Neuza Maria Bernardino da Silva

# Growing up with asthma:

## Adaptation processes and outcomes in children and adolescents with asthma and their parents

Doctoral thesis in Interuniversity Doctorate in Psychology, Specialty Clinical Psychology – Subject area: Family Psychology and Family Intervention, supervised by Professor Maria Cristina Canavarro and Dr. Carla Crespo, and submitted to the Faculty of Psychology and Education Sciences of the University of Coimbra

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## Title

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More than the endpoint of a long and gratifying journey, I hope this dissertation may be the beginning of future challenges and partnerships.

# Table of Contents

## Chapter I | Theoretical Framework

## Chapter II | Objectives and Method

## Chapter III | Meta-Analytic Review and Empirical Studies

## Chapter IV | General Discussion

Attachments

# Index of Tables

## Chapter I | Theoretical Framework

## Chapter II | Objectives and Methods

## Chapter III | Meta-Analytic Review and Empirical Studies

Meta-analytic review | *Quality of life in pediatric asthma patients and their parents: A meta-analysis on 20 years of research*

Empirical study 1 | *The Portuguese DISABKIDS Asthma Module: A global index of asthma-specific quality of life for children and adolescents*

Empirical study II | *Why the (dis)agreement? Family context and child-parent perspectives on health-related quality of life and psychological problems in pediatric asthma*

Empirical study III | *Mapping the caregiving process in pediatric asthma: Parental burden, acceptance/denial coping and quality of life*

Empirical study IV | *Parental positive meaning-making when caregiving for children with asthma*

Empirical study V | *Caregiving burden and uplifts: A contradiction or a protective partnership for the quality of life of parents and their children with asthma?*

Empirical study VI | *Transactional paths between children and parents in pediatric asthma: Associations between family relationships and adaptation*

## Attachments

Preliminary study | *Avaliação da qualidade de vida em crianças e adolescentes com asma: Validação semântica* e *estudo piloto do DISABKIDS – Módulo para a Asma*

# Index of Figures

## Chapter I | Theoretical Framework

## Chapter III | Meta-Analytic Review and Empirical Studies

Meta-analytic review | *Quality of life in pediatric asthma patients and their parents: A meta-analysis on 20 years of research*

Empirical study I | *The Portuguese DISABKIDS Asthma Module: A global index of asthma-specific quality of life for children and adolescents*

Empirical study II | *Why the (dis)agreement? Family context and child-parent perspectives on health-related quality of life and psychological problems in pediatric asthma*

Empirical study III | *Mapping the caregiving process in pediatric asthma: Parental burden, acceptance/denial coping and quality of life*

Empirical study IV | *Parental positive meaning-making when caregiving for children with asthma*

Empirical study V | *Caregiving burden and uplifts: A contradiction or a protective partnership for the quality of life of parents and their children with asthma?*

Empirical study VI | *Transactional paths between children and parents in pediatric asthma: Associations between family relationships and adaptation*

## Chapter IV | General Discussion

# List of Abbreviations and Acronyms

| | |
|---|---|
| APA | American Psychological Association |
| CFA | Confirmatory factor analysis |
| DAsM | DISABKIDS Asthma Module |
| DCGM | DISABKIDS Chronic Generic Module |
| DSM | Diagnostic and Statistical Manual of Mental Disorders |
| FES | Family Environment Scale |
| FRI | Family Relationships Index |
| GINA | Global Initiative for Asthma |
| HrQoL | Health-related quality of life |
| ICC | Intraclass correlation coefficient |
| ICD | International Classification of Diseases |
| MHI | Mental Health Inventory |
| QoL | Quality of life |
| NHLBI | U.S. National Heart, Lung, and Blood Institute |
| SDQ | Strengths and Difficulties Questionnaire |
| SEM | Structural equation modelling |
| SES | Socio-economic status |
| WHO | World Health Organization |
| WHOQOL | World Health Organization Quality of Life working group |

# Abstract

## Background

Asthma is a chronic inflammatory disorder of the airways with a prevalence exceeding 10% among children and adolescents. The recurrent exacerbations may significantly impair the physical and psychosocial health of both pediatric patients and their parents. Following medical advances in asthma diagnosis and treatment, quality of life (QoL) and mental health have emerged as key outcomes of overall adaptation. However, research has revealed a wide variability in patient-reported outcomes, which may be a result of specific methodological challenges in pediatric outcomes assessment, but may also reflect the complex interplay between the risk and resistance factors mapping the adaptation processes. In this context, the general aims of our study were: 1) to characterize the QoL of children with asthma and their parents, in comparison to controls without asthma; 2) to clarify some methodological issues in pediatric outcomes assessment, namely those related to the utility of generic and condition-specific measures and parent-child agreement; and 3) to identify psychosocial risk and resistance factors and the processes through which they operate to explain the differential adaptation trajectories of children and their parents.

## Methods

This cross-sectional study included three distinct phases. In the first research phase, a systematic search and meta-analysis of empirical studies comparing the QoL of children with asthma and their parents with healthy controls was performed. The second phase focused on the cross-cultural adaptation of the self- and proxy-report versions of the DISABKIDS Asthma Module. Subsequently to the translation of the questionnaires to European Portuguese, a sample of 36 dyads of children/adolescents and their family caregivers appraised the comprehensibility and relevance of the items and response scales (semantic validation). The experimental versions of the instrument were then included in the broad assessment protocol and completed by a subsample of 144 dyads (psychometric field study). For the study of individual and family adaptation (third phase), the sample was comprised of 293 8-18 year-old children/adolescents with asthma and their parents. The pediatric adaptation outcomes (i.e., QoL and psychological problems) were evaluated by the children and by the parents as their proxies. The parents also provided information on their own QoL and mental health, caregiving burden and uplifts, and coping tendencies; family relationships were assessed by both family members. Asthma severity and control levels were classified by the physicians.

## Results

Results from the meta-analysis showed that pediatric asthma patients and their parents were at higher risk for QoL impairments than controls without asthma. The self and proxy versions of the DISABKIDS Asthma Module proved to be reliable and valid measures for QoL assessment in Portuguese children, with the advantage of being more sensitive to the clinical asthma characteristics, in relation to the generic measures. Parent-child agreement in pediatric outcomes assessment was poor to moderate, and the extent and direction of discrepancies were better explained by family-related factors than by clinical and socio-demographic variables. Regarding adaptation processes, different patterns emerged for children and parents: the parents' experience of caregiving burden and uplifts contributed directly to the children's QoL, while for parents these paths were mediated by emotion-focused coping tendencies. In addition, caregiving uplifts buffered the deleterious effect of relationship burden on parents' QoL. Positive family relationships were directly linked to better adaptation outcomes for both children and parents; in turn, better adaptation in a family member was associated with better adaptation in the other family member. Finally, the parents' adaptation processes were invariant across clinical and socio-demographic groups, but asthma severity moderated the positive link between family relationships and children's QoL.

## Conclusions

The results from the present study highlight the need of incorporating routine QoL assessment in pediatric clinical and research contexts, preferably adopting a modular approach including generic and condition-specific measures and "giving voice" to both children and their parents, whilst also considering the family context. Our findings also support the pertinence of a risk-resistance approach to parent-child adaptation and emphasize the role of positive dimensions of caregiving (i.e., uplifts), emotion-focused coping strategies (e.g., acceptance, positive reframing), and adaptive family relationships as family resources/protective factors against the deleterious effects of clinical, socio-economic and stress-related risks. The identification of modifiable variables associated with better individual and family adaptation may contribute to operationalize strength-based interventions in pediatric asthma clinical settings.

## Keywords

Caregiving burden and uplifts • Children/adolescents and parents • Coping mechanisms • Family relationships • Mental health • Pediatric asthma • Quality of life

# Resumo

## Introdução

A asma é uma doença inflamatória crónica das vias respiratórias com prevalência superior a 10% na população pediátrica. As exacerbações recorrentes podem afectar significativamente a saúde física e psicossocial das crianças/adolescentes e dos seus pais. Com os avanços médicos no diagnóstico e tratamento da asma, a qualidade de vida (QdV) e a saúde mental têm emergido como importantes indicadores da adaptação global. No entanto, a investigação tem mostrado grande variabilidade nestes indicadores subjectivos, o que pode dever-se aos desafios metodológicos na avaliação de populações pediátricas, mas pode também reflectir as complexas interacções entre os factores de risco e de resistência que mapeiam os processos de adaptação. Neste contexto, este estudo teve como objectivos: 1) caracterizar a QdV de crianças com asma e dos seus pais, em comparação com controlos sem asma; 2) clarificar algumas questões metodológicas na avaliação de indicadores de adaptação pediátricos, nomeadamente a utilidade de instrumentos genéricos e específicos e a concordância entre os relatos dos pais e dos filhos; e 3) identificar factores psicossociais de risco e de resistência e os processos através dos quais eles contribuem para explicar as trajectórias diferenciais de adaptação individual e familiar.

## Metodologia

Esta investigação transversal integrou três fases distintas. Na primeira fase, foi realizada uma pesquisa sistemática e meta-análise dos estudos empíricos que comparavam a QdV de crianças com asma e dos seus pais com controlos saudáveis. A segunda fase focou-se na adaptação das versões de auto- e hetero-relato do instrumento DISABKIDS Módulo para a Asma. Subsequentemente à tradução dos questionários para Português Europeu, uma amostra de 36 crianças/adolescentes e seus cuidadores familiares avaliaram a compreensibilidade e relevância dos itens e das escalas de resposta (validação semântica). As versões experimentais do instrumento foram então integradas no protocolo de avaliação alargado e preenchidas por uma subamostra de 144 díades (estudo psicométrico de campo). Para o estudo da adaptação individual e familiar (terceira fase), a amostra foi constituída por 293 crianças/adolescentes entre 8 e 18 anos com asma e pelos seus pais. Os indicadores de adaptação pediátricos (i.e., QdV e problemas psicológicos) foram avaliados por meio dos auto-relatos das crianças e dos hetero-relatos dos seus pais. Os pais forneceram ainda informação sobre a sua própria QdV e saúde mental, desgaste e gratificações decorrentes da prestação de cuidados e tendências de *coping*; as relações familiares foram avaliadas por ambos os membros da família. A gravidade e controlo da asma foram classificados pelos médicos.

## Resultados

Os resultados da meta-análise mostraram que as crianças com asma e os seus pais têm menor QdV do que os controlos sem asma. As versões de auto- e hetero-relato do DISABKIDS Módulo para a Asma provaram ser fiáveis e válidas para a avaliação da QdV em crianças Portuguesas, com a vantagem de serem mais sensíveis às características clínicas da asma. O acordo entre pais e filhos na avaliação dos indicadores pediátricos foi fraco a moderado e a extensão e direcção das discrepâncias foi mais bem explicada por factores familiares do que por variáveis clínicas e sociodemográficas. Em relação aos processos de adaptação, emergiram padrões diferentes para as crianças e para os pais: a experiência de desgaste e de gratificações contribuíram directamente para a QdV das crianças/adolescentes, enquanto para os pais estas associações foram mediadas pelas tendências de *coping*. Além disso, as gratificações decorrentes da prestação de cuidados moderaram o efeito negativo do desgaste na QdV dos pais. Relações familiares positivas associaram-se directamente com uma melhor adaptação das crianças e dos pais; por sua vez, melhor adaptação de um membro da família associou-se a melhor adaptação do outro membro da família. Finalmente, os processos de adaptação dos pais mostraram-se estáveis entre grupos clínicos e sociodemográficos, mas a gravidade da asma moderou a associação entre as relações familiares e a QdV das crianças/adolescentes.

## Conclusões

Estes resultados apontam para a necessidade de incorporar rotinas de avaliação da QdV em contextos clínicos e de investigação pediátricos, adoptando preferencialmente uma abordagem modular que inclua medidas genéricas e específicas, e “dando voz” tanto às crianças como aos seus pais. Os nossos resultados suportam ainda a pertinência de uma abordagem de risco-resistência no estudo dos processos de adaptação e enfatizam o papel das dimensões positivas da prestação de cuidados, tendências de *coping* (e.g., aceitação, reinterpretação positiva) e relações familiares como recursos/factores protectores contra os efeitos negativos dos riscos clínicos, socioeconómicos e familiares. A identificação de variáveis modificáveis associadas a melhor adaptação individual e familiar pode contribuir para operacionalizar intervenções psicossociais focadas nos pontos fortes das famílias.

## Palavras-chave

Asma pediátrica • Crianças/adolescentes e pais • Desgaste e gratificações na prestação de cuidados • Mecanismos de coping • Qualidade de vida • Relações familiares • Saúde mental

# Introductory Note

Asthma is the most common chronic condition among children and adolescents, with worldwide prevalence rates over 10% (Pearce et al., 2007). This chronic inflammatory disorder of the airways is characterized by recurrent episodes of wheeze, shortness of breath, chest tightness and cough (Global Initiative for Asthma [GINA], 2008) and exerts substantial burden on pediatric patients and their families, including the direct costs of medical treatments, the number of missed days from school/work, and the effects on their physical and psychosocial functioning (Sennhauser, Braun-Fahrländer, & Wildhaber, 2005). Over the past few decades, medical advances in the diagnosis and treatment of pediatric chronic health conditions have resulted in an increasing dissatisfaction with the traditional health indicators (e.g., survival rates, symptom reduction; Varni, Limbers, & Burwinkle, 2007). In addition, improving quality of life (QoL) has become the primary goal of interventions and subjective patient-reported outcomes have been increasingly acknowledged as the key indicators of overall adaptation. However, empirical research has yielded heterogeneous findings regarding the magnitude of QoL impairments and which QoL domains are mostly affected in pediatric asthma patients and their parents. Accordingly, the first aim of the present research project was to estimate the differences in QoL scores between pediatric asthma patients/parents and controls.

The assessment of pediatric populations poses particular methodological challenges, which may contribute to explain some of the heterogeneity in results across studies (Bullinger, Schmidt, Peterson, & Ravens-Sieberer, 2006). Two of the most controversial issues in pediatric literature that remain empirically understudied in the asthma context refer to the advantages and disadvantages of using broad-scope or condition-specific instruments for QoL assessment (Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003) and the reliability of children/adolescents' self-reports and the pros and cons of relying on parent-reports as their proxies (Eiser & Morse, 2001b). For a comprehensive assessment of QoL outcomes in our study, we adopted a three-level modular system comprised of self- and proxy-report forms of generic, chronic-generic and specific measures. Because no asthma-specific instruments were available for the Portuguese pediatric population, the DISABKIDS Asthma Module was translated and cross-culturally validated within the context of the present study. Subsequently, we examined the psychometric performance of the asthma-specific questionnaires with reference to the generic KIDSCREEN and chronic-generic DISABKIDS measures, and examined the extent and direction of agreement/disagreement between child- and parent-reports of QoL and psychological problems.

Despite the disease clinical features and the methodological constraints in pediatric outcome assessment, evidence-based research has demonstrated that few children/adolescents and parents present clinically significant adaptation problems (Barlow & Ellard, 2006). Based on the Disability-Stress-Coping model (Wallander, Varni, Babani, Banis, & Wilcox, 1989a), the third general aim of our research project was to identify psychosocial risk and resistance factors and the processes through which they might contribute to explain the wide variability in individual adaptation trajectories for children/adolescents with asthma and their parents. In order to address some of the current research gaps in pediatric literature, we embedded the reading and empirical testing of this conceptual model in a family-centered and transactional approach to child development (Fiese & Sameroff, 1989; Sameroff, 2009). Specifically, we focused on family stress (e.g., caregiving burden, stress processing mechanisms) and psychological resources (e.g., caregiving uplifts, family relationships) and on the transactional processes through which children/adolescents and parents shape each other's adaptation.

The present dissertation is organized in four chapters, herein succinctly described. **Chapter I | Theoretical Framework** provides an overview of the current state of the art on the topic of psychosocial adaptation processes and outcomes in children/adolescents with asthma and their parents. This first chapter begins with a brief description of asthma clinical and epidemiological features, including etiology and pathophysiology, tools and procedures for differential diagnosis and classification, available medications and non-pharmacological strategies for effective asthma management, prevalence rates and indicators of overall burden of asthma for pediatric patients, their families and society. Subsequently, we discuss some conceptual and methodological issues in pediatric outcomes assessment, and then we proceed with a critical review of the theoretical and empirical literature on the risk and resistance factors and the processes through which they might operate to explain the differential adaptation outcomes in children/adolescents with asthma and their parents. This introductory section ends with a summary of the research gaps and limitations identified in the current literature, which guided the formulation of specific objectives for our research project.

**Chapter II | Objectives and Methods** integrates the operational aspects of our research project, by describing the general aims and broad methodological options that interconnect the different empirical studies. Overall, our research project comprised three distinct phases: (1) a systematic review of the current literature on the topic of QoL of children/adolescents with asthma and their parents; (2) the cross-cultural adaptation and psychometric validation of the European Portuguese self- and proxy-report versions of the asthma-specific DISABKIDS questionnaires; and (3) the examination of adaptation processes and outcomes in children/adolescents with asthma and their parents, in different clinical and socio-demographic groups. In this second chapter, the study design, procedures, participants and assessment instruments are presented for each empirical research phase. The statistical methods that allowed us to test our theoretically-driven hypotheses and operationalize a dyadic and developmental approach to outcomes assessment and adaptation processes are also commented. A final reflection focused on the ethical principles that guided our research work, since its conception to the implementation of the assessment protocol and dissemination of results.

**Chapter III | Meta-Analytic Review and Empirical Studies** includes seven original studies presented in the format of scientific papers, published in national and international peer-reviewed periodicals.

In the first study, entitled *Quality of life in pediatric asthma patients and their parents: A meta-analysis on 20 years of research*, we systematically reviewed the existing quantitative research and examined its pooled results to characterize the QoL of pediatric asthma patients and their parents in relation to controls without asthma.

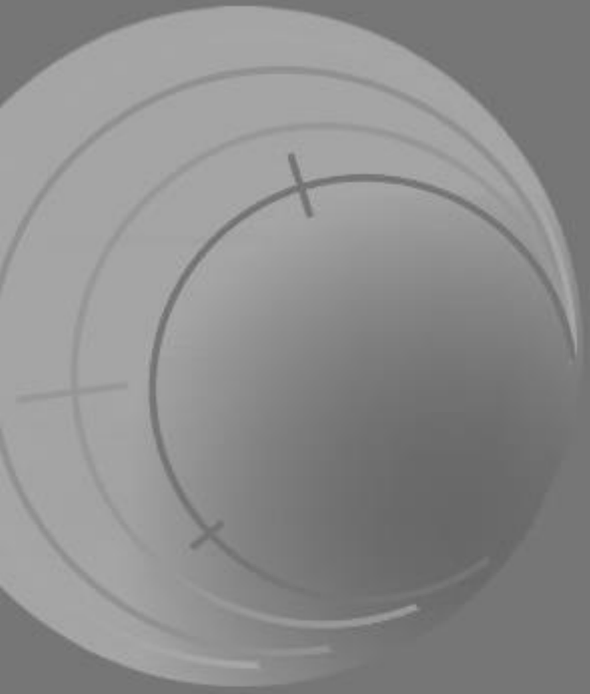
The empirical studies I and II were generally aimed at clarifying some methodological issues in the assessment of QoL outcomes and psychological problems in pediatric patients. In the paper entitled *The Portuguese DISABKIDS Asthma Module: A global index of asthma-specific quality of life for children and adolescents*, we explored the psychometric performance of the European Portuguese self- and proxy-report versions of the DISABKIDS Asthma Module and discussed its utility in a modular system comprising generic, chronic-generic and condition-specific questionnaires for QoL assessment in children/adolescents with asthma. The empirical study II, *Why the (dis)agreement? Family context and child-parent perspectives on health-related quality of life and psychological problems in pediatric asthma*, focused on the "proxy problem" by examining the levels of agreement between child- and parent-reports of QoL and psychological problems and by identifying socio-demographic, clinical and family-related variables explaining the extent and direction of child-parent disagreement.

A third set of empirical studies sought to identify specific psychosocial risk and resistance factors and to understand the processes through which they contribute to differential adaptation outcomes in children/adolescents with asthma and their parents. In the paper *Mapping the caregiving process in pediatric asthma: Parental burden, acceptance

> *and denial coping strategies and quality of life* (empirical study III), we tested the complex mechanisms underpinning the caregiving process and parents' adaptation outcomes, namely the direct and indirect links (via acceptance and denial coping strategies) between caregiving burden and parents' QoL. Complementarily, the empirical study IV, entitled *Parental positive meaning-making when caregiving for children with asthma*, focused on the positive dimension of family caregiving (i.e., uplifts), by testing the mechanism through which positive reframing coping may sustain parents' perceptions of gratifications and positive emotions arising from caregiving and contribute to their positive adaptation. The co-occurrence of caregiving uplifts in the stressful context of parenting a child with asthma and their buffering role against the deleterious effects of caregiving burden on parents' and their children's QoL was addressed in the empirical study V – *Caregiving burden and uplifts: A contradiction or a protective partnership for the quality of life of parents and their children with asthma?*. The last empirical study is called *Transactional paths between children and parents in pediatric asthma: Associations between family relationships and adaptation* (empirical study VI), reflecting the adoption of a transactional framework to analyze the direct and indirect links between children/adolescents' and parents' perceptions of family relationships and adaptation, both separately (the within-subjects effects) and across family members (the cross-lagged effects).

Finally, **Chapter IV | General Discussion** offers a brief summary and discussion of the core results derived from our empirical studies. The general research objectives and the theoretically-driven hypotheses are revisited, by conceptually integrating the main findings within a risk-resistance framework, while incorporating a developmental and ecological approach to children/adolescents' and their parents' adaptation to pediatric asthma. In this chapter, we also critically reviewed the methodological strengths and limitations of our study. The concluding remarks of the present dissertation are dedicated to the discussion of the theoretical and practical contributions of our work and to the outlining of evidence-based guidelines for future research, clinical practice and health policy making in pediatric settings.

Attached to this dissertation, we also present a preliminary study describing the semantic validation study of the DISABKIDS asthma-specific questionnaires for the European Portuguese language and cultural context. This pilot study was presented in the format of a Portuguese-language scientific paper, with the title ***Avaliação da qualidade de vida em crianças e adolescentes com asma: Validação semântica e estudo piloto do DISABKIDS – Módulo para a Asma*** [Assessing quality of life in children and adolescents with asthma: Semantic validation and pilot study of the DISABKIDS – Asthma Module], and published in national conference proceedings.



# Chapter I

## Theoretical Framework

# I. PEDIATRIC ASTHMA: CLINICAL AND EPIDEMIOLOGICAL FEATURES

Asthma is a chronic inflammatory disorder of the airways that affects people of all ages worldwide. Because of the complexity and heterogeneity of genetic, environmental, psychosocial and biological factors in its pathogenesis, course and manifestations, the attempts to define asthma have been predominantly descriptive. The most recent update of the Global Initiative for Asthma (GINA) report presented a consensual definition of asthma, based on its typical characteristics that distinguish it from other respiratory conditions:

> *Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation* (GINA, 2014, p. 2).

## 1.1. Etiology and pathophysiological features

The inception of asthma can occur at any point along the lifespan, with greater incidence in infancy or early childhood (Lemanske & Busse, 2010). Its pathogenesis is not entirely clear, involving an intricate interplay of multiple host factors and environmental exposures that occur at a crucial time in the development of the immune system and determine both the inception and the expression of asthma. Asthma susceptibility is primarily determined by host factors such as genetic predisposition to atopy or airway hyper-responsiveness, obesity and sex; the risk factors underlying asthma exacerbations are mainly environmental and include allergens (e.g., house dust mite, furred animals, fungi, pollens and molds), viral respiratory tract infections, occupational sensitizers, tobacco smoke, outdoor and indoor air pollution and diet (GINA, 2008; Lemanske & Busse, 2010). However, this division is not straightforward: specific genes, alone or in combination, are likely to interact with environmental factors and modify the risk of developing asthma and/or acute responses to direct or indirect stimuli (von Mutius, 2009). In addition, developmental aspects such as the maturation of the immune system and the timing of infectious exposures (GINA, 2008), and psychosocial factors such as anxiety and passive coping tendencies (Lehrer, 1998; Wright, Rodriguez, & Cohen, 1998), have also been acknowledged as potential asthma triggers in genetically susceptible persons.

The pathophysiological mechanisms in the development of airway inflammation involve several inflammatory cell types (e.g., lymphocytes, mucosal mast cells, eosinophils, macrophages) that, when activated, release multiple inflammatory and bronchoconstrictor mediators (e.g., histamine, cytokines, cysteinyl-leukotrienes); in turn, these mediators amplify the inflammatory response, that eventually results in the asthma characteristic pathophysiological features (Busse & Lemanske, 2001; National Heart, Lung, and Blood Institute [NHLBI], 2007). The interaction of these asthma features determines the clinical symptom exacerbation (i.e., the recurrent episodes of cough, wheeze and shortness of breath, also known as "asthma attacks"), as well as asthma severity and responsiveness to treatments (NHLBI, 2007). Even when symptom exacerbations are absent for long periods of time, the asthma pathophysiological features usually persist and contribute to its chronicity (GINA, 2014). Moreover, permanent airway structural changes – referred to as airway remodeling – can occur in some patients, particularly those with severe asthma (Busse, Banks-Schlegel, & Wenzel, 2000; Holgate & Polosa, 2006). These structural changes may include thickening of the sub-basement membrane, sub-epithelial fibrosis, airway smooth muscle hypertrophy, blood vessel proliferation and dilation and mucous gland hyper-secretion, and are associated with a progressive loss of lung function that is not fully reversible by current therapy (NHLBI, 2007).

In order to better understand the heterogeneous clinical nature of asthma, there have been several attempts to cluster patients in different asthma phenotypes, based on age of onset, atopy, lung function and requirement for medication. The most common phenotypes include allergic asthma, exercise-induced asthma, late-onset asthma, aspirin-exacerbated respiratory disease, allergic bronchopulmonary mycosis and asthma with obesity (Corren, 2013; Moore et al., 2010). However, the presence of underlying airway inflammation remains a consistent pattern across distinct phenotypes and, to date, there is scarce evidence for the association between specific phenotypes and clinical patterns or treatment responses (Anderson, 2008).

## 1.2. Diagnosis and classification

The diagnosis of asthma (code J45, according to the International Classification of Diseases [ICD-10]; World Health Organization [WHO], 2010) is fundamentally based on the identification of patterns of respiratory symptoms that are characteristic of asthma and variable expiratory airflow limitation. Although some variations exist for special populations, including children aged 5 years and younger, the commonly recommended diagnostic tools include: (1) a detailed medical history investigating the patterns of daytime and nocturnal symptoms (e.g., wheeze, shortness of breath, cough and/or chest tightness, often worse at night or in the early morning), environmental triggers of symptom exacerbation and family history of asthma or atopic diseases; (2) a physical exam focused on the upper respiratory tract, chest and skin, namely hyperexpansion of the thorax, wheezing during normal breathing or a prolonged phase of forced exhalation, increased nasal secretion and manifestation of allergic skin conditions; and (3) a spirometry (i.e., measurement of the forced expiratory volume at a timed interval of one second ($FEV_1$) at baseline and after inhalation of a short-acting bronchodilator or after a 6-minute exercise challenge) or peak expiratory flow to assess pulmonary function variability and reversibility (Levy et al., 2006, 2009; NHLBI, 2007). The diagnosis of asthma requires clinical judgment because symptoms may vary widely between patients and in a patient over time (NHLBI, 2007). Moreover, other respiratory and non-respiratory diseases may produce symptoms that are similar to those characteristic of asthma; alternative diagnoses, such as bronchiolitis, gastro-esophageal reflux, foreign body aspiration, cystic fibrosis, congenital heart disease, developmental anomalies and somatoform respiratory disorders, must be considered in wheezy children (Grüber, Lehmann, Weiss, & Niggemann, 2012; Levy et al., 2006). Additional pulmonary function testing (e.g., lung volumes), bronchial provocation testing, chest radiograph, allergy testing and measurement of biomarkers of inflammation may facilitate the differential diagnosis of asthma and the assessment of its severity (Holgate & Polosa, 2006).

Over the years, several attempts have been made to classify asthma according to the severity of the underlying disease (Yawn, Brenneman, Allen-Ramey, Cabana, & Markson, 2006). Following the introduction of the concepts of intermittent and persistent asthma by the US National Asthma Education and Prevention Program (NHLBI, 1997), asthma severity has been traditionally classified into four levels – intermittent, mild persistent, moderate persistent or severe persistent – considering the level of symptoms, airflow limitation, and lung function variability before treatment (Table 1).

**Table 1** | Classification of asthma severity by clinical features before treatment (adapted from GINA, 2008, p. 22)

| | *Intermittent* | *Mild Persistent* | *Moderate Persistent* | *Severe Persistent* |
|---|---|---|---|---|
| Daytime symptoms | Less than once a week; brief exacerbations | More than once a week but less than once a day | Daily | Daily; frequent exacerbations |
| Nocturnal symptoms | No more than twice a month | More than twice a month | More than once a week | Frequently |
| Activity limitation | - | Exacerbations may affect activity and sleep | Exacerbations may affect activity and sleep | Limitation of physical activities |
| Lung function ($PEF^a$ or $FEV_1{}^b$) | ≥ 80% predicted | ≥ 80% predicted | 60-80% predicted | ≤ 60% predicted |
| $PEF^a$ or $FEV_1{}^b$ variability | < 20% | < 20%-30% | > 30% | > 30% |

Note: the worst feature determines the severity classification. [a] Peak expiratory flow. [b] Forced expiratory volume at a timed interval of one second.

This classification of asthma by severity levels is still regarded as a valuable cross-sectional tool for patient selection and characterization in research contexts. However, asthma clinical features may change over time, depending not only on the severity of the underlying disease but also on its responsiveness to treatment, i.e., the ease with which asthma control is achieved by therapy. Therefore, in the 2008 revision of the *Global Strategy for Asthma Management and Prevention*, the GINA Executive Committee recommended a classification of asthma by control levels, based on symptoms, activity limitation and use of rescue medication – a paradigm shift that reflects the advances in diagnostic methods and pharmacological care and that is recognized as particularly useful for clinical management and decision-making (Table 2).

**Table 2** | Levels of asthma control (adapted from GINA, 2008, p. 23)

| | *Controlled* | *Partly controlled* | *Uncontrolled* |
|---|---|---|---|
| Daytime symptoms | Twice a week or less | More than twice a week | Three or more features of partly controlled asthma present in any week |
| Activity limitation | None | Any | |
| Nocturnal symptoms/ awakening | None | Any | |
| Need for reliever/ rescue treatment | Twice a week or less | More than twice a week | |
| Lung function (PEF[a] or $FEV_1$[b]) | Normal | < 80% predicted or personal best (if known) | |
| Exacerbations | None | Once a year or more | One in any week |

[a] Peak expiratory flow. [b] Forced expiratory volume at a timed interval of one second.

Quite recently, the notion of asthma control was expanded to include the assessment of both symptom control and future risk of adverse outcomes (GINA, 2014). These guidelines specifically point toward the assessment of symptom control over the last four weeks, the identification of any other risks for asthma exacerbations (e.g., poor medication adherence, exposure to allergens/irritants, major psychological or socio-economic problems and comorbid obesity or other atopic diseases) and periodic assessment of pulmonary function.

## 1.3. Asthma management

The long-term goals of asthma management are to achieve optimal symptom control and to minimize future risk of exacerbations, fixed airflow limitation and side effects from pharmacological interventions (GINA, 2014; Lemanske & Busse, 2010), and to improve patients' quality of life (QoL). Standard procedures for effective asthma management (GINA, 2014; NHLBI, 2007) take into account multiple components, namely pharmacological therapy, identification and control of environmental factors and comorbid conditions that affect asthma, self-management education and skills training. As a result of asthma pathophysiological heterogeneity and variability, therapeutic interventions must be individualized and adjusted on the basis of regular assessment and monitoring of symptom control and patient responsiveness.

Asthma medications can be classified into two categories: (1) controller medications to be taken daily on a long-term basis to reduce airway inflammation, control symptoms and reduce future risk of exacerbation and decline in lung function in persistent asthma (e.g., inhaled and systemic glucocorticosteroids, long-acting inhaled $\beta_2$-agonists); and (2) reliever or rescue medications to be used on an as-needed basis to reverse bronchoconstriction and relieve its symptoms during asthma exacerbations or to prevent exercise-induced bronchoconstriction, in both adults and children/adolescents of all ages (e.g., short-acting inhaled $\beta_2$-agonists; NHLBI, 2007). Daily controller treatment should start the earliest possible with low doses of inhaled corticosteroids (Busse et al., 2008; Selroos, 2008) and be subsequently adjusted within a stepwise approach in order to find the patient's minimum effective treatment (GINA, 2014). For children older than 5 years, continuous treatment with inhaled glucocorticosteroids leads to better control of asthma symptoms and decreases the number of hospital admissions and urgent care visits (The Childhood Asthma Management Program Research Group, 2000). Conversely, the use of reliever medication must be reserved for the treatment of exacerbations and its increased use indicates deterioration of asthma control and the need to reassess treatment (Holgate & Polosa, 2006). The initial selection and subsequent adjustment of pharmacological treatment should take into account the patients' age, asthma clinical features/phenotypes (Lemanske & Busse, 2010) and the potential side effects of medication (which in pediatric patients may include suppression of growth velocity and delay in puberty onset, skin thinning and easy bruising, reduced bone mineral density, increased incidence of dental caries, etc.; Barnes, Pedersen, & Busse, 1998), together with the patient/caregiver's preferences and barriers to its implementation (e.g., capacity to afford medication and ability to use the inhaler correctly after training). A shared decision-making approach to the selection of asthma therapy is likely to improve medication adherence and health outcomes, including asthma-related QoL, healthcare utilization, use of reliever medication, asthma control and lung function (Wilson et al., 2010).

In fact, the establishment of a partnership between the patient/caregiver and the healthcare provider is a key component for a successful long-term asthma management. This partnership enables the patient to acquire the necessary knowledge, confidence and skills to assume a major role in asthma self-management (GINA, 2014). Asthma self-management education involves providing specific information, training and advice about the diagnosis and available treatments, the use of inhaler devices and strategies to identify and reduce exposure to environmental asthma triggers, as well as the establishment of a written action plan to assist patients in daily self-monitoring and in the recognition and handling of symptoms of worsening asthma. Even if the focus of asthma education for young children is on their parents/family caregivers, a large body of research has demonstrated the benefits of self-management education in reducing asthma symptoms, risk of acute exacerbations, use of reliever medication, emergency room visits, hospitalizations and absenteeism from school, and in improving asthma knowledge, self-efficacy and QoL in children/adolescents (e.g., Bhogal, Zemek, & Ducharme, 2006; Cicutto et al., 2005; Guevara, Wolf, Grum, & Clark, 2003; Krishna et al., 2003; MeGhan et al., 2003). In addition, there is scarce but promising evidence for the effectiveness of psychological interventions (e.g., cognitive-behavioral therapy, relaxation techniques, psychodynamic therapies and counseling) in improving health outcomes, such as medication adherence and health-related QoL, in children/adolescents with asthma (Yorke, Fleming, & Shuldham, 2005).

## 1.4. Epidemiology: Asthma prevalence and burden

Despite the multiplicity of diagnostic tests and classification methods that hinder the accurate ascertainment of asthma prevalence, it is estimated that about 300 million people of all ages and ethnic backgrounds have current asthma (Masoli, Fabian, Holt, & Beasley, 2004). In pediatric populations, asthma is the most common chronic health condition with global rates of 10.8% (self-reported asthma ever) and 11.6% (current wheezing) in 6-7 year-old children and 13.8% (asthma ever) and 13.7% (current wheezing) in 13-14 year-old adolescents (Pearce et al., 2007). Prior to the age of 14 years, the asthma prevalence is nearly twice as large in boys, while in adolescence the sex difference narrows (GINA, 2008; Horwood, Fergusson, & Shannon, 1985). The prevalence rates of pediatric asthma also vary worldwide, depending on the genetic background and environmental risk factors such as different allergen and infection exposure in early life, dietary changes and socio-economic dissimilarities, with an increasing trend in the westernized countries (Asher et al., 2006; Pearce et al., 2007).

In Portugal, the International Study of Asthma and Allergies in Childhood (ISAAC) revealed that 9.4% of 6-7 year-old children and 14.7% of 13-14 year-old adolescents reported having had asthma ever, and 12.9% of children and 11.8% of adolescents had self-reported wheezing in the last 12 months, which represents a significant increase in asthma prevalence between 1995 and 2002 for the older group (Figure 1). Most patients have mild to moderate asthma that can be easily controlled with inhaled corticosteroids and short-acting bronchodilators; however, it is estimated that up to 10% have severe asthma that is difficult to control with standardized treatments (Gaspar, Almeida, & Nunes, 2006). Similarly to other developed countries, the asthma mortality rates in the Portuguese pediatric population are low, with a total of 10 deaths in children under the age of 15 years between 1994 and 2004, which represents less than 1% of the total asthma deaths (Gaspar et al., 2006).

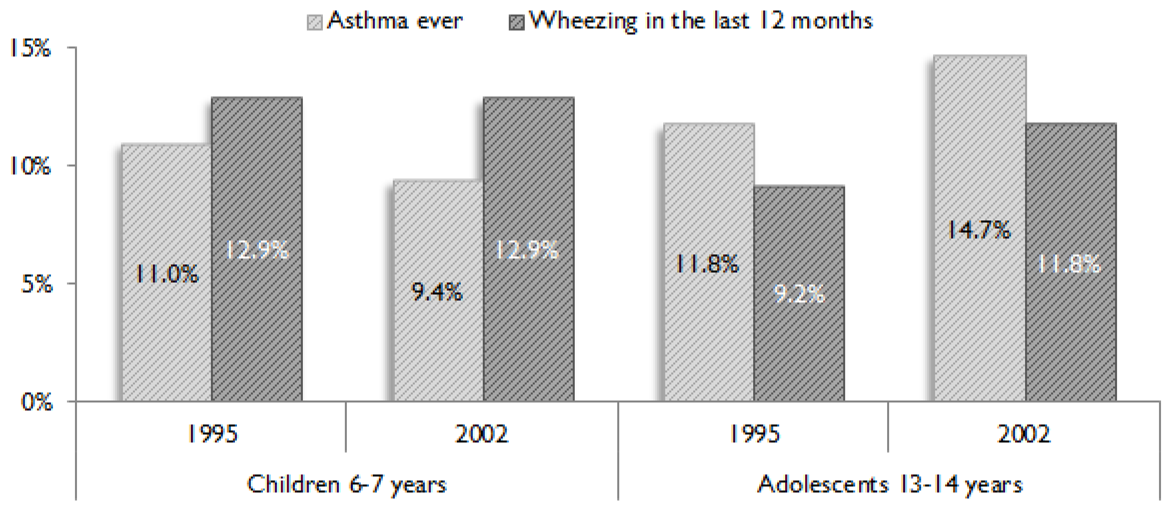


**Figure 1** | Prevalence of asthma and current wheezing in Portuguese children and adolescents (data from the ISAAC study; Pinto, 2011)

The overall asthma burden is best defined by the combination of the prevalence rates, mortality figures, health and QoL outcomes, and direct and indirect healthcare costs for families, the healthcare system and society as a whole (Sennhauser, Braun-Fahrländer, & Wildhaber, 2005; Von Mutius, 2000). The direct costs refer to hospitalizations, emergency department visits and medications, as well as non-medical costs such as transportation to and from healthcare services and household modifications. In fact, asthma is one of the major causes of hospital admissions among children younger than 15 years and, along with medications, represents the most significant driver of the economic burden of asthma (Bahadori et al., 2009). In the 25 European Union countries, the average annual cost per child with asthma is estimated at EUR 613 and the total annual costs of asthma amount to EUR 3,000 million (Van den Akker-van Marle, Bruil, & Detmar, 2005). The indirect costs arising from asthma mortality and morbidity include, amongst others, school absences as an impairment of long-term educational achievement, time off work for parents/ family caregivers and missed socialization opportunities, and can be assessed in terms of the "economic value" of the time lost due to the disease or in health-related QoL parameters (Sennhauser et al., 2005; Van den Akker-van Marle et al., 2005).

### 1.4.1. Asthma burden in pediatric patients

Beyond the clinical and treatment-related parameters (e.g., number of exacerbations, rate of recurrence of hospitalizations/emergency department visits and use of reliever medication, side effects of medications, etc.), the number of missed days from school and the effect on daily activities and psychosocial adaptation outcomes are integral indicators of asthma morbidity in pediatric patients (Sennhauser et al., 2005). In a qualitative study aimed at examining how children and adolescents with asthma experienced their everyday lives, the main themes that emerged in their narratives were, on the one hand, the struggle to participate in everyday activities and, on the other hand, the feeling of being outsiders when they do not succeed (Rydström, Englund, & Sandman, 1999). In fact, asthma may limit the child's participation in sports and other social activities, and even affect school attendance (Von Mutius, 2000). Empirical research showed that children/adolescents with asthma miss more school days per year than their healthy peers (Van Gent et al., 2007) and that the likelihood of missing school days, arriving late or leaving early, missing school-related activities, developing asthma symptoms and using a rescue inhaler while at school is even greater among those with poorly controlled asthma (Dean et al., 2010; Schmier et al., 2007). Moreover, wheezing children/adolescents have more sleep disturbances (Desager, Nelen, Weyler, & De Backer, 2005), which may affect their concentration and productivity at school, as well as their long-term academic achievement, particularly when asthma is inadequately controlled (Schmier et al., 2007).

Emotional burdens may also arise, particularly in adolescence because of the role change and conflict between the developmental tasks related to independence and the need for support from family caregivers during asthma exacerbations (Sennhauser et al., 2005). A meta-analysis of the empirical studies focused on the mental health of pediatric asthma patients revealed that, in general, children/adolescents with asthma are at greater risk for psychological problems compared to their healthy peers, and these differences are particularly evident in the internalizing domain (i.e., anxiety and depression symptoms; McQuaid, Kopel, & Nassau, 2001). Posteriorly, Ortega, Huertas, Canino, Ramirez, and Rubio-Stipec (2002) clarified that pediatric asthma, as opposed to other chronic health conditions, is associated with having an anxiety disorder, but not an affective disorder. Consistently, a systematic review on the prevalence of psychological problems in patients with asthma reiterated that up to one third of children/adolescents with asthma meet the criteria for a comorbid anxiety disorder (Katon, Richardson, Lozano, & McCauley, 2004). The development of psychological problems seems to be related to increased asthma severity (Calam, Gregg, & Goodman, 2005; McQuaid et al., 2001; Waxmonsky et al., 2006), greater use of quick-relief medication (Feldman et al., 2013), number of days of wheeze per year and poorer functional health status (Weil et al., 1999). However, Feldman, Lehrer, Borson, Hallstrand, and Siddique (2005) call attention to the potential overlap between symptoms of asthma exacerbations and anxiety, such as dyspnea, dizziness, chest tightness and sensations of smothering, which could result in patients' over-perception of respiratory compromise and greater use of quick-relief medication.

A growing body of research has focused on QoL as a measure of the broad impact of asthma in patients' physical, psychological and social functioning. However, studies comparing the QoL between children/adolescents with asthma and their healthy peers have yielded inconsistent findings. Specifically, some studies have reported decreased QoL in pediatric asthma patients (e.g., Sawyer et al., 2001; Van Gent et al., 2007; Varni, Limbers, & Burwinkle, 2007), while other studies have failed in detecting significant differences (e.g., Matterne, Schmitt, Diepgen, & Apfelbacher, 2011; Moreira et al., 2013). Methodological constraints in pediatric QoL assessment (as further discussed in the next section) and the clinical characteristics of the samples may explain this heterogeneity across studies. The associations between QoL and the levels of asthma severity and control are, in fact, well established in pediatric literature, with children/adolescents whose symptoms are not well-managed experiencing more QoL impairments and children/adolescents with controlled asthma presenting QoL scores that fall within the expected range of population norms (Dean et al., 2010; Everhart & Fiese, 2009; Schmier et al., 2007). In addition, Josie, Greenley, and Drotar (2007) suggested that the accumulated burden of risk factors, including illness-related factors (e.g., lung functioning and comorbid health conditions), adherence to medication and family functioning (e.g., caregiver's physical and mental health, number of siblings), is strongly associated with greater asthma severity and decreased QoL, regardless of children's age and gender.

### 1.4.2. Asthma burden in family caregivers

Pediatric asthma also exerts a substantial burden in the entire family and particularly in the parents who assume the primary role in the child's asthma management and are the main responsible for purchasing and administering medications, identifying and avoiding potential asthma triggers and monitoring and handling their child's symptoms of worsening asthma. The standard parameters to assess the burden of pediatric asthma in family caregivers include the direct costs of medical care, the number of missed days from work and consequences on their professional career and the effects on their lifestyle, activities, psychosocial functioning and QoL outcomes (Sennhauser et al., 2005).

Some empirical studies found that nearly 30% of parents report missed days from work due to their child's asthma and that their absenteeism is associated with poorly controlled asthma (Laforest et al., 2004; Schmier et al., 2007). In addition, parents of children/adolescents with uncontrolled asthma report significantly greater impairment in regular daily activities such as household affairs, shopping or exercising, impairment while working and overall work productivity loss compared to parents of children/adolescents with controlled asthma (Dean et al., 2010). Although Dean and colleagues (2010) did not find significant differences in the employment status between North American caregivers of children/adolescents with controlled and uncontrolled asthma, in countries with higher unemployment rates parents may fear losing their job or suffering income reduction. Along with the additional financial burden of asthma treatments, the difficulties in balancing work and caregiving demands can be particularly challenging for parents with low socio-economic status [SES] and significantly interfere with their QoL (Gates & Akabas, 2012). Moreover, financial constraints may affect the treatment choices and medication adherence by not buying the medication or lowering the dosage (Sennhauser et al., 2005).

Symptoms of anxiety and depression are also frequent in parents/family caregivers of children/adolescents with asthma. Some studies using clinical diagnostic interviews found rates in the range of 21%-38% for current anxiety disorders and 27%-28% for depressive disorders (Brown et al., 2006; Feldman et al., 2013); these proportions are even higher when considering clinically significant levels of anxiety and depression symptoms as assessed by screening measures (Bartlett et al., 2001, 2004; Waxmonsky et al., 2006). Depressive symptoms in mothers were associated with greater interference in their normal daily routine, along with increased difficulties in child's asthma management practices such as using the inhaler incorrectly or forgetting medication (Bartlett et al., 2004). Children of caregivers with clinically significant symptoms of anxiety and depression were found to present lower pulmonary function (Feldman et al., 2013) and were also more likely to use emergency services than children/adolescents whose parents had fewer psychopathological symptoms (Bartlett et al., 2001; Brown et al., 2006; Weil et al., 1999).

To date, research focused on QoL outcomes in parents/family caregivers of children/adolescents with asthma is scarce. The few existing studies have found strong evidence for decreased sleep quality (Yilmaz et al., 2008) and physical functioning (Gau at al., 2010; Hatzmann, Heymans, Ferrer-i-Carbonell, van Praag, & Grootenhuis, 2008; Van Gent et al., 2007) in parents of pediatric asthma patients compared to parents of healthy children/adolescents; however, the results have been less consistent regarding the psychological and social QoL dimensions. Dean and colleagues (2010) found that parents of children/adolescents with uncontrolled asthma report significantly lower emotional functioning and time to meet their own needs and great interference in family activities. Conversely, Halterman and colleagues (2004) suggested that different indicators of asthma severity (e.g., number of symptom-free days, use of daily medication, school absenteeism, etc.) have a differentiated effect on the activity and emotion dimensions of parents' QoL. These heterogeneous findings can be best understood when considering the cumulative effect of clinical and socio-economic risk factors on parents' QoL (Everhart, Fiese, & Smyth, 2008).

# 2. ADAPTATION OUTCOMES: CONCEPTUAL AND METHODOLOGICAL ISSUES

The contemporary conceptualization of health as a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1948) and the medical advances in the diagnosis and treatment of pediatric chronic health conditions have led to an increasing dissatisfaction with the classical endpoints of disease burden such as symptom reduction and survival rates (Bullinger, Schmidt, Peterson, & Ravens-Sieberer, 2006; Varni et al., 2007). As a consequence, patient-reported outcomes reflecting a more holistic approach to disease management and overall adaptation have emerged as the fundamental focus of comprehensive healthcare. Within the strength-based approach that has prevailed in the health psychology field in the past few years (Pais-Ribeiro, 2009; Seligman & Csikszentmihalyi, 2000), positive adaptation indicators have become the more valued outcomes in pediatric chronic conditions and disabilities. Extending beyond the psychopathological framework in which the children/adolescents' and families' responses to chronic conditions were often considered as emotional problems or psychological maladjustment, the concept of adaptation can be broadly regarded as a process that accounts for resiliency and variability in health outcomes (Harper, 1991). A sensitive measurement of the wide-ranging construct of adaptation involves the integration of indicators of mental health (in its broadest sense and not only in pathological terms), physical health, and social functioning (Wallander, Pitt, & Mellins, 1990; Wallander, Varni, Babani, Banis, & Wilcox, 1989a). Accordingly, mental health and QoL were considered as indicators of children/adolescents' and parents' adaptation in the context of the present research. Next, some conceptual issues and methodological challenges in the assessment of these adaptation outcomes are further discussed.

## 2.1. Quality of life as a multi-dimensional indicator of adaptation

QoL was formally defined by the World Health Organization Quality of Life [WHOQOL] working group, in 1994, as:

> *A person's perception of his/her position in life within the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards, and concerns. It is a broad-ranging concept incorporating, in a complex way, the person's physical health, psychological state, level of independence, social relationships, personal beliefs, and relationship to salient features of the environment* (The WHOQOL Group, 1994, p. 28).

Two major practical implications can be directly derived from this worldwide accepted definition. First, the subjective nature of the QoL construct implies the assessment of the individual's perception of objective conditions (e.g., economic resources, quantity of sleep and work productivity), as well as his/her global and highly personalized evaluation of behaviors, states and capacities (e.g., satisfaction with economic resources and satisfaction with the quality of sleep; Felce & Perry, 1995; The WHOQOL Group, 1995). It follows that each person has unique perceptions of his/her QoL, depending on present lifestyle, past experiences and future expectations and, therefore, QoL can only be rated by the individual himself. Second, it is consensual that QoL is a multi-dimensional construct, encompassing both positive and negative facets of the broad physical, mental and social domains of functioning as universal values across cultures (Saxena, Carlson, Billington, & Orley, 2001).

This general definition also applies to children/adolescents, provided that specific age-related QoL markers are considered. Research on QoL has progressed exponentially over the past 20 years; however, most studies have been conducted in adult populations and pediatric QoL is a more recent and unexplored research field (Bullinger et al., 2006; Varni, Burwinkle, & Lane, 2005). In the pediatric asthma context, the same trend is observed: a succinct bibliometric study[1] showed that, of the 2,938 papers indexed by the MEDLINE database that mentioned the terms "quality of life" and "asthma" in their titles and/or abstracts, only 445 papers (15.1%) focused on children/adolescents (Figure 2). This slower research progress may be justified by some methodological challenges in QoL assessment in pediatric populations, as discussed next.

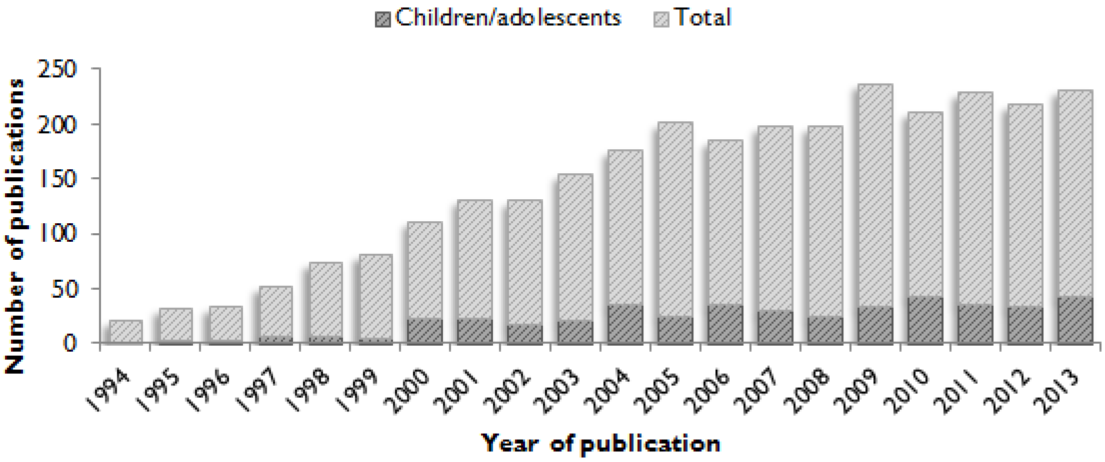


**Figure 2** | Bibliometric study of QoL research in the context of asthma (data retrieved from the PubMed database, US National Library of Medicine, in December 2014)

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[1] The search was performed in the PubMed database (US National Library of Medicine) in December 11th 2014, using combinations of the following keywords: "quality of life" and "asthma" and "child" or "adolescent" or "pediatric". The search results were restricted to titles and abstracts, "humans", and papers published between January 1994 and December 2013.

The term “health-related quality of life” (HrQoL), defined as “a multi-dimensional construct covering physical, emotional, mental, social, and behavioral components of well-being and function as perceived by patients and/or other observers” (Bullinger et al., 2006), was introduced in the healthcare field as a specific component of the broader QoL construct, focusing on the subjective impact of health conditions, medical treatments and healthcare policies (De Civita et al., 2005; Spieth & Harris, 1996). However, this notion is controversial, because QoL has been regarded as a holistic concept; as such, the influence of the disease on physical, psychological and social well-being cannot be conceptually or operationally separated from that of individual current and past life experiences (Wallander, Schmitt, & Koot, 2001). Moreover, these authors argued that the standards for a life of quality should be universal and referenced to the general population, without discriminating against those with chronic health conditions. Assuming that HrQoL is closer to the concept of “disease impact” and theoretically distinct (albeit related) from the QoL broader construct, in the present research the terms QoL and HrQoL were adopted in the contexts of generic and condition-specific assessment, respectively.

## 2.2. Methodological considerations in pediatrics

To assess QoL outcomes in children/adolescents, the Division of Mental Health of the WHO stated that instruments should (1) be child-centered; (2) resort to subjective self-report whenever possible (proxy judgments may be used if the child is too young or too disabled to complete self-reports); (3) be age-related or at least developmentally appropriate; (4) be cross-culturally comparable; (5) have a generic core and specific modules; and (6) put an emphasis on health-enhancing aspects of QoL rather than merely on negative aspects (WHO, 1993). However, the application of these recommendations is not straightforward, and some methodological issues have warranted further debate.

### 2.2.1. The utility of generic and condition-specific QoL measures

The assessment of QoL in healthcare contexts has been operationalized in two different categories of instruments: generic and condition-specific measures (Guyatt, 1995). The generic approach focuses on the assessment of relevant QoL dimensions as broadly defined by the WHOQOL Group (1994), regardless of the respondents’ health condition. The use of generic QoL instruments allows for screening in healthy populations and provides benchmarking data for comparisons across different health conditions (Bullinger et al., 2006; Ravens-Sieberer et al., 2006; Varni et al., 2005). The WHOQOL-100/BREF (The WHOQOL Group, 1998a, 1998b) and the KIDSCREEN questionnaires (The KIDSCREEN Group Europe, 2006) are examples of generic QoL measures. These broad-ranging measures are preferred in epidemiological studies involving decision-making regarding the allocation of public health resources (Eiser & Morse, 2001a; Gerharz, Eiser, & Woodhouse, 2003). However, they are not recommended for QoL assessment in clinical randomized controlled trials because of their lack of sensitivity to small but clinically significant changes over time due to treatments (Clarke & Eiser, 2004).

In contrast, condition-specific measures are designed to assess the HrQoL of populations suffering from a specific chronic condition and they include items assessing specific aspects of functioning that may be impacted directly by the condition and/or its treatments. For example, limitations due to environmental triggers, use of medication, being bullied because of their limited physical capacities or being excluded from sports and other social activities may be particularly relevant for pediatric asthma patients (Van den Bemt et al., 2010). Compared to generic measures, condition-specific measures tend to be more responsive to clinically significant differences or changes (Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003) and, thus, they are more suitable for use in clinical trials designed to assess intervention effects. In addition, this specific approach can be particularly informative for disease management at the individual patient level (Varni et al., 2005). The disadvantages of using condition-specific measures relate to the preclusion of comparative studies across different health conditions, including benchmarking with healthy population norms, the unsuitability to persons with comorbid health conditions, and the impracticality of developing specific instruments for conditions with low incidence (Eiser & Morse, 2001a; Gerharz et al., 2003; Varni et al., 2005).

For a comprehensive assessment of QoL outcomes in healthcare contexts, the development of a core generic instrument supplemented by condition-specific modules has been recommended. In opposition to the traditional battery approach, this modular approach was introduced by Aaronson, Bullinger, and Ahmedzai (1988) as a flexible and practical alternative to devise QoL measures that allow for direct comparison across healthy and chronically ill populations without sacrificing the sensitivity to clinically significant changes/differences. In addition, chronic-generic instruments have been developed to bridge the gap between generic and specific measures. These chronic-generic instruments are built upon a non-categorical approach, which suggests that nosologically different health conditions may lead to similar impacts on patients' well-being and functioning (Holden, Chmielewski, Nelson, Kager, & Foltz, 1997; Stein & Jessop, 1982). The generic KIDSCREEN and the chronic-generic and condition-specific DISABKIDS questionnaires constitute a commendable example of this three-level modular approach to QoL assessment in children/adolescents (Ravens-Sieberer et al., 2007).

### 2.2.2. A developmental approach to QoL assessment

First and foremost, it should be highlighted that the notion of "child development" does not fully equate to "child's age", but is rather a combination of age, cognitive level, adaptive maturity and individual experiences (Harper, 1991). This distinction is particularly important in the pediatric context because chronic health conditions or disabilities may delay or hinder the normative developmental tasks of childhood and adolescence, particularly those related to functional independence and socialization (Drotar, 1981). Moreover, children's cognitive developmental stage, as outlined by Piaget and Inhelder (1966/1993), is closely related to their understanding of the illness, its causes and its treatments (Bibace & Walsh, 1980; Koopman, Baars, Chaplin, & Zwinderman, 2004) and may interfere with self-management practices and perception of adaptation outcomes. For example, before the development of formal logical thinking, children are unable to understand that, although asthma exacerbations may be triggered by environmental (i.e., external) stimuli, the source of the symptoms lies in specific internal physiological structures and functions.

It is fairly consensual that children between 4 and 6 years of age can provide information on concrete health concepts such as pain and use of medication; however, only children over the age of 8 years are able to judge more complex situations and emotions and, thus, provide reliable and valid self-reports of their subjective QoL (Matza, Swensen, Flood, Secnik, & Leidy, 2004; Ravens-Sieberer et al., 2006). It is also important to consider children's cognitive development regarding language comprehension and reading proficiency, powers of abstraction, memory and time perception. To meet children's verbal comprehension abilities, some authors have provided different versions of a questionnaire for different age groups, with fewer items and response categories or using "smileys" as response scales for younger children (e.g., Childhood Asthma Questionnaires; French, Christie, & Sowden, 1994). Regarding the time frame to which the items refer, Ravens-Sieberer and colleagues (2006) suggested that 8-year-old children are usually able to recall periods of 4 weeks with sufficient exactitude.

Finally, the specificities and commonalities between childhood and adolescence must be acknowledged in QoL assessment (Wallander et al., 2001). Even if the core QoL dimensions are age-universal, their operationalization are likely to vary across developmental stages (Bullinger et al., 2006). Specifically, pediatric QoL assessment should consider the relevant social contexts in which children/adolescents are embedded, including their family, school and peer group (Eiser & Morse, 2001a; Matza et al., 2004). In addition, the weight of each context and experience may differ between children and adolescents: while younger children tend to value family attachment, peer play and development of cognitive competencies, a comprehensive assessment of adolescents' QoL must include items related to opposite-sex relationships, body image, autonomy and future aspirations (Gerharz et al., 2003; Schlarmann, Metzing-Blau, & Schnepp, 2008). In a literature review, Eiser (1990) observed that children/adolescents' age may affect adaptation to chronic health conditions differently, with younger children presenting more impairments in school functioning and adolescents presenting more impairments in the social domain. These developmental differences in QoL markers can be addressed by devising age-appropriate questionnaires containing items that reflect the specific developmental tasks of the targeted age group (De Civita et al., 2005). An alternative approach is to select a consistent set of items focused on age-universal QoL markers. One the one hand, this latter approach to QoL assessment is likely to miss age-specific information, but, on the other hand, it enables the comparison of information across age groups and time points (Wallander et al., 2001).

### 2.2.3. Proxy-reported outcomes: A problem or an asset?

A conservative interpretation of the QoL definition suggests the exclusive use of self-report measures for QoL assessment. In fact, children/adolescents' subjective perspective should be assessed, whenever possible, to obtain information on domains of functioning and contexts that are unknown to parents (Matza et al., 2004) and to involve pediatric patients in the disease self-management (Eiser & Morse, 2001a). However, when children are too young, physically ill or disabled, self-report measures may lack reliability and validity and, thus, the advantages and disadvantages of using their parents as proxies must be considered. The same arguments also apply to the assessment of children/adolescents' mental health (Becker, Hagenberg, Roessner, Woerner, & Rothenberger, 2004; Van Roy, Groholt, Heyerdahl, & Clench-Aas, 2010). Over the last few years, a number of instruments with self- and proxy-report forms have been developed for pediatric populations. It is the case, for example, of the KIDSCREEN/DISABKIDS instruments (The DISABKIDS Group Europe, 2006; The KIDSCREEN Group Europe, 2006) and the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997).

Even if parents are asked to describe their children's perceptions and feelings, the patient- and proxy-reports cannot be considered as measures of the exact same construct because parents are unable to detach from their own perceptions of the disease, expectations and additional life stresses (Eiser & Morse, 2001a; Gerharz et al., 2003). In addition, children/adolescents and parents may differ in their interpretation of the items, have different response styles and evoke different events and time frames (Davis et al., 2007). Considerable empirical research has confirmed low to moderate levels of parent-child agreement on pediatric outcomes assessment (e.g., Van der Meer, Dixon, & Rose, 2008; White-Koning et al., 2007), which has been referred to as "the proxy problem" (Sattoe, van Staa, & Moll, 2012; Theunissen et al., 1998). A systematic literature review on children's and parents' ratings of pediatric HrQoL (Eiser & Morse, 2001b; updated by Upton, Lawford, & Eiser, 2008) revealed that levels of agreement may depend on several factors, including the observability of the domains being assessed and the child/adolescent' health status. Specifically, higher levels of agreement have been found for physical symptoms and observed behaviors compared to social and emotional dimensions (e.g., Becker et al., 2004), and for clinical groups compared to healthy controls (e.g., Russell, Hudson, Long, & Phipps, 2006). Different directional patterns of disagreement were also described depending on the child/adolescent's health status: in general populations, parents tend to overrate their children's adaptation outcomes (e.g., Sawyer, Baghurst, & Mathias, 1992; Theunissen et al., 1998), while in pediatric medical contexts parents are more likely to report lower QoL and more psychological problems than the children/adolescents themselves (e.g., Klinnert, McQuaid, McCormick, Adinoff, & Bryant, 2000; Sattoe et al., 2012). Whether patterns of parent-child (dis)agreement differ across socio-demographic characteristics is still unclear, even though age and gender have been addressed in a considerable amount of research (e.g., Petsios et al., 2011; Theunissen et al., 1998).

To solve "the proxy problem", several authors have recommended the use of parent-reports not as proxies but as complementary sources of information (Bullinger et al., 2006; Eiser & Morse, 2001b; Wallander et al., 2001). In fact, the value of parent-reports in clinical and research settings must be recognized even when children/adolescents' reliable self-reports can be obtained. First, parents are the main responsible for clinical decision-making and their perceptions of children/adolescents' health and well-being may greatly influence healthcare utilization, treatment options and adherence (Janicke, Finney, & Riley, 2001; Varni et al., 2005). Second, parent-reports are likely to be more responsive to clinical changes over time, independently of the child's developmental stage, and, thus, should be preferred in longitudinal studies (Le Coq, Boeke, Bezemer, Colland, & van Eijk, 2000). Finally, parents can provide relevant information on the impact of the pediatric health condition on family functioning, which is an important correlate of their children's adaptation outcomes (Matza et al., 2004).

## 2.3. Psychological problems: A predictor or an outcome of asthma morbidity?

As opposed to QoL, which has been consistently addressed as an adaptation outcome, the role of mental health has been more debated in the context of pediatric asthma. The traditional model of psychosomatic illness in children/adolescents postulated that, in some cases, asthma exacerbations are a psychosomatic response to underlying psychological problems resulting from a family functioning characterized by enmeshment, overprotectiveness, rigidity and lack of conflict resolution (Minuchin et al., 1975). Over the past few decades, the increasing understanding of the pathophysiology of asthma has tempered this view (Graham, Rutter, Yule, & Pless, 1967). However, the potential mechanisms that account for the associations between asthma and psychological problems are not entirely clear and the most recent hypotheses emphasize a complex pattern of reciprocal influences between asthma morbidity, psychological factors and contextual variables. Specifically, the occurrence of asthma-related stressors (e.g., recurrent hospitalizations, school absence and loss of social activities) may interfere with normative developmental tasks and lead to increased rates of psychological problems (McQuaid et al., 2001). In turn, psychological problems in the child/adolescent and/or family caregiver may reduce their ability to manage asthma properly (e.g., poor adherence to medication), resulting in increased asthma morbidity (Bender et al., 2000; Kaugars, Klinnert, & Bender, 2004; Weil et al., 1999). The physiological mechanisms underlying anxiety and depression symptoms, namely the autonomic nervous system activation, may also modulate airway constriction (Carr, 1998; Miller & Wood, 1997). Moreover, contextual risk factors (e.g., low SES) may contribute to both asthma functional morbidity and psychological problems.

Although infrequently, children/adolescents' mental health has also been proposed as a predictor of QoL outcomes. For example, Annett, Turner, Brody, Sedillo, and Dalen (2010) found that children's psychological problems were directly and indirectly, via long-term asthma control, linked to children's and parents' QoL. Another study described children's internalizing problems, rather than asthma severity, as the strongest predictor of pediatric HrQoL (Goldbeck, Koffmane, Lecheler, Thiessen, & Fegert, 2007). However, these studies had a cross-sectional design and, without a solid theoretical background supporting their hypotheses, no conclusions can be drawn regarding the direction of these associations. Hence, it is most likely that the relationship between psychological problems and QoL is reciprocal (Vila et al., 2003), representing different indicators of the broader construct of adaptation.

# 3. ADAPTATION PROCESSES OF CHILDREN/ADOLESCENTS WITH ASTHMA AND THEIR PARENTS

Children/adolescents with asthma and their parents are at increased risk for psychological problems and QoL impairments, particularly when asthma is severe and/or inadequately controlled. However, evidence-based research has revealed a wide variability of individual and family adaptation trajectories and outcomes in pediatric contexts (Barlow & Ellard, 2006) that cannot be fully explained by the disease clinical features. Therefore, the fundamental question raised by clinicians and researchers has been: "why some children and their families cope successfully with the challenges they face in adjusting to a chronic disease, whilst others with the same condition fare less well?" (Bradford, 1997, p. 21). Whereas the deficit-based models have failed in addressing this question, the emergence of pediatric psychology as a distinct discipline has offered a novel and promising framework to the understanding of the complex mechanisms that underpin adaptation:

> *Pediatric psychology is a multifaceted and integrated field of both scientific research and clinical practice that focuses on addressing a wide range of physical and psychological issues related to promoting the health and development of children, adolescents, and their families, with an emphasis on evidence-based methods. These health-related issues are considered by pediatric psychologists within a developmental context and reflect a systems-oriented approach to examining the multitude of factors that can affect children and their families* (Aylward, Bender, Graves, & Roberts, 2009, p. 3).

Under this macro paradigm, empirical research has progressively shifted its focus to the identification of risk and resistance psychosocial factors associated with the differentiated adaptation of chronically ill children and their parents (Eiser, 1990; Wallander & Varni, 1998). Although a number of common threads have emerged, their integration in solid and coherent theoretical models is paramount to guide future research and to render evidence-based research into best practices in clinical settings (Bradford, 1997).

## 3.1. Conceptual models of adaptation to pediatric chronic health conditions

Over the last decades, several conceptual models have attempted to explain how specific risk and resistance psychosocial factors might operate to determine individual and family adaptation outcomes in the context of chronic health conditions, including the Model of Child Adjustment to Chronic Disease (Lipowski, 1970; Pless & Pinkerton, 1975) and the Theory of

Crisis of Physical Illness (Moos & Schaefer, 1984). These conceptual models share some common ground. First, they were built upon a non-categorical approach, which assumes that the psychosocial consequences of chronic illness are more similar than different across nosological categories (Stein & Jessop, 1982) and, thus, are common to a wide range of chronic health conditions and disabilities. Second, they assume that the presence of a chronic health condition or disability does not necessarily result in individual and family maladaptation; rather, it may lead to diverse adaptation outcomes depending on how potential stressful events are managed. Third, they emphasize the interactive role of personal competence (e.g., personality, self-concept) and social-ecological environment (e.g., family characteristics, social support) in determining coping responses and the resulting adaptation outcomes. Afterwards, Wallander and colleagues (1989a) proposed the Disability-Stress-Coping Model, which integrates the aforementioned models and a number of dispersed empirical evidences into a single, up-to-date and coherent conceptual model that addresses the differentiated adaptation in terms of risk and resistance factors.

### 3.1.1. The Disability-Stress-Coping Model

The central tenet of the Disability-Stress-Coping Model (Figure 3) is that the impact of risk factors (i.e., disease clinical features, child's functional independence and disease-related or other co-existing stressors) is moderated by three broad categories of resistance factors, namely intrapersonal resources, social-ecological factors and stress processing mechanisms. The model also foresees specific direct and indirect pathways through which risk and resistance factors may influence adaptation outcomes. According to the refined distinction proposed by Rose, Holmbeck, Coakley, and Franks (2004), the specific variables under the rubric of resistance factors can be conceptualized both as resource (i.e., variables that positively influence the outcomes, regardless of the presence of adversity) and/or as protective factors (i.e., variables that decrease the likelihood of negative outcomes under adverse conditions). For example, if a cohesive family environment is directly associated with better QoL in children with asthma, regardless of disease severity, then family cohesion would be conceptualized as a resource factor; however, if the positive association between family cohesion and children's QoL is stronger for those with uncontrolled asthma, buffering the deleterious effect of recurrent exacerbations, then it would be conceptualized as a protective factor.

Guided by Lazarus and Folkman's general Stress and Coping Model (1984), the impact of risk and resistance factors is hypothesized to be mediated by stress processing mechanisms. These include the cognitive appraisal of a particular event as stressful and involving harm-loss, threat or challenge (primary appraisal; e.g., recurrent hospitalizations and consequent school absences perceived as potential threats to academic achievement) and of available resources (secondary appraisal; e.g., availability of social support from classmates). In turn, the cognitive appraisal will determine the use of specific coping strategies to master the stressful situation (e.g., seek support from classmates or do homework while at hospital).

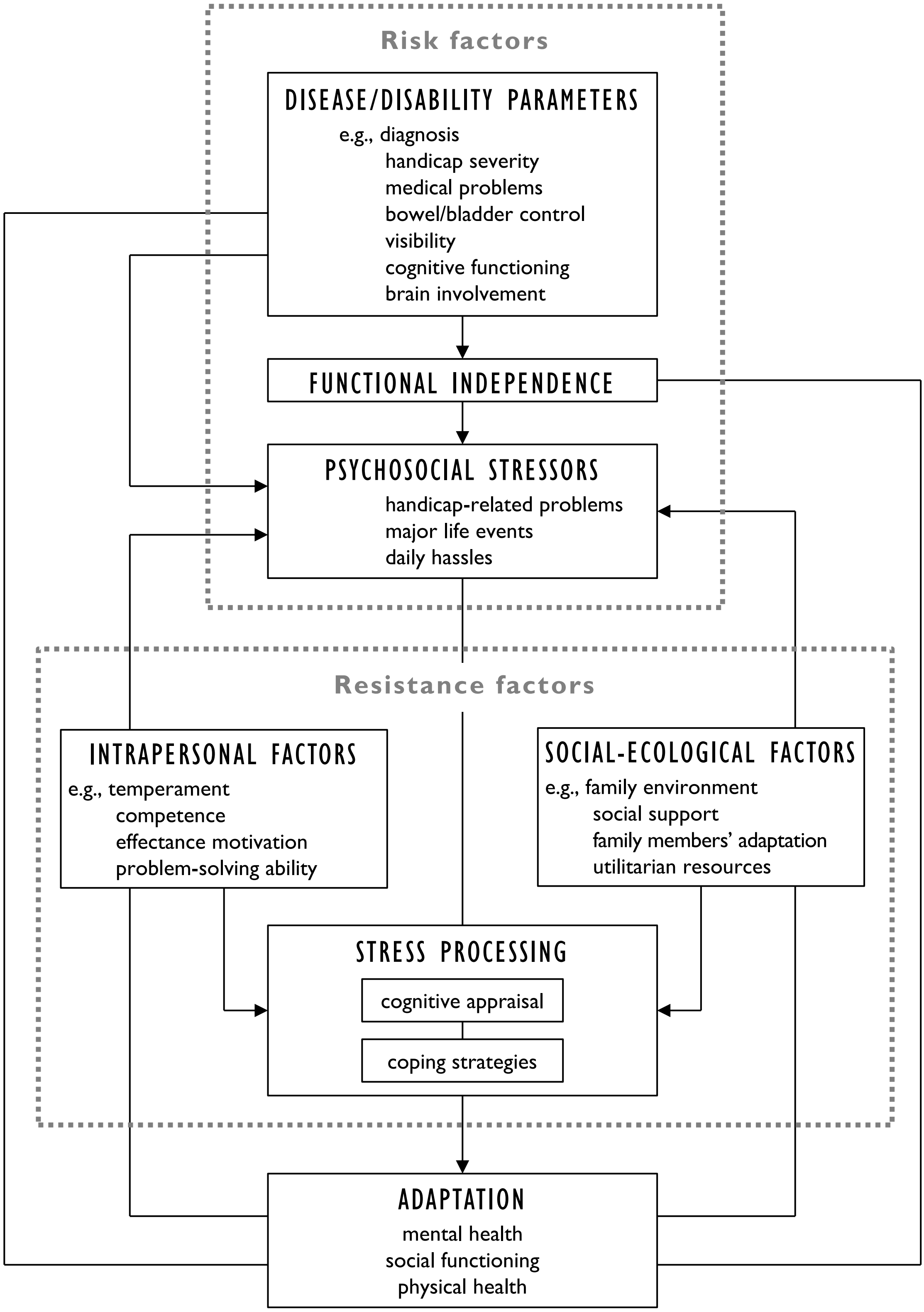

**Figure 3** | The Disability-Stress-Coping Model (reproduced with permission from the authors; Wallander et al., 1989a, p. 171)

In summary, this model has several strengths that justified its adoption as the main theoretical framework of the present research. First, given its non-categorical approach, it is applicable to any pediatric chronic condition, including asthma. Second, it identifies specific risk and resistance factors, as well as the direct, indirect and conditional pathways through which they might operate to determine adaptation outcomes, which enables the operationalization of specific hypotheses to be tested in empirical research. Third, it conceptualizes adaptation as a multi-dimensional construct, including physical, mental and social functioning, which is in line with the emerging concept of QoL (Wallander & Varni, 1998). Moreover, this risk-resistance framework is suitable to map the adaptation processes in both pediatric patients and other family members (Wallander et al., 1990) and it laid the foundation for the development of more specific models of the caregiving process (Raina et al., 2004)[2]. However, Wallander's model may be subjected to two major criticisms: the disregard for children's developmental stage and the conceptualization of children's and parents' adaptation as individual, even if related, processes.

### 3.1.2. A transactional approach to parent-child adaptation processes

The Social-Ecological Model of Human Development (Bronfenbrenner, 1977) offers a comprehensive hierarchical framework of the family and societal contexts that have bidirectional influences on the child. Represented by four concentric rings each contained within the next, the Bronfenbrenner's model organizes ecological environment in a nested arrangement of structures: the microsystem (i.e., the interrelations between the child and the immediate settings in which he/she is actively involved); the mesosystem (i.e., the transitions between major settings in which the child is inserted at a particular point in his/her life); the exosystem (i.e., the distal formal and informal social structures that indirectly influence the child's development); and the macrosystem (i.e., the overarching institutional and cultural patterns such as the economic, social, educational, legal and political systems). Based on the assumption that pediatric chronic health conditions would be better understood within the context of normative family functioning (Kazak, 1989), the development of a chronically ill child would be influenced not only by his/her proximal settings (e.g., family, neighborhood, school), but also by the external settings that have an indirect impact on his/her development, through their effects on parents' mental health and general well-being (e.g., parents' workplace, healthcare system, socio-economic factors and societal influences; Turner-Henson, Holaday, & Swan, 1992). Within this social-ecological perspective, the present research focused on the microsystem: the child and the caregiving environment.

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[2] The main distinctive feature of the conceptual Model of Caregiving Process and Caregiver Burden is the focus on caregiving demands and perception of formal care as foremost risk factors for the caregivers' physical and psychological health. This model is further discussed in the empirical studies III and V.

A common criticism to this systems framework is the disregard for the child's attributes, perceptions and behaviors and how they interact with those of other family members. From a transactional perspective, "the child is not a case of an illness but rather an active member of a family that changes over time to meet new challenges through family transactions" (Fiese, 1997, p. 194). The generic Transactional Model of Development (Fiese & Sameroff, 1989; Sameroff, 2009) and the Transactional Stress and Coping Model for chronic childhood illness (Thompson, Gustafson, Hamlett, & Spock, 1992) emphasize the continuous parent-child reciprocal interactions, embedded in their social-ecological foreground. As a complement to the traditional view (as denoted in Wallander's Disability-Stress-Coping Model) that only considers the unidirectional effect of family environment and family members' adaptation on the child's outcomes, the transactional models acknowledge the child as an active and influential participant in his/her life contexts and, therefore, the effects of the child's functioning and behaviors on the parents' caregiving experiences and adaptation outcomes are regarded as equally important (Fiese & Sameroff, 1989). Although only longitudinal research can attest these two causal pathways, there is compelling evidence of bidirectional associations between children's and their parents' QoL (e.g., Everhart et al., 2008; Marsac, Funk, & Nelson, 2007; Vila et al., 2003) and mental health (e.g., Waxmonsky et al., 2006; Weil et al., 1999) in the context of pediatric asthma. Finally, it is worthwhile to note that the transactional models are not restricted to maladaptive outcomes; rather, they are recognized as central in understanding health-related issues and parent-child positive adaptation at any point in time (Fiese, 1997).

### 3.2. Psychosocial risk and resistance factors and differential adaptation outcomes in pediatric asthma patients and their parents

Given the complexity of the Disability-Stress-Coping Model, Wallander and Varni (1998) advocated that it is not possible to test this comprehensive model of adaptation to pediatric chronic health conditions as a whole; instead they encouraged the examination of small groups of variables and specific components or "sub-models", to ascertain whether they operate in the hypothesized direction. Accordingly, only three groups of variables were selected for the present research: caregiving-related experiences of burden and uplifts, parents' specific coping tendencies and family relationships. The focus on the family and parents' psychosocial risk and resistance factors was justified by the recognition that the family is the primary context for child development in general (Bronfenbrenner, 1986) and for the understanding and treatment of pediatric chronic health conditions in particular (Kazak, 1989, 1997). In addition, a pediatric chronic health condition is not contained within the child but rather affects all members of the family system, particularly those assuming the role of primary caregivers, and the relationships between them. However, parents' adaptation processes have been neglected in pediatric asthma research, despite the growing awareness of the reciprocity of influences and interdependence of adaptation outcomes between family members (Fiese, 1997; Fiese & Sameroff, 1989).

### 3.2.1. Caregiving-related stress and coping mechanisms

Although providing care, protecting and enhancing each other's well-being are inherent to any close relationship such as wife-husband or parent-child relationships, the emergence of a chronic health condition may transform the ordinary exchange of assistance into an extraordinary and unequally distributed source of stress (Pearlin, Mullan, Semple, & Skaff, 1990). The potential adverse effects of the stress involved in the caregiving role that supersedes the caregiver's capacity to adapt has been called "caregiving burden" (Raina et al., 2004). Caregiving burden has been traditionally studied in family caregivers of the elderly. In particular, the study of Montgomery, Gonyea, and Hooyman (1985) provided a major contribution for the conceptualization of caregiving burden as a multi-dimensional construct related to the *perceived* impact of care tasks on caregivers' lives, and not only as an indicator of the extent of workload (e.g., number and type of care tasks performed; number of hours performing these tasks). The authors also addressed the important distinction between the impact of care tasks on caregivers' resources, such as physical health, finances and free time, and the impact on caregivers' emotional state, by considering objective and subjective burden as distinct variables. This pioneering distinction was further refined, eventually yielding the current definition of caregiving burden as a tri-dimensional construct covering the negative impact of caregiving-related responsibilities and instrumental activities on dyadic relationships (relationship burden), on caregivers' free time and other daily life activities such as relationships with other family members, work responsibilities or personal privacy (objective burden), and on emotional stress and anxiety (subjective burden; Savundranayagam, Montgomery, & Kosloski, 2011).

The stress resulting from caregiving demands was emphasized by Raina and colleagues (2004), in their Conceptual Model of Caregiving Process and Caregiver Burden among the pediatric population, as a main risk factor for parents' poor physical and psychological health. In fact, parents of children with chronic health conditions are responsible not only for the physical care of their children, but also for dealing with medical, educational and other service providers, for helping children cope with the physical and emotional demands of their condition, and for balancing competing family needs (Silver, Westbrook, & Stein, 1998). Empirical research has confirmed that mothers of children with chronic health conditions spend twice as much time in caregiving-related activities and substantially less time playing with their children and in leisure activities when compared to mothers of healthy children (Quittner, Opipari, Regoli, Jacobsen, & Eigen, 1992) and that the amount of assistance provided to a chronically ill child during daily living activities (i.e., objective burden) is negatively associated with caregivers' psychological and physical health (Raina et al., 2005). However, very little research has addressed the impact of subjective dimensions of caregiving burden. The differential impact of burden dimensions on parents' adaptation outcomes is no minor issue, since Canning, Harris, and Kelleher (1996) found that higher levels of caregiving burden, as perceived by parents, but not by physicians, are associated with psychological maladjustment in caregivers of children with chronic medical conditions. In addition, subjective burden emerged as a foremost predictor of QoL outcomes in parents of children with cerebral palsy (Carona, Pereira, Moreira, Silva, & Canavarro, 2013). In the specific context of pediatric asthma, the perceived burden of routine asthma care is negatively associated with adaptation outcomes in several family members, namely parents' QoL and children's QoL and anxiety (Fiese, Wamboldt, & Anbar, 2005; Fiese, Winter, Anbar, Howell, & Poltrock, 2008). However, these links are not always direct, but rather mediated by mother-child interaction patterns characterized by rejection/criticism (Fiese et al., 2008) and by a family environment marked by low levels of cohesion and expressiveness (Crespo, Carona, Silva, Canavarro, & Dattilio, 2011).

These empirical evidences highlight the complex mechanisms underlying children's and parents' adaptation outcomes in the context of family caregiving. According to the general Stress and Coping Model (Lazarus & Folkman, 1984) and the conceptual models of adaptation to pediatric chronic health conditions (Raina et al., 2004; Wallander et al., 1989a, 1990), the negative impact of psychosocial stressors (e.g., caregiving burden) on adaptation outcomes are hypothesized to be mediated by stress processing mechanisms, including the individual's appraisal of the stressful situation (i.e., primary appraisal) and the available resources (i.e., secondary appraisal), which in turn would determine the use of specific coping strategies. Coping, defined as "the cognitive and behavioral efforts made to master, tolerate, or reduce external and internal demands and conflicts among them" (Folkman & Lazarus, 1980, p. 223), has been referred to as a dynamic process with a protective function, removing or changing the stressor through the reappraisal of its meaning (i.e., problem-focused coping) or by the regulation of subsequent negative emotions or restoration of self-esteem and personal relationships (i.e., emotion-focused coping; Folkman & Lazarus, 1980; Pearlin & Schooler, 1978).

There have been several attempts to categorize coping strategies according to their focus and adaptive function (i.e., problem-focused *vs.* emotion-focused coping), the person's approach or avoidance orientation in response to a stressor and the method of coping (i.e., whether a response involves primarily cognitive or behavioral efforts; Moos & Holahan, 2007; Roesch & Weiner, 2001). An integrative taxonomy was proposed by Moos and Schaefer (1993), who classified coping into four broad domains: cognitive-approach (e.g., planning/logical analysis, positive reappraisal and active acceptance), behavioral-approach (e.g., seeking information, guidance and support and taking problem-solving action), cognitive-avoidance (e.g., denial, resigned acceptance and mental disengagement), and behavioral-avoidance (e.g., seeking alternative rewards, emotional discharge and behavioral disengagement). More than a conceptual issue, this classification has important implications for the understanding of coping processes in specific stressful circumstances. For example, when the stressful situation is appraised as persisting over time and unlikely to undergo beneficial changes, as in many chronic health conditions, emotion-focused coping strategies aimed at managing the consequent emotional distress are preferred (Carver, Scheier, & Weintraub, 1989; Folkman & Lazarus, 1980). In the context of parenting a child with a chronic health condition or disability, avoidant emotion-focused coping strategies such as wishful thinking, denial and avoidance are associated with parents' decreased QoL and increased psychological symptoms of depression, anxiety and stress (Sales, Fivush, & Teague, 2008; Whittingham, Wee, Sanders, & Boyd, 2013) and negatively related with family strengths (Judge, 1998). Although parental avoidant coping is also associated with decreased HrQoL in pediatric patients (Sales et al., 2008), its mediating effect on the negative link between caregiving burden and QoL outcomes was found to be significant only in parents (Carona, Silva, Crespo, & Canavarro, 2014). Conversely, acceptance is associated with increased life satisfaction and positive affect and decreased anxiety and depression in caregivers of adult patients (Pakenham, 2008); however, empirical research examining how approach-coping strategies may sustain positive adaptation outcomes in parents of children with asthma is definitely lacking.

### 3.2.2. Psychological family resources and parent-child positive adaptation

Despite the deleterious effect of caregiving demands on parents' and their children's adaptation outcomes, a comprehensive understanding of the diversity of adaptation trajectories in pediatric contexts calls for a transition from deficit-based models to a risk-resistance framework and for the consideration of intrapersonal and social-ecological resources. Among social-ecological factors, psychological family resources, which were broadly defined as "the family's characteristic mode of perceiving and interacting with the social world, including within and external to the family" (Wallander et al., 1989a, p. 159), have received considerable attention as resource/protective factors in families dealing with stressful situations, such as pediatric chronic health conditions. According to the family stress theory, families engage in active processes to balance family demands and family resources, as these interact with family meanings to achieve positive adaptation of vulnerable members and the family unit (McCubbin et al., 1980; McCubbin & Patterson, 1983; Patterson, 2002; Walsh, 2002).

The attribution of positive meanings to the experience of parenting a chronically ill child may result in parents' perceptions of gratifications and positive emotions arising from caregiving (Green, 2007; Larson, 2010). This positive dimension of caregiving, often referred to as caregiving uplifts (Montgomery & Kosloski, 2006; Pinquart & Sörensen, 2003), benefit finding (Green, 2007; Kim, Schulz, & Carver, 2007), rewards of caregiving (Bolden & Wicks, 2010), positive perceptions (Gupta & Singhal, 2004) or stress-related growth (Finzi-Dottan, Triwitz, & Golubchnik, 2011)[3], has been acknowledged as an important part of the caregiving process (Sales, 2003). In fact, parents of children with developmental disabilities have described their caregiving experience as an opportunity to develop new skills, widen interests, redefine priorities, strengthen family relationships and expand personal and social networks (Grant, Ramcharan, McGrath, Nolan, & Keady, 1998; Green, 2007; Stainton & Besser, 1998). Comparative research with healthy controls confirmed that parents of chronically ill children are more satisfied with their family situation (Goldbeck, 2006) and have higher levels of family involvement (Thornton et al., 2008) and higher-density social networks (Kazak, 1987). The parents' perception of gratifications and positive emotions arising from caregiving may also sustain effective coping mechanisms (Folkman, 1997; Folkman & Moskowitz, 2000). Specifically, the adoption of meaning-based coping (i.e., cognitive-approach coping strategies based on the reinterpretation of stressful events to reduce the incongruence between the appraised meaning of a specific event – i.e., situational meaning – and the individual's preexisting goals and beliefs – i.e., global meanings; Park, 2010; Park & Folkman, 1997), is linked to increased psychological well-being in caregivers of children with disabilities (Larson, 2010). Besides operating as family resources, caregiving uplifts may co-occur and interact with high levels of caregiving burden, buffering its negative impact on individual and family adaptation outcomes (Carona, Pereira, et al., 2013; Gupta & Singhal, 2004). However, this protective function of caregiving uplifts remains understudied in the context of pediatric asthma.

The conceptual models of adaptation to pediatric chronic health conditions (Raina et al., 2004; Wallander et al., 1989a) have also acknowledged family environment as a resource contributing to children's and parents' improved physical and psychosocial health. In fact, broadly defined family characteristics such as cohesion (i.e., the emotional bonding among family members, a midpoint between disengagement and enmeshment; Olson & Gorall, 2003), conflict, warmth and support have been consistently identified as primary influences on children's psychological outcomes in both healthy and chronically ill populations (Fiese, 1997). Specifically, higher levels of family cohesion and lower levels of family conflict are associated with fewer internalizing, externalizing and attention problems in both normal and low birth weight children

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[3] The term "caregiving uplifts" was adopted in the context of the present research, in accordance with the terminology used by the authors of the Revised Burden Measure (Montgomery & Kosloski, 2006).

(Lucia & Breslau, 2006); moreover, the quality of parent-child relationships have been found to mediate the link between parents' psychological distress and children's internalizing and externalizing problems and depressive symptoms (Papp, Cummings, & Goeke-Morey, 2005). In a literature review of studies linking parent and family functioning to the psychological adjustment of children with chronic health conditions, Drotar (1997) found that, in general, supportive family relationships (e.g., high levels of family cohesion) are associated with fewer behavioral symptoms and more competent psychological functioning in pediatric patients; conversely, family conflict and maternal psychological problems are typically identified as predictors of children's maladjustment.

Family environment and parent-child relationships have been regarded as essential variables in the study of pediatric asthma for a long time, especially in psychosomatic research. However, most studies have focused on negative family emotional climate and how it contributes to increased physical and psychological morbidity in pediatric asthma patients (e.g., Bender et al., 2000; Reichenberg & Broberg, 2005; Wood et al., 2007, 2008). Moreover, the traditionally accepted psychogenesis of asthma symptoms was proved not to be universal: some authors have commented on the influence of family characteristics on asthma onset and outcomes (Kaugars et al., 2004), while others reported no direct associations between family functioning and respiratory function or asthma control (Rodríguez-Orozco, Núñez-Tapia, Ramírez-Silva, & Gómez-Alonso, 2013). Although QoL is emerging as a primary outcome in healthcare contexts in general and in pediatric psychology in particular, it is surprising the scarcity of empirical evidence linking family functioning to QoL outcomes in pediatric asthma patients and their parents. The few existing studies have found convincing evidence that a family environment ruled by low levels of parent-child conflict and high levels of cohesion, expressiveness and adaptability is associated with better QoL for both children and their parents (Crespo et al., 2011; Murdock, Adams, Pears, & Ellis, 2012; Sawyer et al., 2001; Vinson, 2002). Finally, it is important to note that these links are not always direct, but they can be mediated by the child's psychological functioning (Annett et al., 2010).

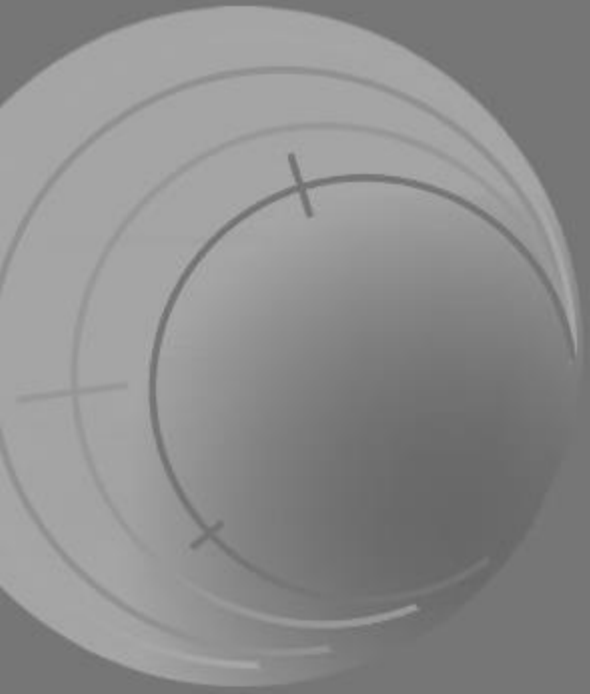
# 4. RESEARCH GAPS AND CURRENT CHALLENGES

This succinct literature review provides an overview of the current state of the art on the topic of psychosocial adaptation processes and outcomes in children/adolescents with asthma and their parents and allows the identification of some research gaps and limitations, as summarized next.

A major critical issue refers to the scarcity of empirical research addressing mental health and QoL as indicators of adaptation in pediatric patients and their families. This research gap may be justified, first, by the traditional psychosomatic view of asthma as an expression of underlying psychological problems (Minuchin et al., 1975), and, second, by the methodological constraints in outcome assessment in pediatric contexts (Bullinger et al., 2006). Moreover, the existing research has yielded inconsistent findings regarding the adaptation outcomes of pediatric asthma patients and their parents in relation to their healthy peers. While a meta-analytic review gathering the empirical studies focused on the mental health of children/adolescents with asthma established that they are at greater risk for internalizing problems compared to children without asthma and population norms (McQuaid et al., 2001), no such task was yet performed for QoL outcomes. Thus, it is imperative to summarize the results of empirical studies comparing the QoL of children/adolescents with asthma and their parents with age-matched controls to ascertain the magnitude of QoL impairments and to identify the QoL domains that are mostly affected in this population.

Regarding the adaptation outcomes assessment in the pediatric asthma context, two methodological gaps have emerged. First, pediatric QoL defined in relation to patients' and/or parents' goals, expectations, standards and concerns may be greatly influenced by cultural background; however, validated asthma-specific questionnaires to assess HrQoL in Portuguese children and adolescents are not available to date. The European KIDSCREEN and DISABKIDS projects provide a set of developmentally appropriate and cross-culturally comparable questionnaires in a three-level modular system for assessing QoL outcomes in healthy and chronically ill children and adolescents (Ravens-Sieberer et al., 2007). Given that the European Portuguese versions of the generic KIDSCREEN and the chronic-generic DISABKIDS modules have already been developed (Carona, Crespo, et al., 2013; Gaspar & Matos, 2008), the following step is the translation and cross-cultural adaptation of the self- and proxy-report versions of the DISABKIDS Asthma Module (DAsM) to the European Portuguese language and culture. Second, the existing studies on the topic of (dis)agreement between children's and parents' reports of QoL and psychological problems have focused mainly in determining the extent to which children and parents agree/disagree and whether parents are more likely to over or underrate pediatric adaptation outcomes, but little is known about its determinants (Eiser & Morse, 2001b; Upton et al., 2008). Clinical and socio-demographic factors have been repeatedly tested, but their explanatory contribution has proven to be small and the results have been inconsistent across studies. Therefore, the current challenge is the identification of modifiable psychosocial variables, such as family functioning and relationships, associated with the extent and direction of parent-child (dis)agreement.

A final set of criticisms relate to the empirical research that has attempted to explain the complex mechanisms underlying the variability in adaptation trajectories of pediatric asthma patients and their parents. An overriding issue refers to the lack of solid theoretical frameworks guiding the formulation of hypotheses in empirical research in pediatric psychology. Besides, the majority of studies have relied on "traditional" analytic approaches (e.g., linear regression models) to examine the linear and additive effects of hypothesized independent variables on adaptation outcomes and few regression-based studies have examined potential interaction effects among explanatory factors. As noted by Raina and colleagues (2004), "single factor changes are relatively rare outside of the context of a natural or laboratory experiment" and, thus, research needs to test theoretically-driven hypotheses using advanced statistical techniques, such as regression-based moderation analyses and structural equation modeling (SEM), to understand the complex web of direct, indirect and conditional effects mapping the adaptation processes in children with asthma and their parents. A related concern is the recurrent disregard for the interdependence of family members in the context of pediatric asthma; even the studies that used more complex statistical approaches (e.g., Annett et al., 2010) examined parents' adaptation independently from children's adaptation. In addition, research has been relatively inactive regarding the identification of risk factors predicting maladaptation, and little is known about the role of positive dimensions of caregiving, specific coping strategies or adaptive family functioning as contributors for improved mental health and QoL in pediatric asthma patients and their parents. Subsequent research needs to adopt a transactional approach to understand how parents and children shape each other's adaptation and to focus on the "existing family strengths and capabilities so that interventions are built on things a particular family already does well" (Judge, 1998, p. 263). Although children's developmental stage was not explicitly included in the Disability-Stress-Coping Model, there is some evidence of age-related specificities in QoL markers (Eiser, 1990; Wallander et al., 2001). A final challenge is to apply a developmental approach to children's and parents' adaptation processes and not only to outcome assessment (Holmbeck, 2002a). This could be accomplished by examining the effects of age group (e.g., children *vs.* adolescents) on the psychosocial risk and resistance factors and on the strength of their direct and indirect associations with adaptation outcomes (i.e., the [in]variance of adaptation mechanisms across age groups).



# Chapter II

## Objectives and Method

This research project was carried out within the *Relationships, Development and Health* Research Group, of the Cognitive and Behavioral Center for Research and Intervention (CINEICC; R&D unit of the Portuguese Foundation for Science and Technology), at the Faculty of Psychology and Education Sciences of the University of Coimbra (http://gaius.fpce.uc.pt/saude/pc2.htm). The preparation of this dissertation also included a 3-month period of supplementary research activities, conducted between May 15 and August 15, 2012, at the Department of Medical Psychology – Centre for Psychosocial Medicine of the University Medical Center Hamburg-Eppendorf, University of Hamburg, in Germany, under the supervision of Professor Dr. phil. Monika Bullinger.

The body of this dissertation comprises a meta-analytic review and six empirical studies; all the seven studies are presented in the format of scientific articles and currently published/ accepted for publication in national (one study) and international (six studies) peer-reviewed journals. The specific objectives and methods (e.g., participants, instruments, statistical analyses) of each study are described in the articles' appropriate sections (see Chapter III). In this second chapter, we will present an integrative overview of the research project, by describing the general objectives and broad methodological options interconnecting the different studies.

# 1. RESEARCH OBJECTIVES

The objectives for the present research project were defined to address important research gaps on the topic of the psychosocial adaptation of children/adolescents with asthma and their parents and methodological limitations of existing studies, which were identified in the previous chapter. Considering the current state of the art, this project intends to be an innovative contribution to the description of the impact of pediatric asthma in children/adolescents' and their parents' psychosocial functioning and well-being, as well as to the understanding of risk and resistance factors underlying their adaptation processes and outcomes. Accordingly, three general objectives were outlined for our study:

1. To characterize the QoL of children/adolescents with asthma and their parents, in comparison to controls without asthma;

2. To clarify key methodological issues in the assessment of QoL outcomes and psychological problems in pediatric asthma patients:
   2.1. To cross-culturally adapt an asthma-specific questionnaire – The DISABKIDS Asthma Module (DAsM) – and to evaluate its utility within a modular system comprising generic, chronic-generic and condition-specific measures for assessing

QoL in Portuguese children and adolescents with asthma;

2.2. To understand the (dis)agreement between child- and parent-reports of QoL and psychological problems;

3. To identify individual and family risk and resistance factors, and to understand the processes through which they contribute to explain the differentiated adaptation outcomes (i.e., mental health and QoL) in children/adolescents with asthma and their parents:
   - 3.1. To characterize psychosocial variables (i.e., coping tendencies, caregiving burden and uplifts and perceptions of family relationships) and children/adolescents' and their parents' adaptation outcomes in distinct socio-demographic and clinical groups;
   - 3.2. To identify socio-demographic, clinical and psychosocial variables associated with children/adolescents' and their parents' adaptation outcomes;
   - 3.3. To examine the processes through which psychosocial variables contribute to better adaptation outcomes (i.e., mediating effects) and to ascertain the socio-demographic and clinical conditions in which they occur (i.e., moderating effects);
   - 3.4. To understand how children/adolescents and parents shape each other's adaptation (i.e., transactional processes).

The first general objective was addressed in a meta-analytic review of published research comparing the scores in overall QoL and in its core domains (physical, psychological, social and school functioning) of pediatric asthma patients and their parents with community/healthy controls. The participants' socio-demographic and clinical characteristics and the methodological quality of the included studies, and their role in explaining the heterogeneity of results, were also examined in this meta-analytic review.

The second general objective was addressed in three different empirical studies. In a preliminary study, we described the procedures for the translation and cross-cultural adaptation of the European Portuguese self- and proxy-report versions of the DAsM questionnaires (semantic validation study), as well as the exploratory psychometric analyses in a small sample of Portuguese children/adolescents (pilot study). In the empirical study I, we described the psychometric properties of the DAsM questionnaires in a large sample of Portuguese children/adolescents (field study), including its factorial structure and the invariance of the measurement model across age groups (children aged 8-12 *vs.* adolescents aged 13-18 years) and informants (child- *vs.* parent-reports). The empirical study II was specifically aimed at examining the (dis)agreement between child- and parent-reports of QoL and psychological problems, at the individual and the group levels, and at identifying socio-demographic, clinical and family variables explaining the extent and direction of child-parent discrepancies.

To address the third general objective, four empirical studies were conducted. The specific objectives of each empirical study are displayed in Table 1. Two distinctive features of these studies should be emphasized. First, we adopted a family-centered perspective, which was operationalized by capturing the perspectives of two family members – a child/adolescent and a parent – regarding psychosocial variables and adaptation outcomes, by examining the role of the whole family relationships in the adaptation outcomes of children/adolescents and their parents and by studying the parent-child transactional paths, i.e., how children/adoelscents and parents influence each other's adaptation (Kazak, 1997; Sameroff, 2009). Second, we embraced a developmental approach by using developmentally appropriate measurement instruments with parallel child- and parent-report versions and by examining age-related differences and common markers in the adaptation processes and outcomes of children aged 8-12 years and adolescents aged 13-18 years and their parents (Carona, Silva, & Moreira, 2015; Wallander et al., 2001).

**Table 1** | Specific research objectives for the empirical studies

| *Empirical study* | *Specific objectives* |
|---|---|
| Empirical study III | • To characterize parents' caregiving burden, acceptance and denial coping tendencies, and QoL in different groups regarding children/adolescents' age, asthma severity and family SES<br>• To examine the direct and indirect links, via acceptance and denial coping, between parents' caregiving burden and QoL, and its (in)variance across children/adolescents' age, asthma severity and socio-economic groups |
| Empirical study IV | • To examine the direct and indirect links, via positive reframing coping, between parents' caregiving uplifts and QoL, and its (in)variance across children/adolescents' age and asthma severity groups |
| Empirical study V | • To characterize the negative and positive dimensions of family caregiving and the QoL of parents and their children in different age, asthma severity and asthma control groups<br>• To examine the moderating role of caregiving uplifts on the associations between caregiving burden and QoL of parents and their children |
| Empirical study VI | • To characterize family relationships and children/adolescents' and their parents' adaptation outcomes in different asthma severity groups<br>• To examine the direct and indirect links between family relationships and adaptation, for children/adolescents and parents separately (within-subjects) and across family members (cross-lagged effects), and its (in)variance across children/adolescents' age and gender and asthma severity groups<br>• To test the moderating role of asthma severity on the links between family relationships and children/adolescents' adaptation outcomes |

# 2. METHOD

Our research project included three distinct phases. In the first research phase, the current literature on the topic of QoL of children/adolescents with asthma and their parents was systematically reviewed to determine whether pediatric asthma patients and their parents have decreased QoL in comparison to their peers without asthma (cf. meta-analytic review study). In the second research phase, we undertook the cross-cultural adaptation and the psychometric validation of the European Portuguese self- and proxy-report versions of the asthma-specific DISABKIDS questionnaires. Finally, the third research phase focused on the examination of adaptation processes and outcomes in children/adolescents with asthma and their parents, in different socio-demographic and clinical groups. Next, we describe the study design, participants and general procedures for the empirical research phases II and III.

## 2.1. Study design

Our research project had a cross-sectional dyadic design, which means that the data were collected at a single moment from two non-independent individuals – a child/adolescent and a parent/family caregiver (Kenny, Kashy, & Cook, 2006). The participants were selected in accordance with the non-probabilistic sampling method of convenience, which involved the collection of data from children/adolescents and parents who attended medical appointments between March 2010 and February 2012 in the healthcare institutions where our study was held and were willing to participate.

The cross-cultural adaptation of the European Portuguese versions of the DAsM questionnaires (research phase II) was conducted in accordance with the DISABKIDS Group Europe guidelines for sequential translation and validation of existing instruments to other languages and cultural contexts (The DISABKIDS Group Europe, 2004) and included qualitative and quantitative methods: (1) forward-backward translation procedures and international harmonization of items and response scales; (2) cognitive interviews with children/adolescents with asthma and their parents (semantic validation); (3) exploratory testing of the psychometric properties of the questionnaires in a small Portuguese sample (pilot study); and (4) comprehensive assessment of the psychometric properties of the questionnaires in a cross-sectional sample of at least 100 children/adolescents with asthma and their parents (field study).

The subsequent empirical studies (research phase III) were quantitative in nature and the data were mainly collected through self-completion datasheets and questionnaires assessing socio-demographic and clinical data, psychosocial variables and adaptation outcomes. Some of these variables were assessed at the individual level, while other variables were assessed at the dyadic level, i.e., children/adolescents' and parents' assessments of the same variables were collected. According to the terminology proposed by Kenny and colleagues (2006) for dyadic research designs, we included between-dyads variables, which have the same score for both members of the dyad but may differ from other dyads (e.g., family SES), and mixed variables, which may have different scores for each dyad member and are also expected to differ, on average, between dyads (e.g., children/adolescents' and parents' perceptions of family relationships).

## 2.2. Procedures and participants

For both empirical research phases, a sample of pediatric asthma patients and their parents/family caregivers was collected at the Pediatric and Immunoallergology outpatient services of three public hospitals in the central region of Portugal (Hospital Universitário de Coimbra [HUC][4], Hospital Pediátrico do Centro Hospitalar de Coimbra [CHC][4], and Hospital de Santo André do Centro Hospitalar Leiria – Pombal, EPE), after the study has been approved by the respective Ethical Committees and/or Direction Boards. The sample collection was conducted by a research team composed of the main researcher and trained research assistants, acquainted with the project objectives and method (students in the final year of the Integrated Master in Psychology, specialty in Clinical Psychology and Health, at the Faculty of Psychology and Education Sciences of the University of Coimbra).

The eligible children/adolescents were identified by their physicians, based on their medical files, according to the following general inclusion criteria:

1. Chronological age between 8 and 18 years;
2. Clinical diagnosis of asthma according to the ICD-10, code J45 (WHO, 2010), established by a physician;
3. Disease duration of at least 12 months;
4. Ability to understand and answer the questionnaires in the Portuguese language.

Two additional inclusion criteria were considered for parents/family caregivers:

5. Self-identification as the family member assuming the role of primary caregiver of the child/adolescent's health-related issues, at the time;
6. Literacy level enabling the self-completion of the assessment protocol in the Portuguese language.

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[4] Currently, both hospitals are integrated into *Centro Hospitalar e Universitário de Coimbra* (CHUC), EPE.

The assessment protocol was completed in person by the children/adolescents and their parents, in a consultation office assigned for research purposes at the healthcare institution they attended, after obtaining informed consent from parents/family caregivers and adolescents older than 13 years and informal assents from younger children. The specific procedures and the sample description for the empirical research phases II and III are presented below.

### 2.2.1. Research phase II: Cross-cultural adaptation of the DAsM questionnaires

Prior to the sample collection, the self- and proxy-report versions of the DAsM questionnaires were translated into the European Portuguese language following the DISABKIDS Group Europe guidelines (Schmidt & Bullinger, 2003; The DISABKIDS Group Europe, 2004). To ensure the cross-cultural conceptual equivalence of the items, we used the forward-backward translation technique, which involved: (1) forward translation of the items and response scales from the original English versions to the European Portuguese language by two independent translators; (2) reconciliation of both translations into a single version by a researcher; (3) backward translation by a third translator; (4) review of forward and backward translations and construction of the experimental Portuguese versions of the questionnaires.

For the semantic validation study of the DAsM questionnaires, a convenience sample of 9 children aged 8-12 years, 9 adolescents aged 13-18 years, and 18 parents/family caregivers was collected between November and December 2010. Cognitive interviews based on the General Probing Method and Paraphrasing as a variant of the Think Aloud Method were conducted to assess the comprehensibility and relevance of each item and the adequacy of its response scale. In addition, the participants were asked to comment on the overall quality of the questionnaires by answering some closed and open-ended questions. Subsequently, we conducted an international harmonization of problematic items by discussing them with the coordinator of the DISABKIDS Group Europe, Professor Dr. phil. Monika Bullinger (Department of Medical Psychology, University Medical Center Hamburg-Eppendorf, Germany).

The experimental Portuguese versions of the DAsM questionnaires were first completed by 18 children aged 8-12, 18 adolescents aged 13-18 and by their parents/family caregivers, selected by convenience between June and July 2011, to explore the first psychometric properties of the questionnaires (pilot study). For the psychometric field study, a subsample of participants from the third research phase also completed the Portuguese versions of the DAsM as part of the broader assessment protocol. This subsample was composed of 144 children/adolescents and their parents/family caregivers, collected by convenience between June 2011 and February 2012. The children/adolescents who were not taking regular or emergency medication for asthma (*n* = 4) were excluded from the DISABKIDS field study, to allow the examination of the treatment-related items. The sampling frames used in the second research phase are summarized in Table 2 and fully described in the adequate sections of the preliminary study and the empirical study I.

**Table 2** | Sample size and description for the empirical studies conducted in research phase II

| ***Research phase II*** | Semantic validation | Pilot study | Field study |
|---|---|---|---|
| Data collection period | Nov. – Dec. 2010 | June – July 2011 | June 2011 – Feb. 2012 |
| Sample size | 9 children<br>9 adolescents<br>18 caregivers | 18 children<br>18 adolescents<br>36 caregivers | 81 children<br>63 adolescents<br>144 caregivers |
| Exclusion criteria | | | |
| No prescription for regular or emergency medication | ✓ | ✓ | ✓ |
| Comorbidity with other chronic health conditions or severe psychiatric disorders | ✓ | ✓ | ✓ |
| Missing data ≥ 5% of the scores | ✓ | ✓ | ✓ |
| Excluded participants | *n* = 0 | *n* = 0 | *n* = 4 |
| Participants included in each study | Preliminary study (*n* = 18 + 36 dyads) | | Empirical study I (*n* = 140 dyads) |

### 2.2.2. Research phase III: Study of adaptation processes and outcomes in pediatric asthma

In the third research phase, a convenience sample of 293 dyads of children/adolescents with asthma and their parents/family caregivers was collected between March 2010 and February 2012. Subsequent to obtaining informed consent/informal assent from the participants, the researchers delivered the assessment protocols to the children/adolescents and their parents, and provided verbal instructions regarding their completion. The importance of the subjective perception of each family member was emphasized and, therefore, the children/adolescents and the parents were instructed to answer according to their own feelings and beliefs because there were no wrong or right answers and to complete the questionnaires independently, without exchanging any information between them. The questionnaires were completed in the presence of a researcher, who was available to help the participants with difficulties in reading or understanding the items. In the few cases when the parents were unable to complete the assessment protocol in the healthcare institutions, pre-stamped envelopes were provided so that they could return it by post to the research team.

Because in this third research phase we were particularly interested in examining parent-child dyadic adaptation processes and outcomes in the context of pediatric asthma, children/adolescents with comorbid chronic health conditions or severe psychiatric disorders (e.g., epilepsy, arthritis, congenital heart disease, Asperger's syndrome, etc.; *n* = 10) and primary caregivers other than parents and who did not live in the same household as the children/adolescents (e.g., grandparents; *n* = 8) were excluded. Additionally, 97 cases were excluded from the empirical studies examining the role of caregiving burden and/or uplifts in explaining the variance in parents' and their children's adaptation outcomes, to avoid overlap with the sample used in the psychometric study of the Portuguese version of the Revised Burden Measure[5]. Finally, we excluded cases in which missing values in the target variables were greater than 5%, which resulted in slight random variations in the final sample size for each empirical study. The exclusion criteria and sample size for each empirical study are summarized in Table 3.

**Table 3** | Sample size and description for the empirical studies conducted in research phase III

| ***Research phase III*** | | | | | |
|---|---|---|---|---|---|
| Data collection period | March 2010 – February 2012 | | | | |
| Sample size | 167 children<br>126 adolescents<br>293 parents/family caregivers | | | | |
| | Empirical study | | | | |
| Exclusion criteria | II | III | IV | V | VI |
| Comorbidity with other chronic health conditions or severe psychiatric disorders | ✓ | ✓ | ✓ | ✓ | ✓ |
| Primary caregivers other than parents | ✓ | ✓ | ✓ | ✓ | ✓ |
| Subsample used in the psychometric study of the Portuguese version of the Revised Burden Measure | × | ✓ | ✓ | ✓ | × |
| Missing data ≥ 5% of the scores | ✓ | ✓ | ✓ | ✓ | ✓ |
| Excluded participants | *n* = 14 | *n* = 111 | *n* = 113 | *n* = 113 | *n* = 36 |
| Participants included in each study | Study II (*n* = 279 dyads) | Study III (*n* = 182 parents) | Study IV (*n* = 180 parents) | Study V (*n* = 180 dyads) | Study VI (*n* = 257 dyads) |

## 2.3. Variables and instruments

With the purpose of operationalizing the variables targeted in the empirical studies, we compiled a set of socio-demographic and clinical datasheets and self-completion questionnaires assessing psychosocial variables and adaptation outcomes, for both the children/adolescents and

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[5] Ongoing study not presented in this dissertation.

their parents/family caregivers. The assessment instruments were selected based on the following generic methodological criteria: (1) suitability for the operationalization of multi-dimensional constructs, including the complementary assessment of both positive and negative dimensions of adaptation and potential psychosocial risks and resource/protective factors; (2) short length self-completion questionnaires, allowing the economic and brief assessment of a large number of variables/dimensions, while minimizing the participants' response burden; (3) availability of translated versions in the European Portuguese language; and (4) psychometric robustness, in terms of reliability and validity, confirmed in previous studies with Portuguese samples. The variables and data collection methods for each empirical study are summarized in Table 4.

**Table 4** | Variables and data collection methods for each empirical study

| Instruments | Variables | Informant | Preliminary study | Empirical studies | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | I | II | III | IV | V | VI |
| ***Socio-demographic and clinical information*** | | | | | | | | | |
| Socio-demographic and clinical datasheets | | Parent | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| GINA[a] | Asthma severity | Physician | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| | Asthma control | Physician | ✓ | | | | | ✓ | |
| ***Children/adolescents' adaptation outcomes*** | | | | | | | | | |
| KIDSCREEN-10 | Generic QoL | Child | | ✓ | ✓ | | | ✓ | ✓ |
| | | Parent | | ✓ | ✓ | | | | |
| DCGM[b] | Chronic-generic HrQoL | Child | | ✓ | ✓ | | | | ✓ |
| | | Parent | | ✓ | ✓ | | | | |
| DAsM[c] | Asthma-specific HrQoL | Child | ✓ | ✓ | | | | | |
| | | Parent | ✓ | ✓ | | | | | |
| SDQ[d] | Psychol. problems | Child | | | ✓ | | | | ✓ |
| | | Parent | | | ✓ | | | | |
| ***Parents' adaptation outcomes*** | | | | | | | | | |
| WHOQOL-BREF[e] | Generic QoL | Parent | | | | ✓ | ✓ | ✓ | ✓ |
| MHI-5[f] | Psychol. distress | Parent | | | | | | | ✓ |
| | Psychol. well-being | Parent | | | | | | | ✓ |
| ***Psychosocial variables*** | | | | | | | | | |
| Revised Burden Measure | Caregiving burden | Parent | | | ✓ | ✓ | | ✓ | |
| | Caregiving uplifts | Parent | | | | | ✓ | ✓ | |
| Brief-COPE | Coping tendencies | Parent | | | | ✓ | ✓ | | |
| FES[g] | Family relationships | Child | | | ✓ | | | | ✓ |
| | | Parent | | | ✓ | | | | ✓ |

[a] Global Initiative for Asthma. [b] DISABKIDS Chronic Generic Module. [c] DISABKIDS Asthma Module. [d] Strengths and Difficulties Questionnaire. [e] World Health Organization Quality of Life assessment. [f] Mental Health Inventory – brief version. [g] Family Environment Scale.

In addition, we favored a developmental approach to pediatric outcomes assessment, which implies that instruments designed for adult populations are inappropriate for use with children/adolescents because of the level of abstraction required for decision-making, the lack of developmental considerations, and the inclusion of domains that can be less relevant or the exclusion of age-related domains (Bullinger et al., 2006; Spieth & Harris, 1996). Following current recommendations (Matza et al., 2004; Schlarmann et al., 2008; Wallander et al., 2001), we carefully selected questionnaires that meet the following developmental requirements: (1) coverage of specific domains within the relevant contexts for children/adolescents (e.g., school functioning, peer relationships, etc.), preferably identified in focus groups with the target population; (2) identification of common markers across developmental periods, assessed by a consistent set of items that enables comparative analyses between age groups; (3) inclusion of a small number of items, since younger children have a limited capacity to maintain attention and process great amounts of information; (4) item and response scale wording and formatting that are appropriate to children's general cognitive ability and expressive/receptive language proficiency (e.g., simple statements that avoid an excessive level of abstract decision-making or the recalling of events and behaviors that occurred before the last four weeks); and (5) availability of similar versions for child and parent-proxy reports.

Next, we present a detailed description of each variable included in our study and the instruments used for its assessment.

### 2.3.1. Socio-demographic and clinical information

The participants' socio-demographic information was collected through a datasheet purposely developed for this study, to be completed by the parents/family caregivers. Specifically, the parents provided information on their own age, sex, educational level, current job, marital status, number of children and household composition, as well as their children's age, sex, school absenteeism and academic achievement. Based on the educational level and current job of the primary caregiver, the family SES was classified into low (e.g., unqualified employees in construction or manufacturing, housekeepers or aids in educational/healthcare services, who did not complete the 9th grade of school education), medium (e.g., employees in bureaus or banks, nurses, social workers or teachers in primary and secondary education with an educational level ranging from the 9th grade to intermediate or university degrees) and high (e.g., senior officials of government, commerce or industry, physicians, magistrates, architects, engineers, economists, teachers of higher education or senior officers of army with bachelor, master, doctorate or other post-graduate degrees), according to the classification system proposed by Simões (1994) for the Portuguese context.

The children/adolescents' clinical information was collected through three different methods. First, classification grids of asthma severity and control levels were rated by the children's physicians according to the GINA guidelines (2008) and the *Portuguese National Program for Asthma Control* (Direcção-Geral da Saúde [DGS], 2000)[6], that were in place at the time of the study preparation and data collection. Thus, asthma severity was classified into four levels (intermittent, mild persistent, moderate persistent and severe persistent), considering the level of symptoms, airflow limitation and lung function variability before treatment. In order to also consider treatment responsiveness, the physicians classified asthma control into three levels (controlled, partly controlled and uncontrolled), based on clinical manifestations, laboratory markers of inflammation and pathophysiological features of the disease as recorded in the children's medical files. Second, the parents/family caregivers completed a clinical datasheet asking about their children's clinical characteristics, namely age at the time of the asthma diagnosis, length of time since the asthma diagnosis, asthma medication, hospitalizations during the last year and comorbidity with other physical or mental health conditions. Third, the children/adolescents and their parents also reported on their perceptions of asthma symptoms during the last year, as part of the asthma-specific DISABKIDS questionnaires (The DISABKIDS Group Europe, 2006). This section of the DAsM questionnaires includes three items related to the recency of the last asthma attack ("When was the last time you/your child had an asthma attack?"), frequency of asthma attacks ("How many asthma attacks did you/your child have during the last year?") and asthma severity ("How severe was your/your child's asthma during the last year?"), which are answered in a 5-point Likert-type response scale.

## 2.3.2. Children/adolescents' adaptation outcomes

### 2.3.2.1. QUALITY OF LIFE OUTCOMES

Following the WHO (1993) recommendations, the children/adolescents' QoL was assessed in our study at three different levels (i.e., generic, chronic-generic and asthma-specific) and using developmentally appropriate and cross-culturally comparable instruments with similar versions to be completed by the children/adolescents and by the parents/family caregivers as their proxies. These requirements for pediatric QoL assessment (WHO, 1993) were thoroughly met by the KIDSCREEN (*Screening for and Promotion of Health-Related Quality of Life in Children and Adolescents – a European Public Health Perspective*; Ravens-Sieberer et al., 2001) and DISABKIDS (*Quality of Life in Children and Adolescents with Disabilities and their Families – Assessing Patient Views and Patient Needs for Comprehensive Care*; Bullinger, Schmidt, Petersen, & The Disabkids Group, 2002) projects, which were promoted by the 5th Framework-Program "Quality

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[6] The National Program for Asthma Control ceased following the development of the *Portuguese National Programme for Respiratory Diseases 2012-2016* (Antunes, Bárbara, & Gomes, 2013), which was approved by dispatch from the Ministry of Health on January 3rd, 2012.

of Life and Management of Living Resources" of the European Union with the aim of constructing questionnaires for assessing the QoL of healthy and chronically ill children and adolescents between 8 and 18 years of age. Both research projects were simultaneously conducted in several European countries, involving a range of work steps that followed the methodological approach proposed by the WHOQOL Group (1995) for international instrument development: (1) item generation based on extensive literature research, insight from international experts (Herdman et al., 2002) and focus groups with children/adolescents and parents (Detmar, Bruil, Ravens-Sieberer, Gosch, & Bisegger, 2006); (2) items translation into the languages of the participating countries, following international guidelines for the cross-cultural adaptation of QoL measures (Guillemin, Bombardier, & Beaton, 1993); (3) reduction of the item pool according to qualitative cognitive debriefings and initial psychometric performance (pilot test phase); and (4) extensive examination of the questionnaires psychometric properties of the questionnaires in a representative sample of the target population (field test phase).

These two co-operating research projects produced two sets of developmentally appropriate and cross-culturally comparable questionnaires, which can be used conjointly in a three-level modular system for QoL assessment: the KIDSCREEN instruments (The KIDSCREEN Group Europe, 2006), which are screening measures suitable for assessing the subjective general health and well-being of healthy and chronically ill children and adolescents and are available in long (KIDSCREEN-52) and short forms (KIDSCREEN-27 and KIDSCREEN-10 Index); and the DISABKIDS tool set (The DISABKIDS Group Europe, 2006), which includes the DISABKIDS Chronic Generic Module in its long and short forms (DCGM-37 and DCGM-12, respectively), as well as seven disease-specific modules for asthma, arthritis, cerebral palsy, cystic fibrosis, atopic dermatitis, diabetes, and epilepsy. Both sets of questionnaires are available in self- and proxy-report forms with parallel items to be answered in a Likert-type response scale ranging from 1 (*not at all/never*) to 5 (*extremely/always*). Next, we present a further description of the questionnaires selected for our study and their psychometric properties.

### *The KIDSCREEN-10 Index*

For assessing the generic QoL of the children/adolescents in our study, we selected the self- and proxy-report versions of the KIDSCREEN-10 Index because these short forms are less time-consuming and may minimize fatigue bias, loss of motivation and dropouts resulting from assessment protocols that are too long, while preserving the good psychometric performance of the instrument (Mühlan, Bullinger, Power, & Schmidt, 2008). Moreover, summary score measures can be useful to assess the impact of a specific health condition and to examine overall differences/changes in QoL (Ravens-Sieberer et al., 2010). The KIDSCREEN-10 Index includes 10 items measuring the level of physical activity, energy and fitness, experiences of depressive moods and emotions and stressful feelings, the quality of the relationship with the parents, feelings of having enough age-appropriate freedom, relationships with other children/adolescents and the children/adolescents' perceptions of their cognitive capacity and satisfaction with school performance. An overall mean score (0-5) or standardized score (0-100) of generic QoL can be computed from the 10 items, with higher values indicating better QoL.

The psychometric properties of the KIDSCREEN questionnaires were tested in a representative community-based sample of 22,830 children/adolescents and 16,237 parents from 13 European countries (Ravens-Sieberer et al., 2010). The KIDSCREEN-10 Index presented good internal consistency (Cronbach's alpha value of .82 for the self-report version and .78 for the proxy-report version), as well as satisfactory criterion validity with the long version (i.e., KIDSCREEN-52) and convergent validity with other QoL measures. In addition, both self- and proxy-report versions enabled the detection of known-group differences by physical and mental health status, age group, gender, SES and country. The KIDSCREEN instruments were sequentially translated to the European Portuguese language using standard methods of forward-backward translation and validated in a random national representative sample of 3,195 Portuguese students attending the 5th and 7th grades (Gaspar & Matos, 2008). For the psychometric studies of the Portuguese version of the KIDSCREEN-10 Index (Matos, Gaspar, & Simões, 2012), the previous sample was enlarged to include children/adolescents attending the 6th, 8th and 10th grades (*n* = 8,072). The self-report questionnaire presented good internal consistency (Cronbach's $\alpha$ = .78). Moreover, the confirmatory factor analysis attested the good fit of the one-dimensional model to the Portuguese data, as well as its structural invariance across age groups, nationality and SES.

*The DISABKIDS Chronic Generic Module (DCGM-37)*

The self- and proxy-report versions of the DCGM-37 were used in our study to assess the impact of chronic health conditions and treatments on the children/adolescents' HrQoL, as perceived by themselves and by their parents/family caregivers. These chronic-generic modules comprise 37 Likert-scaled items, assigned to six facets and three broad-ranging QoL domains: the Physical domain, which includes the facets of Physical Limitation (six items assessing functional limitations, perceived health status and sleeping difficulties) and Treatment (six items measuring the perceived impact of taking medication); the Mental domain, which includes the facets of Independence (six items assessing confidence about the future and living without impairments caused by the health condition) and Emotion (seven items assessing worries, concerns, anger and emotional problems due to the health condition); and the Social domain, which includes the facets of Social inclusion (six items focused on the understanding of others and positive social relationships) and Social exclusion (six items assessing stigma and feelings of being left out). The instruments provide mean scores (0-5) or standardized scores (0-100) for each facet and domain, as well as a global score of chronic-generic HrQoL, with higher scores indicating better chronic-generic HrQoL[7].

The psychometric properties of the original version of the DCGM-37 were tested in a sample of 1,153 children/adolescents with chronic health conditions (asthma, arthritis, atopic dermatitis, diabetes, cerebral palsy, cystic fibrosis or epilepsy) and 1,061 parents/family caregivers, from seven European countries (Simeoni et al., 2007). The instrument had good reliability, with Cronbach's alpha values ranging from .70 to .87 and from .77 to .90 for the sub-scales, while the total score presented alpha coefficients of .93 and .95, for the self- and proxy-report versions, respectively. The agreement between self- and proxy-reports was moderate to high (intraclass correlation coefficients [ICC] between .53 and .65). The instrument also showed good convergent validity with other QoL measures and discriminant validity between age, gender, SES and disease severity groups. The DISABKIDS project in Portugal followed recent guidelines for sequential cross-cultural instrument adaptation (Schmidt & Bullinger, 2003). Accordingly, the DCGM-37 was translated and semantically validated in a pilot study (Carona, Bullinger, & Canavarro, 2011) and subsequently applied to a larger sample of children/adolescents with asthma or epilepsy and their parents for comprehensive psychometric testing (Carona, Crespo, et al., 2013). The Portuguese self- and proxy-report versions of the DCGM-37 presented good internal consistency, with Cronbach's alpha values ranging from .68 to .84 (child version) and from .74 to .92 (proxy version) for the six facets, and values of .91and .94 for the self- and proxy-reported total score, respectively. The parent-child agreement in HrQoL reports was moderate, with ICC between .37 and .49. The examination of convergent and divergent validities showed moderate to strong correlations with generic QoL (*r* between .30 and .63) and psychological problems (*r* between -.30 and -.64). In addition, both versions of the instrument showed discriminant validity between conditions (asthma *vs.* epilepsy), while controlling for age and gender.

*The DISABKIDS – Asthma Module (DAsM)*

The self- and proxy-report versions of the asthma-specific DISABKIDS questionnaires can be used conjointly with the chronic-generic module to measure the specific physical and emotional impact of having asthma. These questionnaires comprise 11 items, clustered into two domains: Impact (six items assessing the experience of limitations and symptoms during sports

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[7] In the empirical study I, which aimed to examine the psychometric performance of the Portuguese versions of the asthma-specific questionnaires with reference to the generic and chronic-generic modules, we sought to include questionnaires of similar length because instrument reliability is highly influenced by item number. Therefore, we computed a total score of chronic-generic HrQoL based on the 12 items that compose the DCGM-12. The psychometric study of the Portuguese version (Carona, Silva, Moreira, Canavarro, & Bullinger, 2014) showed good internal consistency ($\alpha$ = .83 for self-reports and $\alpha$ = .90 for parent-reports) and confirmed the goodness-of-fit of the one-dimensional factor structure, as well as its invariance across age groups, genders and informants.

and activities) and Worry (five items assessing asthma-related fears, such as having an asthma attack or going to the emergency room). Mean scores (0-5) or standardized scores (0-100) can be computed for each HrQoL dimension, with higher values indicating better asthma-specific HrQoL.

The asthma module was the only condition-specific module that was tested in all seven countries participating in the DISABKIDS project, gathering an international sample of 405 children/adolescents and 382 parents for the field test phase (Baars et al., 2005). The self-report version presented good internal consistency (Cronbach's alpha values of .83 for Impact and .84 for Worry), as well as satisfactory test-retest reliability, convergent validity with generic QoL and discriminant validity between asthma severity groups as categorized by physicians. In addition, moderate to high levels of agreement were found between self- and proxy-reports (ICC ranging from .52 to .67). To our best knowledge, this is the first study using the DAsM to assess the disease-specific HrQoL in a Portuguese sample of children/adolescents with asthma. Therefore, the self- and proxy-report versions of the instrument were translated and cross-culturally adapted to the European Portuguese language and context as part of the present research project (cf. preliminary study and empirical study I).

#### 2.3.2.2. PSYCHOLOGICAL PROBLEMS

For assessing psychological problems, we used the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997; Goodman, Meltzer, & Bailey, 1998), which is a brief screening questionnaire that was developed with reference to the main nosological categories recognized by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association, 1994). This questionnaire has a number of valuable design features that justify its inclusion in our study, namely the focus on children/adolescents' strengths and not just their difficulties, the coverage of several domains of contemporary interest (e.g., concentration, impulsivity-reflectiveness, peer relationships, experience of being bullied and prosocial behavior), the compact presentation to fit easily on one page and the availability of identical questionnaires to be completed by children/adolescents between 11 and 16 years of age and by parents or teachers of 4-16 year olds (Goodman, 1997). The SDQ assesses 25 attributes, 10 of which would generally be thought of as strengths and 15 of which as difficulties, divided by five sub-scales with five items each: Emotional symptoms, Hyperactivity-inattention symptoms, Conduct problems, Peer problems, and Prosocial behavior. The items are answered using a Likert-type response scale with three options (0 = *not true*, 1 = *somewhat true* and 2 = *certainly true*), providing sum or mean scores for each sub-scale. Apart from the Prosocial behavior sub-scale (which was not used in our research project), the remaining 20 items can be summed into a total Difficulties score, with higher scores indicating more psychological problems. In addition, for low-risk or general population samples, the authors recommend an alternative coding into Internalizing and Externalizing problems, the first combining the 10 items pertaining to the Emotional symptoms and Peer problems sub-scales and the latter combining the 10 items pertaining to the Hyperactivity-inattention symptoms and Conduct problems sub-scales (Goodman, Lamping, & Ploubidis, 2010).

The psychometric properties of the SDQ were extensively examined in a nationwide community British sample comprised of 3,983 11-15 year-old adolescents and 9,998 parents of 5-15 year-old children/adolescents (Goodman, 2001). The internal consistencies of the instrument were generally satisfactory, with Cronbach's alpha values ranging from .57 to .82 for the parent-report version and from .41 to .80 for the child-report version. The inter-rater correlations showed moderate levels of parent-child agreement (*r* between .30 and .48). In addition, high SDQ scores were significantly associated with independently diagnosed DSM-IV disorders, attesting its validity for detecting non-referred cases of pediatric mental health problems in the community. The most recent psychometric study with the SDQ revealed that the alternative scoring into Internalizing and Externalizing problems is advantageous for assessing low-risk samples, with Cronbach's alpha values of .73 (parent-report) and .66 (child-report) for Internalizing problems and .78 (parent-report) and .76 (child-report) for Externalizing problems (Goodman et al., 2010). The Portuguese version of the SDQ (SDQ-Por; Fleitlich, Loureiro, Fonseca, & Gaspar, 2005) has been used in several studies with different age groups and its psychometric properties resembled those found with British samples (Marzocchi et al., 2004). In particular, a study with 760 youths between 12 and 20 years of age, recruited from public schools (low-risk sample) and juvenile justice centers (high-risk sample), attested the concurrent validity of the Emotional symptoms and Conduct problems sub-scales with the DSM-IV diagnosis of conduct disorder and the discriminant validity of the SDQ total score between low- and high-risk samples (Pechorro, Poiares, & Vieira, 2011). Although the self-report version of the SDQ has been originally designed for children/adolescents aged around 11-16, depending on their level of understanding and literacy (Goodman, Meltzer, & Bailey, 1998), previous studies with Portuguese healthy and chronically ill samples confirmed its adequacy for a broader age range (Moreira et al., 2013).

### 2.3.3. Parents' adaptation outcomes

#### 2.3.3.1. QUALITY OF LIFE

For assessing the QoL of parents of children with asthma, we used the WHOQOL-BREF questionnaire (The WHOQOL Group, 1998a). This instrument thoroughly operationalizes the QoL definition as a subjective and multi-dimensional construct, by assessing the individuals' perception of their objective physical health, psychological state, social relationships and relationships to salient features of the environment, and the individual's subjective evaluation/level of satisfaction with these multiple facets of their lives (The WHOQOL Group, 1994). The WHOQOL-BREF includes 26 items clustered into a generic facet (two items) and four QoL domains: the Physical domain (seven items assessing the facets of pain and discomfort, energy and fatigue, sleep and rest, mobility, daily living activities, dependence on medication and work capacity); the Psychological domain (six items addressing the facets of positive feelings, thinking, learning, memory and concentration, self-esteem, body image, negative feelings and spirituality, religion and personal beliefs); the Social relationships domain (three items assessing the facets of personal relationships, social support and sexual activity); and the Environment domain (eight items measuring the facets of physical safety and security, home environment, financial resources, access to health and social care, opportunities for acquiring new information and skills, recreation and leisure activity, physical environment and transport). The 26 items are to be answered with a 5-point Likert scale in terms of intensity (*not at all* to *extremely*), capacity (*not at all* to *completely*), frequency (*never* to *always*) or evaluation (*very dissatisfied* to *very satisfied*), with higher values indicating better QoL[8].

The cross-cultural psychometric study of the WHOQOL-BREF, involving 15 centers worldwide, attested that the instrument had good internal consistency (Cronbach's alpha values ranging from .66 for the Social relationships domain to .84 for the Physical domain), test-retest reliability, construct validity and discriminant validity between healthy and ill respondents (The WHOQOL Group, 1998a). In addition, the clinical applicability of the WHOQOL-BREF for QoL assessment in mothers of children with asthma was recently ascertained in a Taiwanese study (Gau et al., 2010). The European Portuguese version of the WHOQOL-BREF was sequentially developed by a research team from the University of Coimbra, which founded the Portuguese WHOQOL Center (Vaz-Serra et al., 2006). The psychometric properties obtained in the Portuguese validation studies were quite similar to those described in the international studies, with Cronbach's alpha values ranging from .64 (the Social relationships) to .87 (the Physical domain), good divergent validity with psychopathological symptoms (*r* between -.41 and -.71) and discriminant validity between healthy and ill respondents for all QoL domains.

### 2.3.3.2. PSYCHOLOGICAL DISTRESS AND WELL-BEING

Reflecting a paradigm shift in mental health assessment, the Mental Health Inventory

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[8] Although not provided by the WHOQOL-BREF, we also computed an overall QoL score based on the 8 items that compose the EUROHIS-QOL 8-index (Schmidt, Mühlan, & Power, 2006). This brief screening measure derived from the extraction of 8 items from the WHOQOL questionnaires and has shown good reliability, convergent validity with physical and mental health measures, and discriminant validity between healthy and ill populations, both in the cross-cultural field study (Cronbach's $\alpha$ ranging from .74 to .85; Schmidt et al., 2006) and in the psychometric study for the Portuguese version ($\alpha$ = .83; Pereira, Melo, Gameiro, & Canavarro, 2011).

(MHI; Veit & Ware, 1983) was developed for assessing the general population, and not only psychiatric patients, and broadens the definition of mental health beyond the identification of psychological distress symptoms to incorporate the assessment of psychological well-being features. The long version of the instrument comprises 38 items assessing the most prevalent symptoms of psychological distress in the general population, namely Anxiety, Depression and Loss of behavioral/emotional control, as well as General positive affect and Emotional ties. In turn, these five distinct mental health constructs can be clustered into two unipolar negatively correlated factors – Psychological distress and Psychological well-being, and into a high-order factor of general Mental Health. The short version of the instrument (MHI-5) was developed based on the five items that best reproduce its total score (Berwick et al., 1991). The five items are to be answered in a 6-point response scale ranging from 1 (*none of the time*) to 6 (*all of the time*), allowing the computation of mean scores for Psychological distress (three items) and Psychological well-being (two items); in addition, the scores for the three items measuring negative psychological states can be reversed, in order to calculate a high-order factor of general Mental Health, such that higher scores indicate better mental health.

Good reliability was found in the original study for the long version (Cronbach's α values ranging from .81 to .92 for the five sub-scales, α = .94 for Psychological distress, α = .92 for Psychological well-Being, and α = .96 for the high-order factor of general Mental Health; Veit & Ware, 1983). The MHI-5 has also presented good internal consistency (α = .84; McCabe, Thomas, Brazier, & Coleman, 1996) and a performance similar to the longer version in detecting significant mental disorders (Berwick et al., 1991). As a brief, easy to complete, reliable and valid measure, the MHI-5 is considered a sound method for mental health screening in the general population across different countries and cultural contexts. The MHI was translated into the Portuguese language and tested in a sample of 609 Portuguese healthy adults by Pais-Ribeiro (2001). The original second-order factor structure of the instrument was preserved and its psychometric properties of reliability and validity resembled those found in the original study, with a Cronbach's alpha value of .96 for general Mental Health and a correlation coefficient of .95 between the MHI-5 and the 38-item version.

### 2.3.4. Psychosocial variables

#### 2.3.4.1. PARENTS' EXPERIENCE OF CAREGIVING BURDEN AND UPLIFTS

The Revised Burden Measure (Montgomery & Kosloski, 2006) has two idiosyncratic features that justified its inclusion in our study for assessing the parents' caregiving experience in our study: first, the operationalization of a multi-dimensional approach to caregiving burden through the assessment of its relationship, objective and subjective components; and second, the inclusion of a distinctive but complementary measure of caregiving uplifts. For both the Burden and the Uplift measures, respondents are asked to indicate the extent to which various aspects of their lives have changed due to caregiving ("As a result of assisting the care receiver, have the following aspects of your life changed?"). The Burden measure comprises 16 items focused on changes in parent-child relationships (Relationship burden), time constraints resulting from instrumental caregiving activities (Objective burden) and generalized negative affect (Subjective burden). Quite recently, confirmatory factor analyses (CFA) attested this multi-dimensional structure of the caregiving burden construct, as well as its invariance across different groups of caregivers, namely spouses and adult children of adult patients with chronic illnesses (Savundranayagam et al., 2011). Complementarily, the Uplifts measure comprises six items assessing gratifications and positive psychological states arising from caregiving, namely the direct enjoyment from caregiving tasks, an improved relationship with the care receiver and generalized positive affect. The 22 items are to be answered in a 5-point Likert scale ranging from 1 (*not at all*) to 5 (*a great deal*). Mean scores can be calculated for each burden dimension and for uplifts, with higher scores indicating a greater change in those negative or positive dimensions of caregiving. In addition, the 16 items pertaining to the Burden measure can be combined to provide an overall score of caregiving burden.

Although this instrument has been originally developed and tested in geriatric contexts, the authors acknowledge that children are the most prevalent group of dependents, with mothers usually being the main responsible for general nurturing and care, as well as for the special care required by children with chronic conditions or disabilities (Montgomery, Borgatta, & Borgatta, 2000). Considering this, the Portuguese version of the Revised Burden Measure was pilot-tested in a sample of parents of children/adolescents with asthma or epilepsy (C. Carona, N. Silva, & M. C. Canavarro, personal communication, July 27, 2011). Results from the preliminary psychometric study showed good reliability (Cronbach's alpha values ranging from .75 to .87), convergent validity with parents' psychological distress and well-being and discriminant validity between children/adolescents' age groups and health conditions, thus attesting the applicability of this instrument for assessing parents' caregiving experience in pediatric settings.

#### 2.3.4.2. PARENTS' DISPOSITIONAL COPING TENDENCIES

The parents' coping tendencies were assessed with the Brief-COPE (Carver, 1997). The major strength of this instrument is its theoretically-driven development, based on the Stress and Coping Model (Lazarus & Folkman, 1984) and on the Model of Behavioral Self-Regulation (Scheier & Carver, 1988), while also considering empirical data derived from previous research (Carver et al., 1989). This approach to instrument development represents an improvement over the pre-existing coping measures, by allowing the identification and inclusion of all the domains which were considered relevant by the authors and assuring the linkage between the constructs being assessed and the underlying theoretical principles. Developed from the extended version of the COPE inventory to minimize the participants' response burden due to the large number and redundancy of items, the Brief-COPE (Carver, 1997) is composed of 28 items, assigned to 14 coping scales with two items each: Active coping, Planning, Positive reframing, Acceptance, Humor, Religion, Use of emotional support, Use of instrumental support, Self-distraction, Denial, Venting, Substance use, Behavioral disengagement and Self-blame. The items can be framed in terms of what the person *usually* does under stressful circumstances (i.e., dispositional coping tendencies) or in terms of what the person did, or is currently doing, to deal with a *specific stressor* (i.e., situational coping responses).

For both the extended and brief versions, exploratory factor analyses showed that the composition of most factors was in accordance with *a priori* assignment of the items to the scales, although some exceptions were observed. In addition, most correlation coefficients among the coping scales were weak to moderate ($r$ between .00 and .69), suggesting that different coping responses may co-occur following a particular stressful event, even when conceptualized in a somewhat opposite way (e.g., Acceptance and Denial), and that the coping scales are independent and can, therefore, be used separately. The Brief-COPE presented acceptable reliability, with Cronbach's alpha coefficients ranging from .50 (Venting) to .90 (Substance use). Moreover, the correlation coefficients for the test-retest reliability with an 8-week interval, calculated for the dispositional form of the extended version of the COPE inventory, ranged from .46 (Suppression of competing activities) to .86 (Religion), indicating relative stability for dispositional coping tendencies.

The Portuguese version of the Brief-Cope (Pais-Ribeiro & Rodrigues, 2004) presented a factor structure similar to the original instrument. For all coping scales, the Cronbach's alpha values exceeded the threshold of .50 ($\alpha$ between .55 for Acceptance and .84 for Venting), which was considered by Carver (1997) as the minimally acceptable reliability value for scales comprising only two items. The inter-scale correlations were weak to moderate ($r$ ranging from .00 to .55), thus attesting the independence of the coping scales. Accordingly, for our study only three scales assessing emotion-focused dispositional coping tendencies were used: Acceptance (i.e., the recognition and acceptance that the stressful event has occurred and is real), Denial (i.e., the cognitive and behavioral attempts to reject or ignore the actual existence of the stressor) and Positive reframing (i.e., the attempt to look at the stressful situation in a more beneficial way, in order to manage distressing emotions). The respondents were asked to complete the items using a dispositional response format with four options: 0 = *I usually don't do this at all*, 1 = *I usually do this a little bit*, 2 = *I usually do this a medium amount* and 3 = *I usually do* *this a lot*. Mean scores were computed for each scale, with higher scores indicating a greater tendency for using the coping strategy.

### 2.3.4.3. CHILDREN/ADOLESCENTS' AND PARENTS' PERCEPTIONS OF FAMILY RELATIONSHIPS

The Family Environment Scale (FES; Moos & Moos, 1981, 1994) was selected for our study for several reasons. First, the initial selection and wording of the items was guided by a combination of conceptual and empirical criteria, including a conceptual formulation of general dimensions that might differentiate among families, data obtained from structured interviews with members of different types of families and data obtained from other social climate scales. Second, this questionnaire is a valuable tool for describing the family social environment from an insider's view, by reporting the perceptions of family members who form durable impressions of the social climate from their own experiences in the family. Moreover, the FES can be completed by parents and by children as young as 5 years of age, thus allowing the comparison of different family members' perceptions. Finally, several empirical studies have ascertained the utility of the FES dimensions in identifying at-risk families and in predicting adaptation to diverse life stressors, including pediatric health conditions (e.g., Hilliard, Fritz, & Lewiston, 1985; Silva et al., 1987).

In brief, the FES evaluates the family social climate through 90 items clustered into 10 sub-scales and three underlying dimensions: the Relationship dimension (Cohesion, Expressiveness and Conflict sub-scales), the Personal growth/goal orientation dimension (Independence, Achievement orientation, Intellectual-cultural orientation, Active-recreational orientation and Moral-religious emphasis sub-scales) and the System maintenance dimension (Organization and Control sub-scales; Moos & Moos, 1994). The items can be worded in three distinct forms, in order to assess the family members' perceptions of their family as it currently is (Real form), their preferences about how the family should function in a perfect situation (Ideal form), or their expectations of what the family would be like in a new situation (Expectations form). In our study, the overall quality of the social relationships in the family environment was assessed by the FES Relationship dimension. This dimension primarily reflects the internal family functioning and refers to the emotional bonds that emerge from the family members' interactions throughout the family life cycle and that hold the family unit. Its three sub-scales, with nine items each, were described by Moos and Moos (1994) as follows: Cohesion is the degree of commitment, help and support that family members provide for one another; Expressiveness is the extent to which family members are encouraged to act openly and to express their feelings directly; and Conflict is the extent to which the open expression of anger and aggression and generally conflictual interactions are characteristic of the family. We used the FES Real form and the items were answered with a 6-point Likert-type response scale ranging from 1 (*completely disagree*) to 6 (*completely agree*). Mean scores were computed for each subscale, along with a Family Relationships Index (FRI; Holahan & Moos, 1983; Moos, 1990) based on the combination of the 27 items, after reverse coding the nine items pertaining to the Conflict sub-scale, so that higher scores can be interpreted as indicators of better family relationships.

The original FES was psychometrically tested in a diverse sample, including non-distressed families at different phases of the family life cycle and families dealing with different types of stressful circumstances (Moos & Moos, 1994). The instrument in its Real form presented acceptable reliability, with Cronbach's alpha values of .78, .69 and .75 for the Cohesion, Expressiveness and Conflict sub-scales, respectively. The FRI proposed by Holahan and Moos (1983) also presented good internal consistency ($\alpha = .89$) and construct validity, evaluated through its negative correlations with indicators of physical and psychological symptoms and positive correlations with a traditional measure of social support. The Portuguese adaptation of the FES was conducted by Matos and Fontaine (1992). Subsequently, Santos and Fontaine (1995) used the Portuguese version of the FES – Real form for assessing a school sample that included 311 children/adolescents between 8 and 14 years of age. However, the internal consistency was less than satisfactory with Cronbach's alpha values lower than .70 for all the sub-scales, which was justified by the authors based on the participants' age group, since children and adolescents may not be able to discriminate finely between constructs related to the complex family system (Santos & Fontaine, 1995).

## 2.4. Statistical options

The statistical software and procedures used to accomplish the specific objectives of each empirical study are thoroughly described in their respective methodological sections. At this point, we will discuss some broad-ranging analytic options that have guided empirical research in pediatric psychology in general and our research project in particular.

### 2.4.1. The parent-child dyad as the unit of analysis

The fundamental concept of dyadic analysis is non-independence, i.e., "two scores from the two members of the dyad are more similar to (or different from) one another than are two scores from two people who are not members of the same dyad" (Kenny et al., 2006, p. 25). In our sample, the children/adolescents and the parents are linked by kinship and they also share risk and resistance factors within the family environment. Accordingly, our data set was structured so that each parent-child dyad was treated as a single unit: a single score was considered for dyad-level variables (e.g., disease length, family SES) and two scores were considered for individual-level variables (e.g., children/adolescents' and parents' QoL). For some empirical studies we conducted individual-level analyses (e.g., separate analyses for children/adolescents and parents), while dyadic-level analyses were endorsed in empirical studies II and VI.

Following the latest recommendations (e.g., Eiser & Morse, 2001b; Van Roy, Groholt, Heyerdahl, & Clench-Aas, 2010), we used a multi-informant approach to pediatric adaptation outcomes assessment. Consequently, two sets of scores for pediatric QoL outcomes and psychological problems were obtained – the children/adolescents' self-reports and the parents' proxy-reports. The differences between scores were examined at the group level by performing analyses of covariance for repeated measures, entering the informant as the within-subjects factor. At the individual level, two distinct dyadic indexes were computed: intraclass correlation coefficients, as measures of agreement between the two raters of pediatric outcomes; and child-parent absolute and directional discrepancies as measures of dissimilarity across a set of items for each dyad (Kenny et al., 2006). These dyadic indexes were particularly useful for transforming two individual-level variables into a dyad-level variable, and provided information on the extent and direction of child-parent agreement (cf. empirical study II).

Moreover, the transactional model tested in the empirical study VI can be considered a particular application of the Actor-Partner Interdependence Model (Cook & Kenny, 2005) for pediatric psychology and was designed to integrate the non-independence of dyadic relationships. We used SEM to test the direct and indirect links between children/adolescents' and parents' perceptions of family relationships and adaptation, both separately (i.e., the within-subjects or actor effects) and across family members (i.e., the cross-lagged or partner effects). The dyadic nature of our data-analytic strategy was operationalized by the following model's specifications: (1) the dyad was considered the unit of analysis (*N* = number of dyads); (2) multiple equations were estimated, testing both the actor effects (the effects of a person's own characteristics on his/her own outcomes) and the partner effects (the effects of a partner's characteristics on a person's outcome); and (3) the independent variables were allowed to correlate, so that the actor effects were estimated while controlling for the partner effects and vice-versa. In this model, the partner effects were, by definition, the indicators of parent-child interdependence.

### 2.4.2. Testing of process-oriented theoretical models

The data-analytic strategy designed for the present study sought to address two major research gaps, as identified in our literature review: first, the absence of solid theoretical frameworks to guide the formulation of hypothesis on the complex mechanisms underlying children/adolescents' and their parents' adaptation outcomes (Drotar, 1997; Raina et al., 2004);

and second, the lack of conceptual and statistical clarity in the study of mediation and moderation effects (Holmbeck, 1997). Accordingly, we formulated a number of theoretically-driven hypotheses that might contribute to explain the variability in adaptation outcomes for children/adolescents and their parents, and we tested them with advanced statistical techniques, such as regression-based moderation analyses and SEM for direct and indirect effects.

Based on the conceptual models of adaptation to pediatric chronic health conditions that guided our research project, key psychosocial variables were hypothesized to operate as resources promoting adaptive functioning or as buffers/protective factors against the deleterious effect of disease burden. More than a terminological issue, the distinction between resource and protective factors implies different statistical testing procedures: resource factors represent additive main effects, whereas protective factors represent moderation effects (Rose et al., 2004). In statistical terms, a moderator is "a qualitative (…) or quantitative (…) variable that affects the direction and/or strength of the relation between an independent or predictor variable and a dependent or criterion variable" (Baron & Kenny, 1986, p. 1174). A moderation effect is represented by the interaction between an independent variable and a factor (the moderator) that specifies the conditions under which (*when*) a given effect occurs or varies in its direction or strength (Holmbeck, 1997). The preferred analytic strategy involved multiple regression techniques, in which the predictor, the moderator and the interaction term were entered into the regression equation in hierarchical steps (Aiken & West, 1991; Hayes, 2013). The interpretation of statistically significant interactions was based on post-hoc probing of moderation effects (i.e., computation of simple slopes with statistical tests; Holmbeck, 2002b) and plotting of regression lines for different values of the moderating variable (Jose, 2013).

On the other hand, a mediation effect represents the "generative mechanism through which the focal independent variable is able to influence the dependent variable of interest" and specifies *how* or *why* a given effect occurs (Baron & Kenny, 1986, p. 1173). According to these authors, a mediation effect exists when the independent variable is significantly associated with the hypothesized mediator (*path a*); the mediator is significantly associated with the dependent variable (*path b*); and, when *paths a* and *b* are controlled, a previously significant association between the independent and dependent variables (*path c*) is no longer significant or significantly decreases its strength. To test mediation effects in our study, the SEM[9] strategy was preferred because it provides information on the goodness-of-fit for the overall model after controlling for measurement error, it is particularly useful for specifying multi-dimensional constructs that are reflected by multiple observed indicators (Byrne, 2010) and it is applicable to cross-sectional data, providing that the direction of causal paths is hypothesized in accordance with solid

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[9] When testing a mediational hypothesis with SEM, it is important to distinguish between mediation and indirect effects, the latter occurring when there is no previously significant association between the independent and dependent variables (*path c*), despite the fact that the predictor-mediator and mediator-criterion paths are significant (Holmbeck, 1997).

theoretical foundations (Lei & Wu, 2007). In addition, the theoretical models explaining adaptation in pediatric contexts include several risk and protective factors, which calls for complex statistical models testing multiple mediators, as well as conditional indirect effects (Rose et al., 2004). The use of multi-group analyses for SEM allowed for testing the strength of an indirect effect as a function of the levels of a fourth variable (i.e., the moderator; Preacher, Rucker, & Hayes, 2007), thus providing clinically relevant information about the developmental and clinical conditions in which adaptation processes may occur.

### 2.4.3. Statistical operationalization of a developmental approach

When establishing general guidelines for assessing QoL outcomes in children/adolescents, the WHO clearly stated that instruments should be "age-related or at least developmentally appropriate" (WHO, 1993, p. 3), calling attention to the relevance of considering both specificities and common markers across different developmental phases. For the pediatric outcomes assessment in our study, we used questionnaires designed to be administered to children/adolescents across a broad age range. This methodological approach based on age-universal markers has been criticized because it may miss important information about the specific developmental tasks and experiences, such as opposite-sex relationships or play *vs.* educational opportunities (Wallander et al., 2001). However, we endorsed a developmental approach across our empirical studies, by using diverse statistical procedures to test age and age group effects (Carona et al., 2015).

The effects of the children/adolescents' age as a continuous variable were examined by including it as a covariate in analyses of covariance or as a correlate/predictor of adaptation outcomes in correlation/regression analyses. However, statistical analyses that differentiate age groups were preferred because they allow detecting differences and similarities in both predictors and outcomes and they are particularly useful to inform clinical practice on adaptation processes that are not necessarily invariant across sub-groups of pediatric asthma patients. Two age groups were defined according to the Medical Subject Headings (MeSH terms) of the US National Library of Medicine, which also coincide with the benchmarks adopted in the KIDSCREEN and DISABKIDS projects: children between 8 and 12 years of age, and adolescents between 13 and 18 years of age. Accordingly, we performed analyses of variance/covariance to compare the psychosocial variables and the adaptation outcomes between children and adolescents, as well as multi-group analyses with SEM to examine the (in)variance of direct and indirect pathways across age groups. This developmental approach to pediatric outcomes assessment was also applied in the psychometric studies, because even common QoL dimensions may encompass different features in the daily life experiences of children and adolescents (Wallander et al., 2001) and the psychometric quality of broadband QoL measures may differ across age groups (Carona, Crespo, et al., 2013).

### 2.4.4. Statistical significance and effect sizes

To assess the statistical significance of our results, we adopted the conventional level of significance $\alpha = .05$, which means that we had a 5% chance of rejecting a true null hypothesis (type I error). However, the level of significance depends not only on the effect size but also on the sample size, and, consequently, significant differences/associations are likely to be identified in large samples, even when they are very small. Therefore, a significant statistical result does not necessarily imply clinical relevance, and the reporting of effect sizes has been strongly recommended (American Psychological Association [APA], 2010b). In our research project, the statistical power (i.e., the probability of rejecting false null hypotheses) was calculated *a posteriori*, using the G*Power computational tool (Faul, Erdfelder, Lang, & Buchner, 2007). Considering the number of participants included in our empirical studies, the level of significance ($\alpha = .05$) and the power of the test (1 – type II error probability = .80), the power analyses indicated that small-medium effects could be detected ($f$ ranging from .17 to .25 for multivariate analyses of covariance; $f^2$ ranging from .04 to .08 for regression analyses; Cohen, 1992)[10]. The effect sizes of our results are reported in each empirical study. Overall, for analyses of variance/covariance we reported the partial eta squared ($\eta_p^2$; i.e., the proportion of variability in the dependent variable that is attributable to a factor, after partially excluding other non-error sources of variance; Cohen, 1973); and for correlations and regression analyses we reported, respectively, the Pearson's correlation coefficient ($r$) and the coefficient of determination ($R^2$; Cohen, 1992).

## 2.5. Ethical considerations

Our research project was conducted in compliance with the APA ethical principles regarding research with human participants (APA, 2002, with the 2010a amendments), the World Medical Association declaration of Helsinki (1964, as revised in 2008), and the Order of Portuguese Psychologists (Regulation number 258/2011, April 20th, 2011). These professional associations have encouraged medical/psychological research involving human subjects to understand the causes, development and effects of diseases and to improve diagnostic and therapeutic interventions. Nevertheless, they stress that the rights, dignity and best interests of the participants must prevail over research goals and enunciate a number of ethical principles concerning the researchers' professional conduct. First, the general principle of *Beneficence and*

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[10] For the psychometric study of the DISABKIDS-AsM (empirical study I, $n = 140$), the statistical power calculations indicated that only medium-large effects could be detected ($f = .28$). In order to address this limitation, marginally significant effects ($p < .10$) were also discussed.

*Non-maleficence* compels researchers to seek to benefit the participants by safeguarding their welfare and ensuring that the research procedures do not cause them any physical or psychological harm. The principle of *Respect for People's Rights and Dignity* adds that researchers must respect the rights of the participants to privacy, confidentiality and self-determination. This ethical principle emphasizes the need for the special protection of vulnerable persons or communities, including those who are unable to make decisions autonomously because of their age and/or health condition. Moreover, researchers must comply with the general principles of *Integrity* and *Social Responsibility* towards the production and reporting of accurate, honest and truthful scientific knowledge that may contribute to the improved health and well-being of the targeted populations. Finally, the ethical principle of *Competence* states that psychologists should only conduct research with populations and scientific areas within the boundaries of their competence and advises researchers to undertake specialized and constantly updated theoretical and practical training. These general ethical principles were reflected in the specific procedures adopted during the conception of the study, the implementation of the research protocol and the dissemination of the results, as described below.

### 2.5.1. Study design and preparation for implementation

Our study was integrated in *The DISABKIDS Project in Portugal: Assessing QoL in Children and Adolescents with Chronic Health Conditions* (http://gaius.fpce.uc.pt/saude/projdisabkids.htm), which was approved by the Ethics Committees and/or Direction Boards of the hospital institutions where the sample was collected. The amendments to the initial DISABKIDS research protocol were discussed within the research group *Relationships, Development & Health* and with the health professionals that participated in the study, taking into account the potential risks, burdens and benefits for the participants. The datasheets and questionnaires included in the research protocol aimed to gather the information strictly necessary to accomplish the research goals and the collection of redundant and superfluous information was avoided. Special caution was taken regarding the extent of the questionnaires to minimize the participants' response burden (i.e., brief versions were preferred, when available), as well as regarding the formatting and wording of the questionnaires for the pediatric patients.

All researchers involved in this project were qualified with an academic degree in Clinical Psychology. The research assistants who contributed to the sample collection were students in the final year of their Integrated Master's degree in Psychology, and they had received adequate training and supervision. Moreover, the ethical standard of *Competence* was accomplished during the conception of the research project through the participation of the researchers in conferences and workshops in the pediatric psychology field, the study of relevant literature, and the discussion of the research objectives and procedures with national and international experts.

### 2.5.2. Implementation of the research protocol

The sample collection in the healthcare institutions followed the methods described in the research protocol previously approved by the respective Ethics Committees. To all eligible children/adolescents and their parents/family caregivers, the researchers provided oral information about the research objectives, procedures and expected duration, and anticipated benefits and potential risks of the study; the confidentiality of their answers was also guaranteed. In addition, the prospective participants were assured that their participation would be completely voluntary, that they had the right to decline participation in the study and to withdraw consent at any time without any reprisal regarding the medical care they would receive and that no financial or other compensation would be received. The potential participants had the opportunity to ask questions and clarify any piece of information. After ensuring that this information was totally understood by the children/adolescents and their parents/family caregivers, those who were willing to participate were asked to complete an informed consent form. This document reiterated, in written form, the aforementioned information and also described the researchers' role, including their ethical obligations, institutional affiliations and contacts.

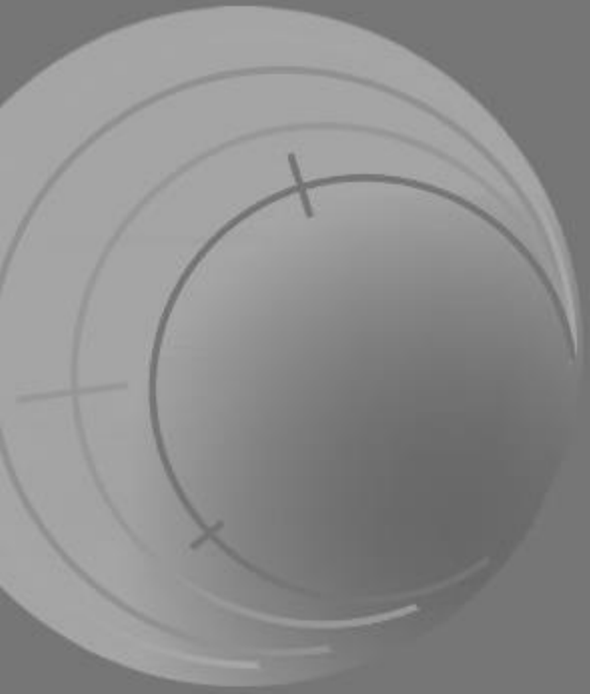
All parents/family caregivers signed an informed consent form regarding their own participation in the study. Regarding the participation of children/adolescents, additional ethical concerns were taken into account, since pediatric patients are considered a group of increased vulnerability and legally incapable of providing informed consent (Vale & Oliveira, n.d.). The participation of children and adolescents was encouraged because our study sought to address relevant issues directly related to their health and well-being that could not be appropriately answered by research in adults, and because the research procedures entailed only minimal risks and burden for the participants. Although any person under the age of 18 is legally considered a minor, the Portuguese law determines that consent can be provided by adolescents with the necessary discernment to evaluate its meaning and scope (Vale, n.d.). Accordingly, the adolescents over 13 years old were considered to have the level of cognitive and moral development required to give informed consent, which was supplemented by parental assent. For pediatric patients under the age of 13 years, we asked for informed consent from their legally authorized representative. In addition, we provided an appropriate explanation of the study objectives and procedures, using language that was considered reasonably understandable to children as young as 8 years old, and we sought the child's informal assent/dissent, which prevailed over parental consent.

To protect the participants' right of *Privacy and Confidentiality*, we only collected personal data that were absolutely essential to the socio-demographic characterization of the sample.

Moreover, in order to prevent the identification of the respondents, each assessment protocol was exclusively identified by a numerical code and was kept separate from any document using personal identification, including the medical files and signed consent forms. The data collected from the participants were entered in an electronic database and treated collectively only for research purposes.

### 2.5.3. Publication and dissemination of the results

Following the ethical principle of *Integrity*, the data analyses and dissemination of our results were conducted with accuracy, honesty and truthfulness. The results were made available to the scientific community through oral and poster presentations in national and international meetings and scientific papers published in peer-reviewed journals. Only original and not fabricated data were submitted for publication; proper credit was given to the authors of any citations or quotations, thus not incurring in plagiarism. Moreover, we sought to disseminate both the positive and inconclusive/unexpected results. The authorships were defined according to the relative scientific or professional contributions of the researchers involved in any research phase, regardless of their relative status, and the sources of funding, institutional affiliations and conflicts of interest were stated in each manuscript. In addition, the main outcomes of our study, including the Portuguese versions of the DISABKIDS-AsM questionnaires, were presented to healthcare professionals in the hospitals' clinical meetings. We have also published our main results on the project's website (http://gaius.fpce.uc.pt/saude/pc2.htm), in order to inform the participants and the general public.



# Chapter III

## Meta-Analytic Review and Empirical Studies

Meta-Analytic Review

# Quality of life in pediatric asthma patients and their parents: A meta-analysis on 20 years of research

Neuza Silva • Carlos Carona • Carla Crespo • Maria Cristina Canavarro

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# Quality of life in pediatric asthma patients and their parents: A meta-analysis on 20 years of research

Neuza Silva • Carlos Carona • Carla Crespo • Maria Cristina Canavarro

## Abstract

***Introduction.*** This meta-analytic review was conducted to estimate the magnitude of quality of life (QoL) impairments in children/adolescents with asthma and their parents. ***Method.*** A systematic search in four electronic databases revealed 15 quantitative studies published between 1994-2013 that directly compared the QoL of 7- to 18-year-old asthma patients/parents to community/healthy controls. Pooled mean differences (MD) with 95% CI were estimated using the inverse-variance random-effects method. ***Results.*** Pediatric asthma patients (*n* = 1,797) presented lower overall QoL (MD = -7.48, CI = -10.67/ -4.29), physical functioning (MD = -9.36, CI = -11.85/ -6.86), psychological functioning (MD = -5.00, CI = -7.17/ -2.82), and social functioning (MD = -3.76, CI = -5.80/ -1.72), compared to controls (*n* = 13,266). For parents (666 cases and 7,328 controls), asthma was associated with lower physical functioning (MD = -10.15, CI = -12.21/ -8.08). Between-studies heterogeneity was explained by type of informant and selection of controls. ***Conclusion.*** The ascertainment of the magnitude of QoL impairments and the most affected QoL dimensions for pediatric asthma patients/parents may contribute to the outlining of realistic goals for multidisciplinary interventions in healthcare settings and evaluate its cost-effectiveness.

## Keywords

Asthma • Children and adolescents • Meta-analysis • Parents • Patient- and parent-reported outcomes • Quality of life

# Introduction

Asthma is the most common chronic health condition in childhood, with an estimated worldwide prevalence of 11.6% in 6- to 7-year-old children and 13.7% in 13- to 14-year-old adolescents (Pearce et al., 2007). Defined as a chronic inflammatory disease of the airways, asthma is characterized by episodic exacerbations of shortness of breath, coughing, wheezing, and chest tightness, which may be life threatening and are a major cause of hospitalizations among pediatric patients (Global Initiative for Asthma [GINA], 2008). Additionally, dependence on medication, sleep disturbances, daytime fatigue, and school/work absenteeism and underachievement may also impair the quality of life (QoL) of children and adolescents and their families (Dean et al., 2010; Schmier et al., 2007).

QoL was formally defined by the World Health Organization Quality of Life (WHOQOL) Group, in 1994, as “a person’s perception of his/her position in life within the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards, and concerns” (The WHOQOL Group, 1994, p. 28). This definition assumes that QoL is a holistic concept, and it considers both the disease and individual life experiences as influences on physical, psychological and social well-being (Wallander, Schmitt, & Koot, 2001). For QoL assessment in children and adolescents, the World Health Organization (World Health Organization [WHO], 1993) recommends using self-reports whenever possible, as well as developmentally appropriate and cross-culturally comparable instruments. Moreover, generic and specific assessment modules should be used to both allow comparisons between healthy and clinical populations and to ensure sensibility to disease-related impairments and healthcare needs (Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003). Although children as young as 7/8 years old are able to provide reliable reports of subjective QoL (Matza, Swensen, Flood, Secnik, & Leidy, 2004; Ravens-Sieberer et al., 2006), the use of parent-reports as complementary sources of information has been strongly recommended in pediatric contexts, because parents are the main people responsible for clinical decision-making, which is likely to be influenced by their own perceptions of their children’s functioning and well-being (Carona, Silva, & Moreira, 2015; Eiser & Morse, 2001).

Over the past 20 years, QoL has emerged as an essential outcome in epidemiological, clinical and health economic/policy research in the context of pediatric chronic conditions (Bullinger, Schmidt, Peterson, & Ravens-Sieberer, 2006; Clarke & Eiser, 2004). However, pediatric asthma research has yielded heterogeneous findings regarding the magnitude of QoL impairments and the QoL domains that are mostly affected in pediatric patients and their parents. Summarizing the results of studies comparing the QoL of children and adolescents with asthma and their parents with age-matched controls, not only with arbitrary norms (Gerharz, Eiser, & Woodhouse, 2003), is needed to improve current understanding of the consequences of pediatric asthma on children/adolescents' and their parents' overall adaptation, identify specific areas of functioning that should be targeted in multidisciplinary interventions, and evaluate the efficacy of medical treatments and psychosocial interventions. Accordingly, the main objective of this meta-analytic review was to estimate the differences in QoL overall scores and core domains (physical, psychological, social and school functioning; the latter only for pediatric patients) between 7- to 18-year-old children and adolescents with asthma, or parents of children and adolescents with asthma, and community/healthy controls.

## Method

### Search strategy

To identify literature published between 1994 and 2013, the first author conducted a systematic search in four electronic databases: PubMed (US National Library of Medicine), PsycINFO, SocINDEX and Thomson Reuters' Web of Science. Combinations of the following keywords were searched: "quality of life", "asthma", "child", "adolescent", "youth" and "pediatric". The detailed strategy used for searching the PsycINFO database is given in Table 1. This search strategy was used for all databases, with slight adaptations to fit different web interfaces. The Medical Subject Headings (MeSH terms) were used in the PubMed search. The final search was conducted on January 28-30, 2014. Additionally, the reference lists of all eligible articles were screened to identify other potentially relevant articles.

**Table 1** | Strategy used for searching the PsycINFO electronic database

| *Number* | *Search term* |
|---|---|
| 1. | *"Quality of Life"/ |
| 2. | asthma.af. |
| 3. | asthma.mp. or exp Asthma/ |
| 4. | child*.af. |
| 5. | adolescent*.af. |
| 6. | youth.af. |
| 7. | (pediatric or paediatric).af. |
| 8. | 2 or 3 |
| 9. | 4 or 5 or 6 or 7 |
| 10. | 1 and 8 and 9 |
| 11. | limit 10 to yr="1994 - 2013" |

Note: Searches were performed using OvidSP, in which ".af." represents all fields, ".mp." represents multipurpose search, "exp" represents explode to include broader terms (e.g., dyspnea) and related terms (e.g., immunologic disorders), and "yr" represents year of publication.

## Study selection and eligibility criteria

Study selection was conducted in two stages. Initially, the first author screened the titles and abstracts of all retrieved records to identify articles with relevant research objectives and methods and decide whether to obtain the full text. Subsequently, the full texts were independently assessed for eligibility by the first and second authors.

Eligibility criteria were defined by types of studies, participants, comparisons and outcome measures (Liberati et al., 2009). Only empirical quantitative studies that were published in peer-reviewed journals since the definition of QoL by the WHOQOL Group (1994-2013) and written in English were considered. Duplicate or secondary publications on the same sample were excluded to avoid multiple-publication bias. In such cases, priority was given to the article reporting data from the largest sample. For types of participants, criteria included samples of 7- to 18-year-old children and adolescents with clinical diagnoses of asthma or parents of children and adolescents with asthma. For types of comparisons, studies were required to report direct comparisons between children and adolescents with asthma or their parents and age-matched community/healthy controls. Finally, the primary outcome for this review was the mean difference (MD) between asthma and control groups on overall QoL for children and adolescents, either by self- or parent-report, and parents' overall QoL. Because QoL is multi-dimensional in nature and several QoL questionnaires provide a profile instead of a single index (Ravens-Sieberer et al., 2006), we considered the MD on QoL core domains (physical, emotional, social and school functioning) as secondary outcomes. For assessing pediatric QoL, both generic and disease-specific instruments were included, provided that they assessed QoL as a broad-ranging multi-dimensional construct, and not only health status, and were applicable, at least in part, to healthy children and adolescents. Following the recommendations of Braido and colleagues (2010) for QoL assessment in respiratory allergy, the studies were also required to use instruments that were psychometrically validated for the targeted age range and language/cultural context.

Inter-rater agreement on reasons for study exclusion was calculated with Cohen's Kappa coefficient, considering $k < .00$ as poor, $k \leq .20$ as slight, $k \leq .40$ as fair, $k \leq .60$ as moderate, $k \leq .80$ as substantial and $k > .81$ as almost perfect agreement (Landis & Koch, 1977). Disagreements were resolved by discussion to reach consensus.

## Data extraction

A data collection form was developed for this review using the Data Extraction Template for Cochrane Reviews (The Cochrane Consumers and Communication Review Group, 2013) as a guide. Data were extracted by the first author and verified for accuracy by the second author. For each study, we extracted information on: publication information (i.e., authors, year and contact information for the corresponding author); methods (i.e., study design, methods and settings for participant recruitment, and inclusion/exclusion criteria for participation in the study); participants (i.e., number of eligible and included participants, non-response rate, country of origin, age, sex and clinical characteristics, including asthma severity, medication and comorbidities with other health conditions); outcomes (i.e., conceptual definitions of primary and secondary outcomes adopted by the authors, methods and instruments used for assessing outcomes, and reliability and validity of outcome measures); and results for asthma and control groups (i.e., sample size, mean [*M*] and standard deviation [*SD*] for continuous outcome, subgroup analyses and controlled variables).

When summary data (*M*, *SD*) were not available for each group, other descriptive statistics (e.g., medians and interquartile ranges, standard errors or CI) or results from comparative analyses (e.g., *t* or *F* statistics) were extracted and converted into the desirable format (Higgins & Green, 2008; Hozo, Djulbegovic, & Hozo, 2005). For studies reporting data separately for subgroups of participants (e.g., children and adolescents; boys and girls), data were gathered into a single sample size that combined *M* and *SD* values (Higgins & Green, 2008). When data were not directly reported in the article and could not be computed from the available data, additional information was requested from the corresponding author by email. Data from the same study that was reported in multiple journal articles were extracted together.

## Quality assessment

The methodological quality of individual studies included in the systematic review was independently assessed by the first and second authors, using an adapted version of the Newcastle-Ottawa Quality assessment scale (Wells et al., 2010). Studies were awarded up to 11 points based on selection of participants (maximum of 5 points), comparability between asthma cases and controls (maximum of 2 points) and QoL ascertainment (maximum of 4 points). Specifically for selection of participants, 1 point was allotted for adequate definition of cases (i.e., asthma diagnosis established by a physician based on medical records or physiological indicators), 1 point for representativeness of cases (i.e., selection of a random sample of patients, all eligible patients in a defined healthcare/educational institution or consecutive series of patients over a defined period of time), 1 point for adequate definition controls (i.e., healthy controls with no history of chronic health conditions), 1 point for selection of controls within the same community/geographic area as cases, and 1 point for response rate that was similar for cases and controls or higher than 80% for the total sample. Regarding comparability between asthma cases and controls, 1 point was allotted if the study controlled for children/adolescents' age and 1 point if the study controlled for any additional confounders. Finally, for ascertainment of QoL, 1 point was allotted for the use of age-appropriate measures that were psychometrically tested in the study sample and presented good psychometric properties in terms of reliability and validity, 1 point for the use of patients' or parents' self-reported measures or 2 points for inclusion of both patients and parents, and 1 point for the use of the same procedures for assessing cases and controls. Studies awarded 0-3 points were considered to be low quality, 4-7 points were average quality and 8-11 points were high quality. Inter-rater agreement was calculated with Cohen's Kappa coefficient (Landis & Koch, 1977) and disagreements were resolved by discussion until consensus.

## Data analyses

Meta-analyses for continuous data were performed with the Review Manager, Version 5.2. (The Cochrane Collaboration, 2012), using the inverse-variance random-effects method. Because this statistical method assumes that the outcomes have a normal distribution, skewness was inspected for both asthma and control groups in each study by checking whether the mean was smaller than twice the standard deviation (Altman & Bland, 1996).

Although QoL instruments often use different response scales, standardized scores ranging from 0 to 100 were the most widely used response scale across studies because they allow for comparisons between questionnaires and/or subscales with different numbers of items. Accordingly, we converted the *M* and *SD* values to the unit of the most commonly used scale for both asthma and control groups in each study. This approach enhances interpretability of summary estimates while preserving power and precision (Thorlund, Walter, Johnston, Furukawa, Guyatt, 2011). Once all results of individual studies were standardized, the MD between asthma and control groups and its associated 95% CI were computed for each outcome measure as the summary statistic for the estimate of effects.

Several covariates have been related to children/adolescents' and parents' QoL (e.g., socio-economic status) and they were likely to vary across studies; therefore, the random-effects model was chosen to incorporate between-studies heterogeneity. The $\tau^2$ statistic (i.e., the squared estimated *SD* of underlying effects across studies) described between-studies variance and the $I^2$ index described the percent of variability in effect estimates due to heterogeneity (Borenstein, Hedges, Higgins, & Rothstein, 2009; Higgins, Thompson, Deeks, & Altman, 2003). When considerable heterogeneity was observed ($I^2$ > 50%; Higgins et al., 2003), differences between subgroups of studies were examined to identify possible causes. To explore diversity in participants, we conducted subgroup analyses by age groups, considering participants aged 7-12 ears with a mean age ≤ 10 years as children and participants aged 11-18 years with a mean age ≥ 13 years as adolescents. To investigate methodological diversity, subgroup analyses comparing informants (self- *vs.* proxy-reports), type of controls (healthy *vs.* community controls), and quality ratings (high *vs.* moderate quality) were performed using $\chi^2$-tests.

# Results

## Study selection

The literature search identified 3,887 non-duplicated articles, of which 272 articles were selected for full-text eligibility assessment (Figure 1). Two hundred and fifty two articles were excluded for the following reasons: absence of a sample of pediatric asthma patients/parents, or inclusion of a sample of pediatric patients/parents of patients with chronic health conditions including asthma, but no data reported separately for each condition ($n$ = 54); the pediatric sample included children younger than 7 or older than 18 years and no data was reported for different age groups ($n$ = 94); absence of community/healthy controls or use of normative data as a reference group ($n$ = 77); no report of direct comparisons between asthma and control groups ($n$ = 9); no data on children/adolescents' or parents' QoL as an outcome measure ($n$ = 9); QoL definitions that were different from the one proposed by the WHOQOL Group ($n$ = 4); qualitative research ($n$ = 1); insufficient or inconsistent data ($n$ = 3); and secondary publication on the same data and analyses ($n$ = 1). Inter-rater agreement for exclusion reason was almost perfect, with $k$ = .90 ($p$ < .001).

Nineteen different studies reported in 20 journal articles met all inclusion criteria and were included in the systematic review.

## Study characteristics

Of the 19 included studies, 17 (reported in 18 articles; Altiparmak, Altiparmak, & Sari, 2011; Covaciu, Bergström, Lind, Svartengren, & Kull, 2013; Danansuriya & Rajapaksa, 2012; French, Christie, & Sowden, 1994; French, Carroll, Christie, 1998; Grootenhuis, Koopman, Verrips, Vogels, & Last, 2007; Hallstrand, Curtis, Aitken, & Sullivan, 2003; Hutchings et al., 2007, 2008; Kojima et al., 2009; Matterne, Schmitt, Diepgen, & Apfelbacher, 2011; Merikallio, Mustalahti, Remes, Valovirta, & Kaila, 2005; Montalto, Bruzzese, Moskaleva, Higgins-D'Alessandro, & Webber, 2004; Moreira et al., 2013; Sawyer et al., 2001; Upton et al., 2005; Van Gent et al., 2007; Wang, Wang, Wang, Xu, & Zhang, 2012) examined the QoL of 32,874 children and adolescents and four studies (Gau et al., 2010; Hatzmann, Heymans, Ferrer-i-Carbonell, Van Praag, & Grootenhuis, 2008; Moreira et al., 2013; Van Gent et al., 2007) examined the QoL of 8,062 parents, from 13 different countries. The study design and sample characteristics are detailed in Table 2.

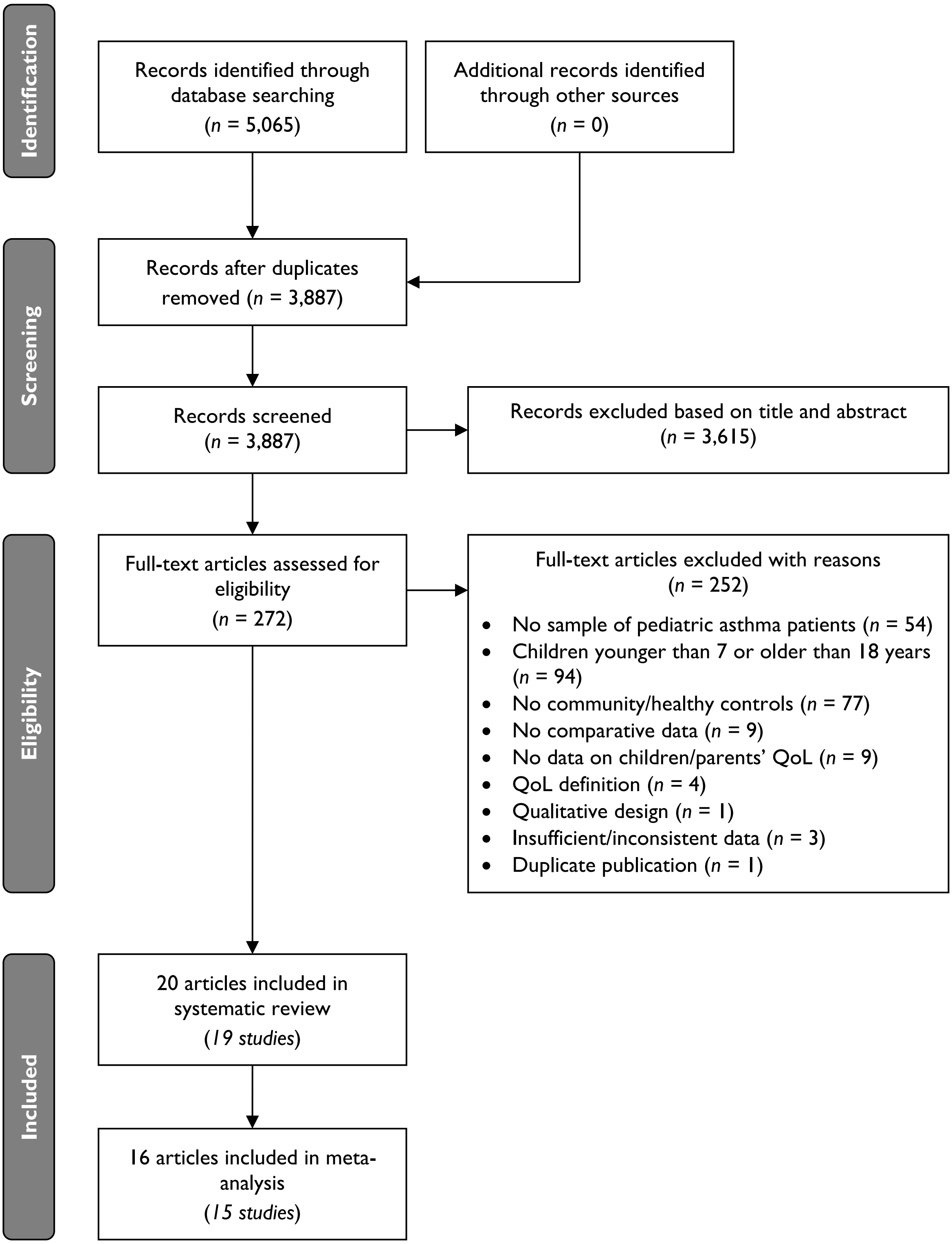


**Figure 1** | Flowchart for selection of studies

**Table 2** | Study design and sample characteristics reported in the 19 studies included in the systematic review

| *Authors, date of publication; country* | *Study design; period of data collection* | *Selection criteria* | *Sample size* | *Age in years M ±SD; range* | *Sex (%) male* | *Outcome measures* | *Quality of life dimensions* |
|---|---|---|---|---|---|---|---|
| Altiparmak et al., 2011; Turkey | Cross-sectional March 2008 – June 2008 | NR | Cases: 94 adolescents with asthma<br>Controls: 669 adolescents without asthma diagnosed by a doctor | Total sample: 13.2±0.9<br>Range: 11-15 | Total sample: 49.0% | Kiddo-KINDL (generic self-report measure) | Physical functioning*, Emotional functioning*, Self-esteem, Family, Friends/social functioning*, School functioning/everyday activities*, QoL overall score** |
| Covaciu et al., 2013; Sweden | Prospective (comparative data from the 8-year follow-up) 2002-2004 | NR | Cases: 199 children with asthma<br>Controls: 3,021 children without asthma | Range: 8 years | Total sample: 49.7% | EuroQoL-5D (generic proxy-report measure) | QoL overall score (visual analogue scale)** |
| Danansuriya et al., 2012; Sri Lanka | Cross-sectional February 2008 – April 2008 | Cases and controls with comorbidities or lacking parental consent were excluded | Cases: 115 adolescents with asthma<br>Controls: 142 healthy adolescents | Cases: 13.0± 0.9<br>Controls: 12.8±0.8<br>Range: 12-14 | Cases: 56.5%<br>Controls: 52.1% | PedsQL™ 4.0 Generic Core Scales (generic self-report measure) | Physical functioning*, Emotional functioning*, Social functioning*, School functioning*, QoL overall score** |
| French et al., 1994; UK | Longitudinal (comparative data reported for both time 1 and 2) | Cases and controls with other chronic illnesses were excluded | Cases: 103 children with asthma<br>Controls: 153 healthy children | Cases: 9.8±NR<br>Controls: 9.5±NR<br>Range: 8-11 | Cases: 54%<br>Controls: 52% | CAQ-Form B (asthma-specific self-report measure) | Active quality of living/physical functioning*, Passive quality of living, Distress, Severity |
| French et al., 1998; Australia | Cross-sectional | NR | Cases: 115 children and 120 adolescents with asthma (total = 235)<br>Controls: 221 children and 185 adolescents without asthma (total = 406) | Cases: 10.23±NR<br>Controls: 10.17±NR<br>Range: 7-16 | Cases: 56.2%<br>Controls: 49.8% | CAQ-Form B; CAQ-Form C (asthma-specific self-report measures) | Active quality of living/ physical functioning*, Passive quality of living (Form B)/ Teenage quality of living (Form C), Distress, Severity, Reactivity (Form C) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Gau et al., 2010; Taiwan | Cross-sectional December 2001 – May 2002 (cases); August 2001 – January 2002 (controls) | For cases, mothers who have children with chronic health conditions other than asthma and who discontinued their child's visits to the doctor were excluded; Selection criteria not reported for controls | Cases: 229 mothers of children with asthma<br>Controls: 6,431 female participants from the community | Cases: 36.76±5.07<br>Controls: NR<br>Range: 21-54 | NA | WHOQOL-BREF (generic self-report measure) | Physical functioning$^{*}$, Psychological functioning$^{*}$, Social relationships$^{*}$, Environment, Overall QoL$^{**}$ |
| Grootenhuis et al., 2007; The Netherlands | Cross-sectional (data from several ongoing studies) | Controls with a chronic disease were excluded | Cases: 32 children with asthma<br>Controls: 913 healthy children | Range: 8-11 | Cases: 66%<br>Controls: NR | TACQoL (generic self-report measure) | Physical functioning$^{*}$, Motor functioning, Autonomy, Cognitive/school functioning$^{*}$, Social functioning$^{*}$, Emotional functioning (positive and negative emotions combined)$^{*}$ |
| Hallstrand et al., 2003; U.S.A. | Cross-sectional | NR | Cases: 37 adolescents with asthma<br>Controls: 123 adolescents with no prior diagnosis of asthma | Total sample: 14.0±1.8 | Total sample: 53.8% | PedsQL™ 3.0 Generic Core Scales (generic self-report measure) | Physical functioning$^{*}$, Emotional functioning$^{*}$, Social functioning$^{*}$, School functioning$^{*}$, General well-being, QoL overall score$^{**}$ |
| Hatzmann et al., 2008; The Netherlands | Retrospective study (cross-sectional data for QoL) January 2006 - September 2007 | Parents were included if they have a child between 1 and 19 years of age with a chronic illness diagnosed > 1 year (cases) or without chronic illnesses (controls), living at home, and were able to fill out the questionnaire in Dutch or English | Cases: 87 parents of children/ adolescents with asthma<br>Controls: 425 parents of healthy children/ adolescents | Cases: 42.2±6.7<br>Controls: 43.7±5.5 | Cases: 13.8%<br>Controls: 16.7% | TAAQoL (generic self-report measure) | Physical functioning (gross and fine motor functioning, sleep, pain, daily activities and vitality combined)$^{*}$, Sexuality, Emotional functioning (positive emotions, depressive emotions and aggressiveness combined)$^{*}$, Social functioning$^{*}$, Cognitive functioning |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Hutchings et al., 2007, 2008; UK | Longitudinal (comparative data reported for time 1) | Cases and controls with learning difficulties or with first language other than English, and controls having a health problem or currently using healthcare resources were excluded | Cases: 56 children/ adolescents with asthma and 37 parents<br>Controls: 563 healthy children/ adolescents and 296 parents | Range: 8-18 | NR | MMQL-Youth and Parent Form (generic self- and proxy-report measures) | Physical functioning*, Appearance, Emotional functioning*, Social functioning*, School functioning* |
| Kojima et al., 2009; Japan | Cross-sectional May 2005 – June 2005 | NR | Cases: 1,438 adolescents with asthma<br>Controls: 10,740 adolescents without asthma | Range: 13-14 | NR | Kiddo-KINDL (generic self-report measure) | Physical functioning*, Emotional functioning*, Self-esteem, Family cohesion, Friends/social functioning*, School functioning/everyday activities*, QoL overall score** |
| Matterne et al., 2011; Germany | Cross-sectional May 2003 – May 2006 | NR | Cases: 263 adolescents with asthma<br>Controls: 6,244 adolescents without asthma | Range: 11-17 | Total sample: 51.0% | KINDL-R (generic self-report measure) | Physical functioning*, Emotional functioning*, Self-esteem, Family, Friends/social functioning*, School functioning/everyday activities*, QoL overall score** |
| Merikallio et al., 2005; Finland | Cross-sectional February 2001 – March 2001 | Cases and controls were excluded due to missing parental consent or missing data | Cases: 192 adolescents with asthma<br>Controls: 1,792 adolescents without asthma | Total sample: 13.2±1.4<br>Range: 11-15 | Total sample: 45.6% | CHQ-Child form (generic self-report measure) | Physical functioning*, Role/social-physical*, General health**, Bodily pain and discomfort, Family activities, Role/social-emotional, Role/social-behavioral, Self-esteem, Mental health/emotional functioning*, Behavior, Family cohesion |
| Montalto et al., 2004; U.S.A. | Cross-sectional 1999/ 2000 school year | NR | Cases: 238 children with asthma<br>Controls: 1,054 children without asthma | Total sample: 8.5±0.78<br>Range: 7-11 | Cases: 53%<br>Controls: 45% | KINDL (generic self-report measure) | Physical state*, Psychological well-being*, Social relationships*, Functional capacity in everyday life*, QoL overall score** |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Moreira et al., 2013; Portugal | Cross-sectional<br>January 2010 – June 2012 | Cases and controls with comorbid chronic health conditions or developmental delay and lacking parental consent were excluded | Cases: 175 children and 133 adolescents with asthma (total = 308); 308 parents<br>Controls: 171 healthy children and 128 healthy adolescents (total = 299); 299 parents | Cases: 12.24±2.64 for children; 41.27± 5.82 for parents<br>Controls: 11.75±3.25 for children; 41.72± 5.54 for parents<br>Range: 8-18 | Cases: 63% of children; 14.3% of parents<br>Controls: 46.2% of children; 9.0% of parents | KIDSCREEN-10 Index<br>EUROHIS-QoL-8 Index<br>(generic self-report measures) | QoL overall score (children/ adolescents)$^{**}$<br>QoL overall score (parents)$^{**}$ |
| Sawyer et al., 2001; Australia | Cross-sectional | NR | Cases: 236 children with asthma and 236 parents<br>Controls: 251 community children and 1,625 parents | Cases: 10.4±1.1<br>Controls: 10.5±NR<br>Range: 8-13 | Cases: 55%<br>Controls: 51% | CHQ-Child form and CHQ-Parent form (generic self- and proxy-report measures) | General health perceptions$^{**}$, Physical activities$^{*}$, Pain and discomfort, Self-esteem, Emotional functioning$^{*}$, Behavioral problems, Role/social functioning-physical$^{*}$, Role/social functioning-emotional, Role/social functioning-behavioral |
| Upton et al., 2005; UK | Cross-sectional | Controls with any chronic health problem were excluded | Cases: 99 children/ adolescents with asthma and 74 parents<br>Controls: 1,034 healthy children/ adolescents and 665 parents | Total sample: 12.58±2.6 for self-reports; 11.86±2.3 for proxy-reports<br>Range: 8-18 | Total sample: 48.9% for self-reports; 47.3% for proxy-reports | PedsQL™ 4.0 Generic Core Scales (generic self- and proxy-report measures) | Physical functioning$^{*}$, Emotional functioning$^{*}$, Social functioning$^{*}$, School functioning$^{*}$, QoL overall score$^{**}$ |
| Van Gent et al., 2007; The Netherlands | Cross-sectional<br>September 2002 – April 2005 | Cases were excluded due to missing data, refusal to participate in bronchial challenge test, or inability to meet technical conditions; Healthy controls had no asthma diagnosis or symptoms in the last 12 months and no reversible airway obstruction | Cases: 81 children with asthma and 81 parents<br>Controls: 202 healthy children and 202 parents | Cases: 9.4±0.8<br>Controls: 9.4±0.7<br>Range: 7-10 | Cases: 58%<br>Controls: 50% | PAQLQ<br>PACQLQ<br>(asthma-specific self-report measures) | Activity/physical functioning$^{*}$, Emotions$^{*}$, Symptom, QoL overall score$^{**}$ (children)<br>Activity/physical functioning$^{*}$, Emotions$^{*}$, QoL overall score$^{**}$ (parents) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Wang et al., 2012; China | Cross-sectional<br>June 2007 – December 2007 | Cases and controls with other systemic or neurological disorders, IQ < 85 and those who refused to participate were excluded | Cases: 81 adolescents with asthma<br>Controls: 87 healthy adolescents | Cases: 15.20±1.10<br>Controls: 15.20±1.09<br>Range: 14-18 | Cases: 64.2%<br>Controls: 56.3% | MOS-SF-36 (generic self-report measure) | Physical functioning*, Role-physical, Bodily pain, General health, Vitality, Social functioning*, Role-emotional, Mental health/emotional functioning*, Health transition, QoL overall score** |

CAQ – Childhood Asthma Questionnaire; CHQ – Child Health Questionnaire; *M* – mean; MMQL – Minneapolis-Manchester Quality of Life instrument; MOS-SF-36 – Medical Outcomes Study - Short Form; NR – not reported; PACQLQ - Pediatric Asthma Caregiver's Quality of Life Questionnaire; PAQLQ – Pediatric Asthma Quality of Life Questionnaire; *SD* – standard deviation; TAAQoL – TNO-AZL Questionnaire for Adult's Health-related Quality of Life; TACQoL – TNO-AZL Children's Quality of Life questionnaire; WHOQOL-BREF – World Health Organization Quality of Life Assessment - Abbreviated version; ** Considered as a primary outcome for this meta-analytic review; * Considered as a secondary outcome for this meta-analytic review.

The 17 studies examining children's and adolescents' QoL included a total of 3,807 pediatric asthma patients aged 7-18 years (*M* = 11.37; *SD* = 2.37; 54.38% male) and 29,067 controls (mean age = 11.52, *SD* = 2.28; 49.55% male). Of these, six studies (35.3%) assessed children aged 7-12 years with a mean age ≤ 10 years and seven studies (41.2%) assessed adolescents aged 11-18 years with a mean age ≥ 13 years; the remaining four studies included broader age ranges, with two performing independent analyses for different age groups (French et al., 1998; Moreira et al., 2013). The four studies examining differences in parents' QoL sampled 705 parents of children and adolescents with asthma (85.82% female; mean age = 39.75, *SD* = 6.13) and 7,357 parents of community/healthy children and adolescents (86.46% female; mean age = 42.88, *SD* = 5.60).

The majority of studies had a cross-sectional design (*n* = 15, 78.9%); of the four studies with a longitudinal design, only one reported case-control comparisons for both assessment times (French et al., 1994; for consistency, only data from the first assessment was used in quantitative analyses). Several studies did not report asthma clinical characteristics and the few studies that presented comparative data separately for different clinical groups used heterogeneous criteria for clustering (e.g., wheezing attacks during the previous month [Merikallio et al., 2005]; dyspnea during exercise [Hallstrand et al., 2003; Kojima et al., 2009]; peak expiratory flow lower than 80% [Wang et al., 2012]). For comparative analyses, nine studies (47.4%) selected healthy controls with no history of chronic conditions, eight (42.1%) selected children and adolescents without asthma but did not describe their health status, and two (10.5%) used a community sample as controls.

For assessing children's and adolescents' QoL, all studies but one (Covaciu et al., 2013) used self-report measures and three studies (Hutchings et al., 2007, 2008; Sawyer et al., 2001; Upton et al., 2005) followed a multi-informant approach by also including proxy-reports from 347 parents of pediatric asthma patients and 2,586 parents of community/healthy children and adolescents. A variety of instruments were used across studies to measure children's and adolescents' QoL, including eight generic (the KINDL [Ravens-Sieberer & Bullinger, 1998; Eser et al., 2008], the PedsQL™ Generic Core Scales [Danansuriya & Rajapaksa, 2012; Upton et al., 2005; Varni, Seid, & Rode, 1999], the Child Health Questionnaire [Landgraf, Abetz, & Ware, 1996; Pelkonen et al., 2001], the Dutch TNO-AZL Children's Quality of Life questionnaire [Vogels, Verrips, & Koopman, 2000], the Portuguese version of the KIDSCREEN-10 Index [Matos, Gaspar, & Simões, 2012], the British version of the Minneapolis-Manchester Quality of Life instrument [Hutchings et al., 2007, 2008], the EuroQoL-5D [Rabin & de Charro, 2001] and the Chinese version of the Medical Outcomes Study SF-36 Health Survey [Li, Wang, & Shen, 2002]) and two asthma-specific questionnaires (the Childhood Asthma Questionnaire [French et al., 1994; French et al., 1998] and the Dutch version of the Pediatric Asthma Quality of Life

Questionnaire [Raat et al., 2005]). Most questionnaires were age appropriate and specifically designed to assess children/adolescents' QoL, except for the EQ-5D and the SF-36. Even so, a child-friendly version of the EQ-5D, which introduced only slight language modifications to the Swedish EQ-5D adult version, presented good feasibility and discriminant validity between Swedish children/adolescents with and without asthma and/or rhinitis (Burström, Svartengren, & Egmar, 2011). Similarly, the SF-36 was developed to be self-rated by persons 14 years of age and older (Ware & Sherbourne, 1992) and presented good psychometric properties for Chinese adolescents (Wang et al., 2012).

For parents' QoL assessment, three studies used generic instruments (the Taiwanese version of the WHOQOL-BREF [Yao, Chung, Yu, & Wang, 2002], the Portuguese version of the EUROHIS-QoL-8 Index [Pereira, Melo, Gameiro, & Canavarro, 2011] and the Dutch TNO-AZL Questionnaire for Adult's Health-related Quality of Life [Bruil, Fekkes, Vogels, & Verrips, 2004]) and one used an asthma-specific measure (the Pediatric Asthma Caregiver's Quality of Life Questionnaire [Juniper et al., 1996]), all four with well-established psychometric properties. Most studies (*n* = 15, 78.9%) used profile instruments measuring several QoL domains (usually physical, psychological, and social), while only two studies (10.5%) assessed QoL as a single index.

## Methodological quality

Figure 2 illustrates the proportion of studies that met the quality criteria defined according to the Newcastle-Ottawa Quality assessment scale (Wells et al., 2010) adapted for this review. Overall, 15 studies (78.9%) were assessed as average quality (Altiparmak et al., 2011; Covaciu et al., 2013; Danansuriya & Rajapaksa, 2012; French et al., 1994; French, et al., 1998; Gau et al., 2010; Grootenhuis et al., 2007; Hallstrand et al., 2003; Hatzmann et al., 2008; Hutchings et al., 2007, 2008; Kojima et al., 2009; Montalto et al., 2004; Sawyer et al., 2001; Van Gent et al., 2007; Wang et al., 2012) and four studies (21.1%) as high quality (Matterne et al., 2011; Merikallio et al., 2005; Moreira et al., 2013; Upton et al., 2005). The main reasons for low quality scores were the use of nonrepresentative samples (e.g., convenience sampling methods, 57.9%), no description of controls' health status (57.9%), response rates lower than 80% or not reported (84.2%), and the use of different procedures/settings in the completion of QoL questionnaires (52.6%). A detailed description of quality assessment is presented in Supplementary Material, Table S1. Inter-rater agreement for quality assessment was moderate, with $k = .49$ ($p < .001$), and consensus was reached for all studies.

Additional quantitative data were directly requested from the authors for seven studies and summary statistics were obtained for three studies (Grootenhuis et al., 2007; Hatzmann et al., 2008; Moreira et al., 2013); the remaining four studies (French, et al., 1998; Hallstrand et al., 2003; Kojima et al., 2009; Wang et al., 2012) were excluded from quantitative analyses due to insufficient or inconsistent data.

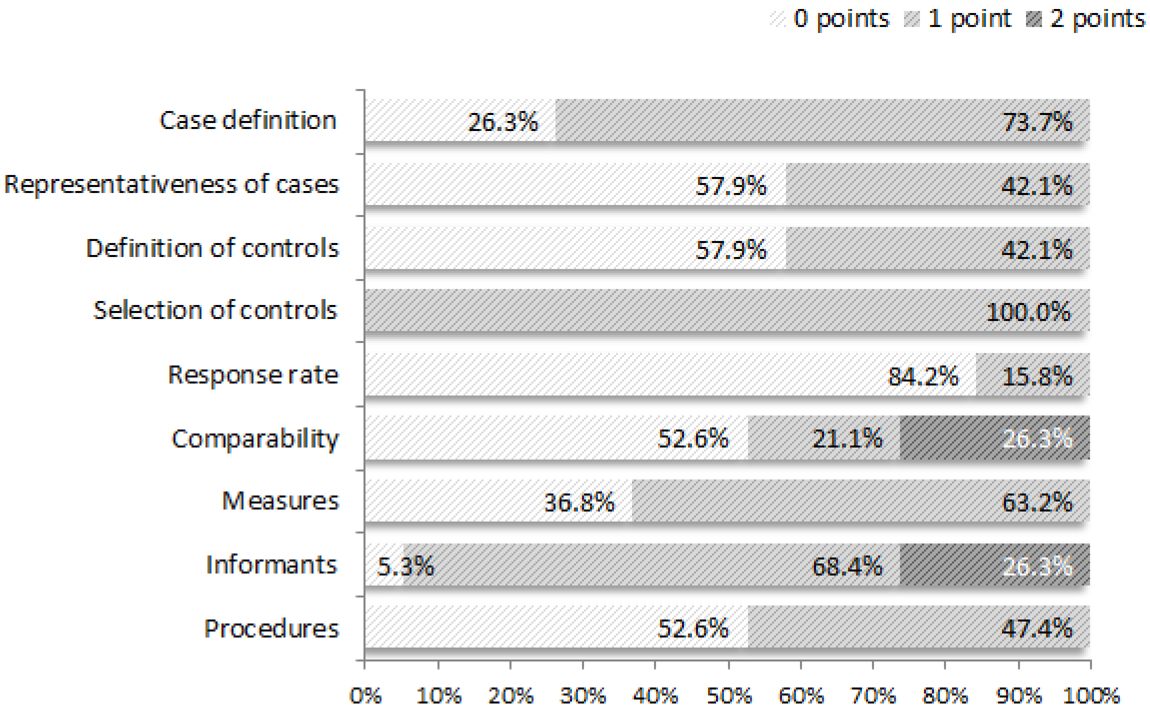
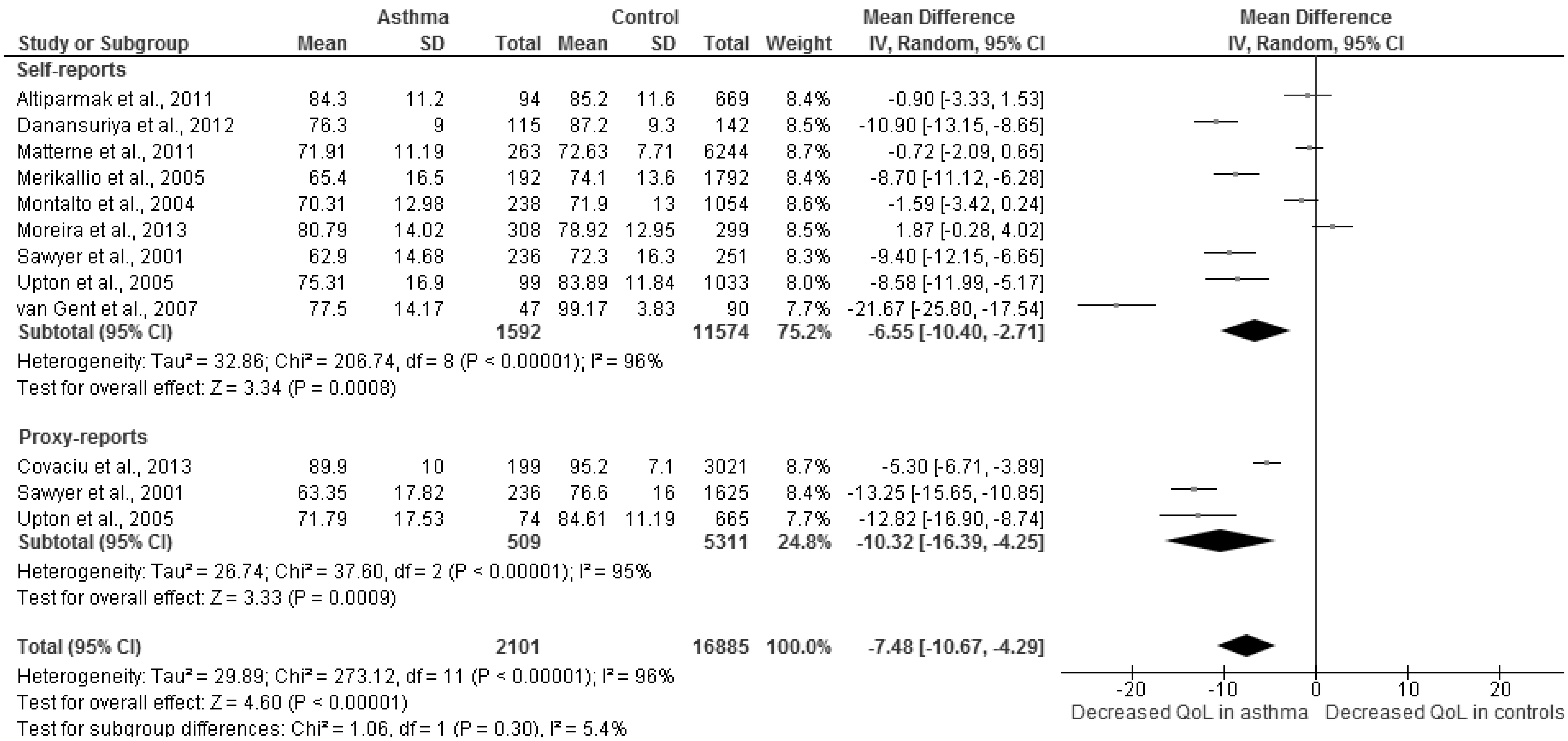


**Figure 2** | Percentage of studies allotted with 0, 1 or 2 points according to the Newcastle-Ottawa Quality assessment scale adapted for the present study

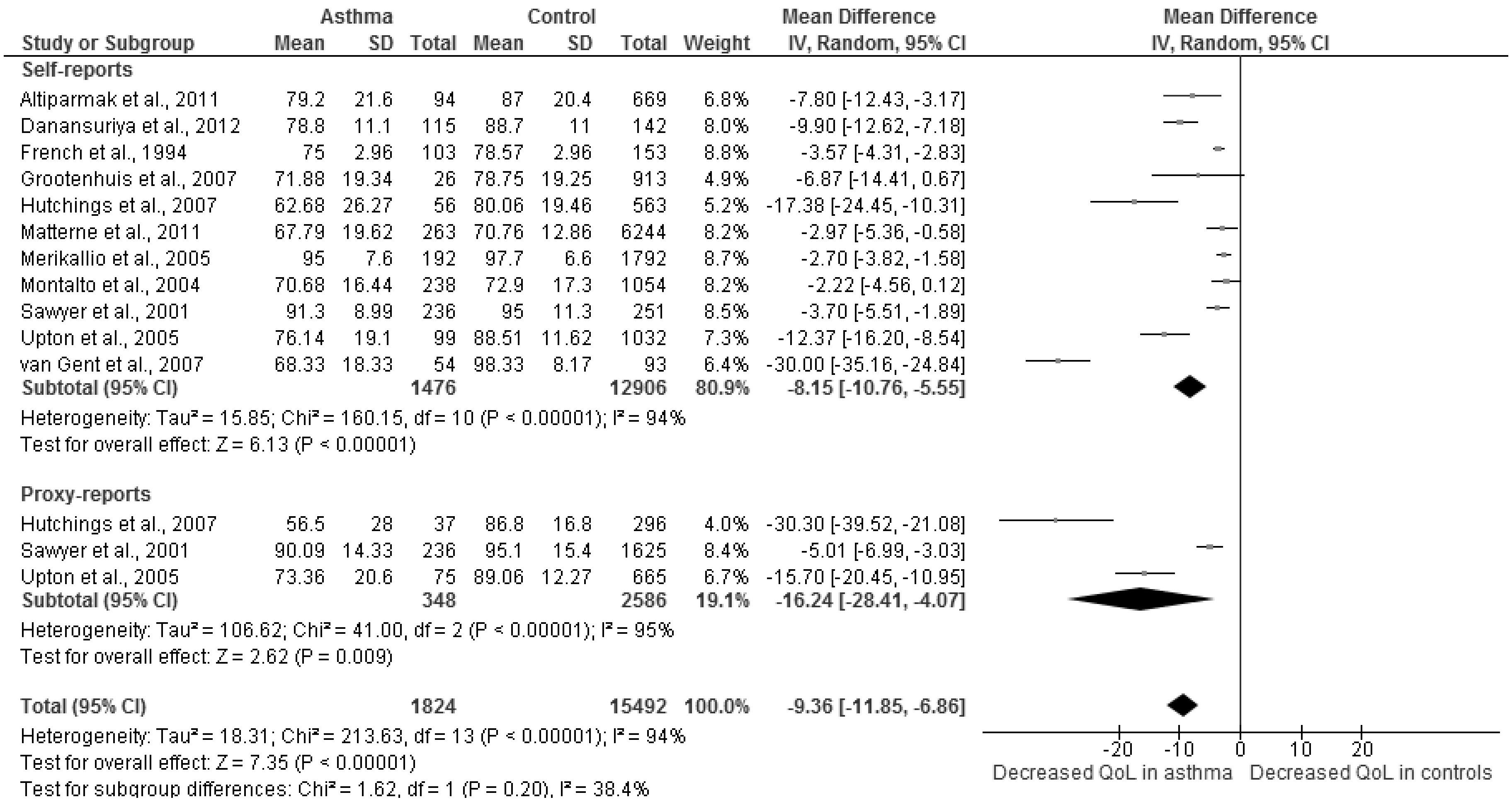
## Quality of life in children and adolescents with asthma

For quantitative synthesis of children's and adolescents' QoL outcomes, data were obtained from 13 studies comprising a total of 1,797 pediatric asthma patients and 13,266 controls, as well as 547 parents of children and adolescents with asthma and 5,607 parents of community/healthy children and adolescents as their proxies. The meta-analyses of the 10 studies presenting data for overall QoL (Figure 3.A) showed that children and adolescents with asthma had significantly lower QoL than their peers, with a MD of -7.48 (95% CI = -10.67/ -4.29, $p$ < .001). Pooled estimates for each core domain of pediatric QoL confirmed a decreased physical (MD = -9.36, 95% CI = -11.85/ -6.86, $p$ < .001; Figure 3.B), psychological (MD = -5.00, 95% CI = -7.17/ -2.82, $p$ < .001; Figure 3.C) and social functioning (MD = -3.76, 95% CI = -5.80/ -1.72, $p$ < .001; Figure 3.D) for pediatric asthma patients when compared to community/healthy controls. No significant differences were observed for school functioning (MD = -4.44, 95% CI = -9.23/ 0.35, $p$ = .07; Figure 3.E). Between-studies variance indicated significant heterogeneity for all QoL domains, with $I^2$ ranging from 82 to 96%.



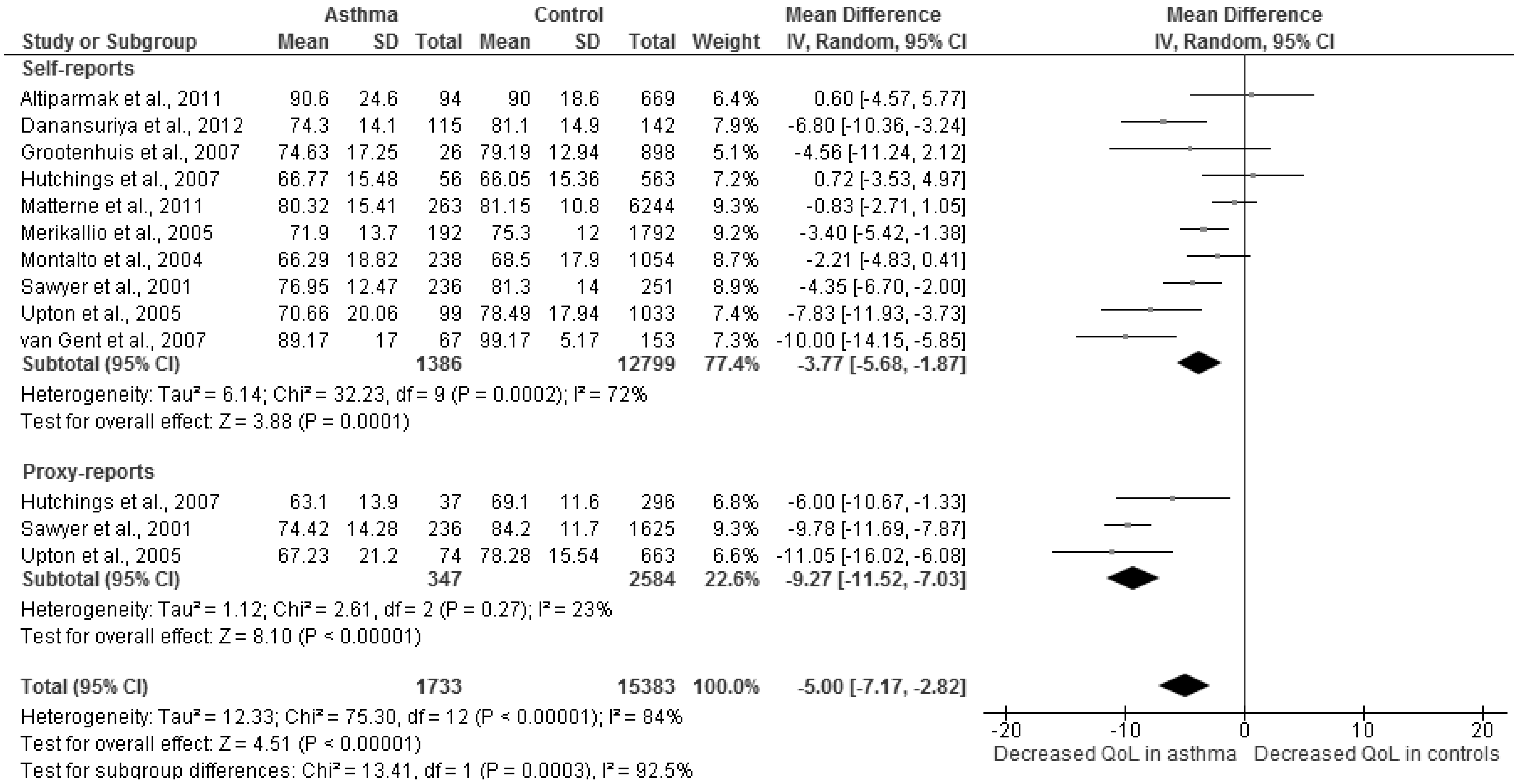
| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Self-reports** | | | | | | | | |
| Altiparmak et al., 2011 | 84.3 | 11.2 | 94 | 85.2 | 11.6 | 669 | 8.4% | -0.90 [-3.33, 1.53] |
| Danansuriya et al., 2012 | 76.3 | 9 | 115 | 87.2 | 9.3 | 142 | 8.5% | -10.90 [-13.15, -8.65] |
| Matterne et al., 2011 | 71.91 | 11.19 | 263 | 72.63 | 7.71 | 6244 | 8.7% | -0.72 [-2.09, 0.65] |
| Merikallio et al., 2005 | 65.4 | 16.5 | 192 | 74.1 | 13.6 | 1792 | 8.4% | -8.70 [-11.12, -6.28] |
| Montalto et al., 2004 | 70.31 | 12.98 | 238 | 71.9 | 13 | 1054 | 8.6% | -1.59 [-3.42, 0.24] |
| Moreira et al., 2013 | 80.79 | 14.02 | 308 | 78.92 | 12.95 | 299 | 8.5% | 1.87 [-0.28, 4.02] |
| Sawyer et al., 2001 | 62.9 | 14.68 | 236 | 72.3 | 16.3 | 251 | 8.3% | -9.40 [-12.15, -6.65] |
| Upton et al., 2005 | 75.31 | 16.9 | 99 | 83.89 | 11.84 | 1033 | 8.0% | -8.58 [-11.99, -5.17] |
| van Gent et al., 2007 | 77.5 | 14.17 | 47 | 99.17 | 3.83 | 90 | 7.7% | -21.67 [-25.80, -17.54] |
| **Subtotal (95% CI)** | | | **1592** | | | **11574** | **75.2%** | **-6.55 [-10.40, -2.71]** |
| Heterogeneity: Tau² = 32.86; Chi² = 206.74, df = 8 (P < 0.00001); I² = 96% | | | | | | | | |
| Test for overall effect: Z = 3.34 (P = 0.0008) | | | | | | | | |
| **Proxy-reports** | | | | | | | | |
| Covaciu et al., 2013 | 89.9 | 10 | 199 | 95.2 | 7.1 | 3021 | 8.7% | -5.30 [-6.71, -3.89] |
| Sawyer et al., 2001 | 63.35 | 17.82 | 236 | 76.6 | 16 | 1625 | 8.4% | -13.25 [-15.65, -10.85] |
| Upton et al., 2005 | 71.79 | 17.53 | 74 | 84.61 | 11.19 | 665 | 7.7% | -12.82 [-16.90, -8.74] |
| **Subtotal (95% CI)** | | | **509** | | | **5311** | **24.8%** | **-10.32 [-16.39, -4.25]** |
| Heterogeneity: Tau² = 26.74; Chi² = 37.60, df = 2 (P < 0.00001); I² = 95% | | | | | | | | |
| Test for overall effect: Z = 3.33 (P = 0.0009) | | | | | | | | |
| **Total (95% CI)** | | | **2101** | | | **16885** | **100.0%** | **-7.48 [-10.67, -4.29]** |
| Heterogeneity: Tau² = 29.89; Chi² = 273.12, df = 11 (P < 0.00001); I² = 96% | | | | | | | | |
| Test for overall effect: Z = 4.60 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 1.06, df = 1 (P = 0.30), I² = 5.4% | | | | | | | | |

**Figure 3.A** | Forest plots for meta-analysis of differences in children/adolescents' overall QoL



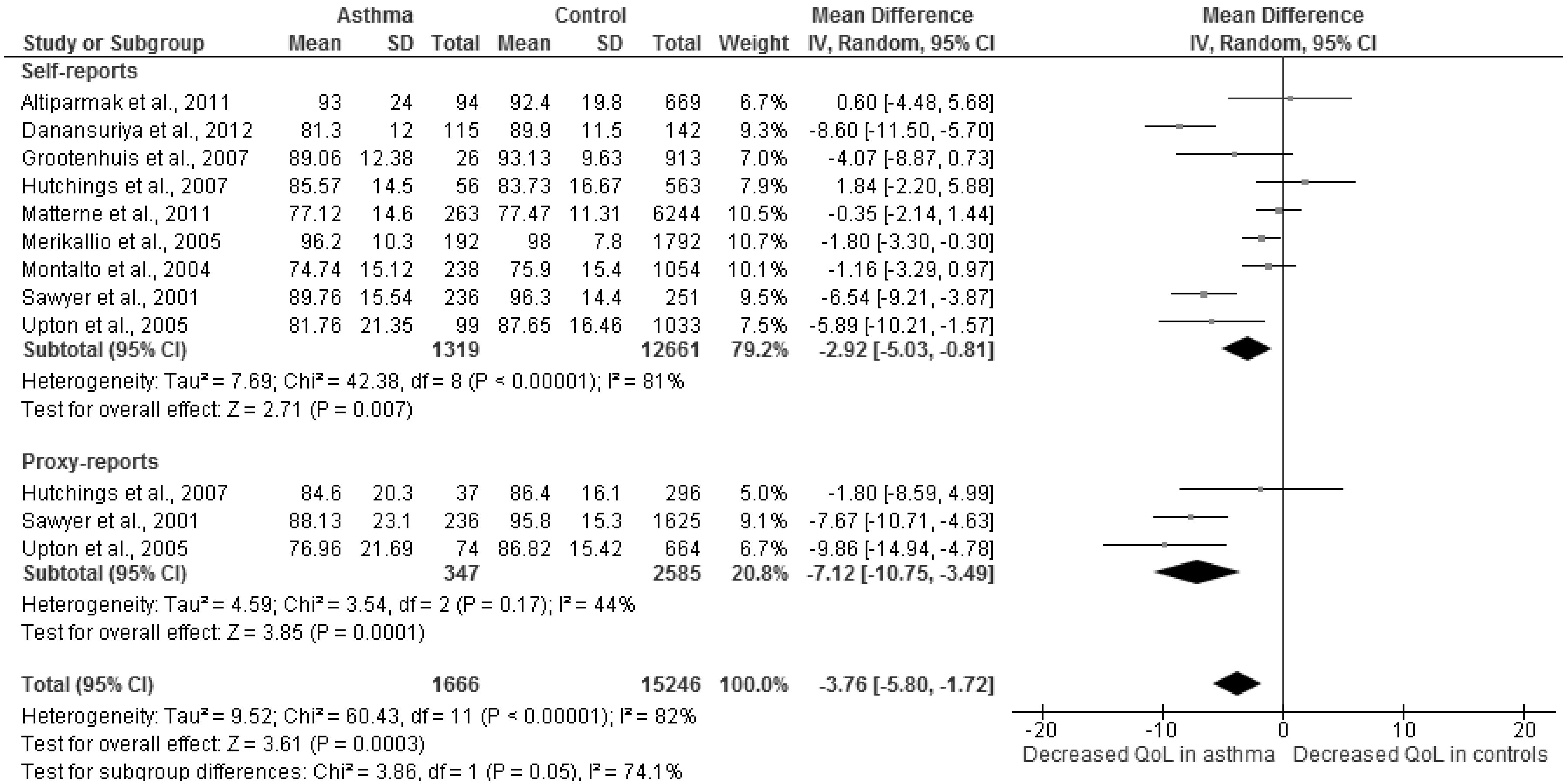
| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Self-reports** | | | | | | | | |
| Altiparmak et al., 2011 | 79.2 | 21.6 | 94 | 87 | 20.4 | 669 | 6.8% | -7.80 [-12.43, -3.17] |
| Danansuriya et al., 2012 | 78.8 | 11.1 | 115 | 88.7 | 11 | 142 | 8.0% | -9.90 [-12.62, -7.18] |
| French et al., 1994 | 75 | 2.96 | 103 | 78.57 | 2.96 | 153 | 8.8% | -3.57 [-4.31, -2.83] |
| Grootenhuis et al., 2007 | 71.88 | 19.34 | 26 | 78.75 | 19.25 | 913 | 4.9% | -6.87 [-14.41, 0.67] |
| Hutchings et al., 2007 | 62.68 | 26.27 | 56 | 80.06 | 19.46 | 563 | 5.2% | -17.38 [-24.45, -10.31] |
| Matterne et al., 2011 | 67.79 | 19.62 | 263 | 70.76 | 12.86 | 6244 | 8.2% | -2.97 [-5.36, -0.58] |
| Merikallio et al., 2005 | 95 | 7.6 | 192 | 97.7 | 6.6 | 1792 | 8.7% | -2.70 [-3.82, -1.58] |
| Montalto et al., 2004 | 70.68 | 16.44 | 238 | 72.9 | 17.3 | 1054 | 8.2% | -2.22 [-4.56, 0.12] |
| Sawyer et al., 2001 | 91.3 | 8.99 | 236 | 95 | 11.3 | 251 | 8.5% | -3.70 [-5.51, -1.89] |
| Upton et al., 2005 | 76.14 | 19.1 | 99 | 88.51 | 11.62 | 1032 | 7.3% | -12.37 [-16.20, -8.54] |
| van Gent et al., 2007 | 68.33 | 18.33 | 54 | 98.33 | 8.17 | 93 | 6.4% | -30.00 [-35.16, -24.84] |
| **Subtotal (95% CI)** | | | **1476** | | | **12906** | **80.9%** | **-8.15 [-10.76, -5.55]** |
| Heterogeneity: Tau² = 15.85; Chi² = 160.15, df = 10 (P < 0.00001); I² = 94% | | | | | | | | |
| Test for overall effect: Z = 6.13 (P < 0.00001) | | | | | | | | |
| **Proxy-reports** | | | | | | | | |
| Hutchings et al., 2007 | 56.5 | 28 | 37 | 86.8 | 16.8 | 296 | 4.0% | -30.30 [-39.52, -21.08] |
| Sawyer et al., 2001 | 90.09 | 14.33 | 236 | 95.1 | 15.4 | 1625 | 8.4% | -5.01 [-6.99, -3.03] |
| Upton et al., 2005 | 73.36 | 20.6 | 75 | 89.06 | 12.27 | 665 | 6.7% | -15.70 [-20.45, -10.95] |
| **Subtotal (95% CI)** | | | **348** | | | **2586** | **19.1%** | **-16.24 [-28.41, -4.07]** |
| Heterogeneity: Tau² = 106.62; Chi² = 41.00, df = 2 (P < 0.00001); I² = 95% | | | | | | | | |
| Test for overall effect: Z = 2.62 (P = 0.009) | | | | | | | | |
| **Total (95% CI)** | | | **1824** | | | **15492** | **100.0%** | **-9.36 [-11.85, -6.86]** |
| Heterogeneity: Tau² = 18.31; Chi² = 213.63, df = 13 (P < 0.00001); I² = 94% | | | | | | | | |
| Test for overall effect: Z = 7.35 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 1.62, df = 1 (P = 0.20), I² = 38.4% | | | | | | | | |

**Figure 3.B** | Forest plots for meta-analysis of differences in children/adolescents' physical functioning



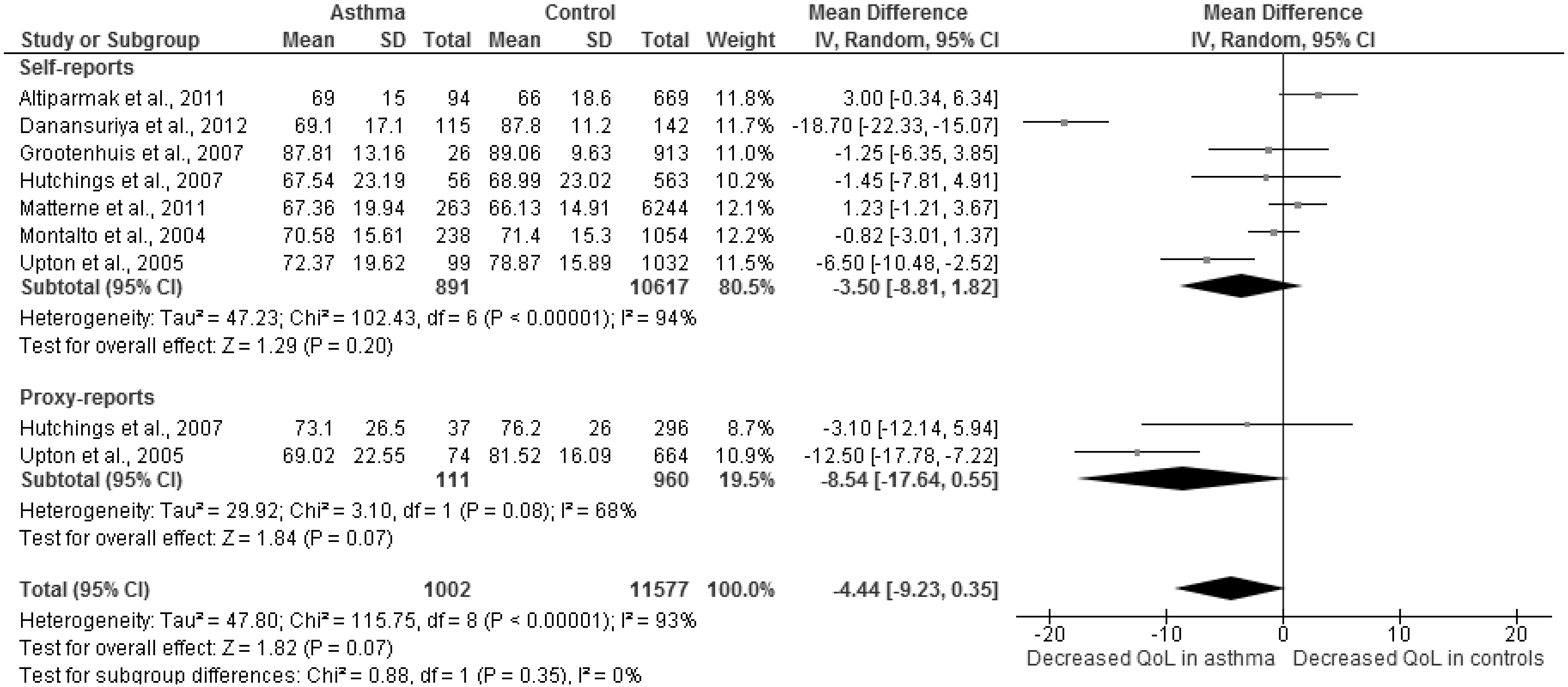
| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Self-reports** | | | | | | | | |
| Altiparmak et al., 2011 | 90.6 | 24.6 | 94 | 90 | 18.6 | 669 | 6.4% | 0.60 [-4.57, 5.77] |
| Danansuriya et al., 2012 | 74.3 | 14.1 | 115 | 81.1 | 14.9 | 142 | 7.9% | -6.80 [-10.36, -3.24] |
| Grootenhuis et al., 2007 | 74.63 | 17.25 | 26 | 79.19 | 12.94 | 898 | 5.1% | -4.56 [-11.24, 2.12] |
| Hutchings et al., 2007 | 66.77 | 15.48 | 56 | 66.05 | 15.36 | 563 | 7.2% | 0.72 [-3.53, 4.97] |
| Matterne et al., 2011 | 80.32 | 15.41 | 263 | 81.15 | 10.8 | 6244 | 9.3% | -0.83 [-2.71, 1.05] |
| Merikallio et al., 2005 | 71.9 | 13.7 | 192 | 75.3 | 12 | 1792 | 9.2% | -3.40 [-5.42, -1.38] |
| Montalto et al., 2004 | 66.29 | 18.82 | 238 | 68.5 | 17.9 | 1054 | 8.7% | -2.21 [-4.83, 0.41] |
| Sawyer et al., 2001 | 76.95 | 12.47 | 236 | 81.3 | 14 | 251 | 8.9% | -4.35 [-6.70, -2.00] |
| Upton et al., 2005 | 70.66 | 20.06 | 99 | 78.49 | 17.94 | 1033 | 7.4% | -7.83 [-11.93, -3.73] |
| van Gent et al., 2007 | 89.17 | 17 | 67 | 99.17 | 5.17 | 153 | 7.3% | -10.00 [-14.15, -5.85] |
| **Subtotal (95% CI)** | | | **1386** | | | **12799** | **77.4%** | **-3.77 [-5.68, -1.87]** |
| Heterogeneity: Tau² = 6.14; Chi² = 32.23, df = 9 (P = 0.0002); I² = 72% | | | | | | | | |
| Test for overall effect: Z = 3.88 (P = 0.0001) | | | | | | | | |
| **Proxy-reports** | | | | | | | | |
| Hutchings et al., 2007 | 63.1 | 13.9 | 37 | 69.1 | 11.6 | 296 | 6.8% | -6.00 [-10.67, -1.33] |
| Sawyer et al., 2001 | 74.42 | 14.28 | 236 | 84.2 | 11.7 | 1625 | 9.3% | -9.78 [-11.69, -7.87] |
| Upton et al., 2005 | 67.23 | 21.2 | 74 | 78.28 | 15.54 | 663 | 6.6% | -11.05 [-16.02, -6.08] |
| **Subtotal (95% CI)** | | | **347** | | | **2584** | **22.6%** | **-9.27 [-11.52, -7.03]** |
| Heterogeneity: Tau² = 1.12; Chi² = 2.61, df = 2 (P = 0.27); I² = 23% | | | | | | | | |
| Test for overall effect: Z = 8.10 (P < 0.00001) | | | | | | | | |
| **Total (95% CI)** | | | **1733** | | | **15383** | **100.0%** | **-5.00 [-7.17, -2.82]** |
| Heterogeneity: Tau² = 12.33; Chi² = 75.30, df = 12 (P < 0.00001); I² = 84% | | | | | | | | |
| Test for overall effect: Z = 4.51 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 13.41, df = 1 (P = 0.0003), I² = 92.5% | | | | | | | | |

**Figure 3.C** | Forest plots for meta-analysis of differences in children/adolescents' psychological functioning



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Self-reports** | | | | | | | | |
| Altiparmak et al., 2011 | 93 | 24 | 94 | 92.4 | 19.8 | 669 | 6.7% | 0.60 [-4.48, 5.68] |
| Danansuriya et al., 2012 | 81.3 | 12 | 115 | 89.9 | 11.5 | 142 | 9.3% | -8.60 [-11.50, -5.70] |
| Grootenhuis et al., 2007 | 89.06 | 12.38 | 26 | 93.13 | 9.63 | 913 | 7.0% | -4.07 [-8.87, 0.73] |
| Hutchings et al., 2007 | 85.57 | 14.5 | 56 | 83.73 | 16.67 | 563 | 7.9% | 1.84 [-2.20, 5.88] |
| Matterne et al., 2011 | 77.12 | 14.6 | 263 | 77.47 | 11.31 | 6244 | 10.5% | -0.35 [-2.14, 1.44] |
| Merikallio et al., 2005 | 96.2 | 10.3 | 192 | 98 | 7.8 | 1792 | 10.7% | -1.80 [-3.30, -0.30] |
| Montalto et al., 2004 | 74.74 | 15.12 | 238 | 75.9 | 15.4 | 1054 | 10.1% | -1.16 [-3.29, 0.97] |
| Sawyer et al., 2001 | 89.76 | 15.54 | 236 | 96.3 | 14.4 | 251 | 9.5% | -6.54 [-9.21, -3.87] |
| Upton et al., 2005 | 81.76 | 21.35 | 99 | 87.65 | 16.46 | 1033 | 7.5% | -5.89 [-10.21, -1.57] |
| **Subtotal (95% CI)** | | | **1319** | | | **12661** | **79.2%** | **-2.92 [-5.03, -0.81]** |
| Heterogeneity: $\text{Tau}^2 = 7.69$; $\text{Chi}^2 = 42.38$, df = 8 ($P < 0.00001$); $I^2 = 81\%$ | | | | | | | | |
| Test for overall effect: $Z = 2.71$ ($P = 0.007$) | | | | | | | | |
| **Proxy-reports** | | | | | | | | |
| Hutchings et al., 2007 | 84.6 | 20.3 | 37 | 86.4 | 16.1 | 296 | 5.0% | -1.80 [-8.59, 4.99] |
| Sawyer et al., 2001 | 88.13 | 23.1 | 236 | 95.8 | 15.3 | 1625 | 9.1% | -7.67 [-10.71, -4.63] |
| Upton et al., 2005 | 76.96 | 21.69 | 74 | 86.82 | 15.42 | 664 | 6.7% | -9.86 [-14.94, -4.78] |
| **Subtotal (95% CI)** | | | **347** | | | **2585** | **20.8%** | **-7.12 [-10.75, -3.49]** |
| Heterogeneity: $\text{Tau}^2 = 4.59$; $\text{Chi}^2 = 3.54$, df = 2 ($P = 0.17$); $I^2 = 44\%$ | | | | | | | | |
| Test for overall effect: $Z = 3.85$ ($P = 0.0001$) | | | | | | | | |
| **Total (95% CI)** | | | **1666** | | | **15246** | **100.0%** | **-3.76 [-5.80, -1.72]** |
| Heterogeneity: $\text{Tau}^2 = 9.52$; $\text{Chi}^2 = 60.43$, df = 11 ($P < 0.00001$); $I^2 = 82\%$ | | | | | | | | |
| Test for overall effect: $Z = 3.61$ ($P = 0.0003$) | | | | | | | | |
| Test for subgroup differences: $\text{Chi}^2 = 3.86$, df = 1 ($P = 0.05$), $I^2 = 74.1\%$ | | | | | | | | |

**Figure 3.D** | Forest plots for meta-analysis of differences in children/adolescents' social functioning



| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| **Self-reports** | | | | | | | | |
| Altiparmak et al., 2011 | 69 | 15 | 94 | 66 | 18.6 | 669 | 11.8% | 3.00 [-0.34, 6.34] |
| Danansuriya et al., 2012 | 69.1 | 17.1 | 115 | 87.8 | 11.2 | 142 | 11.7% | -18.70 [-22.33, -15.07] |
| Grootenhuis et al., 2007 | 87.81 | 13.16 | 26 | 89.06 | 9.63 | 913 | 11.0% | -1.25 [-6.35, 3.85] |
| Hutchings et al., 2007 | 67.54 | 23.19 | 56 | 68.99 | 23.02 | 563 | 10.2% | -1.45 [-7.81, 4.91] |
| Matterne et al., 2011 | 67.36 | 19.94 | 263 | 66.13 | 14.91 | 6244 | 12.1% | 1.23 [-1.21, 3.67] |
| Montalto et al., 2004 | 70.58 | 15.61 | 238 | 71.4 | 15.3 | 1054 | 12.2% | -0.82 [-3.01, 1.37] |
| Upton et al., 2005 | 72.37 | 19.62 | 99 | 78.87 | 15.89 | 1032 | 11.5% | -6.50 [-10.48, -2.52] |
| **Subtotal (95% CI)** | | | **891** | | | **10617** | **80.5%** | **-3.50 [-8.81, 1.82]** |
| Heterogeneity: Tau² = 47.23; Chi² = 102.43, df = 6 (P < 0.00001); I² = 94% | | | | | | | | |
| Test for overall effect: Z = 1.29 (P = 0.20) | | | | | | | | |
| **Proxy-reports** | | | | | | | | |
| Hutchings et al., 2007 | 73.1 | 26.5 | 37 | 76.2 | 26 | 296 | 8.7% | -3.10 [-12.14, 5.94] |
| Upton et al., 2005 | 69.02 | 22.55 | 74 | 81.52 | 16.09 | 664 | 10.9% | -12.50 [-17.78, -7.22] |
| **Subtotal (95% CI)** | | | **111** | | | **960** | **19.5%** | **-8.54 [-17.64, 0.55]** |
| Heterogeneity: Tau² = 29.92; Chi² = 3.10, df = 1 (P = 0.08); I² = 68% | | | | | | | | |
| Test for overall effect: Z = 1.84 (P = 0.07) | | | | | | | | |
| **Total (95% CI)** | | | **1002** | | | **11577** | **100.0%** | **-4.44 [-9.23, 0.35]** |
| Heterogeneity: Tau² = 47.80; Chi² = 115.75, df = 8 (P < 0.00001); I² = 93% | | | | | | | | |
| Test for overall effect: Z = 1.82 (P = 0.07) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I² = 0% | | | | | | | | |

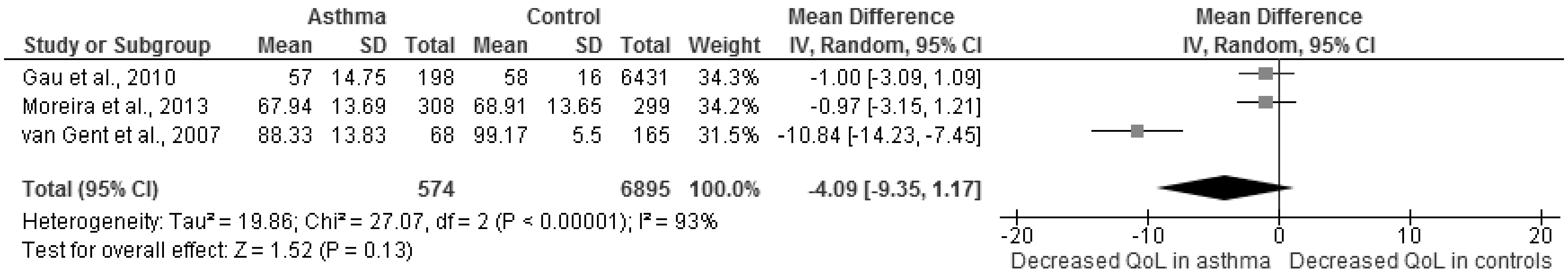
**Figure 3.E** | Forest plots for meta-analysis of differences in children/adolescents' school functioning

## Quality of life in parents of pediatric asthma patients

Data on parents' QoL outcomes were obtained from a total of 666 parents of pediatric asthma patients and 7,328 parents of community/healthy children and adolescents that were reported in four studies. Of these, three studies presented data for overall QoL (Gau et al., 2010; Moreira et al., 2013; Van Gent et al., 2007), three examined physical and psychological functioning (Gau et al., 2010; Hatzmann et al., 2008; Van Gent et al., 2007) and two assessed social functioning (Gau et al., 2010; Hatzmann et al., 2008). The results from the meta-analysis (Figures 4.A, 4.B, 4.C and 4.D) showed that parents of pediatric asthma patients had significantly impaired physical functioning when compared to parents of community/healthy children and adolescents (MD = -10.15, 95% CI = -12.21/ -8.08, $p < .001$), with low heterogeneity across the three included studies ($I^2$ = 32%). Conversely, pooled estimates indicated no significant differences for parents' overall QoL (MD = -4.09, 95% CI = -9.35/ 1.17, $p = .13$), psychological functioning (MD = -6.60, 95% CI = -14.10/ 0.91, $p = .08$) or social functioning (MD = -1.84, 95% CI = -4.37/ 0.69, $p = .15$), but high heterogeneity across studies was observed for overall QoL ($I^2$ = 93%) and psychological functioning ($I^2$ = 94%).

## Subgroup analyses

Table 3 presents the results for subgroup analyses by informant (self- *vs.* proxy-report), age group (children aged 7-12 years with a mean age ≤ 10 years *vs.* adolescents aged 11-18 years with a mean age ≥ 13 years), type of controls (healthy controls *vs.* community controls) and quality rating (high quality *vs.* medium quality) for children's and adolescents' QoL outcomes. The high heterogeneity across studies was explained by informants and controls' health status. Specifically, studies that relied on parent-reports presented significantly decreased children/adolescents' psychological and social functioning than studies based on patient-reported measures (Figures 3.C and 3.D). Moreover, greater impairments were found for physical, psychological, and school functioning of children and adolescents with asthma (although only marginally significant for the last two domains) when studies compared them to healthy controls with no history of chronic conditions, than when studies selected community children and adolescents without asthma as controls, without adjusting for the presence of other health conditions. No significant differences were observed between subgroups of studies according to age group or quality rating. The forest plots for subgroup differences are presented in Supplementary Material, Figures S1-S3.

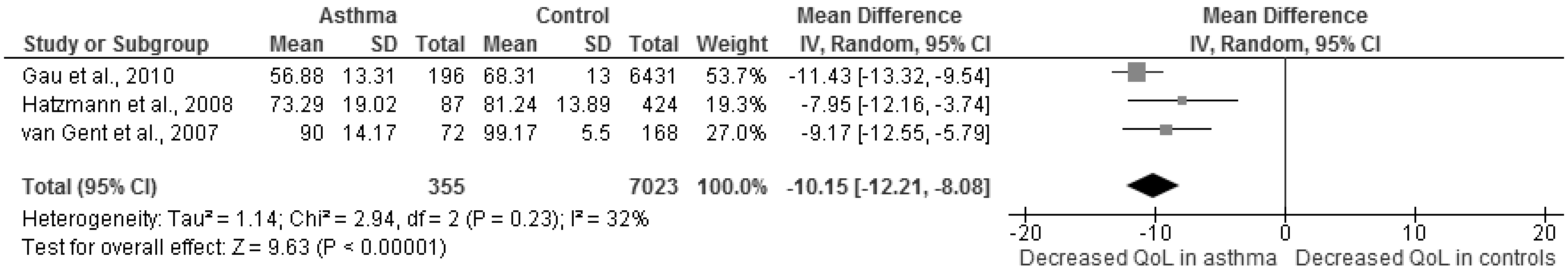


| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| Gau et al., 2010 | 57 | 14.75 | 198 | 58 | 16 | 6431 | 34.3% | -1.00 [-3.09, 1.09] |
| Moreira et al., 2013 | 67.94 | 13.69 | 308 | 68.91 | 13.65 | 299 | 34.2% | -0.97 [-3.15, 1.21] |
| van Gent et al., 2007 | 88.33 | 13.83 | 68 | 99.17 | 5.5 | 165 | 31.5% | -10.84 [-14.23, -7.45] |
| **Total (95% CI)** | | | **574** | | | **6895** | **100.0%** | **-4.09 [-9.35, 1.17]** |

Heterogeneity: Tau² = 19.86; Chi² = 27.07, df = 2 (P < 0.00001); I² = 93%

Test for overall effect: Z = 1.52 (P = 0.13)

**Figure 4.A** | Forest plots for meta-analysis of differences in parents' overall QoL

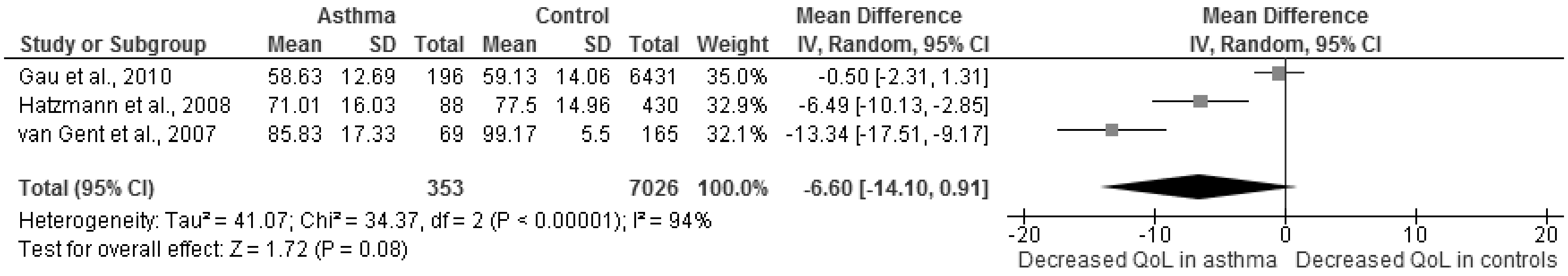


| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| Gau et al., 2010 | 56.88 | 13.31 | 196 | 68.31 | 13 | 6431 | 53.7% | -11.43 [-13.32, -9.54] |
| Hatzmann et al., 2008 | 73.29 | 19.02 | 87 | 81.24 | 13.89 | 424 | 19.3% | -7.95 [-12.16, -3.74] |
| van Gent et al., 2007 | 90 | 14.17 | 72 | 99.17 | 5.5 | 168 | 27.0% | -9.17 [-12.55, -5.79] |
| **Total (95% CI)** | | | **355** | | | **7023** | **100.0%** | **-10.15 [-12.21, -8.08]** |

Heterogeneity: Tau² = 1.14; Chi² = 2.94, df = 2 (P = 0.23); I² = 32%

Test for overall effect: Z = 9.63 (P < 0.00001)

**Figure 4.B** | Forest plots for meta-analysis of differences in parents' physical functioning

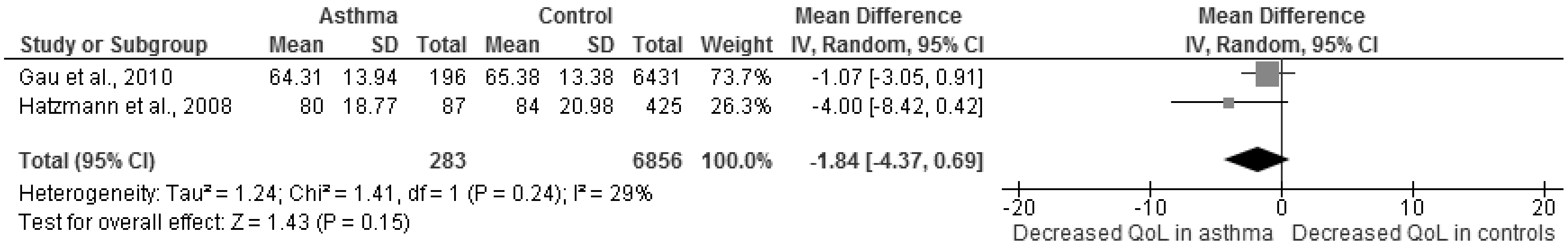


| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Gau et al., 2010 | 58.63 | 12.69 | 196 | 59.13 | 14.06 | 6431 | 35.0% | -0.50 [-2.31, 1.31] |
| Hatzmann et al., 2008 | 71.01 | 16.03 | 88 | 77.5 | 14.96 | 430 | 32.9% | -6.49 [-10.13, -2.85] |
| van Gent et al., 2007 | 85.83 | 17.33 | 69 | 99.17 | 5.5 | 165 | 32.1% | -13.34 [-17.51, -9.17] |
| **Total (95% CI)** | | | **353** | | | **7026** | **100.0%** | **-6.60 [-14.10, 0.91]** |

Heterogeneity: $Tau^2 = 41.07$; $Chi^2 = 34.37$, df = 2 ($P < 0.00001$); $I^2 = 94\%$

Test for overall effect: Z = 1.72 (P = 0.08)

**Figure 4.C** | Forest plots for meta-analysis of differences in parents' psychological functioning



| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Gau et al., 2010 | 64.31 | 13.94 | 196 | 65.38 | 13.38 | 6431 | 73.7% | -1.07 [-3.05, 0.91] |
| Hatzmann et al., 2008 | 80 | 18.77 | 87 | 84 | 20.98 | 425 | 26.3% | -4.00 [-8.42, 0.42] |
| **Total (95% CI)** | | | **283** | | | **6856** | **100.0%** | **-1.84 [-4.37, 0.69]** |

Heterogeneity: $Tau^2 = 1.24$; $Chi^2 = 1.41$, df = 1 ($P = 0.24$); $I^2 = 29\%$

Test for overall effect: Z = 1.43 (P = 0.15)

**Figure 4.D** | Forest plots for meta-analysis of differences in parents' social functioning

**Table 3** | Children/adolescents' QoL according to subgroup analyses

| | *Informants* | | *Age group* | | *Type of controls* | | *Methodological quality* | |
|---|---|---|---|---|---|---|---|---|
| **Outcome** | Self-reports | Proxy-reports | Children | Adolescents | Healthy | Community | High | Average |
| Overall QoL | | | | | | | | |
| Number of studies | 9 | 3 | 3 | 5 | 4 | 5 | 4 | 5 |
| MD | -6.55 | -10.32 | -7.76 | -3.27 | -9.72 | -4.16 | -3.91 | -8.72 |
| 95% CI | [-10.40/ -2.71] | [-16.39/ -4.25] | [-17.85/ 2.33] | [-8.35/ 1.81] | [-18.78/ -0.65] | [-7.65/ -0.68] | [-8.75/ 0.93] | [-14.79/ -2.65] |
| $\chi^2$ | 1.06 | | 0.61 | | 1.25 | | 1.48 | |
| Physical functioning | | | | | | | | |
| Number of studies | 11 | 3 | 4 | 4 | 6 | 5 | 3 | 8 |
| MD | -8.15 | -16.24 | -10.38 | -5.59 | -13.20 | -3.14 | -5.63 | -9.57 |
| 95% CI | [-10.76/ -5.55] | [-28.41/ -4.07] | [-18.26/ -2.50] | [-9.12/ -2.07] | [-20.22/ -6.17] | [-4.19/ -2.10] | [-10.07/ -1.19] | [-13.49/ -5.65] |
| $\chi^2$ | 1.62 | | 1.18 | | **7.70**$^{**}$ | | 1.70 | |
| Psychological functioning | | | | | | | | |
| Number of studies | 10 | 3 | 3 | 4 | 5 | 5 | 3 | 7 |
| MD | -3.77 | -9.27 | -5.51 | -2.73 | -5.80 | -2.40 | -3.56 | -3.88 |
| 95% CI | [-5.68/ -1.87] | [-11.52/ -7.03] | [-10.90/ -0.13] | [-5.38/ -0.09] | [-9.51/ -2.09] | [-3.93/ -0.87] | [-6.78/ -0.34] | [-6.47/ -1.30] |
| $\chi^2$ | **13.41**$^{**}$ | | 0.82 | | **2.76**$^{\dagger}$ | | 0.02 | |
| Social functioning | | | | | | | | |
| Number of studies | 9 | 3 | 2 | 4 | 4 | 5 | 3 | 6 |
| MD | -2.92 | -7.12 | -1.79 | -2.66 | -4.28 | -1.98 | -1.92 | -3.18 |
| 95% CI | [-5.03/ -0.81] | [-10.75/ -3.49] | [-4.14/ 0.56] | [-6.02/ 0.71] | [-9.00/ 0.44] | [-4.01/ 0.04] | [-4.06/ 0.23] | [-6.52/ 0.16] |
| $\chi^2$ | **3.86**$^{*}$ | | 0.17 | | 0.77 | | 0.39 | |
| School functioning | | | | | | | | |
| Number of studies | 7 | 2 | 2 | 3 | 4 | 3 | 2 | 5 |
| MD | -3.50 | -8.54 | -0.89 | -4.78 | -7.16 | 0.86 | -2.47 | -3.88 |
| 95% CI | [-8.81/ 1.82] | [-17.64/ 0.55] | [-2.90/ 1.12] | [-17.19/ 7.63] | [-15.86/ 1.54] | [-1.22/ 2.95] | [-10.04/ 5.10] | [-11.62/ 3.86] |
| $\chi^2$ | 0.88 | | 0.37 | | **3.09**$^{\dagger}$ | | 0.07 | |

CI – confidence interval; MD – mean difference

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$; $^{\dagger}$ $p \leq .10$

# Discussion

## Summary of evidence

This is the first meta-analytic review to gather comparative studies of QoL outcomes between pediatric asthma patients or their parents and community/healthy controls. The results from the meta-analyses showed that children and adolescents with asthma are at a greater risk for decreased QoL than their peers without asthma, particularly in physical, psychological, and social domains. Parents of children and adolescents with asthma also presented diminished QoL, but only in the physical domain. These results were strengthened by the ascertainment of type of informant (self- or proxy-reports) and controls' health status as methodological features explaining the heterogeneous results across studies.

The deleterious effect of asthma on children's and adolescents' QoL is consistent with previous research on other psychosocial adaptation outcomes. A previous meta-analysis on behavioral adjustment described a higher risk for internalizing and externalizing problems among pediatric asthma patients compared to healthy controls or normative data (McQuaid, Kopel, & Nassau, 2001). However, the broad CI associated with differences in QoL mean scores between asthma and control groups that were found in most studies included in this meta-analysis reveal considerable within-studies variability, which suggests that children and adolescents with asthma may experience different levels of QoL impairments.

Pooled results also showed high between-studies heterogeneity, which was partially explained by the informant of pediatric QoL. A major trend for using self-report measures was observed; however, studies that relied on parent-reports as proxies identified larger impairments in children's and adolescents' psychological and social functioning than studies that used self-report measures. A previous systematic review on parent-child agreement in the context of pediatric chronic conditions had shown that parents were more likely to underrate pediatric QoL than children and adolescents themselves, with lower levels of agreement for non-observable domains, such as emotional or social QoL (Eiser & Morse, 2001). On the one hand, these findings may reflect a bias resulting from parents' expectations and concerns; on the other hand, parents may be more reliable in detecting psychosocial problems associated with pediatric asthma – the so-called "hidden morbidities" (Varni, Burwinkle, & Lane, 2005).

Between-studies heterogeneity was also explained by controls' health status as there were greater differences on physical, psychological and school functioning in studies that compared pediatric asthma patients to healthy controls than in studies that selected community children and adolescents without asthma as controls. Over recent years, technological advances in medicine have resulted in increased survival rates and greater prevalence of chronic conditions in childhood and adolescence (Varni, Limbers, & Burwinkle, 2007). Consequently, community samples are likely to include a number of children and adolescents with other chronic conditions and QoL impairments, which may bring the QoL scores of community and asthma groups closer, thus leading to a lower magnitude of differences.

For parents' QoL, the existing studies are too scarce to draw robust conclusions. However, the few included studies consistently reported decreased physical functioning among parents of children and adolescents with asthma in comparison to parents of community/healthy children and adolescents. On the one hand, the decreased physical functioning may reflect asthma morbidity in the parents since asthma has a heritable component with an overall prevalence above 13% in the first-degree relatives of pediatric asthma patients (Sibbald, Horn, Brain, & Gregg, 1980). On the other hand, the burden of caring for a child with asthma may affect parents' everyday life and functioning, particularly in terms of lower quantity and quality of sleep, greater daytime fatigue, and poorer work attendance and productivity (Fiese, Winter, Anbar, Howell, & Poltrock, 2008; Raina et al., 2004). Conversely, no significant differences were found for psychological and social domains, but high levels of between-studies heterogeneity were observed.

## Limitations

Some limitations at the individual study and review levels should be acknowledged. First, diverse QoL measures were used across studies, resulting in a dissimilar methodological operationalization of the QoL construct in terms of number and content of items and response scales. Moreover, the minimally important difference, i.e., the smallest difference/change in an outcome measure perceived, on average, as beneficial by the patients (Guyatt, Osoba, Wu, Wyrwich, & Norman, 2002) was not established for the great majority of QoL measures. Even if a half standard deviation has been acknowledged as a "universal" threshold of discrimination for differences/changes in health-related QoL (Norman, Sloan, & Wyrwich, 2003), the minimally important difference is likely to vary across clinical and demographic characteristics of the sample and across instruments with dissimilar measurement properties (e.g., different number of items, floor and ceiling effects, etc.; Thorlund et al., 2011). In this meta-analytic review, variability in outcome measures was addressed by performing distinct meta-analyses for QoL total scores and each domain of functioning and converting response scales into standardized scores to allow comparability across QoL domains. Future research should translate and adapt the existing reliable and valid measures to facilitate cross-cultural comparisons and determine the minimally important difference for patient-reported outcomes to enhance interpretability in both clinical trials and meta-analyses.

Second, our results should be interpreted with caution due to high levels of between-studies heterogeneity. Participant and methodological diversity was addressed by using random-effects models and subgroup analyses by informant, age group, type of controls and quality rating. However, because of the different criteria for clustering asthma clinical groups that were used across studies, we were unable to explore asthma severity and control levels as potential factors explaining heterogeneity. Additionally, despite the high heterogeneity observed for parents' overall QoL and psychological functioning, subgroup analyses could not be performed because at least one of the subgroups would have only one study.

Finally, our literature search was restricted to English-language articles and the "grey literature" was not considered, which may have introduced publication bias. However, the small number of studies included in each meta-analysis limited the use of tests for detecting funnel plots asymmetry because they have low power to distinguish chance from real asymmetry when there are less than 10 studies (Egger, Davey Smith, Schneider, & Minder, 1997; Higgins & Green, 2008).

## Implications for research and clinical practice

The ascertainment of the magnitude of QoL impairments and the identification of the most affected QoL domains among children and adolescents with asthma and their parents, in comparison to community/healthy controls, has important implications for research and clinical practice. First, the QoL of pediatric asthma patients and their parents should be routinely assessed in pediatric healthcare services and included as a broad-ranging outcome in clinical trials. For assessing pediatric QoL, our findings reiterate the need to include self- and parent-reports as complementary sources of information and the importance of selecting reliable and valid, age-appropriate and cross-culturally comparable measures. Even if single-index measures may be attractive as screening tools in clinical and research contexts due to their small number of items, our results suggest that profile measures covering physical, psychological and social functioning may be more sensitive in detecting the most impaired areas of patients' and parents' QoL.

Second, further case-control studies on QoL outcomes are required in the pediatric asthma context, especially for parents' QoL. Future comparative research should carefully select healthy controls and avoid using community samples or normative data, and also adjust for potential clinical and socio-demographic confounders. Moreover, it is urgent to disseminate valid procedures for assessing asthma clinical characteristics that can be used worldwide, such as the Global Initiative for Asthma guidelines (GINA, 2008), to enable cross-cultural comparisons by asthma severity and control levels.

Third, research can now move from merely descriptive and comparative studies to the examination of adaptation processes explaining within-studies heterogeneity. Addressing the complex interactions between disease-related risks and resistance factors, namely, family functioning, social support and coping strategies, may contribute to explain the variability in children/adolescents' and parents' QoL outcomes (Wallander, Pitt, & Mellins, 1990; Wallander, Varni, Babani, Banis, & Wilcox, 1989).

Finally, the identification of specific domains of decreased functioning can assist healthcare providers to cost-effectively allocate resources, define appropriate goals for multidisciplinary interventions and evaluate its effectiveness. Preliminary evidence for the efficacy of psychosocial interventions in children/adolescents with asthma (e.g., cognitive-behavioral therapies, relaxation techniques, supportive counseling), in addition to pharmacological treatments, was found for a variety of adaptation outcomes (Yorke, Fleming, & Shuldham, 2005). Psychosocial interventions in pediatric settings should also aim to reduce the parental burden of caring for a child with asthma and improve physical well-being. Family functioning, social support and coping strategies (Wallander et al., 1989; Wallander et al., 1990) are specific intervention targets that can moderate the impact of asthma on children/adolescents' and their parents' QoL outcomes.

## Conclusion

Over the past couple of decades, a number of descriptive studies have been conducted to characterize the QoL outcomes of pediatric asthma patients, in comparison to healthy or community children and adolescents. Current evidence, as based on a meta-analysis of those results, indicates that children and adolescents with asthma are at a greater risk for impairments in overall QoL and present lower levels of physical, psychological and social functioning, in comparison to community/healthy controls. Complementarily, a synthesis of results observed in studies addressing the assessment of QoL outcomes in parents who have children with asthma points to a more impaired QoL in the physical domain, which generally encompasses those facets related to sleep, fatigue and work attendance/productivity, in comparison to controls. QoL outcomes research conducted in the context of pediatric asthma has been marked by a preferred use of self-reported measures; however, larger QoL impairments tend to be observed in studies that employed proxy-report measures. Pediatric QoL differences also tend to be larger in comparative studies that used healthy controls instead of general community controls. Taken altogether, these results illustrate the decisive need of incorporating a parent-child perspective in assessment and intervention processes targeting the QoL of pediatric patients with asthma.

Research conducted over the past 20 years on the QoL of children with asthma and their parents enabled the ascertainment of QoL impairments for this pediatric group. The challenge is now to move from outcomes description to QoL outcomes prediction. In this line of thought, the research on QoL in pediatric asthma is expected to flourish in the years to come, with an increased number of studies examining bio-psycho-social mediating pathways for QoL outcomes, while incorporating a dyadic parent-child perspective in their designs. To improve their clinical and ecological validity, those studies must increase their methodological complexity by optimally including multiple informants, examining individual and family levels of analysis, and crossing biological and psychosocial variables. Hopefully, a greater substantiation of a parent-child perspective in QoL research for pediatric asthma will result in a greater number of studies simultaneously employing self- and proxy-reports and linking the children's and their parents' adaptation processes and outcomes.

## Key issues

- The large amount of papers on quality of life (QoL) of children/adolescents with asthma and/or their parents that were published in the past 20 years illustrates the growing importance of QoL as an essential endpoint in pediatric research and healthcare contexts.
- Children and adolescents with asthma are at a greater risk for decreased QoL, in general, and physical, psychological and social functioning, in particular, compared to their peers without asthma.
- A major trend for using self-report QoL measures was observed across studies; however, patient- and parent-reports provide different but complementary data, and thus a multi-informant approach to pediatric QoL assessment is recommended.
- Over the past two decades, there has been a proliferation of instruments specifically designed for QoL assessment in children and adolescents, resulting in a dissimilar methodological operationalization of the QoL construct and hindering cross-cultural comparisons.
- Apart from the type of informants and the health status of controls, the severity of the underlying disease and responsiveness to treatments may contribute to explain the high levels of between-studies heterogeneity; however, the different criteria that were used across studies for clustering asthma clinical groups prevented the examination of clinical variables in this meta-analysis.
- The QoL of parents of children/adolescents with asthma has been understudied; still, the few studies examining their QoL in relation to parents of healthy children

consistently indicate QoL impairments in the physical domain.

- The ascertainment of the magnitude of QoL impairments and the identification of the most affected QoL domains among pediatric asthma patients and their parents may contribute to outline realistic goals for medical treatments and psychosocial interventions and to evaluate its cost-effectiveness.
- Research can now move from descriptive studies to the examination of risk and resistance factors underpinning the adaptation processes to explain the within-study variability in children/adolescents’ and their parents’ QoL outcomes.

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# Supplementary Material

**Table S1** | Quality ratings for the 19 studies included in the systematic review using an adapted version of the Newcastle-Ottawa Quality assessment scale

| ***Study*** | ***Selection of participants*** [a] | | | | | ***Comparability*** [b] | ***Ascertainment of QoL*** [c] | | | ***Overall quality rating*** [d] |
|---|---|---|---|---|---|---|---|---|---|---|
| | Case definition | Representativeness | Definition of controls | Selection of controls | Response rate | | Measures | Informants | Procedures | |
| Altiparmak et al., 2011 | Asthma diagnosed by a doctor ★ | Stratified random + cluster sampling methods ★ | NR | Community controls, within the same schools as cases ★ | NR | No control for confounding variables | Kiddo-KINDL (Cronbach's α for the Turkish version: .78) ★ | Adolescents ★ | Same procedures for assessment of cases and controls ★ | 6 (average) |
| Covaciu et al., 2013 | Asthma defined as 4 episodes of wheeze or at least 1 episode of wheeze in combination with prescribed inhaled steroids in the last 12 months ★ | NR | NR | Community controls, with-in the same community as cases ★ | 84% (total sample at the 8-year follow-up) ★ | The study controls for hereditary for allergy, sex, being a first born child and having a young mother ★ | EuroQoL-5D (psychometric properties not reported for the Swedish children) | Parents | Same procedures for assessment of cases and controls ★ | 5 (average) |
| Danansuriya et al., 2012 | Asthma diagnosis made by a physician ★ | Consecutive cases from 4 hospitals selected on convenience basis ★ | Healthy controls, with no physical or mental disabilities, chronic conditions or acute severe illness ★ | Community controls randomly selected from schools ★ | 91.1% (control group) | No control for confounding variables | PedsQL™ 4.0 Generic Core Scales (Cronbach's α for the Sinhala version: .85) ★ | Adolescents ★ | Cases were assessed at the clinics in the presence of researchers; controls were assessed at classroom | 6 (average) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| French et al., 1994 | Current diagnosis of asthma and/or recent prescription for asthma medication ★ | NR | Healthy controls, with no chronic illnesses ★ | Community controls from the same schools as 20% of cases ★ | 72% (test-retest for cases) | No control for confounding variables | CAQ-Form B (Cronbach's α between .44 and .82 for cases and between .21 and .69 for controls) | Children ★ | 80% of the cases were contacted through their doctor and assessed at home; 20% of the cases and controls completed questionnaires at classroom, supervised by 2 researchers | 4 (average) |
| French et al., 1998 | Asthma diagnosis based on medical (64%) or school records (36%) ★ | NR | Community controls without asthma (other comorbidities not reported) | Community controls from the same schools as 36% of cases ★ | 32% for cases recruited at the Asthma Foundation of Western Australia; 79% for the school sample | No control for confounding variables | CAQ-Form B (Cronbach's α between .62 and .76);<br>CAQ-Form C (Cronbach's α between .71 and .76) ★ | Children ★ | Cases recruited from the Asthma Foundation received and returned the questionnaires by post; the school sample was assessed in classrooms under the supervision of a researcher | 4 (average) |
| Gau et al., 2010 | Asthma cases referred by a pediatric immunologist ★ | Convenience sample | NR | Female participants aged 21-54 years from the nationwide Taiwan community ★ | 95.4% (cases);<br>93.8% (controls) ★ | No control for confounding variables | WHOQOL-BREF (Cronbach's α between .53 and .86 for cases and between .68 and .76 for controls) ★ | Parents ★ | Cases completed the questionnaires during a schedule clinical visit; Data collection method for controls was not described | 5 (average) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Grootenhuis et al., 2007 | NR | Cases selected by convenience at 2 healthcare institutions | Healthy controls, with no history of chronic disease ★ | Dutch school-going children aged 8-11 years (data from the original TACQoL study) ★ | NR | No control for confounding variables | TACQoL (Cronbach's α values in the original Dutch study ranged from .60 to .90) ★ | Children ★ | Patients completed the questionnaires in the waiting room of the outpatient clinic; Data collection method for controls was not described | 4 (average) |
| Hallstrand et al., 2003 | Asthma diagnosis based on interviews, self-report questionnaires and exercise challenge tests followed by spirometry ★ | NR | Controls with no prior diagnosis of asthma | Adolescent athletes from the same three suburban western Washington schools as cases ★ | 62.5% (total sample; non-respondents were described) | No control for confounding variables | PedsQL™ 3.0 Generic Core Scales (Cronbach's α for the core items in the original study: .83) ★ | Adolescents ★ | Same procedures for assessment of cases and controls ★ | 5 (average) |
| Hatzmann et al., 2008 | NR | NR | Parents of children/ adolescents with no chronic illnesses ★ | Controls recruited from schools in the same geographic area as cases ★ | 91.9% (total sample) ★ | Cases and controls were comparable with regard parents' age, sex, marital status, educational level, and number of children ★ | TAAQoL (Cronbach's α value in this study ranged from .60 to .96) ★ | Parents ★ | Same procedures for assessment of cases and controls ★ | 7 (average) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Hutchings et al., 2007, 2008 | Asthma diagnosis made by a clinician according to the British Thoracic Society ★ | NR | Healthy children/adolescents without health problems and not currently using healthcare resources ★ | Convenience sample recruited from local schools ★ | 64.2% (total sample) | No control for confounding variables | MMQL- Youth Form (Cronbach's α values between .72 and .90)<br>MMQL- Parent Form (Cronbach's α values between .75 and .93) ★ | Children/adolescents and parents ★★ | Cases completed the questionnaires either in clinic or at home; controls completed the questionnaires in the classroom under the supervision of a researcher | 6 (average) |
| Kojima et al., 2009 | Asthma diagnosis based on self-report questions | Random sample of 10% of the total population of adolescents in the 8th grade ★ | NR | Community controls from the same randomly selected schools as cases ★ | 64.0% (total sample) | No control for confounding variables | Kiddo-KINDL (psychometric properties for the Japanese version not reported) | Adolescents ★ | Same procedures for assessment of cases and controls ★ | 4 (average) |
| Matterne et al., 2011 | Asthma was defined based on parents' reports of a medical diagnosis in the last 12 months ★ | Representative sample of children and adolescents in 167 communities in Germany (data from the KiGGS study) ★ | NR | Representative sample of children and adolescents in the same communities as cases ★ | 66.6% (total sample) | The study controls for age, sex, country of origin, SES, weight, and presence of mental health problems ★★ | KINDL-R (Cronbach's α in the original psychometric study was .82 for the total score and ranged from .53 to .72 for sub-scales) ★ | Adolescents ★ | Same procedures for assessment of cases and controls ★ | 8 (high) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Merikallio et al., 2005 | Parent's reports of asthma diagnosed by a doctor ★ | Cases recruited from 175 randomly selected school classes ★ | Controls with no history of wheezing attacks or asthma diagnosis | Controls recruited from the same randomly selected school classes as cases ★ | 60% (total sample) | The study controls for age, sex, geographical area, SES, family size, death/divorce in the family, smoking of the child and presence of other serious illnesses of the child ★★ | CHQ-Child form (Cronbach's α for the Finish version was .94 for the total score and ranged from .65 to .84 for domains) ★ | Adolescents ★ | Same procedures for assessment of cases and controls ★ | 8 (high) |
| Montalto et al., 2004 | Asthma diagnosis based on parent-report questionnaire | All 3rd and 4th grade students attending 6 elementary schools ★ | NR | Controls recruited from the same schools as cases ★ | 72% (total sample) | The study controls for sex and ethnicity ★ | KINDL (psychometric properties for the modified version used in this study were not reported) | Children ★ | Same procedures for assessment of cases and controls (both cases and controls completed the survey in school) ★ | 5 (average) |
| Moreira et al., 2013 | Asthma diagnosis made by a physician ★ | Convenience sample recruited in 3 healthcare institutions | Controls with no history of chronic health conditions or developmental delay ★ | Controls recruited in 2 regular schools in the same geographic area as cases ★ | NR | The study controls for age and sex ★★ | KIDSCREEN-10 Index (Cronbach's α value in this study was .77)<br>EUROHIS-QoL-8 Index (Cronbach's α value was .83) ★ | Children/ adolescents and parents ★★ | Cases completed the questionnaires in the health, supervised by a researcher; controls completed the questionnaires in the classroom | 8 (high) |

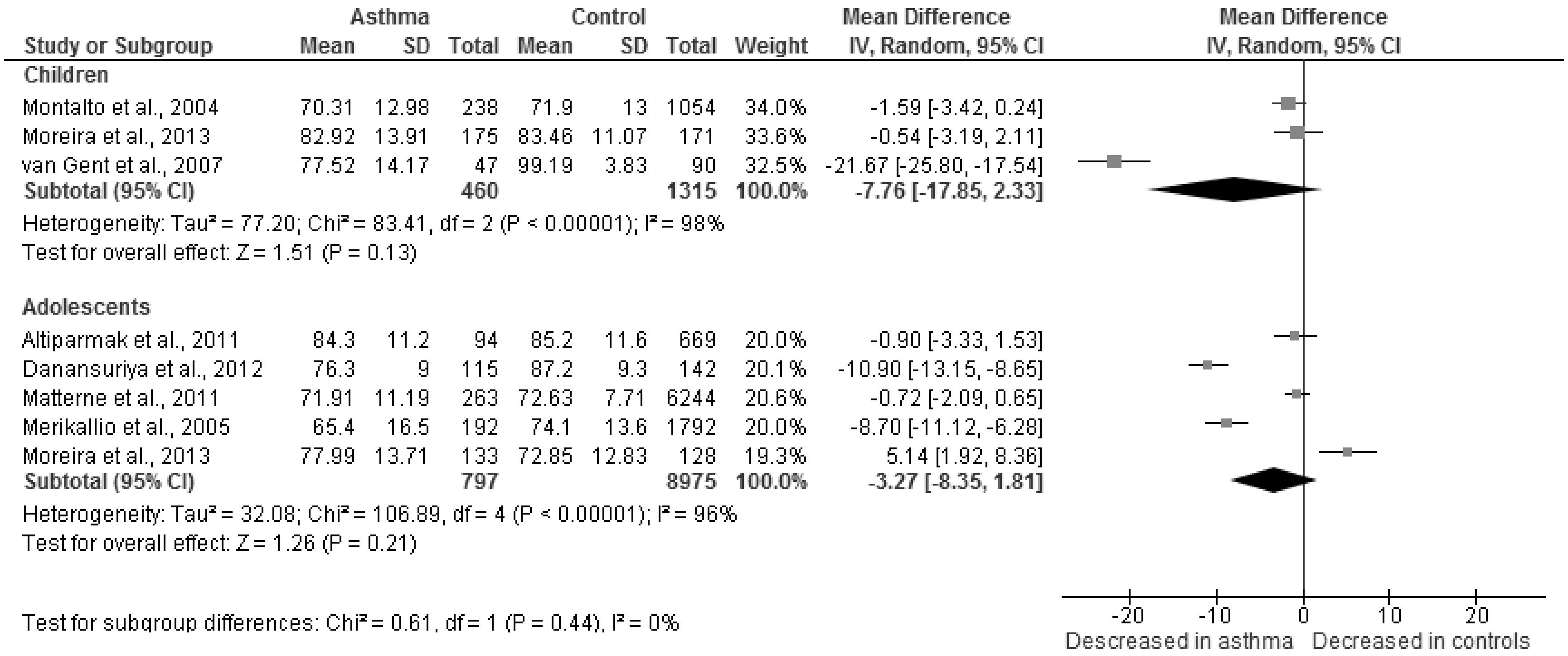
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sawyer et al., 2001 | Asthma diagnosis based on parent-report questionnaire | Random sample of 59 schools ★ | NR | Controls randomly selected across Australia (sample from the National Child and Adolescent Mental Health Survey) ★ | 79% (for cases) | No control for confounding variables | CHQ-Child form and CHQ-Parent form (psychometric properties in this study were not reported) | Children and parents ★★ | Cases completed the questionnaires during home visits; Data collection method for controls was not described | 4 (average) |
| Upton et al., 2005 | Cases were identified based on medical records ★ | NR | Healthy controls with no chronic health problems ★ | Healthy controls recruited from 23 schools in South Wales ★ | 58.97% for cases; 74.77% for controls | The study controls for age and sex ★★ | PedsQL™ 4.0 Generic Core Scales (Cronbach's α values exceeded .70 for all self- and proxy-report sub-scales and .90 for the total score) ★ | Children/adolescents and parents ★★ | Cases completed the questionnaires either in clinic or at home under the supervision of a researcher; controls completed the questionnaires in class, under the supervision of a researcher | 8 (high) |
| Van Gent et al., 2007 | Asthma diagnosis based on parents' reports of physician-diagnosed asthma in the last 12 months ★ | All eligible cases in 41 primary schools ★ | Healthy controls with no asthma diagnosis or symptoms in the last 12 months and no reversible airway obstruction | Controls were randomly selected from the same schools as cases ★ | 64% (total sample) | The study controls for body weight ★ | PAQLQ<br>PACQLQ<br>(psychometric properties in this study were not reported) | Children and parents ★★ | Same procedures for assessment of cases and controls ★ | 7 (average) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Wang et al., 2012 | Asthma diagnosis based on Global Initiative for Asthma (2005) and peak expiratory flow (PEF) ★ | NR | Healthy controls without any severe progressive neurological diseases or systemic disorders ★ | Controls were selected from the same outpatient units as cases ★ | NR | No significant differences on sex, age, education level or family size were found between cases and controls ★★ | MOS-SF-36 (psychometric properties not reported for the asthma group) | Adolescents ★ | NR | 6 (average) |

CAQ – Childhood Asthma Questionnaire; CHQ – Child Health Questionnaire; MMQL – Minneapolis-Manchester Quality of Life instrument; MOS-SF-36 – Medical Outcomes Study-Short Form; NR – not reported; PACQLQ - Pediatric Asthma Caregiver's Quality of Life Questionnaire; PAQLQ – Pediatric Asthma Quality of Life Questionnaire; SES – Socio-economic status; TAAQoL – TNO-AZL Questionnaire for Adult's HrQoL; TACQoL – TNO-AZL Children's Quality of Life questionnaire; WHOQOL-BREF – World Health Organization Quality of Life Assessment - Abbreviated version; ★ = 1 point

[a] For selection of participants, 1 point was allotted for adequate definition of cases (i.e., asthma diagnosis established by a physician, based on medical records or physiological indicators), 1 point if the study reports on a random sample of patients, all eligible patients in a defined healthcare/educational institution or consecutive series of patients over a defined period of time, 1 point for adequate definition of healthy controls with no history of chronic health conditions, 1 point for selection of controls within the same community/geographic area as cases, and 1 point if the response rate was similar for cases and controls or > 80% for the total sample. [b] For comparability, 1 point was allotted if the study controls for children/adolescents' age, and 1 point if the study controls for any additional confounders. [c] For ascertainment of quality of life, 1 point was allotted for use of reliable, valid and age-appropriate measures, 1 point for use of patients' or parents' self-reported outcomes or 2 for inclusion of both patients and parents, and 1 point for use of the same method of ascertainment for cases and controls. [d] Studies can be awarded a maximum of 11 points: 0-3 points = low quality; 4-7 points = average quality; 8-11 points = high quality.

# Supplementary Material

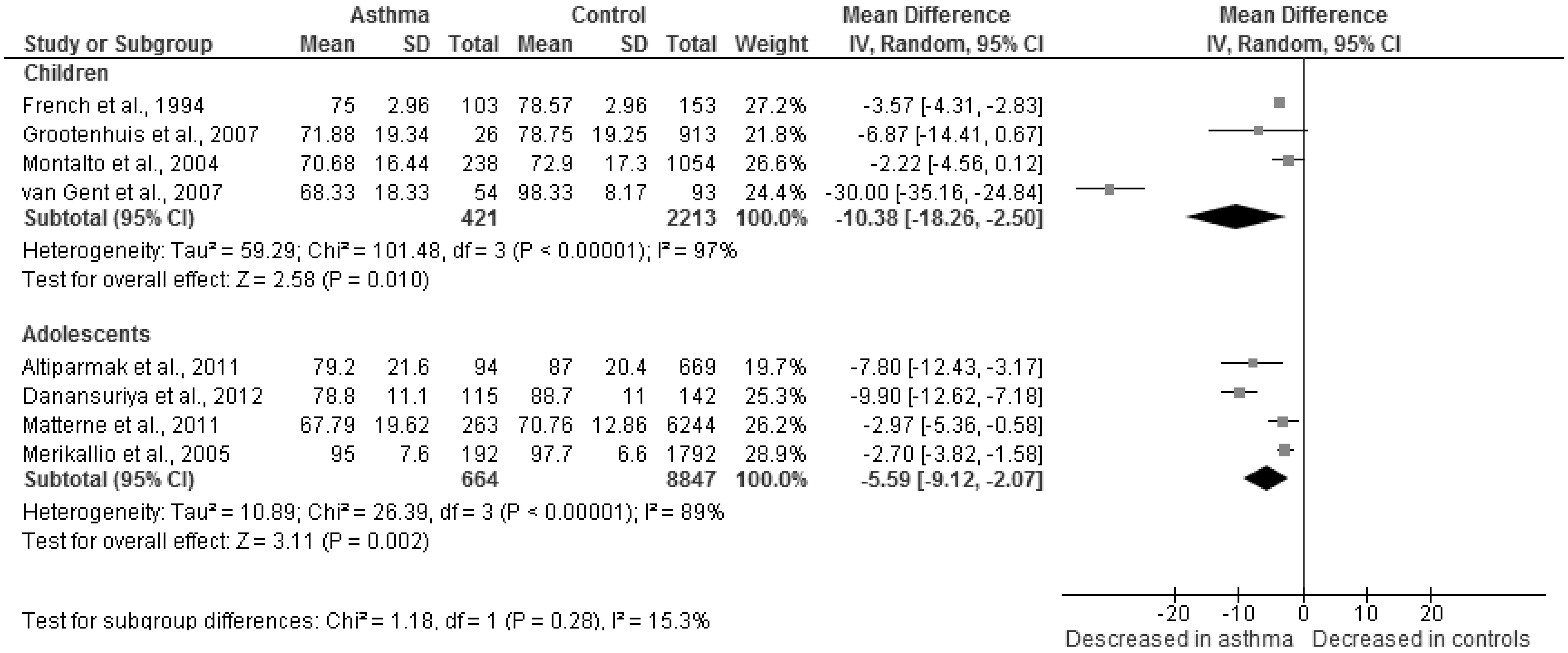


|  | Asthma |  |  | Control |  |  |  | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| **Children** |  |  |  |  |  |  |  |  |
| Montalto et al., 2004 | 70.31 | 12.98 | 238 | 71.9 | 13 | 1054 | 34.0% | -1.59 [-3.42, 0.24] |
| Moreira et al., 2013 | 82.92 | 13.91 | 175 | 83.46 | 11.07 | 171 | 33.6% | -0.54 [-3.19, 2.11] |
| van Gent et al., 2007 | 77.52 | 14.17 | 47 | 99.19 | 3.83 | 90 | 32.5% | -21.67 [-25.80, -17.54] |
| **Subtotal (95% CI)** |  |  | **460** |  |  | **1315** | **100.0%** | **-7.76 [-17.85, 2.33]** |
| Heterogeneity: $\text{Tau}^2 = 77.20$; $\text{Chi}^2 = 83.41$, df = 2 ($P < 0.00001$); $I^2 = 98\%$ |  |  |  |  |  |  |  |  |
| Test for overall effect: $Z = 1.51$ ($P = 0.13$) |  |  |  |  |  |  |  |  |
| **Adolescents** |  |  |  |  |  |  |  |  |
| Altiparmak et al., 2011 | 84.3 | 11.2 | 94 | 85.2 | 11.6 | 669 | 20.0% | -0.90 [-3.33, 1.53] |
| Danansuriya et al., 2012 | 76.3 | 9 | 115 | 87.2 | 9.3 | 142 | 20.1% | -10.90 [-13.15, -8.65] |
| Matterne et al., 2011 | 71.91 | 11.19 | 263 | 72.63 | 7.71 | 6244 | 20.6% | -0.72 [-2.09, 0.65] |
| Merikallio et al., 2005 | 65.4 | 16.5 | 192 | 74.1 | 13.6 | 1792 | 20.0% | -8.70 [-11.12, -6.28] |
| Moreira et al., 2013 | 77.99 | 13.71 | 133 | 72.85 | 12.83 | 128 | 19.3% | 5.14 [1.92, 8.36] |
| **Subtotal (95% CI)** |  |  | **797** |  |  | **8975** | **100.0%** | **-3.27 [-8.35, 1.81]** |
| Heterogeneity: $\text{Tau}^2 = 32.08$; $\text{Chi}^2 = 106.89$, df = 4 ($P < 0.00001$); $I^2 = 96\%$ |  |  |  |  |  |  |  |  |
| Test for overall effect: $Z = 1.26$ ($P = 0.21$) |  |  |  |  |  |  |  |  |

Test for subgroup differences: $\text{Chi}^2 = 0.61$, df = 1 ($P = 0.44$), $I^2 = 0\%$

**Figure S1.A** | Forest plots for subgroup analyses by age group for children/adolescents' overall QoL

# Supplementary Material

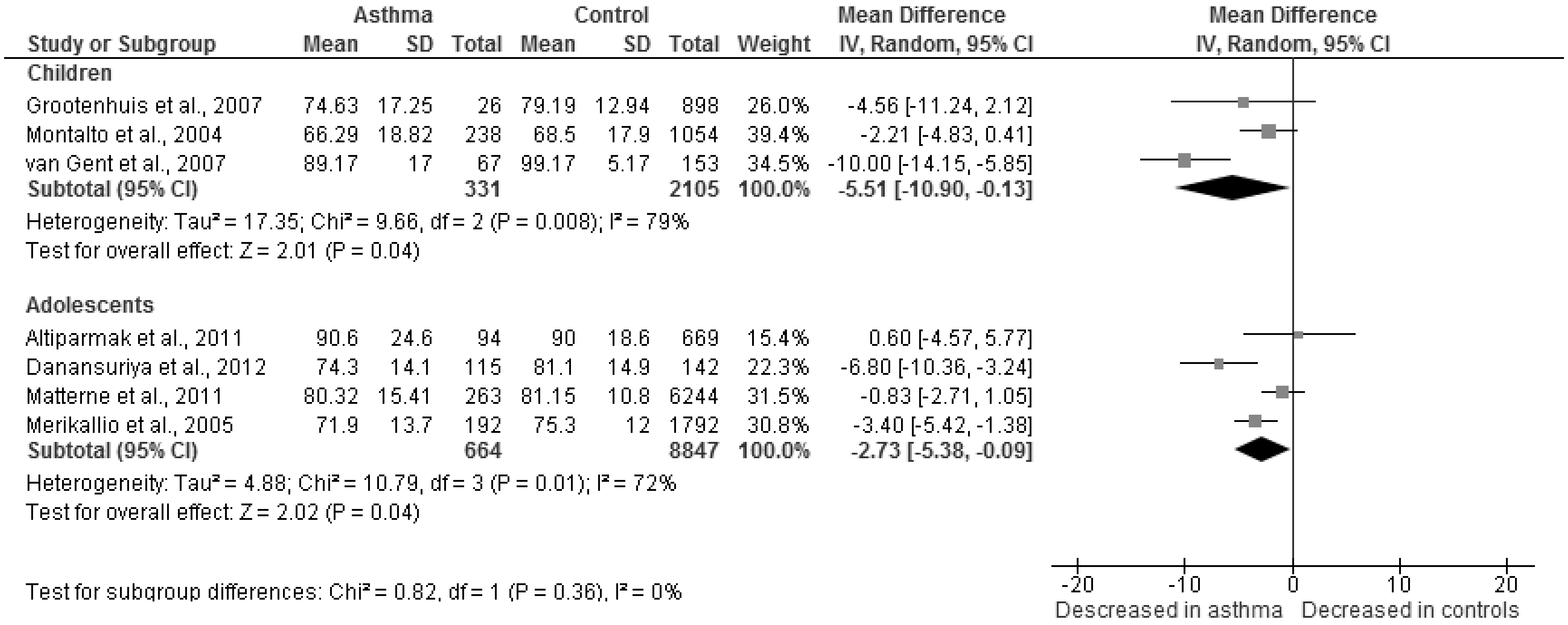


| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Children** | | | | | | | | |
| French et al., 1994 | 75 | 2.96 | 103 | 78.57 | 2.96 | 153 | 27.2% | -3.57 [-4.31, -2.83] |
| Grootenhuis et al., 2007 | 71.88 | 19.34 | 26 | 78.75 | 19.25 | 913 | 21.8% | -6.87 [-14.41, 0.67] |
| Montalto et al., 2004 | 70.68 | 16.44 | 238 | 72.9 | 17.3 | 1054 | 26.6% | -2.22 [-4.56, 0.12] |
| van Gent et al., 2007 | 68.33 | 18.33 | 54 | 98.33 | 8.17 | 93 | 24.4% | -30.00 [-35.16, -24.84] |
| **Subtotal (95% CI)** | | | **421** | | | **2213** | **100.0%** | **-10.38 [-18.26, -2.50]** |
| Heterogeneity: Tau² = 59.29; Chi² = 101.48, df = 3 (P < 0.00001); I² = 97% | | | | | | | | |
| Test for overall effect: Z = 2.58 (P = 0.010) | | | | | | | | |
| **Adolescents** | | | | | | | | |
| Altiparmak et al., 2011 | 79.2 | 21.6 | 94 | 87 | 20.4 | 669 | 19.7% | -7.80 [-12.43, -3.17] |
| Danansuriya et al., 2012 | 78.8 | 11.1 | 115 | 88.7 | 11 | 142 | 25.3% | -9.90 [-12.62, -7.18] |
| Matterne et al., 2011 | 67.79 | 19.62 | 263 | 70.76 | 12.86 | 6244 | 26.2% | -2.97 [-5.36, -0.58] |
| Merikallio et al., 2005 | 95 | 7.6 | 192 | 97.7 | 6.6 | 1792 | 28.9% | -2.70 [-3.82, -1.58] |
| **Subtotal (95% CI)** | | | **664** | | | **8847** | **100.0%** | **-5.59 [-9.12, -2.07]** |
| Heterogeneity: Tau² = 10.89; Chi² = 26.39, df = 3 (P < 0.00001); I² = 89% | | | | | | | | |
| Test for overall effect: Z = 3.11 (P = 0.002) | | | | | | | | |

Test for subgroup differences: Chi² = 1.18, df = 1 (P = 0.28), I² = 15.3%

**Figure S1.B** | Forest plots for subgroup analyses by age group for children/adolescents' physical functioning

# Supplementary Material



|  | Asthma |  |  | Control |  |  |  | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| **Children** |  |  |  |  |  |  |  |  |
| Grootenhuis et al., 2007 | 74.63 | 17.25 | 26 | 79.19 | 12.94 | 898 | 26.0% | -4.56 [-11.24, 2.12] |
| Montalto et al., 2004 | 66.29 | 18.82 | 238 | 68.5 | 17.9 | 1054 | 39.4% | -2.21 [-4.83, 0.41] |
| van Gent et al., 2007 | 89.17 | 17 | 67 | 99.17 | 5.17 | 153 | 34.5% | -10.00 [-14.15, -5.85] |
| **Subtotal (95% CI)** |  |  | **331** |  |  | **2105** | **100.0%** | **-5.51 [-10.90, -0.13]** |

Heterogeneity: Tau² = 17.35; Chi² = 9.66, df = 2 (P = 0.008); I² = 79%

Test for overall effect: Z = 2.01 (P = 0.04)

|  | Asthma |  |  | Control |  |  |  | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| **Adolescents** |  |  |  |  |  |  |  |  |
| Altiparmak et al., 2011 | 90.6 | 24.6 | 94 | 90 | 18.6 | 669 | 15.4% | 0.60 [-4.57, 5.77] |
| Danansuriya et al., 2012 | 74.3 | 14.1 | 115 | 81.1 | 14.9 | 142 | 22.3% | -6.80 [-10.36, -3.24] |
| Matterne et al., 2011 | 80.32 | 15.41 | 263 | 81.15 | 10.8 | 6244 | 31.5% | -0.83 [-2.71, 1.05] |
| Merikallio et al., 2005 | 71.9 | 13.7 | 192 | 75.3 | 12 | 1792 | 30.8% | -3.40 [-5.42, -1.38] |
| **Subtotal (95% CI)** |  |  | **664** |  |  | **8847** | **100.0%** | **-2.73 [-5.38, -0.09]** |

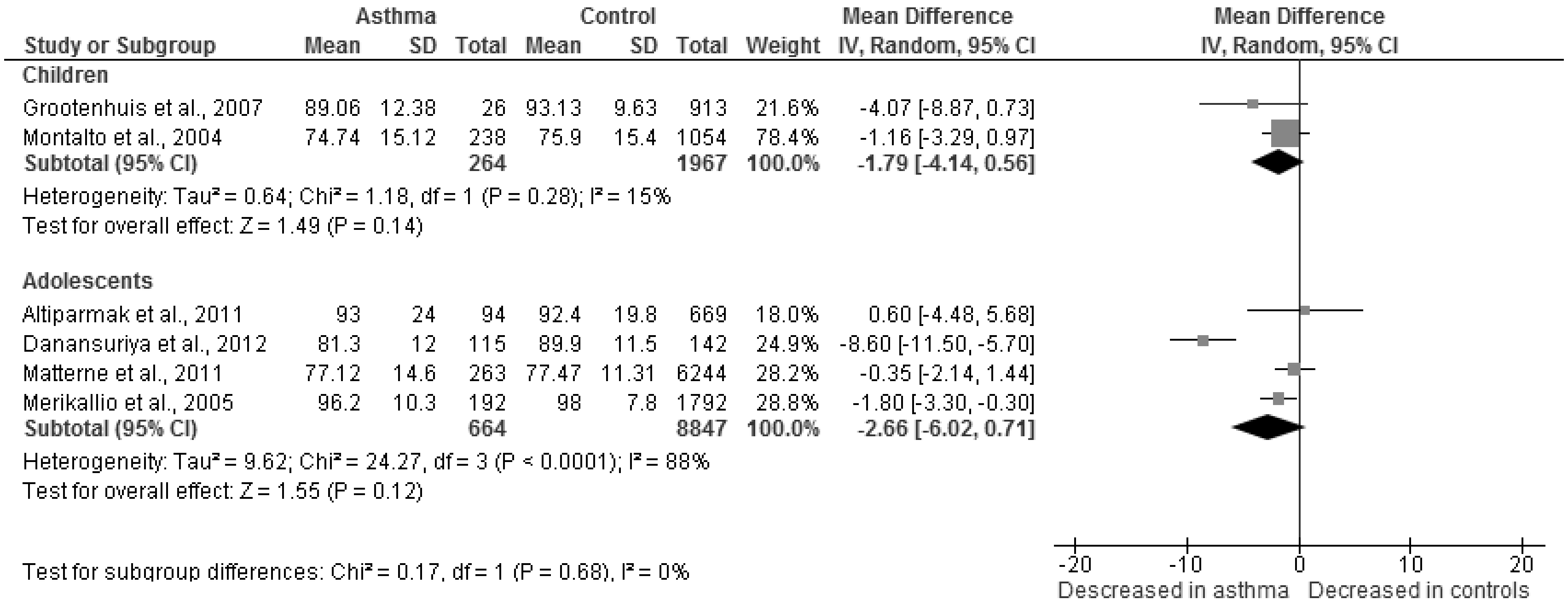
Heterogeneity: Tau² = 4.88; Chi² = 10.79, df = 3 (P = 0.01); I² = 72%

Test for overall effect: Z = 2.02 (P = 0.04)

Test for subgroup differences: Chi² = 0.82, df = 1 (P = 0.36), I² = 0%

**Figure S1.C** | Forest plots for subgroup analyses by age group for children/adolescents' psychological functioning

# Supplementary Material



| Study or Subgroup | Asthma<br>Mean | <br>SD | <br>Total | Control<br>Mean | <br>SD | <br>Total | Weight | Mean Difference<br>IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Children** | | | | | | | | |
| Grootenhuis et al., 2007 | 89.06 | 12.38 | 26 | 93.13 | 9.63 | 913 | 21.6% | -4.07 [-8.87, 0.73] |
| Montalto et al., 2004 | 74.74 | 15.12 | 238 | 75.9 | 15.4 | 1054 | 78.4% | -1.16 [-3.29, 0.97] |
| **Subtotal (95% CI)** | | | **264** | | | **1967** | **100.0%** | **-1.79 [-4.14, 0.56]** |
| **Adolescents** | | | | | | | | |
| Altiparmak et al., 2011 | 93 | 24 | 94 | 92.4 | 19.8 | 669 | 18.0% | 0.60 [-4.48, 5.68] |
| Danansuriya et al., 2012 | 81.3 | 12 | 115 | 89.9 | 11.5 | 142 | 24.9% | -8.60 [-11.50, -5.70] |
| Matterne et al., 2011 | 77.12 | 14.6 | 263 | 77.47 | 11.31 | 6244 | 28.2% | -0.35 [-2.14, 1.44] |
| Merikallio et al., 2005 | 96.2 | 10.3 | 192 | 98 | 7.8 | 1792 | 28.8% | -1.80 [-3.30, -0.30] |
| **Subtotal (95% CI)** | | | **664** | | | **8847** | **100.0%** | **-2.66 [-6.02, 0.71]** |

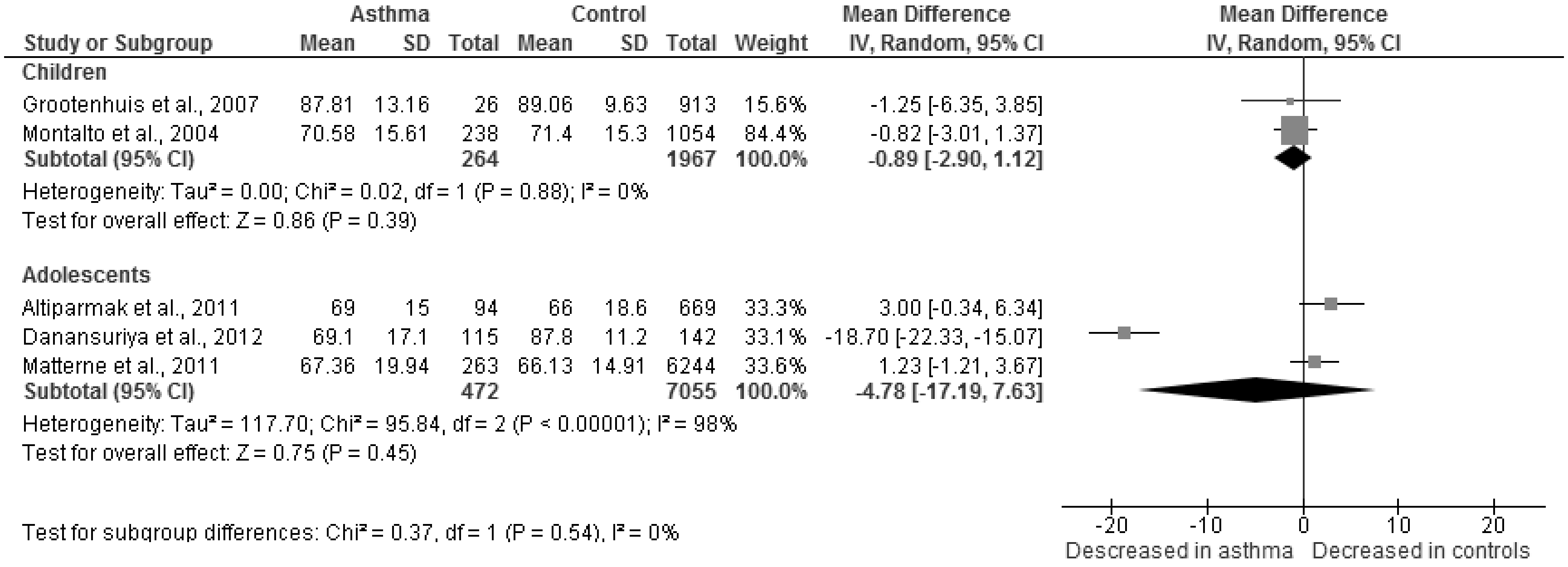
Children:
Heterogeneity: Tau$^2$ = 0.64; Chi$^2$ = 1.18, df = 1 (P = 0.28); I$^2$ = 15%
Test for overall effect: Z = 1.49 (P = 0.14)

Adolescents:
Heterogeneity: Tau$^2$ = 9.62; Chi$^2$ = 24.27, df = 3 (P < 0.0001); I$^2$ = 88%
Test for overall effect: Z = 1.55 (P = 0.12)

Test for subgroup differences: Chi$^2$ = 0.17, df = 1 (P = 0.68), I$^2$ = 0%

**Figure S1.D** | Forest plots for subgroup analyses by age group for children/adolescents' social functioning

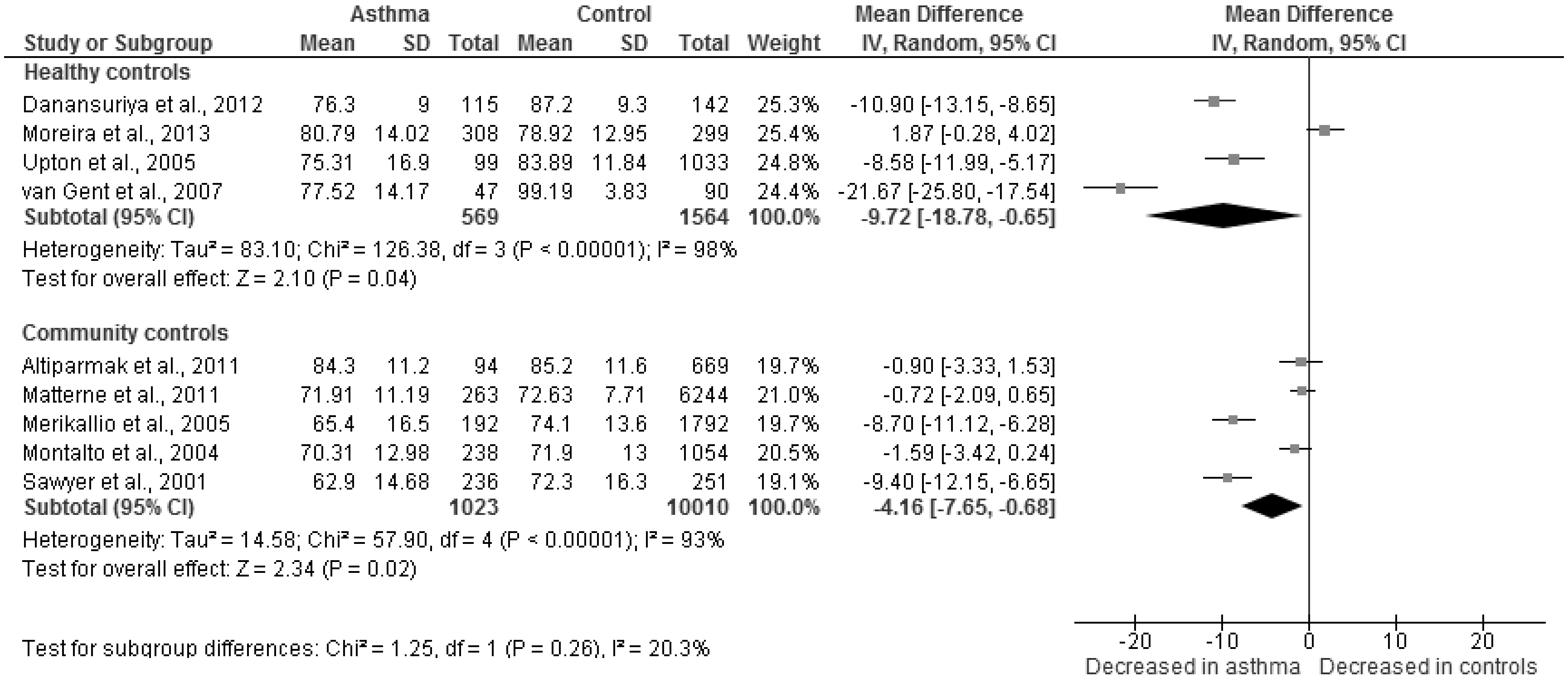
# Supplementary Material



| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| **Children** | | | | | | | | |
| Grootenhuis et al., 2007 | 87.81 | 13.16 | 26 | 89.06 | 9.63 | 913 | 15.6% | -1.25 [-6.35, 3.85] |
| Montalto et al., 2004 | 70.58 | 15.61 | 238 | 71.4 | 15.3 | 1054 | 84.4% | -0.82 [-3.01, 1.37] |
| **Subtotal (95% CI)** | | | **264** | | | **1967** | **100.0%** | **-0.89 [-2.90, 1.12]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 0.86 (P = 0.39) | | | | | | | | |
| **Adolescents** | | | | | | | | |
| Altiparmak et al., 2011 | 69 | 15 | 94 | 66 | 18.6 | 669 | 33.3% | 3.00 [-0.34, 6.34] |
| Danansuriya et al., 2012 | 69.1 | 17.1 | 115 | 87.8 | 11.2 | 142 | 33.1% | -18.70 [-22.33, -15.07] |
| Matterne et al., 2011 | 67.36 | 19.94 | 263 | 66.13 | 14.91 | 6244 | 33.6% | 1.23 [-1.21, 3.67] |
| **Subtotal (95% CI)** | | | **472** | | | **7055** | **100.0%** | **-4.78 [-17.19, 7.63]** |
| Heterogeneity: Tau² = 117.70; Chi² = 95.84, df = 2 (P < 0.00001); I² = 98% | | | | | | | | |
| Test for overall effect: Z = 0.75 (P = 0.45) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.37, df = 1 (P = 0.54), I² = 0% | | | | | | | | |

**Figure S1.E** | Forest plots for subgroup analyses by age group for children/adolescents' school functioning

# Supplementary Material

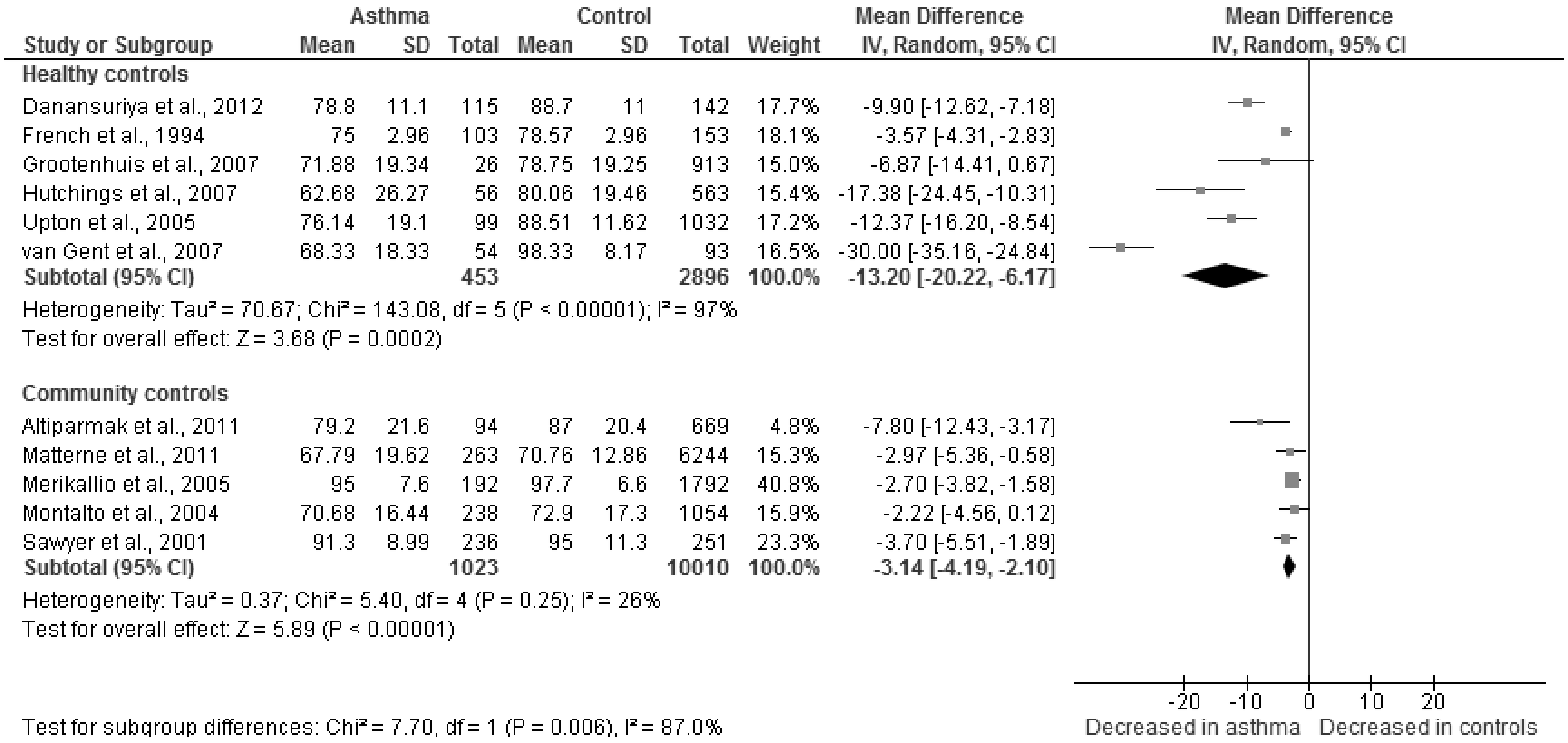


| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Healthy controls** | | | | | | | | |
| Danansuriya et al., 2012 | 76.3 | 9 | 115 | 87.2 | 9.3 | 142 | 25.3% | -10.90 [-13.15, -8.65] |
| Moreira et al., 2013 | 80.79 | 14.02 | 308 | 78.92 | 12.95 | 299 | 25.4% | 1.87 [-0.28, 4.02] |
| Upton et al., 2005 | 75.31 | 16.9 | 99 | 83.89 | 11.84 | 1033 | 24.8% | -8.58 [-11.99, -5.17] |
| van Gent et al., 2007 | 77.52 | 14.17 | 47 | 99.19 | 3.83 | 90 | 24.4% | -21.67 [-25.80, -17.54] |
| **Subtotal (95% CI)** | | | **569** | | | **1564** | **100.0%** | **-9.72 [-18.78, -0.65]** |
| Heterogeneity: Tau² = 83.10; Chi² = 126.38, df = 3 (P < 0.00001); I² = 98% | | | | | | | | |
| Test for overall effect: Z = 2.10 (P = 0.04) | | | | | | | | |
| **Community controls** | | | | | | | | |
| Altiparmak et al., 2011 | 84.3 | 11.2 | 94 | 85.2 | 11.6 | 669 | 19.7% | -0.90 [-3.33, 1.53] |
| Matterne et al., 2011 | 71.91 | 11.19 | 263 | 72.63 | 7.71 | 6244 | 21.0% | -0.72 [-2.09, 0.65] |
| Merikallio et al., 2005 | 65.4 | 16.5 | 192 | 74.1 | 13.6 | 1792 | 19.7% | -8.70 [-11.12, -6.28] |
| Montalto et al., 2004 | 70.31 | 12.98 | 238 | 71.9 | 13 | 1054 | 20.5% | -1.59 [-3.42, 0.24] |
| Sawyer et al., 2001 | 62.9 | 14.68 | 236 | 72.3 | 16.3 | 251 | 19.1% | -9.40 [-12.15, -6.65] |
| **Subtotal (95% CI)** | | | **1023** | | | **10010** | **100.0%** | **-4.16 [-7.65, -0.68]** |
| Heterogeneity: Tau² = 14.58; Chi² = 57.90, df = 4 (P < 0.00001); I² = 93% | | | | | | | | |
| Test for overall effect: Z = 2.34 (P = 0.02) | | | | | | | | |

Test for subgroup differences: Chi² = 1.25, df = 1 (P = 0.26), I² = 20.3%

**Figure S2.A** | Forest plots for subgroup analyses by type of controls for children/adolescents' overall QoL

# Supplementary Material



|  | Asthma |  |  | Control |  |  |  | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| **Healthy controls** |  |  |  |  |  |  |  |  |
| Danansuriya et al., 2012 | 78.8 | 11.1 | 115 | 88.7 | 11 | 142 | 17.7% | -9.90 [-12.62, -7.18] |
| French et al., 1994 | 75 | 2.96 | 103 | 78.57 | 2.96 | 153 | 18.1% | -3.57 [-4.31, -2.83] |
| Grootenhuis et al., 2007 | 71.88 | 19.34 | 26 | 78.75 | 19.25 | 913 | 15.0% | -6.87 [-14.41, 0.67] |
| Hutchings et al., 2007 | 62.68 | 26.27 | 56 | 80.06 | 19.46 | 563 | 15.4% | -17.38 [-24.45, -10.31] |
| Upton et al., 2005 | 76.14 | 19.1 | 99 | 88.51 | 11.62 | 1032 | 17.2% | -12.37 [-16.20, -8.54] |
| van Gent et al., 2007 | 68.33 | 18.33 | 54 | 98.33 | 8.17 | 93 | 16.5% | -30.00 [-35.16, -24.84] |
| **Subtotal (95% CI)** |  |  | **453** |  |  | **2896** | **100.0%** | **-13.20 [-20.22, -6.17]** |

Heterogeneity: Tau$^2$ = 70.67; Chi$^2$ = 143.08, df = 5 ($P < 0.00001$); I$^2$ = 97%

Test for overall effect: Z = 3.68 (P = 0.0002)

|  | Asthma |  |  | Control |  |  |  | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Community controls** |  |  |  |  |  |  |  |  |
| Altiparmak et al., 2011 | 79.2 | 21.6 | 94 | 87 | 20.4 | 669 | 4.8% | -7.80 [-12.43, -3.17] |
| Matterne et al., 2011 | 67.79 | 19.62 | 263 | 70.76 | 12.86 | 6244 | 15.3% | -2.97 [-5.36, -0.58] |
| Merikallio et al., 2005 | 95 | 7.6 | 192 | 97.7 | 6.6 | 1792 | 40.8% | -2.70 [-3.82, -1.58] |
| Montalto et al., 2004 | 70.68 | 16.44 | 238 | 72.9 | 17.3 | 1054 | 15.9% | -2.22 [-4.56, 0.12] |
| Sawyer et al., 2001 | 91.3 | 8.99 | 236 | 95 | 11.3 | 251 | 23.3% | -3.70 [-5.51, -1.89] |
| **Subtotal (95% CI)** |  |  | **1023** |  |  | **10010** | **100.0%** | **-3.14 [-4.19, -2.10]** |

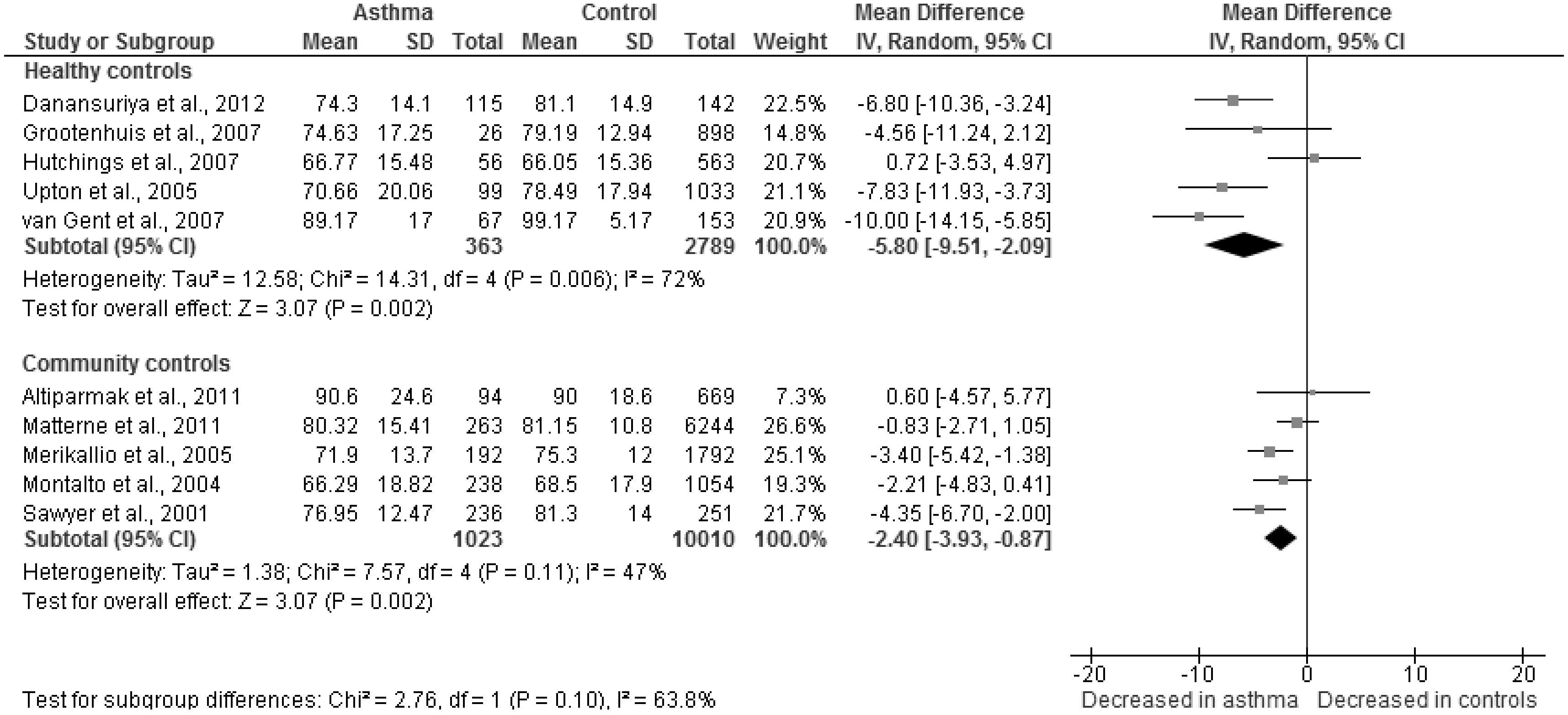
Heterogeneity: Tau$^2$ = 0.37; Chi$^2$ = 5.40, df = 4 (P = 0.25); I$^2$ = 26%

Test for overall effect: Z = 5.89 ($P < 0.00001$)

Test for subgroup differences: Chi$^2$ = 7.70, df = 1 (P = 0.006), I$^2$ = 87.0%

**Figure S2.B** | Forest plots for subgroup analyses by type of controls for children/adolescents' physical functioning

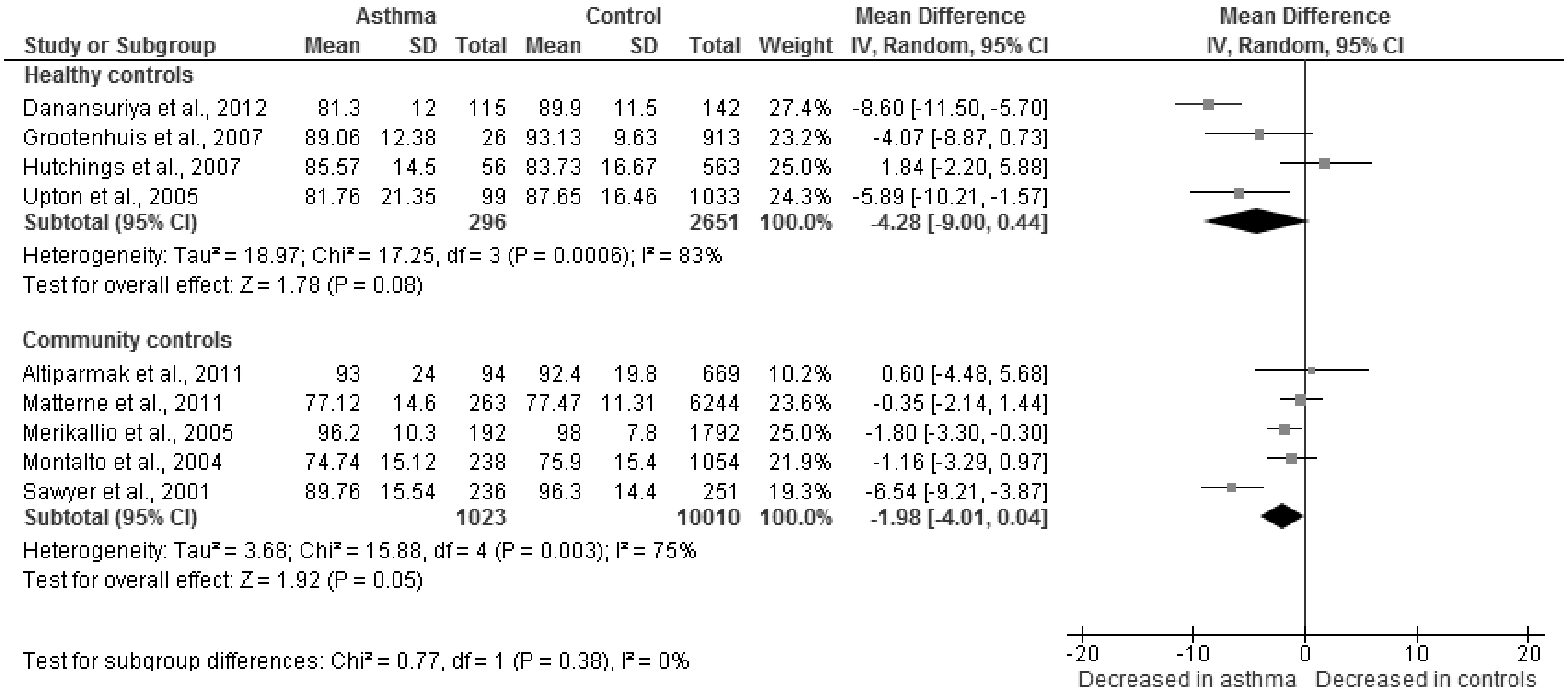
# Supplementary Material



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Healthy controls** | | | | | | | | |
| Danansuriya et al., 2012 | 74.3 | 14.1 | 115 | 81.1 | 14.9 | 142 | 22.5% | -6.80 [-10.36, -3.24] |
| Grootenhuis et al., 2007 | 74.63 | 17.25 | 26 | 79.19 | 12.94 | 898 | 14.8% | -4.56 [-11.24, 2.12] |
| Hutchings et al., 2007 | 66.77 | 15.48 | 56 | 66.05 | 15.36 | 563 | 20.7% | 0.72 [-3.53, 4.97] |
| Upton et al., 2005 | 70.66 | 20.06 | 99 | 78.49 | 17.94 | 1033 | 21.1% | -7.83 [-11.93, -3.73] |
| van Gent et al., 2007 | 89.17 | 17 | 67 | 99.17 | 5.17 | 153 | 20.9% | -10.00 [-14.15, -5.85] |
| **Subtotal (95% CI)** | | | **363** | | | **2789** | **100.0%** | **-5.80 [-9.51, -2.09]** |
| Heterogeneity: Tau² = 12.58; Chi² = 14.31, df = 4 (P = 0.006); I² = 72% | | | | | | | | |
| Test for overall effect: Z = 3.07 (P = 0.002) | | | | | | | | |
| **Community controls** | | | | | | | | |
| Altiparmak et al., 2011 | 90.6 | 24.6 | 94 | 90 | 18.6 | 669 | 7.3% | 0.60 [-4.57, 5.77] |
| Matterne et al., 2011 | 80.32 | 15.41 | 263 | 81.15 | 10.8 | 6244 | 26.6% | -0.83 [-2.71, 1.05] |
| Merikallio et al., 2005 | 71.9 | 13.7 | 192 | 75.3 | 12 | 1792 | 25.1% | -3.40 [-5.42, -1.38] |
| Montalto et al., 2004 | 66.29 | 18.82 | 238 | 68.5 | 17.9 | 1054 | 19.3% | -2.21 [-4.83, 0.41] |
| Sawyer et al., 2001 | 76.95 | 12.47 | 236 | 81.3 | 14 | 251 | 21.7% | -4.35 [-6.70, -2.00] |
| **Subtotal (95% CI)** | | | **1023** | | | **10010** | **100.0%** | **-2.40 [-3.93, -0.87]** |
| Heterogeneity: Tau² = 1.38; Chi² = 7.57, df = 4 (P = 0.11); I² = 47% | | | | | | | | |
| Test for overall effect: Z = 3.07 (P = 0.002) | | | | | | | | |
| Test for subgroup differences: Chi² = 2.76, df = 1 (P = 0.10), I² = 63.8% | | | | | | | | |

**Figure S2.C** | Forest plots for subgroup analyses by type of controls for children/adolescents' psychological functioning

# Supplementary Material

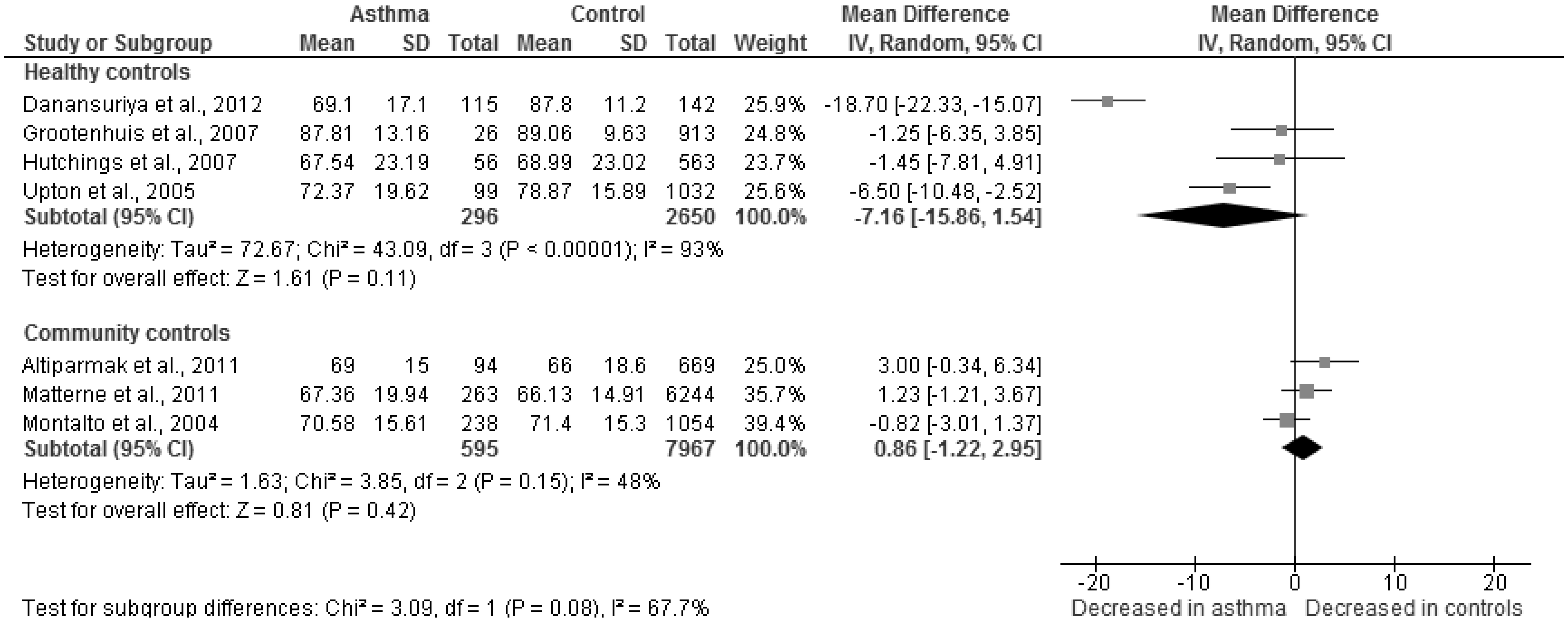


| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| **Healthy controls** | | | | | | | | |
| Danansuriya et al., 2012 | 81.3 | 12 | 115 | 89.9 | 11.5 | 142 | 27.4% | -8.60 [-11.50, -5.70] |
| Grootenhuis et al., 2007 | 89.06 | 12.38 | 26 | 93.13 | 9.63 | 913 | 23.2% | -4.07 [-8.87, 0.73] |
| Hutchings et al., 2007 | 85.57 | 14.5 | 56 | 83.73 | 16.67 | 563 | 25.0% | 1.84 [-2.20, 5.88] |
| Upton et al., 2005 | 81.76 | 21.35 | 99 | 87.65 | 16.46 | 1033 | 24.3% | -5.89 [-10.21, -1.57] |
| **Subtotal (95% CI)** | | | **296** | | | **2651** | **100.0%** | **-4.28 [-9.00, 0.44]** |
| Heterogeneity: Tau² = 18.97; Chi² = 17.25, df = 3 (P = 0.0006); I² = 83% | | | | | | | | |
| Test for overall effect: Z = 1.78 (P = 0.08) | | | | | | | | |
| **Community controls** | | | | | | | | |
| Altiparmak et al., 2011 | 93 | 24 | 94 | 92.4 | 19.8 | 669 | 10.2% | 0.60 [-4.48, 5.68] |
| Matterne et al., 2011 | 77.12 | 14.6 | 263 | 77.47 | 11.31 | 6244 | 23.6% | -0.35 [-2.14, 1.44] |
| Merikallio et al., 2005 | 96.2 | 10.3 | 192 | 98 | 7.8 | 1792 | 25.0% | -1.80 [-3.30, -0.30] |
| Montalto et al., 2004 | 74.74 | 15.12 | 238 | 75.9 | 15.4 | 1054 | 21.9% | -1.16 [-3.29, 0.97] |
| Sawyer et al., 2001 | 89.76 | 15.54 | 236 | 96.3 | 14.4 | 251 | 19.3% | -6.54 [-9.21, -3.87] |
| **Subtotal (95% CI)** | | | **1023** | | | **10010** | **100.0%** | **-1.98 [-4.01, 0.04]** |
| Heterogeneity: Tau² = 3.68; Chi² = 15.88, df = 4 (P = 0.003); I² = 75% | | | | | | | | |
| Test for overall effect: Z = 1.92 (P = 0.05) | | | | | | | | |

Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0%

**Figure S2.D** | Forest plots for subgroup analyses by type of controls for children/adolescents' social functioning

# Supplementary Material

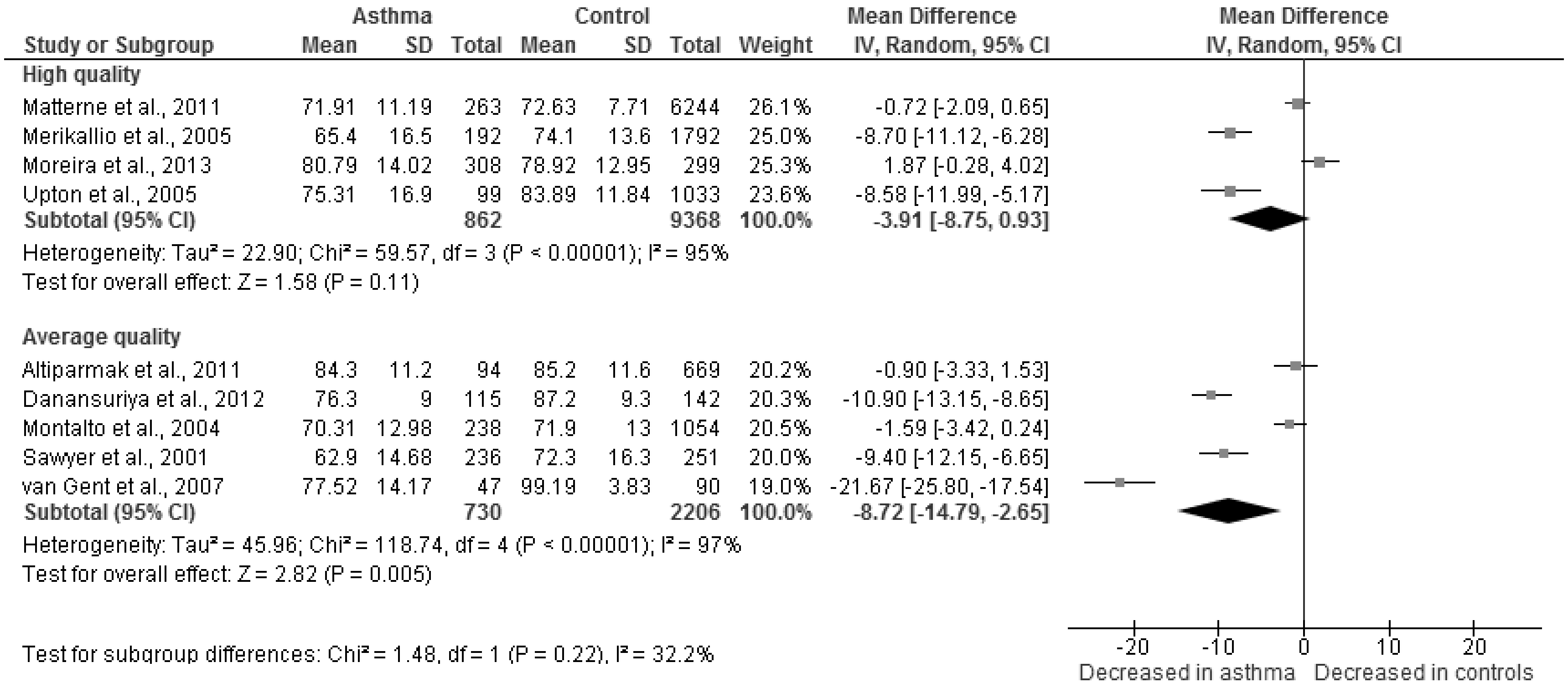


| | Asthma | | | Control | | | | Mean Difference | Mean Difference |
|---|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** | **IV, Random, 95% CI** |
| **Healthy controls** | | | | | | | | | |
| Danansuriya et al., 2012 | 69.1 | 17.1 | 115 | 87.8 | 11.2 | 142 | 25.9% | -18.70 [-22.33, -15.07] | |
| Grootenhuis et al., 2007 | 87.81 | 13.16 | 26 | 89.06 | 9.63 | 913 | 24.8% | -1.25 [-6.35, 3.85] | |
| Hutchings et al., 2007 | 67.54 | 23.19 | 56 | 68.99 | 23.02 | 563 | 23.7% | -1.45 [-7.81, 4.91] | |
| Upton et al., 2005 | 72.37 | 19.62 | 99 | 78.87 | 15.89 | 1032 | 25.6% | -6.50 [-10.48, -2.52] | |
| **Subtotal (95% CI)** | | | **296** | | | **2650** | **100.0%** | **-7.16 [-15.86, 1.54]** | |
| Heterogeneity: Tau² = 72.67; Chi² = 43.09, df = 3 (P < 0.00001); I² = 93% | | | | | | | | | |
| Test for overall effect: Z = 1.61 (P = 0.11) | | | | | | | | | |
| **Community controls** | | | | | | | | | |
| Altiparmak et al., 2011 | 69 | 15 | 94 | 66 | 18.6 | 669 | 25.0% | 3.00 [-0.34, 6.34] | |
| Matterne et al., 2011 | 67.36 | 19.94 | 263 | 66.13 | 14.91 | 6244 | 35.7% | 1.23 [-1.21, 3.67] | |
| Montalto et al., 2004 | 70.58 | 15.61 | 238 | 71.4 | 15.3 | 1054 | 39.4% | -0.82 [-3.01, 1.37] | |
| **Subtotal (95% CI)** | | | **595** | | | **7967** | **100.0%** | **0.86 [-1.22, 2.95]** | |
| Heterogeneity: Tau² = 1.63; Chi² = 3.85, df = 2 (P = 0.15); I² = 48% | | | | | | | | | |
| Test for overall effect: Z = 0.81 (P = 0.42) | | | | | | | | | |

Test for subgroup differences: Chi² = 3.09, df = 1 (P = 0.08), I² = 67.7%

**Figure S2.E** | Forest plots for subgroup analyses by type of controls for children/adolescents' school functioning

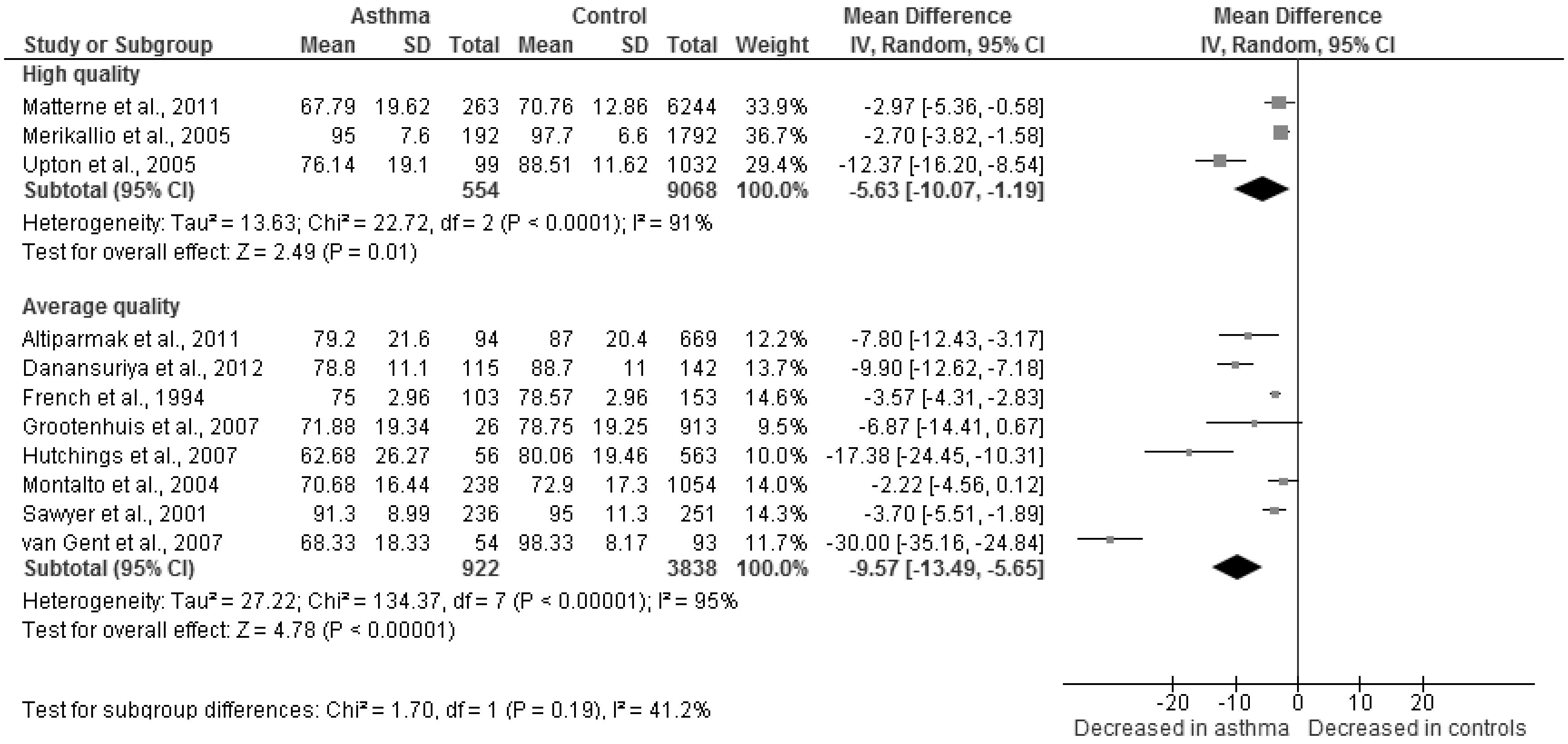
# Supplementary Material



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **High quality** | | | | | | | | |
| Matterne et al., 2011 | 71.91 | 11.19 | 263 | 72.63 | 7.71 | 6244 | 26.1% | -0.72 [-2.09, 0.65] |
| Merikallio et al., 2005 | 65.4 | 16.5 | 192 | 74.1 | 13.6 | 1792 | 25.0% | -8.70 [-11.12, -6.28] |
| Moreira et al., 2013 | 80.79 | 14.02 | 308 | 78.92 | 12.95 | 299 | 25.3% | 1.87 [-0.28, 4.02] |
| Upton et al., 2005 | 75.31 | 16.9 | 99 | 83.89 | 11.84 | 1033 | 23.6% | -8.58 [-11.99, -5.17] |
| **Subtotal (95% CI)** | | | **862** | | | **9368** | **100.0%** | **-3.91 [-8.75, 0.93]** |
| Heterogeneity: Tau² = 22.90; Chi² = 59.57, df = 3 (P < 0.00001); I² = 95% | | | | | | | | |
| Test for overall effect: Z = 1.58 (P = 0.11) | | | | | | | | |
| **Average quality** | | | | | | | | |
| Altiparmak et al., 2011 | 84.3 | 11.2 | 94 | 85.2 | 11.6 | 669 | 20.2% | -0.90 [-3.33, 1.53] |
| Danansuriya et al., 2012 | 76.3 | 9 | 115 | 87.2 | 9.3 | 142 | 20.3% | -10.90 [-13.15, -8.65] |
| Montalto et al., 2004 | 70.31 | 12.98 | 238 | 71.9 | 13 | 1054 | 20.5% | -1.59 [-3.42, 0.24] |
| Sawyer et al., 2001 | 62.9 | 14.68 | 236 | 72.3 | 16.3 | 251 | 20.0% | -9.40 [-12.15, -6.65] |
| van Gent et al., 2007 | 77.52 | 14.17 | 47 | 99.19 | 3.83 | 90 | 19.0% | -21.67 [-25.80, -17.54] |
| **Subtotal (95% CI)** | | | **730** | | | **2206** | **100.0%** | **-8.72 [-14.79, -2.65]** |
| Heterogeneity: Tau² = 45.96; Chi² = 118.74, df = 4 (P < 0.00001); I² = 97% | | | | | | | | |
| Test for overall effect: Z = 2.82 (P = 0.005) | | | | | | | | |
| Test for subgroup differences: Chi² = 1.48, df = 1 (P = 0.22), I² = 32.2% | | | | | | | | |

**Figure S3.A** | Forest plots for subgroup analyses by quality rating for children/adolescents' overall QoL

# Supplementary Material



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **High quality** | | | | | | | | |
| Matterne et al., 2011 | 67.79 | 19.62 | 263 | 70.76 | 12.86 | 6244 | 33.9% | -2.97 [-5.36, -0.58] |
| Merikallio et al., 2005 | 95 | 7.6 | 192 | 97.7 | 6.6 | 1792 | 36.7% | -2.70 [-3.82, -1.58] |
| Upton et al., 2005 | 76.14 | 19.1 | 99 | 88.51 | 11.62 | 1032 | 29.4% | -12.37 [-16.20, -8.54] |
| **Subtotal (95% CI)** | | | **554** | | | **9068** | **100.0%** | **-5.63 [-10.07, -1.19]** |
| **Average quality** | | | | | | | | |
| Altiparmak et al., 2011 | 79.2 | 21.6 | 94 | 87 | 20.4 | 669 | 12.2% | -7.80 [-12.43, -3.17] |
| Danansuriya et al., 2012 | 78.8 | 11.1 | 115 | 88.7 | 11 | 142 | 13.7% | -9.90 [-12.62, -7.18] |
| French et al., 1994 | 75 | 2.96 | 103 | 78.57 | 2.96 | 153 | 14.6% | -3.57 [-4.31, -2.83] |
| Grootenhuis et al., 2007 | 71.88 | 19.34 | 26 | 78.75 | 19.25 | 913 | 9.5% | -6.87 [-14.41, 0.67] |
| Hutchings et al., 2007 | 62.68 | 26.27 | 56 | 80.06 | 19.46 | 563 | 10.0% | -17.38 [-24.45, -10.31] |
| Montalto et al., 2004 | 70.68 | 16.44 | 238 | 72.9 | 17.3 | 1054 | 14.0% | -2.22 [-4.56, 0.12] |
| Sawyer et al., 2001 | 91.3 | 8.99 | 236 | 95 | 11.3 | 251 | 14.3% | -3.70 [-5.51, -1.89] |
| van Gent et al., 2007 | 68.33 | 18.33 | 54 | 98.33 | 8.17 | 93 | 11.7% | -30.00 [-35.16, -24.84] |
| **Subtotal (95% CI)** | | | **922** | | | **3838** | **100.0%** | **-9.57 [-13.49, -5.65]** |

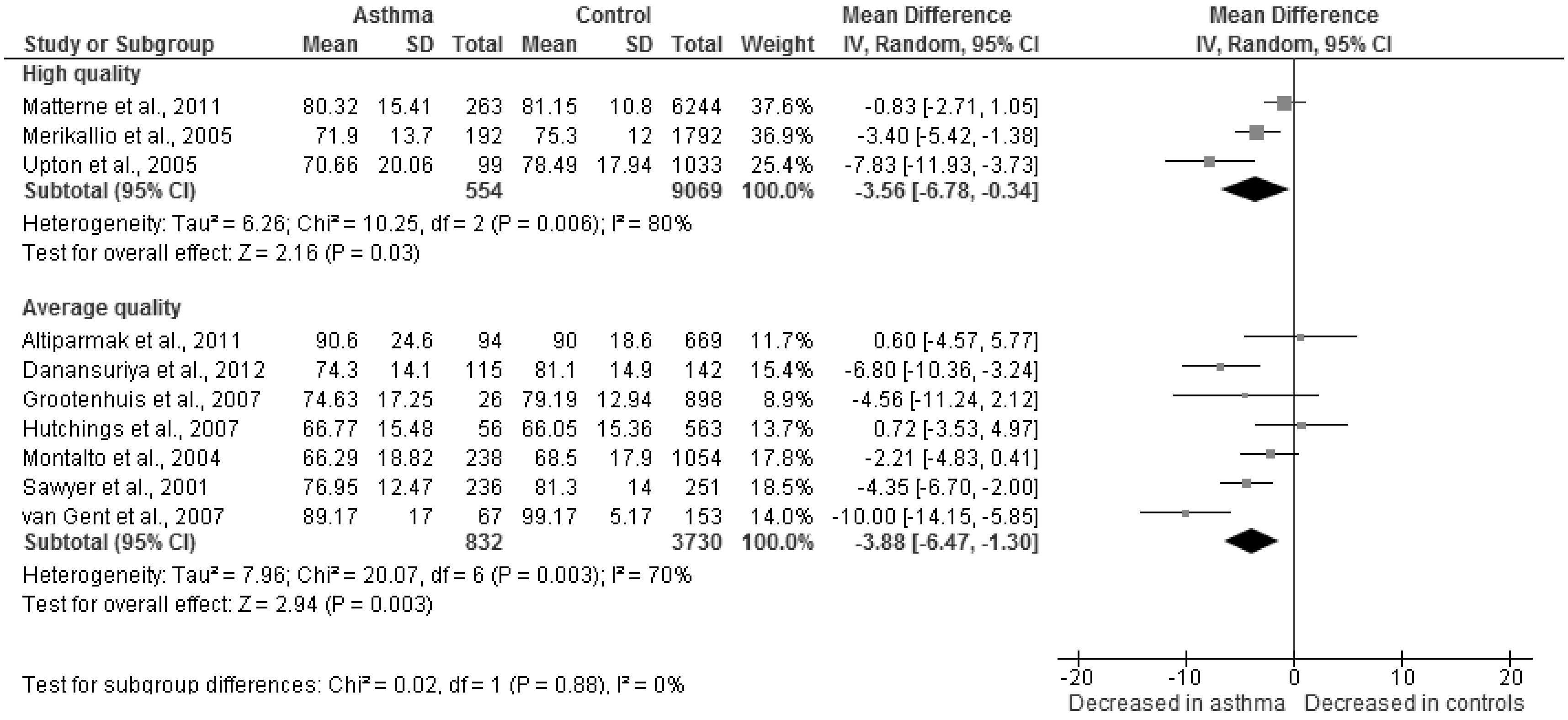
High quality: Heterogeneity: Tau² = 13.63; Chi² = 22.72, df = 2 (P < 0.0001); I² = 91%
Test for overall effect: Z = 2.49 (P = 0.01)

Average quality: Heterogeneity: Tau² = 27.22; Chi² = 134.37, df = 7 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.78 (P < 0.00001)

Test for subgroup differences: Chi² = 1.70, df = 1 (P = 0.19), I² = 41.2%

**Figure S3.B** | Forest plots for subgroup analyses by quality rating for children/adolescents' physical functioning

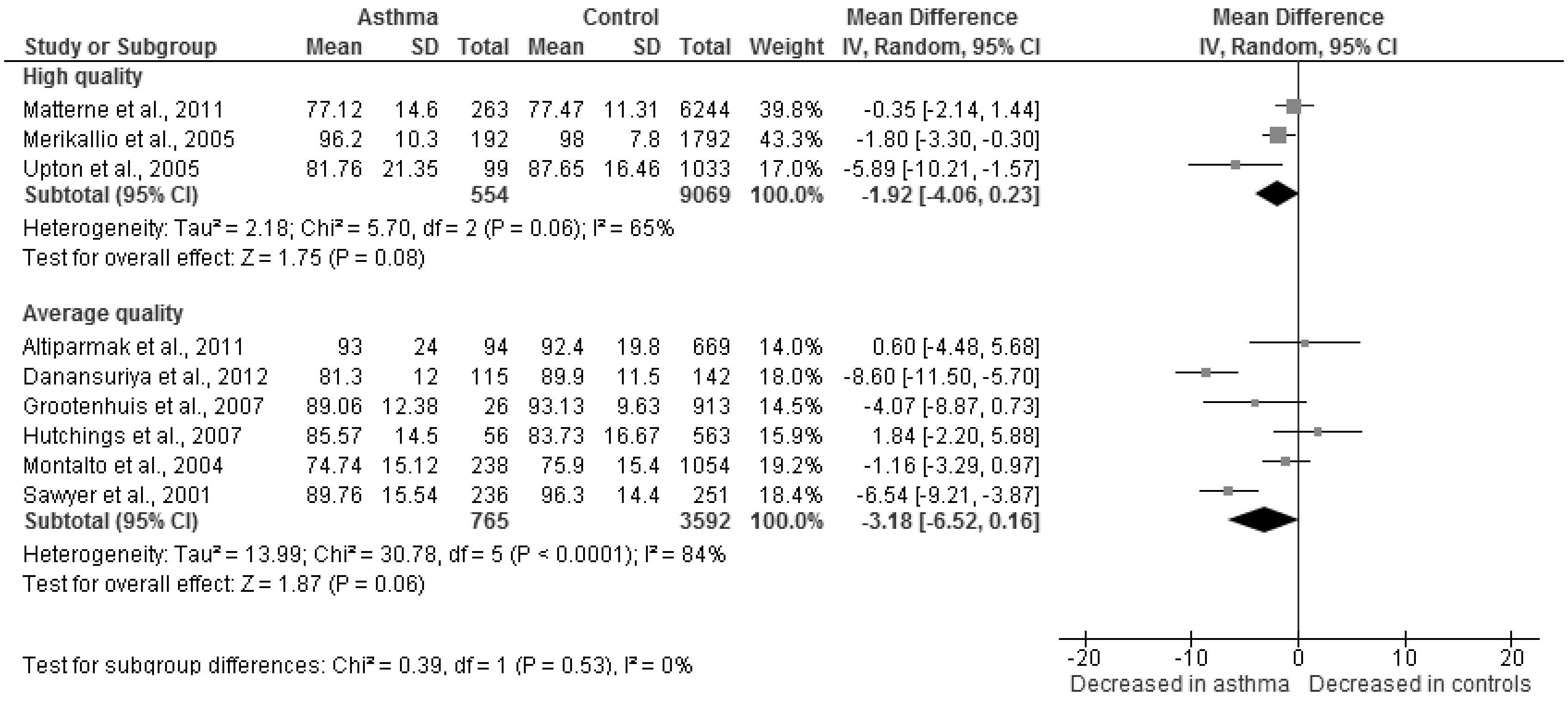
# Supplementary Material



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **High quality** | | | | | | | | |
| Matterne et al., 2011 | 80.32 | 15.41 | 263 | 81.15 | 10.8 | 6244 | 37.6% | -0.83 [-2.71, 1.05] |
| Merikallio et al., 2005 | 71.9 | 13.7 | 192 | 75.3 | 12 | 1792 | 36.9% | -3.40 [-5.42, -1.38] |
| Upton et al., 2005 | 70.66 | 20.06 | 99 | 78.49 | 17.94 | 1033 | 25.4% | -7.83 [-11.93, -3.73] |
| **Subtotal (95% CI)** | | | **554** | | | **9069** | **100.0%** | **-3.56 [-6.78, -0.34]** |
| Heterogeneity: Tau² = 6.26; Chi² = 10.25, df = 2 (P = 0.006); I² = 80% | | | | | | | | |
| Test for overall effect: Z = 2.16 (P = 0.03) | | | | | | | | |
| **Average quality** | | | | | | | | |
| Altiparmak et al., 2011 | 90.6 | 24.6 | 94 | 90 | 18.6 | 669 | 11.7% | 0.60 [-4.57, 5.77] |
| Danansuriya et al., 2012 | 74.3 | 14.1 | 115 | 81.1 | 14.9 | 142 | 15.4% | -6.80 [-10.36, -3.24] |
| Grootenhuis et al., 2007 | 74.63 | 17.25 | 26 | 79.19 | 12.94 | 898 | 8.9% | -4.56 [-11.24, 2.12] |
| Hutchings et al., 2007 | 66.77 | 15.48 | 56 | 66.05 | 15.36 | 563 | 13.7% | 0.72 [-3.53, 4.97] |
| Montalto et al., 2004 | 66.29 | 18.82 | 238 | 68.5 | 17.9 | 1054 | 17.8% | -2.21 [-4.83, 0.41] |
| Sawyer et al., 2001 | 76.95 | 12.47 | 236 | 81.3 | 14 | 251 | 18.5% | -4.35 [-6.70, -2.00] |
| van Gent et al., 2007 | 89.17 | 17 | 67 | 99.17 | 5.17 | 153 | 14.0% | -10.00 [-14.15, -5.85] |
| **Subtotal (95% CI)** | | | **832** | | | **3730** | **100.0%** | **-3.88 [-6.47, -1.30]** |
| Heterogeneity: Tau² = 7.96; Chi² = 20.07, df = 6 (P = 0.003); I² = 70% | | | | | | | | |
| Test for overall effect: Z = 2.94 (P = 0.003) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.88), I² = 0% | | | | | | | | |

**Figure S3.C** | Forest plots for subgroup analyses by quality rating for children/adolescents' psychological functioning

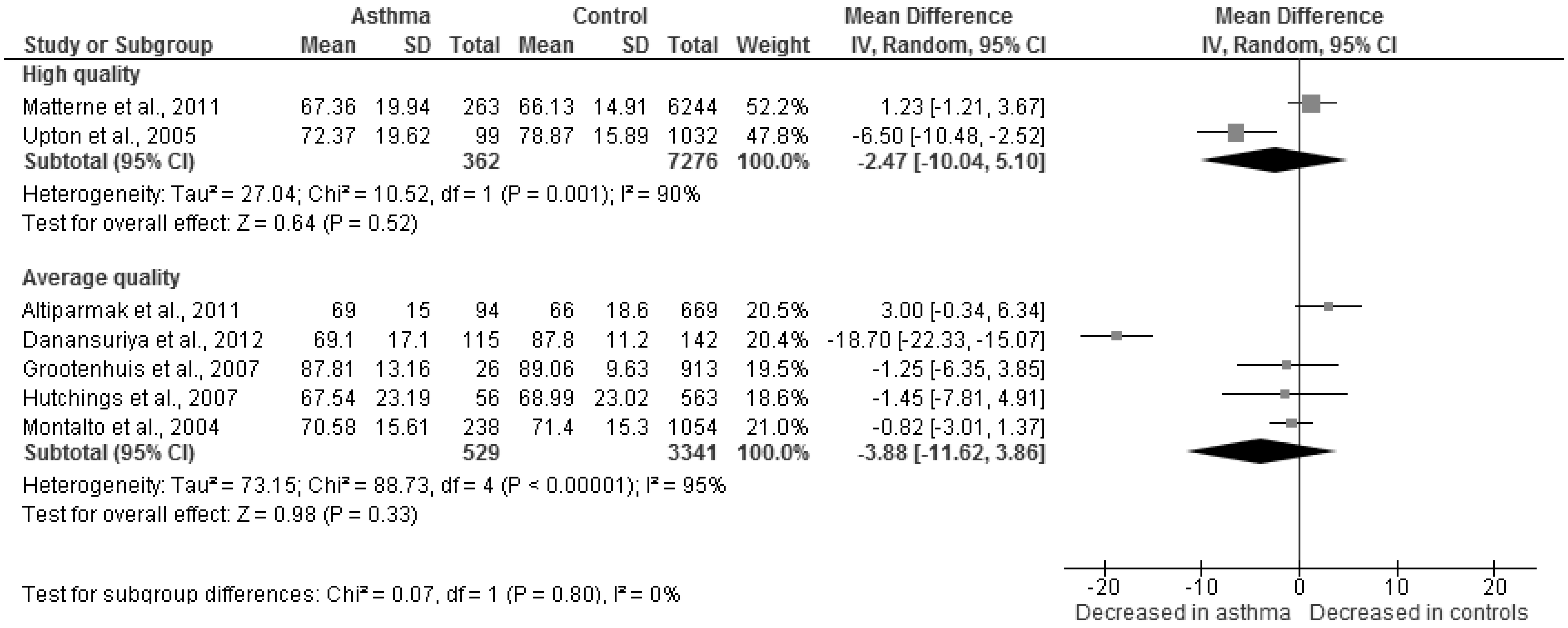
# Supplementary Material



| | Asthma | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| **High quality** | | | | | | | | |
| Matterne et al., 2011 | 77.12 | 14.6 | 263 | 77.47 | 11.31 | 6244 | 39.8% | -0.35 [-2.14, 1.44] |
| Merikallio et al., 2005 | 96.2 | 10.3 | 192 | 98 | 7.8 | 1792 | 43.3% | -1.80 [-3.30, -0.30] |
| Upton et al., 2005 | 81.76 | 21.35 | 99 | 87.65 | 16.46 | 1033 | 17.0% | -5.89 [-10.21, -1.57] |
| **Subtotal (95% CI)** | | | **554** | | | **9069** | **100.0%** | **-1.92 [-4.06, 0.23]** |
| Heterogeneity: Tau² = 2.18; Chi² = 5.70, df = 2 (P = 0.06); I² = 65% | | | | | | | | |
| Test for overall effect: Z = 1.75 (P = 0.08) | | | | | | | | |
| **Average quality** | | | | | | | | |
| Altiparmak et al., 2011 | 93 | 24 | 94 | 92.4 | 19.8 | 669 | 14.0% | 0.60 [-4.48, 5.68] |
| Danansuriya et al., 2012 | 81.3 | 12 | 115 | 89.9 | 11.5 | 142 | 18.0% | -8.60 [-11.50, -5.70] |
| Grootenhuis et al., 2007 | 89.06 | 12.38 | 26 | 93.13 | 9.63 | 913 | 14.5% | -4.07 [-8.87, 0.73] |
| Hutchings et al., 2007 | 85.57 | 14.5 | 56 | 83.73 | 16.67 | 563 | 15.9% | 1.84 [-2.20, 5.88] |
| Montalto et al., 2004 | 74.74 | 15.12 | 238 | 75.9 | 15.4 | 1054 | 19.2% | -1.16 [-3.29, 0.97] |
| Sawyer et al., 2001 | 89.76 | 15.54 | 236 | 96.3 | 14.4 | 251 | 18.4% | -6.54 [-9.21, -3.87] |
| **Subtotal (95% CI)** | | | **765** | | | **3592** | **100.0%** | **-3.18 [-6.52, 0.16]** |
| Heterogeneity: Tau² = 13.99; Chi² = 30.78, df = 5 (P < 0.0001); I² = 84% | | | | | | | | |
| Test for overall effect: Z = 1.87 (P = 0.06) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0% | | | | | | | | |

**Figure S3.D** | Forest plots for subgroup analyses by quality rating for children/adolescents’ social functioning

# Supplementary Material



| Study or Subgroup | Asthma Mean | Asthma SD | Asthma Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **High quality** | | | | | | | | |
| Matterne et al., 2011 | 67.36 | 19.94 | 263 | 66.13 | 14.91 | 6244 | 52.2% | 1.23 [-1.21, 3.67] |
| Upton et al., 2005 | 72.37 | 19.62 | 99 | 78.87 | 15.89 | 1032 | 47.8% | -6.50 [-10.48, -2.52] |
| **Subtotal (95% CI)** | | | **362** | | | **7276** | **100.0%** | **-2.47 [-10.04, 5.10]** |
| Heterogeneity: Tau² = 27.04; Chi² = 10.52, df = 1 (P = 0.001); I² = 90% | | | | | | | | |
| Test for overall effect: Z = 0.64 (P = 0.52) | | | | | | | | |
| **Average quality** | | | | | | | | |
| Altiparmak et al., 2011 | 69 | 15 | 94 | 66 | 18.6 | 669 | 20.5% | 3.00 [-0.34, 6.34] |
| Danansuriya et al., 2012 | 69.1 | 17.1 | 115 | 87.8 | 11.2 | 142 | 20.4% | -18.70 [-22.33, -15.07] |
| Grootenhuis et al., 2007 | 87.81 | 13.16 | 26 | 89.06 | 9.63 | 913 | 19.5% | -1.25 [-6.35, 3.85] |
| Hutchings et al., 2007 | 67.54 | 23.19 | 56 | 68.99 | 23.02 | 563 | 18.6% | -1.45 [-7.81, 4.91] |
| Montalto et al., 2004 | 70.58 | 15.61 | 238 | 71.4 | 15.3 | 1054 | 21.0% | -0.82 [-3.01, 1.37] |
| **Subtotal (95% CI)** | | | **529** | | | **3341** | **100.0%** | **-3.88 [-11.62, 3.86]** |
| Heterogeneity: Tau² = 73.15; Chi² = 88.73, df = 4 (P < 0.00001); I² = 95% | | | | | | | | |
| Test for overall effect: Z = 0.98 (P = 0.33) | | | | | | | | |

Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.80), I² = 0%

**Figure S3.E** | Forest plots for subgroup analyses by quality rating for children/adolescents' school functioning

# Empirical Study 1

## The Portuguese DISABKIDS Asthma Module: A global index of asthma-specific quality of life for children and adolescents

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# The Portuguese DISABKIDS Asthma Module: A global index of asthma-specific quality of life for children and adolescents

Neuza Silva • Carlos Carona • Carla Crespo • Monika Bullinger • Maria Cristina Canavarro

## Abstract

***Introduction.*** The KIDSCREEN and DISABKIDS questionnaires constitute a modular system for assessing the health-related quality of life (HrQoL) of children/adolescents. Objective: This study was aimed at examining the factorial structure of the Portuguese patient- and parent-reported versions of the DISABKIDS-Asthma Module (AsM) and its invariance across age groups and informants, as well as to examine their reliability and construct validity. ***Method***. The sample included 140 children/adolescents aged 8-18 years, who were diagnosed with asthma, and one of their parents. Both family members assessed HrQoL at the generic (KIDSCREEN-10), chronic-generic (DISABKIDS-12) and asthma-specific (DISABKIDS-AsM) levels. Asthma severity was classified by physicians using Global Initiative for Asthma (GINA) guidelines. ***Results.*** Confirmatory factor analysis attested the factorial validity of the correlated two-factor model of the DISABKIDS-AsM, but the low average variance extracted by each factor (Impact and Worry) suggested that a one-factor structure would better fit the Portuguese data. The one-factor model had an acceptable fit ($\chi^2/df = 1.97$; comparative fit index = 0.94; root mean square error of approximation = 0.08) and was invariant between age groups (children *vs.* adolescents) and informants (patient-reports *vs.* parent-reports). The resulting global index of asthma-specific HrQoL presented good reliability and convergent validity with the generic and chronic-generic measures. The DISABKIDS instruments also detected significant differences in HrQoL regarding asthma severity groups. ***Conclusion***. The DISABKIDS-AsM may be regarded as a specific one-dimensional questionnaire, which, besides suiting pediatric patients in different developmental stages and enabling reliable proxy-reports, is sensitive to asthma clinical characteristics and is cross-culturally comparable, thus representing a valuable tool for assessing asthma-specific HrQoL as a primary health outcome in clinical practice and research contexts.

## Keywords

Asthma-specific assessment • Children and adolescents • DISABKIDS questionnaires • Health-related quality of life • Patient-reported and parent-reported outcomes • Psychometrics

# Introduction

Asthma is a chronic inflammatory disease of the airways with a high prevalence worldwide, particularly among pediatric patients (Pearce et al., 2007). In Portugal, its prevalence is nearly 9% in children and 14% in adolescents (Pinto, 2011). Episodic exacerbations of asthma symptoms can be life threatening and are a major cause of hospitalizations among pediatric patients (Global Initiative for Asthma Program [GINA], 2008). Moreover, the dependence on medication, sleep disturbances, daytime fatigue, physical limitations, school absenteeism and academic underachievement may impair the health-related quality of life (HrQoL) of children and adolescents, particularly when asthma is poorly controlled (Dean et al., 2010; Schmier et al., 2007). Some comparative studies with healthy controls have reported decreased generic HrQoL in pediatric asthma patients (Grootenhuis, Koopman, Verrips, Vogels, & Last, 2007; Upton et al., 2005; Varni, Limbers, & Burwinkle, 2007); however, other studies have failed to detect significant differences (Chan, Mangione-Smith, Burwinkle, Rosen, & Varni, 2005; Moreira et al., 2013). When comparing children/adolescents with asthma to children/adolescents with other medical conditions, no significant impairments have been found in HrQoL total scores (Anderson, Czosek, Knilans, & Marino, 2012; Bullinger, Schmidt, Petersen, & Ravens-Sieberer, 2006; Moreira et al., 2013), but lower scores in the physical domain have been reported for pediatric asthma patients (Austin, Smith, Risinger, & McNelis, 1994; Varni et al., 2007).

These inconsistent findings may be the result of methodological constraints, namely, the use of broad-scope instruments that may neglect the most specific HrQoL domains affected by asthma. Therefore, a multilevel assessment of pediatric HrQoL, including generic and disease-specific measures, is recommended (World Health Organization [WHO], 1993). The European KIDSCREEN and DISABKIDS projects provide a set of age-appropriate and cross-culturally comparable questionnaires in a three-level modular system for assessing pediatric HrQoL (Baars et al., 2005; Bullinger et al., 2006; Ravens-Sieberer et al., 2007). While the generic measures are suitable for all children and adolescents and allow comparisons between healthy and clinical populations, the chronic-generic and disease-specific measures ensure sensitivity to disease-related impairments and healthcare needs and allow the detection of subtle but clinically relevant differences or changes in the health status of patients (Guyatt, 1995; Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003).

This article reports the results from the field validation study of a specific instrument to assess the HrQoL in Portuguese children and adolescents with asthma. Following standard procedures for cross-cultural instrument adaptation (Schmidt & Bullinger, 2003), the patient- and parent-reported versions of the DISABKIDS-Asthma Module (AsM) (The DISABKIDS Group

Europe, 2006) were previously translated into Portuguese language and internationally harmonized to ensure the conceptual equivalence of items. Semantic validation and pilot testing were also performed to verify the comprehensibility, relevance and adequacy of items and response scales (Silva, Carona, Crespo, & Canavarro, 2011). The main goal of this study was to ascertain the psychometric properties of the Portuguese patient- and parent-reported versions of the DISABKIDS-AsM questionnaires. Specifically, we aimed to examine the following: (1) the original correlated two-factor model of the DISABKIDS-AsM, as well as an alternative one-factor model; (2) the invariance of the measurement model across age groups (children aged 8-12 years *vs.* adolescents aged 13-18 years) and informants (patient-reports *vs.* parent-reports); (3) the reliability of the questionnaires; (4) their construct validity (convergent validity with the generic and chronic-generic instruments and known-groups validity with regard to asthma severity levels as assessed by physicians), as well as their correlations with asthma symptoms as perceived by children/adolescents and their parents; and (5) the child-parent agreement on ratings of asthma-specific HrQoL.

# Method

## Participants and procedure

The participants were dyads of children/adolescents diagnosed with asthma and one of their parents. Data collection occurred between June 2011 and February 2012 in the outpatient services of three Portuguese public hospitals, upon the study's approval by the respective Ethics Committees and/or Direction Boards, and in agreement with the following inclusion criteria: (1) age between 8 and 18 years; (2) diagnosis of asthma, established by a physician according to the International Classification of Diseases-10, for at least one year; (3) requiring regular or emergency medication intake; (4) absence of comorbidity with other health conditions; and (5) be accompanied by a parent currently assuming the role of primary family caregiver (i.e. the parent self-identified as mainly responsible for the child's asthma management). The children and adolescents who attended medical routine appointments in the period of data collection were screened by their physicians based on their medical files, and those who met the aforementioned criteria were invited to participate in the study (non-probabilistic convenience sampling method).

Following the World Medical Association Declaration of Helsinki's guidelines (World Medical Association [WMA], 2008) and national legal requirements, detailed information about the study aims and procedures was provided to all participants, and informed consent was obtained from parents and adolescents older than 13 years, and informal assent was obtained from younger children. The children/adolescents and parents who agreed to participate (*n* = 144 dyads) completed the questionnaires independently, in a room designated for research purposes in the health institution they attended. A research assistant was available to provide support whenever necessary and to prevent the exchange of information between children and parents.

## Measures

Pediatric HrQoL was assessed by children/adolescents and their parents using the Portuguese patient- and parent-reported versions of the generic KIDSCREEN-10 index (Ravens-Sieberer et al., 2010), the DISABKIDS-12 chronic-generic module (The DISABKIDS Group Europe, 2006) and the DISABKIDS asthma-specific module (The DISABKIDS Group Europe, 2006). The KIDSCREEN-10 index comprises 10 items assessing general subjective health and well-being (e.g., "Have you felt fit and well?"/ "Has your child felt fit and well?"), and the DISABKIDS-12 includes 10 items measuring the impact of chronic health conditions (e.g., "Does your condition get you down?"/ "Does your child's condition get him/her down?") and two items measuring the impact of treatments on patients' lives (e.g., "Does taking medication bother you?"/ "Does taking medication bother your child?"). The DISABKIDS-AsM comprises 11 items focused on the experience of limitations and symptoms (Impact, six items; e.g., "Do you feel that you get easily exhausted?"/ "Does your child feel that he/she gets easily exhausted?") and on fears and worries about having asthma (Worry, five items; e.g., "Are you worried that you might have an asthma attack?"/ "Is your child worried that he/she might have an asthma attack?"). The DISABKIDS-AsM questionnaires also include three questions assessing the participants' perceptions of asthma symptoms. The three questionnaires were answered using a five-point Likert scale, ranging from 1 (*never/not at all*) to 5 (*always/extremely*). Standardized scores (0-100) were calculated, with higher scores indicating better HrQoL.

Parents also completed a socio-demographic datasheet soliciting for their age, gender, educational level and occupational status, as well as their children's age, gender and clinical information (e.g., age at the time of asthma diagnosis and use of medication). Following the Global Initiative for Asthma guidelines (GINA, 2008), the clinical severity of asthma was classified by physicians into four categories: intermittent, mild persistent, moderate persistent and severe persistent.

## Statistical analyses

The statistical analyses were performed with the Statistical Package for the Social Sciences, v.20 (SPSS Inc., Chicago, IL). Except for clinical and socio-demographic variables, missing data, which were random and less than 5% of the values, were handled by replacement with the individual mean score for each scale. Descriptive statistics were calculated for socio-demographic and clinical variables.

The factor structure of the Portuguese patient- and parent-reported versions of the DISABKIDS-AsM was examined with confirmatory factor analyses (CFA) using the Analysis of Moment Structures, v.20 (AMOS Development Corporation, Meadville, PA). The models' goodness-of-fit was assessed based on the maximum-likelihood $\chi^2$ statistic, the comparative fit index (CFI), the root mean square error of approximation (RMSEA) and the standardized root mean squared residual (SRMR). A model was considered to have a good fit when CFI ≥ .95, RMSEA ≤ .06 and SRMR ≤ .08, and was considered to have an acceptable fit when CFI ≥ .90 and RMSEA ≤ .10 (Browne & Cudeck, 1993; Hu & Bentler, 1999). The factorial validity of the DISABKIDS-AsM questionnaires was evaluated based on the significance and strength of factor loadings. The measurement invariance of the model across age groups (children 8-12 years *vs.* adolescents 13-18 years) and informants (patient-reports *vs.* parent-reports) was addressed at a strong level by performing multi-group analyses comparing the unconstrained model with a model in which factor loadings (metric invariance) and factor loading and item intercepts (scalar invariance) were fixed equally across groups (Dimitrov, 2010).

The reliability of the DISABKIDS-AsM questionnaires was assessed by using Cronbach's alpha coefficients and composite reliability (CR) values, calculated from the squared sum of standardized factor loading divided by the squared sum of standardized factor loading and error variance terms. Good construct reliability was established if CR was higher than .70 (Hair, Black, Babin, & Anderson, 2010). Construct validity was examined by calculating Pearson correlation coefficients between the DISABKIDS-AsM questionnaires and the generic and chronic-generic HrQoL measures (convergent validity), and by comparing HrQoL across groups expected to differ in this health construct (known-groups validity) (DeVellis, 2012). Multivariate analyses of covariance (MANCOVA) were performed to compare the generic, chronic-generic and asthma-specific HrQoL between asthma severity groups (intermittent asthma *vs.* persistent asthma), while controlling for children's age and gender by including them as covariates. When multivariate effects were significant, univariate analyses were performed to examine which levels of HrQoL were significantly different between groups. In addition, correlation coefficients between HrQoL and asthma symptoms as perceived by the children/adolescents and by parents were examined. Agreement between patient- and parent-reports of pediatric generic, chronic-generic and asthma-specific HrQoL was tested at the individual and group levels (Sneeuw, Sprangers, & Aaronson, 2002) by using, respectively, intraclass correlation coefficients (ICC) (two-way mixed model, absolute agreement, 95% confidence interval) and MANCOVA for repeated measures (entering the informant as the within-subject factor and the children's age and gender as covariates).

# Results

## Sample characteristics

Four cases were excluded due to missing values in a ratio greater than 5% of the data. The final sample included 140 dyads of children/adolescents diagnosed with asthma and one of their parents. The socio-demographic and clinical characteristics of the sample are presented in Table 1. Due to the low frequency of participants at each asthma severity level, this variable was dichotomized into intermittent (*n* = 83, 59.3%) and persistent asthma (*n* = 57, 40.7%) for the subsequent analyses.

**Table 1** | Socio-demographic and clinical characteristics of the sample

| | Pediatric patients (*n* = 140) | Parents (*n* = 140) |
|---|---|---|
| ***Socio-demographic characteristics*** | | |
| Age (in years), *M* (*SD*) | 12.18 (2.70) | 42.04 (7.11) |
| Age group, *n* (%) | | |
| Children (8-12 years) | 79 (56.4%) | |
| Adolescents (13-18 years) | 61 (43.6%) | |
| Gender, *n* (%) | | |
| Male | 89 (63.6%) | 27 (19.3%) |
| Female | 51 (36.4%) | 113 (80.7%) |
| Socio-economic level [a], *n* (%) | | |
| Low | | 83 (59.3%) |
| Medium | | 52 (37.1%) |
| High | | 5 (3.6%) |
| ***Clinical characteristics*** | | |
| Asthma severity [b], *n* (%) | | |
| Intermittent | 83 (59.3%) | |
| Mild persistent | 33 (23.6%) | |
| Moderate persistent | 20 (14.3%) | |
| Severe persistent | 4 (2.9%) | |
| Disease length (in years), *M* (*SD*) | 7.66 (4.17) | |

[a] The socio-economic level was determined using a classification system for the Portuguese context based on parents' job and educational level (Simões, 1994). [b] Asthma severity as assessed by physicians according to the GINA guidelines (2008).

## Confirmatory factor analyses

The original correlated two-factor model of the DISABKIDS-AsM questionnaire had an unacceptable fit to the patient-reported data, with $\chi^2_{(43)} = 138.72$, $p \leq .001$; CFI = .84; RMSEA = .13; and SRMR = .08. The inspection of modification indices suggested that items 1, 3 and 4 might be correlated. Although these three items were hypothesized to load on different domains, all three were related to physical activity; therefore, their measurement errors were allowed to correlate. The modified model had an acceptable fit, with $\chi^2_{(40)} = 76.22$, $p \leq .001$; CFI = .94; RMSEA = .08; and SRMR = .07, which was significantly better than the original model, with $\Delta\chi^2_{(3)} = 62.50$, $p \leq .001$. All factor loadings were statistically significant and, except for item 2, were above the threshold of .50. However, the average variance extracted (AVE) by each factor, as calculated from the sum of squared standardized factor loadings divided by the sum of squared standardized factor loadings and error terms (Fornell & Larcker, 1981) (AVE = .40 for Impact and .41 for Worry), was lower than the squared correlation between the two factors ($r^2 = .88$), indicating that they did not measure different constructs.

A one-factor model, in which all items loaded on a global index of asthma-specific HrQoL, was also tested. The one-factor model (Figure 1) had an acceptable fit, $\chi^2_{(41)} = 80.57$, $p \leq .001$; CFI = .94; RMSEA = .08; and SRMR = .07. Although the chi-square difference test between the modified correlated two-factor model and the one-factor model was statistically significant, $\Delta\chi^2_{(1)} = 4.35$, $p = .037$, indicating a better fit for the two-factor model, the remaining goodness-of-fit indexes were nearly identical. The similarities on goodness-of-fit indexes, as well as the limitations of the two-factor model, namely the low AVE by each factor and the correlations between items which were hypothesized to load on different domains, suggested that the one-factor model would better fit the Portuguese patient-reported data. Therefore, the one-factor model, hereinafter referred to as asthma-specific HrQoL index, was adopted for the subsequent analyses.

The multi-group analysis by age group confirmed that the one-factor model was valid for both children and adolescents, with $\Delta\chi^2_{(11)} = 15.41$, $p = .165$ (metric invariance) and $\Delta\chi^2_{(11)} = 7.89$, $p = .723$ (scalar invariance).

The one-factor model was also tested for parent-reported data, given our aim of validating an equivalent model for both versions of the instrument (Figure 1). The model had a nearly acceptable fit, with $\chi^2_{(40)} = 112.11$, $p \leq .001$; CFI = .89; RMSEA = .11; and SRMR = .09. In addition, the multi-group analysis confirmed that factor loadings and item means did not differ significantly between informants (patient-reported data *vs.* parent-reported data), with $\Delta\chi^2_{(11)} = 13.94$, $p = .236$ (metric invariance) and $\Delta\chi^2_{(11)} = 15.68$, $p = .154$ (scalar invariance).

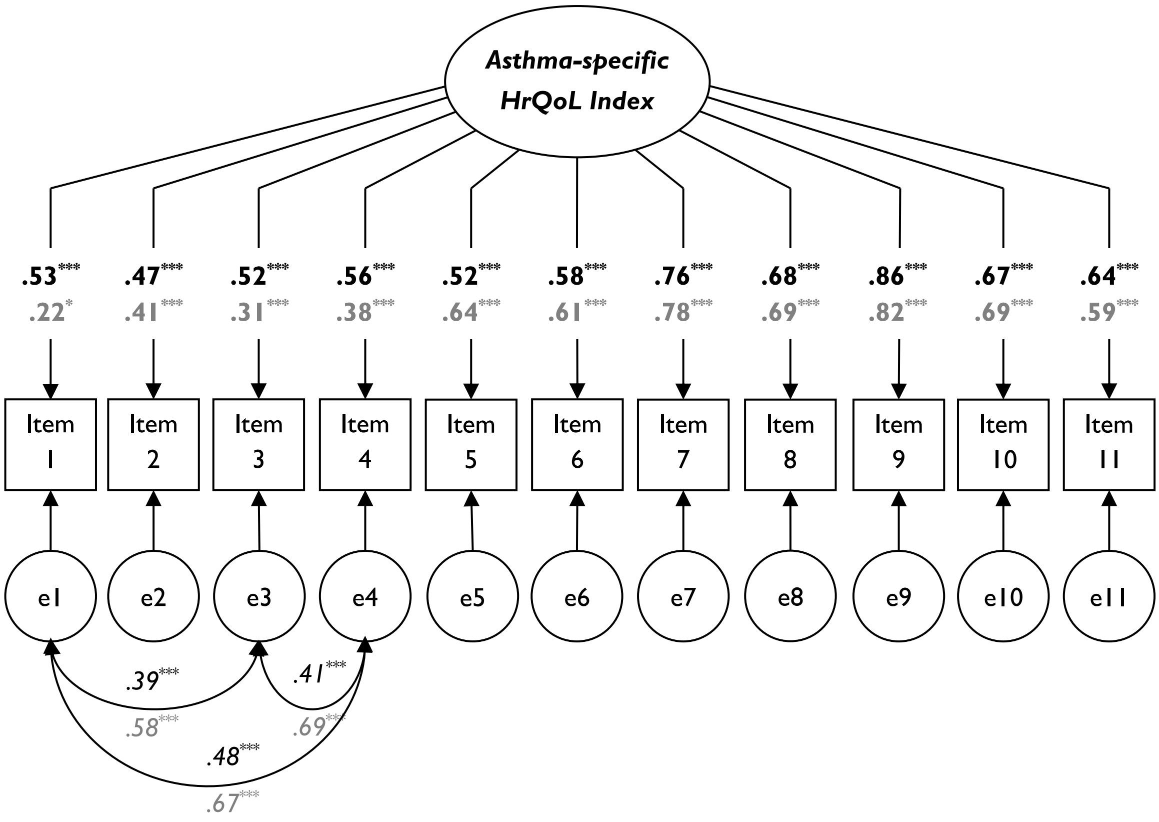

**Figure 1** | One-factor model for patient- and parent-reported versions of the DISABKIDS-AsM questionnaire

*Note*. Black bold figures represent standardized regression weights of factor loadings for the patient-reported version; gray bold figures represent standardized regression weights of factor loadings for the parent-reported version; black italicized figures represent Pearson correlation coefficients for the patient-reported-version; gray italicized figures represent Pearson correlation coefficients for the parent-reported version.
$^{***}$ $p \leq .001$; $^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

## Reliability

The Cronbach's alpha coefficients indicated good internal consistency for the patient-reported (α = .88) and parent-reported (α = .86) global index of asthma-specific HrQoL. In addition, CR values calculated from the factor loadings of the 11 items of the DISABKIDS-AsM questionnaires (.87 for patient- and .84 for parent-reports) were higher than the recommended threshold of .70 (Hair et al., 2010).

Adequate internal consistency was also found for the generic and chronic-generic HrQoL measures, with Cronbach's alpha values of .80 (patient-reports) and .77 (parent-reports) for the KIDSCREEN-10 instrument; and α = .65 (patient-reports) and α = .78 (parent-reports) for the DISABKIDS-12 chronic-generic module.

## Construct validity

The global index of asthma-specific HrQoL was moderately correlated with the generic HrQoL and strongly correlated with the chronic-generic HrQoL, supporting the convergent validity of the DISABKIDS-AsM (Table 2). In addition, patient-reported asthma-specific HrQoL was negatively correlated with children/adolescents' perceptions of asthma symptoms, and parent-reported asthma-specific HrQoL was negatively correlated with parents' perceptions of asthma symptoms (Table 2).

**Table 2** | Inter-correlation matrix of patient- and parent-reported HrQoL and asthma symptoms

| *Variable/ Measure* | *Informant* | *Pearson correlation coefficients* | | | | |
|---|---|---|---|---|---|---|
| | | | | Asthma symptoms | | |
| | | 1 | 2 | Recency $^{a}$ | Frequency $^{b}$ | Severity $^{c}$ |
| 1. Generic HrQoL | Patient | - | - | -.16 | -.13 | -.11 |
| (KIDSCREEN-10) | Parent | - | - | .05 | -.03 | -.17$^{*}$ |
| 2. Chronic-generic HrQoL | Patient | .61$^{***}$ | - | -.11 | -.08 | -.12 |
| (DISABKIDS-12) | Parent | .52$^{***}$ | - | -.09 | -.19$^{*}$ | -.30$^{***}$ |
| 3. Asthma-specific HrQoL | Patient | .39$^{***}$ | .68$^{***}$ | -.06 | -.10 | -.27$^{**}$ |
| (DISABKIDS-AsM) | Parent | .36$^{***}$ | .66$^{***}$ | -.17$^{*}$ | -.28$^{**}$ | -.39$^{***}$ |

$^{a}$ Time since last asthma attack, as assessed by pediatric patients and by parents ("When was the last time you/your child had an asthma attack?"). $^{b}$ Frequency of asthma attacks during the last year, as assessed by pediatric patients and by parents ("How many asthma attacks did you/your child have during the last year?"). $^{c}$ Asthma severity during the last year, as assessed by pediatric patients and by parents ("How severe was your/your child's asthma during the last year?").
$^{***}$ $p \leq .001$; $^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$, two-tailed.

A significant multivariate effect of asthma severity levels, as assessed by physicians, was found for both patient- and parent-reports, with Wilks' Lambda = .92, $F_{(3, 134)} = 3.81$, $p = .012$, $\eta_p^2 = .08$ and Wilks' Lambda = .89, $F_{(3, 134)} = 5.58$, $p = .001$, $\eta_p^2 = .11$, respectively. The univariate effects (Table 3) showed that children/adolescents with persistent asthma had lower chronic-generic and asthma-specific HrQoL than patients with intermittent asthma, attesting the known-groups validity of both generic and asthma-specific modules of the DISABKIDS instruments.

## Child-parent agreement

At the individual level, the examination of the ICC indicated poor to moderate levels of agreement between patient- and parent-reports of pediatric HrQoL (Table 4). At the group level, the MANCOVA for repeated measures showed no significant multivariate differences between informants, Wilks' Lambda = .99, $F_{(3, 135)} = 0.55$, $p = .651$ (univariate effects are presented in Table 4). In addition, no significant multivariate effects of the interaction between informant and children's age, Wilks' Lambda = .99, $F_{(3,\ 135)}$ = 0.12, $p$ = .949, or gender, Wilks' Lambda = .95, $F_{(3,\ 135)}$ = 2.17, $p$ = .094, were found.

**Table 3** | Univariate analyses of covariance of HrQoL between asthma severity levels

| *Variable/Measure* | *Informant* | *Asthma severity levels* [a] | | | | |
|---|---|---|---|---|---|---|
| | | Intermittent | Persistent | | | |
| | | *M (SD)* | *M (SD)* | $F_{(1,136)}$ | $p$ | $\eta_p^2$ |
| Generic HrQoL | Patient | 81.60 (13.38) | 79.30 (14.89) | 0.96 | .328 | .01 |
| (KIDSCREEN-10) | Parent | 74.73 (14.99) | 75.00 (13.35) | 0.06 | .811 | .00 |
| Chronic-generic HrQoL | Patient | 83.18 (11.71) | 77.19 (14.63) | 9.91 | .002 | .07 |
| (DISABKIDS-12) | Parent | 81.75 (12.58) | 75.55 (15.17) | 9.79 | .002 | .07 |
| Asthma-specific HrQoL | Patient | 67.42 (20.17) | 62.56 (19.31) | 3.49 | .064 | .03 |
| (DISABKIDS-AsM) | Parent | 64.46 (15.99) | 61.40 (18.18) | 1.66 | .200 | .01 |

[a] Dichotomized asthma severity levels as assessed by physicians, according to the GINA guidelines (2008).

**Table 4** | Agreement between patient- and parent-reports of generic, chronic-generic and asthma-specific HrQoL

| *Variable/Measure* | *Informant* | *M (SD)* | $F_{(1,\ 137)}$ | $p$ | $\eta_p^2$ | ICC [a] |
|---|---|---|---|---|---|---|
| Generic HrQoL | Patient | 80.66 (14.01) | 0.68 | 0.410 | 0.01 | 0.35*** |
| (KIDSCREEN-10) | Parent | 74.84 (14.30) | | | | |
| Chronic-generic HrQoL | Patient | 80.74 (13.26) | 0.21 | 0.650 | 0.00 | 0.54*** |
| (DISABKIDS-12) | Parent | 79.23 (13.98) | | | | |
| Asthma-specific HrQoL | Patient | 65.44 (19.90) | 1.07 | 0.302 | 0.01 | 0.36*** |
| (DISABKIDS-AsM) | Parent | 62.21 (16.92) | | | | |

[a] Intraclass correlation coefficients reference values: ICC ≤ .40 = poor agreement, ICC between .41 and .60 = moderate agreement, ICC between .61 and .80 = good agreement, ICC ≥ .81 = excellent agreement (Landis & Koch, 1977).

*** $p \leq .001$; ** $p \leq .01$; * $p \leq .05$, two-tailed.

## Discussion

This is the first cross-cultural adaptation of an asthma-specific HrQoL questionnaire to the Portuguese pediatric context and the first study to examine the factorial structure of the DISABKIDS-AsM using CFA. Following the introduction of minor modifications (i.e. allowing the measurement error terms of the items related to physical activity to correlate), the correlated two-factor model presented good factorial validity; however, the low AVE by each factor suggested that a one-factor model would fit the Portuguese data better. The one-factor model had good fit to the patient-reported data and a nearly acceptable fit to the parent-reports. In addition, all items loaded significantly on the proposed global index of asthma-specific HrQoL, and the model was invariant across age groups (children *vs.* adolescents) and informants (patient-reports *vs.* parent-reports). The psychometric qualities of reliability and validity of the Portuguese patient- and parent-reported versions of the DISABKIDS-AsM questionnaires as a global index of asthma-specific HrQoL resembled those described in the original study with an international sample from seven European countries (Baars et al., 2005).

The items included in the DISABKIDS asthma-specific module were originally derived from focus groups conducted with children and adolescents and primarily reflect the perspective of pediatric patients (Baars et al., 2005; The DISABKIDS Group Europe, 2006). Concordantly, the analytical strategy used in our study valued the patient-reported data to adjust the factorial model of the questionnaire, and subsequently the resulting model was tested for parent-reported data. Although consistent with the World Health Organization recommendations for pediatric quality of life assessment (WHO, 1993), the child-centered approach may explain the poorer goodness-of-fit indexes for the parent-reported version of the instrument. These results, which were similar to those found in the psychometric studies of the chronic-generic module (Carona, Silva, Moreira, Canavarro, & Bullinger, 2014; Muehlan, 2010), should not constitute an obstacle to the use of parent-reports as proxies, but instead imply that HrQoL assessment should employ patients' self-reports whenever possible.

The DISABKIDS-AsM questionnaires presented good reliability, confirming that their 11 items consistently reflect the latent construct of asthma-specific HrQoL, either assessed by children/adolescents or parents. Regarding convergent validity, the moderate and strong correlations with the generic and chronic-generic measures, respectively, provide additional evidence of the conceptual distinction between generic HrQoL and disease-specific impact (Wallander, Schmitt, & Koot, 2001), even if they are hierarchically interrelated. The three HrQoL measures correlated differently with patients' and parents' perceptions of recency, frequency and severity of asthma symptoms, with stronger associations for the asthma-specific measure. Moreover, the chronic-generic and asthma-specific instruments have detected significant differences between asthma severity levels as assessed by physicians, in contrast to the generic measure. Thus, we advocate a multilevel assessment of HrQoL, including both generic domains and disease-specific impact, to ensure sensitivity to the differences in health status and to the specific healthcare needs of pediatric patients (Wiebe et al., 2003).

The absence of significant differences between informants on factor loadings and on item means, as well as on DISABKIDS-AsM total scores, attested to the strong agreement between patient- and parent-reports at the group level (Sneeuw et al., 2002). Nevertheless, at the individual level, the examination of ICC indicated poor to moderate levels of agreement. In addition, the parent-reports were strongly correlated with asthma symptoms, whereas patient-reports were more sensitive in detecting differences between clinical severity levels. Taken together, these findings support the utility of a dyadic parent-child approach to HrQoL assessment (Bullinger et al., 2006), which may provide unique information about the impact of asthma on children/adolescents' psychosocial functioning and allow the identification of the so-called "hidden morbidities" (Varni, Burwinkle, & Lane, 2005).

Although the original structure of the DISABKIDS-AsM consists of two correlated domains (Impact and Worry), these analyses suggested a one-dimensional measure. Nevertheless, these results do not preclude the use of the two domains for cross-cultural comparisons. This study is an example of a sequential approach to instrument development, in which a previously published measure is then translated and validated for a different language and culture (Schmidt & Bullinger, 2003). These analyses should be replicated with samples from other countries in order to further examine whether a one-dimensional measure would better suit the asthma-specific HrQoL assessment in children and adolescents.

## Limitations and strengths

The main limitation of this study was the non-probabilistic sample collection method and the heterogeneous distribution of children by asthma severity levels. The high percentage of participants with intermittent asthma, although consistent with the distribution of asthma severity levels that are typically observed in the Portuguese pediatric population (Gaspar, Almeida, & Nunes, 2006), required the variable to be dichotomized and increased intragroup variability. In addition, the classification of asthma severity levels was based on expert opinion, rather than on physiological measures, which may disguise important differences in asthma-specific HrQoL. Our study was also limited by its cross-sectional design, which precluded the examination of the test-retest reliability of the instrument and the ascertainment of a threshold for discrimination of clinically important changes in asthma-specific HrQoL. Although a score difference higher than a half a standard deviation has been proposed as a minimally important difference for HrQoL instruments (Norman, Sloan, & Wyrwich, 2003), future longitudinal research with a higher number of children with severe asthma is required to further examine the sensitivity of the DISABKIDS-AsM questionnaires to developmental and clinical changes.

Despite these limitations, CFA is as a sophisticated and robust analytic procedure to ascertain construct reliability and factorial validity across age groups and informants. Our study was also strengthened by the multilevel assessment of HrQoL, including both generic, chronic-generic and asthma-specific measures, and by the dyadic parent-child approach for data collection and analyses. The adopted multi-informant approach was also extended to the physicians' classification of asthma severity, thus enhancing the information collected from parents, which is likely to be biased by parental perceptions and expectations (Everhart & Fiese, 2009). Therefore, we can conclude that the Portuguese patient- and parent-reported versions of the DISABKIDS-AsM questionnaires are reliable and valid measures for assessing the specificities of HrQoL in pediatric asthma patients.

## Conclusion

In summary, this study validates the pertinence of using the Portuguese patient- and parent-reported versions of the DISABKIDS-AsM as a global index of asthma-specific HrQoL. An asthma-specific HrQoL instrument, which can be briefly completed by children/adolescents and by parents and that is sensitive to the clinical characteristics of asthma, is recommended as a primary health outcome for routine assessment in medical care and for research, particularly clinical trials and health policy/economy studies. The combined use of generic and specific modules allows clinicians and researchers to compare the HrQoL across children/adolescents with different health conditions or comorbidities without neglecting the sensitivity to the asthma-related impairments and healthcare needs. Moreover, the use of standard procedures to translate and validate the questionnaires ensures their cross-cultural equivalence and expands their utility in the international research context.

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# Empirical Study II

## Why the (dis)agreement? Family context and child-parent perspectives on health-related quality of life and psychological problems in pediatric asthma

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# Why the (dis)agreement? Family context and child-parent perspectives on health-related quality of life and psychological problems in pediatric asthma

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## Abstract

***Introduction.*** Children's health-related quality of life (HrQoL) and psychological problems are important outcomes to consider in clinical decision making in pediatric asthma. However, children's and parents' reports often differ. The present study aimed to examine the levels of agreement/disagreement between children's and parents' reports of HrQoL and psychological problems and to identify socio-demographic, clinical and family variables associated with the extent and direction of (dis)agreement. ***Method.*** The sample comprised 279 dyads of Portuguese children with asthma who were between 8 and 18 years of age (*M* = 12.13; *SD* = 2.56) and one of their parents. The participants completed self- and proxy-reported questionnaires on pediatric generic HrQoL (KIDSCREEN-10), chronic-generic HrQoL (DISABKIDS-37) and psychological problems (Strengths and Difficulties Questionnaire). Children's and parents' perceptions of family relationships were measured with the Family Environment Scale and the caregiving burden was assessed using the Revised Burden Measure.
***Results.*** The child-parent agreement on reported HrQoL and psychological problems was poor to moderate (intraclass correlation coefficients between .32 and .47). The rates of child-parent discrepancies ranged between 52.7% (psychological problems) and 68.8% (generic HrQoL), with 50.5% and 31.5% of the parents reporting worse generic and chronic-generic HrQoL, respectively, and 33.3% reporting more psychological problems than their children. The extent and direction of disagreement were better explained by family factors than by socio-demographic and clinical variables: a greater caregiving burden was associated with increased discrepancies in both directions and children's and parents' perceptions of less positive family relationships were associated with discrepancies in different directions. ***Conclusion.*** Routine assessment of pediatric HrQoL and psychological problems in healthcare and research contexts should include self- and parent-reported data as complementary sources of information, and also consider the family context. The additional cost of conducting a more in-depth assessment of pediatric adaptation outcomes can be offset through more efficient allocation of health resources.

## Keywords

Caregiving burden • Child-parent (dis)agreement • Family relationships • Health-related quality of life • Pediatric asthma • Psychological problems

# Introduction

Health-related quality of life (HrQoL) and psychological problems have emerged as important health outcomes to consider in clinical decision making and research related to pediatric chronic conditions, such as asthma, because managing symptoms and improving psychosocial adaptation are now the primary goals of interventions (Clarke & Eiser, 2004; Le Coq, Boeke, Bezemer, Colland, & van Eijk, 2000). The assessment of pediatric populations poses particular methodological challenges, namely the reliability of children's self-reports and the advantages/disadvantages of using their parents as proxies (Bullinger, Schmidt, Peterson, & Ravens-Sieberer, 2006; Matza, Swensen, Flood, Secnik, & Leidy, 2004). Parents' reports are essential when children are too young or unable to report their own experiences (Eiser & Morse, 2001; Wallander, Schmitt, & Koot, 2001), and these reports play an important role in decision making about treatment and healthcare use (Annett, Bender, DuHamel, & Lapidus, 2003; Matza et al., 2004) and in detecting clinical changes over time (Le Coq et al., 2000). Nevertheless, the World Health Organization (WHO, 1993) recommends assessing children's individual perceptions of their quality of life (QoL) whenever possible. In addition, children's reports are more sensitive than their parents' in detecting minor emotional and behavioral disturbances (Becker, Hagenberg, Roessner, Woerner, & Rothenberger, 2004; Van Roy, Groholt, Heyerdahl, & Clench-Aas, 2010). Therefore, a multi-informant approach that includes both children's and parents' reports has been widely recommended to enable a comprehensive assessment of pediatric adaptation outcomes (Eiser & Morse, 2001; Van Roy et al., 2010).

Over the last few years, several instruments with self- and proxy-reported forms for assessing pediatric HrQoL and psychological problems have been developed (Bullinger et al., 2006; Goodman, 2001). Despite the common assumption that the reports from children and parents should be similar, most studies have found low to moderate levels of agreement on HrQoL (e.g., Sattoe, van Staa, Moll, & On Your Own Feet Research Group, 2012; White-Koning et al., 2007) and psychological problems (e.g., Ender, Stachow, Petermann, & Tiedjen, 2011; Van der Meer, Dixon, & Rose, 2008), with lower rates for social and emotional domains than for physical symptoms and observed behaviors (Becker et al., 2004; Eiser & Morse, 2001).

Children's health status seems to impact both the degree to which children and parents agree/disagree [the extent of (dis)agreement] and whether parents are more likely to over or underrate pediatric HrQoL and psychological problems (the direction of disagreement). Higher levels of agreement have been reported between parents and children with chronic conditions, compared with healthy controls (Russell, Hudson, Long, & Phipps, 2006). Research on pediatric chronic conditions has found that parents reported significantly lower HrQoL (Sattoe et al., 2012; White-Koning et al., 2007) and more psychological problems (Becker et al., 2004) than the children themselves, which is the opposite of the directional pattern of disagreement found in the general population (Cremeens, Eiser, & Blades, 2006; Gaspar, Matos, Batista-Foguet, Pais-Ribeiro, & Leal, 2010; Sawyer, Baghurst, & Mathias, 1992; Theunissen et al., 1998). Moreover, Upton, Lawford, and Eiser, (2008) stated that the levels of agreement would also depend on the relevance of different domains for a specific clinical group because parents would be most alert to the frailest domains of their children's HrQoL. This argument is supported by research that shows positive associations between the extent of agreement and disease severity and length (April, Feldman, Platt, & Duffy, 2006; Petsios et al., 2011).

Children's developmental characteristics have also been investigated in the child-parent (dis)agreement research, which has produced inconsistent findings to date. Some studies have found higher levels of agreement for older children, supporting the hypothesis that the levels of agreement depend on cognitive and communication skills (e.g., Petsios et al., 2011). Conversely, other studies have described greater agreement between parents and younger children, suggesting that increasing independence in adolescence may limit the sharing of experiences with parents (e.g., April et al., 2006; Jokovic, Locker, & Guyatt, 2004). Children's and parents' genders have also been suggested as important determinants of (dis)agreement (Eiser & Morse, 2001; Upton et al., 2008); however, few empirical studies have addressed the role of these variables (e.g., Theunissen et al., 1998) and no clear findings have emerged.

The examination of family-related factors remains an important gap in (dis)agreement research in general and in pediatric asthma in particular. There is, nonetheless, some evidence suggesting that the study of family relationships may add valuable contributions to our current understanding of the extent and direction of child-parent (dis)agreement (De Civita et al., 2005). For example, White-Koning and colleagues (2007) described a significant association between higher levels of parenting stress and parents' underrating the HrQoL of their children with cerebral palsy. Family relationships characterized by poor parental engagement and communication have also been linked to an increased likelihood of disagreement on reports of emotional and behavioral problems, most often with children reporting more problems than their parents (Van Roy et al., 2010). In addition, in a pediatric asthma study, the illness-related burdens experienced by parents were negatively associated with parents' reports of pediatric HrQoL (Annett et al., 2003), which may contribute to child-parent disagreement.

In the context of pediatric asthma, the present study aimed to examine the (dis)agreement between child- and parent-reported adaptation outcomes (HrQoL and psychological problems) and to identify the socio-demographic, clinical and family variables that may account for the extent and direction of disagreement. Three hypotheses were formulated: (H1) child-parent agreement on reports of adaptation outcomes will be moderate; (H2) parents will report lower HrQoL and more psychological problems than children; (H3) the extent of disagreement, particularly in parents' underrating of adaptation outcomes, will be associated with the clinical characteristics of their child's asthma (i.e., lower severity and a shorter time since diagnosis), with less positive family relationships and with greater caregiving burden.

# Method

## Participants and procedure

The participants (279 dyads of children with asthma and one of their parents) were enrolled between March 2010 and February 2012 in the outpatient services of three Portuguese public hospitals (Coimbra University Hospitals, Coimbra Pediatric Hospital and Leiria Saint Andre Hospital) after the study had been approved by the institutions' ethic committees. Using a non-probabilistic convenience sampling method, the children were selected based on their medical files, according to the following criteria: (1) age between 8 and 18 years; (2) diagnosis of asthma according to the International Classification of Disease (ICD-10) for at least 1 year; (3) absence of other chronic conditions; and (4) accompanied by the parent self-identified as the primary caregiver. The participants' socio-demographic and clinical characteristics are presented in Table 1.

**Table 1** | Socio-demographic and clinical characteristics of the sample

| | Children<br>(*n* = 279) | Parents<br>(*n* = 279) |
|---|---|---|
| ***Socio-demographic characteristics*** | | |
| Age (in years), *M* (*SD*) | 12.13 (2.56) | 41.33 (5.90) |
| Age group [a], *n* (%) | | |
| Children | 162 (58.1%) | |
| Adolescents | 117 (41.9%) | |
| Gender, *n* (%) | | |
| Male | 175 (62.7%) | 41 (14.7%) |
| Female | 104 (37.3%) | 238 (85.3%) |
| Socio-economic level [b], *n* (%) | | |
| Low | | 168 (60.2%) |
| Medium | | 78 (28.0%) |
| High | | 20 (7.2%) |
| *Missing* | | 13 (4.7%) |

[a] The pediatric sample was divided into two age groups based on The DISABKIDS Group Europe's (2006) categories: children (8-12 years old) and adolescents (13-18 years old). For simplicity, we adopted the term children to refer to the pediatric sample, which includes both age groups. [b] Socio-economic level was determined using a classification system for the Portuguese context based on the parents' jobs and educational levels (Simões, 1994).

**Table 1** | Socio-demographic and clinical characteristics of the sample (cont.)

| | Children | Parents |
|---|---|---|
| ***Clinical characteristics*** | | |
| Asthma severity [c], *n* (%) | | |
| Intermittent | 157 (56.3%) | |
| Mild persistent | 73 (26.2%) | |
| Moderate persistent | 41 (14.7%) | |
| Severe persistent | 8 (2.9%) | |
| Age (in years) at the time of diagnosis, *M* (*SD*) | 4.74 (3.89) | |
| Time (in years) since asthma diagnosis, *M* (*SD*) | 7.64 (4.04) | |
| Using medication, *n* (%) | 273 (97.8%) | |

[c] Asthma severity was classified by physicians, according to the Global Initiative for Asthma [GINA] (2008) guidelines. Due to the heterogeneous distribution of asthma severity in our sample, this variable was dichotomized and dummy-coded [0 – intermittent asthma, *n* = 157; 1 – persistent asthma (mild, moderate and severe), *n* = 122].

The pediatric sample was mainly composed of boys and most of the children had intermittent asthma, which is consistent with the prevalence of asthma by gender and with the distribution of asthma severity levels typically observed in the Portuguese pediatric population (Gaspar, Almeida, & Nunes, 2006). The great majority of caregivers was female and had low/medium socio-economic status, reflecting the users' profile in public pediatric healthcare services in Portugal.

Informed consent was obtained from all parents and adolescents older than 13 years, and informal assent was obtained from younger children. The protocols were completed by the children and parents in the health institution they attended, under the supervision of a trained research assistant who ensured that no information was exchanged between the children and their parents.

## Measures

### *Children's adaptation outcomes*

The children's HrQoL was measured by the Portuguese self- and proxy-reported versions of the KIDSCREEN-10 Index (Ravens-Sieberer et al., 2010; Portuguese version: Matos, Gaspar, & Simões, 2012) and the DISABKIDS-37 Chronic-Generic Module (The DISABKIDS Group Europe, 2006; Portuguese version: Carona et al., 2013). The KIDSCREEN-10 provides a general index of subjective health and well-being, whereas the DISABKIDS-37 assesses the impact of the chronic condition on six facets of the children's QoL: Independence, Emotion, Social inclusion, Social exclusion, Physical limitation and Treatment. Both questionnaires were answered using a five-point Likert scale ranging from 1 (*never*) to 5 (*always*), with higher scores indicating better HrQoL.

Psychological problems were assessed using the Difficulties scale of the Portuguese self- and parent-rated versions of the Strengths and Difficulties Questionnaire (Goodman, 2001; Portuguese version: Fleitlich, Loureiro, Fonseca, Gaspar, 2005). This scale comprises 20 items that were clustered into Internalizing and Externalizing problems (Goodman, Lamping, & Ploubidis, 2010) and answered using a Likert-type response scale with three options (0 = *not true*, 1 = *somewhat true* and 2 = *certainly true*). Higher values indicated more psychological problems. The Cronbach's alpha values found in our sample for each measure are presented in Table 2.

### *Family variables*

The overall quality of family relationships was assessed by the children and parents using the Portuguese version of the Family Relationships Index (Moos, 1990). This scale is comprised of the Cohesion, Expressiveness and Conflict dimensions of the Family Environment Scale (Moos & Moos, 1986), which assess how involved family members are in their family and how openly they express both positive and negative feelings, using 27 items scored on a six-point Likert scale ranging from 1 (*completely disagree*) to 6 (*completely agree*), with higher scores indicating better perceived family relationships. In the current sample, the Cronbach's alpha values were .86 and .85 for children's and parents' reports, respectively.

The caregiving burden was measured using the Portuguese version of the Revised Burden Measure (Montgomery & Kosloski, 2006; Portuguese version: Carona, Silva, & Canavarro, 2011). This scale assesses the parents' perceptions of changes in dyadic parent-child relationships (Relationship burden), time constraints resulting from caregiving activities (Objective burden) and generalized negative affect (Subjective burden), with 16 items scored on a five-point Likert scale ranging from 1 (*not at all*) to 5 (*a great deal*), with higher values indicating a greater caregiving burden. Good internal consistency was observed for our sample (Cronbach's alpha = .93).

## Statistical analyses

Statistical analyses were performed with SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The child-parent (dis)agreement on adaptation outcomes was examined at the individual and the group levels (Sneeuw, Sprangers, & Aaronson, 2002), by using, respectively, intraclass correlation coefficients (ICC) [two-way mixed model, absolute agreement, 95% confidence interval (CI)] and analyses of covariance for repeated measures (univariate analyses for the total scores and multivariate analyses for the six facets of chronic-generic HrQoL and for the two dimensions of psychological problems). Absolute and directional discrepancies were computed as dyadic indexes of the extent and direction of disagreement, respectively (Kenny, Kashy, & Cook, 2006). Directional discrepancies were categorized into three groups ("child-report > parent-report", "agreement" and "child-report < parent-report") based on the threshold for clinically important differences in QoL (Norman, Sloan, & Wyrwich, 2003). Thus, agreement was defined as an absolute child-parent difference that was lower than or equal to half of the standard deviation (*SD*) of the score with the greatest variability. In order to identify the clinical, socio-demographic and family-related variables associated with the extent and direction of child-parent discrepancies, hierarchical multiple regression analyses and multinomial logistic regression analyses using "agreement" as the reference category were respectively performed (Field, 2009). For multinomial logistic regressions, the goodness-of-fit of the overall model was evaluated using likelihood ratio tests and the statistical significance of individual predictors was evaluated by calculating the Wald statistic and the odds ratio (OR) with a 95% CI.

# Results

## Child-parent (dis)agreement

At the individual level, there were poor to moderate correlations between children's and parents' reports of pediatric HrQoL and psychological problems (Table 2). At the group level, after controlling for socio-demographic and clinical variables, the results indicated a multivariate effect of the informant on chronic-generic HrQoL, Wilks' Lambda = .95, $F_{(6,\ 258)}$ = 2.13, $p$ = .05, and on psychological problems, Wilks' Lambda = .96, $F_{(2,\ 268)}$ = 5.30, $p$ = .01. However, as shown in Table 2, no univariate effects reached statistical significance.

The examination of the child-parent discrepancies indicated rates of agreement ranging from 31.2% (generic HrQoL) to 47.3% (psychological problems). Overall, the parents tended to score pediatric HrQoL lower and psychological problems higher than did the children (Figure 1).

## Regression analyses explaining the extent of disagreement

The regression analyses showed that children's age and gender explained only a small portion of the variance in child-parent absolute discrepancies. After controlling for clinical and socio-demographic variables, the family variables explained a significant portion of the variance (Table 3). Specifically, better family relationships were negatively associated with the extent of disagreement in HrQoL reports and a greater caregiving burden was positively associated with the extent of disagreement in the reported HrQoL and psychological problems.

**Table 2** | Descriptive statistics, intraclass correlation coefficients, ANCOVA for repeated measures, and absolute and directional discrepancies

| | ***Child-report*** | | ***Parent-report*** | | ***ICC*** [a] | ***ANCOVA for repeated measures*** [b] | | ***Discrepancy*** | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | ***Absolute*** [c] | ***Directional*** [d] |
| | *M* (*SD*) | α | *M* (*SD*) | α | | *F* | *p* | *M* (*SD*) | *M* (*SD*) |
| Generic HrQoL | 4.26 (0.55) | .80 | 4.01 (0.57) | .78 | .38 | 0.23 | .63 | 0.79 (0.41) | 0.26 (0.60) |
| Chronic-generic HrQoL | 4.25 (0.48) | .91 | 4.21 (0.49) | .93 | .47 | 0.72 | .40 | 0.77 (0.34) | 0.05 (0.50) |
| Independence | 4.23 (0.58) | .73 | 4.31 (0.57) | .77 | .33 | 2.76 | .10 | 0.72 (0.45) | -0.08 (0.66) |
| Emotion | 4.26 (0.71) | .86 | 4.22 (0.73) | .91 | .37 | 0.94 | .33 | 0.80 (0.54) | 0.05 (0.81) |
| Social inclusion | 4.26 (0.58) | .64 | 4.22 (0.59) | .70 | .32 | 2.88 | .09 | 0.81 (0.45) | 0.03 (0.68) |
| Social exclusion | 4.66 (0.48) | .71 | 4.60 (0.53) | .81 | .41 | 0.23 | .63 | 0.47 (0.50) | 0.06 (0.54) |
| Physical limitation | 3.87 (0.65) | .68 | 3.70 (0.67) | .77 | .41 | < 0.01 | .96 | 0.89 (0.47) | 0.17 (0.71) |
| Treatment | 4.16 (0.81) | .81 | 4.14 (0.79) | .84 | .36 | 2.75 | .10 | 0.91 (0.62) | 0.04 (0.91) |
| Psychological problems | 0.53 (0.25) | .75 | 0.59 (0.30) | .81 | .40 | 0.07 | .79 | 0.49 (0.19) | -0.06 (0.30) |
| Internalizing | 0.47 (0.28) | .62 | 0.52 (0.34) | .71 | .37 | 2.39 | .12 | 0.50 (0.23) | -0.05 (0.35) |
| Externalizing | 0.58 (0.34) | .75 | 0.66 (0.38) | .78 | .46 | 3.48 | .06 | 0.49 (0.24) | -0.08 (0.37) |

[a] Intraclass correlation coefficients reference values: ICC < .40 = poor agreement, ICC between .41 and .60 = moderate agreement, ICC between .61 and .80 = good agreement, ICC > .81 = excellent agreement (Landis & Koch, 1977). All ICCs were statistically significant at the .01 level. [b] Univariate analyses of covariance for repeated measures, entering the informant (child *vs.* parent) as the within-subject factor and the socio-demographic and clinical variables (children's age and gender, parents' gender, asthma severity and time since diagnosis) as covariates. [c] Σ (|child score - parent score|) / number of items for each dimension. [d] Σ (child score - parent score) / number of items for each dimension.

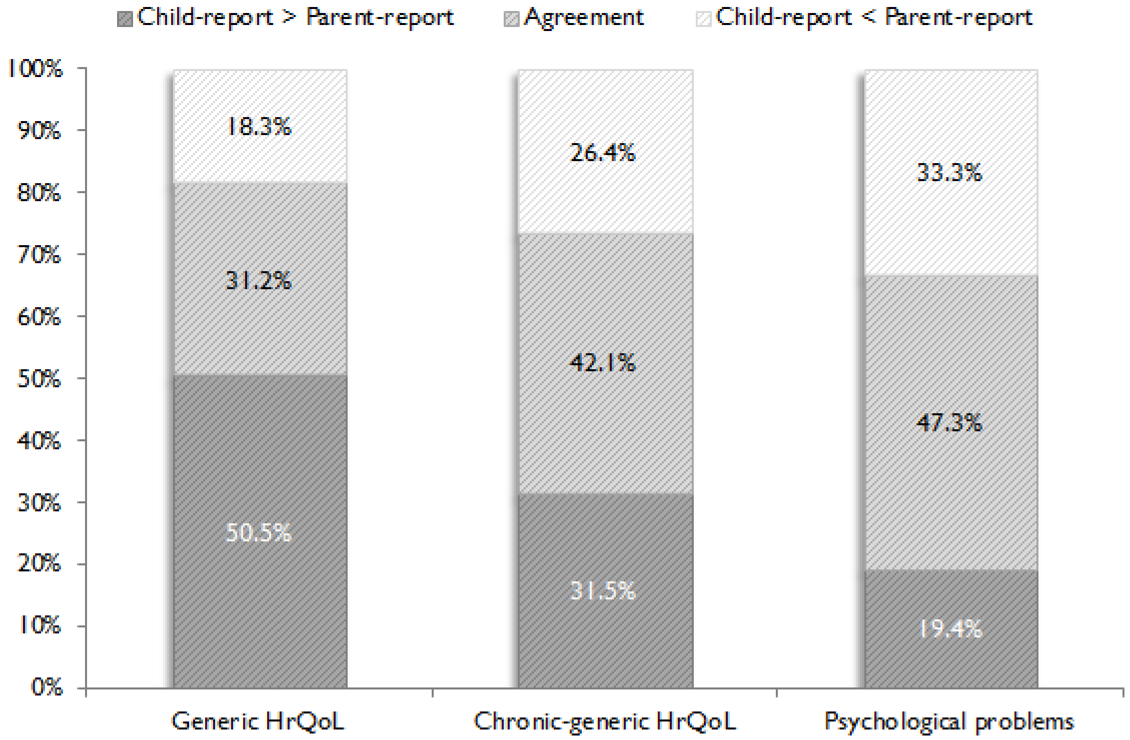

**Figure 1** | Distribution of child-parent directional discrepancies on generic HrQoL, chronic-generic HrQoL and psychological problems

*Note.* Agreement was defined as an absolute difference between the child's and parent's scores that was lower than or equal to half of the *SD* of the score with the greatest variability.

## Regression analyses explaining the direction of disagreement

The results from the multinomial logistic regression analyses examining "child-report > parent-report" and "child-report < parent-report" *vs.* "agreement" are presented in Table 4. The socio-demographic and clinical variables were not significantly associated with the direction of disagreement. A greater caregiving burden was associated with an increased likelihood of disagreement in both directions: parents' overrating of generic HrQoL and psychological problems and children's overrating of chronic-generic HrQoL. Family relationships had varying associations with the direction of disagreement: when children perceived less positive family relationships, they were more likely to report worse HrQoL and more psychological problems than their parents; when parents perceived less positive family relationships, they reported worse HrQoL; and when parents perceived better family relationships, they reported fewer psychological problems than the children.

**Table 3** | Hierarchical regression model explaining the extent of the child-parent discrepancies

| | **Absolute child-parent discrepancies** [a] | | | | | |
|---|---|---|---|---|---|---|
| | Generic HrQoL<br>$\mathbf{R^2 = .19; F_{(8, 257)} = 7.62^{***}}$ | | Chronic-generic HrQoL<br>$\mathbf{R^2 = .35; F_{(8, 252)} = 16.69^{***}}$ | | Psychological problems<br>$\mathbf{R^2 = .18; F_{(8, 257)} = 6.90^{***}}$ | |
| ***First step:<br>Socio-demographic and clinical variables*** | $\Delta R^2 < .01; F_{(5, 260)} = .17$ | | $\Delta R^2 = .06; F_{(5, 255)} = 3.00^{*}$ | | $\Delta R^2 = .04; F_{(5, 260)} = 1.89$ | |
| | β | *t* | β | *t* | β | *t* |
| Children's age | -.03 | -0.44 | -.18 | -2.65$^{**}$ | -.16 | -2.40$^{*}$ |
| Children's gender [b] | .02 | 0.36 | .14 | 2.25$^{*}$ | -.09 | -1.51 |
| Parents' gender [b] | .04 | 0.56 | -.03 | -0.55 | -.05 | -0.73 |
| Asthma severity [c] | .02 | 0.31 | .11 | 1.77 | -.02 | -0.29 |
| Time since asthma diagnosis | -.01 | -0.11 | .09 | 1.38 | .12 | 1.84 |
| ***Second step:<br>Family variables*** | $\Delta R^2 = .19; F_{(3, 257)} = 19.97^{***}$ | | $\Delta R^2 = .29; F_{(3, 252)} = 37.37^{***}$ | | $\Delta R^2 = .14; F_{(3, 257)} = 14.74^{***}$ | |
| | β | *t* | β | *t* | β | *t* |
| Children's age | .04 | 0.63 | -.10 | -1.67 | -.09 | -1.38 |
| Children's gender [b] | .02 | 0.30 | .13 | 2.56$^{*}$ | -.10 | -1.81 |
| Parents' gender [b] | .02 | 0.33 | -.06 | -1.23 | -.07 | -1.13 |
| Asthma severity [c] | .04 | 0.71 | .13 | 2.56$^{*}$ | -.01 | -0.15 |
| Time since asthma diagnosis | -.02 | -0.37 | .08 | 1.34 | .10 | 1.68 |
| Family relationships (children) | -.11 | -1.65 | -.19 | -3.21$^{**}$ | -.09 | -1.39 |
| Family relationships (parents) | -.18 | -2.83$^{**}$ | -.20 | -3.39$^{**}$ | -.06 | -0.96 |
| Caregiving burden | .30 | 4.88$^{***}$ | .35 | 6.32$^{***}$ | .33 | 5.30$^{***}$ |

[a] Hierarchical multiple regression analyses, entering the clinical and socio-demographic variables in the first block and the family variables in the second block of the regression equation. [b] Reference group: 0 = male; [c] Reference group: 0 = intermittent asthma.

$^{***}$ $p < .001$, two-tailed. $^{**}$ $p < .01$, two-tailed. $^{*}$ $p < .05$, two-tailed.

**Table 4** | Multinomial logistic regression model explaining the direction of the child-parent discrepancies

| | **Directional child-parent discrepancies** [a] | | | | | |
|---|---|---|---|---|---|---|
| | Generic HrQoL | | Chronic-generic HrQoL | | Psychological problems | |
| | $R^2_{(\text{Cox \& Snell})} = .13$; $R^2_{(\text{Nagelkerke})} = .14$<br>Model $\chi^2_{(16)} = 35.60^{**}$ | | $R^2_{(\text{Cox \& Snell})} = .24$; $R^2_{(\text{Nagelkerke})} = .27$<br>Model $\chi^2_{(16)} = 69.85^{***}$ | | $R^2_{(\text{Cox \& Snell})} = .12$; $R^2_{(\text{Nagelkerke})} = .14$<br>Model $\chi^2_{(16)} = 35.28^{**}$ | |
| | *B* (SE) | Odds Ratio | *B* (SE) | Odds Ratio | *B* (SE) | Odds Ratio |
| **Child-report < Parent-report *vs.* Agreement** | | | | | | |
| Children's age | .03 (.08) | 1.03 (0.88/ 1.21) | -.14 (.07) | 0.87 (0.75/ 1.00) | -.03 (.07) | 0.97 (0.85/ 1.10) |
| Children's gender [b] | .04 (.38) | 1.04 (0.49/ 2.20) | -.32 (.33) | 0.73 (0.38/ 1.39) | .07 (.30) | 1.07 (0.60/ 1.93) |
| Parents' gender [b] | .68 (.47) | 1.98 (0.79/ 4.98) | .52 (.42) | 1.69 (0.74/ 3.84) | -.68 (.46) | 0.51 (0.21/ 1.26) |
| Asthma severity [c] | .05 (.38) | 1.05 (0.50/ 2.20) | .20 (.32) | 1.22 (0.65/ 2.29) | .23 (.29) | 1.25 (0.71/ 2.22) |
| Time since asthma diagnosis | -.07 (.05) | 0.93 (0.85/ 1.03) | .03 (.04) | 1.03 (0.95/ 1.12) | .04 (.04) | 1.04 (0.97/ 1.13) |
| Family relationships (children) | -.65 (.32)$^{*}$ | 0.52 (0.28/ 0.99) | -.84 (.29)$^{**}$ | 0.43 (0.25/ 0.76) | .45 (.26) | 1.56 (0.94/ 2.60) |
| Family relationships (parents) | .40 (.39) | 1.49 (0.69/ 3.20) | -.08 (.31) | 0.93 (0.50/ 1.71) | -.35 (.28) | 0.70 (0.41/ 1.21) |
| Caregiving burden | .61 (.30)$^{*}$ | 1.84 (1.02/ 3.35) | .31 (.28) | 1.36 (0.78/ 2.37) | .51 (.23)$^{*}$ | 1.66 (1.06/ 2.60) |
| **Child-report > Parent-report *vs.* Agreement** | | | | | | |
| Children's age | .03 (.07) | 1.03 (0.90/ 1.17) | -.01 (.08) | 0.99 (0.86/ 1.15) | -.15 (.08) | 0.86 (0.74/ 1.00) |
| Children's gender [b] | .29 (.30) | 1.33 (0.74/ 2.39) | -.34 (.34) | 0.71 (0.37/ 1.37) | -.25 (.35) | 0.78 (0.39/ 1.56) |
| Parents' gender [b] | -.64 (.43) | 0.53 (0.23/ 1.23) | -.75 (.54) | 0.47 (0.17/ 1.35) | .58 (.44) | 1.79 (0.75/ 4.25) |
| Asthma severity [c] | -.28 (.29) | 0.75 (0.43/ 1.34) | -.09 (.33) | 0.92 (0.48/ 1.75) | -.22 (.34) | 0.80 (0.41/ 1.57) |
| Time since asthma diagnosis | -.04 (.04) | 0.96 (0.89/ 1.04) | -.02 (.04) | 0.98 (0.90/ 1.07) | .03 (.05) | 1.03 (0.94/ 1.13) |
| Family relationships (children) | .32 (.26) | 1.38 (0.83/ 2.29) | .53 (.30) | 1.70 (0.95/ 3.06) | -.77 (.30)$^{*}$ | 0.47 (0.26/ 0.83) |
| Family relationships (parents) | -.76 (.29)$^{*}$ | 0.47 (0.26/ 0.83) | -.69 (.32)$^{*}$ | 0.50 (0.27/ 0.94) | .84 (.36)$^{*}$ | 2.32 (1.15/ 4.71) |
| Caregiving burden | .41 (.24) | 1.50 (0.94/ 2.41) | 1.35 (.28)$^{***}$ | 3.85 (2.23/ 6.65) | .26 (.28) | 1.29 (0.75/ 2.24) |

[a] Multinomial logistic regression analyses, using "agreement" as the reference category and entering the child's and parent's genders and the child's asthma severity as categorical factors and the child's age, time since diagnosis and family factors as covariates. [b] Reference group: 0 = male; [c] Reference group: 0 = intermittent asthma.

$^{***}$ $p < .001$, two-tailed. $^{**}$ $p < .01$, two-tailed. $^{*}$ $p < .05$, two-tailed.

# Discussion

To our knowledge, this is the first study examining the role of family relationships and caregiving burden in explaining the extent and direction of child-parent (dis)agreement. Three main findings should be considered. First, most of the children with asthma and their parents differed in their perceptions of pediatric adaptation outcomes. Second, although disagreement occurred in both directions, the parents were more likely to report worse HrQoL and more psychological problems than the children. Finally, the extent and direction of disagreement were better explained by family-related factors than by socio-demographic and clinical variables. The strengths of this research include the use of developmentally appropriate instruments for assessing HrQoL and psychological problems with strictly parallel versions for children and parents and the adoption of a multi-informant approach; both children and parents reported on family relationships, and the physicians reported on asthma severity.

The low to moderate levels of agreement found at the individual level confirmed our first hypothesis and coincide with previous studies (e.g., Ender et al., 2011; White-Koning et al., 2007). These results can be understood within a cognitive-developmental framework, which suggests that children and adults differ in their understanding of the concept of illness, its causes and the effects of treatment (Bibace & Walsh, 1980). Although the instruments used to assess children's adaptation outcomes have been semantically and psychometrically validated for children as young as 8 years and for family caregivers, children and parents may support their answers with different experiences (Davis et al., 2007). At the group level, no significant differences were found between child and parent-reported adaptation outcomes, regardless of the domains being assessed, which refutes the hypothesis raised by Upton and colleagues (2008).

Consistent with most of the previous research conducted with clinical samples (e.g., Becker et al., 2004; Sattoe et al., 2012; White-Koning et al., 2007) and as predicted in our second hypothesis, when disagreement occurred, it was likely to be in the direction of parents reporting worse HrQoL and more psychological problems. These results may reflect, on the one hand, the children's tendency to emphasize the positive aspects of adaptation (Oeffinger et al., 2007). On the other hand, parents may be more reliable in identifying the most strongly affected areas of their children's functioning and the so-called "hidden morbidities" (Varni, Burwinkle, & Lane, 2005). Therefore, a dyadic child-parent approach to assessing pediatric outcomes may provide unique information about the children's risk factors and resilience.

The extent and direction of child-parent disagreement on adaptation outcomes were primarily explained by family-related factors. Children's and parents' perceptions of less positive family relationships were significantly associated with greater disagreement on HrQoL reports. These findings suggest that a family context that is characterized by high levels of cohesion and low levels of conflict, which allows children to openly express their worries and feelings, might be more important in explaining child-parent (dis)agreement than developmental characteristics and communication skills. Regarding the direction of disagreement, we observed a tendency for children and parents underrate the pediatric adaptation outcomes when they also perceived family relationships as less positive. These findings may reflect informant biases, but they could also indicate that individual perceptions of family relationships may affect how each family member evaluates the children's health status. Furthermore, a greater caregiving burden was significantly associated with increased disagreement, regardless of its direction. Parents' perceptions of caregiving tasks and asthma management routines as overly demanding and burdensome have been associated with negative mother-child interactions (Fiese, Winter, Anbar, Howell, & Poltrock, 2008), which may limit the exchange of information between children and parents. Moreover, the caregiving burden is also likely to negatively affect children's and parents' perceptions of the family environment (Crespo, Carona, Silva, Canavarro, & Dattilio, 2011) and thus contribute indirectly to child-parent disagreement on adaptation outcomes.

Two main limitations should be acknowledged in the present study. First, the non-probabilistic sampling strategy may have influenced the levels of agreement because parents who participated were more involved in pediatric healthcare than parents in the general population. In addition, the low frequency of children with severe asthma required the dichotomization of the asthma severity variable and increased the intragroup variability. Furthermore, the sample of caregivers included mostly mothers, which limited the ability to assess the potential role of the caregivers' gender in explaining the extent and direction of child-parent disagreement. Second, the study's cross-sectional design precluded causal inferences among the variables. Given the possibility that the associations between family-related factors and child-parent disagreement are bidirectional, longitudinal studies should further investigate this hypothesis.

Despite the aforementioned limitations, our findings have important implications for pediatric asthma research and clinical practice. The tendency for parents to report worse HrQoL and more psychological problems than children suggests, on the one hand, that parents may underestimate children's abilities to adapt to adverse circumstances and, on the other hand, that they may be more aware of children's current and future functional limitations. Moreover, parents assume important responsibilities in asthma management and healthcare decision making. Child-parent disagreement may influence the way parents respond to children's healthcare and emotional needs, which may influence their adaptation over time. Therefore, routine assessment of children's adaptation outcomes should include both children's and parents' perspectives as complementary sources of information and should also consider the family factors that are likely to influence child-parent (dis)agreement. The additional cost of conducting a more in-depth assessment of adaptation outcomes can be offset by more efficiently allocating health resources and implementing clinical interventions.

## Key messages

- The agreement between children with asthma and their parents on pediatric adaptation outcomes was low to moderate.
- Parents were more likely to report worse pediatric HrQoL and more psychological problems than children themselves.
- Both the extent and direction of child-parent disagreement were better explained by family relationships and caregiving burden than by clinical or socio-demographic variables.
- When possible, information about children's adaptation outcomes should be collected from both children and parents, while also consider the family context.
- An in-depth assessment of pediatric adaptation outcomes can enhance a more efficient allocation of health resources.

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# Empirical Study III

## Mapping the caregiving process in pediatric asthma: Parental burden, acceptance and denial coping strategies and quality of life

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# Mapping the caregiving process in pediatric asthma: Parental burden, acceptance and denial coping strategies and quality of life

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## Abstract

***Introduction.*** Based on a multi-dimensional model of the caregiving process, the main goal of this study was to examine the direct and indirect links, via acceptance and denial coping, between the caregiving burden and the quality of life (QoL) in parents of children with asthma. ***Method.*** The sample was composed of 182 parents of a child/adolescent between 8 and 18 years of age with a clinical diagnosis of asthma. Data were obtained via self-report questionnaires assessing the caregiving burden, acceptance and denial coping strategies and QoL. ***Results.*** Results from structural equation modelling indicated a good fit for the mediation model, which explained 30% of the variability of the parents' QoL. Higher levels of caregiving burden were negatively and indirectly associated with the parents' QoL, via less use of acceptance and greater use of denial coping strategies. Multi-group analyses ascertained the invariance of these links across the children's asthma severity, age and socio-economic groups. ***Conclusion.*** These findings emphasize acceptance and denial as important coping mechanisms in the caregiving process. Thus, broad-spectrum family-centered interventions in pediatric asthma settings can target the development of the parents' coping tendencies characterized by greater acceptance and less denial as a way of reappraising caregiving demands as less burdensome and improving their QoL.

## Keywords

Acceptance/ denial coping strategies • Caregiving burden • Multi-dimensional model of caregiving process and caregiver burden • Parental quality of life • Pediatric asthma

# Introduction

Pediatric asthma has been suggested as a potentially stressful context for parental caregiving. The presence of this chronic condition implies the rearrangement of family routines to incorporate its management, such as avoiding environmental and emotional triggers of asthma exacerbations, monitoring symptoms and medication intake, and coordinating family and work responsibilities (Fiese, Winter, Anbar, Howell, & Poltrock, 2008; Gates & Akabas, 2012). These caregiving demands can become burdensome and may have a deleterious effect on the parents' quality of life (QoL) outcomes (Crespo, Carona, Silva, Canavarro, & Dattilio, 2011; Fiese, Wamboldt, & Anbar, 2005). In fact, impaired physical functioning has been consistently described for parents of pediatric asthma patients when compared with the parents of healthy children (Gau et al., 2010; Hatzmann, Heymans, Ferrer-i-Carbonell, van Praag, & Grootenhuis, 2008; van Gent et al., 2007); conversely, research comparing the parents' psychological and social functioning has yielded heterogeneous findings across studies, as well as substantial within-study variability (Silva, Carona, Crespo, & Canavarro, 2015). The variability in parental adaptation trajectories may be better explained not only by caregiving demands and perceived burden but also by a complex interplay between the risk factors and the resources, namely the coping processes (King, King, Rosenbaum, & Goffin, 1999; Raina et al., 2004; Wallander et al., 1989). However, specific coping mechanisms remain empirically understudied in the pediatric asthma context. The examination of the mediating role of specific coping strategies on the associations between the caregiving burden and the parents' QoL may contribute to a better understanding of the caregiving process and to the identification of modifiable variables that could be targeted in psychosocial interventions aimed at promoting the adaptation of these parents.

## A multi-dimensional approach to the caregiving process and parental adaptation

Raina and colleagues (2004) have proposed a multi-dimensional model of the caregiving process aimed at mapping the complex associations between contextual variables (e.g., socio-economic status [SES]), child characteristics (e.g., disease severity), psychosocial stressors (e.g., caregiving burden), intrapersonal factors (e.g., perception of caregiving mastery), social-ecological factors (e.g., family functioning and social support), stress processing mechanisms (e.g., cognitive appraisal and coping strategies) and adaptation outcomes. Within this conceptual framework, the caregiving burden has been typically addressed as a risk factor for poor parental adaptation outcomes. Even if providing daily care to children is a normative assignment of parenting, the increased responsibilities and limitations experienced by parents caring for a child with a chronic condition may elicit caregiving stress related to the parent-child dyadic relationship (relationship burden), instrumental activities and consequent time constraints (objective burden), and emotional stress and anxiety (subjective burden; Savundranayagam, Montgomery, & Kosloski, 2011). Higher levels of caregiving burden have been associated with psychological maladjustment in the caregivers of children with chronic medical conditions (Canning, Harris, & Kelleher, 1996) and with impaired QoL in the parents of children with asthma (Fiese et al., 2005). However, these pathways have not always emerged directly, but were mediated by social-ecological factors, such as family functioning (Crespo et al., 2011) and social support (Carona, Crespo, & Canavarro, 2013).

The disease severity, the child's age and family SES are also relevant risk factors, which can operate at different levels of the caregiving process. For example, disease severity has been associated with a greater caregiving burden in parents caring for a child with a chronic condition (Canning et al., 1996) and with decreased QoL in parents in the particular context of pediatric asthma (Everhart, Fiese, & Smyth, 2008; Halterman et al., 2004). The effects of the child's age on the caregiving burden and QoL outcomes have also been tested, but studies have yielded divergent results, depending on the child's health condition. For example, higher levels of objective burden and lower QoL were described for parents of adolescents compared to parents of younger children with cerebral palsy (Carona, Pereira, Moreira, Silva, & Canavarro, 2013). However, the inverse pattern of age-group differences emerged in non-clinical groups (Carona, Pereira et al., 2013) and mixed samples of parents of pediatric patients with chronic health conditions and disabilities (Floyd & Gallagher, 1997). Considering that pediatric asthma does not seriously threaten the development of autonomy in adolescence (as in the case of cerebral palsy), it can be hypothesized that younger children would require greater assistance in the activities of daily living and asthma management, which may result in an increased caregiving burden and a lower parental QoL. Furthermore, providing treatments and additional care required by a child with asthma may increase the financial burden (Gates & Akabas, 2012), and thus family SES has been acknowledged as a significant risk factor for QoL impairments in the caregivers of children with asthma (Everhart et al., 2008).

Consistent with the stress and coping theory, which advocates that adaptation outcomes are determined by an individual's appraisal of stressors and resources (Lazarus & Folkman, 1984), the caregiving process model considers the stress management strategies as constraining resources with regard to the caregiver's adaptation outcomes (Raina et al., 2004). Coping, defined as "the cognitive and behavioral efforts made to master, tolerate, or reduce external and internal demands and conflicts among them" (Folkman & Lazarus, 1980, p. 223), has been referred to as a dynamic process with a protective function, removing or changing the stressor through the reappraisal of its meaning (i.e., problem-focused coping) or by the regulation of subsequent emotions (i.e., emotion-focused coping; Pearlin & Schooler, 1978). The use of specific coping strategies would be mainly determined by the individual's appraisal of the stressful situation (primary appraisal) and the available resources (secondary appraisal; Lazarus & Folkman, 1984), and could influence the subsequent adaptation outcomes or even enhance personal growth (Blount et al., 2008). Some authors have advocated that when the stressful situation is appraised as persisting over time and unlikely to undergo beneficial changes, as in many cases of chronic health conditions, emotion-focused coping strategies aimed at managing the consequent emotional distress are preferred (Carver, Scheier, & Weintraub, 1989; Folkman & Lazarus, 1980).

### Acceptance and denial as coping strategies in the caregiving process

One specific emotion-focused coping strategy is accepting the reality of the stressful situation, which was argued by Carver and colleagues (1989) to be a functional coping response, because it would motivate active attempts to address the stressor. In the context of family caregiving, acceptance may reflect an attempt to make sense of the child's health condition and a reconciliation of the caregiving demands with the caregiver's goals, values and beliefs, as well as a sense of control over emotional reactions (Pakenham, 2008). The coping response of acceptance has been related to a greater life satisfaction and positive affect, and less anxiety and depression in the caregivers of adult patients (Pakenham, 2008). The third wave of cognitive-behavioral therapies (e.g., Acceptance and Commitment Therapy [ACT], Hayes, 2004; Mindfulness-Based Stress Reduction [MBSR], Kabat-Zinn, 1990) relies specifically on strategies such as mindfulness, acceptance or cognitive defusion to change the meaning of the stressful events and to develop more flexible and effective coping repertoires (Hayes, 2004; Larson, 2010). There is scarce but promising evidence that this intervention approach may be effective in reducing parenting stress, depression and negative affect, and in improving psychological well-being and QoL outcomes in the parents of children with chronic conditions or disabilities (e.g., Bazzano et al., 2015; Benn, Akiva, Arel, & Roeser, 2012; Minor, Carlson, Mackenzie, Zernicke, & Jones, 2006).

In opposition, denial has been considered a particular form of cognitive avoidance (Moos & Schaefer, 1993), which is characterized by attempts to deny or minimize the importance of a stressful event or its consequences, and by behavioral efforts to ignore the stressor (Carver et al., 1989). Although denial is considered a dynamic process that may have a protective function depending on the context and the time in which it operates (e.g., following the diagnosis of a chronic illness; Livneh, 2009), avoidant strategies have been systematically associated with poorer psychological adjustment to a physical illness (Roesch & Weiner, 2001). In parents caring for a child with cerebral palsy, experiential avoidance was positively related to the parenting burden and symptoms of depression, anxiety and stress (Whittingham, Wee, Sanders, & Boyd, 2013). Moreover, disengagement coping strategies, including cognitive avoidance, were identified as mediators of the associations between the caregiving burden and anxiety and depression in the caregivers of adult patients with Alzheimer's disease (García-Alberca et al., 2012).

It is also important to note that although acceptance and denial have been conceptualized in a somewhat opposite way, they are likely co-occurring responses to different aspects of the stressful situation (Carver et al., 1989). For instance, a parent may tend to accept the disruption of daily routines implied by caregiving, and yet being prone to deny negative emotional states aroused by the child's physical impairment and/or treatment procedures. Hence, acceptance and denial responses and their links to parents' QoL must be examined separately, instead of being considered as opposite and mutually exclusive sides of the same coping strategy.

## The present study: Aims and hypotheses

Within the broader concept of "adaptation", the parents' QoL was defined as the "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (The WHOQOL Group, 1998, p. 551) and considered as an overall indicator of their physical, psychological and social well-being. In the context of family caregiving for a child with asthma, the following objectives were outlined for the present study: (1) to characterize the parents' caregiving burden, coping tendencies and QoL in different clinical (intermittent *vs.* persistent asthma) and socio-economic groups (low *vs.* medium/high SES), and at different developmental periods (childhood *vs.* adolescence); (2) to examine the direct and indirect links, via acceptance and denial as dispositional coping strategies, between the caregiving burden and the parents' QoL; and (3) to attest if the mediation model was moderated by asthma severity, child's age and family SES. Following the recommendations of Raina and colleagues (2004), we used advanced statistical techniques (structural equation modelling [SEM]) that allowed the operationalization of the caregiving burden and QoL as multi-dimensional constructs and the examination of the complex mechanisms (i.e., direct and indirect pathways) underpinning the caregiving process and the parents' adaptation outcomes.

Accordingly, the following theoretically driven hypotheses were formulated. First, we expected higher levels of caregiving burden and lower QoL in the parents caring for a child with persistent asthma, the parents of younger children and the parents with low SES when compared with the parents caring for a child with intermittent asthma, the parents of adolescents and the parents with medium/high SES. Second, we predicted that higher levels of caregiving burden would be associated with lower parental QoL and that this negative association would be mediated by coping strategies, such as a reduced use of acceptance and a greater use of denial.

We also tested the invariance of the mediation model across the asthma severity, the children's age and the socio-economic groups, but, given the exploratory nature of these analyses, no predictions were made in this regard.

## Method

### Participants and procedure

The present study is part of a broader research project, which was approved by the ethics committees and/or direction boards of three Portuguese public hospitals (Coimbra University Hospitals, Coimbra Pediatric Hospital, and Leiria Santo André Hospital). Parents were enrolled at the Pediatric and Immunoallergology outpatient services of the aforementioned hospitals between September 2010 and February 2012 if they had a child who met the following criteria: (1) between 8 and 18 years of age; (2) diagnosis of asthma for at least one year that was established by a physician according to the International Classification of Diseases system (ICD-10); and (3) absence of comorbidities with other chronic health conditions or severe psychiatric disorders, except for comorbid allergic diseases (e.g., allergic rhinitis, atopic dermatitis/ eczema, and hypersensitivity to inhalant or food allergens). In addition, an inclusion criterion for parents was considered: being the parent self-identified as currently assuming the role of primary caregiver for the child's asthma management.

The medical files of the children attending medical routine appointments in the period of data collection were screened by their physicians. Adopting a non-probabilistic convenience sampling method, the primary caregivers of the eligible children were invited to participate in the study. Detailed information about the study's aims and procedures was provided to all eligible participants, and informed consent was obtained from the parents who agreed to participate. The parents completed a set of self-report questionnaires in a room assigned for research purposes in the health institution that their child attended. A research assistant was available to provide occasional support to the participants with difficulties in reading or understanding item content.

### Measures

#### *Caregiving burden*

The three burden subscales of the Revised Burden Measure (Montgomery & Kosloski, 2006; Portuguese version: ongoing psychometric studies) were used to assess the extent to which various aspects of parents' lives had changed due to caregiving for their children with asthma ("As a result of assisting the care receiver, have the following aspects of your life changed?"). The Relationship burden subscale (five items) assesses the negative psychological state that directly derives from the caregiver's unique relationship with the care receiver, particularly as a result of demands for care and attention over and above the level that the caregiver perceives is warranted by the care receiver's condition (e.g., "Have your caregiving responsibilities caused conflicts with your relative?"). The Objective burden subscale (six items) assesses the negative psychological state that results from the interference of caregiving activities on the caregiver's free time (e.g., "Have your caregiving responsibilities kept you from recreational activities?"). The Subjective burden subscale (five items) refers to a generalized form of negative affect resulting from caregiving, but not as a direct consequence of any specific event, task or interaction (e.g., "Have your caregiving responsibilities created a feeling of hopelessness?"). The parents answered a total of 16 items using a five-point Likert scale, which ranged from 1 (*not at all*) to 5 (*a great deal*), with higher scores indicating greater levels of caregiving burden. For SEM, the three subscales were considered observed indicators, loading on a latent variable representing the multi-dimensional construct of caregiving burden. As displayed in Table 2, good reliability was found in the current sample for the three subscales and for the latent variable, resembling the Cronbach's α values described in the original study with a sample of spouses and adult children caregivers of persons with chronic illnesses (α ranging from .85 to .93; Savundranayagam et al., 2011).

### *Acceptance and denial coping strategies*

The parents' use of acceptance and denial as dispositional coping strategies was evaluated with the respective subscales of the Brief-COPE (Carver, 1997; Portuguese version: Pais-Ribeiro & Rodrigues, 2004). The Acceptance subscale is composed of two items that assess the parents' recognition and acceptance that the stressful event has occurred and is real ("I've been accepting the reality of the fact that it has happened."; "I've been learning to live with it."). The Denial subscale, which is also composed of two items, assesses the parents' cognitive and behavioral attempts to reject or ignore the actual existence of the stressful event ("I've been saying to myself 'this isn't real'."; "I've been refusing to believe that it has happened."). For both subscales, the answers were provided using a dispositional response format with four options, ranging from 0 (*I usually don't do this at all*) to 3 (*I usually do this a lot*), with higher scores indicating more frequent use of the coping strategy. For SEM, we considered acceptance and denial as latent variables, which were reflected in their respective two items as observed indicators. In the current sample, the Cronbach's α coefficients were .63 for the Acceptance subscale and .58 for the Denial subscale (composite reliability values for the latent variables are presented in Table 2). These reliability values exceeded those reported in the original studies of the Brief-COPE instrument (α = .57 for Acceptance and .54 for Denial) and that were considered to be acceptable by the author (Carver, 1997).

### *Quality of life*

The parents' QoL was assessed with the abbreviated version of the World Health Organization Quality of Life questionnaire (WHOQOL- BREF; The WHOQOL Group, 1998; Portuguese version: Vaz-Serra et al., 2006). This questionnaire includes 26 items clustered into a generic facet composed of two items (which were not used in the present study) and four QoL domains. The Physical domain assesses the facets of pain and discomfort, energy and fatigue, sleep and rest, dependence on medication, mobility, activities of daily living and working capacity (seven items; e.g., "Do you have enough energy for everyday life?"). The Psychological domain encompasses the facets of positive and negative feelings, self-esteem, thinking, learning, memory and concentration, body image and spirituality, religion and personal beliefs (six items; e.g., "How often do you have negative feelings such as blue mood, despair, anxiety, depression?"). The Social Relationships domain comprises the facets of personal relationships, sexual activity and social support (three items; e.g., "How satisfied are you with the support you get from your friends?"). The Environment domain evaluates the facets of physical safety and security, the home and physical environments, financial resources, access to health and social care, transport, opportunities for acquiring new information and skills, and recreation and leisure activity (eight items; e.g., "How healthy is your physical environment?"). The items were answered using a five-point Likert scale in terms of intensity (*not at all* to *extremely*), capacity (*not at all* to *completely*), frequency (*never* to *always*) or evaluation (*very dissatisfied* to *very satisfied*), with higher values indicating a better QoL. A latent variable representing the multi-dimensional construct of QoL, which comprised the four domains as observed indicators, was designed for the SEM. The cross-cultural psychometric study of the WHOQOL-BREF, involving 15 centers worldwide, attested the instrument's good internal consistency (Cronbach's α values ranging from .66 for Social Relationships domain to .84 for Physical domain; The WHOQOL Group, 1998). Similarly, good reliability was observed in the current sample for all four domains and for the latent variable (Table 2).

### *Socio-demographic and clinical data*

The parents also completed a socio-demographic datasheet, which collected information on their age, gender, marital status, educational level and occupational status, as well as their children's age, gender and clinical information (e.g., use of medication, comorbidities with other health conditions). Using a classification system specifically developed for the Portuguese context and based on the educational level and current job of the primary caregiver (Simões, 1994), the family SES was classified into low (e.g., unqualified employees in construction or manufacturing without completing the 9th grade of school education), medium (e.g., employees in bureaus or banks, nurses, social workers or teachers with intermediate or university courses) and high (e.g., senior officials of government, army, commerce or industry, physicians, magistrates or engineers with bachelor, master, doctorate or other post-graduate degrees).

Asthma severity was classified by the child's physician into four levels (intermittent, mild persistent, moderate persistent and severe persistent), according to the Global Initiative for Asthma [GINA] guidelines (2008). This classification was based on asthma clinical features before treatment, as recorded in the child's medical files, namely the level of symptoms, airflow limitation and lung function variability.

### Statistical analyses

The statistical analyses were conducted with SPSS v.20.0 (SPSS Inc., Chicago, IL, USA). Except for socio-demographic and clinical variables, missing data, which were random and less than 5% of the values, were replaced with the individual mean score for each variable. Descriptive statistics were calculated for the socio-demographic, clinical and psychosocial variables. Due to the heterogeneous distribution of the asthma severity and the SES levels observed in our sample, for the group comparison analyses, these variables were dichotomized and dummy-coded (asthma severity: 0 – intermittent [n = 95], 1 – persistent [mild, moderate or severe, n = 87]; SES: 0 – low [n = 108], 1 – medium/high [n = 74]). Multivariate analyses of covariance (MANCOVA) were performed to examine the main and interaction effects of the asthma severity (intermittent *vs.* persistent), the children's age (children aged 8-12 *vs.* adolescents aged 13-18) and the SES groups (low *vs.* medium/high) on the caregiving burden, the coping strategies and the parents' QoL. The remaining clinical and socio-demographic variables that were significantly associated with the main study variables were included as covariates. When multivariate effects were significant, univariate analyses were performed to examine which dimensions of the caregiving burden, coping and QoL significantly differed between the groups.

SEM was performed with Analysis of Moment Structures (AMOS Development Corporation, Meadville, PA). The method of estimation was the maximum likelihood, and the overall model fit was evaluated based on the chi-square statistic ($\chi^2$) and on the main approximate goodness-of-fit indexes, namely, the comparative fit index (CFI), the root mean square error of approximation (RMSEA) and the standardized root mean squared residual (SRMR). A model was considered to have a good fit when $\chi^2$ was non-significant ($p > .05$), the CFI ≥ .95, the RMSEA ≤ .06 ($p > .05$) and the SRMR ≤ .08; an acceptable fit was defined by a CFI

≥ .90 and a RMSEA ≤ .10 (Browne & Cudeck, 1993; Hu & Bentler, 1999). To ensure the pertinence of multi-dimensional constructs (latent variables), we first examined the measurement model testing the hypothesized links between the latent variables and their observed indicators. The construct reliability of the latent variables was assessed using composite reliability values, calculated from the squared sum of the standardized factor loading divided by the squared sum of the standardized factor loading and the error variance terms (Hair, Black, Babin, & Anderson, 2010). Second, we examined the structural model testing the direct and indirect links, via acceptance and denial coping, of the caregiving burden on the parents' QoL. Following recent recommendations (Preacher & Hayes, 2008), the statistical significance of the indirect effects was estimated using bootstrap resampling procedures with 2000 samples and a 95% bias-corrected confidence interval (BC 95% CI). Finally, to ascertain that the parameters tested in the mediation model were valid for the asthma severity, the children's age and the family socio-economic groups, we examined the baseline model for each group separately, and we subsequently conducted multi-group analyses testing the model's invariance between the groups. As suggested by Little (2013), we first tested the invariance on the associations between the latent variables and their observed indicators; once the measurement invariance was established, we examined the structural invariance, i.e., the invariance on the strength of the associations among the latent variables. The chi-square difference ($\Delta\chi^2$) method was used to compare the unconstrained model with the models in which the measurement weights and the structural weights were fixed to be equal across groups.

## Results

### Sample characteristics

The sample was composed of 182 parents who assumed the role of primary caregivers of 112 children with asthma aged 8-12 years (*M* = 10.23, *SD* = 1.27; 69.6% male) and 70 adolescents with asthma aged 13-18 years (*M* = 14.71, *SD* = 1.49; 55.7% male). The parents included 153 mothers (84.1%) and 29 fathers (15.9%), between 27 and 71 years of age (*M* = 41.06; *SD* = 5.85). The majority of the parents were married or were living with a partner (*n* = 145, 79.7%) and had low (*n* = 108, 59.3%) or medium (*n* = 63, 34.6%) SES, while 37 families (20.3%) lived in single-parent households (i.e., they were single, divorced or widowed) and only 11 families (6%) had high SES.

Regarding the children's clinical characteristics, 95 children (52.2%) had intermittent asthma, 52 children (28.6%) had mild persistent asthma, 29 children (15.9%) had moderate persistent asthma and 6 children (3.6%) had severe persistent asthma. Thirty-seven children (20.3%) also had comorbidities with other allergic diseases, such as allergic rhinitis ($n$ = 13, 7.1%), atopic dermatitis/eczema ($n$ = 8, 4.4%) and hypersensitivity to inhalant or food allergens ($n$ = 16, 8.8%). The average length of time since asthma diagnosis was 7.37 years ($SD$ = 3.93) and most children were taking regular or emergency medication ($n$ = 178, 97.8%).

## Descriptive statistics and multivariate analyses of covariance

Preliminary correlation analyses indicated that a greater use of denial as a coping strategy was significantly associated with parents' female gender ($r = .19$, $p = .01$) and with the absence of comorbidities with other allergic diseases in the child ($r = -.15$, $p = .04$). In addition, living in single-parent households was negatively associated with the parents' QoL in the psychological ($r = -.18$, $p = .02$) and social domains ($r = -.18$, $p = .01$). Accordingly, these variables were included as covariates in the multivariate analyses of covariance when appropriate. No significant associations were found for parents' age, children's gender and length of time since asthma diagnosis.

The descriptive statistics for the caregiving burden dimensions, coping and parents' QoL are presented in Table 1. Regarding the caregiving burden, we found significant multivariate main effects of asthma severity, Wilks' $\lambda = .94$; $F_{(3,\ 172)} = 3.79$, $p = .01$; $\eta_p^2 = .06$, children's age group, Wilks' $\lambda = .94$; $F_{(3,\ 172)} = 3.38$, $p = .02$; $\eta_p^2 =.06$, and SES, Wilks' $\lambda = .90$; $F_{(3,\ 172)} = 6.29$, $p < .01$; $\eta_p^2 = .10$. The univariate analyses (Table 1) showed higher levels of caregiving burden for parents of children with intermittent asthma when compared with parents of children with persistent asthma, but only on the relationship dimension. In addition, the parents of younger children presented higher levels of objective and subjective burden than parents of adolescents. Finally, parents with low SES had higher levels of relationship and subjective burden, than parents with medium/high SES. No significant interaction effects between asthma severity, age and SES group were found.

In addition, we found multivariate main effects of SES on coping, while controlling for parents' gender and comorbidities with other allergic diseases, Wilks' $\lambda = .96$; $F_{(2,\ 171)} = 3.43$, $p = .04$; $\eta_p^2 = .04$, and on parents' QoL, while controlling for type of household, Wilks' $\lambda = .92$; $F_{(4,\ 170)} = 3.97$, $p < .01$; $\eta_p^2 = .09$. The univariate analyses revealed that parents with low SES tended to use denial as a coping strategy more often and reported a poorer QoL on the psychological and environment domains than parents with medium/high SES (Table 1). No multivariate main effects of asthma severity levels or children's age group or interaction effects between the factors were found for coping strategies and parents' QoL.

**Table 1** | Descriptive statistics and univariate analyses of covariance by asthma severity, children's age and SES groups

| | ***Asthma severity*** | | | ***Age group*** | | | ***Socio-economic status*** | | |
|---|---|---|---|---|---|---|---|---|---|
| | Intermittent (*n* = 95) | Persistent (*n* = 87) | | Children (*n* = 112) | Adolescents (*n* = 70) | | Low (*n* = 108) | Medium/high (*n* = 74) | |
| Variable | *M* (*SD*) | *M* (*SD*) | $F_{(1, 172)}$ | *M* (*SD*) | *M* (*SD*) | $F_{(1, 172)}$ | *M* (*SD*) | *M* (*SD*) | $F_{(1, 172)}$ |
| Caregiving burden | | | | | | | | | |
| Relationship | 1.64 (0.80) | 1.40 (0.57) | $5.76^{*}$ | 1.57 (0.68) | 1.44 (0.76) | 3.51 | 1.61 (0.79) | 1.39 (0.55) | $5.91^{*}$ |
| Objective | 1.82 (0.81) | 1.80 (0.77) | 0.06 | 1.94 (0.81) | 1.60 (0.71) | $9.73^{**}$ | 1.83 (0.79) | 1.79 (0.79) | 0.74 |
| Subjective | 2.11 (0.92) | 1.99 (0.85) | 1.10 | 2.14 (0.90) | 1.92 (0.85) | $5.29^{*}$ | 2.21 (0.97) | 1.83 (0.69) | $10.79^{**}$ |
| Coping strategies | | | | | | | | | |
| Acceptance | 1.97 (0.65) | 2.08 (0.70) | 0.45 | 2.01 (0.61) | 2.04 (0.77) | 0.11 | 2.01 (0.71) | 2.04 (0.63) | 0.03 |
| Denial | 0.85 (0.70) | 0.84 (0.79) | 0.37 | 0.88 (0.74) | 0.79 (0.75) | 1.15 | 0.97 (0.81) | 0.67 (0.60) | $6.67^{*}$ |
| Quality of life | | | | | | | | | |
| Physical | 3.89 (0.61) | 3.90 (0.57) | 0.03 | 3.86 (0.58) | 3.95 (0.61) | 1.94 | 3.86 (0.63) | 3.96 (0.51) | 2.28 |
| Psychological | 3.83 (0.58) | 3.90 (0.62) | 0.82 | 3.86 (0.58) | 3.87 (0.63) | 0.50 | 3.80 (0.64) | 3.95 (0.52) | $4.79^{*}$ |
| Social relationships | 3.86 (0.63) | 4.03 (0.69) | 3.14 | 3.91 (0.64) | 3.99 (0.70) | 1.13 | 3.89 (0.73) | 4.02 (0.55) | 2.75 |
| Environment | 3.61 (0.57) | 3.62 (0.50) | 0.03 | 3.60 (0.54) | 3.65 (0.53) | 0.98 | 3.49 (0.55) | 3.80 (0.46) | $15.37^{**}$ |

$^{**}$ $p < .01$; $^{*}$ $p < .05$, two-tailed.

## The measurement model

The measurement model testing the hypothesized links between the latent variables (caregiving burden, acceptance, denial and QoL) and their observed indicators had a good fit, with $\chi^2_{(38)} = 59.68$, $p = .01$; CFI = .97; RMSEA = .06 ($p = .33$; 90% CI = .03/.08); and SRMR = .05. All observed indicators presented good factorial validity: standardized regression weights were above the threshold of .50 and statistically significant (Table 2). The squared multiple correlations ($R_{smc}^2$) between each observed indicator and all other observed indicators were lower than .90, and the tolerance values ($1 - R_{smc}^2$) were higher than .10, indicating that each variable explained a substantial proportion of the total variance, and, thus, the model was not limited by multicollinearity problems (Kline, 2005).

In addition, the construct reliability of the latent variables was good for caregiving burden and parents' QoL, with composite reliability values above the threshold of .70, and satisfactory for the acceptance and denial coping strategies, with composite reliability values near .60. Weak to moderate associations were found between the latent variables: caregiving burden was positively correlated with denial and negatively correlated with acceptance and with parents' QoL; acceptance and denial coping strategies were negatively associated with each other, and they were associated with parents' QoL, with positive correlations found between acceptance and QoL, and negative correlations found between denial and QoL.

## The mediation model

The structural model testing the direct and indirect effects, via acceptance and denial coping strategies, of caregiving burden on parents' QoL (Figure 1) had a good fit, with $\chi^2_{(39)} = 63.88$, $p = .01$; CFI = .96; RMSEA = .06 ($p = .26$; 90% CI = .03/.09); and SRMR = .06, and explained 30% of parents' QoL. Significant direct effects of caregiving burden were found on coping strategies ($\beta = -.27$, $p = .02$ for acceptance; $\beta = .40$, $p < .01$ for denial). In turn, acceptance and denial had significant direct effects on parents' QoL, with $\beta = .29$, $p = .01$; and $\beta = -.32$, $p = .01$, respectively. No direct effect of caregiving burden on parents' QoL was found ($\beta = -.16$, $p = .10$), but the indirect effects via coping strategies were statistically significant ($\beta = -.20$, $p < .01$; BC 95% CI = -.40/-.09). We also examined the simple mediation models for each coping strategy, and both acceptance ($\beta = -.08$, $p = .04$, BC 95% CI = -.24/-.02) and denial ($\beta = -.14$, $p < .01$; BC 95% CI = -.32/-.05) emerged as significant mediators of the association between caregiving burden and parents' QoL.

**Table 2** | Inter-correlations, factor loadings and reliability for observed indicators and latent variables

| | Caregiving burden | | | Acceptance | | | Denial | | | Parents' QoL | | | | $1\text{-}R_{smc}^2$ | Factor | Reliability |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 | 2 | 3 | B | 4 | 5 | C | 6 | 7 | D | 8 | 9 | 10 | | loadings | $^a$ |
| A. Caregiving burden | | | | **-.26$^{**}$** | | | **.39$^{**}$** | | | **-.36$^{**}$** | | | | | | **.85** |
| 1. Relationship | - | | | | | | | | | | | | | .33 | .82$^{**}$ | .86 |
| 2. Objective | .72$^{**}$ | - | | | | | | | | | | | | .23 | .88$^{**}$ | .88 |
| 3. Subjective | .57$^{**}$ | .67$^{**}$ | - | | | | | | | | | | | .45 | .74$^{**}$ | .85 |
| B. Acceptance | | | | | | | **-.34$^{**}$** | | | **.40$^{**}$** | | | | | | **.63** |
| 4. Acceptance 1 | -.20$^{**}$ | -.08 | -.14 | | - | | | | | | | | | .61 | .62$^{**}$ | - |
| 5. Acceptance 2 | -.25$^{**}$ | -.12 | -.12 | | .46$^{**}$ | - | | | | | | | | .46 | .74$^{**}$ | - |
| C. Denial | | | | | | | | | | **-.46$^{**}$** | | | | | | **.58** |
| 6. Denial 1 | .25$^{**}$ | .20$^{**}$ | .28$^{**}$ | | -.12 | -.14 | | - | | | | | | .56 | .66$^{**}$ | - |
| 7. Denial 2 | .25$^{**}$ | .14 | .15$^{*}$ | | -.17$^{*}$ | -.18$^{*}$ | | .41$^{**}$ | - | | | | | .61 | .62$^{**}$ | - |
| D. Parents' QoL | | | | | | | | | | | | | | | | **.85** |
| 8. Physical | -.28$^{**}$ | -.18$^{*}$ | -.29$^{**}$ | | .19$^{*}$ | .23$^{**}$ | | -.16$^{*}$ | -.25$^{**}$ | | - | | | .57 | .66$^{**}$ | .81 |
| 9. Psychological | -.28$^{**}$ | -.20$^{**}$ | -.35$^{**}$ | | .21$^{**}$ | .23$^{**}$ | | -.24$^{**}$ | -.24$^{**}$ | | .58$^{**}$ | - | | .24 | .87$^{**}$ | .83 |
| 10. Social | -.23$^{**}$ | -.11 | -.19$^{**}$ | | .22$^{**}$ | .28$^{**}$ | | -.22$^{**}$ | -.18$^{*}$ | | .42$^{**}$ | .68$^{**}$ | - | .44 | .75$^{**}$ | .73 |
| 11. Environmental | -.29$^{**}$ | -.21$^{**}$ | -.37$^{**}$ | | .15$^{*}$ | .20$^{**}$ | | -.30$^{**}$ | -.24$^{**}$ | | .54$^{**}$ | .63$^{**}$ | .56$^{**}$ | .44 | .75$^{**}$ | .82 |

Note. Inter-correlations and composite reliability for latent variables are shown in boldface.

$^a$ Cronbach's $\alpha$ values were calculated for observed indicators and composite reliability values were computed for latent variables.

$^{**}$ $p < .01$; $^{*}$ $p < .05$, two-tailed.

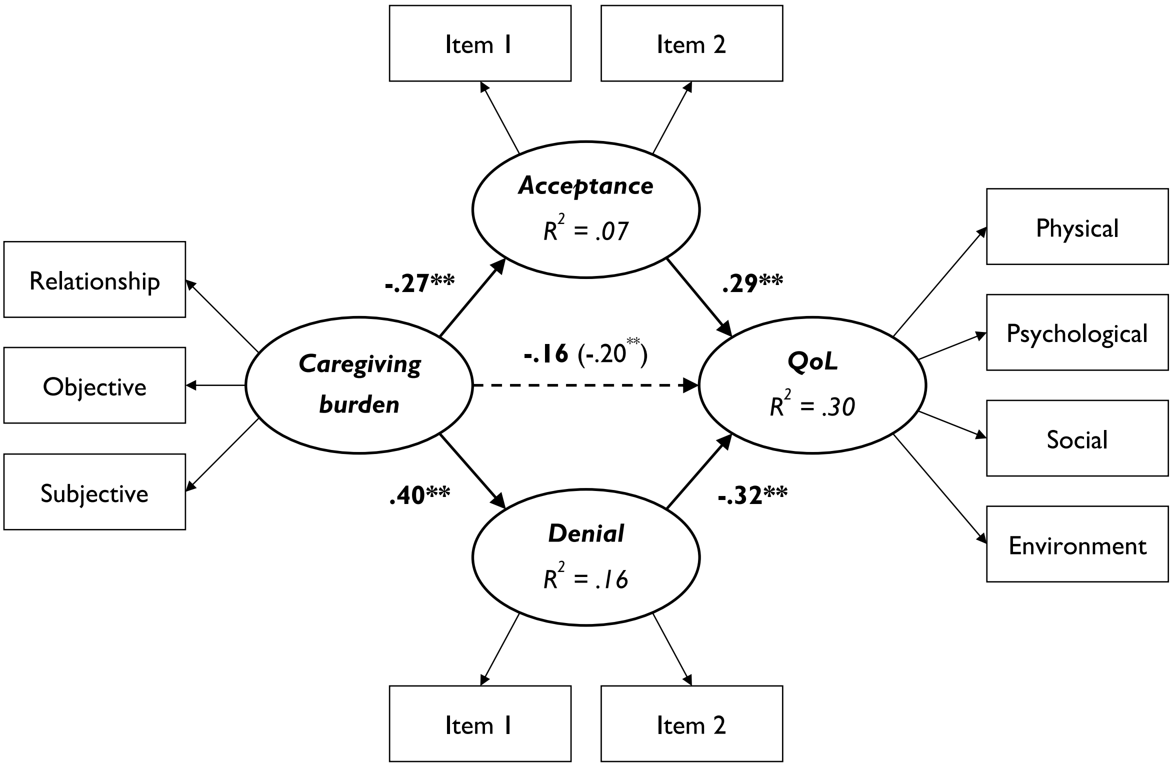

**Figure 1** | SEM testing the direct and indirect effects, via acceptance and denial coping strategies, of caregiving burden on parents' QoL

*Note*. Bold figures represent the standardized regression weights for the direct paths; non-bold figures in brackets represent the standardized regression weights for the indirect path. For simplicity, measurement error terms are not shown.
$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

## Multi-group analyses

Table 3 presents the summary of fit statistics for the mediation model tested separately for the asthma severity groups (intermittent *vs.* persistent), the children's age groups (children aged 8-12 *vs.* adolescents aged 13-18) and the SES groups (low *vs.* medium/high), as well as the results from multi-group analyses comparing the unconstrained model with the nested models in which factor loadings and structural weights were sequentially and cumulatively fixed to be equal across groups. Regarding measurement invariance, the factor loadings of the observed indicators on their respective latent variables did not significantly differ between parents of children with intermittent asthma and parents of children with persistent asthma ($\Delta\chi^2_{(7)}$ = 6.25, $p$ = .51), between parents of children and parents of adolescents ($\Delta\chi^2_{(7)}$ = 9.06, $p$ = .25), or between families with low SES and families with medium/high SES ($\Delta\chi^2_{(7)}$ = 4.22, $p$ = .75). Assuming that the measurement model is invariant across groups, the results from the multi-group analyses also yielded no significant differences in the structural weights across asthma severity ($\Delta\chi^2_{(5)}$ = 1.40, $p$ = .92), children's age ($\Delta\chi^2_{(5)}$ = 4.37, $p$ = .50) or family SES ($\Delta\chi^2_{(5)}$ = 9.10, $p$ = .11) groups.

**Table 3** | Multi-group analyses testing measurement and structural invariance across asthma severity, children's age and SES groups

| | $\chi^2$ | *df* | CFI | RMSEA [90% CI] | SRMR | $\Delta\chi^2$ | $\Delta df$ | $\Delta$CFI |
|---|---|---|---|---|---|---|---|---|
| ***Asthma severity groups*** | | | | | | | | |
| Summary of fit statistics | | | | | | | | |
| Intermittent | 53.70 | 39 | .97 | .06 [.00/.10] | .06 | | | |
| Persistent | 40.72 | 39 | .99 | .02 [.00/.08] | .08 | | | |
| Multi-group analyses | | | | | | | | |
| Unconstrained model | 94.42 | 78 | .98 | .03 [.00/.06] | .06 | - | - | - |
| Measurement weights | 100.67 | 85 | .98 | .03 [.00/.05] | .06 | 6.25 | 7 | < .01 |
| Structural weights | 102.07 | 90 | .98 | .03 [.00/.05] | .06 | 1.40 | 5 | < .01 |
| ***Children's age groups*** | | | | | | | | |
| Summary of fit statistics | | | | | | | | |
| Children 8-12 | 58.33$^{*}$ | 39 | .95 | .07 [.03/.10] | .06 | | | |
| Adolescents 13-18 | 66.47$^{**}$ | 39 | .91 | .10 [.06/.14]$^{*}$ | .08 | | | |
| Multi-group analyses | | | | | | | | |
| Unconstrained model | 124.90$^{**}$ | 78 | .93 | .06 [.04/.08] | .06 | - | - | - |
| Measurement weights | 133.96$^{**}$ | 85 | .93 | .06 [.04/.07] | .07 | 9.06 | 7 | < .01 |
| Structural weights | 138.33$^{**}$ | 90 | .93 | .06 [.04/.07] | .07 | 4.37 | 5 | < .01 |
| ***SES groups*** | | | | | | | | |
| Summary of fit statistics | | | | | | | | |
| Low | 60.29$^{*}$ | 39 | .95 | .07 [.03/.11] | .07 | | | |
| Medium/high | 51.08 | 39 | .95 | .07 [.00/.11] | .08 | | | |
| Multi-group analyses | | | | | | | | |
| Unconstrained model | 111.39$^{**}$ | 78 | .95 | .05 [.03/.07] | .07 | - | - | - |
| Measurement weights | 115.61$^{*}$ | 85 | .96 | .05 [.02/.06] | .07 | 4.22 | 7 | .01 |
| Structural weights | 124.71$^{**}$ | 90 | .95 | .05 [.02/.07] | .09 | 9.10 | 5 | .01 |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

## Discussion

The main contribution of the present study was the examination of a mediational hypothesis based on a solid theoretical background, namely the multi-dimensional model of the caregiving process and the stress and coping theory. The findings allowed the ascertainment of the caregiving burden as an important risk factor for parent's QoL impairments, as well as the identification of the mediating role of specific coping strategies, namely, a greater use of acceptance and a lower use of denial, for positive adaptation outcomes, which remain fundamental to research and clinical practice.

Our first set of results showed that parents of children with intermittent asthma, parents of younger children and parents with low SES were at greater risk of experiencing higher levels of caregiving burden. Although higher levels of caregiving burden reported by parents of children with intermittent asthma when compared with parents of children with persistent asthma were somewhat unexpected, they were significant only for the relationship burden domain. These findings suggest that, when asthma does not inflict severe limitations on the child's functioning, the parents may be more prone to interpret their child's demands for care and attention as over and above the needs warranted by the pediatric health condition. Furthermore, the asthma management routines may be less rigid in the daily functioning of families of children with intermittent asthma and, consequently, imply specific contingencies in therapeutic monitoring and adherence. For instance, decision-making about avoiding environmental triggers of asthma exacerbations (e.g., going out or meet up with friends) or using emergency medication can cause additional parent-child conflicts, which are eventually reflected in higher levels of relationship burden. Even if this explanatory hypothesis requires further research, our results strengthen the importance of addressing caregiving burden as a multi-dimensional construct (Savundranayagam et al., 2011), because clinical asthma characteristics may have a differential impact on the specific dimensions of parental burden.

Regarding the children's age groups, the higher levels of caregiving burden found for parents of children in comparison with parents of adolescents were consistent with our assumption that younger children could be more dependent on parental care and less able to communicate their healthcare needs, thus increasing the parents' responsibilities and worries. Similarly, Floyd and Gallagher (1997) described greater time demands in providing care to children with chronic illnesses or disabilities in mothers of children aged 6-12 years compared with mothers of adolescents aged 13 years and older. Along with the functional limitations related to the health condition, normative developmental capabilities may also influence the caregiving process. Therefore, conceptual models of adaptation to pediatric health conditions could be improved through the inclusion of child's age-related characteristics as important factors associated with the caregivers' outcomes.

Higher levels of caregiving burden and lower QoL were also found for parents with low SES when compared with parents with medium/high SES. These results were consistent with our hypothesis and support previous findings showing that the opportunity to afford additional support from healthcare service providers and to successfully balance work-caregiving responsibilities may ease caregiving demands and contribute to positive adaptation outcomes in parents (Gates & Akabas, 2012). Moreover, parents with low SES were more likely to use denial as a coping strategy suggesting that when parents have insufficient external resources to help them cope with the stressful events, avoidant strategies are preferred. These results should be interpreted within the Portuguese current economic context and healthcare system, because additional financial burdens may have inflated the levels of caregiving burden and, consequently, contributed to poorer QoL outcomes.

Caregiving burden was negatively associated with parents' QoL, but only indirectly via a greater use of denial and a lower use of acceptance as coping strategies, confirming our second hypothesis. The absence of direct associations between the caregiving burden and the parents' adaptation outcomes has previously been observed in other studies (e.g., King et al., 1999), and emphasizes the important role of stress processing mechanisms for the well-being of parents caring for a child with a chronic condition (Raina et al., 2004; Wallander et al., 1989). The parents' perceptions of increased burden and negative affect related to caregiving may hinder the use of acceptance coping and predispose them to deny or minimize stressful events, either related or unrelated to parental caregiving. The reduced use of acceptance as a coping strategy may also reflect the parents' difficulties in accommodating and reconciling the caregiving demands with their individual goals and expectations (Pakenham, 2008). In turn, and as expected, these coping tendencies were negatively linked to the parents' QoL, which is basically conceptualized in relation to individual goals, expectations, standards and concerns (The WHOQOL Group, 1998).

These results were strengthened by the ascertainment of the model's invariance across asthma severity, children's age and SES groups. Although parents of children with intermittent asthma, young age and low SES presented higher levels of caregiving burden, coping dispositions marked by greater use of acceptance and less use of avoidance strategies have operated as resource factors positively linked to parents' QoL outcomes, regardless of the socio-demographic and clinical conditions. The acceptance coping mechanisms underlying the adaptation outcomes for parents caring for a child with asthma are similar to those described for normative parenting (Duncan, Coatsworth, & Greenberg, 2009), which suggests a general applicability of mindful parenting models and acceptance-based interventions in the context of pediatric asthma.

## Limitations of the study

The results from our study should be interpreted with caution due to some limitations in the study design and procedures. First, even though the directional paths tested in the mediation analyses have been hypothesized according to widely accepted theoretical models, the study's cross-sectional design prevents the establishment of causal relationships among the variables. Second, the required sample size for SEM has been suggested to vary between a minimum of 100-200 individuals, but more complex models (i.e., with higher number of distinct parameters to be estimated) may require larger sample sizes in order to achieve the necessary power to detect small effects (Kline, 2005). Third, the non-probabilistic sample collection method may have biased the distribution of clinical (e.g., asthma severity levels) and socio-demographic characteristics (e.g., family SES and parents' gender) of the sample and may limit the generalizability of the results. The low percentage of parents of children classified by persistent levels of asthma severity, although consistent with the distribution of asthma severity levels typically observed in the Portuguese pediatric population (Gaspar, Almeida, & Nunes, 2006), required the dichotomization of the asthma severity variable, which increased the intragroup variability and may have overlooked potential group differences. In addition, the classification of asthma severity levels by the child's physician was based on existing guidelines at the time of sample collection (GINA, 2008), and they do not represent the current recommendation of using both the parents' and the child's information for the assessment of asthma symptom control (GINA, 2014). Similarly, our sample was mainly composed of mothers with low/medium SES, which precluded the examination of gender differences and required the dichotomization of the SES variable even if this distribution was consistent with the users' profile in Portuguese outpatient public healthcare services and with previous studies with family caregivers (e.g., Canning et al., 1996; Everhart et al., 2008). Finally, the reliability values in our sample for the coping variables (acceptance and denial) were below the threshold of .70, which should be recognized as a limitation of the study even if they were slightly higher than those reported in the original studies of the Brief-COPE instrument and are considered by the author to be acceptable since each scale consists of two items only (Carver, 1997).

## Implications for clinical practice and research

Two main implications for clinical practice in pediatric asthma settings can be drawn from the present study. First, it is important that health professionals recognize that pediatric asthma affects not only the child but the family as a whole (Fiese et al., 2008) and that parents, particularly those caring for a younger child or with scarce socio-economic resources, may be at greater risk for experiencing higher levels of caregiving burden. Therefore, the caregiving burden should be routinely assessed and elected as a strategic intervention target for family-centered psychosocial interventions aimed at promoting parents' adaptation processes and outcomes. Second, coping tendencies characterized by greater use of acceptance and less use of denial can be encouraged in parents caring for a child with asthma, regardless of asthma severity or socio-demographic characteristics, in order to diminish the deleterious effects of the caregiving burden on the parents' QoL outcomes. Cognitive-behavioral therapies have been extensively recognized for their effectiveness in promoting more realistic appraisals of stressful events and the adequate use of coping resources in patients with health conditions (Ridder & Schreurs, 2001). In the specific context of caring for a child with asthma, acceptance-based interventions are expected to be effective in reappraising the caregiving demands and parent-child relationships as less burdensome, in developing coping tendencies marked by acceptance as an alternative to experiential avoidance, and, ultimately, in improving parental adaptation. Specifically, mindfulness training is likely to decrease caregiving-related stress, through the exposure to negative emotional states and the broadening of attention to more varied aspects of the caregiving experience and ways of coping with it (Bazzano et al., 2015; Minor et al., 2006).

Further longitudinal research should be undertaken to clarify the direction of the direct and indirect pathways proposed in our mediation model, as well as to examine the role of awareness, distraction, prevention of negative emotions and constructive self-assertion as specific mindful coping strategies (Tharaldsen, Bru, & Wilhelmsen, 2011) mediating the caregiving process. Besides, the efficacy of acceptance and mindful-based interventions to promote parental adaptation to pediatric asthma and the benefits of its availability as a public resource in pediatric healthcare services can only be ascertained by longitudinal research, namely, randomized controlled clinical trials and cost-effectiveness studies.

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# Empirical Study IV

## Parental positive meaning-making when caregiving for children with asthma

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# Parental positive meaning-making when caregiving for children with asthma

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## Abstract

***Introduction.*** Providing informal care to children/adolescents with chronic conditions has been associated with high levels of caregiving burden and impaired quality of life (QoL); however, parents can also experience uplifts which, by facilitating the attribution of positive meanings to caregiving, may contribute to better adaptation outcomes. The present study aimed at examining the direct and indirect links, via positive reframing as a coping strategy, between caregiving uplifts and quality of life (QoL) of parents who have a child/adolescent with asthma, as well as the invariance of the mediation model across children's age groups and asthma severity levels. ***Method.*** A total of 180 parents of children/adolescents aged 8-18 reported their experience of caregiving uplifts (Revised Burden Measure), the use of positive reframing coping (Brief Cope) and their QoL (WHOQOL-Bref). ***Results.*** Structural equation modeling showed a good fit for the mediation model ($\chi^2/df$ = 1.74, CFI = .95, RMSEA = .06), which explained 14% of the variability of parents' QoL. The caregiving uplifts were positively associated with positive reframing coping ($\beta$ = .19, $p$ = .02), which in turn was positively associated with QoL ($\beta$ = .36, $p$ < .01). No direct effect of uplifts on parents' QoL was found, but the indirect effect via positive reframing coping was statistically significant ($\beta$ = .07, BC 95% CI = .01/.14). Multi-group analyses demonstrated the strong structural invariance of the model across age groups ($\Delta\chi^2$ = .89, $p$ = .35) and asthma severity levels ($\Delta\chi^2$ = 1.91, $p$ = .17). ***Conclusion.*** These results suggest that psychological interventions focused on recognizing and valuing caregiving uplifts and on positive reappraisal of the stressful situation may support more adaptive coping processes and improve parents' QoL.

## Keywords

Caregiving uplifts • Coping • Parents/ family caregivers • Pediatric asthma • Positive reframing • Quality of life

# Introduction

Parental caregiving for children with chronic health conditions is a complex experience, encompassing both negative and positive dimensions, such as caregiving burdens and uplifts (Green, 2007; Larson, 2010). While the deleterious effects of caregiving burden on parents' adaptation outcomes are documented in pediatric literature for chronic medical conditions in general (Canning, Harris, & Kelleher, 1996), and for asthma in particular (Crespo, Carona, Silva, Canavarro, & Dattilio, 2011; Fiese, Wamboldt, & Anbar, 2005), the associations between caregiving uplifts and adaptation outcomes remain a neglected research topic. Even if some authors have suggested a positive impact of perceived benefits of caregiving on parents' emotional and physical health (Green, 2007), and some evidence has been gathered for the buffering effect of caregiving uplifts on the associations between caregiving burden and parents' quality of life (QoL) when caring for a child with a disability (Carona, Pereira, Moreira, Silva, & Canavarro, 2013), the examination of the role of positive coping strategies on these parental adaptation processes has not been yet conducted. The study of potential positive coping mechanisms in the context of pediatric conditions, namely asthma, can improve parental adaptation outcomes through a better understanding of specific modifiable variables and mechanisms to be targeted in intervention processes. This study could, thus, contribute to refine the current operationalization of a strength-based approach to family interventions in pediatric settings (Beresford, 1994).

## Family caregiving as developmental context for positive meaning-making

Despite the consensual claim that parents caring for a child with a chronic health condition face considerable stress and caregiving demands, a transition from deficit-based models to a risk-resilience framework has been increasingly acknowledged as a mean of enabling a more comprehensive understanding on the diversity of trajectories related to parental stress, coping and adaptation processes in those situations (Beresford, 1994). In the disability-stress-coping model, a risk-resilience framework on individual and family adaptation to chronic physical conditions, stress processing variables, such as cognitive appraisal and coping strategies, are assumed as resistance factors that increase the likelihood of positive adaptation outcomes, including positive mental health, social functioning and physical health (Wallander, Varni, Babani, Banis, & Wilcox, 1989). Since common criticisms to psychosocial research on parental adaptation to pediatric conditions include the disregard of positive dimensions related to adaptation processes (Barlow & Ellard, 2006), the study of positive dimensions of parental caregiving and coping seems imperative to support family-centered pediatric interventions, which are essentially aimed at targeting "existing family strengths and capabilities so that interventions are built on things a particular family already does well" (Judge, 1998, p. 263).

Interestingly, the observation that positive and negative psychological states may co-occur during caregiving processes, has led researchers to explore the role of positive emotion in disposing individuals to appraise stressful situations more as a challenge than as a threat (Folkman, 1997; Folkman & Moskowitz, 2000). The experience of positive emotions and psychological states during stressful situations is related to the adoption of meaning-based coping (e.g., positive reappraisal), and hypothesized to sustain adaptive coping processes (Folkman, 1997). Meaning-making is a cognitive coping process based on the reinterpretation of stressful events to minimize distress, and may occur at the global (e.g., reprioritization of family goals) or situational levels (e.g., benefit finding and personal growth) (Larson, 2010). In the specific case of pediatric asthma, it has been considered that families face considerable stress and demands, such as worry, restrictions of daily activities and interference with family routines, aside with the development of alternative, optimistic coping strategies that may serve as buffers from stress (Garro, 2011).

## Caregiving uplifts and caregivers' adaptation outcomes: The hypothesis of positive reframing as mediator

Although some authors commented on the relationship of positive caregiving perceptions with increased subjective well-being (Larson, 2010) and greater psychological flexibility (Gupta & Singhal, 2004), such tenets remain empirically unexamined, particularly for family caregiving in the context of pediatric conditions. In a recent study, the experience of uplifts tended to be more frequent in parents of children when compared to parents of adolescents in both groups of parents who had a child with a disability or a typically developing child, and caregiving uplifts were linked to the psychosocial QoL outcomes of parents of a child with a disability (Carona, Pereira, et al., 2013). The experience of caregiving uplifts has been also observed for parents of children with asthma, who tended to acknowledge positive gain from caregiving, such as personal growth from assuming a caregiver role (Gates & Akabas, 2012). Nevertheless, even with promising data on the beneficial effects of caregiving uplifts on parental adaptation, the mechanisms underlying these pathways have not been ascertained.

As proposed by the broaden-and-build model, the experience of positive emotions broadens the individual's scope of attention (e.g., mindful attention focus), cognition (e.g., creative thinking) and action (e.g., behavioral variety), which ultimately promote the development of his/her physical (e.g., vitality), intellectual (e.g., psychological flexibility) and social (e.g., pro-social mentality) resources (Fredrickson, 1998). Assuming family caregiving for a child with asthma as a significant developmental context, one can hypothesize that caregiving uplifts may improve parental adaptation outcomes through the development of positive dispositional coping tendencies. In line with the aforementioned stress and coping models, one of those coping tendencies is positive reframing or reappraisal, a dispositional, emotion-focused coping strategy, which has been defined as changing the situation's meaning by focusing on the good aspects of what has happened or what is happening (Carver, 1997; Carver, Scheier, & Weintraub, 1989; Folkman & Moskowitz, 2000).

### The present study: Aims and hypotheses

In the present study, caregiving uplifts were assumed as positive emotions and gratifications arising from caring for a child with a chronic health condition, and QoL was understood as an overall parental adaptation outcome within the developmental context of family caregiving. The main objective of this study was to examine the direct and indirect associations, via positive reframing coping, between caregiving uplifts and QoL outcomes of parents caring for a child with asthma. Accordingly, it was hypothesized that the experience of more caregiving uplifts would be associated with parents' better QoL, and that positive reframing coping would mediate that link. We also tested the invariance of the mediation model across children's age groups and asthma severity levels, but no specific predictions were made on this regard.

## Method

### Participants

A total of 110 parents of children with asthma aged 8-12 years and 70 parents of adolescents with asthma aged 13-18 years were included in the sample. Descriptive statistics for parents' and their children's socio-demographic and clinical variables are displayed in Table 1.

Comparison tests of socio-demographic and clinical characteristics (independent samples t-tests for continuous variables and chi-square tests for categorical variables) between parents of children aged 8-12 years and parents of adolescents aged 13-18 years showed no significant differences regarding parents' gender, socio-economic status, asthma severity levels and child's age at the time of asthma diagnosis. However, the group of parents of adolescents was significantly older, had a higher portion of daughters and had lived with the child's condition for a longer time when compared with the group of parents of children.

**Table 1** | Socio-demographic and clinical characteristics of the sample

| | Parents of children ($n$ = 110) | Parents of adolescents ($n$ = 70) | Differences between groups |
|---|---|---|---|
| ***Parents' socio-demographic characteristics*** | | | |
| Age (in years), $M$ ($SD$) | 39.83 (6.06) | 42.96 (4.71) | $t = -3.65^{**}$ |
| Gender, $n$ (%) | | | |
| Male | 15 (3.6%) | 13 (18.6%) | $\chi^2 = 0.79$ |
| Female | 95 (86.4%) | 57 (81.4%) | |
| Socio-economic status, $n$ (%) | | | |
| Low | 60 (54.5%) | 46 (65.7%) | $\chi^2 = 1.77$ |
| Medium/ high | 46 (41.8%) | 23 (32.9%) | |
| *Missing* | 4 (3.6%) | 1 (1.4%) | |
| ***Children's socio-demographic characteristics*** | | | |
| Age (in years), $M$ ($SD$) | 10.24 (1.26) | 14.71 (1.49) | - |
| Gender, $n$ (%) | | | |
| Male | 77 (70.0%) | 39 (55.7%) | $\chi^2 = 3.81^{*}$ |
| Female | 33 (30%) | 31 (44.3%) | |
| ***Clinical characteristics*** | | | |
| Asthma severity, $n$ (%) | | | |
| Intermittent | 56 (50.9%) | 39 (55.7%) | $\chi^2 = 1.46$ |
| Mild persistent | 35 (31.8%) | 17 (24.3%) | |
| Moderate persistent | 15 (13.6%) | 12 (17.1%) | |
| Severe persistent | 4 (3.6%) | 2 (2.9%) | |
| Age at diagnosis, $M$ ($SD$) | 4.25 (2.86) | 5.25 (4.68) | $t = -1.59$ |
| Disease length, $M$ ($SD$) | 6.05 (2.96) | 9.47 (4.41) | $t = -5.66^{**}$ |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$, two-tailed.

## Measures

### *Caregiving uplifts*

The parents' experience of gratification and positive psychological states arising from caregiving, such as the direct enjoyment from caregiving tasks, an improved relationship with their child, and generalized positive affect, was assessed with the Uplifts subscale of the Revised Burden Measure (Montgomery & Kosloski, 2006; Portuguese version: Carona, Silva, & Canavarro, 2011). This subscale comprises six items (e.g., "Have your caregiving responsibilities given your life more meaning?"), which were answered in a 5-point Likert scale, ranging from 1 (*not at all*) to 5 (*a great deal*). Higher scores indicate the experience of more caregiving uplifts. In our sample, the Uplifts subscale presented good reliability, with a Cronbach's alpha value of .85. For the structural equation modeling, the six items were considered observed indicators, which loaded on a latent variable of caregiving uplifts (factor loadings and composite reliability for the latent variable are presented in Table 3).

*Positive reframing*

The parents' use of positive reframing as a dispositional coping strategy was evaluated with the Positive Reframing subscale of the Portuguese brief version of the Cope inventory (Carver, 1997; Portuguese version: Pais-Ribeiro & Rodrigues, 2004). This subscale comprises two items assessing the parents' attempts to look at the stressful situation in a more beneficial way and grow from it ("I've been trying to see it in a different light, to make it seem more positive"; "I've been looking for something good in what is happening"). The answers were provided in a Likert-type response scale with four options, ranging from 0 (*I haven't been doing this at all*) to 3 (*I've been doing this a lot*), with higher scores indicating more frequent use of the coping strategy. In our sample, the positive reframing coping subscale proved to have adequate reliability, with a Cronbach's alpha value of .70. A latent variable, comprising the two items as observed indicators, was designed for the analyses of structural equation models (factorial validity and composite reliability for the latent variable are presented in Table 3).

*Quality of life*

Parent's QoL was measured with the Portuguese brief version of the World Health Organization Quality of Life (WHOQOL) instrument (The WHOQOL Group, 1998; Portuguese version: Vaz-Serra, et al., 2006). This questionnaire comprised 26 items clustered into a generic facet (2 items; not used in the present study) and four QoL domains, namely Physical (7 items; e.g., "Do you have enough energy for everyday life?"), Psychological (6 items; e.g., "How often do you have negative feelings such as blue mood, despair, anxiety, depression?"), Social relationships (3 items; e.g., "How satisfied are you with the support you get from your friends?") and Environmental (8 items; e.g., "How satisfied are you with your access to health services?"). The items were answered using a 5-point Likert scale addressing intensity (*not at all* to *extremely*), capacity (*not at all* to *completely*), frequency (*never* to *always*) or evaluation (*very dissatisfied* to *very satisfied*), with higher values indicating better QoL. All of the four QoL domains presented good reliability, with Cronbach's alpha values ranging from .74 (Social relationships domain) to .83 (Psychological domain). For the structural equation modeling we considered the four QoL domains as observed indicators loading on a latent variable of parents' QoL (factor loadings and composite reliability for the latent variable are presented in Table 3).

*Socio-demographic and clinical variables*

Asthma severity was classified by the child's physician into four categories (intermittent, mild persistent, moderate persistent and severe persistent), according to the Global Initiative for Asthma guidelines (GINA, 2008). Due to the low frequency of children/adolescents in the persistent asthma levels, this variable was dichotomized and dummy-coded (0 – intermittent asthma, *n* = 95; 1 – persistent asthma [mild, moderate, persistent], *n* = 85). Other clinical data (e.g., age at the time of diagnosis) and socio-demographic information (e.g., parents' and their children's age and gender) was collected from parents. The socio-economic status (SES) was determined using a classification system for the Portuguese context, based on parents' job and educational level (Simões, 1994).

## Procedure

The present study was approved by the Ethics Committee and/or Direction Board of three Portuguese public hospitals (Coimbra University Hospitals, Coimbra Pediatric Hospital, and Leiria Santo André Hospital). The sample was collected in the Pediatric and Immunoallergology outpatient services of the aforementioned health institutions, between September 2010 and February 2012, using the non-probabilistic convenience sampling method. For inclusion in the sample, parents had to meet the following criteria: 1) having a child aged between 8 and 18 years, with clinical diagnosis of asthma established by a physician according to the International Classification of Diseases system (ICD-10) for at least one year, and with no comorbidities with other chronic health conditions or severe psychiatric disorders; and 2) being the parent who, at the time of assessment, assumed the primary caregiver role on child's health related issues. The study's aims and procedures were explained in detail and written informed consent forms were obtained from all of the parents who agreed to participate. The parents completed a set of self-reported questionnaires in an office assigned for research purposes, in the health institution that their child attended. A trained research assistant was available to provide support during the completion of the assessment protocol, whenever necessary.

## Statistical analyses

Statistical analyses were conducted with SPSS (SPSS Inc., Chicago, IL, USA). Except for socio-demographic and clinical variables, missing data, that were random and low level (less than 5%), were handled by individual mean score substitution. Descriptive statistics were calculated for socio-demographic, clinical and psychosocial variables and Pearson correlation coefficients among study variables were examined.

Structural Equation Modeling (SEM) was performed with Analysis of Moments Structures (AMOS). The method of estimation was the maximum likelihood and the overall model fit was evaluated based on the chi-square statistic ($\chi^2$) and on the main approximate goodness-of-fit indexes, namely the comparative fit index (CFI), the root mean square error of approximation (RMSEA) and the standardized root mean squared residual (SRMR). A model was considered to have a good fit when $\chi^2$ was non-significant ($p > .05$), CFI ≥ .95, RMSEA ≤ .06 ($p > .05$) and SRMR ≤ .08, and an acceptable fit when CFI ≥ .90 and RMSEA ≤ .10 (Browne & Cudeck, 1993; Hu & Bentler, 1999). In the first step, to ensure the pertinence of multi-dimensional constructs (latent variables), we examined the measurement model by conducting a confirmatory factor analysis (CFA) testing the hypothesized links between the latent variables and their observed indicators. For each latent variable, the construct reliability was assessed by calculating composite reliability values, i.e., the ratio between the squared sum of standardized factor loading and the squared sum of standardized factor loading plus the sum of the error variance terms; good construct reliability was established if composite reliability value was higher than .70 (Hair, Black, Babin, & Anderson, 2010). In the second step, we examined the structural model testing the direct and indirect effects, via positive reframing coping, of caregiving uplifts on parents' QoL. The statistical significance of the indirect effects was evaluated using bootstrap resampling procedures (Preacher & Hayes, 2008; Williams & MacKinnon, 2008), with 2000 samples and 95% bias-corrected bootstrap confidence interval (BC 95% CI).

The invariance of the mediation model across children's age groups and asthma severity levels was tested in two steps: first we examined the baseline model for each group separately, and, subsequently, we conducted multi-group analyses comparing the unconstrained model with models in which measurement weights, measurement intercepts, structural weights and structural covariances were sequentially and cumulative fixed to be equal across groups. Strong structural invariance was established when the chi-square difference between models ($\Delta\chi^2$) was non-significant (Little, 2013).

## Results

### Descriptive statistics and inter-correlations among study variables

Descriptive statistics and correlations among study variables are presented in Table 2. Higher levels of caregiving uplifts were associated with more frequent use of positive reframing as a coping strategy and with better QoL in the social relationships domain. Moreover, positive reframing was positively associated with all dimensions of parents' QoL. Regarding socio-demographic and clinical variables, no significant associations with caregiving uplifts, positive reframing or parents' QoL were found, except for marginally significant association between children' age and caregiving uplifts ($p = .06$); children' age and positive reframing ($p = .07$); and asthma severity and parents' social QoL ($p = .06$).

**Table 2** | Descriptive statistics and matrix of inter-correlations among study variables

| ***Psychosocial variables*** | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1. Caregiving uplifts | - | | | | | |
| 2. Positive reframing | .16$^{*}$ | - | | | | |
| 3. Physical QoL | .05 | .17$^{*}$ | - | | | |
| 4. Psychological QoL | .10 | .22$^{**}$ | .57$^{**}$ | - | | |
| 5. Social QoL | .16$^{*}$ | .34$^{**}$ | .41$^{**}$ | .68$^{**}$ | - | |
| 6. Environmental QoL | .12 | .17$^{*}$ | .54$^{**}$ | .63$^{**}$ | .55$^{**}$ | - |
| ***Socio-demographic and clinical variables*** | | | | | | |
| Children's age | -.14$^{\dagger}$ | .13$^{\dagger}$ | .12 | .07 | .01 | .11 |
| Asthma severity | -.01 | .08 | .05 | .05 | .14$^{\dagger}$ | .06 |
| Mean (*SD*) | 3.06 (0.99) | 2.00 (0.71) | 3.90 (0.58) | 3.86 (0.60) | 3.95 (0.66) | 3.62 (0.54) |
| Cronbach's alpha | .85 | .70 | .81 | .83 | .74 | .82 |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$, $^{\dagger}$ $p < .10$, two-tailed.

## The measurement model

The measurement model (CFA) testing the hypothesized links between the latent variables (caregiving uplifts, positive reframing and parents' QoL) and their observed indicators had a good fit, with $\chi^2_{(52)} = 90.55$, $p < .01$; CFI = .95; RMSEA = .06 ($p = .14$; 90% CI =.04/ .09); and SRMR = .06. As presented in Table 3, all of the observed indicators had standardized regression weights above the threshold of .50 and were statistically significant. In addition, the latent variables presented adequate construct reliability, with composite reliability values above .70. Except for the item PR2, the squared multiple correlations ($R^2_{smc}$) between each observed indicator and all other observed indicators were lower than .90 and the tolerance values ($1 - R^2_{smc}$) were higher than .10 (Table 3), indicating that each one of the observed variables explained a substantial proportion of the total standardized variance (Kline, 2005).

## The structural model

After confirming the adequacy of the measurement model, a structural model testing the direct and indirect effects, via positive reframing coping, of caregiving uplifts on parents' QoL was tested. The model, which is displayed in Figure 1, had a good fit, with $\chi^2_{(52)} = 90.55$, $p < .01$; CFI = .95; RMSEA = .06 ($p = .14$; 90% CI =.04/.09); and SRMR = .06, and explained 14% of the variability of parents' QoL. We found significant direct links between caregiving uplifts and positive reframing ($\beta = .19$, $p = .02$) and between positive reframing and parents' QoL ($\beta = .36$, $p < .01$). Although the direct effect of caregiving uplifts on parent's QoL was not statistically significant ($\beta = .08$, $p = .33$), a significant indirect effect via positive reframing coping was found (β = .07, $p$ = .02; BC 95% CI =.01/.14).

**Table 3** | Multicollinearity diagnosis, factor loadings of observed indicators and composite reliability for latent variables

| Latent variable | Observed indicators | $R^2_{smc}$ | Tolerance $(1 - R^2_{smc})$ | Factor loadings | Composite reliability |
|---|---|---|---|---|---|
| Caregiving uplifts | Item U1 | .44 | .56 | .66** | .85 |
| | Item U2 | .48 | .52 | .69** | |
| | Item U3 | .49 | .51 | .70** | |
| | Item U4 | .53 | .47 | .73** | |
| | Item U5 | .49 | .51 | .70** | |
| | Item U6 | .56 | .44 | .75** | |
| Positive reframing | Item PR1 | .30 | .70 | .55** | .77 |
| | Item PR2 | .99 | .01 | .99** | |
| Parents' QoL | Physical | .41 | .59 | .64** | .84 |
| | Psychological | .76 | .24 | .87** | |
| | Social | .58 | .42 | .76** | |
| | Environmental | .54 | .46 | .74** | |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$, two-tailed.

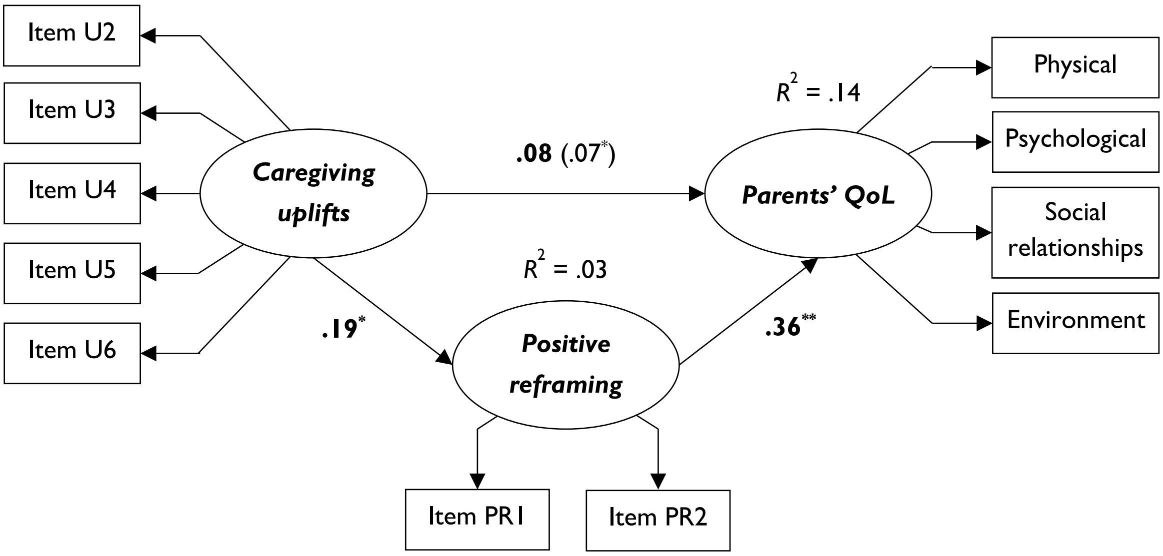

**Figure 1** | SEM testing the direct and indirect effects, via positive reframing, of caregiving uplifts on parents' QoL

*Note*. Bold figures represent standardized regression weights for direct paths; non-bold figures in brackets represent standardized regression weights for indirect paths. For simplicity, measurement error terms are not shown. $^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

## Multi-group analyses

The examination of the baseline mediation model for children's age groups separately revealed that the model had a good fit for parents of children aged 8-12 and an acceptable fit for parents of adolescents aged 13-18 years-old (summary of fit statistics are presented in Table 4). Regarding asthma severity groups, the mediation model had an acceptable fit for both parents of children with intermittent asthma and parents of children with persistent asthma. As presented in Table 4, no significant differences between the unconstrained model and the models with fixed measurement weights, fixed measurement intercepts, fixed structural weights and fixed structural covariances were found, confirming that the parameters tested in the mediation model were similar for both children's age and asthma severity groups.

**Table 4** | Model's invariance by children's age groups and asthma severity levels

| | $\chi^2$ | *df* | CFI | RMSEA [90% CI] | SRMR | $\Delta\chi^2$ | $\Delta df$ |
|---|---|---|---|---|---|---|---|
| ***Children's age groups*** | | | | | | | |
| Summary of fit statistics | | | | | | | |
| Children 8-12 | 72.25$^{*}$ | 52 | .96 | .06 [.02/ .09] | .06 | | |
| Adolescents 13-18 | 81.48$^{**}$ | 52 | .92 | .09 [.05/ .13] | .09 | | |
| Multi-group analyses | | | | | | | |
| Unconstrained model | 153.85$^{**}$ | 104 | .94 | .05 [.03/ .07] | .06 | - | - |
| Measurement weights | 163.62$^{**}$ | 113 | .94 | .05 [.03/ .07] | .06 | 9.77 | 9 |
| Measurement intercepts | 182.14$^{**}$ | 125 | .93 | .05 [.03/ .07] | .06 | 18.52 | 12 |
| Structural weights | 182.75$^{**}$ | 128 | .93 | .05 [.03/ .06] | .07 | 0.61 | 3 |
| Structural covariances | 183.64$^{**}$ | 129 | .93 | .05 [.03/ .06] | .07 | 0.89 | 1 |
| ***Asthma severity groups*** | | | | | | | |
| Summary of fit statistics | | | | | | | |
| Intermittent asthma | 84.62$^{**}$ | 52 | .93 | .08 [.05/ .11] | .08 | | |
| Persistent asthma | 86.52$^{**}$ | 52 | .91 | .09 [.05/ .12]$^{*}$ | .07 | | |
| Multi-group analyses | | | | | | | |
| Unconstrained model | 171.15$^{**}$ | 104 | .92 | .06 [.04/ .08] | .08 | - | - |
| Measurement weights | 180.74$^{**}$ | 113 | .92 | .06 [.04/ .07] | .08 | 9.60 | 9 |
| Measurement intercepts | 188.98$^{**}$ | 125 | .92 | .05 [.04/ .07] | .08 | 8.24 | 12 |
| Structural weights | 189.07$^{**}$ | 128 | .93 | .05 [.04/ .07] | .08 | 0.08 | 3 |
| Structural covariances | 190.97$^{**}$ | 129 | .92 | .05 [.04/ .07] | .08 | 1.91 | 1 |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$, two-tailed.

# Discussion

The present study is an innovative contribution on the processes explaining parents' adaptation outcomes in the challenging context of caring for a child with asthma. In summary, we found that caregiving uplifts were associated with parents' QoL outcomes, although only indirectly via positive reframing as a coping strategy. These findings were strengthened by ascertaining the invariance of this mediation model across different groups of parents who, due to their children's developmental stage and asthma clinical severity, have distinct caregiving demands. Taken together, our results support the pertinence of considering the positive dimensions of caregiving (e.g., uplifts) and meaning-making coping mechanisms for an improved understanding of parents' adaptation within a risk-resilience framework, namely the role of positive reappraisals in the context of stress processing mechanisms.

As stated in our hypothesis, parents' perception of benefits and gratifications arising from caring for a child with asthma was positively associated with their QoL, but only for the social domain. Complementary to the social support deterioration model, according to which chronic parenting stress may exhaust social resources and elicit inadequate responses from network members and, consequently, increase parents' maladjustment (Carona, Crespo, & Canavarro, 2013), the distinctive association between parents' uplifts and social QoL may reflect the importance of positive emotions in establishing and maintaining supportive social relationships (Fredrickson, 1998). In addition, parents of children with chronic health conditions or disabilities have similar social network structures to other families, but they may use their social resources differently in order to reappraise caregiving strains and improving their adaptation outcomes (Kazak, 1987). Further research is required to clarify the impact of social support on positive meaning-making coping strategies and parental adaptation outcomes in pediatric contexts.

However, when considering QoL as a multi-dimensional construct including physical, psychological, social and environmental domains, the beneficial effect of caregiving uplifts emerged only in an indirect way, via positive reframing coping, confirming our mediation hypothesis. Our findings support the applicability of the broaden-and-build model of positive emotions (Fredrickson, 1998) in the developmental context of caring for a child with asthma. The experience of uplifts, which involves positive emotions related to caregiving, may facilitate the development of general positive coping dispositions, such as positive reframing (e.g., maintaining a positive look over life and its circumstances). In turn, positive meaning-making reappraisals on caregiving demands have been stated as effective coping mechanisms to sustain the well-being of parents who have children with disabilities (Judge, 1998; Larson, 2010). Moreover, there is scarce but important evidence that parental coping patterns may also influence the psychological functioning and health-related QoL of their children with asthma (e.g., Sales, Fivush, & Teague, 2008). Thus, future research should clarify the potential role of caregiving uplifts and positive meaning-making reappraisal on the transactional processes between children's and parents' adaptation.

Finally, we examined the mediation model's (in)variance across children's age groups and asthma severity levels but no significant differences on the strength of the aforementioned associations were found. Although important differences on parental adaptation outcomes may exist according to asthma severity levels (Everhart, Fiese, & Smyth, 2008) and children's age groups (Carona, Pereira, et al., 2013), our findings suggested that the experience of caregiving uplifts may operate through similar mechanisms (i.e., via positive reframing coping) in both developmental and clinical groups. Thus, our study also adds preliminary evidence for the general applicability of this specific parental adaptation mechanism, regardless of their children's age group or asthma severity level, which may guide and facilitate parental psychological assessment and intervention in pediatric asthma settings.

The results from the present study should be read with caution due to some limitations in the study's design and procedures. The main limitation was the study's cross-sectional design, which prevents the establishment of causality among the variables. Although the directional paths tested in the mediation model have been hypothesized according to the literature, further longitudinal research should be undertaken to clarify the direction of these associations and to examine whether changes in the attribution of meanings to the caregiving experience may influence the parental adaptation processes over time. Our study was also limited by the non-probabilistic sampling method and the consequent heterogeneous distribution of sample characteristics. The pediatric literature has advocated that the role of primary caregivers of children with chronic health conditions is commonly assumed by mothers, and that mothers are likely to be more vulnerable to psychological symptoms and lower QoL than fathers (Goldbeck, 2006; Silver, Westbrook, & Stein, 1998). Consistently with these studies, our sample was mainly composed of mothers; however, the low frequency of fathers precluded the examination of the role of caregivers' gender on the mediating processes explaining parents' QoL. Furthermore, about a half of the parents had a child with intermittent asthma, which forced the dichotomization of the asthma severity variable. Although the distribution of children by asthma severity levels in our sample has been similar to the Portuguese pediatric population distribution (Gaspar, Almeida, & Nunes, 2006), the increased variability within the persistent asthma group may have overlooked potential differences in the parameters tested in the mediation model according to asthma severity levels.

Despite these limitations, several implications for clinical practice and research can be drawn. The impact of childhood health conditions on the family and the reciprocal influences between parents' and their children's adaptation are extensively recognized in pediatric psychology (Sameroff, 2009). Therefore, clinical interventions in pediatric settings should be family-centered and consider parents' adaptation processes and outcomes. The assessment of positive dimensions of caregiving (e.g., uplifts) is essential to provide a comprehensive depiction of the caregiving experience and may contribute to operationalize a strength-based approach in promoting family adaptation. Therefore, encouraging parents' perception of caregiving gratifications and personal growth is an important target for interventions aiming at promoting coping strategies in adverse circumstances and long-term adaptation (Joseph & Linley, 2006). Mindful-based interventions have already proven to be effective in reducing stress and anxiety and increasing personal growth in caregivers of children with special needs (Benn, Akiva, Arel, & Roeser, 2012), which may then "broaden and build" their coping repertoires (Larson, 2010), and specifically meaning-based coping mechanisms such as positive reframing or reappraisal. However, applications of meaning-making coping models to promote parental positive adaptation in the context of pediatric asthma still need further research, particularly longitudinal studies and randomized controlled clinical trials. Moreover, future research should examine the mediating role of other specific meaning-based coping mechanisms, such as acceptance or self-compassion, on the associations between caregiving-related emotions and parental adaptation, and also on the transactional processes between parental coping patterns and children's adaptation outcomes.

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## Empirical Study V

# Caregiving burden and uplifts: A contradiction or a protective partnership for the quality of life of parents and their children with asthma?

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# Caregiving burden and uplifts: A contradiction or a protective partnership for the quality of life of parents and their children with asthma?

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## Abstract

***Introduction.*** Parental caregiving in the context of pediatric chronic conditions is a multifaceted experience that encompasses negative (burdens) and positive dimensions (uplifts), which may support risk and protective processes that influence family adaptation. This study aimed to examine the caregiving experience of parents caring for a child with asthma and the moderating role of caregiving uplifts on the associations between caregiving burden and quality of life (QoL) of parents and their children. ***Method.*** Participants were 180 dyads of children/adolescents with asthma between 8 and 18 years of age and one of their parents. The parents reported on caregiving burden and uplifts and on their QoL, and the children/adolescents completed a self-report measure of generic QoL. ***Results.*** Results showed that although parents of children with intermittent asthma and parents of younger children presented higher levels of caregiving burden, non-controlled asthma was the only clinical variable representing a significant risk factor for decreased QoL in children. Significant negative and positive associations were found between burden dimensions and QoL and between caregiving uplifts and QoL, respectively, in parents and children. Additionally, caregiving uplifts moderated the negative link between relationship burden and parents' QoL. ***Conclusion.*** These results suggest that, far from being contradictory, caregiving uplifts may co-occur with high levels of burden and may constitute a protective factor against the deleterious effect of the caregiving burden on parents' QoL and a resource that directly contributes to children's QoL. This risk-resistance approach to family caregiving may contribute to operationalizing strength-based interventions in the context of pediatric asthma.

## Keywords

Caregiving burden • Caregiving uplifts • Parent-child quality of life • Pediatric asthma • Risk and resistance factors

# Introduction

Pediatric chronic health conditions such as asthma are challenging contexts for parents, who, in addition to providing daily care to children as a normative task of parenting, must embrace the unexpected and stressful "caregiver career" (Raina et al., 2004). The burden resulting from caregiving demands, which include avoiding the environmental and emotional triggers of asthma exacerbation and monitoring symptoms and treatment (Fiese, Winter, Anbar, Howell, & Poltrock, 2008), has been associated with quality of life (QoL) impairments for children with asthma and their parents (Crespo, Carona, Silva, Canavarro, & Dattilio, 2011; Fiese, Wamboldt, & Anbar, 2005). However, parental caregiving is a complex experience and the co-occurrence of uplifts (e.g., gratifications and positive emotions) arising from caring for a child with a chronic condition or disability has also been described (Green, 2007; Larson, 2010). Although there is some evidence that caregiving uplifts may buffer the negative impact of the caregiving burden on QoL in parents of children with cerebral palsy (Carona, Pereira, Moreira, Silva, & Canavarro, 2013), few studies have examined this positive dimension of caregiving and its links to the adaptation outcomes in parents and their children with asthma. Understanding the role of caregiving uplifts may assist in the operationalization of a strength-based approach to pediatric asthma and may contribute to improving family adaptation in that context (Beresford, 1994; Judge, 1998).

Clinicians and researchers have long recognized that a pediatric chronic condition does not only affect the child; it also affects all family members and the relationships among them (Kazak, 1989). Although families facing such a chronic condition are at greater risk for psychosocial adaptation impairments, few children and parents present clinically significant psychological symptoms (Barlow & Ellard, 2006). Moreover, studies comparing the QoL of children with asthma and their parents with healthy controls have yielded inconsistent findings (e.g., Moreira et al., 2013; Van Gent et al., 2007). To explain the wide variability in family adaptation trajectories, the disability-stress-coping model highlights the importance of considering specific risk and resistance factors and the complex interactions between them (Wallander, Pitt, & Mellins, 1990; Wallander, Varni, Babani, Banis, & Wilcox, 1989). Within this model, disease parameters (e.g., severity), child functional dependence, and psychosocial stressors (e.g., daily hassles) have been proposed as important risk factors affecting children's and their parents' adaptation. In addition, the negative impact of disease-specific risk factors has been hypothesized to be moderated by several resistance factors, namely intrapersonal factors (e.g., problem-solving ability), social-ecological factors (e.g., family environment) and stress processing mechanisms (e.g., cognitive appraisal).

Raina and colleagues (2004) also emphasized caregiving burden as an important risk factor for poor parental adaptation outcomes. The burden of caregiving has been broadly defined as the "caregiver's perceived responsibilities and associated limitations on self and family" (Canning, Harris, & Kelleher, 1996, p. 737). Even if most research tends to use global measures resulting from the integration of different burden dimensions (Pinquart & Sörensen, 2003), the caregiving burden should be further differentiated into relationship burden (i.e., disruptions in the relationship between the caregiver and the care receiver), objective burden (i.e., time constraints resulting from caregiving instrumental activities), and subjective burden (i.e., emotional stress and anxiety; Savundranayagam, Montgomery, & Kosloski, 2011). This multi-dimensional approach is justified by the differential impact of burden dimensions on key outcomes. In fact, some authors found evidence for a direct association between the amount of assistance provided to a child during activities of daily living (i.e., objective burden) and the caregivers' psychological and physical health (Raina et al., 2005), while in other studies the subjective burden emerged as a foremost predictor of caregivers' distress (Canning et al., 1996) and QoL outcomes (Carona et al., 2013).

The associations between the additional practical demands and concerns arising from parenting a child with a chronic condition and the parents' impaired QoL are also well documented in empirical research conducted in the context of pediatric asthma (Crespo et al., 2011; Fiese et al., 2005). However, little is known about the potential influences of parents' caregiving burden on their children's adaptation outcomes. The family is the primary context for child development, in general, and for the understanding and treatment of pediatric chronic conditions, in particular (Fiese & Sameroff, 1989; Kazak, 1989). Moreover, a considerable amount of research has demonstrated that the children's ability to adapt to adversity is influenced by the quality of parental caregiving (Armstrong, Birnie-Lefcovitch, & Ungar, 2005). Specifically, the parents' caregiving burden has been associated with impaired QoL for their children with asthma (Crespo et al., 2011; Fiese et al., 2005), both directly and indirectly through mother-child interaction patterns (Fiese et al., 2008).

The disease parameters and child characteristics are also relevant risk factors, which can operate at different levels of the adaptation process. Disease severity has been associated with greater caregiving burden in parents caring for a child with a chronic condition (Canning et al., 1996). In the particular context of pediatric asthma, worse QoL has been found for parents and their children with greater asthma severity and poorly controlled symptoms (Dean et al., 2010; Everhart & Fiese, 2009; Everhart, Fiese, & Smyth, 2008). Although children's age has not been explicitly included in the disability-stress-coping model, there is some evidence of excessive time demands in providing care to children with chronic conditions or disabilities among mothers of younger children when compared with mothers of adolescents (Floyd & Gallagher, 1997).

In addition to the deleterious effect of risk factors, research is now moving toward the study of how and when families can restore the balance between demands and capabilities to achieve the positive adaptation of vulnerable members and the family unit, in a context of significant adversity (McCubbin & Patterson, 1983; Patterson, 2002; Walsh, 2002). Family psychological resources, which have been defined as "the family's characteristic mode of perceiving and interacting with the social world, including within and external to the family" (Wallander et al., 1989, p. 159), have assumed particular relevance in determining family adaptation in the context of pediatric chronic conditions. For example, research has consistently shown that a positive family environment is associated with better family adaptation outcomes in pediatric samples, in general (for a review, see Drotar, 1997), and in pediatric asthma, in particular (e.g., Silva, Crespo, & Canavarro, 2014). In addition to operating as resources (i.e., they can positively influence adaptation outcomes regardless of the presence of a stressor), Wallander et al. (1989) have suggested that family variables may operate as protective factors (i.e., they can ameliorate negative outcomes or promote adaptive functioning under adverse conditions; Rose, Holmbeck, Coakley, & Franks, 2004). The caregiving uplifts, as the parents' perceptions of gratifications and positive emotions arising from caregiving (Green, 2007; Larson, 2010), also fall within the definition of "family psychological resources". However, the role of caregiving uplifts as a resource contributing directly for the parents' and their children's QoL, or as a protective factor against the deleterious effects of caregiving burden, remains understudied for pediatric asthma.

Gratifications and positive emotions can emerge by attributing positive meanings to the caregiving experience, also known as the meaning-making process, which may occur at the global (e.g., reprioritization of family goals) or situational levels (e.g., benefit finding and personal growth; Park, 2010). Qualitative studies with families of children with developmental disabilities have described caregiving as an opportunity to develop new skills, widen interests, strengthen family relationships and expand personal and social networks, and as a source of personal growth (Grant, Ramcharan, McGrath, Nolan, & Keady, 1998; Stainton & Besser, 1998). A quantitative study with parents of children with cerebral palsy showed that the experience of caregiving uplifts directly contributed to better parental QoL and buffered the negative effect of the caregiving burden (Carona et al., 2013). Three adaptive functions of positive emotions occurring in stressful circumstances have been identified: broadening the "thought-action repertoire" and sustaining coping efforts, providing a "breather" or a distraction from daily hassles, and building new personal physical, intellectual, and social resources or restoring depleted ones (Folkman, 1997; Folkman & Moskowitz, 2000; Fredrickson, 1998). Within family caregiving, parents' positive perceptions of their experience may buffer the negative impact of the child's health condition on family members and, ultimately, contribute to better QoL for parents and their children (Gupta & Singhal, 2004).

## The present study: Aims and hypotheses

Our study implemented a multi-dimensional approach to the caregiving experience, through the assessment of different components of caregiving burden and the examination of both burdens and uplifts as, respectively, risk and resource/protective factors for the adaptation of parents and their children with asthma. In the scope of the comprehensive concept of "adaptation", QoL has been defined as "a person's perception of his/her position in life within the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards, and concerns" (The WHOQOL Group, 1994, p. 28). From this standpoint, we considered the parents' and their children's QoL as overall adaptation outcomes that reflect both the disease and the broader individual life experiences as influences on physical, psychological, and social well-being.

Based on a risk-resistance approach to family adaptation (Wallander et al., 1989, 1990), the objective of this study was twofold. First, we intended to describe the negative (burdens) and positive (uplifts) dimensions of family caregiving and the QoL of parents and their children in different clinical groups of asthma severity (intermittent *vs.* persistent) and control (controlled *vs.* partly controlled or uncontrolled), and at different developmental periods (childhood *vs.* adolescence). The second aim of our study was to examine the moderating role of caregiving uplifts on the associations between burden dimensions and the QoL of parents and their children. According to the conceptualization of disease parameters as risk factors for poor family adaptation outcomes, we expected higher levels of caregiving burden and worse QoL in the persistent and non-controlled asthma groups (H1). Considering that younger children require greater assistance in the activities of daily living and asthma management, we also predicted higher levels of caregiving burden and worse QoL among their parents compared with the parents of adolescents (H2). Given the scarce literature on the positive dimensions of caregiving, we made no predictions regarding the direction of group differences in caregiving uplifts. Moreover, we expected that caregiving burden would be negatively associated with parents' and their children's QoL (H3). Finally, based on the potential role of gratifications and positive emotions as protective factors against the adverse consequences of family stressors (Folkman, 1997; Gupta & Singhal, 2004), we hypothesized that these associations would be moderated by caregiving uplifts (i.e., the negative associations between caregiving burden and QoL would be buffered by the parents' concomitant perceptions of caregiving uplifts; H4).

# Method

## Participants

The participants were 180 dyads of children and adolescents with asthma and one of their parents. The families were enrolled at the Pediatric and Immunoallergology outpatient services of three Portuguese public hospitals. Data collection took place between September, 2010 and February, 2012. For inclusion in the sample, the children/adolescents had to meet the following criteria: (a) between 8 and 18 years of age, (b) diagnosis of asthma established by a physician according to the International Classification of Diseases system (ICD-10), (c) asthma diagnosis for at least one year, and (d) absence of comorbidities with other chronic health conditions or severe psychiatric disorders, except for comorbid allergic diseases (e.g., allergic rhinitis, atopic dermatitis/ eczema, and hypersensitivity to inhalant or food allergens). In addition, an inclusion criterion for parents was considered: being the parent self-identified as currently assuming the role of primary caregiver for the child in health-related issues. The participants' socio-demographic and clinical characteristics are presented in Table 1.

**Table 1** | Socio-demographic and clinical characteristics of the sample

| | | Parents (*n* = 180) | Children (*n* = 180) |
|---|---|---|---|
| ***Socio-demographic characteristics*** | | | |
| Age (in years), *M* (*SD*) | | 41.03 (5.77) | 11.98 (2.57) |
| Age group [a], *n* (%) | Children 8-12 years | - | 110 (61.1%) |
| | Adolescents 13-18 years | - | 70 (38.9%) |
| Gender, *n* (%) | Male | 28 (15.6%) | 116 (64.4%) |
| | Female | 152 (84.4%) | 64 (35.6%) |
| Socio-economic status [b], *n* (%) | Low | 106 (58.9%) | |
| | Medium | 58 (32.2%) | |
| | High | 14 (7.8%) | |
| | *Missing* | 2 (1.1%) | |
| ***Clinical characteristics*** | | | |
| Asthma severity, *n* (%) | Intermittent | - | 95 (52.8%) |
| | Mild persistent | - | 52 (28.9%) |
| | Moderate persistent | - | 27 (15.0%) |
| | Severe persistent | - | 6 (3.3%) |
| Asthma control, *n* (%) | Controlled | - | 120 (66.7%) |
| | Partly controlled | - | 51 (28.3%) |
| | Uncontrolled | - | 9 (5.0%) |
| Comorbidities with other allergic diseases, *n* (%) | Allergic rhinitis | - | 13 (7.2%) |
| | Atopic dermatitis/eczema | - | 7 (3.9%) |
| | Unspecified allergies | - | 16 (8.9%) |
| Use of regular or emergency medication, *n* (%) | | - | 176 (97.8%) |
| Length of time since asthma diagnosis (in years), *M* (*SD*) | | - | 7.36 (3.95) |

[a] The pediatric sample was divided into two age groups: children (8-12 years old) and adolescents (13-18 years old). For simplicity, we adopted the term children to refer to the pediatric sample, which includes both age groups. [b] Socio-economic status was determined using a classification system for the Portuguese context based on the parents' job and educational level (Simões, 1994).

## Procedure

The present study is part of a broader research project approved by the ethics committees and/or direction boards of three Portuguese public hospitals (Coimbra University Hospitals, Coimbra Pediatric Hospital, and Leiria Santo André Hospital). Using the non-probabilistic convenience sampling method, children who had routine medical appointments during the data collection period were screened by their physicians based on their medical files, and those who met the aforementioned criteria were invited to participate in the study. Detailed information about the study's aims and procedures was provided to all participants. Informed consent was obtained from parents and from adolescents older than 13 years, and informal assent was obtained from younger children. The parents and their children completed a set of self-report questionnaires in a room assigned to research purposes in the health institution they attended. A research assistant was available to provide support to participants with difficulties in reading or understanding the items' content.

## Measures

### *Caregiving burden and uplifts*

The Portuguese version of the Revised Burden Measure (Montgomery & Kosloski, 2006; Portuguese version: ongoing psychometric studies) was used to assess the parents' experience of caregiving burden and uplifts. The parents were asked to indicate the extent to which various aspects of their lives had changed due to caregiving for their children with asthma ("As a result of assisting the care receiver, have the following aspects of your life changed?"), through 22 items clustered into three burden subscales and a distinct but complementary measure of caregiving uplifts. The Relationship burden subscale (five items) assesses the negative psychological state that directly derives from the caregiver's unique relationship with the care receiver, particularly as a result of demands for care and attention over and above the level that the caregiver perceives is warranted by the care receiver's condition (e.g., "Have your caregiving responsibilities increased attempts by your relative to manipulate you?"). The Objective burden subscale (six items) assesses the negative psychological state that results from the interference of caregiving activities on the caregiver's free time (e.g., "Have your caregiving responsibilities kept you from recreational activities?"). The Subjective burden subscale (five items) refers to a generalized form of negative affect resulting from caregiving, but not as a direct consequence of any specific event, task, or interaction (e.g., "Have your caregiving responsibilities created a feeling of hopelessness?"). The Uplifts measure comprises six items assessing the experience of gratifications and positive psychological states arising from caregiving, such as the direct enjoyment of caregiving tasks, an improved relationship with the child, and generalized positive affect (e.g., "Have your caregiving responsibilities given your life more meaning?"). All of the items were scored on a 5-point Likert scale ranging from 1 (*not at all*) to 5 (*a great deal*). Mean scores were calculated for each burden dimension and for the uplifts measure, with higher scores indicating the parents' perception of greater burden and more uplifts, respectively. Good internal consistency was obtained in our sample for all burden subscales, with Cronbach's alpha coefficients ranging from .84 (Subjective burden) to .88 (Objective burden), as well as for the Uplifts measure ($\alpha$ = .85).

*Parents' quality of life.*

Parents' QoL was measured by the Portuguese version of the EUROHIS-QOL 8-item index (Pereira, Melo, Gameiro, & Canavarro, 2011; Schmidt, Mühlan, & Power, 2006). This self-report questionnaire is derived from the World Health Organization Quality of Life Assessment (WHOQOL-100 and WHOQOL-Bref instruments) and includes eight items representing the physical (e.g., "Do you have enough energy for everyday life?"), psychological (e.g., "How satisfied are you with yourself?"), social (e.g., "How satisfied are you with your personal relationships?"), and environmental (e.g., "How satisfied are you with the conditions of your living place?") domains of QoL. The eight items were scored on a 5-point Likert scale ranging, for instance, from *not at all* to *completely*. An overall QoL score was computed from the mean score of the items, with higher scores indicating better QoL. In the current sample, the questionnaire presented good reliability, with a Cronbach's alpha value of .83.

*Children's quality of life.*

Children's generic QoL was measured by the Portuguese child-report version of the KIDSCREEN-10 Index (Matos, Gaspar, & Simões, 2012; Ravens-Sieberer et al., 2010). This one-dimensional questionnaire contains 10 items measuring physical well-being (e.g., "Have you felt fit and well?"), psychological well-being (e.g., "Have you felt sad?"), parent relations and autonomy (e.g., "Have your parent(s) treated you fairly?"), social support and peers (e.g., "Have you had fun with your friends?"), and school environment (e.g., "Have you got on well at school?"), and is answered on a 5-point Likert scale ranging from 1 (*never/ not at all*) to 5 (*always/ extremely*). A global score was calculated from the mean score of the items, with higher scores indicating better QoL. In our sample, the Cronbach's alpha coefficient was .78, indicating good reliability.

*Socio-demographic and clinical data*

The asthma severity and control levels were classified by the child's physician according to the Global Initiative for Asthma (2008) guidelines. Asthma severity was categorized into four levels (intermittent, mild persistent, moderate persistent, and severe persistent), considering the level of symptoms, airflow limitation, and lung function variability. In addition to the clinical severity of the underlying disease, the physicians also classified the asthma control into three levels (controlled, partly controlled, and uncontrolled), in order to consider the responsiveness to treatment according to the asthma clinical manifestations, laboratory markers of inflammation, and pathophysiological features of the disease as recorded in the children's medical files.

Additional clinical data (e.g., use of medication, comorbidities with other health conditions, and length of time since asthma diagnosis) and socio-demographic information (e.g., parents' and their children's ages and genders, educational level and current job) were collected from the parents. Using a classification system specifically developed for the Portuguese context and based on the educational level and current job of the primary caregiver (Simões, 1994), the family socio-economic status (SES) was classified into low (e.g., unqualified employees in construction or manufacturing without completing the 9th grade of school education), medium (e.g., employees in bureaus or banks, nurses, social workers, or teachers with intermediate or university courses) and high (e.g., senior officials of government, army, commerce or industry, physicians, magistrates, or engineers with bachelor, master, doctorate, or other post-graduate degrees).

## Statistical analyses

The statistical analyses were conducted with SPSS v.20.0 (SPSS Inc., Chicago, IL). Except for socio-demographic and clinical variables, missing data, which were random and less than 5% of the total values, were replaced with the individual mean score for each variable. Descriptive statistics were calculated for socio-demographic and clinical variables. Due to the heterogeneous distribution of family SES, asthma severity, and control levels observed in our sample, these variables were dichotomized and dummy-coded (family SES: 0 – low [$n$ = 106], 1 – medium/high [$n$ = 72]; asthma severity: 0 – intermittent [$n$ = 95], 1 – persistent [mild, moderate, or severe, $n$ = 85]; asthma control: 0 – controlled [$n$ = 120], 1 – non-controlled [partly controlled or uncontrolled, $n$ = 60]). Differences in the mean scores of the study variables between age groups (children aged 8-12 *vs.* adolescents aged 13-18), asthma severity groups (intermittent *vs.* persistent), and asthma control groups (controlled *vs.* non-controlled) were tested with one-way multivariate analyses of covariance for caregiving burden dimensions and with one-way univariate analyses of covariance (ANCOVA) for caregiving uplifts, parents' QoL and children's QoL, while controlling for the remaining factors as well as family SES and length of time since asthma diagnosis. For caregiving burden, when multivariate effects were significant, univariate analyses were performed to examine which dimensions significantly differed between groups.

Prior to conducting the regression analyses, we computed Pearson's correlation coefficients between the main socio-demographic (parents' and children's ages and genders and family SES) and clinical variables (asthma severity, asthma control, length of time since asthma diagnosis, and comorbidities with other allergic diseases) and the other study variables. The socio-demographic and clinical variables that were significantly associated with one or both of the independent/moderator and dependent variables were included as covariates in the regression models (MacKinnon & Luecken, 2008). Following the procedures recommended by Aiken and West (1991), hierarchical regression analyses were performed to examine the main and interaction effects of caregiving burden and uplifts on parents' and their children's QoL. To reduce multicollinearity with the interaction terms and to render the regression coefficients more meaningful and interpretable, the independent (burden dimensions) and moderator (uplifts) variables were mean centered before computing the interaction terms (Aiken & West, 1991; Hayes, 2013). After the inclusion of covariates in the first step of the regression equation, the independent variables, the moderator, and the interaction terms were entered as predictors in subsequent steps. According to the guidelines for testing multiple moderating effects (Frazier, Tix, & Barron, 2004), we introduced the interaction terms together in the same step of the regression equation. Using the Modgraph computational tool (Jose, 2013), the significant interaction effects were plotted from the estimates of the dependent variable at different values of the moderator, and the strength and significance of each regression line was analyzed with post-hoc simple slope computations.

# Results

## Descriptive statistics and analyses of covariance

Descriptive statistics for caregiving burden and uplifts and for parents' and children's QoL are presented in Table 2. Significant multivariate effects of the asthma severity group, Wilks' $\lambda = .94$; $F_{(3,\ 167)} = 3.39$, $p = .02$; $\eta_p^2 = .06$, and the children's age group, Wilks' $\lambda = .94$; $F_{(3,\ 167)} = 3.48$, $p = .02$; $\eta_p^2 = .06$, were found for caregiving burden. The univariate analyses (see Table 2) indicated higher levels of relationship burden for parents caring for a child with intermittent asthma compared with the persistent asthma group, and higher levels of objective and subjective burden for parents of younger children than for parents of adolescents. The ANCOVAs for caregiving uplifts and for parents' QoL also presented significant differences between the children's age groups, with parents of younger children reporting more uplifts but lower QoL than parents of adolescents. Regarding children's QoL, a significant difference between asthma control groups was found, with children with controlled asthma reporting better QoL than children with non-controlled asthma.

**Table 2** | Descriptive statistics and univariate analyses of covariance by asthma severity, asthma control and children's age groups

| | ***Asthma severity*** | | | |
|---|---|---|---|---|
| | ***Intermittent*** (*n* = 91) | ***Persistent*** (*n* = 84) | | |
| | *M* (*SD*) | *M* (*SD*) | $F_{(1, 169)}$ | $\eta_p^2$ |
| Relationship burden | 1.61 (0.77) | 1.40 (0.57) | $4.67^{*}$ | .03 |
| Objective burden | 1.77 (0.76) | 1.80 (0.77) | 0.00 | .00 |
| Subjective burden | 2.05 (0.87) | 1.99 (0.83) | 0.08 | .00 |
| Uplifts | 3.06 (0.91) | 3.02 (1.06) | 0.00 | .00 |
| Parents' QoL | 3.75 (0.54) | 3.78 (0.51) | 0.83 | .01 |
| Children's QoL | 4.34 (0.48) | 4.29 (0.56) | 0.04 | .01 |
| | **Asthma control** | | | |
| | **Controlled** (*n* = 116) | **Non-controlled** (*n* = 59) | | |
| | *M* (*SD*) | *M* (*SD*) | $F_{(1, 169)}$ | $\eta_p^2$ |
| Relationship burden | 1.52 (0.72) | 1.49 (0.63) | 0.40 | .00 |
| Objective burden | 1.77 (0.73) | 1.80 (0.82) | 0.00 | .00 |
| Subjective burden | 2.04 (0.85) | 1.98 (0.84) | 0.21 | .00 |
| Uplifts | 3.08 (0.98) | 2.97 (0.99) | 0.58 | .00 |
| Parents' QoL | 3.79 (0.48) | 3.70 (0.60) | 1.46 | .01 |
| Children's QoL | 4.38 (0.46) | 4.20 (0.61) | $4.37^{*}$ | .03 |
| | **Age group** | | | |
| | **Children** (*n* = 107) | **Adolescents** (*n* = 68) | | |
| | *M* (*SD*) | *M* (*SD*) | $F_{(1, 169)}$ | $\eta_p^2$ |
| Relationship burden | 1.57 (0.68) | 1.41 (0.69) | 3.32 | .02 |
| Objective burden | 1.92 (0.79) | 1.57 (0.66) | $9.91^{**}$ | .06 |
| Subjective burden | 2.11 (0.85) | 1.89 (0.82) | $4.92^{*}$ | .03 |
| Uplifts | 3.15 (0.93) | 2.88 (1.05) | $4.34^{*}$ | .03 |
| Parents' QoL | 3.72 (0.50) | 3.83 (0.56) | $5.51^{*}$ | .03 |
| Children's QoL | 4.35 (0.56) | 4.27 (0.46) | 0.53 | .00 |

$^{*}$ $p \leq .05$; $^{**}$ $p \leq .01$, two-tailed.

## Main and interaction effects of caregiving burden and uplifts on parents' and their children's QoL

As presented in Table 3, preliminary correlation analyses indicated weak to moderate positive associations between burden dimensions and caregiving uplifts and negative associations between burden dimensions and parents' and their children's QoL. Conversely, caregiving uplifts were not significantly associated with parents' or children's QoL. Regarding socio-demographic and clinical characteristics, children's younger age, lower SES, and intermittent asthma were significantly associated with greater relationship burden; children's younger age was associated with greater objective burden; and low SES was associated with greater subjective burden. In addition, medium/high SES was correlated with parents' and their children's better QoL, and controlled asthma was positively associated with children's QoL (see Table 3). Accordingly, these variables were included as covariates in the regression analyses when appropriate. No significant associations were found for parents' age, parents' and children's gender, length of time since asthma diagnosis, and presence of comorbidities with other allergic diseases.

**Table 3** | Inter-correlations among study variables and socio-demographic and clinical characteristics

| *Psychosocial variables* | *Burden dimensions* | | | *Uplifts* | *QoL outcomes* | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| 1. Relationship burden | - | | | | | |
| 2. Objective burden | .72$^{**}$ | - | | | | |
| 3. Subjective burden | .57$^{**}$ | .66$^{**}$ | - | | | |
| 4. Uplifts | .16$^{*}$ | .30$^{**}$ | .20$^{**}$ | - | | |
| 5. Parents' QoL | -.25$^{**}$ | -.15$^{*}$ | -.34$^{**}$ | .13 | - | |
| 6. Children's QoL | -.30$^{**}$ | -.20$^{**}$ | -.24$^{**}$ | .12 | .25$^{**}$ | - |
| *Socio-demographic and clinical variables* | | | | | | |
| Children's age (in years) | -.16$^{*}$ | -.27$^{**}$ | -.14 | -.14 | .12 | -.06 |
| Children's gender [a] | .01 | -.04 | .09 | .00 | -.03 | -.04 |
| Parents' age (in years) | -.05 | -.10 | -.11 | -.10 | -.07 | -.03 |
| Parents' gender [a] | -.05 | .02 | .12 | -.04 | -.08 | .06 |
| Family SES [b] | -.16$^{*}$ | -.02 | -.22$^{**}$ | -.07 | .19$^{*}$ | .22$^{**}$ |
| Length of time since asthma diagnosis (in years) | -.02 | -.03 | <.01 | <.01 | -.11 | -.06 |
| Comorbidities with other allergic diseases [c] | .03 | .01 | <.01 | .04 | -.02 | .05 |

[a] Children's and parents' gender: 0 – male; 1 – female. [b] Family SES: 0 – low; 1 – medium/high. [c] Comorbidities with other allergic diseases: 0 – no; 1 – yes. $^{*}$ $p \leq .05$; $^{**}$ $p \leq .01$, two-tailed.

Results from the regression analyses examining the main and interaction effects of the burden dimensions and caregiving uplifts on the parents' QoL are displayed in Table 4. Significant main effects of caregiving burden and uplifts were found, explaining 11% and 4% of the variance in parents' QoL, respectively. The main effects model showed that, while controlling for socio-demographic and clinical variables, the parents' experience of higher levels of subjective burden were significantly associated with lower QoL, and higher levels of caregiving uplifts significantly accounted for better QoL.

As depicted in Table 5, significant negative main effects of caregiving burden were also found on children's QoL, explaining 9% of its variance. Specifically, higher levels of relationship burden were associated with children's lower QoL. In addition, higher levels of caregiving uplifts were associated with children's better QoL, explaining 3% of its variance.

**Table 4** | Main and interaction effects of caregiving burden and uplifts on parents' QoL

| | ***Step 1: Covariates*** | | ***Step 2: Main effects of burden dimensions*** | | ***Step 3: Main effects of caregiving uplifts*** | | ***Step 4: Interaction effects*** | |
|---|---|---|---|---|---|---|---|---|
| | $\Delta R^2 = .05$, $\Delta F_{(3, 174)} = 3.26^{*}$ | | $\Delta R^2 = .11$, $\Delta F_{(3, 171)} = 7.35^{***}$ | | $\Delta R^2 = .04$, $\Delta F_{(1, 170)} = 7.92^{**}$ | | $\Delta R^2 = .05$, $\Delta F_{(3, 167)} = 3.44^{*}$ | |
| Variables | *b* (*SE*) | *t* | *b* (*SE*) | *t* | *b* (*SE*) | *t* | *b* (*SE*) | *t* |
| Constant | 3.33 (.20) | $16.99^{***}$ | 3.44 (.19) | $17.88^{***}$ | 3.40 (.19) | $17.97^{***}$ | 3.45 (.19) | $18.43^{***}$ |
| Children's age | .03 (.02) | 1.77 | .02 (.02) | 1.55 | .03 (.02) | 1.74 | .02 (.02) | 1.40 |
| Family SES [a] | .21 (.08) | $2.67^{**}$ | .10 (.08) | 1.26 | .12 (.08) | 1.52 | .10 (.08) | 1.31 |
| Asthma severity [b] | .03 (.08) | 0.37 | -.03 (.08) | -0.35 | -.02 (.08) | -0.23 | < -.01 (.07) | -0.03 |
| Relationship burden | | | -.17 (.08) | $-2.10^{*}$ | -.15 (.08) | -1.87 | -.20 (.08) | $-2.38^{*}$ |
| Objective burden | | | .19 (.08) | $2.31^{*}$ | .14 (.08) | 1.67 | .12 (.08) | 1.47 |
| Subjective burden | | | -.21 (.06) | $-3.60^{***}$ | -.21 (.06) | $-3.68^{***}$ | -.20 (.06) | $-3.48^{***}$ |
| Uplifts | | | | | .11 (.04) | $2.81^{**}$ | .16 (.04) | $3.69^{***}$ |
| Relationship burden X Uplifts | | | | | | | .22 (.10) | $2.31^{*}$ |
| Objective burden X Uplifts | | | | | | | -.09 (.08) | -1.11 |
| Subjective burden X Uplifts | | | | | | | .07 (.06) | 1.10 |
| Model summary | $R^2 = .05$, $F_{(3, 174)} = 3.26^{*}$ | | $R^2 = .16$, $F_{(6, 171)} = 5.48^{***}$ | | $R^2 = .20$, $F_{(7, 170)} = 6.02^{***}$ | | $R^2 = .25$, $F_{(10, 167)} = 5.42^{***}$ | |

[a] Family SES: 0 – low; 1 – medium/high. [b] Asthma severity: 0 – intermittent; 1 – persistent. $^{*}$ $p \leq .05$; $^{**}$ $p \leq .01$; $^{***}$ $p \leq .001$, two-tailed.

**Table 5** | Main and interaction effects of caregiving burden and uplifts on children's QoL

| | ***Step 1: Covariates*** | | ***Step 2: Main effects of burden dimensions*** | | ***Step 3: Main effects of caregiving uplifts*** | | ***Step 4: Interaction effects*** | |
|---|---|---|---|---|---|---|---|---|
| | $\Delta R^2 = .07$, $\Delta F_{(4,\ 173)} = 3.41^{**}$ | | $\Delta R^2 = .09$, $\Delta F_{(3,\ 170)} = 6.40^{***}$ | | $\Delta R^2 = .03$, $\Delta F_{(1,\ 169)} = 6.28^{*}$ | | $\Delta R^2 = .01$, $\Delta F_{(3,\ 166)} = 0.81$ | |
| Variables | *b* (*SE*) | *t* | *b* (*SE*) | *t* | *b* (*SE*) | *t* | *b* (*SE*) | *t* |
| Constant | 4.37 (.19) | $22.64^{***}$ | 4.56 (.19) | $23.82^{***}$ | 4.52 (.19) | $23.90^{***}$ | 4.53 (.19) | $23.67^{***}$ |
| Children's age | -.01 (.02) | -0.56 | -.02 (.02) | -1.30 | -.02 (.02) | -1.16 | -.02 (.02) | -1.29 |
| Family SES [a] | .23 (.08) | $2.91^{**}$ | .15 (.08) | 1.93 | .17 (.08) | $2.17^{*}$ | .16 (.08) | $2.01^{*}$ |
| Asthma severity [b] | .03 (.09) | 0.33 | -.02 (.08) | -0.27 | -.02 (.08) | -0.24 | -.01 (.08) | -0.16 |
| Asthma control [c] | -.18 (.09) | $-2.03^{*}$ | -.18 (.09) | $-2.07^{*}$ | -.17 (.09) | -1.96 | -.17 (.09) | $-2.01^{*}$ |
| Relationship burden | | | -.19 (.08) | $-2.41^{*}$ | -.18 (.08) | $-2.22^{*}$ | -.20 (.08) | $-2.44^{*}$ |
| Objective burden | | | .03 (.08) | 0.32 | -.02 (.08) | -0.23 | -.04 (.08) | -0.43 |
| Subjective burden | | | -.08 (.06) | -1.34 | -.08 (.06) | -1.36 | -.07 (.06) | -1.10 |
| Uplifts | | | | | .10 (.04) | $2.51^{*}$ | .13 (.04) | $2.85^{**}$ |
| Relationship burden X Uplifts | | | | | | | .11 (.10) | 1.12 |
| Objective burden X Uplifts | | | | | | | < .01 (.08) | 0.04 |
| Subjective burden X Uplifts | | | | | | | -.01 (.06) | -0.07 |
| Model summary | $R^2 = .07$, $F_{(4,\ 173)} = 3.41^{**}$ | | $R^2 = .17$, $F_{(7,\ 170)} = 4.88^{***}$ | | $R^2 = .20$, $F_{(8,\ 169)} = 5.19^{***}$ | | $R^2 = .21$, $F_{(11,\ 166)} = 3.98^{***}$ | |

[a] Family SES: 0 – low; 1 – medium/high. [b] Asthma severity: 0 – intermittent; 1 – persistent. [c] Asthma control: 0 – controlled; 1 – partly controlled/uncontrolled. $^{*}$ $p \leq .05$; $^{**}$ $p \leq .01$; $^{***}$ $p \leq .001$, two-tailed.

In addition to the main effects of caregiving burden and uplifts, the insertion of the interaction terms between these variables explained an additional variance of 5% in parents' QoL. Post hoc simple slope analyses (see Figure 1) revealed that higher levels of relationship burden were associated with lower parental QoL when parents experienced low (*b* = -.42, SE = .14; *t* = -2.97, *p* < .01) or medium (*b* = -.20, SE = .08; *t* = -2.39, *p* = .02) levels of uplifts but not when they experienced high levels of uplifts (*b* = -.02, SE = .11; *t* = 0.16, *p* = .87).

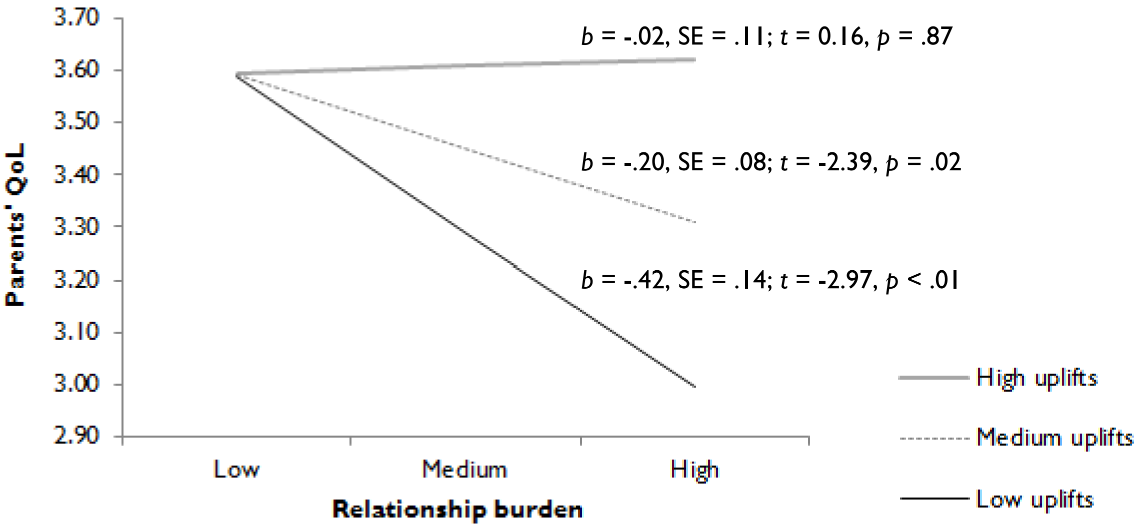

**Figure 1** | The moderating effect of caregiving uplifts on the association between relationship burden and parents' QoL

No significant moderation effects of caregiving uplifts on the associations between objective or subjective burden and parents' QoL, or between any of the burden dimensions and children's QoL, were found.

# Discussion

Grounded in the disability-stress-coping model (Wallander et al., 1989, 1990), the present study examined the caregiving experience and the QoL of parents and their children with different clinical characteristics of asthma and at different developmental stages, and the buffering role of caregiving uplifts on the negative associations between burden dimensions and QoL outcomes. Overall, our results showed that, although significant differences were found in caregiving dimensions according to asthma severity and children's age groups, these variables did not represent direct risk factors for parents' or their children's decreased QoL. In contrast, asthma control was not associated with the caregiving dimensions or with parents' adaptation, but it was a significant risk factor for children's QoL impairment. After controlling for clinical and socio-demographic variables, higher levels of caregiving burden were associated with worse QoL and higher levels of uplifts were associated with better QoL for both family members (main effects). In addition, caregiving uplifts moderated the negative association between relationship burden and parents' QoL (interaction effects).

Our first set of results showed different effects of asthma clinical characteristics on the QoL outcomes of parents and children. Parents were more likely to perceive their children's demands for care and attention as over and above the needs warranted by the pediatric health condition when asthma was intermittent and did not inflict strict limitations on the children's functioning than when asthma was persistent. However, no significant effects of asthma severity or control were found on objective and subjective caregiving burdens or on parents' QoL. These results shall not exclude the possibility of indirect effects of asthma severity on parents' QoL, through its effect on caregiving burden dimensions. The hypothesis that intermittent asthma may result in increased relationship burden, which, in turn, negatively affects parents' QoL, needs further investigation. In contrast, and partially confirming our first hypothesis, children with controlled asthma reported better QoL than children with partly controlled or uncontrolled asthma. According to previous research reporting greater school/work absenteeism, lower productivity, and more impaired QoL for children with uncontrolled asthma and their caregivers when compared to the controlled asthma group (Dean et al., 2010; Schmier et al., 2007), significant differences in the caregiving burden dimensions and parents' QoL were also expected. The absence of significant differences between asthma control groups in our study may reflect the high portion of patients with partly controlled asthma that were included in the non-controlled asthma group, but it could also indicate that parents may be concerned with the broader aspects of their child's psychosocial functioning (Varni, Burwinkle, & Lane, 2005) and constant involvement in asthma management routines (Fiese et al., 2008), regardless of asthma clinical characteristics.

Consistent with previous research on the time demands of caring for a child with a chronic condition or disability (Floyd & Gallagher, 1997) and confirming our second hypothesis, parents of younger children presented higher levels of objective and subjective burden and lower QoL than parents of adolescents. These findings support the assumption that as the child ages and becomes more able to manage self-care routines, the responsibilities for asthma management are likely to be shared by family members, thereby alleviating caregiver burden (Kaugars, Klinnert, & Bender, 2004; Kazak, 1989). Therefore, we advocate that conceptual models of family adaptation to pediatric chronic conditions should adopt a developmental perspective by including, among other aspects, children's younger age as a risk factor for parents' greater burden and impaired adaptation outcomes.

Interestingly, parents of younger children also presented more caregiving uplifts compared with parents of adolescents. In addition, higher levels of caregiving burden were associated with parents' perception of more uplifts. Taken together, these results suggest that parents are more likely to find benefits in the most stressful caregiving circumstances, which may reflect two different scenarios. On the one hand, and according to the differential susceptibility hypothesis (Belsky & Pluess, 2009), some parents may be more vulnerable to environmental influences and, thus, more affected by both negative and positive features of their caregiving context. On the other hand, even if caring for a child with asthma is not considered a traumatic experience, it seems to include mechanisms similar to those underlying the genesis of post-traumatic growth (Tedeschi & Calhoun, 2004), particularly if we take into account a recent study of breast cancer survivors showing that a negative life event may not necessarily be perceived as traumatic but may be stressful enough to shatter beliefs and expectations and to motivate a reappraisal of the stressful event and individual goals and capabilities (Silva, Moreira, & Canavarro, 2011).

Regarding the second aim of our study, and confirming our third hypothesis, the results showed a negative contribution of caregiving burden dimensions, except for objective burden, to explain parents' and their children's QoL. These findings suggest that, more than objective risk factors, parents' subjective perceptions of stressor events and family relationships may determine coping processes and may ultimately influence their adaptation outcomes (Lazarus & Folkman, 1984; Patterson, 2002). Regarding the positive effects of caregiving uplifts on QoL outcomes, different patterns have emerged for parents and children. For parents, caregiving uplifts were positively associated with their QoL and moderated the negative effect of relationship burden on QoL, whereas for children, only positive main effects of caregiving uplifts, but not moderating effects, were found. According to the conceptual distinction proposed by Rose et al. (2004), the perception of caregiving-related gratifications and positive emotions operated as a protective factor for the parents, that is, it contributed to buffering the negative effect of high levels of caregiving burden on QoL (moderation effect), and operated as a resource for the children, that is, contributed to better QoL, regardless of the presence of greater parental stress (main effect). A possible explanation of the moderation effects is the potential role of caregiving-related positive emotions in facilitating the development of positive meaning-based coping dispositions (e.g., positive reappraisal; Folkman, 1997; Fredrickson, 1998), which may serve as a buffer from emotional stress (Garro, 2011).

In conclusion, our results strengthen the importance of addressing the caregiving burden as a multi-dimensional construct, including its relationship, objective, and subjective dimensions (Savundranayagam et al., 2011), because each dimension may be differentially related to both asthma clinical characteristics and parents' and their children's adaptation outcomes. In addition, to provide a comprehensive depiction of the parental caregiving experience, the positive dimension of caregiving and its effects on family adaptation should also be examined (Green, 2007; Larson, 2010). Although it may seem contradictory at first, parents' perceptions of gratifications and positive emotions arising from caring for their children with asthma seems to occur in the most burdensome contexts (e.g., caring for a younger child). Finding positive meanings in the caregiving experience may constitute a protective factor against the deleterious effect of the caregiving burden on parents' QoL and an important resource that directly contributes to children's adaptation, thus benefiting all family members and fortifying the relational bonds among them (Walsh, 2002).

## Strengths and limitations

The main strength of our study was the innovative approach to the caregiving experience, including its negative and positive dimensions. To our knowledge, this is the first study to address the interaction effects of caregiving burden and uplifts on the QoL of parents and their children as a means of operationalizing a risk-resistance approach to family adaptation in the context of pediatric asthma. Our findings were strengthened by the inclusion of data from the child and his or her primary caregiver, which allows us to capture some of the complexity of family systems and to examine the inter-relationships among family members (Kazak, 1997). This methodological strategy was extended to the inclusion of data from individuals outside the family system (the child's physician, who reported on asthma severity and control), thus reducing the bias resulting from parent-reported asthma outcomes, which are likely to be influenced by parents' emotional status, perceptions, and expectations (Everhart & Fiese, 2009; Kaugars at al., 2004; Kazak, 1997). In addition, the assessment of families living with pediatric asthma for at least one year sought to minimize the effect of acute stress responses caused by a recent diagnosis (Gupta & Singhal, 2004) and to enable families to stabilize their functioning and meaning-making processes in this adverse context.

However, our findings should be interpreted with caution due to some limitations in the study's design and procedures. First, the study's cross-sectional design only allowed us to capture a snapshot of the ongoing dynamic process of family adaptation and precluded the establishment of causal links among study variables. Second, the non-probabilistic sample collection method and the heterogeneous distribution of socio-demographic and clinical characteristics of the sample may limit the generalizability of the results. The high percentage of children with intermittent and controlled asthma, although consistent with the distribution of asthma severity levels typically observed in the Portuguese pediatric population (Gaspar, Almeida, & Nunes, 2006), required the dichotomization of asthma severity and control variables, which increased the intragroup variability and excluded the examination of interaction effects between age, severity, and control groups on the caregiving dimensions and QoL outcomes. Moreover, the great majority of caregivers was female and had low/medium SES, reflecting the users' profile in public pediatric healthcare services in Portugal. Even if the family SES was controlled in our analyses, the results should be interpreted within the Portuguese economic context, because the additional financial burdens may have influenced the caregiving experiences and, consequently, the parents' and their children's QoL outcomes. Third, only children with asthma and their primary caregivers were included, and the analyses were performed at the individual level (i.e., parents' and children's QoL were examined separately). Considering preliminary evidence showing that parents' and their children's QoL are interrelated (e.g., Everhart et al., 2008; Moreira et al., 2013; Silva et al., 2014; Vila et al., 2003) and that the way in which families represent their experiences is based on transactional influences between family members over time (Fiese & Sameroff, 1989), future research should adopt longitudinal designs, include other family members/units (e.g., couples and siblings) and rely on dyadic analyses of family adaptation processes. Finally, the parents' caregiving burden and uplifts contributed for explaining only a small amount of the variance in their own and their children's QoL. The child's characteristics (e.g., child behavior), caregiver's intrapersonal factors (e.g., self-esteem and sense of mastery over the caregiving situation), and coping resources (e.g., social support, family functioning, and stress processing mechanisms) have been acknowledged as highly relevant predictors of the caregiving experience and family adaptation outcomes (Fiese & Sameroff, 1989; Raina et al., 2004) and, therefore, future research on this topic is warranted.

## Clinical implications

The findings from this study have important implications for clinical interventions in pediatric asthma settings. In contrast to a healthcare approach focused only on the child and his or her health condition (Gupta & Singhal, 2004), our results suggest that, in addition to symptom control, effective clinical interventions aimed at promoting family adaptation to pediatric asthma should be family centered and should encourage a positive outlook on caregiving demands and parent-child relationships. A risk-resistance approach to family adaptation (Wallander et al., 1989, 1990) offers a valuable conceptual map to identify and target key family processes that may reduce the risk of psychosocial problems, buffer stress, and even enable personal and relational growth in stressful contexts. In clinical practice, this framework is operationalized by strength-based interventions, particularly those focused on family meaning-making (e.g., positive reinterpretation of stressful events; appraisal of family capacities as sufficient to successfully manage distress) and coping strategies to withstand and rebound from adversity (Patterson, 2002; Walsh, 2002).

A multi-dimensional assessment and intervention targeting both negative (e.g., burdens) and positive (e.g., uplifts) dimensions of parental caregiving may contribute to operationalizing this strength-based approach to family adaptation. Therefore, it is important to avoid pathologizing parents' experience of gratifications and positive emotions when caring for a child with a health condition (e.g., considering them a form of denial of their child's condition) and to understand their adaptive function (Larson, 2010). Encouraging and supporting parents' perceptions of gratifications and positive emotions arising from caregiving may sustain adaptive coping processes (Folkman, 1997) and contribute to adaptation for parents and their children. Identifying thoughts and beliefs that interfere with positive experiences, facilitating coping strategies based on positive reappraisal, acceptance, and problem-solving, planning positive meaningful events, and infusing ordinary events with positive meaning (Folkman, 1997; Folkman & Moskowitz, 2000) are specific intervention strategies that may help parents meet the challenge of "embracing the paradox" of their caregiving experience and perceive gratifications and positive emotions while they are also regulating distress (Carona et al., 2013; Larson, 1998).

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# Empirical Study VI

# Transactional paths between children and parents in pediatric asthma: Associations between family relationships and adaptation

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# Transactional paths between children and parents in pediatric asthma: Associations between family relationships and adaptation

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## Abstract

***Introduction.*** The particular challenges posed by pediatric asthma may have a negative impact on the adaptation of children and their parents. From a transactional approach it is important to examine how reciprocal links between children and parents contribute to explain their adaptation and under which conditions these associations occur. This cross-sectional study aimed at examining the direct and indirect links between children's and parents' perceptions of family relationships and adaptation, separately (within-subjects) and across participants (cross-lagged effects), and the role of asthma severity in moderating these associations. ***Method.*** The sample comprised 257 children with asthma, aged between 8 and 18 years-old, and one of their parents. Both family members completed self-reported questionnaires on family relationships (cohesion and expressiveness) and adaptation indicators (quality of life and psychological functioning). Physicians assessed asthma severity. Structural Equation Modeling was used to test within-subjects and cross-lagged paths between children's and parents' family relationships and adaptation. ***Results.*** The model explained 47% of children's and 30% of parents' adaptation: family relationships were positively associated with adaptation, directly for children and parents, and indirectly across family members. Asthma severity moderated the association between family relationships and health-related quality of life for children: stronger associations were observed in the presence of persistent asthma. ***Conclusion.*** These results highlight the need of including psychological interventions in pediatric healthcare focused on family relationships as potential targets for improving children's and parents' quality of life and psychological functioning, and identified the children with persistent asthma as a group that would most benefit from family-based interventions.

## Keywords

Adaptation • Asthma severity • Children and parents • Family relationships • Pediatric asthma

# Introduction

Asthma is an episodic chronic health condition that is characterized by asymptomatic periods alternating with exacerbation episodes (i.e., asthma attacks or acute asthma). The exacerbations are marked by progressive increases in shortness of breath, coughing, wheezing, or chest tightness or by a combination of these symptoms (Global Initiative for Asthma Program [GINA], 2008). A complex interaction between genetic susceptibility and environmental factors (e.g., air pollution, tobacco smoke, and microbial exposure) influences the development and manifestations of asthma (Von Mutius, 2009). Beyond these well-known environmental triggers, psychological factors, such as emotional stress, negative emotions, and passive coping strategies, have also been identified as emotional triggers of asthma symptoms (Lehrer, 1998; Wood et al., 2007). In the pediatric context, asthma affects not only the child but also the entire family and implies rearranging family organization and interaction patterns to avoid environmental and emotional triggers and manage treatment (Fiese, 2008; Morris, Silk, Steinberg, Myers, & Robinson, 2007), thereby requiring cooperation of all the family members. The influence of family and parental functioning on children's adaptation has been extensively addressed and is well documented in pediatric literature. In a literature review, Drotar (1997) concluded that supportive family relationships (e.g., families with high levels of cohesion) were associated with more positive psychological outcomes of children with chronic health conditions (e.g., fewer behavioral problems and better self-esteem). Conversely, family conflict, maternal distress and parental child-rearing practices characterized by overprotection consistently predicted children's psychological problems, such as lower self-control, behavioral problems and psychological distress (Drotar, 1997). However, scholars and researchers are increasingly acknowledging the reciprocity of influences between parents and children to better understand family adaptation in pediatric contexts (Fiese, 1997; Fiese & Sameroff, 1989). The present study used a transactional framework (Sameroff, 2009) to examine the ways in which family relationships were associated with adaptation for children and parents.

Studies of family processes and family interventions in pediatric asthma have a deep-rooted history (Fiese, 2008). Since the pioneering work of Minuchin and colleagues with families with a child with a psychosomatic illness (Minuchin et al., 1975), the psychobiological influence of family relationships on the emotional and physiological regulation of pediatric asthma patients has been addressed by several studies. Specifically, studies have demonstrated that higher levels of family cohesion are associated with children's better self-worth and few emotional and behavioral problems (Reichenberg & Broberg, 2005) and that a negative family emotional climate, characterized by low levels of expressiveness, is linked to children's depressive symptoms, which in turn are linked to asthma severity (Wood et al., 2007, 2008). The links between family relationships and adaptation outcomes of children with asthma are complex. Most studies have found that these pathways are not always direct and are potentially mediated by individual and relational characteristics. For example, parent-child interaction patterns were found to mediate the links between a negative family emotional climate and children's depressive symptoms (Wood et al., 2008) and between the burden related to family routines to manage asthma and children's anxiety and quality of life (QoL) (Fiese, Winter, Anbar, Howell, & Poltrock, 2008). Annett, Turner, Brody, Sedillo, and Dalen (2010) also found that the association between a positive family environment and children's QoL was mediated by children's psychological functioning.

Undertaking research with children with chronic health conditions implies considering their social-ecological foreground, where the continuous reciprocal interactions between children and family members provide a context for understanding the individual and family adaptation (Kazak, 1989). Additionally, the transactional model of development emphasizes that children are active and influential participants in their life contexts (Fiese & Sameroff, 1989; Sameroff, 2009). Despite the growing awareness of the reciprocity of influences between children and parents, few empirical studies have addressed the influence of children's functioning on parents' adaptation in the specific context of pediatric asthma, and even those have examined parents' adaptation independently from children's adaptation (e.g., Annett et al., 2010; Bender et al., 2000). However, there is evidence of bidirectional associations between the QoL of children with asthma and their parents (Marsac, Funk, & Nelson, 2007; Vila et al., 2003) and of the influence of the psychological functioning of children with asthma on parents' QoL (Annett et al., 2010) and on the quality of parent-child relationships (Papp, Cummings, & Goeke-Morey, 2005).

The chronic nature of asthma and the unpredictability of its exacerbations pose particular challenges to children and their families and thus hinder the adaptation of all family members (Rolland, 2004). Physical limitations and restrictions on daily and social activities, dependence on medication and healthcare services, absence from school and work, and sleep disturbances are a few of the effects of pediatric asthma on the everyday life of children and their parents (Dean et al., 2010; Schmier et al., 2007). A growing body of research has demonstrated that children with asthma have more compromised global health-related quality of life (HrQoL) than their healthy peers (e.g., Schmier et al., 2007; Van Gent et al., 2007) and lower physical domain sub-scores than children with other chronic health conditions (e.g., Austin, Smith, Risinger, & McNelis, 1994). Additionally, asthma has been linked to a higher risk of developing emotional and behavioral problems (e.g., Goldbeck, Koffmane, Lecheler, Thiessen, & Fegert, 2007; McQuaid, Kopel, & Nassau, 2001; Vila et al., 2003), even though most children do not present with clinically significant psychopathological symptoms (Barlow & Ellard, 2006).

Asthma severity has been addressed extensively in empirical research; however, the role of this variable on children's QoL (for a review, see Everhart & Fiese, 2009) and psychological problems (McQuaid et al., 2001) remains unclear. Some studies have reported decreased HrQoL among children with severe asthma (e.g., Sawyer et al., 2001), but other studies have failed to detect significant associations between asthma severity and children's QoL or emotional and behavioral symptoms (e.g., Goldbeck et al., 2007). These inconsistent findings highlight the limitations of clinical parameters for predicting patients' QoL (Juniper et al., 1999) and suggest possible interaction effects between clinical and psychosocial factors. For example, Patterson (2002) has suggested that when family members are exposed to increased stress, as in severe asthma, family organizational and communication patterns might improve adaptation by serving as coping strategies for withstanding and rebounding from adversity. For the parents of children with asthma, QoL impairments (e.g., Dean et al., 2010; Everhart, Fiese, & Smyth, 2008) and increased depression and anxiety prevalence (e.g., Brown et al., 2006) have been consistently linked to higher asthma severity indicators. In these studies, however, severity has been mainly reported by parents, and less is known about the role of severity as assessed through clinical parameters or expert opinion.

The rationale for the present study was based on evidence supporting the central but complex associations between family relationships and children's and parents' adaptation indicators, and on the transactional model of development that assumes a dynamic interplay between children and parents (Sameroff, 2009). The examination of the role of asthma severity on adaptation indicators was based on the hypothesis raised by Patterson (2002), according to which family relationships would be more important for family members' adaptation in more stressful circumstances. In the context of the present study, we considered "adaptation" within a positive theoretical framework, extending beyond the psychopathological conceptualization of the child and family responses to chronic illness and considering adaptation as a process that accounted for resiliency and variability on adaptation indicators (Harper, 1991). The children's and parents' adaptation was cross-sectionally evaluated through multiple indicators. We assessed children's internalizing and externalizing psychological problems and parents' psychological distress, including depression and anxiety symptoms, based on a more traditional research line pointing to these specific psychological functioning outcomes as potentially compromised in pediatric asthma patients and their parents. Following a more positive and recent trend that has emphasized the QoL as an important outcome criterion for assessing physical, emotional and social well-being and function in pediatric contexts (Bullinger, Schmidt, Petersen, & Ravens-Sieberer, 2006) we also included children's HrQoL and parents' QoL as adaptation indicators.

Within this conceptual framework, we sought to address some of the aforementioned gaps in the pediatric asthma literature by examining (a) the direct and indirect links between children's and parents' perceptions of family relationships and adaptation both separately (the within-subjects effects) and across family members (the cross-lagged effects); and (b) the moderating role of asthma severity on these associations. Three main hypotheses were formulated. First, we predicted positive associations between better family relationships and individual adaptation for both children and parents, separately. Second, we hypothesized that: (a) children's perception of more positive family relationships would be linked to parents' better adaptation both directly and indirectly through children's adaptation; and (b) parents' perception of more positive family relationships would be associated with children's better adaptation both directly and indirectly via parents' adaptation. Finally, we expected that these links within and across family members would be stronger in families in which a child had more severe asthma. We also assessed whether these links were moderated by children's age and gender but made no specific predictions on this issue.

## Method

### Participants

The sample comprised 257 dyads consisting of Portuguese children with asthma, users of Pediatric and Immunoallergology outpatient services of three Portuguese public hospitals, and one of their parents. The children (163 boys and 94 girls) were between 8 and 18 years old (*M* = 12.14; *SD* = 2.54) and had had a clinical diagnosis of asthma for at least one year (*M* = 7.54 years; *SD* = 3.98). Regarding the asthma severity as assessed by physicians, 144 children (56%) had intermittent asthma, 65 children (25.3%) had mild persistent asthma, 40 children (15.6%) had moderate persistent asthma, and 8 children (3.1%) had severe persistent asthma. Most of children were using medication (98.1%, *n* = 252). The parents' sample, which consisted of 221 mothers (86%) and 36 fathers (14%), included those parents who were assuming the primary caregiver role in the children's healthcare issues. The parents' ages ranged from 27 to 64 years (*M* = 41.11; *SD* = 5.71). The great majority of parents were married or were living with a partner (80.5%, *n* = 207), while 18.7% (*n* = 48) of families lived in a single-parent household. Most of the families had low (60.3%, *n* = 155) and middle (26.8%, *n* = 69) socio-economic status.

### Procedure

The present study was approved by the Ethics Committees of the following three Portuguese public hospitals: Coimbra University Hospitals, Coimbra Pediatric Hospital, and

Leiria Santo Andre Hospital. The participants were selected from the readily available cases, i.e., the children who had medical appointments in the aforementioned health institutions' outpatient services during the period between March 2010 and January 2012 (non-probabilistic convenience method). For inclusion in the sample, the children had to meet the following criteria: (1) be between 8 and 18 years old; (2) be diagnosed with asthma by a physician according to the International Classification of Diseases system (ICD-10); (3) have asthma for at least one year; (4) have no significant developmental delays, comorbidities with other chronic health conditions, or severe psychiatric disorders; and (5) be accompanied by a parent currently assuming the primary caregiver role. The children who met the aforementioned criteria were identified by the physicians, based on their medical file. A trained research assistant approached the children and their parents, while they were waiting for their medical appointments, and invited them to a separate room designated for research purposes in the health institution they attended. The study's aims and procedures were explained to all participants, and informed consent forms were requested from all of the parents and children older than 13 years; informal assents were obtained from the younger children. The children and parents who agreed to participate completed the protocols with the assistance of the assigned researcher, who helped the participants with difficulties in reading or understanding the item content and prevented the exchange of information between children and parents.

## Measures

### *Family relationships*

The children's and parents' perceptions of family relationships were measured as latent variables comprising two subscales – Cohesion and Expressiveness – from the relationship dimension of the Portuguese version of the Family Environment Scale (Moos & Moos, 1986; Portuguese version: Matos & Fontaine, 1992), as assessed by the children and parents, respectively. The Cohesion subscale (nine items) assessed the family members' perceptions of the degree of commitment, help and support that family members provided to each other, and the Expressiveness subscale (nine items) measured the extent to which family members were encouraged to express their feelings. Both subscales used a 6-point Likert scale ranging from 1 (*completely disagree*) to 6 (*completely agree*), with higher scores indicating better family relationships. The reliability and validity of these two subscales were demonstrated in the original validation studies, conducted with a heterogeneous sample consisting of children as young as 8 years, adolescents and adults (Moos & Moos, 1986). Additionally, studies with the Portuguese version of the Family Environment Scale have shown adequate reliability of the Cohesion and Expressiveness subscales for use in different age groups (e.g., Crespo, Carona, Silva, Canavarro, & Dattilio, 2011). The Cronbach's alpha values in the current sample exceeded .70 for all subscales, except for the Expressiveness subscale as reported by the children, and .80 for the latent variables (see Table 2).

*Children's adaptation*

Children's adaptation was considered a latent variable that consisted of three observed indicators as assessed by the children: generic HrQoL, generic HrQoL for chronic health conditions and psychological problems. Generic and chronic-generic HrQoL were respectively measured by the Portuguese self-reported versions of the KIDSCREEN-10 Index (Ravens-Sieberer et al., 2010; Portuguese version: Gaspar & Matos, 2008), a 10-item questionnaire assessing children's general subjective health and well-being, and of the DISABKIDS Chronic Generic Module (The DISABKIDS Group Europe, 2006; Portuguese version: Carona et al., 2013), a 37-item questionnaire assessing the impact of chronic conditions and treatments on children's QoL. Both questionnaires were answered using a 5-point Likert scale ranging from 1 (*never*) to 5 (*always*), with higher scores indicating better HrQoL. These two questionnaires were specifically designed and tested for use in children and adolescents aged between 8 and 18 years-old (Ravens-Sieberer et al., 2007). The Portuguese versions of the KIDSCREEN and DISABKIDS questionnaires were semantically and psychometrically validated in studies conducted with children and adolescents from the general population aged between 10 and 16 years (Gaspar & Matos, 2008) and with children and adolescents with asthma or epilepsy aged between 8 and 18 years (Carona et al., 2013), respectively.

Psychological problems were measured with the total Difficulties score of the Portuguese self-rated version of the Strengths and Difficulties Questionnaire [SDQ] (Goodman, 2001; Portuguese version: Fleitlich, Loureiro, Fonseca, & Gaspar, 2005). This scale included the assessment of emotional symptoms, conduct problems, hyperactivity/inattention and peer relationship problems, based on 20 items that used a Likert-type response scale with three options (*not true*, *somewhat true*, or *certainly true*), with higher values indicating more psychological problems. The self-rated version of the SDQ was originally developed for use with children aged between 11 and 16 years-old, depending on their cognitive abilities and educational level (Goodman, 2001). However, the Portuguese self-rated version has presented good psychometric properties in samples of children as young as 8 years-old (e.g., Santos, Crespo, Silva, & Canavarro, 2012).

The Cronbach's alpha in the current sample was .94 for the latent variable and ranged from .76 (psychological problems) to .92 (chronic-generic HrQoL) for the observed indicators (see Table 2).

### *Parents' adaptation*

Parents' adaptation was a latent variable composed of three observed indicators, as assessed by the parents: QoL, which was measured by the Portuguese version of the EUROHISQOL-8 (Schmidt, Mühlan, & Power, 2006; Portuguese version: Pereira, Melo, Gameiro, & Canavarro, 2011), psychological distress and psychological well-being, both of which were measured by the Portuguese brief version of the Mental Health Inventory [MHI-5] (Veit & Ware, 1983; Portuguese version: Pais-Ribeiro, 2001). The EUROHIS-QOL 8-item Index provided an overall QoL score that evaluated the physical, psychological, social and environmental QoL domains using eight items scored on a 5-point Likert scale ranging from 1 (*not at all/ very dissatisfied*) to 5 (*completely/very satisfied*), with higher scores indicating better QoL.

The MHI-5 consisted of five items that focused on the psychological symptoms of depression, anxiety, loss of emotional and behavioral control, and positive affect. These items were clustered in two dimensions – Distress (three items) and Well-being (two items) and were measured using a Likert-type response scale with six responses ranging from 1 (*none of the time*) to 6 (*all of the time*).

In the current sample, Cronbach's alpha was .89 for the latent variable and ranged from .69 (psychological well-being) to .87 (psychological distress) for the observed indicators (see Table 2).

### *Asthma severity*

Following the Global Initiative for Asthma [GINA] guidelines (2008), the asthma severity was classified by physicians into four categories: intermittent, mild persistent, moderate persistent and severe persistent. This classification was based on the expert opinion, considering the level of symptoms, airflow limitation and lung function variability. Due to the heterogeneous severity level distribution observed in our sample, this variable was dichotomized and dummy coded (0 – intermittent, *n* = 144; 1 – persistent [mild, moderate, and severe], *n* = 113).

### *Clinical and socio-demographic characteristics*

Other relevant clinical information (e.g., disease length and medication) and socio-demographic data were collected from the parents. The socio-economic level was determined using a classification system for the Portuguese context, based on parents' job and educational level (Simões, 1994). For the group comparison analyses, children were divided into two age groups based on the DISABKIDS Group Europe's (2006) approach: children (8-12 years old) and adolescents (13-18 years old). For remaining analyses, we adopted the term children when referring to the pediatric sample, which included both age groups.

## Statistical analyses

The statistical analyses were performed with the Statistical Package for the Social Sciences v. 17.0 (SPSS Inc., Chicago, IL). Missing data, that were random and constituted less than 5% of the values, were handled by replacement with the individual mean score for each variable, excluding clinical and demographic data. For all observed variables, descriptive statistic were calculated and differences between asthma severity groups (intermittent *vs.* persistent) were tested with multivariate analyses of covariance (MANCOVA). These analyses were controlled for age and gender, by including them as covariates. Effect-size measures (partial Eta squared) were presented for the comparison analyses, considering $\eta_p^2 \geq .01$ as small effects, $\eta_p^2 \geq .06$ as medium effects and $\eta_p^2 \geq .14$ as large effects (Cohen, 1988).

The structural equation modeling (SEM) was implemented with the Analysis of Moments Structures (AMOS, v.18). The models' goodness of fit was assessed in two steps (the measurement model and the structural model) using the reference values for the main fit indexes: maximum-likelihood $\chi^2$ *p*-value ≥ .05, comparative fit index (CFI) ≥ .95 and root mean square error of approximation (RMSEA) ≤ .06 (Hu & Bentler, 1999). In the first step, to analyze the appropriateness of the multi-dimensionality of the theoretical constructs, we conducted a confirmatory factor analysis (CFA) testing the hypothesized links between latent variables (family relationships as reported by the children, family relationships as reported by the parents, children's adaptation and parents' adaptation) and their observed indicators (Byrne, 2010). In the second step, we constructed a structural model to test the direct and indirect effects of children's and parents' perceptions of family relationships on adaptation, separately (within-subjects) and across participants (cross-lagged effects). Following recent recommendations (Preacher & Hayes, 2008; Williams & MacKinnon, 2008), the statistical significance of the indirect effects was estimated using bootstrap resampling procedures with 2,000 samples [95% bias-corrected bootstrap confidence interval (BC 95% CI)]. Multi-group analyses were conducted to determine whether the parameters tested in the model were valid for different groups (children's age, gender and asthma severity groups). We used the Chi square difference method to compare the unconstrained measurement weights model with the structural weights model in which the factor loadings and variances/covariances were fixed and equal across groups (Byrne, 2010). Post-hoc *Z*-tests were performed to examine which structural coefficients significantly differed between the groups.

Finally, to further investigate the paths that significantly differed between the groups, we conducted separate moderation analyses for each adaptation indicator (children's generic HrQoL, chronic-generic HrQoL and psychological problems). We performed multiple regression analyses by entering the centered independent variable (family relationships as assessed by the children), the categorical moderator (asthma severity levels: intermittent *vs.*

persistent) and the interaction term (family relationships x asthma severity) into the equation, in sequential steps. The significant interaction effects were plotted using Mod-Graph (Jose, 2008), and the statistical significance of each regression line was analyzed with post hoc simple slope computations.

# Results

## Descriptive statistics and multivariate analyses of covariance

Descriptive statistics for all observed variables are presented in Table 1. For children's adaptation indicators, there was a statistically significant multivariate effect according to asthma severity groups (intermittent *vs*. persistent), controlling for age and gender, Wilks' Lambda = .97, $F_{(3, 251)} = 2.85$, $p = .04$, $\eta_p^2 = .03$. The univariate analyses, which are presented in Table 1, showed that children with intermittent asthma reported better chronic-generic HrQoL and fewer psychological problems than children with persistent asthma. While controlling for age and gender, no multivariate effects of asthma severity groups were found for parent's adaptation indicators, Wilks' Lambda = .99, $F_{(3, 251)} = 0.43$, $p = .73$, $\eta_p^2 = .01$, neither for family relationships as assessed by the children, Wilks' Lambda = .99, $F_{(2, 252)} = 0.68$, $p = .51$, $\eta_p^2 = .01$, or as assessed by the parents, Wilks' Lambda = .99, $F_{(2, 252)} = 1.23$, $p = .29$, $\eta_p^2 = .01$.

**Table 1** | Descriptive analyses and differences in children's and parents' perceptions of family relationships and adaptation indicators between asthma severity groups

| | Intermittent asthma (*n* = 144) | Persistent asthma (*n* = 113) | Asthma severity effects | | |
|---|---|---|---|---|---|
| | *M* (*SD*) | *M* (*SD*) | $F_{(1, 253)}$ | *p* | $\eta_p^2$ |
| ***Children*** | | | | | |
| Family relationships | | | | | |
| Cohesion | 4.96 (0.85) | 4.94 (0.90) | 0.03 | .87 | .00 |
| Expressiveness | 4.52 (0.71) | 4.43 (0.69) | 0.92 | .34 | .00 |
| Adaptation indicators | | | | | |
| Generic HrQoL | 4.29 (0.52) | 4.19 (0.62) | 2.01 | .16 | .01 |
| Chronic-generic HrQoL | 4.32 (0.43) | 4.15 (0.54) | 7.70 | .01 | .03 |
| Psychological problems | 0.50 (0.25) | 0.57 (0.27) | 3.79 | .05 | .02 |
| ***Parents*** | | | | | |
| Family relationships | | | | | |
| Cohesion | 4.84 (0.77) | 4.89 (0.75) | 0.29 | .59 | .00 |
| Expressiveness | 4.58 (0.72) | 4.71 (0.71) | 1.95 | .16 | .01 |
| Adaptation indicators | | | | | |
| QoL | 3.70 (0.56) | 3.77 (0.53) | 1.15 | .29 | .01 |
| Psychological well-being | 3.85 (1.08) | 3.87 (1.12) | 0.04 | .84 | .00 |
| Psychological distress | 2.64 (0.90) | 2.59 (1.04) | 0.20 | .66 | .00 |

## The measurement model

The measurement model (CFA) with the four latent variables (family relationships as reported by the children and parents and children's and parents' adaptation) had a very good fit, with $\chi^2_{(29)} = 35.60$, $p = .19$; CFI = .99 and RMSEA = .03, and all of the observed indicators showed factorial validity with factor loadings above .50 and statistically significant (see Table 2). The squared multiple correlations between each observed variable and all the other variables ($R_{smc}^2$) were lower than .90 and the tolerance values ($1 - R_{smc}^2$) were higher than .10 (see Table 2), indicating that each one of the observed variables explained a substantial proportion of the total standardized variance, and thus the model was not limited by multicollinearity problems (Kline, 2005). Except for expressiveness reported by the children, the Cronbach's alphas were adequate for the observed indicators and good (above .80) for all four latent variables (see Table 2). As shown in Table 2, the family relationships were moderately to strongly associated with adaptation, and these associations were significant for both children and parents separately, and also across family members. The asthma severity was negatively correlated with the children's chronic-generic HrQoL.

## The structural equation model

A structural model was constructed to examine the direct and indirect links between family relationships and adaptation, for children and parents separately (within-subjects) and across participants (cross-lagged effects). Following the trimming procedures described by Kline (2005), the non-significant paths were removed. The final model, which is depicted in Figure 1, had a very good fit, with $\chi^2_{(31)} = 38.24$, $p = .17$; CFI = .99 and RMSEA = .03, and explained 46.7% of the variability in children's adaptation, and 29.7% of the variability in parents' adaptation. Significant indirect effects were found between family relationships and adaptation across family members. The standardized indirect effect of family relationships as reported by children on parents' adaptation, via children's adaptation, was .10 ($p = .002$; BC 95% CI = .04/ .17), and the standardized indirect effect of family relationships as reported by parents on children's adaptation, via parents' adaptation, was .05 ($p = .002$; BC 95% CI = .02/ .10).

The multi-group analyses confirmed that the model was valid for the children's age and gender groups. However, the model significantly differed for the two asthma severity groups (intermittent and persistent), with $\Delta\chi^2_{(3)} = 10.21$, $p = .02$. Only the coefficient of the regression path between the children's perception of family relationships and children's adaptation was significantly different ($Z = -2.08$, $p < .05$) in the post hoc $Z$-tests. A stronger regression weight was observed in the persistent asthma group ($B = .45$, $SE = .07$) than in the intermittent asthma group ($B = .26$, $SE = .06$).

**Table 2** | Matrix of inter-correlations (Pearson), factor loadings and Cronbach's alphas for observed and latent variables

| | Children | | | | | | Parents | | | | | | | $R_{smc}^2$ | Tolerance | Factor | α |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 | 2 | B | 3 | 4 | 5 | C | 6 | 7 | D | 8 | 9 | 10 | | (1- $R_{smc}^2$) | loadings | |
| ***Children*** | | | | | | | | | | | | | | | | | |
| A. Family relationships | | | **.64**$^{**}$ | | | | **.47**$^{**}$ | | | **.29**$^{**}$ | | | | | | | **.84** |
| 1. Cohesion | | | | | | | | | | | | | | .89 | .11 | .95$^{**}$ | .85 |
| 2. Expressiveness | .68$^{**}$ | | | | | | | | | | | | | .52 | .48 | .72$^{**}$ | .56 |
| B. Adaptation | | | | | | | **.44**$^{**}$ | | | **.41**$^{**}$ | | | | | | | **.94** $^{a}$ |
| 3. Generic HrQoL | .52$^{**}$ | .40$^{**}$ | | | | | | | | | | | | .65 | .35 | .81$^{**}$ | .81 |
| 4. Chronic-generic HrQoL | .46$^{**}$ | .33$^{**}$ | | .65$^{**}$ | | | | | | | | | | .64 | .36 | .80$^{**}$ | .92 |
| 5. Psychological problems | -.41$^{**}$ | -.30$^{**}$ | | -.52$^{**}$ | -.53$^{**}$ | | | | | | | | | .44 | .57 | -.66$^{**}$ | .76 |
| ***Parents*** | | | | | | | | | | | | | | | | | |
| C. Family relationships | | | | | | | | | | **.51**$^{**}$ | | | | | | | **.87** |
| 6. Cohesion | .37$^{**}$ | .30$^{**}$ | | .30$^{**}$ | .31$^{**}$ | -.27$^{**}$ | | | | | | | | .76 | .24 | .87$^{**}$ | .81 |
| 7. Expressiveness | .39$^{**}$ | .33$^{**}$ | | .28$^{**}$ | .28$^{**}$ | -.28$^{**}$ | | .73$^{**}$ | | | | | | .71 | .29 | .84$^{**}$ | .73 |
| D. Adaptation | | | | | | | | | | | | | | | | | **.89** $^{a}$ |
| 8. QoL | .25$^{**}$ | .16$^{**}$ | | .22$^{**}$ | .28$^{**}$ | -.26$^{**}$ | | .36$^{**}$ | .30$^{**}$ | | | | | .46 | .54 | .68$^{**}$ | .84 |
| 9. Psychological well-being | .23$^{**}$ | .20$^{**}$ | | .22$^{**}$ | .26$^{**}$ | -.22$^{**}$ | | .38$^{**}$ | .35$^{**}$ | | .51$^{**}$ | | | .62 | .38 | .79$^{**}$ | .69 |
| 10. Psychological distress | -.21$^{**}$ | -.12 | | -.18$^{**}$ | -.36$^{**}$ | .24$^{**}$ | | -.35$^{**}$ | -.33$^{**}$ | | -.59$^{**}$ | -.68$^{**}$ | | .74 | .26 | -.86$^{**}$ | .87 |
| Asthma severity $^{b}$ | -.01 | -.06 | | -.09 | -.17$^{**}$ | .12 | | .03 | .09 | | .07 | .01 | -.03 | | | | |

Note. Inter-correlations and Cronbach's alphas for latent variables are shown in boldface.

$^{a}$ In order to estimate Cronbach's alpha of the latent variables, the negative dimensions (children's psychological problems and parents' psychological distress) scores were reversed, so that all items were in same direction and positively correlated. $^{b}$ Dummy-coded variable (0 – intermittent asthma; 1– persistent asthma).

$^{**}$ $p \leq .01$, two-tailed; $^{*}$ $p \leq .05$, two-tailed.

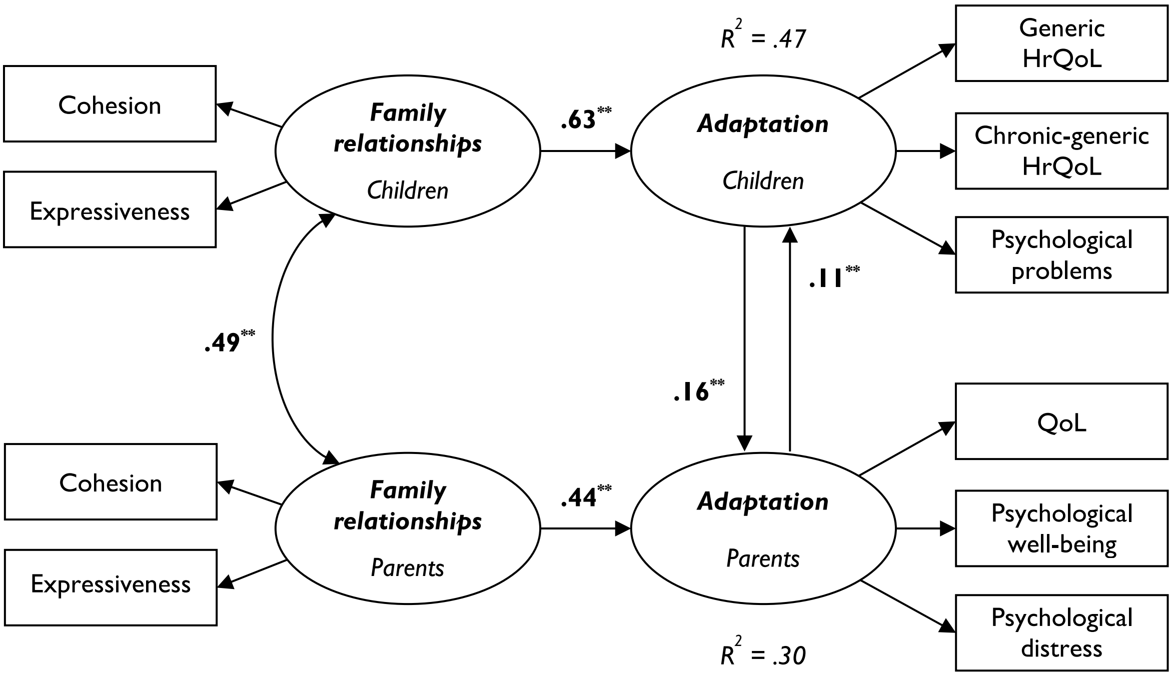

**Figure 1** | SEM testing the direct and indirect effects of family relationships on children's and parents' adaptation

*Note*. Non-significant paths are not represented (trimmed model). Bold figures represent standardized coefficients; italic non-bold figures represent Pearson correlation coefficients. For simplicity, measurement error terms are not shown. $^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

## Moderation analyses

To further investigate the role of asthma severity on the link between family relationships as reported by children and children's adaptation, we separately tested the moderating effect of asthma severity on the associations between the children's perception of family relationships and each of the three indicators of children's adaptation (generic and chronic-generic HrQoL and psychological problems). The interaction between asthma severity and family relationships was significantly associated with generic HrQoL ($b$ = .19; $t$ = 2.63, $p$ < .01) and with chronic-generic HrQoL ($b$ = .20; $t$ = 2.66, $p$ < .01) (see Figure 2) but was only marginally associated with psychological problems ($b$ = -.13; $t$ = -1.68, $p$ = .09).

The post hoc simple slope analyses revealed that family relationships were more strongly associated with HrQoL for the children with persistent asthma ($b$ = .52; $t$ = 8.22, $p$ < .001 for generic HrQoL, and $b$ = .40; $t$ = 6.32, $p$ < .001 for chronic-generic HrQoL) than for the children with intermittent asthma ($b$ = .30; $t$ = 5.46, $p$ < .001 for generic HrQoL, and $b$ = .20; $t$ = 4.52, $p$ < .001 for chronic-generic HrQoL).

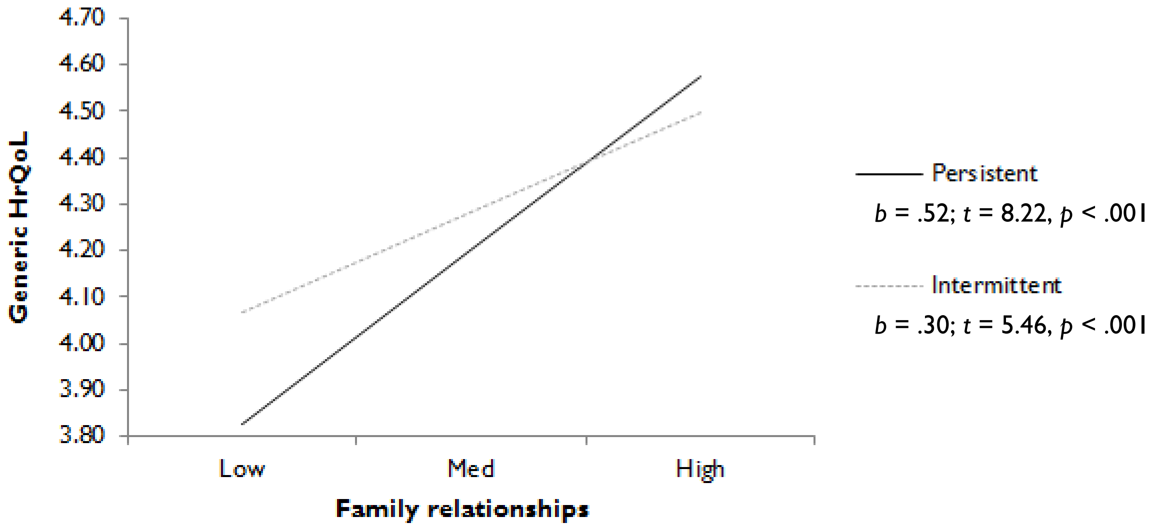

**Figure 2 |** The moderating effect of asthma severity on the associations between children's perception of family relationships and children's generic HrQoL

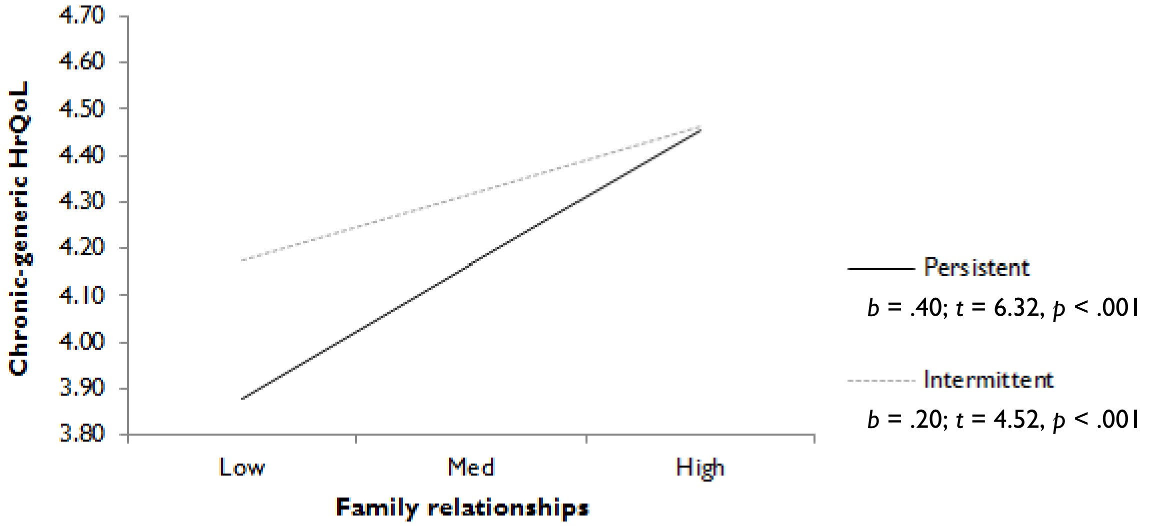

**Figure 3 |** The moderating effect of asthma severity on the associations between children's perception of family relationships and children's chronic-generic HrQoL

## Discussion

This study described an examination, via SEM, of the direct and indirect links between children's and parents' perceptions of family relationships and adaptation, within and across family members. The model had a very good fit, which empirically supported the relevance of a transactional approach to understanding the adaptation of children with asthma and their parents. Three main findings should be considered. First, positive family relationships, as assessed by the children, were directly associated with children's better adaptation and also positive family relationships, as assessed by the parents, were directly associated with parents' better adaptation. Second, the links between family relationships and adaptation were also verified across family members, although only indirectly. Specifically, the children's perception of more positive family relationships were linked to parents' better adaptation, via children's own adaptation; and the parents' perception of more positive family relationships were linked to children's better adaptation, through a positive association with parents' adaptation. Finally, asthma severity moderated the positive associations between the children's perception of family relationships and generic and chronic-generic HrQoL, with stronger associations found for the children with persistent asthma.

The first set of results from the present study supports previous research on the relevance of family relationships for understanding the adaptation of children with asthma and their parents (e.g., Annett et al., 2010; Wood et al., 2008), but also clarifies how family relationships contribute to explaining the adaptation variability. As stated in our first hypothesis, better family relationships, characterized by higher levels of cohesion and expressiveness as assessed by the children and parents, were positively associated with children's and parents' adaptation, respectively. Differently from the enmeshment, which is associated with exacerbated psychosomatic asthma symptoms (Minuchin et al., 1975), family cohesion (emotional bounding among family members, that is balanced between disengagement and enmeshment) has been identified as a facilitator of family functioning in general (Olson & Gorall, 2003) and of the psychological adjustment of children with asthma in particular (Reichenberg & Broberg, 2005). Family communication has been conceptualized as a facilitatory process that regulates family functioning (Olson & Gorall, 2003), promoting families' ability to adapt through its affective function (i.e., sharing feelings and emotional support) and its instrumental function, which includes role assignments, decision making and conflict resolution (Patterson, 2002). In the pediatric asthma context, a family environment perceived as a safe haven for openly express feelings, opinions and concerns could be significantly associated with children's and parents' adaptation, by promoting emotional regulation and decreasing family conflict, thus minimizing emotional asthma triggers (Minuchin et al., 1975; Wood et al., 2007). Such a family environment is also likely to facilitate the beneficial effect of well-organized daily family routines on the family members' adaptation (Santos et al., 2012), and to buffer the negative impact of the burden associated with asthma management (Crespo et al., 2011; Fiese et al., 2008).

Beyond the direct links with both children's and parents' adaptation, children's and parents' perceptions of more positive family relationships were also associated with better adaptation across family members, however only indirectly, which partially confirmed our second hypothesis. In a previous study (Crespo et al., 2011), a significant association was observed between the parents' perception of family environment and the QoL of children with asthma. Similarly, supportive family relationships as assessed by the parents and parental psychological functioning have been widely identified in the pediatric literature as important predictors of children's adaptation outcomes (Drotar, 1997). The present study is unique in its examination of the transactional links between children and parents and the indirect pathways by which they occur. The bidirectional links between children's and parents' adaptation have barely been investigated in the particular context provided by pediatric asthma, although they are well established in the normative development literature (Sameroff, 2009) and there is growing recognition of the similarities between the functioning of families who have a child with a chronic health condition and other families (Fiese, 2008; Kazak, 1989). The associations between mother-child interaction patterns and children's QoL and anxiety found by Fiese et al. (2008) and the positive bidirectional link between children's and mothers' QoL presented by Marsac et al. (2007) are important evidence of the interdependence of family members' adaptation.

A second original contribution of the present study is the identification of the clinical conditions in which family relationships can be more relevant to adaptation. The comparative analyses according to the asthma severity levels presented no significant differences in family relationships, either reported by the children or reported by the parents, but showed that children with persistent asthma had poorer chronic-generic HrQoL and more psychological problems than children with intermittent asthma. Additionally, asthma severity moderated the association between family relationships as assessed by the children and children's HrQoL, with stronger associations found for children with persistent asthma. These results suggest that children's HrQoL may be better explained by the interaction between clinical and psychosocial variables rather than single clinical indicators, thus partially confirming our third hypothesis. Asthma's clinical characteristics (e.g., severity) impose different physical and psychosocial demands on children (Rolland, 2004); the means by which these demands are fulfilled within a specific family environment may influence children's adaptation. In contrast to previous studies, which have demonstrated that asthma severity and caregiving burden are the risk factors with most impact on parents' QoL (e.g., Everhart et al., 2008), for the participants in the present research, asthma severity had no effect on parents' adaptation indicators. These results may be due to the low percentage of children with severe asthma in our sample, which were included in the persistent asthma group. The absence of differences in parent's adaptation indicators regarding asthma severity levels could also be explained by the episodic nature of asthma and the uncertainty associated with asthma exacerbations. To improve asthma symptoms control, parents' concerns and involvement in caregiving tasks, including routine healthcare services attendance, medication management and avoiding environmental triggers, are kept unchanged, which may be linked to parents' decreased QoL and psychological functioning regardless of asthma severity.

Children's developmental stages and family life-cycle phases can affect how chronic health conditions and family resources are perceived and managed by family members (Kazak, 1989; Rolland, 2004), yet our model did not change for children's age and gender. These findings suggest that, when family relationships are perceived as adequately balancing the different needs of autonomy and emotional sharing that are intrinsic to children's developmental phases (Collins & Laursen, 2004), families provide a safe haven for their members, facilitating individual adaptation.

The interpretation of our findings should be read with caution, considering some limitations in the study design and procedures. The main limitation of this study is its cross-sectional design. Using SEM to test indirect effects with cross-sectional data assumed that the reciprocal causal processes had already occurred and that the system was at an equilibrium point (Kline, 2005). The latter assumption was addressed in our study by including children who had asthma for at least one year, thereby minimizing the effects of acute stress responses to recent diagnoses and enabling families to stabilize their functioning in the novel context created by pediatric asthma. However, this approach can only provide a snapshot of the ongoing dynamic processes between parents and children (Sameroff, 2009). Although the directional paths addressed in our study have been hypothesized according to the theoretical and empirical literature, the cross-sectional design excludes inferring causality among the variables. Further longitudinal research should be undertaken to clarify the direction of these associations and to examine whether individual and family developmental changes influence the parent-child interaction patterns and the adaptation process over time. Our study was also limited by the non-probabilistic sample collection method and the heterogeneous distribution of children by asthma severity levels. Although consistent with the distribution of asthma severity levels typically observed in the Portuguese pediatric population (Gaspar, Almeida, & Nunes, 2006), the low frequency of children with severe asthma required the variable to be dichotomized and increased intragroup variability. Additionally, the classification of asthma severity based on the expert opinion rather than on objective measures, although indicated for cross-sectional research purposes (GINA, 2008), should be acknowledged as a study's limitation. The specificity of our sample, namely the inclusion of families mostly from low and middle socio-economic background, a characteristic of the users of public health services in Portugal, might restrict the generalizability of the results to other contexts.

Despite these limitations, our study addressed some important gaps in the pediatric asthma literature. Assessing the perceptions of two family members regarding the relationships among the whole family provided further insight into the interactions among family members (Kazak, 1997). The importance of multiple informants extends to the children's self-reported adaptation indicators and the clinicians' assessments of asthma severity. Both of these sources can enhance parent-reported data, which is likely to be biased by parental perceptions and expectations (Everhart & Fiese, 2009). Using SEM allowed analyzing the indirect and conditional effects, thereby contributing to understanding the processes through which family relationships are linked to children's and parents' adaptation and to examining under which clinical and developmental conditions these associations occur. Moreover, assessing the children's and parents' adaptation as latent variables allowed including general and specific indicators of adaptation, thus confirming the important role of family variables on the physical, psychological and social domains of subjective health and functioning.

Identifying the central role of family relationships for explaining the adaptation of children with asthma and their parents reinforced the need to include multidisciplinary interventions in pediatric healthcare. In addition to medical treatments aimed at controlling asthma symptoms and improving physical functioning, including intervention strategies designed to promote positive family factors would help enhance children's and parents' quality of life and psychological functioning (Fiese, 1997; Sawyer et al., 2001). Family communication and interaction patterns are specific potential targets that should be addressed by interventions aimed at strengthening a family's ability to cope with pediatric asthma demands, particularly in severe cases (Patterson, 2002).

Additionally, the reciprocal paths between children's and parents' adaptation have important clinical implications, given that less positive family relationships may lead to the deterioration of family members' adaptation over time. Interventions focused on promoting a sense of belonging to the family and communication skills may be an effective method of promoting both individual and family-wide adaptation. These interventions should target all family members to maximize their efficacy (Kazak, 1989; Minuchin et al., 1975). However, our results suggest that, when involving the entire family is impossible or undesirable, individual interventions focused on the children's or parents' perceptions of family relationships would also be effective at improving individual and family-wide adaptation.

Finally, our results identified children with more severe asthma as the group that would benefit most from family-based psychological interventions. Allocating psychological interventions to children and families within healthcare systems should be based on comprehensive evaluations of asthma severity levels and family relationships.

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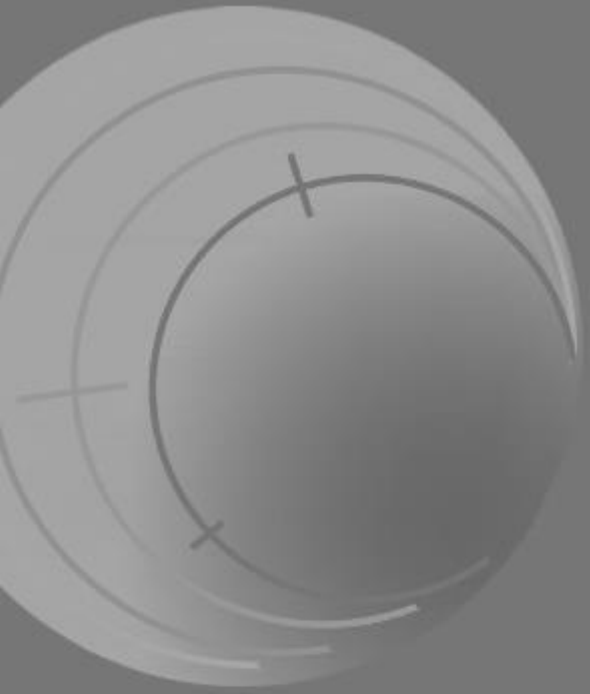


# Chapter IV

## General Discussion

In the final chapter of the present dissertation, a brief summary and discussion of the main findings from our research work will be presented, in compliance with the general research questions and specific objectives outlined for each research phase. This chapter intends to portray an integrative overview of the main results, without overlapping with their detailed discussion as presented in the appropriate section of the empirical studies that comprise the previous chapter. Overall, the results will be theoretically integrated within a risk-resistance framework, as proposed by the conceptual models of individuals' and caregivers' adaptation to pediatric chronic health conditions that broadly guided this research project (Raina et al., 2004; Wallander et al., 1989a), taking into account a transactional approach to child development (Fiese & Sameroff, 1989; Sameroff, 2009). Afterward, the core methodological strengths and limitations will be critically commented. Finally, the contributions of our findings will be discussed in terms of evidence-based guidelines for future research and clinical practice.

## 1. SUMMARY AND GENERAL DISCUSSION OF THE MAIN FINDINGS

The first aim of our research project was to characterize the QoL of children/adolescents with asthma and their parents in relation to their peers without asthma. For that purpose, we performed a meta-analytic review of quantitative studies, published in the English language between 1994 and 2013, that directly compared the overall QoL and/or QoL core domains (physical, psychological, social and school functioning) of 7-18 year-old asthma patients and/or their parents to community or healthy controls. The most important findings emerging from this study can be summarized as follows:

- Children/adolescents with asthma were at a greater risk for QoL impairments, in general, and for decreased physical, psychological and social functioning (but not school functioning), compared to their peers without asthma.

- Despite the scarcity of comparative research on parents' QoL, the few existing studies consistently indicated QoL impairments in the physical domain among parents of pediatric asthma patients, compared to parents of children/adolescents without asthma.

- High levels of heterogeneity were observed across studies, which were partly explained by type of informant and health status of the controls: larger QoL impairments were described in studies that relied on parent-reports and that included children/adolescents with no history of medical conditions as controls.

The second research aim was to clarify key methodological issues in the assessment of QoL outcomes and psychological problems in pediatric asthma patients. To address this objective, three empirical studies were conducted: a preliminary study describing the cross-cultural adaptation procedures and the semantic validation of the Portuguese self- and proxy-report versions of the DISABKIDS asthma-specific questionnaire; the empirical study I focusing on the psychometric adequacy of the DAsM questionnaire for assessing HrQoL in Portuguese children/adolescents with asthma, within a modular system comprising generic, chronic-generic and disease-specific measures; and the empirical study II examining the levels of (dis)agreement between children/adolescents' and parents' reports of QoL and psychological problems, and the contribution of socio-demographic, clinical and family-related variables to explain the extent (i.e., the degree to which children/adolescents and parents disagreed) and the direction of child-parent discrepancies (i.e., which family member was more prone to underrate the adaptation outcomes). The main results from these studies were:

- After ensuring the comprehensibility, relevance and adequacy of the items and response scales of the DAsM questionnaire in the Portuguese cultural context, the instrument revealed adequate reliability and validity for HrQoL assessment in both 8-12 year-old children and 13-18 year-old adolescents, reported by the patients themselves and their parents.

- The DAsM scores were moderately and strongly correlated with the generic KIDSCREEN and chronic-generic DISABKIDS scores, respectively; in addition, the three levels of QoL measurement presented different sensitivity to asthma clinical characteristics: significant differences between asthma severity levels as assessed by physicians were detected by both DISABKIDS questionnaires (but not by the generic module) and the associations between HrQoL and patients/parents' perceptions of asthma symptoms were stronger for the asthma-specific measure.

- Child-parent agreement on pediatric adaptation outcomes assessment was poor to moderate, with parents being more prone to report worse QoL outcomes and more psychological problems than children/adolescents.

- The extent and direction of child-parent disagreement were better explained by family-related factors than by socio-demographic and clinical variables: greater caregiving burden was associated with increased discrepancies in both directions (i.e., parents' under and overratings of pediatric outcomes), while children's and parents' underestimations of pediatric adaptation outcomes were associated with the concomitant perception of less positive family relationships.

The identification of QoL impairments in both pediatric asthma patients and their parents, along with the high levels of between- and within-studies heterogeneity, brought up the question of why some families adapt better to pediatric asthma than others. We sought to address this issue by examining risk and resistance factors and the processes through which they contribute to explain the differentiated adaptation outcomes in this population. The four empirical studies that were conducted yielded the following results:

- Significant differences were found in children/adolescents' adaptation outcomes according to asthma clinical characteristics: patients with intermittent and/or controlled asthma reported better QoL and fewer psychological problems than the patients in persistent and non-controlled asthma groups.

- The parents of younger children and/or with low SES reported worse QoL and more caregiving burden than the parents of adolescents and/or with medium/high SES. Higher levels of caregiving uplifts were also found among parents of younger children. In addition, parents of children/adolescents with intermittent asthma experienced greater caregiving burden compared to parents of children/adolescents with persistent asthma, but only on the relationship dimension of burden.

- Higher levels of caregiving burden were indirectly associated with worse QoL in parents, via less use of acceptance and greater use of denial coping strategies. Similarly, the parents' experience of more caregiving uplifts was indirectly linked to better QoL, via positive reframing coping. In addition, caregiving uplifts moderated the deleterious effect of relationship burden on parents' QoL.

- For children/adolescents, direct negative and positive effects of relationship burden and caregiving uplifts, respectively, were found on their QoL outcomes.

- Positive perceptions of the family relationships were directly associated with better adaptation outcomes for both family members. In turn, children/adolescents' adaptation outcomes were positively linked to their parents' adaptation, and vice-versa (cross-lagged indirect effects).

- Parents' adaptation processes were invariant across asthma severity, children's age and SES groups. Conversely, the positive link between the children/adolescents' perception of the family relationships and their adaptation outcomes was moderated by asthma severity, with stronger associations for the persistent asthma group.

### 1.1. Pediatric asthma as a developmental context marked by significant QoL impairments in children/adolescents and their parents

In 2001, a meta-analysis established that pediatric asthma patients are at greater risk for developing psychological problems, particularly anxious and depressive symptoms, in relation to their healthy peers (McQuaid et al., 2001). Nonetheless, the growing recognition of QoL as a key outcome in healthcare contexts has produced, in the past 20 years, a number of scattered studies yielding inconsistent findings. By summarizing the results of the existing research comparing the QoL of children/adolescents with asthma and their parents with age-matched controls, our meta-analytic review showed that pediatric asthma patients were, indeed, at greater risk for decreased QoL than their peers without asthma, particularly in the physical, psychological and social domains. Similarly, their parents also presented diminished QoL, but only in the physical domain.

Despite the high heterogeneity across studies (which had been detected in our preliminary literature review and was, in fact, the main motivation for this meta-analytic review), the ascertainment of the magnitude of QoL impairments among pediatric asthma patients provided an important contribution for the current understanding of the burden of asthma in children/adolescents' psychosocial functioning, thus extending beyond the traditional and unsatisfactory indicators of asthma morbidity (Bullinger et al., 2006; Varni et al., 2007). The identification of the most affected domains of functioning has also important implications to outline multidisciplinary interventions and to evaluate the efficacy of medical treatments and psychosocial interventions in pediatric healthcare settings. In relation to the methodological trends in the reviewed studies, we noticed an unwarranted proliferation of QoL instruments specifically designed for children/adolescents, with some of them disregarding the WHO recommendations for pediatric QoL assessment (WHO, 1993) or lacking adequate psychometric studies, which limits the conclusions drawn from the pooled results. In addition, research on pediatric QoL has been marked by the preferred use of patient-report measures, which is consistent with a conservative interpretation of the QoL construct, as defined by the WHOQOL Group (1994). However, the few studies that relied on parent-reports as proxies identified larger impairments in children/adolescents' psychosocial and social functioning, reinforcing the value of parents' perceptions for the detection of psychosocial and functional disabilities in pediatric patients (Varni et al., 2005).

Regarding the QoL of parents of pediatric asthma patients, we observed a surprising scarcity of comparative studies with parents of healthy children/adolescents, despite the great amount of theoretical literature and empirical evidence advocating that pediatric asthma also exerts a substantial burden in the entire family and particularly in the parents who assume the role of primary caregivers. The decreased physical functioning among parents was not surprising and may reflect the loss of sleep quantity and quality, the fatigue associated with the additional caregiving demands, the interference of asthma management practices in their normal daily routine and the loss of work capacity/productivity (Fiese et al., 2008; Laforest et al., 2004; Schmier et al., 2007). In addition, asthma has an important heritable component, with an overall prevalence above 13% in first-degree relatives of pediatric asthma patients (Sibbald, Horn, Brain, & Gregg, 1980), which may contribute to explain the diminished physical functioning among parents. We also expected that the burden of pediatric asthma in parents would impact their psychosocial functioning (Sennhauser et al., 2005); however, the high between-studies heterogeneity limited the drawing of robust conclusions on this regard.

This systematic literature review inspired the outlining of objectives and methodological options for our subsequent empirical studies. First, the observation of dissimilar magnitudes of QoL impairments, depending on the QoL domains being assessed, brought up the question of whether the impact of a chronic health condition and its treatments would be better detected by asthma-specific measures. Moreover, the limitations inherent to the use of different instruments for QoL assessment across studies highlighted the importance of adapting existing reliable and valid measures, rather than developing new ones, to facilitate future meta-analytic studies and cross-cultural comparisons. Second, the reduced number of studies using parent-report measures and the high between-studies heterogeneity, which was partly explained by the health status of controls and type of informants, stressed the need of examining the levels of parent-child agreement on outcomes reports, and the clinical, socio-demographic and family-related factors associated with the extent and direction of the discrepancies. Finally, the great within-study variability (i.e., the broad confidence-intervals associated with differences in QoL mean scores between asthma and control groups) motivated us to move from the mere outcomes description to the study of risk and resistance factors underpinning the differentiated adaptation processes and outcomes in children/adolescents with asthma and their parents.

### 1.2. A comprehensive assessment of pediatric adaptation outcomes: The DISABKIDS project within the Portuguese context

The present study benefited greatly from its articulation with *The DISABKIDS Project in Portugal: Validation of the Portuguese versions of the DISABKIDS instruments – quality of life questionnaires for children and adolescents with chronic health conditions*, which was coordinated by Dr. Carlos Carona and Professor Maria Cristina Canavarro and conducted in the Faculty of Psychology and Education Sciences of the University of Coimbra, in close collaboration with the international coordinator Professor Dr. phil. Monika Bullinger (University Medical Center Hamburg-Eppendorf, Germany). The combination of the generic KIDSCREEN, chronic-generic and asthma-specific DISABKIDS modules, all translated and adapted to the Portuguese language and cultural context according to standard procedures (Schmidt & Bullinger, 2003) and available in both patient- and proxy-report forms, enabled the clarification of key methodological issues in pediatric QoL assessment, namely the distinctive utility of condition-specific measures and the agreement between children/adolescents and their parents in outcomes reports, as further discussed in the next paragraphs.

### 1.2.1. The KIDSCREEN/DISABKIDS modular approach to QoL assessment in Portuguese pediatric asthma patients

One of the major contributions of our study is the provision of the European Portuguese self- and proxy-report versions of the DAsM (The DISABKIDS Group Europe, 2006), thus completing the three-level (i.e., generic, chronic-generic and condition-specific) modular structure of the KIDSCREEN/DISABKIDS questionnaires for children/adolescents with asthma in our country. These questionnaires were cross-culturally adapted within a sequential approach, that is, they were transferred from one culture to another, based on the assumption that subjective indicators of QoL are anthropologically universal (Bullinger, 1997). Using the terminology proposed by Herdman, Fox-Rushby, and Badia (1998), the results from our semantic validation and pilot study confirmed their conceptual equivalence (i.e., the items and response scales were considered relevant by the children/adolescents and their parents), item equivalence (i.e., only a minor modification in one item was required), semantic equivalence (i.e., the items were easily forward and backward translated, and their comprehensibility was attested by the participants), operational equivalence (i.e., the original mode of administration, format and time frame were appropriate for the Portuguese population), and measurement equivalence (i.e., the preliminary psychometric properties in terms of reliability and construct validity resembled those found in the original international studies; Baars et al., 2005).

However, the results from a CFA in a larger sample of pediatric asthma patients and parents (field study) suggested that a one-factor model would fit the Portuguese data better than the correlated two-factor (Impact and Worry) model. After the discussion of this unexpected result with the international coordinator of the DISABKIDS project, we concluded that the use of the instrument as a global index of asthma-specific HrQoL in the Portuguese population should not constitute an obstacle to cross-cultural research. However, replication studies in other countries are required to further examine whether a one-dimensional measure would better suit the condition-specific HrQoL assessment in children/adolescents. In turn, brief measures that summarize scores into a single value (or index) can be especially useful in the context of routine monitoring and screening, because they can be sensitive to differences or changes in patients' perceived HrQoL, while reducing response burden and saving administration costs (Ravens-Sieberer et al., 2006). The use of a single-index result also allows the calculation of quality-adjusted life years (QALYs) – a measure that weighs both the quality and the quantity of years of life that would be added by a specific intervention and that has been extensively used in cost-effectiveness studies. Nevertheless, global-index measures are inadequate to obtain detailed profile assessments, and should be complemented, whenever possible, by generic measures accounting for the multi-dimensionality of the QoL construct.

In addition, the one-factor model was valid for both age groups (i.e., children and adolescents), and for both patient- and parent-reported data, and the psychometric qualities of reliability and validity of the proposed global index of asthma-specific HrQoL were confirmed in the field test sample. On this regard, we highlight the moderate and strong correlations between this asthma-specific HrQoL global score and those of the generic and chronic-generic measures, respectively, which provided additional evidence for the conceptual distinction between generic QoL and disease-specific impact (Wallander et al., 2001), even if they are hierarchically interrelated. In contrast with the generic KIDSCREEN measure, the DISABKIDS instruments were more sensitive in detecting differences between clinical groups (intermittent *vs.* persistent asthma) and were strongly correlated with patients' and parents' perceptions of asthma symptoms. These results support the pertinence of a multi-level assessment of children/adolescents' QoL, including generic, chronic-generic and condition-specific measures, for a comprehensive assessment of the impact of asthma and its treatments in the broader context of their physical, psychological and social functioning.

### 1.2.2. The importance of the family context for improving the validity of patient- and parent-reported outcomes

The low to moderate levels of parent-child agreement on reports of QoL and psychological problems (i.e., the extent of the agreement), and the major trend for parents to report worse QoL and more psychological problems than the children/adolescents (i.e., the direction of the discrepancies), were in accordance with previous studies conducted with clinical samples (Ender, Stachow, Petermann, & Tiedjen, 2011; Sattoe et al., 2012; Van der Meer et al., 2008; White-Koning et al., 2007). The questions that are worthy of further discussion relate to the reasons for disagreement and the clinical validity of patient- and parent-reports.

Previous studies have attempted to address these questions but they have focused mainly on clinical variables, such as disease severity and length (e.g., April, Feldman, Platt, &

Duffy, 2006; Petsios et al., 2011), and socio-demographic factors, namely children's age and gender (e.g., Jokovic, Locker, & Guyatt, 2004; Theunissen et al., 1998), which have revealed limited value for explaining the (dis)agreement between children/adolescents and parents on outcomes reports. Our study provided an innovative contribution by testing the role of family-related variables (i.e., caregiving burden and family relationships) in explaining both the extent and the direction of parent-child (dis)agreement. In fact, our results suggested that a family context that allows children/adolescents to openly express their worries and feelings may contribute for higher levels of parent-child agreement regarding pediatric adaptation outcomes. Conversely, parents' perceptions of caregiving-related tasks and asthma management routines as overly demanding and burdensome may interfere with parent-child interactions (Fiese, Winter, Anbar, Howell, & Poltrock, 2008) and, consequently, limit the exchange of information and contribute to larger discrepancies in pediatric outcomes reports, in both directions.

The use of developmentally appropriate instruments that were semantically and psychometrically validated for children as young as eight years, reinforced our conclusion that the parent-child discrepancies were not mainly due to patients' and parents' different understandings of the concept of illness, its causes and the treatment effects (Bibace & Walsh, 1980), levels of language comprehension and reading proficiency or response styles (e.g., a tendency to provide more extreme scores and base their responses in different experiences; Davis et al., 2007). Accordingly, we believe that the parent-child discrepancies on their assessments of QoL and psychological problems overcomes the methodological issues and reflects, on the one hand, children/adolescents' tendency to emphasize the positive aspects of their adaptation (Oeffinger et al., 2007) and, on the other hand, parents' greater reliability in identifying the most strongly affected areas of their children's functioning. Therefore, we advocate that both patient- and parent-reports are valid and may provide different but complementary information with great clinical relevance.

### 1.3. Conceptual integration of risk and resistance factors explaining the differentiated adaptation of children/adolescents with asthma and their parents

Our third set of results allowed the identification of a number of specific risk and resistance factors and the processes through which they may operate to explain the wide variability in adaptation outcomes of children/adolescents with asthma and their parents. Our hypotheses were framed within solid and coherent theoretical models, namely the Disability-Stress-Coping Model (Wallander et al., 1989a), considering its specifications to the understanding of caregiving processes (Raina et al., 2004). Nonetheless, our empirical studies addressed some major research gaps, as identified in our literature review (cf. the Theoretical Framework section of the present dissertation) and provided an innovative contribution to the scientific knowledge in the pediatric psychology field, by:

1. Testing the moderating effects of patients' age group (i.e., childhood *vs.* adolescence) on both key predictors and outcomes of their own and their parents' adaptation, and on the strength of the associations between variables;
2. Considering the multi-dimensionality of the caregiving burden construct (Savundranayagam et al., 2011) and examining the differentiated impact of its objective, subjective and relationship dimensions on patients' and parents' adaptation outcomes in the context of pediatric asthma;
3. Moving from the identification of risk factors associated with maladaptation to the study of positive dimensions of caregiving, specific coping strategies and adaptive family functioning as contributors to improved mental health and QoL in pediatric asthma patients and their parents;
4. Adopting a transactional approach that accounted for the interdependence of adaptation processes and outcomes between family members (Fiese & Sameroff, 1989).

Figure 1 graphically depicts the conceptual integration of our main research findings within the Disability-Stress-Coping Model, followed by a brief comment on the most important contributions of our study for the refinement of this theoretical model and consequent better understanding of individual and family adaptation processes and outcomes in the context of pediatric asthma.

### 1.3.1. Pediatric asthma in context: The variability of psychosocial risk and resistance factors and adaptation outcomes according to clinical and socio-demographic features

Pediatric asthma patients and their parents are at greater risk for QoL impairments and decreased psychological functioning, in comparison with peers without asthma and their parents. However, the wide variability in individual adaptation trajectories and outcomes calls for the identification of specific clinical and socio-demographic characteristics that may increase that risk. In our study, we found that children/adolescents with persistent asthma reported more HrQoL impairments (as detected by the DISABKIDS chronic-generic and asthma-specific modules) and psychological problems than children/adolescents with intermittent asthma. In addition, pediatric patients with uncontrolled or partly controlled asthma presented worse generic QoL, compared to those with adequately controlled asthma.

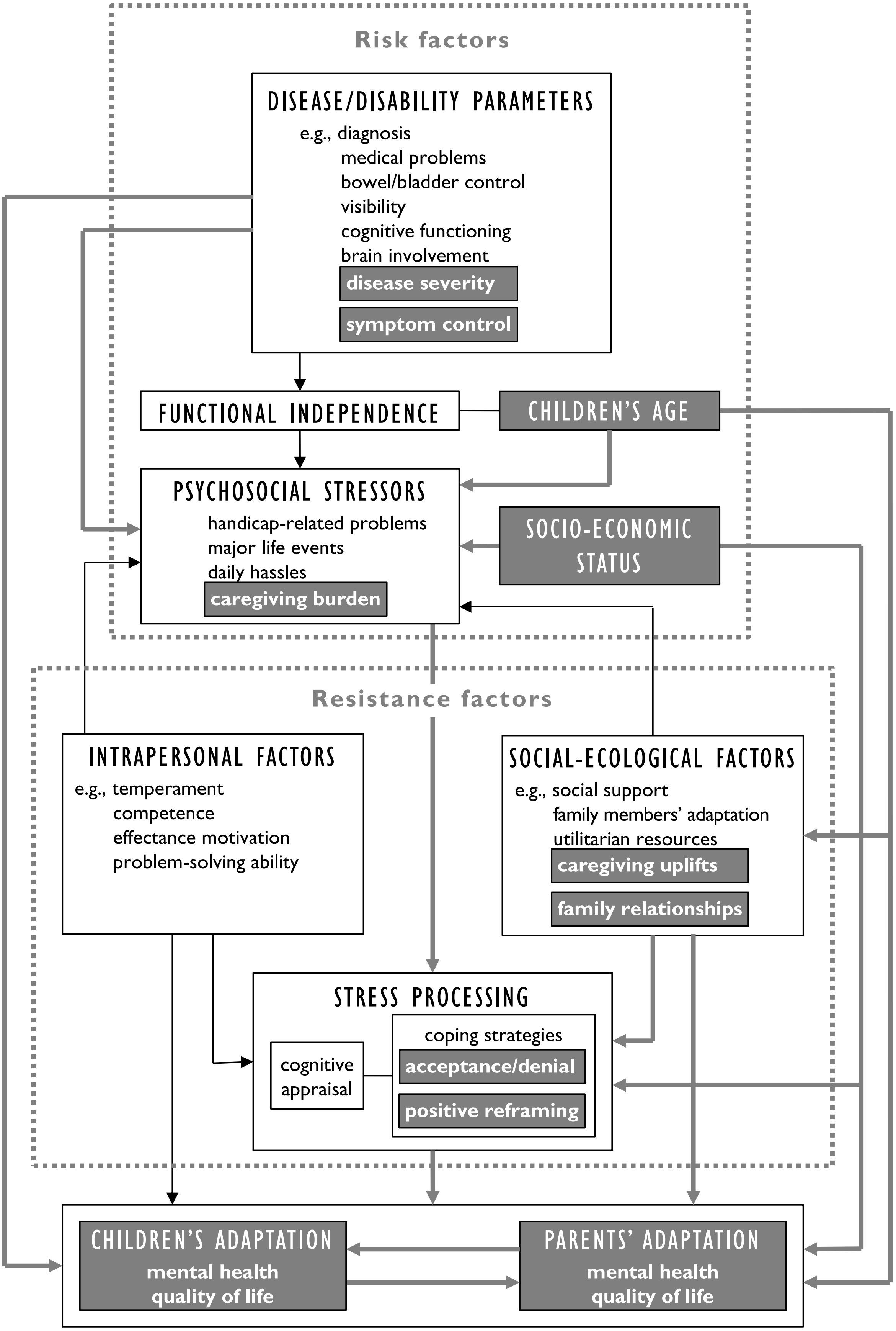


**Figure 1** | Conceptual integration of the results from the present study within the Disability-Stress-Coping Model (Wallander et al., 1989a)

These results were expected based on previous research (Dean et al., 2010; Everhart & Fiese, 2009; McQuaid et al., 2001; Schmier et al., 2007). Conversely, socio-demographic variables (e.g., children/adolescents' age) were not identified as direct risk factors for the adaptation of pediatric patients.

For parents, a different pattern of associations between clinical and socio-demographic variables and their caregiving experiences and adaptation outcomes was found. Although asthma severity and control influenced children/adolescents' adaptation outcomes, no such effect was found on parents' caregiving burden and QoL. The only exception was the greater relationship burden found for parents of children/adolescents with intermittent asthma, compared to the persistent asthma group. The interpretation of this somewhat unexpected result should consider the content of the items included in the relationship burden domain, which essentially assessed parents' perceptions of their children's demands for care and attention as exceeding the needs warranted by the pediatric health condition (Montgomery & Kosloski, 2006). Accordingly, when asthma does not inflict severe limitations on the child's functioning (as in the case of intermittent asthma), parents may be more prone to interpret their child's demands as unjustified, which may result in additional parent-child conflict. A divergent, although complementary, explanatory hypothesis advocates that children/adolescents with intermittent asthma may perceive the specific restrictions imposed by their parents (e.g., avoidance of unhealthy environments) as excessive for their asthma management, which eventually results in the deterioration of the family relationships and higher levels of relationship burden.

Although children/adolescents' age was not considered in the conceptual models of adaptation (Raina et al., 2004; Wallander et al., 1989a), we found that parents of younger children reported higher levels of objective and subjective burden and worse QoL, compared to parents of adolescents. These results are consistent with a previous study describing greater time demands when providing care to children with chronic illnesses or disabilities in mothers of children aged 6-12 years compared with mothers of adolescents aged 13 years and older (Floyd & Gallagher, 1997). In fact, while adolescents are able to share some responsibilities for asthma management, thereby alleviating caregiver burden, younger children could be more dependent on parental care and less able to communicate their healthcare needs, thus increasing parents' responsibilities and worries (Kaugars, Klinnert, & Bender, 2004; Kazak, 1989). Interesting enough, parents of younger children also presented more caregiving uplifts than parents of adolescents, which suggests that the greater amount of time that parents spend caring for younger children may also be viewed as a privileged opportunity for parent-child positive interactions and, consequently, for parents' experiences of caregiving-related gratifications and positive emotions.

Moreover, low family SES has emerged as a significant risk factor for higher levels of relationship and subjective caregiving burden, as well as for parents' decreased QoL, especially in the psychological and environment domains. Similar results were found by Gates and Akabas (2012), which stated that the opportunity to afford additional support from healthcare service providers and to successfully balance work and caregiving responsibilities may ease caregiving demands and contribute to positive adaptation outcomes in parents. Nonetheless, our findings have limited generalizability to other cultural backgrounds and should be interpreted within the current Portuguese economic context and healthcare policies, because additional financial burdens may have inflated the levels of caregiving burden and, consequently, contributed to poorer QoL outcomes. Taken together, these findings suggest that parents' caregiving experiences and adaptation outcomes are most affected by their appraisal of personal and economic resources to manage their child's asthma effectively, than by asthma clinical features and objective demands.

### 1.3.2. Psychosocial risk factors: The deleterious effect of caregiving burden(s) on parents' and their children's QoL outcomes

Beyond the socio-demographic and clinical characteristics, the burden of caring for a chronically ill child has been hypothesized as a foremost predictor of parents' physical and psychological health (Raina et al., 2004). In our study, caregiving burden, addressed as a latent variable reflected by the three burden dimensions (i.e., relationship, objective and subjective burden; cf. empirical study III) as observed indicators, was negatively associated with parents' QoL, but only indirectly via acceptance and denial coping tendencies. The absence of direct links between caregiving burden and parents' adaptation outcomes has been previously observed in other studies (e.g., King et al., 1999) and may reflect two different scenarios. First, it emphasizes the role of stress processing mechanisms in the well-being of parents caring for a child with a chronic condition (Raina et al., 2004; Wallander et al., 1989b). Second, it may indicate a differentiated impact of burden dimensions on parents' QoL that cannot be captured by a latent construct, thus strengthening the importance of addressing burden dimensions as relatively independent constructs (Savundranayagam et al., 2011).

In fact, when the effect of each burden dimension was examined *per se* (cf. empirical study V), results showed a negative contribution of the relationship and subjective burden dimensions, but not objective burden, to explain parents' QoL. According to previous research (Canning et al., 1996; Carona, Pereira, et al., 2013), these findings suggest that, more than the objective parameters of the pediatric health condition and the extent of work load (e.g., objective caregiving demands and amount of time performing care tasks; Montgomery et al., 1985), caregiving-related negative emotions and parent-child conflict may determine coping processes and, ultimately, influence parents' adaptation outcomes (Lazarus & Folkman, 1984). In addition, relationship burden emerged as a significant risk factor for children/adolescents' decreased QoL. A straightforward interpretation of this finding is that higher levels of parental burden associated with routine asthma care may result in overprotective or intrusive parent-child interaction patterns, which, in turn, are likely to affect children's QoL outcomes (Fiese et al., 2008). Nonetheless, the negative link between relationship burden and children/adolescents' QoL may indicate that, when parents perceive their children's demands for care and attention as unwarranted, they may become less responsive to their children's needs or even disengage from providing adequate medical care and emotional support to them, with serious consequences for children/adolescents' physical and psychosocial health. To date, there is little evidence-based research to confirm this hypothesis and, thus, further studies on this topic are required.

### 1.3.3. Family resource/protective factors: The importance of caregiving uplifts and family relationships

Under the rubric of social-ecological factors, we examined the role of caregiving uplifts and positive family relationships as resource/protective factors for children/adolescents' and their parents' better adaptation. The multi-dimensional assessment of parents' caregiving experience, by incorporating both negative (i.e., burdens) and positive dimensions (i.e., uplifts), was a major contribution of our study because it operationalizes the transition from deficit-based models to a risk-resistance approach to caregiving processes. A remarkable finding from our study was the co-occurrence of caregiving-related gratifications and positive emotions in parents experiencing greater levels of burden (e.g., parents caring for younger children). In addition, we found positive associations between caregiving burden and uplifts, suggesting that they are different (even if related) constructs, rather than "two sides of the same coin", and that they may sustain distinctive adaptation processes (Larson, 2010). In fact, different patterns of associations between caregiving uplifts and adaptation outcomes have emerged for parents and children/adolescents in our study. While for children/adolescents, parents' experience of gratifications and positive emotions was directly linked to their QoL, for parents, this association was more complex. In our empirical study IV, we found that caregiving uplifts were indirectly linked to parents' QoL, via positive reframing coping tendencies, which is aligned with the assumption that the experience of positive emotions and psychological states during stressful situations is related to the adoption of meaning-based coping (Folkman, 1997). Besides sustaining adaptive coping mechanisms, caregiving uplifts may also serve the function of restoring exhausted resources (Folkman, 1997; Folkman & Moskowitz, 2000). Based on this premise, we also examined caregiving uplifts as moderators of the associations between caregiving burden and

QoL outcomes (cf. empirical study V). Consistent with previous research (Carona, Pereira, et al., 2013; Gupta & Singhal, 2004), our results showed that caregiving uplifts buffered the negative effect of relationship burden on parents' QoL. It is also worth noting that the results arising from these two studies are not conflicting, given the fact that positive meaning-based coping tendencies may also serve as buffers from emotional stress (Garro, 2011). To summarize these findings in accordance with the refined conceptual and methodological distinction proposed by Rose and colleagues (2004), we can assume that caregiving uplifts may operate as family resources for both family members, as well as protective factors against the deleterious effect of relationship burden on parents' QoL.

In addition, family relationships marked by high levels of cohesion and expressiveness, as perceived by children/adolescents and by parents, emerged as important family resources, contributing for better adaptation, directly for children/adolescents and parents (i.e., the within-subjects or actor effects), and indirectly across family members (i.e., the cross-lagged or partner effects). These findings were expected, based on the vast theoretical and empirical literature acknowledging the role of supportive family relationships as important predictors of psychological functioning in children with chronic health conditions (Drotar, 1997; Wallander et al., 1989a). As regulators of family functioning in general (Olson & Gorall, 2003), family cohesion and communication patterns have two main adaptive functions: the affective function (i.e., sharing feelings and emotional support) and the instrumental function (i.e., role assignments, decision-making and conflict resolution; Patterson, 2002). In the specific context of pediatric asthma, a third adaptive function of family relationships may be considered: the avoidance of emotional asthma triggers and subsequent improvement in asthma control, as a result of patients' fewer psychological symptoms of depression and anxiety (Wood et al., 2007). Although alternative pathways were not examined in the present study, previous studies with pediatric asthma patients and their parents also found some support for the hypothesis of family relationships as a mediator of the beneficial effect of well-organized and meaningful daily family routines on children/adolescents' adaptation (Santos, Crespo, Silva, & Canavarro, 2012) and of the deleterious effect of caregiving burden on both parents' and their children's QoL outcomes (Crespo et al., 2011; Fiese et al., 2008).

### 1.3.4. Stress processing mechanisms: Acceptance/denial and positive reframing as specific coping strategies mediating the caregiving process

Another major contribution of our study was the identification of specific coping strategies mediating the links between parents' caregiving experiences of burden and uplifts and their QoL. Based on the assumption that emotion-focused coping strategies aimed at managing emotional distress would be preferred in the context of pediatric chronic health conditions, because they are unlikely to undergo beneficial changes (Carver et al., 1989), we elected acceptance, denial and positive reframing to be tested in our study. These coping mechanisms have been described as “meaning-based” and operate at a situational level through the reinterpretation of stressful events to reduce the incongruence between their specific meaning and the individual’s global meanings (Park, 2010; Park & Folkman, 1997). In the context of family caregiving, acceptance or positive reframing strategies may reflect the parents’ attempt to make sense of their children’s health condition and a reconciliation of the caregiving demands with the caregivers’ goals, values and beliefs (Pakenham, 2008).

Our results showed that higher levels of caregiving burden were associated with parents’ tendencies to use less acceptance and more denial coping strategies, which, in turn, were linked to their QoL. Complementarily, higher levels of caregiving uplifts sustained positive reframing coping tendencies, thus contributing indirectly to parents’ improved QoL. Although empirical research on the topic of parental coping in the context of pediatric asthma is scarce, similar results have been described for caregivers of adult patients or caregivers of children with other chronic health conditions. For example, Pakenham (2008) found that the coping strategy of acceptance is related to greater life satisfaction and positive affect, and less anxiety and depression in caregivers of adult patients with multiple sclerosis. In opposition, avoidance coping strategies (including denial) have been systematically associated with poorer psychological adjustment to physical illness (for a review, see Roesch & Weiner, 2001). Specifically for parents of children with neurodevelopmental conditions, experiential avoidance and behavioral disengagement are related to increased burden and worse QoL (Carona, Silva, Crespo, et al., 2014; Whittingham, Wee, Sanders, & Boyd, 2013).

Although the links between parents’ coping tendencies and their children’s adaptation outcomes were not examined in the present study, there is some evidence that parental coping patterns characterized by active coping strategies, such as planning, problem-solving and positive reframing (as opposed to avoidance coping), may also influence the adaptation outcomes of children with asthma over time (Sales et al., 2008). Moreover, by contributing for parents’ better QoL, acceptance and positive reframing coping tendencies may have an indirect positive effect on the QoL of pediatric asthma patients.

### 1.3.5. Family context from a transactional perspective: The interdependence of parent-child adaptation processes and outcomes

Although the cross-sectional design of our study precluded the examination of the reciprocal influences between family members over time, it stands clear that children/adolescents' and their parents' adaptation are not independent processes. The influences of parental and family functioning on children's adaptation outcomes are well established in the pediatric literature. In a comprehensive literature review, Drotar (1997) found that supportive family relationships (e.g., high levels of cohesion) are associated with positive psychological outcomes in children with chronic health conditions (e.g., fewer behavioral problems and improved self-esteem), while family conflict, maternal distress and parental child-rearing practices characterized by overprotection consistently predict children's psychological problems, such as lower self-control, behavioral problems and psychological distress. In the specific context of pediatric asthma, direct positive effects of parents' perceptions of a warm and supportive family environment and low levels of caregiving burden on their children's QoL were also described (Crespo et al., 2011). In the same line, our results showed significant associations between parents' caregiving experiences of burden and uplifts and their children's QoL, as well as indirect effects of parents' perceptions of the family relationships as characterized by higher levels of cohesion and expressiveness on their children's better adaptation outcomes, via a positive effect on parents' own adaptation.

Based on the transactional model of development, which advocates that children/adolescents are active and influential participants in their life contexts (Fiese & Sameroff, 1989; Sameroff, 2009), the influences between children/adolescents and parents are expected to be reciprocal. In fact, our study also showed that children/adolescents' perceptions of positive family relationships were associated with their parent's improved adaptation outcomes, although only indirectly via children's own adaptation. Previous research had already found significant effects of children's psychological functioning on parents' QoL (Annett et al., 2010) and on the quality of parent-child relationships (Papp et al., 2005). However, these studies have examined the adaptation outcomes separately for each family member, despite the compelling evidence of bidirectional associations between children's and their parents' QoL in the context of pediatric asthma (Marsac et al., 2007; Vila et al., 2003). By testing a single model accounting for the transactional links between children/adolescents and parents, and the indirect pathways by which they may occur, our study provided an innovative contribution for the understanding of the interdependence between family members' adaptation processes.

### 1.3.6. The (in)variance of individual and family adaptation mechanisms across clinical, developmental and socio-economic conditions

As a final remark on the topic of children/adolescents' and their parents' adaptation processes in the context of pediatric asthma, it is interesting to note that, although significant differences between asthma severity, children/adolescents' age and family SES groups existed on caregiving burden and uplifts, as well as on children's and their parents' adaptation outcomes, the individual and family psychosocial adaptation mechanisms remained invariant across clinical, developmental and socio-economic conditions. The general applicability of the Disability-Stress-Coping Model to sub-groups of pediatric asthma patients and their parents has been remarkably understudied, although stable associations between life stressors, social resources and adaptation outcomes have been reported across chronically ill, psychologically distressed and healthy children/adolescents (Moos, 2002). Therefore, our study provided innovative evidence for the occurrence of general adaptation mechanisms in pediatric asthma patients and their parents, independently of their socio-demographic and clinical characteristics, which, ultimately, may facilitate the outlining of specific interventions for this population.

The only exception was the strength of the associations between children/adolescents' perception of the family relationships and their generic and chronic-generic QoL, which was moderated by asthma severity levels, with stronger associations found for patients with persistent asthma. Daniels, Moos, Billings, and Miller (1987) also showed that family relationships marked by low levels of cohesion and expressiveness and high levels of burden are related to more adjustment problems in patients with chronic health conditions (i.e., juvenile rheumatic disease), their healthy siblings and healthy controls, although those associations were stronger for the clinical group. In the specific context of pediatric asthma, a supportive and expressive family environment is likely to play a major role in helping children/adolescents manage the additional demands posed by severe asthma, thus emerging as more strongly associated with their QoL outcomes. Although these associations were not as strong for the intermittent asthma group, they were also statistically significant, attesting the general role of family relationships as family resources contributing for children/adolescents' and their parents' adaptation outcomes.

## 2. STRENGTHS AND LIMITATIONS OF THE STUDY

A number of theoretical and methodological strengths are notorious in the present research work, thus supporting the validity and pertinence of its contributions for understanding adaptation to pediatric asthma in children/adolescents and their parents. Most importantly, our research questions and objectives were underpinned by solid theoretical frameworks, namely the Disability-Stress-Coping Model of adaptation for chronically ill or handicapped children (Wallander et al., 1989a) and its specifications for the conceptualization of the caregiving process (Raina et al., 2004), as well as the Transactional Model of Development applied to pediatric contexts (Fiese & Sameroff, 1989). The outlining of theoretically-driven hypotheses enabled a deeper understanding of the differentiated adaptation processes and outcomes in children/adolescents with asthma and their parents, and it also facilitated the interpretation of research findings in light of the proposed theoretical principles. In turn, our empirical results may contribute to the refinement of the theoretical models and to convert them into evidence-based guidelines for clinical practice in pediatric settings. In addition, we highlight the comprehensive and multi-dimensional approach to the construct of adaptation, by including mental health and QoL outcomes as broad indicators of physical, mental and social functioning (Harper, 1991; Wallander et al., 1990). Particularly for children/adolescents' QoL, we adopted a three-level modular system composed of broad-ranging questionnaires assessing general subjective health and well-being, and specific questionnaires assessing the impact of asthma and its treatments on patients' lives (Ravens-Sieberer et al., 2007). The multi-dimensional approach was also extended to the assessment of negative (i.e., burdens) and positive (i.e., uplifts) dimensions of parents' caregiving experience (Larson, 2010; Savundranayagam et al., 2011). In contrast to the current "little investigation of opportunities for positive growth following childhood illness" (Barlow & Ellard, 2006, p. 30), the emphasis on positive outcomes and predictors sustained our progression from deficit-based and psychopathological frameworks to the study of processes that account for resiliency and variability in individual and family adaptation trajectories in the context of significant adversity (Patterson, 2002).

At the empirical level, our study was strengthened by the careful selection of developmentally appropriate instruments for pediatric outcomes assessment and by the dyadic parent-child approach to data collection and analyses. All questionnaires used for assessing children/adolescents in our study (i.e., the KIDSCREEN-10, the DISABKIDS chronic-generic and asthma-specific modules and the SDQ) met the methodological standards to be considered "developmentally appropriate", which implied that their items and dimensions were related to the developmental contexts of children and adolescents and that the questionnaires' wording and format were adequate for their language and cognitive skills (Bruil & Detmar, 2005; Carona et al., 2015). Although these questionnaires may be criticized for disregarding age-related specificities (Wallander et al., 2001), their focus on age-universal markers enabled not only the examination of age group differences on adaptation outcomes, but also the assessment of the (in)variance of individual and family adaptation processes along the continuum from childhood to adolescence. Moreover, these questionnaires provided strictly parallel versions to be completed by children/adolescents and by their parents/family caregivers. By capturing the perspectives of two family members, not only on pediatric adaptation outcomes, but also on family relationships, we were able to examine the transactional associations between them, thus providing further insight into the complexity of family systems (Drotar, 1997; Kazak, 1997). This multi-informant approach was also extended to physicians' classification of asthma severity and control levels, since the inclusion of data reported by individuals outside the family system has been considered an effective methodological strategy to reduce the biases resulting from parents' emotional status, perceptions and expectations (Everhart & Fiese, 2009).

Finally, the use of advanced statistical techniques, such as regression-based moderation analyses and SEM, allowed moving from mere outcomes description to the examination of potential direct, indirect and conditional mechanisms underpinning the adaptation processes in pediatric asthma patients and their parents. A major advantage of SEM procedures is the ability to model latent constructs, which statistically operationalized the multi-dimensional approach to adaptation outcomes and psychosocial variables, while controlling for the measurement error inherent to psychological measures (DeShon, 1998). In addition, SEM techniques assume that the paths between the variables are specified *a priori*, and that the fit of the proposed model to the sample data is subsequently tested, thus favoring a theory-driven approach and providing the methods for testing theories in light of empirical data (Kline, 2005). Although under-utilized in pediatric psychology research, SEM techniques have been described as powerful and flexible tools for examining complex theoretical models, especially the social-ecological systems models applied to pediatric conditions (Kazak, 1989; Kazak, Rourke, & Navsaria, 2009), because they capture the complex interacting relationships among hierarchical systems of children's lives that may contribute for explaining important health-related outcomes (Nelson, Aylward, & Steele, 2008).

Notwithstanding the aforementioned strengths, we also acknowledge some methodological limitations that should be considered in the interpretation of our research findings. First, our empirical study had a cross-sectional design, which precluded inferring causality among the variables and implies that our results should be interpreted in terms of inter-relationships among the variables at a certain point in time. Even with the commitment to a theoretically-driven research, the testing of directional paths with cross-sectional data assumes that the causal processes had already occurred and that the system was at an equilibrium point (Kline, 2005). This assumption was addressed in our study by including children/adolescents who had asthma for at least one year, thus minimizing the effects of acute stress responses caused by a recent diagnosis and enabling families to stabilize their functioning in the context of pediatric asthma. However, only longitudinal data can ascertain the reciprocal influences among family members over time, as advocated by the Transactional Model of Development (Fiese & Sameroff, 1989; Sameroff, 2009).

A second set of limitations of our study relates to the non-probabilistic sample collection method, which resulted in a limited representativeness of the sample. Because only pediatric asthma patients referred to pediatricians or pediatric pulmonologists in public urban hospitals were included in our sample, most families had low or medium SES and, thus, the generalizability of our results to wealthier families attending private healthcare services is limited. Although the distribution of socio-economic levels in our sample is consistent with the users' profile in public healthcare services in Portugal, the results should be interpreted within the current Portuguese economic context. In addition to the financial burden of asthma treatments, the high rates of unemployed parents and the consequent family income reduction may result in additional burdens affecting parents' perceptions of their caregiving experiences and their adaptation outcomes. Moreover, the great majority of family caregivers participating in our study were female. This is not surprising, given the fact that mothers tend to assume the role of primary caregivers of children with chronic health conditions in most families and, consequently, they are more likely to accompany their children to hospital visits than fathers. A number of studies have shown that mothers tend to report higher levels of parenting stress and lower QoL compared to fathers (e.g., Goldbeck, 2006; Silver et al., 1998). However, pediatric chronic health conditions also have a deleterious effect on fathers' emotional well-being, particularly in terms of additional concerns about their children's physical health, experiences of stressful life events and feelings of lower self-esteem (Hayes & Savage, 2008; Hovey, 2003; Katz & Krulik, 1999). Besides, fathers' involvement in parental caregiving has been consistently related to improved well-being, cognitive development and social competence (Cabrera, Tamis-LeMonda, Bradley, Hofferth, & Lamb, 2000) and fewer psychological problems in their children (DeKlyen, Speltz, & Greenberg, 1998; Flouri, 2008). Unfortunately, the under-representation of fathers in our sample precluded the examination of gender differences on caregiving experiences and adaptation outcomes for both parents and their children.

Third, the classification of asthma severity and control levels based on expert opinion rather than on objective measures of pulmonary function, as well as the absence of information about the use of daily controller and/or quick-relief medications, adherence and responsiveness to pharmacological treatments, should also be acknowledged as study limitations. The physicians' classification of asthma severity into four levels (intermittent, mild persistent, moderate persistent and severe persistent) and asthma control into three levels (controlled, partly controlled and uncontrolled) was suited for cross-sectional research purposes according to the existing guidelines at the time of sample collection (GINA, 2008). However, this classification system does not represent the current recommendations for asthma outcomes assessment, which should include periodic tests of pulmonary function, evaluation of future risk of adverse outcomes (e.g., medication adherence and exposure to allergens/irritants) and information from both the children/adolescents and their parents (GINA, 2014). Moreover, the high portion of children/adolescents with intermittent and controlled asthma, even though consistent with the distribution of asthma severity and control levels that are typically observed in the Portuguese pediatric population (Gaspar et al., 2006), may limit the generalizability of the results to patients with severe and difficult-to-control asthma. The dichotomization of asthma severity and control levels in our analyses, and the consequent increased variability within the persistent and non-controlled asthma groups, may also have overlooked potential group differences on adaptation processes and outcomes.

Finally, it is worth noting some limitations related to the statistical procedures for data analyses. Few parents refused to participate in the study, mostly because of time constraints, with an estimated rate of participation higher than 90%. Unfortunately, not all of the cases who refused to participate and the reasons for refusal were systematically recorded. Furthermore, some cases were excluded from our dataset because of missing data that were not completely random (e.g., as the result of participants dropping out of the study before completing the last questionnaires in the assessment protocol) or that were higher than 5% of the values. For the remaining cases, we used imputation techniques based on the substitution of the mean of a participants' observed items for each of his/her missing items, under the assumption that the items of a specific scale/sub-scale are highly interrelated (Osborne, 2013). Imputation (i.e., the practice of filling in missing items) has several advantages, namely the prevention of statistical power loss resulting from a diminished sample size (because no cases are excluded, as in case deletion procedures) and the possibility of using standard methods and software for data analyses (Schafer & Graham, 2002). However, unlike case deletion, the individual mean score substitution may introduce bias because the variance of the scale tends to increase and its reliability tends to decrease as the number of observable items drops (Schafer & Graham, 2002). Considering the total sample size, the statistical power analyses conducted *a posteriori* indicated that, in general, small to medium effects could be detected in our empirical studies. Although our sample size was greater than the minimum of 100-200 individuals recommended for SEM procedures, the testing of more complex models (i.e., with higher number of distinct parameters to be estimated) would require larger sample sizes to achieve the necessary power to detect small effects (Kline, 2005). Another important statistical limitation of our study relates to multiple testing, that is, the testing of more than one hypothesis at a time and using the same dataset. At the individual study level, the probability of a type I error (i.e., rejecting the individual null hypothesis although it is, in fact, true), also called individual error rate or error rate per hypothesis, was controlled by using multivariate analyses that accounted for the relationship between the outcome variables, followed by univariate analyses with Bonferroni correction (Field, 2009). However, when multiple hypotheses are tested within a single experiment and each test has a specified type I error probability, the expected number of false significant tests increases with the number of hypotheses per experiment (Bender & Lange, 2001; Shaffer, 1995). This increased familywise error rate should be taken into account when considering a set of conclusions as a whole, as in the case of the present integrated discussion of results arising from multiple statistical tests.

# 3. THEORETICAL IMPLICATIONS AND FUTURE DIRECTIONS FOR RESEARCH

We believe that our study provides an important contribution to a better understanding of adaptation processes and outcomes in pediatric asthma patients and their parents, particularly by clarifying some methodological issues in the assessment of pediatric adaptation outcomes and by enabling the refinement of the existing conceptual models of individual and family adaptation. Based on the results from the studies described in the present dissertation and the methodological considerations stated in the previous section, it stands clear that further studies on the topic of psychosocial adaptation processes and outcomes in pediatric settings in general and in the specific context of pediatric asthma are still required. Next, we highlight some promising avenues for future research.

## 3.1. Designing longitudinal and mixed-methods studies

The findings from our empirical studies provided fresh insights into a number of clinical (e.g., asthma severity and control levels), socio-demographic (e.g., children/adolescent' age and family SES) and psychosocial variables (e.g., caregiving burden and uplifts, family relationships) that were associated with adaptation outcomes in pediatric asthma patients and their parents at a certain point in time. Large prospective studies are required to clarify the directionality of the associations between risk and resistance factors and adaptation outcomes, as well as to examine the reciprocal influences among family members over time. This methodological approach is also essential to ascertain whether these individual and family adaptation processes are stable over time or whether they evolve across the course of illness, children's developmental stages and family life cycle phases (Kazak, 1989; Rolland, 2004). However, we must recognize that longitudinal research can be time- and resource-consuming. To maximize such investment, researchers should consider some predictors of experimental attrition in pediatric samples, namely the participant-researcher relationship, parental well-being and patient's clinical characteristics (Kazak, 1997).

In addition, our results stressed the importance of attributing positive meanings to the caregiving experience and the mediating role of specific cognitive and emotion-focused coping strategies (e.g., acceptance and positive reframing) for positive adaptation outcomes in parents caring for a child with asthma. Based on previous research, it is also expected that parents with more flexible and integrative perceptions of the illness and its treatments adopt more effective coping strategies (Goldbeck & Bundschuh, 2007; Santos, 2010), are more involved in clinical decision-making and comply more with medical prescriptions (Barros & Santos, 1999).

Structured interviews have been considered the preferred method for exploring the complexity of these meaning-making processes and their variability over time (La Greca & Lemanek, 1996). Therefore, future research should adopt mixed-methods designs, combining qualitative and quantitative data (Creswell, 2009) to provide a more in-depth depiction of illness perceptions and meaning-making coping, and the processes through which they contribute to positive adaptation outcomes.

### 3.2. Enhancing the validity of patient- and parent-reported outcome measures

The findings from our empirical studies I and II, which were generally aimed at clarifying key methodological issues in the assessment of QoL outcomes and psychological problems in children/adolescents, have two major practical implications for future research. First, we highlight the need of incorporating a multi-level assessment of QoL, covering the broad physical, psychological and social domains of functioning, as well as the specific impact of health conditions and medical treatments. Depending on their specific objectives, researchers should preferably adopt a modular system composed of generic core and condition-specific modules, to allow comparisons across healthy and chronically ill populations (Ravens-Sieberer et al., 2006), while also ensuring sensitivity to changes or differences in the health status and healthcare needs of pediatric patients (Bullinger et al., 2006; Wiebe et al., 2003). The selection of instruments with a modular structure, in opposition to a battery approach, may also minimize participants' response burden and prevent high rates of drop-outs, particularly in longitudinal studies.

Second, future research should adopt a multi-informant approach by employing both patient- and parent-reported outcomes. Obtaining two scores, from two family members, for a single outcome does not imply the computation of a composite score as a better estimate of the actual value (Kenny et al., 2006); on the contrary, both children/adolescents and their parents may provide unique, though complementary, information on pediatric QoL and psychological problems (Eiser & Morse, 2001b; Wallander et al., 2001). To better understand parent-child agreement on adaptation outcomes reports, researchers should consider the family context, namely the opportunities for information exchange between family members, along with the children's developmental characteristics and communication skills. Beyond the identification of clinical, socio-demographic and family-related factors associated with the extent and direction of (dis)agreement, research should now move to the examination of the predictive role of parent-child agreement on asthma outcomes, including medication adherence, emergency room visits, hospitalizations and school/work absenteeism.

Currently, there are several instruments that meet the aforementioned requirements for a comprehensive assessment of adaptation outcomes. For example, the KIDSCREEN and

DISABKIDS questionnaires (Ravens-Sieberer et al., 2007) and the PedsQL instruments (Varni, Seid, & Rode, 1999) include generic core scales and specific modules for a number of pediatric conditions, and they are available in self- and proxy-report forms. Rather than developing new QoL questionnaires, future studies should translate and adapt existing reliable and valid measures to other languages and cultural contexts to facilitate cross-cultural comparisons. In addition, the great majority of QoL measures do not establish cut-off scores for minimally important differences (i.e., the smallest difference in an outcome measure perceived, on average, as beneficial by the patients; Guyatt, Osoba, Wu, Wyrwich, & Norman, 2002). To enhance the clinical interpretability of screening measures (e.g., identify "at-risk" patients), longitudinal studies providing reference data for pediatric patients, caregivers and healthy peers and determining appropriate cut-off scores for different clinical and socio-demographic groups are essential.

## 3.3. Generalizing research findings to other populations

Based on the generalizability limitations that were mentioned in the previous section, it would be worthwhile to broaden the research population in future studies. The inclusion of larger samples of pediatric asthma patients and their parents would increase the statistical power and allow researchers to test a greater number of variables and inter-relationships among them with more complex statistical procedures. Furthermore, the generalizability of the results would benefit from the collection of more diversified samples, by including a larger number of patients with severe and uncontrolled asthma and a balanced proportion of male and female caregivers, as well as other family members (e.g., siblings), gathered in public and private healthcare services (Barlow & Ellard, 2006). A more homogeneous distribution of sample characteristics would also enable the investigation of group differences in adaptation outcomes and the identification of the socio-demographic and clinical conditions in which the individual and family adaptation processes are more likely to occur (i.e., moderation analyses).

Moreover, our study was focused on pediatric asthma patients attending urban public Portuguese hospitals, which clearly limits the generalizability to broader populations. In fact, most research concerning pediatric conditions has involved small convenience samples collected only at a single site, despite the recognition that some of the variance in psychosocial outcomes may be attributed to characteristics, services and referral patterns of the medical settings where children/adolescents are recruited, and to family environmental and demographic characteristics of the participants (Drotar, 1994). To address this limitation and enhance generalizability, we recommend three different study designs for future research: (1) the replication of findings in different samples and settings, provided that scientific reports have described in detail the recruitment and analytic procedures and the subject characteristics; (2) cross-cultural research comparing data from different countries and cultural contexts; and (3) meta-analytic studies combining existing research and examining between-studies heterogeneity across participants' and settings' characteristics. These methodological strategies may also provide useful contributions to improve individual treatments, as well as healthcare systems organization and policies at regional, national and international levels (Skevington, 2002).

The complex interplay between risk and resistance factors and adaptation outcomes found in our empirical studies is also expected to be generalizable, to some extent, to other pediatric chronic health conditions, as proposed by non-categorical approaches (Stein & Jessop, 1982). Sampling a wide range of pediatric chronic health conditions and using generic and chronic-generic measures may be particularly useful to understand adaptation processes and outcomes in general, and particularly in low-prevalence diseases that cannot constitute large samples. In addition, some authors have advocated the resemblance of family functioning and adaptation processes among typically developing families and those caring for a child with a chronic condition (Herzer et al., 2010; Roberts & Wallander, 1992). To test the (in)variance of the adaptation mechanisms, future studies should include age-matched healthy children/adolescents as controls. Despite the additional costs related to the collection of control samples, this approach should be preferred over the use of population norms, because community samples are likely to include a number of children/adolescents with other chronic conditions or disabilities, which could disguise potential differences (Gerharz et al., 2003).

### 3.4. Expanding research to other ecological systems

Our study provides a major contribution to understanding adaptation to pediatric asthma within the family context, by identifying family-related risk (e.g., caregiving burden) and resource/protective factors (e.g., caregiving uplifts and family relationships), as well as the coping mechanisms mediating the adaptation outcomes in children/adolescents and their parents. Using the social-ecological framework as reference (Bronfenbrenner, 1977), we must recognize that the family system is interrelated to other ecological systems. Therefore, the investigation of potential influences of contextual factors on the adaptation of pediatric patients and their parents should be extended beyond the family microsystem, by also examining the role of social support networks (Kazak, 1987; Wallander & Varni, 1989), school environment and peer acceptance (Barros, Matos, & Batista-Foguet, 2008) and perceptions of family-centered formal caregiving (King, King, Rosenbaum, & Goffin, 1999; Raina et al., 2004).

Among these distal formal and informal social structures, social support has been one of the most studied variables. In pediatric literature, we can find three alternative specific mechanisms through which social support may influence children/adolescents' and their parents' adaptation outcomes. First, social support has been linked to positive adaptation outcomes for children/adolescents with chronic health conditions or disabilities (Goldbeck et al., 2007; Wallander & Varni, 1989) and their mothers (Barakat & Linney, 1992; Wallander et al., 1989c). However, there has been some debate on whether this relationship is always direct (main effect hypothesis) or a result of interaction effects between social support and contextual stressors (buffering hypothesis; Cohen & Wills, 1985). This second hypothesis could be operationalized in future research by testing the moderating effect of social support on the associations between condition- and caregiving-related stressors and adaptation outcomes. Finally, there is some empirical support for the mediating effect of social support on the links between caregiving stress and adaptation outcomes in parents caring for a deaf child (Quittner, Glueckauf, & Jackson, 1990) or a child with cerebral palsy (Carona, Crespo, & Canavarro, 2013). Based on a “social support deterioration model” (Lin & Ensel, 1984), these authors advocate that chronic caregiving stress would elicit more negative perceptions of social support, which, in turn, would increase parents’ maladjustment. However, these hypotheses require further investigation in other developmental contexts, including pediatric asthma.

# 4. CONTRIBUTIONS FOR CLINICAL PRACTICE AND HEALTH POLICY-MAKING

In this last section of this dissertation, we offer some evidence-based guidelines that may contribute to improve clinical practice and healthcare policies in pediatric settings. These considerations are the result of our extensive literature review, discussion of empirical findings with national and international experts in the field of pediatric psychology, and our direct contact with children/adolescents and parents during the sample collection. Based on the two general objectives of pediatric psychology (i.e., prevention/education and remediation/intervention) and on its theoretical and methodological principles (which include the recognition of the importance of child development, the close collaboration with pediatricians and other health professionals and the concern to provide effective and brief interventions; Barros, 2003), we comment, in the first place, on the implications of our research findings to improve general medical care, and secondly, on the specific strategies to be implemented in specialized psychosocial interventions.

## 4.1. Incorporating psychosocial screening in pediatric healthcare

Alongside with the periodical examination of physiological indicators of pulmonary function and asthma symptoms control, the most recent GINA guidelines recommend the assessment of the future risk of adverse outcomes, including major psychological and social problems (GINA, 2014). To this end, QoL measures can be particularly useful, since their potential applications include the "description of function and wellbeing of populations with and without medical conditions (epidemiological perspective), its use as an outcome criterion for interventions (clinical perspective) and its contribution to decision making in the health care field (political perspective)" (Bullinger, 1997, p. 815). Within a clinical perspective, the inclusion of QoL routine assessment into pediatric clinical practice has several advantages, namely: (1) the facilitation of patient-physician communication and shared clinical decision-making; (2) the improvement of patient satisfaction with medical care; and (3) the detection of psychosocial and functional disabilities – the so-called "hidden morbidities" (Varni et al., 2005). Despite these compelling arguments in favor of QoL routine assessment in pediatric medical care, this practice is still poorly disseminated in Portuguese healthcare services, which can be attributed to the scarcity of reliable and valid measures adapted for the Portuguese language and cultural context, the limited amount of professionals' and patients' time for completion, scoring and interpretation of QoL data, as well as some skepticism that still prevails in the medical community regarding the subjective data reported by the patient and/or their family caregivers (Spieth & Harris, 1996).

We believe that our research findings may contribute to overcome some of these barriers, by ascertaining the good psychometric performance of a global index of asthma-specific QoL and the distinctive utility of the generic KIDSCREEN and the chronic-generic and asthma-specific DISABKIDS questionnaires for assessing Portuguese pediatric asthma patients within a modular and, thus, more economic and less time-consuming, approach. These questionnaires proved to be suitable for a wide age range of children/adolescents, by taking into account their cognitive development, level of language comprehension and reading proficiency, which could increase confidence in the validity of patient-reported outcomes. In addition, they are easy to score and interpret and can be administered by different members of the medical staff such as physicians, nurses, social workers or psychologists. Next, we summarize some specific recommendations for pediatric outcomes assessment in medical care.

### 4.1.1. Selecting generic and condition-specific measures

According to Varni and colleagues (2005), screening measures to be used in pediatric medical settings should meet the following criteria: (1) be brief, whilst presenting good reliability and validity; (2) be easily completed by patients/parents and easily scored and interpreted by clinicians; and (3) be responsive to significant differences or changes in patients' health status. The chronic-generic DISABKIDS-12 (Carona, Silva, Moreira, et al., 2014) and the asthma-specific modules proved to be more responsive to asthma clinical severity as assessed by physicians and to patients' and parents' perceptions of asthma symptoms, in relation to generic QoL measures. Therefore, these questionnaires may be particularly informative for asthma-management at the individual patient level. Although health-related contexts may assume a major relevance for pediatric asthma patients, their normative development and overall adaptation should be interpreted in a broader perspective. Generic measures (e.g., KIDSCREEN questionnaires; Gaspar & Matos, 2008) entail the additional advantages of providing information on the broad physical, psychological and social domains of child's functioning and well-being, as well as on the wider life contexts that may result in additional risk for pediatric asthma patients, even if not directly related to their health condition (e.g., going out with friends to a bar or nightclub and the consequent exposure to cigarette smoke). A combination of generic, chronic-generic and condition-specific measures, structured in brief single-index modules, is, thus, recommended for a comprehensive evaluation of children/adolescents' QoL in clinical practice.

### 4.1.2. Listening to both the children/adolescents' and their parents' voices

Patient-reported outcomes have been widely recommended for a comprehensive assessment of overall adaptation in routine clinical care. Specifically, Detmar (2003) stated that patient-reported outcomes are feasible to facilitate patient-physician communication in clinical care and that they may lead to increased recognition of patients' problems and healthcare needs, which, in turn, may result in more effective decision-making (e.g., referrals and medication prescriptions) and, ultimately, in improved adaptation outcomes. This is even more important in pediatric settings, where patient-physician communication can be hampered by the limited verbal skills of young patients; the use of patient-reported QoL measures that are sensitive to children's language and cognitive development may facilitate the accurate report of symptoms or other impairments in daily functioning (Varni et al., 2005). In fact, our sample collection experience confirmed that children/adolescents are often motivated by the questionnaires items to share additional health-related concerns with researchers and also with their parents.

Along with patient-reported outcomes assessment, parents' perspectives on their children's adaptation should also be considered because they may provide complementary information on children/adolescents' current and future functional limitations and help physicians to detect psychosocial impairments in pediatric patients. Moreover, parents assume a major role in asthma management and healthcare decision-making, which are significantly influenced by their own perceptions about illness and medication (Klok, Brand, Bomhof-Roordink, Duiverman, & Kaptein, 2011). For example, parents' beliefs regarding the potential side effects of inhaled corticosteroids are an important cause of poor adherence to medical prescriptions in pediatric asthma patients. The low to moderate levels of parent-child agreement on reports of QoL and psychological problems is more than a methodological issue and may become a potential intervention target. Psychosocial interventions focused on strengthening parent-child communication may help minimize disagreements, thus promoting children/adolescents' involvement in daily asthma management routines and enabling parents to recognize and respond to their children's healthcare needs.

In addition, parents' voices should be listened to in regard to their own caregiving experiences and adaptation outcomes. Since long ago, pediatric healthcare professionals have considered that they almost always work with at least two patients simultaneously – a child and a parent (Allmond, Buckman, & Gofman, 1979). In agreement with previous research, our findings showed that parents are also at risk for QoL impairments and that the adaptation outcomes of parents and their children are reciprocally interrelated. Therefore, the routine assessment of QoL and mental health should be extended to parents or other family members assuming the role of primary caregivers regarding children/adolescents' health-related issues. The screening of caregivers' mental health in pediatric healthcare services and their subsequent referral are particularly important because clinically significant symptoms of depression and anxiety in parents have been consistently associated with increased difficulties in children's asthma management (Bartlett et al., 2004), lower pulmonary functioning in children/adolescents

(Feldman et al., 2013) and more emergency room visits (Brown et al., 2006; Weil et al., 1999). Based on our experience, we can recommend the EUROHIS-QOL 8-index (Pereira et al., 2011) and the brief version of the Mental Health Inventory (MHI-5; Pais-Ribeiro, 2001) for assessing parents' QoL and mental health, respectively, in pediatric medical settings, because they are brief and easy to complete, whilst maintaining good reliability and validity.

### 4.1.3. Periodically assessing psychosocial outcomes throughout the child's development

Individual and family adaptation to pediatric chronic health conditions are dynamic processes that change over time. Therefore, QoL and mental health should be reassessed on a regular basis, particularly for young patients experiencing rapid developmental changes and challenges that may require different treatment approaches. In fact, the reciprocity of effects between the presence of a chronic health condition during childhood and the normative physical and psychosocial development have been described in the literature (Suris, Michaud, & Viner, 2004). On the one hand, pediatric asthma may affect children/adolescents' physical development (e.g., growth velocity and delay in puberty onset; Barnes et al., 1998), psychological functioning (McQuaid et al., 2001), school attendance and academic achievement (Dean et al., 2010; Schmier et al., 2007), social inclusion and peer acceptance (e.g., limited participation in sports and other social activities; Von Mutius, 2000) and family relationships and independence (Sennhauser et al., 2005). On the other hand, the developmental transition from childhood to adolescence may result in high risk-taking behaviors and exposures (e.g., cigarette smoking), poor medication adherence and increased rates of mental health problems, which, in turn, lead to increased asthma morbidity and healthcare services utilization (Desai & Oppenheimer, 2011).

The early detection of such risk behaviors for adverse asthma outcomes calls for a periodical assessment of psychosocial adaptation outcomes in pediatric patients and their parents. For that purpose, clinicians should select developmentally appropriate instruments that cover age-universal QoL markers, to enable comparisons across different developmental stages (Carona et al., 2015). Tracking changes in QoL over time may assist physicians in monitoring symptom control and patients' responsiveness to medications, and, subsequently, in adjusting pharmacological treatments (Lemanske & Busse, 2010). Finally, it is worth noting that the screening of QoL impairments and mental health problems should be regarded as the "starting point" for understanding the healthcare needs of pediatric patients and their families. The identification of children/adolescents and/or parents at risk for developing clinically significant psychosocial problems should be followed by referral to specialized mental health providers for adequate diagnosis and intervention. This more efficient allocation of health resources can offset the additional costs of conducting periodical in-depth assessments of adaptation outcomes.

## 4.2. Implementing psychosocial interventions in pediatric asthma care

At a preventive level, there is a great amount of research confirming the benefits of asthma self-management educational programs to improve children/adolescents' pulmonary function and feelings of self-control and to reduce school absenteeism, number of days with restricted activity and number of visits to an emergency department (for a review, see Guevara et al., 2003). However, less is known about remediation interventions in pediatric asthma care. Within a non-deterministic and non-pathological approach to pediatric chronic health conditions, and taking into account the diversity of adaptation trajectories and outcomes in children/adolescents with asthma and their parents, and the need of efficiently allocating health resources, we advocate that specialized psychological interventions should be delivered only to those families referred as being at higher risk for developing clinically significant problems. Our research findings, namely the identification of modifiable psychosocial risk and resistance factors and the processes through which they may operate to influence adaptation outcomes, provide a valuable contribution for the outlining of specific targets and strategies for interventions aimed at reducing the risk of psychosocial problems, buffering stress and even enabling personal and relational growth in the stressful context of pediatric asthma. The recommendations offered below are primarily based on cognitive-behavioral techniques, because they have been extensively recognized for their effectiveness in promoting more realistic appraisals of stressful events and the adequate use of coping resources in adult patients with chronic health conditions (Ridder & Schreurs, 2001) and in improving parenting behaviors and parents' mental health, as well as their children's symptoms, in pediatric contexts (Eccleston, Palermo, Fisher, & Law, 2012).

### 4.2.1. Adopting a family-centered approach

First and foremost, clinicians must recognize that pediatric asthma affects not only the patient, but the family as a whole, and particularly the parents assuming the role of primary caregivers (Fiese et al., 2008). Therefore, clinical interventions in pediatric asthma settings should be family-centered, which, in our view, may involve two complementary approaches: first, the provision of child's medical care in a family-centered manner, by establishing a parent-physician partnership enabling shared decision-making and meeting parents' preferences, available resources and needs of information and support (King et al., 1999); and, second, the inclusion of psychosocial interventions aimed at promoting positive family relationships and adaptation outcomes in children/adolescents and their parents (Fiese, 1997; Sawyer et al., 2001). The results from our study suggest that assisting families to develop problem-solving and communication skills (thus, minimizing family conflict), fostering a sense of belonging and encouraging emotional expressiveness among family members may constitute specific targets to be addressed in psychosocial interventions aimed at promoting children/adolescents' and their parents' QoL and psychological functioning. These interventions focused on the whole-family environment may be particularly helpful for families coping with severe asthma, because family members' perceptions that the family "still stands" as a stable and reliable context, even when facing major clinical and psychosocial stressors, may buffer the negative impact of those stressors in both children/adolescents' and parents' adaptation outcomes.

An additional issue arising from our findings relates to the format of psychosocial interventions. Ideally, family-centered interventions should target all family members to maximize their efficacy (Kazak, 1989; Minuchin et al., 1975). However, the reciprocal influences between children/adolescents' and their parents' adaptation suggest that individual interventions aimed at promoting one family member's adaptation may have a beneficial indirect effect on other family members' adaptation. Thus, when involving the entire family is impossible or undesirable, addressing individual perceptions of family relationships may be an effective way of enhancing both individual and family-wide adaptation. It is also worth noting that this assumption applies to both parent-child and child-parent directions. Although most researchers and clinicians tend to primarily focus on the influence of parental functioning (e.g., child-rearing and disease-management practices) on their child's physical health and psychosocial development, strategic interventions directed to the child may also contribute to improve family adaptation outcomes.

### 4.2.2. Broadening caregiving experiences

In our study, parents, particularly those caring for younger children, children with intermittent asthma or with scarce socio-economic resources, were at greater risk for experiencing higher levels of caregiving burden. Concomitantly, they also experienced caregiving-related gratifications and positive emotions. In addition, the different dimensions of caregiving burden and uplifts emerged as foremost risk and resource/protective factors, respectively, associated with adaptation outcomes in both parents and their children with asthma. These results call for a multi-dimensional assessment of parents' caregiving experiences, which implies, on the one hand, the assessment of multiple dimensions of burden, including its relationship, objective and subjective dimensions (Savundranayagam et al., 2011), and, on the other hand, the consideration of positive dimensions of caregiving (Larson, 2010; Sales, 2003). Broadening the scope of clinical attention to encompass both negative and positive dimensions of family caregiving may represent a strategic and cost-effective option to operationalize a strength-based approach to family interventions in pediatric clinical settings (Beresford, 1994; Judge, 1998).

The identification of the most affected burden dimensions in parents caring for a child with asthma has straightforward implications for the outlining of specific intervention strategies and more efficient allocation of health resources. For example, parents reporting increased levels of objective burden (e.g., parents of younger children) may mostly benefit from sharing caregiving responsibilities with other family members, developing effective time-management strategies to include the scheduling of pleasant social activities and personal time and widening social support networks, while parents with marked subjective (e.g., parents of younger children or with low SES) or relationship burden (e.g., parents of children/adolescents with intermittent asthma) should be referred to psychological interventions respectively aimed at developing their abilities to manage emotional stress or parenting skills to manage their children's behavioral difficulties (Carona, Pereira, et al., 2013).

Complementarily, encouraging parents' perception of caregiving uplifts may contribute to directly improve parents' and their children's QoL and to attenuate the negative effect of relationship burden on parents' QoL. It is worth noting that caregiving burden and uplifts are not "two sides of the same coin". In fact, our results showed that the experience of caregiving uplifts may co-occur with high levels of caregiving stress. The expression "embrace of the paradox" (Larson, 1998; revisited by Carona, Pereira, et al., 2013) has been used to denote the successful effort of parents caring for a child with a chronic health condition in integrating and finding a balance between positive and negative aspects of their caregiving experience. Therefore, therapeutic strategies aimed at reducing burden do not imply the achievement of caregiving-related gratifications or positive emotions. Identifying and restructuring thoughts and beliefs that interfere with positive experiences, planning positive meaningful events, noting positive events when they occur spontaneously and infusing ordinary events with positive meaning (Folkman, 1997; Folkman & Moskowitz, 2000) are specific strategies that may help parents "embrace the paradox" of their caregiving experience and perceive gratifications and positive emotions while they are also regulating distress. This (re)definition of intervention goals may also require a change in professional and social attitudes to avoid pathologizing parents' positive caregiving experiences, by considering them as a form of denial of their children's condition, and to understand their adaptive function (Larson, 2010).

### 4.2.2. Sustaining meaning-based coping processes

The aforementioned strategies to reduce caregiving burden and improve parents' perceptions of caregiving uplifts may also contribute indirectly to their long-term adaptation, by sustaining adaptive coping mechanisms in adverse circumstances (Folkman, 1997; Joseph & Linley, 2006). Encouraging the experience of caregiving-related positive emotions in parents caring for a child with asthma may "broaden and build" their coping repertoires, by widening their scope of attention (e.g., mindful attention focus), cognition (e.g., creative thinking) and action (e.g., behavioral variety), which ultimately promote long-lasting physical, intellectual and social resources (Fredrickson, 1998). In our study, we identified acceptance (as opposed to denial) and positive reframing as specific “meaning-based” coping strategies mediating the caregiving process and contributing for parents’ improved QoL outcomes.

The third wave of cognitive-behavioral therapies (e.g., Acceptance and Commitment Therapy [ACT], Hayes, 2004; Mindfulness-Based Stress Reduction [MBSR], Kabat-Zinn, 1990) relies specifically on strategies such as mindfulness, acceptance and cognitive defusion to change the meaning of stressful events and to develop more flexible and effective coping repertoires. A mindfulness-based approach has been applied to normative parenting (Duncan, Coatsworth, & Greenberg, 2009) and there is also promising evidence that its techniques may be effective in reducing parenting stress, depression and negative affect and in promoting psychological well-being, QoL and even personal growth in parents of children with chronic conditions or disabilities (e.g., Bazzano et al., 2015; Benn, Akiva, Arel, & Roeser, 2012; Minor, Carlson, Mackenzie, Zernicke, & Jones, 2006). Moreover, mindfulness approaches were found to be effective in increasing the efficacy of coping strategies (Carson, Carson, Gil, & Baucom, 2004). In this sense, Tharaldsen, Bru, and Wilhelmsen (2011) used the term “mindful coping” to refer to the way mindfulness supports a more realistic evaluation of the stressful situation (i.e., primary appraisal) and of the available coping resources (i.e., secondary appraisal). In the specific context of caring for a child with asthma, incorporating mindful awareness into parenting interactions, by intentionally and non-judgmentally paying attention to their child in the present moment, is expected to be effective in reappraising caregiving demands and parent-child relationships as less burdensome, in developing coping tendencies marked by acceptance as an alternative to experiential avoidance and, ultimately, in improving parents’ adaptation outcomes.

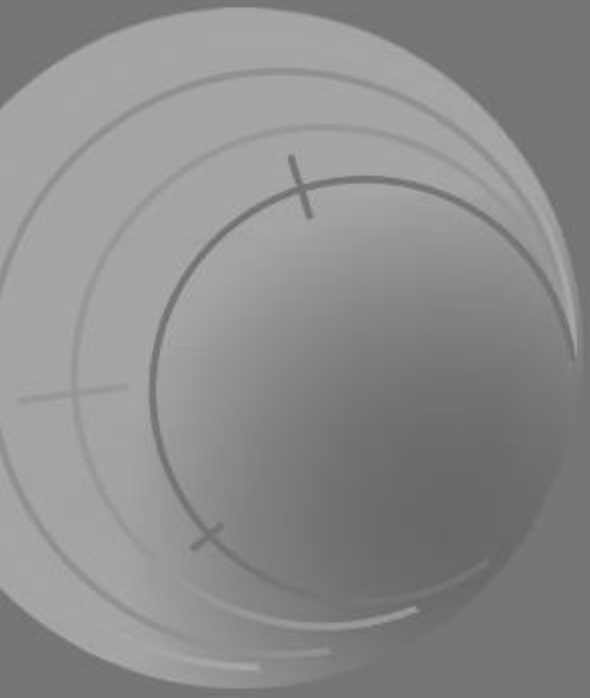
### 4.2.3. Addressing the future: e-Health applications

Although pediatric asthma patients and their parents would benefit from psychological support, there are some barriers that prevent them to access traditional forms of care, including unavailability of skilled professionals in pediatric services, direct and indirect costs with sessions and travel to and from a clinician’s office, geographic distance, lack of time to schedule and attend regular appointments and length of treatments (Ritterband et al., 2003; Ritterband & Tate, 2009). With the advances of computer technologies over the past 20 years, new ways to communicate, provide and deliver psychological treatments have emerged. Internet-based intervention programs and e-Health applications may significantly increase access to care for a wide range of patients, thus reducing health disparities and overcoming geographical and economic barriers (Cushing & Steele, 2010). Additional advantages of e-Health programs include the greater flexibility in terms of treatment progression and access to materials, guarantee of anonymity and the possibility of reaching patients earlier than traditional mental health services

(Proudfoot et al., 2011; Ritterband et al., 2003).

In the context of pediatric asthma, several studies have demonstrated the efficacy of internet-delivered interventions to reduce hospital admissions, particularly for patients with severe asthma (McLean et al., 2010), and to increase asthma control and pulmonary functioning (van der Meer et al., 2009), medication adherence (Petrie, Perry, Broadbent, & Weinman, 2012), asthma knowledge, self-management practices and QoL outcomes (Chan et al., 2007). It is also important to note that these interventions have been designed not only for asthma self-management education purposes, but also to modify patients' beliefs regarding their condition and its treatments (e.g., Petrie et al., 2012), which has been acknowledged as fundamental for maximizing the efficacy of cognitive and cognitive-behavioral interventions in pediatric psychology (Barros, 1996).

In Portugal, the provision of internet-based psychosocial interventions in pediatric healthcare services is still poorly disseminated. However, the high rate of Portuguese people that use the Internet as a source of health information (Santana, 2009) and the willingness of most healthcare professionals to use e-Health platforms more frequently (Moreira, 2012) support the suitability of the Internet as a vehicle for the efficient provision of preventive/educational and treatment programs to pediatric asthma patients and parents, in a brief and cost-effective way.



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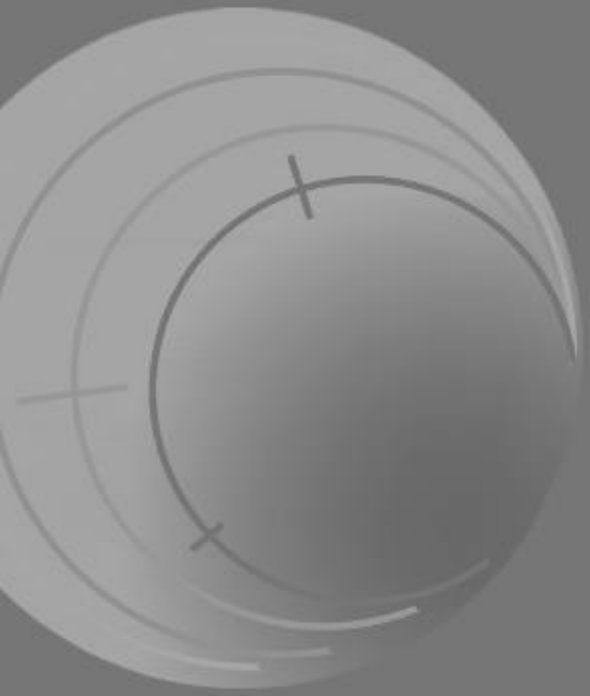

# Attachments

Preliminary Study

# Avaliação da qualidade de vida em crianças e adolescentes com asma: Validação semântica e estudo piloto do DISABKIDS – Módulo para a Asma

## [Assessing quality of life in children and adolescents with asthma: Semantic validation and pilot study of the DISABKIDS – Asthma Module]

Neuza Silva • Carlos Carona • Carla Crespo • Maria Cristina Canavarro

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# Avaliação da qualidade de vida em crianças e adolescentes com asma: Validação semântica e estudo piloto do DISABKIDS – Módulo para a Asma

Neuza Silva • Carlos Carona • Carla Crespo • Maria Cristina Canavarro

## Abstract

A qualidade de vida tem surgido na literatura como um importante indicador de saúde. A elevada prevalência da asma na população pediátrica portuguesa torna particularmente relevante a avaliação da qualidade de vida relacionada com a saúde (QdVrS) nesta condição. ***Objectivos***. (1) Descrever o processo de desenvolvimento das versões Portuguesas do DISABKIDS- Módulo para a Asma; (2) avaliar a importância e compreensibilidade dos seus itens e adequação da escala de resposta (validação semântica); e (3) examinar as suas propriedades psicométricas (estudo-piloto). ***Metodologia***. A amostra, recolhida nos HUC, Hospital Pediátrico (Coimbra) e HSA (Leiria), foi constituída por 36 crianças (8-12 anos) e adolescentes (13-18 anos) com asma, e seus pais/cuidadores familiares. O protocolo incluiu as versões Portuguesas (auto e hetero-relato) do DISABKIDS- Módulo para a Asma e questionários DISABKIDS de validação semântica. A gravidade da asma foi avaliada pelos médicos responsáveis. ***Resultados***. A validação semântica do DISABKIDS- Módulo para a Asma certificou a compreensibilidade, importância e adequação dos itens. O estudo exploratório indicou boa consistência interna [.88 (auto-relato)/ .85 (hetero-relato)]. Os domínios do questionário apresentaram correlações fortes entre si e com a pontuação global (*r* entre .79 e .97). O questionário apresentou ainda poder discriminante entre níveis de gravidade da asma, grupos etários e sexo das crianças/adolescentes. O acordo entre auto e hetero-relatos foi fraco a moderado (ICC entre .20 e .50). ***Conclusões***. A disponibilização deste questionário para a população Portuguesa terá implicações para a investigação, clínica e políticas de saúde, possibilitando a melhoria da QdVrS das crianças/adolescentes com asma.

# Introdução

Num contexto em que os progressos no campo da medicina têm enfatizado a prevenção e controlo das condições crónicas de saúde (CCS), a qualidade de vida relacionada com a saúde (QdVrS) tem vindo a ser considerada um importante *outcome* nos cuidados de saúde pediátricos (Ravens-Sieberer et al., 2006). Enquanto a investigação da qualidade de vida (QdV) em adultos tem vindo a progredir substancialmente nos últimos anos, os desafios conceptuais e metodológicos particulares com que a avaliação da QdVrS em crianças e adolescentes se depara (e.g., De Civita et al., 2005; Matza, Swensen, Flood, Secnik, & Leidy, 2004) podem estar na origem da escassez de investigação da QdV pediátrica (Bullinger, Schmidt, Peterson, & Ravens-Sieberer, 2006). Sendo a asma a CCS mais comum na infância e adolescência (WHO, 2008), estimando-se uma prevalência superior a 11% na população pediátrica portuguesa (Direcção Geral de Saúde, 2000), e cujos sintomas têm um impacto significativo na vida das crianças e adolescentes, ao nível dos tratamentos e hospitalizações recorrentes, limitações nas actividades, problemas de sono, e absentismo escolar, comprometendo a sua QdV (Schmier et al., 2007; Van Gent et al., 2007), torna-se fundamental a adaptação de instrumentos específicos para a avaliação da QdVrS das crianças e adolescentes Portugueses com asma.

O projecto DISABKIDS (*Quality of life in children and adolescents with disabilities and their families – assessing patients' view and patients' needs for comprehensive care*) considera a QdVrS como um constructo multidimensional, que engloba componentes físicos, emocionais, mentais, sociais e comportamentais do bem-estar e do funcionamento percebidos pelos pacientes e/ou outros observadores (Bullinger et al., 2006). Este projecto, seguindo as recomendações da OMS para a avaliação da QdVrS pediátrica (WHO, 1993), distingue-se pela sua perspectiva transcultural e abordagem simultânea em vários países europeus, pelo seu sistema modular que permite a combinação de aspectos genéricos e específicos da QdVrS, pela abrangência de uma ampla faixa etária e pelo foco na perspectiva das crianças e adolescentes e dos seus pais ou cuidadores (Baars et al., 2005; The DISABKIDS Group Europe, 2006). A metodologia utilizada no desenvolvimento dos questionários de avaliação da QdVrS das crianças e adolescentes desenrolou-se em várias fases, combinando métodos qualitativos e quantitativos, desde uma extensa revisão da literatura, discussão em grupos focais com crianças e adolescentes e suas famílias, procedimentos de selecção dos itens e de tradução, estudos-piloto, e estudos de campo em amostras representativas da população (Ravens-Sieberer et al., 2007). Em estreita ligação com o projecto KIDSCREEN (The DISABKIDS Group Europe, 2004), os questionários desenvolvidos formam um sistema modular em 3 níveis de avaliação compreensivos da QdVrS das crianças e adolescentes: módulos genéricos, módulos genéricos para condições crónicas e módulos específicos para a asma, dermatite atópica, diabetes mellitus, fibrose quística, epilepsia, artrite crónica juvenil e paralisia cerebral (Baars et al., 2005; The DISABKIDS Group Europe, 2006). Este sistema modular permite, através dos módulos genéricos, desenvolvidos pelo projecto KIDSCREEN, uma grande abrangência e comparabilidade entre grupos clínicos e população geral, ao mesmo tempo que assegura, a partir dos módulos genéricos e específicos para CCS, concebidos pelo projecto DISABKIDS, a sensibilidade às questões clínicas específicas e a detecção de resultados emergentes de mudanças na condição de saúde ou outros factores a ela associados, importantes na investigação e na prática clínica (Eiser & Morse, 2001b; Wiebe, Guyatt, Weaver, Matijevic, & Sidwell, 2003).

No seguimento dos trabalhos de validação das versões Portuguesas do Módulo Genérico DISABKIDS-37 (Carona, Bullinger, & Canavarro, 2011), este estudo tem como objectivos (1) descrever o processo de desenvolvimento das versões Portuguesas do DISABKIDS – Módulo Específico para a Asma, (2) avaliar a importância e compreensibilidade dos seus itens (validação semântica), e (3) examinar, a um nível de análise exploratório, as propriedades psicométricas do questionário (estudo piloto).

## Metodologia

### Participantes

De acordo com as recomendações do Grupo Europeu DISABKIDS (The DISABKIDS Group Europe, 2004), para o estudo de validação semântica a amostra foi constituída por 9 crianças (entre 8 e 12 anos) e 9 adolescentes (entre 13 e 18 anos) com diagnóstico clínico de asma, e por um dos seus pais/cuidador familiar, e para o estudo piloto, por 18 crianças e 18 adolescentes, e por um dos seus pais/cuidador familiar. Os critérios de inclusão na amostra foram: (1) idade das crianças/adolescentes entre 8 e 18 anos; (2) diagnóstico clínico de asma, efectuado por um médico, de acordo com a CID-10; (3) duração da doença de pelo menos 12 meses; (4) consentimento na participação, após esclarecimento dos objectivos e procedimentos do estudo, por parte dos pais/cuidadores e adolescentes maiores de 14 anos. Foram excluídas da amostra crianças e adolescentes com atrasos desenvolvimentais significativos, e com comorbilidade com patologia psiquiátrica grave ou com outras CCS principais. Os pais/cuidadores familiares foram aqueles que assumiam o papel de cuidadores primários da criança/adolescente nas questões relacionadas com a saúde. As características clínicas e sociodemográficas da amostra são apresentadas na Tabela 1.

**Tabela 1** | Características sociodemográficas e clínicas das crianças/adolescentes e dos pais/cuidadores familiares

| Validação semântica | Crianças (*n* = 9) | Adolescentes (*n* = 9) | Cuidadores familiares (*n* = 18) |
|---|---|---|---|
| ***Características sociodemográficas*** | | | |
| Idade, *M* (*DP*) | 9.89 (1.36) | 14.33 (1.26) | 43.00 (8.01) |
| Sexo, *n* (%) | | | |
| Masculino | 6 (66.7%) | 5 (55.6%) | 3 (16.7%) |
| Feminino | 3 (33.3%) | 4 (44.4%) | 15 (83.3%) |
| Nível socioeconómico, *n* (%) | | | |
| Baixo | | | 8 (44.4%) |
| Médio | | | 8 (44.4%) |
| Alto | | | 1 (5.6%) |
| ***Características clínicas da asma*** | | | |
| Gravidade da asma, *n* (%) | | | |
| Intermitente | 8 (88.9%) | 6 (66.7%) | |
| Ligeira persistente | 1 (11.1%) | 2 (22.2%) | |
| Moderada persistente | - | 1 (11.1%) | |
| Grave persistente | - | - | |
| Controlo da asma, *n* (%) | | | |
| Controlada | 9 (100%) | 7 (77.8%) | |
| Parcialmente controlada | - | 1 (11.1%) | |
| Não controlada | - | 1 (11.1%) | |
| Duração da doença, *M* (*DP*) | 5.89 (4.26) | 9.89 (4.54) | |
| Estudo piloto | Crianças (*n* = 18) | Adolescentes (*n* = 18) | Cuidadores familiares (*n* = 36) |
| ***Características sociodemográficas*** | | | |
| Idade, *M* (*DP*) | 9.89 (1.28) | 14.78 (1.44) | 41.58 (6.95) |
| Sexo, *n* (%) | | | |
| Masculino | 12 (66.7%) | 8 (44.4%) | 4 (11.1%) |
| Feminino | 6 (33.3%) | 10 (55.6%) | 32 (88.9%) |
| Nível socioeconómico, *n* (%) | | | |
| Baixo | | | 21 (58.3%) |
| Médio | | | 13 (36.1%) |
| Alto | | | 1 (2.8%) |
| ***Características clínicas da asma*** | | | |
| Gravidade da asma, *n* (%) | | | |
| Intermitente | 14 (77.8%) | 15 (83.3%) | |
| Ligeira persistente | 3 (16.7%) | 2 (11.1%) | |
| Moderada persistente | 1 (5.6%) | 1 (5.6%) | |
| Grave persistente | - | - | |
| Controlo da asma, *n* (%) | | | |
| Controlada | 17 (94.4%) | 14 (77.8%) | |
| Parcialmente controlada | 1 (5.6%) | 3 (16.7%) | |
| Não controlada | - | 1 (5.6%) | |
| Duração da doença, *M* (*DP*) | 5.39 (3.43) | 9.22 (4.56) | |

## Procedimentos de investigação

Este estudo seguiu os procedimentos recomendados pelo Grupo Europeu DISABKIDS (The DISABKIDS Group Europe, 2004) e contemplou as fases de tradução, validação semântica dos itens e estudo-piloto do questionário DISABKIDS – Módulo para a Asma.

Para a tradução, e de forma a garantir a equivalência conceptual dos itens, foi utilizada a técnica de tradução - retroversão, que contemplou as seguintes etapas: (1) tradução dos itens do questionário da sua versão original em Inglês para Português, por dois tradutores independentes; (2) reconciliação das duas traduções numa única versão, por um membro da equipa de investigação; (3) retroversão por um terceiro tradutor; (4) análise comparativa da retroversão com a versão original do questionário; e (5) revisão da versão reconciliada e construção da versão traduzida. Uma vez que estes procedimentos sucederam a tradução e estudo piloto do Módulo Genérico DISABKIDS-37 (Carona et al., 2011), no qual foi avaliada a equivalência conceptual das versões Portuguesas, e que não surgiram conceitos problemáticos adicionais, foi dispensada a etapa de primeira harmonização internacional.

A amostra foi recolhida entre Dezembro de 2010 e Julho de 2011 em três hospitais públicos da região centro: Hospitais da Universidade de Coimbra, Hospital Pediátrico do Centro Hospitalar de Coimbra e Hospital de Santo André de Leiria, após aprovação do estudo pelas respectivas Comissões de Ética. Os participantes foram recrutados por conveniência, no momento de admissão às consultas externas dos serviços de alergologia e de pediatria, após indicação dos médicos responsáveis. A recolha de dados foi precedida de obtenção de consentimento informado de todos os pais/cuidadores e dos adolescentes maiores de 14 anos. As entrevistas e a administração dos instrumentos de avaliação, de autopreenchimento assistido por um investigador, decorreram nas próprias instituições de saúde.

Após o estudo de validação semântica do questionário, procedeu-se à harmonização internacional dos itens, em reunião com a coordenadora do Grupo Europeu DISABKIDS. Foram então constituídas as versões experimentais Portuguesas do questionário DISABKIDS – Módulo para a Asma, objecto de análise psicométrica no estudo piloto.

## Instrumentos

O protocolo de validação semântica incluiu as versões traduzidas para Português do DISABKIDS – Módulo para a Asma (The DISABKIDS Group Europe, 2006), um questionário de impressão geral/validação semântica geral, e uma ficha de registo da entrevista cognitiva/validação semântica específica (The DISABKIDS Group Europe, s/d). O protocolo para o estudo-piloto incluiu as versões experimentais Portuguesas do DISABKIDS – Módulo para a Asma e a avaliação clínica da gravidade e controlo da asma. Todos os instrumentos foram preenchidos pelas crianças/adolescentes e pelos pais/cuidadores familiares, com excepção da avaliação clínica da gravidade e controlo da asma, que foi efectuada pelos médicos responsáveis.

*DISABKIDS – Módulo para a Asma [versões experimentais Portuguesas de auto- e hetero-relato]*

Este questionário avalia a QdVrS de crianças e adolescentes com asma, entre os 8 e os 18 anos de idade, focando-se especificamente nos aspectos físicos e emocionais relacionados com a asma. É composto por 11 itens, agrupados em dois domínios: Impacto (6 itens), relativo às limitações e sintomas; e Preocupações (5 itens), referente aos aspectos emocionais negativos relacionados com a asma. Os itens são avaliados numa escala de Likert entre 1 (*nunca*) e 5 (*sempre*), tendo como referência temporal as "últimas 4 semanas". A pontuação foi calculada para cada um dos domínios através da soma dos valores obtidos nos itens que compõem o domínio, e para a qualidade de vida relacionada com a asma global (QdVrA) através da soma das pontuações invertidas dos 11 itens. Este questionário inclui ainda 3 questões adicionais que avaliam a gravidade dos sintomas percebidos pelas crianças/adolescentes e pelos pais/cuidadores.

*Questionário de impressão geral relativo ao DISABKIDS – Módulo para a Asma*

Este questionário de validação semântica geral pretende fazer uma avaliação global da qualidade e relevância do questionário, a partir da perspectiva das crianças/adolescentes com asma e dos pais/cuidadores. É composto por 4 questões fechadas que avaliam a qualidade do DISABKIDS – Módulo para a Asma, a compreensibilidade dos itens e das opções de resposta e a pertinência dos itens, e 3 questões abertas onde as crianças/adolescentes e pais/cuidadores foram convidados a sugerir modificações no questionário.

*Ficha de registo da entrevista cognitiva de validação semântica específica*

Através do método de sondagem geral, as crianças/adolescentes e os seus pais/cuidadores familiares manifestaram-se, para cada item em particular, sobre a sua relevância para a CCS da criança/adolescente, a sua compreensibilidade e sobre a adequação das escalas de resposta. Posteriormente, com base no método de parafraseamento (variante do método *think aloud*), as crianças/adolescentes e pais/cuidadores foram convidados a repetir o item por palavras suas e a descrever o seu significado. Devido à exaustão associada a esta tarefa, os 11 itens do questionário foram divididos em 3 subconjuntos: subconjunto A (itens 1 a 4), subconjunto B (itens 5 a 8) e subconjunto C (itens 9 a 11), tendo cada participante realizado a validação semântica específica de apenas um subconjunto de itens.

*Avaliação clínica da gravidade e do controlo da asma*

A gravidade e o controlo da asma pediátrica foram avaliados pelos médicos, a partir das directrizes da *Global Initiative for Asthma Program* (GINA, 2008), que recomendam a avaliação da gravidade da asma em 4 níveis (1 – intermitente, 2 – ligeira persistente, 3 – moderada persistente, 4 – grave persistente) e do controlo em 3 níveis (1 – controlada, 2 – parcialmente controlada, 3 – não controlada).

*Variáveis clínicas e sociodemográficas*

Os pais/cuidadores preencheram ainda uma breve ficha de dados clínicos e sociodemográficos da criança/adolescente e da família.

### Procedimentos estatísticos

Todos os procedimentos estatísticos foram efectuados com recurso ao *software Statistical Package for the Social Sciences*, versão 17.0 (SPSS, v.17.0). Dada a natureza exploratória do estudo, as análises estatísticas foram efectuadas a um intervalo de confiança de 90%. Para o estudo qualitativo de validação semântica, foram calculadas as frequências das respostas obtidas no questionário de impressão geral e na entrevista cognitiva. Para a validação específica dos itens, foi considerada uma frequência mínima de 3 respostas negativas como indicadora de que o item poderá apresentar problemas e deverá ser sujeito a revisão adicional. O estudo da fiabilidade das versões Portuguesas do DISABKIDS – Módulo para a Asma foi efectuado através do cálculo da consistência interna (α de *Cronbach*) para cada um dos domínios e para o total de itens do questionário. A validade de constructo foi analisada através dos coeficientes de correlação de *Pearson* entre os 2 domínios e entre os domínios e a pontuação total do questionário, e a validade discriminante a partir do teste de comparação de medianas para amostras independentes *U de Mann-Whitney*. A concordância entre os auto-relatos das crianças/adolescentes e os hetero-relatos dos pais/cuidadores foi analisada ao nível individual e ao nível grupal (Sneeuw, Sprangers, & Aaronson, 2002), através dos Coeficientes de Correlação Intraclasse (*two-way mixed model, absolute agreement*) e do teste *t-student* de comparação de médias em amostras emparelhadas.

## Resultados

### Validação semântica geral

As crianças e adolescentes com asma, assim como os seus pais/cuidadores familiares, expressaram uma impressão geral positiva das versões experimentais Portuguesas do

DISABKIDS – Módulo para a Asma (cf. Tabela 2). A grande maioria das crianças/adolescentes e dos pais/cuidadores avaliaram os itens do questionário como fáceis de compreender e não demostraram dificuldades na utilização da escala de resposta. As questões foram avaliadas como *muito importantes* ou *por vezes importantes* pela maioria dos participantes, embora tendencialmente os pais/cuidadores tenham atribuído maior relevância às questões. Apenas uma pequena percentagem de crianças/adolescentes e de pais/cuidadores manifestaram vontade de alterar/acrescentar questões ao questionário e nenhum participante considerou as perguntas intrusivas de tal forma que não quisesse responder.

**Tabela 2** | Impressão geral/validação semântica geral das versões portuguesas do DISABKIDS – Módulo para a Asma

| ***Questões*** | | Crianças/ adolescentes (n=18) | Cuidadores familiares (n=18) |
|---|---|---|---|
| 1. De uma maneira geral, o que achas/ acha do nosso questionário? | É muito bom<br>É bom<br>Não é bom | 3 (16.7%)<br>15 (83.3%)<br>- | 8 (44.4%)<br>10 (55.6%)<br>- |
| 2. As perguntas compreendem-se bem? | Fáceis de compreender<br>Algumas são difíceis<br>Não se compreendem | 14 (77.8%)<br>4 (22.2%)<br>- | 17 (94.4%)<br>1 (5.6%)<br>- |
| 3. E em relação às respostas? Tiveste/ Teve alguma dificuldade em compreendê-las? | Sem dificuldades<br>Com algumas dificuldades<br>Com muitas dificuldades | 14 (77.8%)<br>4 (22.2%)<br>- | 18 (100%)<br>-<br>- |
| 4. As perguntas são importantes para o problema de saúde que tu tens/ que o seu filho tem? | São muito importantes<br>Por vezes são importantes<br>Não são nada importantes | 8 (44.4%)<br>9 (50.0%)<br>1 (5.6%) | 14 (77.8%)<br>4 (22.2%)<br>- |
| 5. Gostavas/ Gostava de mudar alguma coisa no questionário? | Não<br>Sim | 16 (88.9%)<br>2 (11.1%) | 16 (88.9%)<br>2 (11.1%) |
| 6. Gostavas/ Gostava de acrescentar alguma coisa ao questionário? | Não<br>Sim | 15 (83.3%)<br>3 (16.7%) | 15 (83.3%)<br>3 (16.7%) |
| 7. Houve alguma pergunta que não quisesses/ quisesse responder? | Não<br>Sim | 18 (100%)<br>- | 18 (100%)<br>- |

## Validação semântica específica

Na fase de validação semântica específica, todos os itens foram considerados importantes para a avaliação da QdVrS na asma pediátrica por pelo menos dois terços dos participantes. As perguntas foram consideradas compreensíveis por todas as crianças/adolescentes, com excepção do item 11 ("Tens medo de noite por causa da asma?"), que suscitou dificuldade de compreensão a uma criança. Também a maioria dos pais/cuidadores não apresentou dificuldade na compreensão dos itens, tendo apenas os itens 2 ("A asma incomoda o seu filho quando ele quer sair?") e 4 ("O seu filho sente dificuldade em respirar quando pratica desporto?") sido avaliados como mais difíceis de compreender por um cuidador. As opções de resposta (1 – *nunca*; 2 – *raramente*; 3 – *algumas vezes*; 4 – *muitas vezes*; 5 – *sempre*) foram avaliadas como adequadas pela maioria dos participantes. Apesar de nenhum item ter sido considerado problemático com base no critério de uma frequência mínima de 3 respostas negativas, o método de parafraseamento revelou que o significado atribuído pelas crianças/adolescentes ao item 11 era diferente do pretendido. Tendencialmente as crianças interpretaram este item como significando "Tens medo da noite/do escuro por causa da asma?", enquanto os adolescentes tenderam a interpretar como "Tens medo de sair de noite por causa da asma?". Face à discrepância conceptual entre as interpretações das crianças e adolescentes e o significado original, este item foi reformulado, tendo a sua redacção sido modificada para "Tens medo durante a noite por causa da asma?". Para os itens restantes, as entrevistas cognitivas confirmaram a equivalência entre os conceitos que se pretendiam avaliar e a interpretação que os participantes fizeram dos itens.

## Fiabilidade

Em ambas as versões de auto-relato das crianças/adolescentes e de hetero-relato dos pais/cuidadores familiares, o questionário apresentou uma boa consistência interna para o total de itens e, com excepção do domínio Preocupações da versão de hetero-relato, uma consistência interna aceitável para os dois domínios (cf. Tabela 3).

**Tabela 3** | Consistência interna das versões portuguesas do DISABKIDS - Módulo para a Asma (versão para crianças e adolescentes/versão para cuidadores familiares)

| | α de *Cronbach* | Número de casos | Número de itens |
|---|---|---|---|
| Domínio Impacto | .76/ .74 | 36/ 36 | 6/ 6 |
| Domínio Preocupações | .78/ .69 | 36/ 36 | 5/ 5 |
| QdVrA global | .88/ .85 | 36/ 36 | 11/ 11 |

## Validade de constructo

Os dois domínios (Impacto e Preocupações) apresentaram correlações fortes (versão de hetero-relato) a muito fortes (versão de auto-relato) entre si e muito fortes com a pontuação total do questionário em ambas as versões de auto e de hetero-relato (cf. Tabela 4).

**Tabela 4 |** Correlações entre os domínios do DISABKIDS – Módulo para a Asma (versão para crianças e adolescentes/versão para cuidadores familiares)

| | Impacto | Preocupações |
|---|---|---|
| Preocupações | .86**/ .79** | - |
| QdVrA global | -.97**/ -.95** | -.96**/ -.94** |

** $p \leq .01$; * $p \leq .05$.

## Validade discriminante

As versões Portuguesas do DISABKIDS – Módulo para a Asma mostraram diferenças na QdVrS das crianças e adolescentes em função dos níveis de gravidade da asma, sendo que as crianças com asma persistente (ligeira, moderada ou grave) apresentaram menor QdVrA global (hetero-relatada), maior impacto dos sintomas (auto e hetero-relatado) e mais preocupações relacionadas com a asma (hetero-relatadas), comparativamente às crianças/adolescentes com asma intermitente. O questionário mostrou ainda sensibilidade discriminativa em função do grupo etário e do sexo das crianças e adolescentes, tendo sido observado um maior comprometimento da QdVrA nas crianças mais novas (auto-relatada) e do sexo feminino (auto e hetero-relatada) (cf. Tabela 5).

**Tabela 5 |** QdVrS em função da gravidade da asma, do grupo etário e do sexo das crianças/adolescentes

| ***Níveis de gravidade da asma*** | | | | | |
|---|---|---|---|---|---|
| | | Asma Intermitente | Asma persistente | | |
| | | *M* (*DP*) | *M* (*DP*) | *Z* | *p* |
| Domínio Impacto | Auto-relato | 13.41 (4.59) | 17.57 (4.50) | -1.92 | .05 |
| | Hetero-relato | 13.69 (3.56) | 16.86 (4.34) | -1.80 | .07 |
| Domínio Preocupações | Auto-relato | 13.66 (4.29) | 16.29 (4.61) | -1.22 | n.s. |
| | Hetero-relato | 12.76 (2.89) | 16.14 (4.60) | -1.81 | .07 |
| QdVrA global | Auto-relato | 38.93 (8.50) | 32.14 (9.03) | -1.64 | n.s. |
| | Hetero-relato | 39.55 (5.94) | 33.00 (8.81) | -1.73 | .09 |
| ***Grupo etário*** | | | | | |
| | | Crianças | Adolescentes | | |
| | | *M* (*DP*) | *M* (*DP*) | *Z* | *p* |
| Domínio Impacto | Auto-relato | 15.44 (3.99) | 13.00 (5.35) | -1.82 | .07 |
| | Hetero-relato | 13.72 (4.04) | 14.89 (3.71) | -0.90 | n.s. |
| Domínio Preocupações | Auto-relato | 15.78 (4.28) | 12.56 (4.03) | -2.37 | .02 |
| | Hetero-relato | 12.67 (3.29) | 14.17 (3.60) | -1.32 | n.s. |
| QdVrA global | Auto-relato | 34.78 (7.81) | 40.44 (9.22) | -2.11 | .03 |
| | Hetero-relato | 39.61 (7.02) | 36.94 (6.84) | -1.18 | n.s. |

**Tabela 5** | QdVrS em função da gravidade da asma, do grupo etário e do sexo das crianças/adolescentes (cont.)

| ***Sexo das crianças/adolescentes*** | | | | | |
|---|---|---|---|---|---|
| | | Masculino | Feminino | | |
| | | *M* (*DP*) | *M* (*DP*) | *Z* | *p* |
| Domínio Impacto | Auto-relato | 12.90 (4.95) | 15.88 (4.21) | -1.84 | .07 |
| | Hetero-relato | 12.50 (3.15) | 16.56 (3.54) | -3.13 | < .01 |
| Domínio Preocupações | Auto-relato | 13.65 (5.07) | 14.81 (3.47) | -1.37 | n.s. |
| | Hetero-relato | 11.70 (2.43) | 15.56 (3.46) | -3.35 | < .01 |
| QdVrA global | Auto-relato | 39.45 (9.69) | 35.31 (7.45) | -1.71 | .09 |
| | Hetero-relato | 41.80 (5.01) | 33.88 (6.64) | -3-34 | < .01 |

## Concordância inter-avaliadores

A nível individual, os Coeficientes de Correlação Intraclasse (ICC) revelaram concordância moderada na avaliação do Impacto e concordância fraca na avaliação da QdVrA global. Ao nível grupal, não foram encontradas diferenças estatisticamente significativas entre as pontuações médias do auto-relato das crianças/adolescentes da sua QdVrS e as pontuações médias do auto-relato dos pais/cuidadores familiares (cf. Tabela 6).

**Tabela 6** | Concordância entre auto-relatos das crianças/adolescentes e hetero-relatos dos cuidadores familiares

| | Auto-relato | Hetero-relato | | | |
|---|---|---|---|---|---|
| | *M* (*DP*) | *M* (*DP*) | ICC | *t* | *p* |
| Domínio Impacto | 14.22 (4.81) | 14.31 (3.87) | .50$^{**}$ | -.11 | n.s. |
| Domínio Preocupações | 14.17 (4.41) | 13.42 (3.48) | .20 | .89 | n.s. |
| QdVrA global | 37.61 (8.90) | 38.28 (6.96) | .39$^{**}$ | -.45 | n.s. |

$^{**}$ $p \leq .01$; $^{*}$ $p \leq .05$.

# Discussão

Face ao crescente interesse a que se tem assistido nos últimos anos pela QdVrS e consequente proliferação de instrumentos para a sua avaliação, os procedimentos de adaptação transcultural têm surgido como uma preocupação premente, assumindo o conceito de equivalência uma importância nuclear, tanto a nível conceptual como metodológico (Herdman, Fox-Rushby, & Badia, 1997). As versões Portuguesas do DISABKIDS – Módulo para a Asma foram construídas com base numa abordagem sequencial (Bullinger, 1997), pelo que os procedimentos de validação semântica se tornam imprescindíveis como forma de assegurar a sua equivalência conceptual aos questionários originais. A impressão geral das versões Portuguesas do DISABKIDS – Módulo para a Asma foi bastante positiva, confirmando a relevância dos itens para a avaliação da QdVrA pediátrica, assim como a sua compreensibilidade e adequação da escala de resposta, indo ao encontro dos resultados obtidos no estudo de validação semântica das versões Portuguesas do Módulo Genérico DISABKIDS-37 (Carona et al., 2011). A entrevista cognitiva revelou-se um procedimento essencial na identificação de problemas na compreensão dos itens, tendo contribuído para a reformulação do item 11 e para confirmar a equivalência conceptual dos itens entre as versões Portuguesas e as versões originais do questionário.

O estudo psicométrico exploratório das versões Portuguesas do DISABKIDS – Módulo para a Asma revelou uma boa consistência interna, com valores superiores ao mínimo de .70 considerado aceitável pelo *Scientific Advisory Committee of the Medical Outcomes Trust* (SAC, 2002), exceptuando o domínio Preocupações da versão de hetero-relato. Embora inferiores aos valores de consistência interna encontrados no estudo psicométrico original do questionário ($\alpha$ = .83 para o domínio Impacto e .84 para o domínio Preocupações, na versão de auto-relato; The DISABKIDS Group Europe, 2006), os valores de $\alpha$ de *Cronbach* encontrados na presente amostra aproximam-se dos encontrados nas amostras parcelares de cada um dos países envolvidos no projecto DISABKIDS (Baars et al., 2005). As correlações fortes a muito fortes encontradas entre os domínios do questionário indicam boa validade de constructo, sugerindo que a interpretação dos seus resultados é suportada pelas implicações teóricas subjacentes ao constructo de QdVrS específica para a asma (SAC, 2002). As versões Portuguesas do DISABKIDS – Módulo para a Asma apresentaram ainda validade discriminante entre níveis de gravidade da asma, entre faixas etárias e entre sexos das crianças/adolescentes. Não obstante a natureza exploratória deste estudo, a menor QdVrS apresentada pelas crianças e adolescentes com asmas mais graves vai ao encontro da literatura (e.g., Everhart & Fiese, 2009). Este resultado é particularmente interessante no sentido em que reflecte a sensibilidade do questionário aos aspectos clínicos da asma e ao seu impacto no funcionamento e bem-estar das crianças/adolescentes, e justifica a necessidade de avaliação da QdVrS específica para esta CCS. As diferenças encontradas na QdVrS em função da idade e do sexo das crianças e adolescentes revelam ainda sensibilidade do questionário às questões desenvolvimentais. A concordância fraca a moderada entre o auto-relato das crianças/adolescentes da sua QdVrS e o hetero-relato dos cuidadores salienta a necessidade de incluir ambas as fontes de informação para uma avaliação compreensiva da QdVrS (e.g., Eiser & Morse, 2001a), privilegiando a informação veiculada pelas crianças/adolescentes e considerando a percepção dos cuidadores não como seus representantes, mas como fontes complementares de informação.

Tratando-se de um estudo exploratório, devem ser consideradas algumas limitações importantes. Apesar de seguir as directrizes do Grupo Europeu DISABKIDS (The DISABKIDS Group Europe, 2004), o tamanho reduzido da amostra é uma das principais limitações deste estudo, pois restringe a utilização de procedimentos estatísticos mais complexos e reduz o poder estatístico dos testes utilizados. Outra limitação prende-se com o método não probabilístico de recolha da amostra que, para além das implicações ao nível da generalização dos resultados, teve como consequência uma distribuição não homogénea de algumas variáveis clínicas e sociodemográficas da amostra. Não obstante estas limitações, o bom desempenho psicométrico do DISABKIDS – Módulo para a Asma nesta amostra de crianças/adolescentes Portugueses motiva a necessidade de prosseguir para o estudo das suas propriedades psicométricas numa amostra mais alargada e representativa – fase de estudo de campo (The DISABKIDS Group Europe, 2004). Os resultados encontrados neste estudo mostram ainda a necessidade de estudos futuros que examinem factores clínicos, sociodemográficos e psicossociais associados a melhor QdVrS das crianças/adolescentes com asma.

Em conclusão, as versões experimentais Portuguesas do DISABKIDS – Módulo para a Asma revelaram-se adequadas para a avaliação auto e hetero-relatada da QdVrS das crianças e adolescentes com asma. A sua tradução e adaptação numa perspectiva transcultural têm implicações a diversos níveis, nomeadamente epidemiológico, clínico e das políticas de saúde (Bullinger, 1997). Ao avaliar as especificidades do impacto físico, social e emocional da asma e dos tratamentos no funcionamento e bem-estar das crianças e adolescentes, este questionário torna-se uma ferramenta fundamental no trabalho multidisciplinar no contexto dos cuidados de saúde pediátricos, possibilitando a avaliação dos custos e benefícios dos tratamentos, a detecção de morbilidades latentes e de necessidades específicas de intervenção, permitindo uma planificação de estratégias e alocação dos recursos de saúde mais eficazes, visando a melhoria da saúde e do bem-estar destas crianças e adolescentes.

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