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ESCP International Secretariat

Theda Mansholtstraat 5b
2331 JE Leiden
The Netherlands
Phone: +31/71-5722430
Fax: +31/71-5722431
E-mail: secretariat@escp.nl
Http: www.escp.nl

Introduction to the proceedings

Pharmaceutical care, hospital pharmacy, clinical pharmacy - what is the difference ?

Evidence-Based Pharmaceutical Care was the title of the 27th Annual Symposium of the European Society of Clinical Pharmacy (ESCP) in Jerusalem in 1998. *The effect of patient-focused care on the activities of clinical pharmacists* was the title of a lecture at the 3rd Congress of the European Society of Hospital Pharmacy in Edinburgh in the same year [1]. Coincidence? Certainly not. It shows a new approach to the pharmaceutical profession and a new understanding of the function of the pharmacist, formulated mainly during the last decade.

After centuries of the acceptance by our societies of the specialised knowledge required in the preparation of medications and a clear separation of the responsibilities of the apothecary from the physician, this pattern was disrupted in the 20th century, when an increasing number of pharmaceutical manufacturers entered in to "competition" with the primary role of the pharmacist as a compounder of drugs. Although the procurement, storage, and dispensing of prescribed medications involve a significant societal responsibility in terms of safety and efficacy of drug therapy, a conviction has developed within the pharmacy profession, that the professional knowledge of pharmacists was not used to its full potential. Activities to assure the safe and appropriate use of drugs became a new target leading to activities in the direction of more patient related aspects of drug therapy [2]. This perception was present at about the same time on both sides of the Atlantic and most pertinently by hospital pharmacists and, mainly in the US, also by pharmacists involved in education. It was logically named "Clinical Pharmacy", meaning a pharmacy activity directed to and in contact with the patient.

The leaders of this new approach wanted to reinforce their message by founding professional organisations preoccupied with the teaching and practical development of Clinical Pharmacy. In 1979 the birth of the American College of Clinical Pharmacy (ACCP) and the European Society of Clinical Pharmacy (ESCP) took simultaneously place. The development of the discipline was impetuous in the States and had an enormous impact on education, changing the image of the pharmacist very consistently in hospital and later also in the ambulatory setting and in community. In commission of the ESCP a scenario analysis concerning the future of the profession was elaborated which showed that the pharmacist, if he wants to keep a key role in our healthcare system, has to move away from his clerk and controller role and assume an active responsibility as care manager [3]. This finding is important, because in Europe - with the exception of the U.K. which for historical and linguistic reasons is stronger influenced by the US – patient-oriented pharmacy was rather slow to develop and often limited to some visionaries. The main reasons considered for the time lag in the development of the new role of the pharmacist in Europe are:

1) the historically warranted monopolistic position of the profession which was not contributing to stimulating the need for change;
2) the many educational systems and languages which separate the numerous European countries from each other;
3) the lethargy of teachers at our universities who lost contact with the new reality of the profession.

If on the academic level initiatives were hardly adopted to implement a new orientation of the profession, hospital pharmacists, directly confronted with the negative impact of poor pharmaco-therapy on patient's health and on costs, recognised first the importance of adopting the concept of Clinical Pharmacy in practice. In the recent years there has therefore been a spread of activities which can be all integrated under the term "Clinical Pharmacy": drug-information centres, drug formularies, elaboration of therapeutic guidelines, pharmaco-epidemiology, pharmaco-economy, clinical nutrition, centralised cytostatic-preparation, intravenous admixture programs, therapeutic drug monitoring, and of course, the presence of the pharmacist in the different departments and units of the hospital, providing clinical pharmacy services directly to the patient.

"Clinical" is in many European languages almost synonymous to "hospital" and the first application of Clinical Pharmacy (in hospitals) reinforced this message. To demonstrate that the new activities are not at all restricted to the hospital, the definition of the goals of the ESCP have been deliberately formulated as follows: " Developing and promoting the rational and appropriate use of medicines by the individual and by society" and there is since many years a strong conviction in the Society, that there is a need to better integrate pharmacists working in community pharmacies and in ambulatory care and in primary care. Many professionals working in these fields are frustrated about the professional perspectives, the gap between studies and practice and are conscious about their changing societal role. The formulation of new opportunities and responsibilities under the denomination "pharmaceutical care" [4] had therefore a world-wide echo and even so pharmaceutical care is an integrated part of the discipline "Clinical Pharmacy", the identification with the new expression was much easier for community pharmacists. The title of last years ESCP Annual Symposium in Jerusalem was hence to stress the message that there is a scientific society which is actively involved in promoting the idea of "pharmaceutical care" in Europe. The increasing professionalism of the International Secretariat of the Society and the building up of a strong collaboration with the SIR (Stevenshof Institute for Research) in Leiden, a University bound Institute with a postgraduate course in practice-oriented pharmaceutical research, shall maintain the pioneer role of the Society in the development of a new professional image and stronger co-ordination in this field in Europe.

The pharmaceutical profession can play an important role in the changing healthcare systems as far as education and training are adequately adjusted to prepare students for their future roles. The early integration of students as a "pressure group" is important to change education. For the first time, a Student's Symposium organised by the European Pharmacy Student Association (EPSA) together with the ESCP will be held in 1999 prior to its Annual Symposium [5], The title "From Student to Clinical Pharmacist: Bridging the Gap" can further contribute to change professional understanding in the upcoming generation. National and international societies can also make pressure to change the curriculum as to integrate a high level background in pharmacotherapeutics, preparing the pharmacist for a greater involvement in the prescribing process, along with the basic underlying sciences which are a condition for the development of pharmacy as a science oriented profession. It is important that more and more practitioners are integrated in the teaching process at University level, to bring science and practice together for the best of the patient.

We should not see any antagonism between clinical pharmacy, hospital pharmacy, community pharmacy and pharmaceutical care. The latter fits easily in the concept of Clinical Pharmacy which will have to integrate a growing part of the activities of community and hospital pharmacists. Clinical Pharmacy is therefore not limited to one of them but has an overlapping character which can contribute to a better understanding between the different professional categories. Moreover it is an extremely helpful concept to prepare pharmacists for an integrated healthcare system with minimal separation between hospital and ambulatory care.

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5 1st EPSA / ESCP Student Symposium 13 October 1999 Berlin, prior to the 28th Annual Symposium of the ESCP.

G.L. Zelger (Past President)

G.Scroccaro (President)

Y.A. Hekster (Vice President)

A. Floor-Schreudering (Director of the ESCP)

ESCP PRESS RELEASE

ESCP 28th European Symposium on Clinical Pharmacy
Bridging the Gaps – The Future of Clinical Pharmacy
14th –16th October 1999
Berlin, Germany

Although our goals are still the same, Clinical Pharmacy had and has to adapt to a changing world. One of the big challenges in the future is to bridge gaps among different health care activities, professions and disciplines. Because of its interdisciplinary orientation and its unique combination of scientific and practical activities Clinical Pharmacy is predestined to do this job.

It is our pleasure to invite you together with the Federal Union of German Associations of Pharmacists (ABDA) and the German Association of Hospital Pharmacists (ADKA) to the 28th European Symposium on Clinical Pharmacy with the main theme "Bridging the Gaps – The Future of Clinical Pharmacy", which will take place in Berlin, Germany, from 14th to 16th October 1999.

The scientific programme will focus on interesting subjects for Clinical Pharmacists in community, hospital and academia, where co-operation and joint efforts are most needed. As in previous years the Symposium is an excellent opportunity to meet up with colleagues and to exchange ideas and experiences on all areas of Clinical Pharmacy.

The Symposium will be held close to the historic centre of the city where you can feel the spirit of different centuries and observe the rise of a new European metropolis bridging Eastern and Western Europe.

We look forward to welcoming you to Berlin in October 1999!

Maria Rivera
President of the Symposium

Giovanna Scroccaro
President ESCP

ESCP Spring Conference on Clinical Pharmacy
Clinical Pharmacy Skills for the New Therapeutic Horizons
11th –13th May 2000
Reykjavik, Iceland

It is our pleasure to invite you together with the Pharmaceutical Society of Iceland to participate in the Spring Conference of the ESCP which will be held in Reykjavik, 11th –13th May 2000. The theme of the Conference is Clinical Pharmacy Skills for the New Therapeutic Horizons.

The scientific programme will appeal to clinical pharmacists both in the hospital and the community settings. In the plenary sessions distinguished practitioners will address the question: What clinical skills does the pharmacist need as a clinical practitioner, as a clinical scientist, as drug evaluator, and as an educator? In the workshops you will get an opportunity to exchange ideas and experiences on research projects, patient monitoring and small group teaching to name a few of the topics. Round table conferences, mini-symposia, short communications and poster sessions will add to the possibilities for pharmacists from all over Europe to meet with colleagues and share views and experiences.

Reykjavik, the venue of the Conference, offers you the opportunity to enjoy the clean atmosphere of a city next door to nature, the charm of the old small town mingled with the vivid development of a modern city. Reykjavik will be one of eight European cultural cities in the year 2000 so a lot of cultural activities can be expected. Besides, 1000 years of Christianity in Iceland will be commemorated this year as well. Not to forget the physical needs, being situated in a geothermal area, Reykjavik offers you a considerable number of swimming pools where you can let the warmth of the natural hot water relax your stressed muscles.

We look forward to welcoming you to Reykjavik in May 2000.

Kristján Linnet
President of the Conference

Giovanna Scroccaro
President ESCP

For more information on the above mentioned Conferences or on ESCP please contact ESCP International Secretariat, Theda Mansholtstraat 5b, 2331 JE Leiden Tel: +31/71-5722430 Fax: +31/71-5722431 E-mail: secretariat@escp.nl.

PLENARY LECTURES

1 WHAT IS THE RATIONALE FOR BASING DECISIONS ON EVIDENCE?

A. Stevens

If the rationale for basing decisions on evidence is itself self-evident, it is curious that it was not always thus. Indeed the evidence based health care movement is something of a revolution. There is a proliferation of journals dealing solely with the evidence base of health care. Conferences on the subject are appearing at an unprecedented pace. And there is serious investment in strengthening the evidence base of health care.

Academic efforts to furnish the evidence base of health care have long existed. The current revolution has three distinct antecedents in: (1) cost-effective analyses produced by health economists in a trickle from the mid 1970s to a torrent in the 1990s; (2) the evidence based medicine movement itself with its roots in clinical settings as a way of defining and resolving clinical problems; (3) health technology assessment initiatives — the earliest in the United States set up in 1972 — but in many other countries since — in which the focus is on the production of evidence with both a clinical and policy relevance.

These three traditions have been brought together by the growing appetite for evidence based health care. This appetite exists at a political public health and clinical level. It follows from three related observations made in many countries on the rapid rise of the cost of health care — with new technologies from a variety of innovations in genetics, biomaterials and IT for example; on increasing anxieties about ineffective health care or its corollary of delayed effective health care; and on the establishment of a cadre of health care management professionals whose job it is to be responsible for cost-effectiveness monitoring — in the UK this was notably mediated by the purchaser-provider split.

The response to these observations have been a multiplicity of initiatives designed to overcome (1) the lack of availability of relevant high quality information e.g. through the Cochrane collaboration; (2) access problems to relevant high quality information e.g. through a variety of evidence based compendia; (3) inadequate skills in finding, appraising and acting on evidence e.g. through the critical appraisal skills programme, and (4) barriers in the organisation of work or care such as through the development of guidelines.

Clearly the underlying rationale for evidence based decision-making rests on anxieties about its alternatives: anecdote experience and conventional wisdom-based decision-making. There is a variety of evidence that the traditions of decision-making not using high quality evidence is flawed, classically in the have of the immediate treatment of coronary artery disease, but in almost every other area of health care delivery too.

However, the rationale for work for those in evidence based health care must also depend on how successful it is in taking the place of alternative means of decision making. When innovations in encouraging evidence-based decisions are themselves put to experimental test, the results are not always encouraging although at a pan-clinical level. There is a growing sea change in the use of evidence in health care.

United Kingdom

2 HOW IS EVIDENCE IN HEALTH CARE EVALUATED?

Antonio Nicolucci

There is a general agreement that clinical decisions should be based on the best scientific evidence, and the need for systematically finding, appraising, and using research findings as the basis for clinical-problem solving (evidence based medicine, EBM) has been often underlined.
The synthesis of the available scientific evidence is obtained by systematic literature reviews, with the aim of establishing the real yield of a medical procedure, the consistency of research findings and their generalisability to different patient populations and settings. The use of explicit methods in the identification, quality assessment and, where appropriate, quantitative combination of study results (mesa-analysis), allows to limit bias and improve reliability and accuracy of conclusions.
While a great attention has been devoted to the development and standardisation of the procedures underlying EBM and to the production of evidence-based clinical practice guidelines, it is still not clear how we can assess whether medical decisions in the real world are evidence based.
The major limitation is indeed related to the discrepancy between the narrow focus of research results, addressing specific questions, and the complexity of most clinical problems. Furthermore, evidence from randomised controlled trials mainly refers to pharmacological interventions, and many areas of uncertainty still remain for other aspects of clinical practice (prevention, diagnosis, rehabilitation).
It has also been emphasised that a truly evidence-based medicine does not consist in the mere application of trials results in routine practice, but must incorporate patient preferences and priorities in the decision process.
In the presentation, possible solutions to overcome the dichotomy ‘evidence based yes/not’ will be proposed by including some measures of the multifaceted doctor-patient interactions.

Department of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, 66030 S. Maria Imbaro (Ch), Italy

3 HOW IS EVIDENCE IMPLEMENTED IN THE USE OF MEDICINES?

J. Bonal

During the last decades, clinical pharmacy has been developed in many hospitals in Europe, sometimes with conflicts related to professional competition with other members of the health care team. Legislation in different countries has stated the need to implement clinical pharmacy practice in hospitals as well as in community setting. WHO recommendations (1) are also underlying clinical pharmacy as a one of the essential activities required for European health systems.

Efficient drug prescription and use is a permanent challenge in health care. Cost/Effective decision making presents many difficulties and limitations, most of them related to the lack of relevant information for a particular health care environment, specially for the effectivity understood as the effect of the therapy out of the frame of randomised clinical trials (RCT). However, when there is evidence, problems are related to a scarce use of it in the decision making process (2). The effectivity of a drug depends on several factors related to the health context, particularly appropriate indication, clinical characteristics of the patient or comorbidities, dose prescribed, compliance of the patient and therapeutic monitoring level.

Research on efficacy and effectivity are frequently based on intermediate indicators instead of final endpoints. This fact is adding confusion on prescribing decision making.
Although poorly validated biological indicators are frequently used as outcomes, they are not useful as final health outcomes (3).

Walker (4), talking about relevance of outcome measures in pharmaceutical care outcomes, stated that desired outcomes can be expressed by the following equation:
Pharmaceutical care outcomes = Pharmacoterapy outcomes + Pharmacy service outcome

This means that to achieve an efficient pharmaceutical care we need not only evidence of pharmacotherapy but also evidence on the effectiveness of pharmacy services we are providing. If evidence on drug prescribing is not easy to obtain and when exist it is not frequently used, evidence on pharmacy service outcomes is even less frequent and there are very few articles showing such evidence as has been pointed by Hekster (5).

Some studies evaluating clinical and pharmaceutical care outcomes will be presented, emphasising those based on solid endpoints demonstrates how clinical pharmacist intervention is improving patient health in terms of cure of the disease, prevention of toxicity and side effects, morbimortality, patient satisfaction and value for money.

Health politics in Europe and inter-professional competition, will drive Pharmacy to a higher degree of specialisation and to document better outcome evaluations in order to offer evidence of the efficacy of clinical pharmacy practice in terms of health care outcomes, as well as evidence on the value for money of such pharmaceutical service.

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Barcelona, Spain

4 EVALUATION OF CLINICAL AND ECONOMIC OUTCOMES: A CASE STUDY WITH HEPATITIS B VACCINES

T. Jefferson

The notable increase in quantity of economic evaluations in the last two decades has not been matched by good methodological standards. This problem has present in the field of economic evaluations of Hepatitis B vaccines, universally used to justify decisions to vaccinate whole populations. Traditionally single studies have been evaluated with little regard to a population of similar studies. However, serious methodological problems are highlighted when a population approach (systematically conducted reviews) is applied to the topic. The results of two systematic reviews conducted by in1993 and 1996 showed three problem areas. A sizeable minority of reports of economic evaluations of HB vaccines are unclear as to the study question, showing a basic ignorance of the first rule of conducting scientific research. Secondly, the basic epidemiological assumptions upon which the economic models are based showed variability that persisted even after stratification. This finding raises the question of the accuracy of the epidemiological knowledge base of hepatitis B and its progression. Lastly, a further minority of studies show weaknesses in the basic methods of conducting and reporting economic evaluations. Examination of these problem areas leads to the conclusion that no assessment of the efficiency of hepatitis B vaccines can be drawn from the evidence. Addressing the problem of poor methodological standards concerns the whole research community but, as a proportion of economic evaluations are published, one obvious mean of exerting pressure to increase and maintain methodological standards is the editorial and peer review process. Readers of economic evaluation literature should beware of uncritical acceptance of study conclusions without appraisal of the methods used in the study.

Edmund Parkes Professor of Preventive Medicine, Cochrane Vaccines Field, Army Medical Directorate, Ministry of Defence, Keogh barracks, Ash Vale, Hants GU12 5RR, E-mail: zorria@epinet.co.uk.

5 PHARMACEUTICAL CARE IN PSYCHIATRIC DISEASE

A. Dorevitch

Psychiatric pharmacy services in Israel include clinical, teaching and research activities. A psychiatric clinical pharmacist monitored medication response over a 10-year period for chronic schizophrenic outpatients. Successful treatment resulted in a decreased rate of re-hospitalisation, shorter length of hospital stay and decreased total neuroleptic dosage as compared to the 10-year period prior to entry into the study. Another study in the inpatient psychiatric facility describes 109 physician-initiated consultations that were directed to the clinical pharmacist. Of the 229 recommendations made by the psychiatric pharmacist 103 (88.2%) were accepted. Major question types included: side-effects, non-response, preventive measures and mixed factors. Sixty-seven percent of patients exhibited a very satisfactory or satisfactory response as measured by global effectiveness of pharmacist interventions. Psychiatric clinical pharmacy services though cost-effective and available in Israel have yet to be sufficiently expanded to meet current needs.

Clinical Senior Lecturer, Hebrew University Faculty of Medicine, and Talbieh Mental Health Center, 18 Disraeli St., Jerusalem, Israel

6 EVIDENCE-BASED PHARMACEUTICAL CARE IN EPILEPSY

M. Bialer

Epilepsy is a common and chronic disease which affects 1 % of the global population. At present there are four major (established) antiepilepltic drugs (AEDs): phenobarbital, phenytoin, carbamazepine and valproic acid. About 25% of epileptic patients do not respond to these major AEDs, and their therapy is associated with side effects including teratogenicity and hepatotoxicity and pharmacokinetic drug interactions. In the last decade a numbers of new AEDs have been approved across the world. These new AEDs are: gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate, vigabatrin and zonisamide. The advent of the new AEDs brought a welcome expansion to the pharmaceutical care and pharmacological armamentarium against epilepsy. However it also made therapeutic decisions more complicated because physicians and clinical pharmacists are now confronted with an array of about 15 different AEDs, whose relative merits have not been fully characterised. A clinical choice of AED should be based firm evidence generated in randomised clinical trials, in which drugs efficacy and tolerability are investigated.
In the current presentation assessment of the pharmacodynamics (PD) and pharmacokinetics (PK) of the new AEDs in patients with refractory (therapy resistant) epilepsy will be assessed. The major PD criterion for outcome assessment or evidence-based pharmaceutical care in epilepsy is seizure counts. There is a clear evidence that each of the above new AEDs is better than placebo at preventing seizures. The analysis of the new AEDs is based on the percent of refractory patients who have a more than 50% reduction in their seizure frequency. In addition, reported side effects and percent withdrawal from clinical trials also have to be included. This comparative PD-PK analysis is done in order to characterise the current status of evidence-based pharmaceutical care in epilepsy.

Department of Pharmaceutics, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem, POB 12056, Jerusalem 91120, Israel.

FREE COMMUNICATIONS

1 EVIDENCE-BASED PHARMACEUTICAL CARE: WHICH EVIDENCE FROM LITERATURE?

M. Romereo, G. Di Sabatino, F. Ravaioli, C. Spoltore, C.N. Venanzi

Background: Evidence-based concept is a new emerging paradigm for medical and pharmaceutical practice. It de-emphasises intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research.

Aims: To know how the evidence based concept fit in with the normal activities of clinical pharmacy and to review the contributions of clinical pharmacy to delivery an evidence-based pharmaceutical care.

Methods: A medline review of the literature from January 1995 through April 1998 was conducted. Various research's strategies were carried out through different keywords combinations, such as 'evidence-based pharmaceutical care', 'evidence-based healthcare', 'evidence-based medicine' and 'clinical pharmacy', 'evidence-based approach' and 'clinical pharmacy' or ' pharmaceutical care'.

Results: The combination of key words has turned out to be unsuccessful. On the contrary, a total of 126 citations were identified using 'pharmaceutical care' alone. The main results of our research can be summarised in three points:

1. Few research studies (18%) have evaluated the provision of pharmaceutical care in a defined population or disease or setting: elderly patients (3 studies); chronic illness (2 studies); diabetes, asthma, HIV (2 studies each); cancer (1 study); acute care setting, outpatient dialysis setting (1 study each), etc.
2. A substantial number of studies (50%) discussed the pharmacist's functions and responsibilities in providing pharmaceutical care. In particular, the following aspects have been considered fundamental: measuring therapeutic outcome; establishing a pharmaceutical care database; developing models of pharmaceutical care for educating students; establishing patient-pharmacist relationships and implementing collaboration with physicians based upon consensus guideline.
3. The practise of evidence based pharmaceutical care seems to be still unusual. No article discussed about the evidence-based concept. The aforementioned studies, however, did not follow the evidence-based approach in asking for considerable clinical questions, finding and appraising relevant data, and harnessing that information for everyday clinical practice.

Conclusion: Evidence based medicine requires new skills of the health care providers, including efficient literature searching and application of formal rules of evidence evaluating the clinical literature. Professional associations have an important role to play in ensuring that research-based information is included in educational activities and clinical as well as pharmaceutical guidelines.

Centro Studi SIFO, Consorzio Mario Negri Sud, Santa Maria Imbaro (Chieti), Italy

2 EFFECTS OF TWO INTERVENTIONS ON THE PHARMACOTHERAPY DURING AND AFTER HOSPITAL STAY IN PATIENTS ADMITTED TO GENERAL MEDICAL WARDS

H.S. Lau, M. Klerkx, A.J. Porsius, A. de Boer

As avoidable iatrogenic illness is common, there is great need for interventions that improve appropriate drug prescribing. We studied the effects of two interventions, one based on providing additional information from the community pharmacy on the medication used before hospital admission (intervention A) and one based on that same information supplemented with a detailed report on drug-related problems set up by on expert panel (intervention B), on the pharmacotherapy during hospital stay and at hospital discharge, and length of hospital stay of patients admitted to general medical wards.
Patients admitted to the general ward of 2 acute care hospitals were included in the study. In one hospital patients were randomised over an intervention group who received intervention A (n=75), and a control group (n=77). In the other hospital, patients were randomised over an intervention group who received intervention B (n=55), and a control group (n=52). The length of admission in the control group, the intervention group A, and the intervention group B were 16.5 (14.4-18.6), 12.6 (10.2-15.0) and 15.3 (11.9-18.8) days, respectively. The number of drugs during admission were 7.5 (6.7-8.2), 7.1 (6.0-8.2), and 8.6 (7.1-10), in the 3 groups, respectively. Results for the number of drugs at discharge were 4.6 (4.1-5.1), 4.4 (3.7-5.2), and 4.9(3.8-5.9), for the number contraindicated drugs in discharge medications 0.45 (0.27-0.63), 0.26(0.10-0.43), and 0.46(0.19-0.74), for the number of drug interactions in discharge medication 0.48(0.30-0.65), 0.47 (0.25-0.69), and 0.73 (0.28-1.2), and for the reduction in the number of drug related problems as evaluated by an expert panel 35%, 25% and 23% in the 3 groups, respectively. The differences between the intervention groups and control group were not statistically significant, except for the length of admission between intervention A and the control group. Regardless of intervention or control group, the proportion of drugs that was not continued during admission was increased for those drugs that were not registered in the medical records (40-61%) in comparison with drugs that were registered (13-20%).
We conclude that interventions that are solely based on written recommendations to improve appropriateness of medication prescribing in patients admitted to general medical wards have no effect on the number of drugs prescribed during hospital stay, the number of drugs, the number of contraindicated drugs or the number of drug interactions at discharge, the length of hospital stay, or the number of drug related problems as evaluated by an expert panel. Failure of registration in the hospital medical records of drug use before admission may be associated with unintentional discontinuation of drug therapy during admission.

Department of Pharmacoepidemiology & Pharmacotherapy, Faculty of Pharmacy, Utrecht University, Utrecht, The Netherlands

3 EVALUATION OF DRUG MONITORING PRACTICES: EFFECTS OF AN EDUCATIONAL CAMPAIGN

E.R. Smith*, A.C. Greenberg, A. Yinnon**

Following the introduction of once-daily aminoglycoside dosing, the clinical pharmacists noticed that some confusion existed in the correct manner of monitoring blood levels for these drugs as well as for the other commonly monitored antimicrobial, vancomycin. An audit was carried out to determine what the problems were and their extent, and to try and improve the process of blood level monitoring of antibiotics through an educational effort directed at the medical staff by the clinical pharmacists of the hospital. The study consisted of two stages interspersed with an educational campaign. Patients eligible for the study were those receiving either gentamicin, amikacin or vancomycin or any aminoglycoside and vancomycin. Patients included all adults, children and neonates who had been receiving therapy with these drugs for at least 48 hours during the study periods. The three steps of drug level monitoring were assessed -1. Reason for ordering 2. Accuracy of blood level taking and 3. The doctor's response to the results of the blood levels. Between the two stages an educational effort was made to increase the medical staff's awareness and knowledge of antibiotic level taking. During this stage a new form for antibiotic drug level requests was introduced. The new form allowed the clinical pharmacist's recommended changes to be documented on the form. The second stage of the study took place after the education campaign and was used to assess whether there had been an improvement in staff competence in the correct manner of ordering, taking and interpretation of serum drug levels after the educational effort. In the first stage of the study 161 patients were entered and in the second stage 198 patients. The results for step one, the reason for ordering showed a small increase in the number of justified requests between the two stages in the medical (70.2% in stage 1 to 72.7% in stage 2) and surgical departments (70.4% justified in stage 1 to 72.9% in stage 2). However the intensive care departments showed a significant decrease in the number of justified requests (65.7% is stage 1 to 42.9% is stage 2). $p<0.005$. For step two - assessment of serum level taking- a small but statistically insignificant improvement in the serum level taking for each of the three drugs is seen between the two stages. When the results were pooled and compared for appropriateness of serum level taking there was also an improvement in all three categories of departments. These results however, did not reach statistical significance. A significant ($p< 0.001$) improvement in the correct interpretation of the serum drug results (step three) was shown between stage one and stage two. When the departments were pooled, improvements in the interpretation of results for all departments groups are seen, but it is only the medical departments that show a statistically significant ($p<0.025$) improvement. When the clinical pharmacist had direct input into the therapeutic drug monitoring process, such as in giving advice on the interpretations of the serum blood level results, then it was seen that a significant improvement ($p< 0.025$) occurred between stage one, when there was no clinical pharmacy involvement and stage two when the clinical pharmacist's recommendations regarding dosage and dosage interval were recorded on the request form that was subsequently returned to the departments. In the other two steps of the drug monitoring process, where there was no direct input of the clinical pharmacist, the results showed no significant improvement between the two stages of the study. The study shows that a clinical pharmacist can exert a significant effect on the monitoring of serum drug levels.

* Department of Pharmacy, Shaare Zedek Medical Center, Jerusalem. Israel
** Department of Infectious Diseases, Shaare Zedek Medical Center, Jerusalem, Israel

4 THE DRUG INFORMATION CENTRE AND ITS SUPPORT TO THERAPEUTIC COMMITTEE

T. Cassani, D. Guzzo, G. Scroccaro

Introduction: The Drug Information Centre (DIC) is located at the Pharmacy of University Hospital of Verona Hospital Firm (two hospitals for a total of 2.300 beds). Among other activities, DIC co-operates with the Therapeutic Committee (P&T), established in 1977 to promote a rational use of drugs within the hospital.

Objectives and methods: The aim of this study is to describe the support provided by DIC of P&T, through the analysis of the work done from 1995 to 1998.

Results: During the years 1995-1998, 16 meetings at P&T were organised as well as 6 meetings of panels of experts constituted by P&T in order to define Guidelines for the correct use of drugs and to carry out periodic revisions of the Hospital Formulary (HF).
On this purpose DIC has prepared, through the evaluation of the literature derived from bibliographical research, 107 dossiers of drugs, 6 dossiers of comprehensive review for specific problems, 13 analysis of the consumption of largely used single drugs and drugs categories.
The material arranged by DIC has allowed the P&T to take the following decisions: 74 inclusions in HF on free distribution, 34 inclusions in HF on justified request, 28 non inclusions in HF, 76 exclusions from HF, 16 suspended judgements waiting to acquire further elements of evaluation, 30 modifications of previously taken decisions, 27 confirmations of previous decisions.
Thanks to the co-operation between DIC, P&T and panels of experts, 4 HF reviews were made and 4 Guide-Lines were defined for appropriate use of specific drugs or drugs categories (antibiotic profilaxis in surgery, gabexate mesilate, octreotide and somatostatine in pancreatic disease, intravenous immunoglobulins, new lipidic formulations of amphotericin B).
In order to, disseminate the decisions of P&T, DIC has prepared 10 Bulletins (from October 1997 also available in Internet http://www.sfm.univr.it/Farmacia/sdf-txt.htm) and 15 informative sheets.
Furthermore, through the analysis of drug consumption and justified requests prepared by DIC, P&T has been able to verify the validity of the measures taken.

Conclusions: The analysis of the activity of P&T during the years 1995-1998 points out that support provided by DIC to P&T is of essential importance and it consists of: 1. Reviews of literature on drugs; 2. Co-operation with panel of experts in order to define Guidelines or HF revisions; 3. Analysis of drug consumption and justified requests to verify possible intervention areas and the impact of P&T decisions on medical practice; 4. Dissemination of P&T decisions within the hospital**.**

Department of Pharmacy - Azienda Ospedaliera 'lstituti Ospitalieri di Verona' – Italy

5 THE CENTRE FOR DRUG DOCUMENTATION: FROM THE HOSPITAL TO THE COMMUNITY

G. Dusi*, L. Bragantini*, G. Scroccaro*

Introduction: The Centre for Drug Documentation and Information (CIF) was established with a regional deliberation in 1975. While proceeding through a progressive change that led it to qualify its role as an active knowledge 'promoter' rather than a passive information 'transcriber'; CIF has become today a steady landmark for informative activity aiming at a rational use of drugs**.**

Purpose and methods: CIF activity in the years 1996-1997 has been examined by dividing answers into queries from inside and queries from outside.
As far as requests from inside are concerned we have focused on those regarding substitution of an ongoing therapy during patient hospitalisation with drugs included in the Official Hospital Formulary (PTO).

Results: During the years 1996 –1997, 418 (24.8%) requests from outside and 1270 (75.2%) requests from inside occurred.
By examining requests from outside in the same period we have observed that most of queries were concerned with side effects (12%) followed by those regarding speciality synonyms of the same active principle (9%) and by literature references (8%).
In particular the main users outside the hospital structure have revealed community pharmacists (16.5%) and citizens (16.0%)
Request from inside on behalf of physicians aiming at replacing patience ongoing therapy with branded pharmaceuticals from the Formulary represent 9% of the whole 1270 requests from inside.
Cardiovascular drugs (54%) represent the main therapeutic category for which a substitution is requested. This fact can be partly explained if we consider that there are about 196 commercially available active principles (including associations), while those included in PTO are 48 (24.5%).
Antibiotics are just following this category (4.5%).
In this latter case there are 107 commercially available active principles (and associations) of which 44 (41.1%) included in PTO.

Conclusions: The analysis performed in these years of activity has shown the importance for a Centre for Drug Documentation being open even to queries coming from outside or to those regarding therapeutics already working during hospitalisation. In order to allow and increase better relationships with general medicine physicians and patients a toll free phone number called 'green number' was created in May 1998.

* Center for Drug Documentation and Information, Verona Hospital, Italy

6 DRUG INFORMATION WEB PAGES: AN UPDATE

Venturelli A,. De Marino C., Zeuli L., *De Rosa M., *Rinieri E., **Giuliani G., Cozzolino S.

Introduction: In 1996 the Italian Society of Hospital Pharmacists planned the creation of a web site 'Eupharma' at the URL http://www.sifo.it.
The site is organised in many sections regarding the different Hospital Pharmacists fields.
The Biomedical Documentation Center of the Cardarelli Hospital of Naples carried out the task of realising the web pages related to drug information.
These pages are divided in two different sections:
- a consultive section;
- an interactive section.

The growing number of users of the Sifonetwork in Eupharma and the necessity to satisfy the mutable requirements of the Hospital Pharmacists induced a continous extension and updating work of the WebPages.
So in 1998 a project was elaborated to activate new sections in the web pages of drug documentation.

Aims:
- to create a network between the Italian Drug Information Centers;
- to create a frequent asked questions (FAQ) page: each Center will put in this page the most interesting questions about drug information;
- to promote an active participation of the Italian Drug Information Centers to on-line projects;
- to allow the use of the on-line Sifo software BBS and Start;
- to provide the Pharmacists with detailed information about all public competitions published on Italian Official Gazette;
- to permit the free use of Martindale;
- to provide the users with a temporary access to the OVID System to show its potentialities
- to create a page in which the people will put in their questions about Health World and where they will find the solution of the drug related problems.

Methods: The project is in progress but some of the aims was already realised; in fact, thanks to the collaboration of CINECA the web page about the public competitions is biweekly update. The page for the people is under construction.
Regarding the free use of Martindale and the temporary access to the OVID System, the Eupharma working group is negotiating respectively with the Medical Economics Italia srl and the Dea International Library to provide the Pharmacists with these services.

Conclusions: The activation of these new sections could promote a greater interest from the Hospital Pharmacists, other health professionals and the people in the Eupharma site.
Eupharma could be the tool:
- to improve the Hospital and Territorial Services efficiency;
- to increase the diffusion of the information and the integration of the experiences;
- to manage the problems about the Hospital Pharmacist Work.

Biomedical Documentation Center, Biofarmacological Sector, Cardarelli Hospital, Via s: giacomo dei Capri no 66, 80131 Naples, Italy.
* Consorzio Interuniversitario Cineca, Bologna
** Servizio Aziende USSL 13, Treviglio

7 AN INFORMATIVE REPORT ABOUT FULL-TEXT RETRIEVAL IN ITALY

De Marino C.,Venturelli A.,Mancini A., Scala D.,Cozzolino S., Zeuli L., *Albano M.

Introduction: In the last years the problem of bibliographic update in the pharmaceutical and biomedical fields has been partly solved thanks to the creation of specific scientific databases; in fact it is now possible to carry out researches on all over the world bibliographic reviews.
The most part of on-line or on CD-ROM bibliographic databases provide the users with the references and often with the abstract. The careful reading of the abstract allows a critical selection of the articles and the screening of the topics for the professional update.
However, for health professionals working in biomedical and pharmaceutical researches, it is often necessary to consult the full-texts or the articles.
In Italy, the full-text retrieval is often a problem so the Biomedical Documentation Center of Naples is carrying out a research to provide the Hospital Pharmacists and the other health professionals with a general picture of the situation about document delivery.

Aim: To organise an informative report about full-text retrieval in Italy.

Methods: The preliminary phase dealt with the selection of the information about the document retrieval tools. Therefore, first a bibliographic research in Medline database then an Internet research by making use of the main search engines were carried out using the keywords 'full text' and 'document delivery'.
In the executive phase, the most specific bibliographic references and the most interesting web sites was selected and then organised in a report that will provide the health operators the following information:
- the most important on-line and CD ROM full-text databases;
- the online full-text journals;
- the main Clearing Houses: document ordering, wait and payment;
- the Italian document delivery services;
- the better, the cheapest and the most reliable way to obtain a full-text.

Conclusions:
In Italy, the lack of structured information from public or independent sources make health professionals' biomedical documentation approach difficult. To facilitate the approach to information sources and to support health operators in their work it is necessary to improve the diffusion an a national scale of the informative report about full-text retrieval in Italy; it may be inserted in the Italian Society of Hospital Pharmacists web site (Eupharma) and/or published on Italian Scientific journals.

Biomedical Documentation Center, Cardarelli Hospital, Via S. Giacomo dei Capri no 66, 80131 Naples, Italy
* Doctorline Viale Certosa 148 Milan, Italy

8 QUALITY OF NUTRITION IN PATIENTS AT AN INTENSIVE CARE UNIT

M.M.P.M. Jansen*, F. Heymer, J.A. Leusink**, A. de Boer***

Adequate nutrition of patients remaining at intensive care units (ICU) is of great important since both over- and undernutrition can lead to serious morbidity and even mortality. The aim of our study was to examine whether patients at an ICU are adequately fed. A prospective follow-up was performed in 39 postoperative and non-surgical patients whom were on artificial ventilation and were at least two-day on the ICU prior to inclusion. These patients were on average 65 years old (range 23 to 88) and 40% was female. For each patient the following data were collected. First, the exact amounts of energy and macronutrients (carbohydrates, fat and proteins) given over 24 hours by parenteral and/or enteral route were calculated ('administered'). Second, on the same day indirect calorimetric measurement (DeltratrecTM II metabolic monitor) was performed over 18 hours and urinary nitrogen loss was measured over 24 hours in order to estimate energy expenditure and macronutrient usage ('measured'). Third, by means of the formula of Harris Benedict we calculated the needs for energy and macronutrients based on the clinical information obtained on the day prior to the day the indirect calorimetric measurements were performed ('calculated'). For each patient the difference between the amounts of energy, carbohydrates, fat and proteins administered, calculated and measured were calculated. Furthermore, correlation coefficients between energy amounts administered, calculated and measured were calculated.
In 30 patients (77%) the administered amount of energy exceeded the measured amount by on average 671 kcal/24h and a maximum of 2166 kcal/24h. Nine patients received insufficient amounts of energy (average 358 kcal/24h and a maximum of 1113 kcal/24h). Sixteen patients had a negative protein balance (on average 33 g of proteins shortage per 24h and maximum of 93 g/24h). Furthermore 25 patients were administered more fats and carbohydrates than were actually needed (on average 73 g and 125 g per 24h, respectively). Coefficients of correlation between measured versus administered, calculated versus administered and measured versus calculated amounts of energy were 0.19 (p=0.25), 0.03 (p=0.87) and 0.57 (p=0.002), respectively.
In conclusion, a substantial part of patients at an intensive care unit are not adequately fed. Improvement of the quality of feeding can be established by using the Harris-Benedict formula in the prescribing of nutrition.

* Department of Pharmacoepidemiology & Pharmacotherapy, Faculty of Pharmacy, Utrecht University, Utrecht
** Intensive Care Unit, St Antonius Hospital, Nieuwegein, The Netherlands

9 NUTRITIONAL SUPPORT IN CANCER PATIENT: AN EPIDEMIOLOGICAL STUDY IN THE LOCAL HEALTH UNIT OF ROVIGO – ITALY

R. Joppi*, C. Battistutta*, L. Monesi*, A. Ferraresc, S. Toso**, E. Ferrazzi****

Introduction: In the last five years, guidelines have been developed for the use of nutritional support at national as well as at international level. These guidelines intend to promote an 'evidence based' and effective use of artificial nutrition in specific diseases and/or conditions.
With regard to cancer patients the artificial nutritional is part of the supportive therapies and its aim (according to the American Society for Parenteral and Enteral Nutrition Guidelines) is to improve:
- the tumor response to anticancer therapy;
- the patient's tolerance towards the therapy;
- the patient's survival.

More and more frequently cancer patients are discharged on artificial nutrition. An European survey shows that Italy was only second to France in the number of outpatients on nutritional support. Home care for these patients strongly highlights the following problems:
1. the rational use of nutritional support;
2. the risk of complications;
3. the need for a specific training for specialists, relatives and caregivers involved in the management of outpatients.

Objectives: The purpose of this study was to evaluate the impact of nutritional support guidelines on the management of cancer patients; the role of the artificial nutrition in a global supportive care, the quality of training and information for the outpatients, their relatives and other caregivers.

Methods: Using two different questionnaires and the 'index day' methodology, data from in- and outpatients were collected. The questions focused on characteristics of the patient, type of tumor, kind of nutritional support, management of cancer related symptoms and information for outpatients and their relatives.
The data were processed according to the epidemiological computer program EPI INFO (version 6.04).

Results: In this study (one day survey) 55 adult patients (49 followed by the Oncology Unit and 6 by the Home Care Service, respectively) were recruited. Out of the 55 patients 22 were male and 33 female, the mean age was 62,9 (range 31 – 97); SD 12,86), 3 were terminal cases, 7 received nutritional support (2 were on Total Parenteral Nutrition and 5 on Enteral Nutrition). In the opinion of physicians and nurses the cancer related symptoms were well controlled in the outpatients while in one inpatient the management was estimated less than satisfactory. The outpatients were visited weekly by the physician and twice a week by the nurse. No training or information was provided to the outpatients and their relatives.

Discussion and conclusion:
1. the terminal cases did not receive TPN according to the guidelines;
2. the artificial nutrition was included in a global supportive care;
3. training or information for outpatients and their relatives or other caregivers were lacking.

These results pointed out that multicenter and collaborative epidemiological studies are needed to gather information about and improve the use of nutritional support in these patients.

Servizio di Farmacia Ospedaliera – Ospedale Civile Viale Tre Martiri – 45100 Rovigo, Italy
* Hospital Pharmacy ** Oncology Unit

10 PHARMACEUTICAL MANAGEMENT OF CLINICAL TRIALS SPONSORED BY PUBLIC ASSISTANCE OF PARIS HOSPITALS: THE INVOLVEMENT OF CENTRAL HOSPITAL PHARMACY

A. Tibi, B. Lehmann, F. Courteille-Laurencon, D. Pradeau

Public Assistance of Paris Hospitals (PA-PH) is the major French institutional sponsor of clinical trials. Pharmaceutical quality of the investigational medicinal products is of particular importance for non-industrial sponsors. In fact, various products are concerned (experimental products, non-pharmaceutical starting materials…).
Moreover, all clinical trials in France are submitted to declaration to French Drug Agency, but not to IND.
In this context, the Central Hospital Pharmacy (C.H.P.) has created a Clinical Trial Unit for the pharmaceutical management of therapeutic trials sponsored by PA-PH.
This unit is in charge of the pharmaceutical analysis of the study protocols and of drug supply (manufacturing, quality control, industrial contracts…). This also includes, for numerous multicentric trials, the packaging and labelling of patients treatment, their shipping, the returns and destruction with respect to good manufacturing practices. This unit has the support of several partners within PA-PH (Analysis Laboratory, Manufacturing unit, Quality Assurance Department of C.H.P., hospital pharmacists…) and the help of pharmaceutical companies for the supply of investigational or comparator products (placebo, marketed product…).
Up to date, Central Hospital Pharmacy works on more than 100 different clinical trials and offers a reliable structure for the management of pharmaceutical requirements of institutional clinical trials.

Central Hospital Pharmacy, Public Assistance of Paris Hospitals, 7 rue du Fer a Moulin 75005 Paris, France

11 CLINICAL TRIALS IN HYPERTENSIVE AND HYPERLIPEMIC DISEASES: REVIEW OF THE ACTIVITY OF AN ETHICAL COMMITTEE

M.P. Alberti, V. Berto, G. Scroccaro

Cardiovascular diseases are the first cause of death in the modern developed society. High blood pressure and hyperlipemia have been shown to be important risk factors for these diseases. Treating such conditions should so lower these events: that's why the clinical trials for antihypertensive and hypolipemic drugs are of great interest for the scientific community.

Aims: Goals of this study were: a) to evaluate the characteristics of trials involving drugs belonging to the hypertensive and hypolipemic agents, according to their design and their objectives; b) to examine the EC's opinions; c) to monitor the development and results of approved studies.

Methods: All of the trials submitted to the EC of Verona since 1992 until now were revised, and those related to antihypertensive and serum lipid reducing agents were set apart. These trials were then examined according to their design, their objectives, and the EC's opinions. Final reports sent to the Committee by investigators and sponsors were also examined and, when they were lacking, requests were sent to complete data.

Results: 45 out of 489 (9%) examined by the EC between April 1992 and May 1998 were related to this kinds of diseases. These trials were connected to 39 different protocols. Drugs investigated were mostly calcium channel blockers (14 protocols), angiotensin II antagonists and ACE inhibitors plain or in combinations (8 protocols each). Diseases studied included 19 times primary hypertension, 13 times hypertension in combination with different diseases (i.e.: nefropathy, diabetes mellitus, cardiopathy), 7 times troubles in lipid metabolism. The analysis of protocols design showed that 36 were controlled and 3 uncontrolled; 4 trials were monocentric and the other 35 multicentric. Only two out of 39 protocols were spontaneous, while the others had a sponsor. 5 studies had less than 50 patients planned, 3 between 50 and 100, 9 between 100 and 200, 14 between 200 and 500, 3 between 500 and 1000, and 5 more than 1000 (range 10 – 18.000). A particular attention was paid to the goals of trials: they were four times the evaluation of effects on mortality and cardiovascular morbidity, 9 times the effect on target organs and 26 times the evaluation of blood pressure reduction or tolerability of drugs on a short perspective, thus showing a persistent tendency to evaluate surrogate endpoints rather than hard ones. Two trials belonged to phase II, 28 to phase III and 9 to phase IV: for the most part they planned to evaluate new chemical entities (NCEs). More than half of these trials (21) were approved by the EC, 16 were approved after amendment and two were suspended waiting for amendments. 32 protocols were approved until the end of 1996: according to investigators reports, 15 of them were finished, 6 were ongoing and one could not start; for 10 of them investigators gave no information. Only 12 reports were sent by sponsor: 2 reported an 'in house' report, 6 said that results were in printing; 3 protocols had a publication of results, and only one was published and presented at a conference.

Conclusions: The analysis of trials in the area of hypertension and hyperlipemia submitted to the EC of Verona Hospitals shows that assessment of efficacy is still focused on surrogate end points and NCEs, that don't always mean innovate drugs, rather than on hard end points for the existing drugs. However trials design is almost always in formal agreement with the CPMP' guidelines. On a single centre level more than half of the trials have been finished while multicentric results are often lacking. This enforces the role of EC as monitor of diffusion of results.

Department of Pharmacy - Ethical Committee's Secretariat - Azienda Ospedaliera 'Istitutiti Ospitalieri di Verona' – Italy

12 ASSESSMENT OF THE IMPACT OF A SPECIALISED OUTPATIENT PSYCHIATRIC CLINIC ON PATIENTS PERCEPTION OF HRQOL

Batel Marques F.J.*, Feio J.A.L.*, Alexandrino M.B.*, Silva A.M., Araujo A**, Ferreira P.L.*****

Specialised outpatient psychiatric clinics deal with special groups of patients characterised by severe forms of psychiatric disorders. Different treatment interventions are performed, outcomes being measured by clinical evaluation. In order to asses, the potential value of humanistic evaluations as outcome measures in the treatment process, the overall impact of interventions performed in the psychiatric clinic on patients' perceptions of Health-Related Quality of Life (HRQoL) was studied.
Patients attending an outpatient psychiatric clinic were invited to participate in the study. The Portuguese version of the Sickness Impact Profile (PSIP) was administered at entry and on two follow-up clinic visits with a 2-month period interval between clinic visits.
One hundred and four patients (72% females, median age 47 range 15-75) completed the study.
Rank scores for the PSIP dimensions at the beginning and at the end of the study are presented on Table I

Table I

Questionnaire dimensions	1st visit	3th visit	'p' value*
O/A - overall PSIP scores	25.48 ± 15.37	16.51 ± 15.76	0.000
PHD - physical dimension	15.74 ± 15.52	10.61 ± 14.79	0.000
PSI) - psychological dimension	39.41 ± 22.74	26.28 ± 24.18	0.000
Independent categories			
SR- sleep and rest	28.50 ± 21.45	15.46 ± 19.72	0.000
HM - home management	24.00 ± 25.39	13.59 ± 20.25	0.000
W - work	13.25 ± 22.52	9.52 ± 19.29	0.168
RP - recreation and pastime	30.58 ± 20.39	18.37 ± 20.01	0.000
E - eating	6.14 ± 7.76	3.33 ± 5.30	0.003

Students T test for paired data (*)

Improvements in patients' perception of HRQoL were consistently found for all PSIP dimensions at the end of the study period, providing evidence for a favourable impact of clinic interventions. This study provided the rational to incorporate HRQoL evaluations in routine practice and evidence for the value of measuring humanistic outcomes in psychiatric outpatients. Although being a general HRQoL instrument, the PSIP was found to be a useful and sensible instrument in detecting differences in perceptions of HRQoL experienced by psychiatric patients enrolled in specialised clinics.

*School of Pharmacy,
**Sobral Cid Psychiatry Hospital
***School of Economics. University of Coimbra, Largo D. Dinis, 3000 Coimbra, Portugal, Fax no + 351 39 835139, Tel no + 351 39 834301

13 QUALITY OF LIFE IN PATIENTS WITH CHRONIC CONDITIONS: BASELINE RESULTS FROM A PHARMACEUTICAL CARE DEMONSTRATION PROJECT

Venturini F.*, Johnson K.A., Tannous R.E., Parker J., Kamath T., Rudolph M.

Introduction: There is increasing recognition that the impact of chronic illnesses and their treatments must be assessed in terms of their influences on quality of life (QoL) in addition to more traditional measures of medical outcome, such as morbidity and mortality. Consequently, measures that address patient perceptions of their health-related well-being have been developed. Two strategies for QoL evaluation have been described: measures that address illness-specific issues and measures that may be used across a wide spectrum of conditions.

Objective: To describe QoL in patients with chronic conditions using both a generic and a disease-specific QoL instrument.

Methods: Patients included in this analysis were part of a pharmaceutical care demonstration project. In that study, patients were selected based on their prescription profile, i.e., if they were prescribed medication for asthma, diabetes, hypertension or a combination of these. At the beginning of the study, they received a mailed questionnaire. The questionnaire comprised questions on QoL, satisfaction with physician services, medication adherence and personal information. The generic QoL instrument used was the SF-36, while the disease specific instruments were: Asthma Quality of Life Questionnaire (asthma), Diabetes Quality of Life Measure (diabetes), and the Vital Signs Quality of Life Questionnaire (hypertension). For analysis purposes, patients were divided into five subgroups based on their prescription profile: patients with asthma only (asthma), diabetes only (diab), hypertension only (htn), hypertension plus diabetes (htn-diab) and hypertension plus asthma (htn-asth).

Results: Quality of life data were available for 513 patients (54.9% female, 86.9% white, mean age 65.7 ± 14.5). The overall sample obtained a mean score of 41.3 and 54.5 in the physical component scale (PCS) and mental component scale (MCS) of the SF-36, respectively (US population norm = 50). Diabetes specific scores were lower (i.e., the higher the score, the worse the level of QOL) than the one found in the DCCT trial (1.97 vs. 2.1 for the satisfaction scale; 1.93 vs. 2.05 for the impact, 1.55 vs. 2.0 for the worry diabetes related), while patients in the diab group had a lower overall diabetes QoL score than their counterparts in the htn-diab group (0.17 vs. 0.19, p=0.0 17). All disease specific QoL scores for asthma patients (activities, symptoms, emotions, and environment) were higher in comparison with previous research. The combination of asthma and hypertension (htn-asth) significantly reduced the scores vs. patients with asthma only. Regarding hypertension related QoL, all the groups (htn, htn-diab, htn-asth) had poorer scores (e.g. higher scores) when compared with previous published research (e.g., overall score 45.9 previous studies vs. 63.8 htn, 73.4 htn-diab. 83.5 htn-asth). When compared with htn-diab and htn-asth, the htn group QoL was higher in all the subscales.

Discussion: QoL of patients is strongly affected by their chronic conditions. Patients with multiple chronic conditions exhibited a lower QoL than patients with just one chronic disease. In spite of the fact that the population under study is quite elderly, the scores on mental component scale of the SF-36 rank higher than those for the general US population. Further analysis needs to be done, correlating disease severity and patient characteristics to QoL information.

University of Southem California, School of Pharmacy, Dept. of Phannaceutical Economics & Policy, 1540 E.Alcazar Street. CHP 140. Los Angeles, CA 90033, USA

14 A DISEASE MANAGEMENT STUDY IN PATIENTS WITH RESECTED COLON CANCER

A. Messori* S. Trippoli* A.M. Grion, M.C. Giron****

A multicentre study was started to evaluate the outcome and the use of resources in patients with resected Stage III or Stage IV colon cancer. The study was designed as a prospective and observational collection of clinical and economic data. Patients are enrolled in the study at the time of surgery and are followed-up for 24 months. The project involves a total of 60 Italian hospitals and will be closed when the target number of patients is reached (250 patients).

The main objective of the study is to provide a pattern of clinical and economic information on this disease condition and to correlate the clinical outcome data with the use of resources. The clinical end-points measured during the follow-up of the patients include survival, quality adjusted survival, cancer recurrence, treatment-related side-effects. The economic end-points include hospitalisation, chemotherapy, visits, and outpatient drug prescription. The number of clinical and economic end-points has been kept as low as possible to facilitate the completeness of data collection.

The study is ongoing. An interim analysis of the results will be carried out in September 1998.

* Laboratorio SIFO di Fannacoeconomia. c/o Centro Informazione Farmaci, U.O. Farmacia I, Azienda Ospedaliera Careggi, Viale Morgagni 85. 50134 Firenze, Italy
** Servizio Farmaceutico, Azienda ULSS 16 del Veneto, Via Berchet 10, 35131 Padova. Italy

15 COST-EFFECTIVENESS OF GEMCITABINE AS FIRST-LINE THERAPY FOR PATIENTS WITH ADVANCED PANCREAS CANCER

S. Trippoli*, A. Messori*, E. Tendi**

Background: Gemcitabine is a new anticancer drug that has recently been proposed for the treatment of advanced pancreas cancer. The therapy with gemcitabine has been reported to confer a survival advantage it comparison with fluorouracil. Since gemcitabine is expensive. we estimated the cost per life-year gained using gemcitabine for this clinical indication.

Methods: The clinical material utilised in our analysis was derived from a randomised clinical trial[1] in which the survival of patients receiving gemcitabine was compared with that of patients receiving fluorouracil. To obtain an estimate of effectiveness, the survival curves published in the trial were analysed using the Gompertz methodology. Gemcitabine acquisition cost was based on wholesale price in Italy, in the UK and in the U.S. The overall cost of treatment is presently being estimated by collecting individual data on the use of resources and morbidity costs.

Results: The analysis of the survival curves showed that the mean survival of patients treated with gemcitabine was 6.29 months, while the corresponding value for patients receiving standard treatment was 3.20 months (both values include discounting at an annual rate of 3%). The survival gain for the gemcitabine group was 2.9 months per patient. Our analysis of cost data for these two treatments is in progress, but preliminary data show that the incremental cost is less than $20,000 per patient.

Conclusions: In pancreatic cancer, gemcitabine determines a survival gain of approximately 3 months. Its cost-effectiveness profile seems so be within acceptable values.

1. Burris HA. Moore MJ, Andersen J. Green MR et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. J Clin Oncol 1997:15:2403-13.

* Laboratorio SIFO di Farmacoeconomia Centro Informazione Farmazi, U.O. Farmacia 1, Azienda Ospedaliera Careggi, Viale Morgagni 85, 50134 Florence Italy.
** U.O. Farmacia 1, Azienda Ospedaliera Careggi, Viale Morgagni 85, 50134 Florence, Italy.

16 COST-EFFECTIVENESS ANALYSIS OF HIGH-DOSE CHEMOTHERAPY WITH HEMATOPOIETIC RESCUE AS PRIMARY TREATMENT FOR METASTATIC BREAST CANCER

S. Moriconi*, M. Puliti V.Viviani**, S. Trippoli*, A. Messori*, E. Tendi****

Background: The analysis of published survival curves can be used as the basis for conducting cost-effectiveness analyses in which two treatments are compared in terms of cost per life year saved. In patients with metastatic breast cancer, high-dose chemotherapy (HDC) with autologous bone marrow transplantation (ABMT) has been reported to improve survival in comparison with control patients who receive standard chemotherapy[1].

Methods: An incremental cost-effectiveness analysis was undertaken in which the Gompertz model was used to determine a lifetime estimate of patient-years gained by subjects given HDC with hematopoietic rescue in comparison with controls. Our study utilised the clinical data reported by Bezwoda et al[1] This randomised clinical trial involved 45 patients subjected to HDC with ABMT and 45 controls given chemotherapy.

Results: Lifetime survival advantage for patients of HDC wills ABMT group was estimated as 72.5 discounted patient-years for every 100 patients. The use of HDC with ABMT, as opposed to standard chemotherapy, was found to imply an incremental cost of about $55.000 per discounted life year gained.

Discussion: The cost-effectiveness ratio of high-dose chemotherapy with autologous bone marrow transplantation in patients with metastatic breast cancer is borderline if one considers that acceptable figures of cost per life year gained are generally below $50.000.

1. Bezwoda WR. Soymour L. Dansey RD et al High-dose chemotherapy with hematopoietic rescue as primary treatment for metastatic breast cancer: a randomized trial. J Clin Oncol 1995: 13 :2483-89.

* Laboratorio SIFO di Farmacoeconomia, c/o Centro Informazione Farmaci, U.O. Farmacia 1, Azienda Ospedaliera Careggi, Viale Morgagni 85, 50134 Florence, Italy.
** U.O. Farmacia 1, Azienda Ospedaliera Careggi. Viale Morgagni 85, 50134 Florence, Italy.

17 QUALITY ASSURANCE AND EVIDENCE-BASED DRUG PRESCRIBING

J.P. Kampmann, S.A. Gunnarsdottir, B. Krølner, J. Meile

Unit of Rational Pharmacotherapy, Copenhagen Health Service, Sjaellandsgade 40, DK2200 Copenhagen N, Denmark

Introduction: The Copenhagen Unit of Rational Pharmacotherapy was established in 1993 as a response to ever increasing drug costs far in excess of inflation. The Unit is staffed with a clinical pharmacologist, 2 part-time general practitioners (GPs), a pharmacist and a secretary.

***Methods**: In 1993 the Unit offered an intensive intervention program of 2 personal visits to almost all of the 300 GPs in Copenhagen, 2 small-group meetings with clinical pharmacological teaching and a quarterly newsletter with personalised prescription statistics. The intervention programme was based upon a thorough clinical pharmaceutical and pharmacological examination of the most rational and evidence-based drug treatment. In 1994 to 1996 the intervention was limited to educational meetings and quarterly newsletters. The impact on drug prescribing habits was evaluated by drug consumption statistics for each GP: prescribing of individual drugs in DKR, DDD and the costs of DDD.

Results: The implementation of such a programme changed the pattern of drug prescribing amongst GPs. Drug reimbursement in Copenhagen was considerably reduced compared to the rest of the country and the drugs used were often more rational. The effect was most pronounced during the personal visits, but maintained in the following years. Since 1993 the increase in drug costs in Copenhagen has been less than half that of the other 15 counties of Denmark.

Conclusion: It is possible with an intensive programme of rational and evidence-based drug prescription to save costs maintaining the same level of drug treatment. A randomised study with various intervention methods is currently in progress.

18 REMIFENTANIL Vs FENTANYL A POLISPECIALISTICAL ECONOMICAL / CLINICAL TRIAL

B. Rebesco, P. Della Casa **, M.E. Amalfitano*

Remifentanil (RE) is a new opioid with a very rapid kinetic. From an economic point of view, this drug costs about twice fentanyl (FE), the opioid presently in use, and its short effect (about 3 min) might increase significantly delivered doses. In our public health system, with limited resources, before introducing a new drug in PTO a careful evaluation of the economic impact on hospital budget must be carried out.
In collaboration with anaesthesiology dpt. a quick and predictive method like a poll was set up to determinate the economic impact due to the delivery of (RE) instead of (FE) in every general anaesthesia. Clinical effects produced were evaluated. Clinical and economic effects of (RE) have been compared with (FE) holding usual anaesthesiologic technical procedures (propofol or thiopentone. isoflurane, N_2O-O_2 and muscle relaxing drugs). Evaluation has been performed in 11 on 54 surgery beds chosen according to disciplines, accepting as randomised 165 (97 ISO+FE, 45M/52F), (68 ISO+RE 31M/37F) patients scheduled along 10 days of routine surgery procedures; (FE) was used in the first five days and (RE) in the remaining ones. Requested data were synthesised in 5 forms and collected: base data about patient, kind of surgical procedure,(RE)-(ISO) delivering time, adverse effects, estubation and discharge time, assessment of recovery all delivered drug and doses. Data were computerised for mathematics and statistic elaboration. Variation of the anaesthesia cost in the (RE) group was of (+) USD 2,5 for opioid and **(-)** USD 0,8 for halogenate anaesthetic, there were no significantly differences of N_2O-O_2 consumption. Therefore we may say that despite to a greater cost, (RE) improves anaesthesia quality thanks to faster awakes times, shorter permanence in surgical theatre and better recovery quality.
Finally, excluding surgical procedure in which the suitable pharmacological characteristic of cardiovascular stability induced by the drug is strictly indicated, pharmacoeconomic evaluation suggests (RE) use in elective surgery with a large number of surgical procedure such as day surgery **,** short -medium elective surgery and diagnostic invasive procedure.

* Pharmacy Service, S. Martino Hospital. L.go Rosanna Benzi 10, 16132 **,** Genova, Italy
** Anaesthesiology and Reanimation Institute, University of Genoa, L.go R.Benzi 10, 16132, Genova, Italy

19 PRESCRIBING PATTERNS AND COST OF ANTIMICROBIAL SURGICAL PROPHYLAXIS IN ITALY

C. N. Venanzi*, C. Spoltore*, F. Venturini*, R. Di Virgilio, M. Romero***

Introduction: Antibiotic prophylaxis is a controversial topic usually characterised by a gap between recommended treatments and clinical practice. Clinical pharmacists should play an active role in developing measures so rationalise antibiotic treatments and reduce cost. Knowledge of the actual pattern of drug use is essential for planning specific interventions.

Aim: A survey was undertaken in a sample of Italian hospitals to identify a cluster of inpatients treated for surgical prophylaxis and to describe the pattern of drug use in terms of antibiotic used, duration of treatment, overall and daily therapy cost.

Methods: All patients treated with a course of parenteral antibiotic therapy during 4 index days in June 1997 in a sample of 82 hospitals were surveyed. Data were collected on 2200 patients including patients demographics, clinical and therapeutic information during hospitalisation. This analysis is focused on usage of antibiotic treatment as surgical prophylaxis.

Results: Preliminary results are available for 800 patients (34.3% of the overall sample). Patients were for 53% male with a mean age of 52 years (range 0-89 years). 275 (34.4%) were taking antibiotics for surgical prophylaxis only, 368 (46%) for therapy only, 75 (9.4%) for medical prophylaxis only, while the remaining 10.2% for a combination of reasons. The mean length of antibiotics course for surgical prophylaxis was 4.9 days (median: 3 days) markedly shorter than for any other reason, but with a very wide range, from 1 to 63 days. The antibiotic usage was as monotherapy in 243 patients (88,3%), whereas a combination of 2 or 3 different antibiotics were used to treat the remaining patients. Overall, 30 different antibiotics were used to prevent surgery infection in 275 patients. The main drugs used were: cefazoline (16.8%). piperacilline (9.5%), ampicilline (7.9%), cefotetan (7.0%), ceftizoxime (7.0%,) and cefotaxime (4.8%). These six antibiotics accounted for 53% of patients treated for surgical prophylaxis. The average overall cost and the mean cost per day (± SD) of antibiotic courses were $ 125 ± 203 ad $22 + 17, respectively.

Discussion and conclusion: Questionable practices include delaying chemoprophylaxis or unnecessarily extending it, as well as using not recommended antibiotics as first line prophylaxis. Several previous studies have shown that these kinds of practice are not only less effective, but also more risky for the patients and more expensive for the health care service. Control measures should be implemented using a multidisciplinary approach where clinical pharmacist should have an important active role. Although these data are preliminary, they suggest that further improving prescribing intervention in surgical prophylaxis can be found.

* Centro Studi SIFO, Consorzio Mario Negri Sud, Santa Maria Imbaro (chieti), Italy
** Direzione Medica, wyeth-Lederle, Aprilia, Italy

20 DEFINITION OF GUIDELINES FOR OFF-LABELLED USE OF INTRAVENOUS IMMUNOGLOBULINS AT VERONA HOSPITAL FIRM

T. Cassani, G. Scroccaro

Introduction: The Therapeutic Committee (P&T) of Verona Hospital Firm, constituted of a general hospital (about 1.400 beds) and of an university hospital (about 900 beds), was established in 1977 to rationalise the use of drugs within the hospital. The Secretariat has been committed from the beginning to the university hospital Pharmacy Service and it avails itself of the collaboration of the Drug Information Centre (DIC) of the Pharmacy.

Objectives and methods: The aim of this study is to describe, through the analysis of the collaboration between P&T, DIC and physicians, the path followed to get to the definition of Guidelines for use of intravenous immunoglobulins (IVIG) at the Verona Hospital Firm.

Results: The P&T Secretariat has analysed the IVIG consumption within the Verona Hospital Firm: at the general hospital the IVIG expenditure from 1995 to 1997 has remained unchanged, while at the university hospital it has constantly increased. The consumption of IVIG in 1995 was of 18.583 g, in 1996 of 25.535 g and in 1997 of 32.734, equal to an expenditure of £. 93.847.197 in 1995, of £. 107.897.466 in 1996 and of £. 303.170.650 in 1997. The analysis of consumption for each department of the university hospital has allowed the identification of the main consumers, which are: Haematology, Rheumatology, Neurology and Paediatric wards.
The reasons for using IVIG have been identified through the analysis of justified requests and it was verified that at the university hospital IVIG are used both for labelled and off-labelled indications and for those not approved by P&T.
A literature evaluation was therefore made (Medline 1991-1997) and, following in particular a consensus statement published in JAMA 1995, vol. 273, no 23, it was possible to establish that the indications labelled in Italy and those approved by P&T are too restrictive while on the other hand, at university hospital IVIG are requested also for indication not supported by published evidence. At this regard, ESCP members of France and Spain, who provided us with extensive material, offered an important contribution. P&T has therefore constitute a panel of experts representative of departments mainly concerned, with the task of drawing up a list of indications which have been assigned the following evaluations: A- IVIG use is recommended; B – IVIG use is recommended only in selected cases; C - evidence does not support IVIG use. Finally, after analysis of cases in which there was discordance between the evaluation of the panel and the published evidence, P&T approved the Guidelines.

Conclusions: The definition of Guidelines by P&T is part of a strategy aimed at the development of a correct use of drugs within hospital.
A successive analysis of consumption and justified requests are planned to verify the impact of this kind of intervention on medical practice at this regard.

Department of Pharmacy - Azienda Ospedaliera 'Intituti Ospitalieri di Verona' - Italy

21 IS THE PRESCRIPTION OF TICLOPIDINE IN U.S.L 7 OF CHIVASSO EVIDENCE-BASED?

R. Corgnati, L. Poggio, C. Pietraru

Ticlopidine is a platelet aggregation inhibitor that may be useful in the prevention of thromboembolic disorders, cardiovascular mortality, stroke, myocardial infarction and vaso-occlusive peripheral arterial disorders. Ticlopidine may also be useful in maintaining graft patency or access sites for hemodialysis. As ticlopidine is associated with a risk of neutropenia/agranulocytosis, which may be life-threatening, it should be reserved for patients who are intolerant to aspirin therapy, if indicated, The recommended adult dose of ticlopidine is 500 milligrams daily given in two divided doses; doses of 750 milligrams daily (given in three divided doses) have also proved to be effective. With the new National Drug Formulary which came into effect on January 1, 1994, Italian doctors can prescribe ticlopidine within the National Health Service only by filling a special form with some information about patient, diagnosis and pharmacological treatment and sending it to U.S.L., where is kept a pathology register. A study of the use of current best evidence in making decision about the prescription of ticlopidine was carried out by examining general practitioners' registration forms come to U.S.L. 7 of Chivasso until April 15, 1998.
533 patients received treatment with ticlopidine: 317 were males with a mean age of 66±10 years and 216 were females with a mean age of 69±11 years. Reported pathologies were: intolerance to aspirin in cardiovascular prevention 138 (83 males - mean age 64,93±10,10 y. - and 55 females -mean age 68,62±9,47 y.); intolerance to aspirin in cerebrovascular prevention 74 (36 males - mean age 72,36±7.39 y. - and 38 females - mean age 71,16±13,45 y.); intolerance to aspirin in obstructive peripheral vascular disease 27 (25 males - mean age 66,16±9,62 y. - and 2 females -mean age 62.50±17,50 y.); intolerance to aspirin and other diagnosis 40 (21 males - mean age 62.14±12,11 y. . and 19 females - mean age 69,21±9,67 y.); intolerance to aspirin and diagnosis not specified 153 (93 males - mean age 64,46±10,53 y. - and 60 females - mean age 69,80±9,07 y.); coronary stenting 8 (3 males - mean age 56.67±7,36 y. - and 5 females - mean age 65,40±12,16 y.); cardiovascular prevention without indication of intolerance to aspirin 20 (18 males - mean age 60.89±6,35 y. - and 2 females - mean age 78,00±15,00 y.): cerebrovascular prevention without indication of intolerance to aspirin 13 (6 males - mean age 70.67±10,92 y. - and 7 females - mean age 69,86±10,44 y.); obstructive peripheral vascular disease without indication of intolerance to aspirin 9 (6 males - mean age 75,67±7,04 y. - and 3 females - mean age 77,33±8,99 y.): other diagnosis without indication of intolerance to aspirin 51(26 males - mean age 65,58±9,78 y. - and 25 females - mean age 66,36±13,93 y.). The dosage of ticlopidine employed were: 125 mg daily in 2 patients (0,38%), 250 mg daily in 444 patients (83.30%), 500 mg daily in 85 patients (15.94%), 750mg daily in 1 patient (0,19%); other dosages in 1 patient (0.19%).
This study shows that for 17,45% of patients receiving ticlopidine, doctors didn't indicate intolerance to aspirin therapy and for 28,70% they omitted to specify pathology. Only 16.13% of treated patients received an affective dose of oral ticlopidine. Additional research is needed to determine non specified diagnosis and to investigate if patients have regular blood tests done when they first start taking ticlopidine. Programs of information to general practitioners seem to be necessary to promote a better integration of their individual clinical expertise with the best available external evidence from systematic research in making decision about the care of individual patients.

U.O.A.Farmaceutica Territoriale A.S.L. 7 Chivasso, via Po 11, 10034 Chivasso (TO) Italy.

22 CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: PHARMACEUTICAL COST IDENTIFICATION ANALYSIS OF FRALLE 93 STUDY

L. Gauthier*, J. Delorme*, R. Gilli*, G. Michel, D. Braguer***

FRALLE 93 is the major protocol treatment for childhood Acute Lymphoblastic Leukemia (ALL), managed by the «Societe Francaise d'Oncologie Pediatrique» in a prospective multicenter study. From 01/95 to 12/97, 101 patients were included in the paediatric hematological unit of our University Hospital. They were enrolled according to their recurrence prognostic in 3 groups A, B and C for low, intermediate and high risk respectively. They were randomised in a methotrexate (MTX) low dose versus high dose subgroup (group A and B) and combined with idarubicin (IDR) or daunorubicin (DNR) in group B. Anticancer and antiinfectious drugs represent $ 34,000 (40%) and $ 27.000 (32%) respectively of the pharmaceutical cost of this protocol. The incidence of infectious risk was identified as the second cost variation factor after anticancer drugs.

Objectives: Evaluate and compare pharmaceutical costs of childhood ALL in the different subgroups of FRALLE 93 study.

Patients and methods: This prospective analysis was conducted on 52 patients for which the follow up was complete. Tight collaboration between clinical and pharmaceutical teams allowed to combine clinical information, protocol of chemotherapy and antiinfectious drugs administered. To calculate pharmaceutical cost according to hospital prices we previously developed a Microsoft Access® database **«** ONCOLOGY a. *(J. DELORME et al. An approach to understanding the increase in oncology therapy use. In G. Scroccaro et al Ed. Progress in clinical Pharmacy Clinical trials and pharmaco-epidemiology. European Society of Clinical Pharmacy. 1994. Agrigento*

Results: Mean pharmaceutical cost per patient was correlated with recurrence prognostic **($** 1,060. $ 2,166 and $ 5,752 for group A, B, C respectively). Moreover. the frequency of infections was linked with the intensity of the chemotherapy (from 24 % to 60%). However, antiinfectious drug costs were statistically increased in IDR subgroup **($** 786 versus **$** 231) associated with prolonged aplastic period. Actually, there is one relapse in daunorubicin and one in idarubicin group.

Conclusions: 1/ For MTX high/low dose randomisation, mean pharmaceutical costs were correlated with anticancer drugs. 2/ For IDR/DNR randomisation, mean pharmaceutical costs were correlated with anticancer and antiinfectious drugs, because of hematological toxicity of IDR. 3/ Idarubicin is a recognised drug in childhood ALL; however response rate comparative studies between DNR and IDR are in progress. A longer follow up is necessary to compare disease free survival and to perform a complete cost efficacy analysis.

* Service Pharmacie Enfants.
** Service d' Hematologie Pediatrique. CHU Timone, Assistance Publique Hopitaux de Marseille. 264 rue Saint Pierre, 13385 Marseille Cedex 05, France

23 CURRENT MANAGEMENT OF COLORECTAL CARCINOMA

M.C. Giron, A.M. Grion, A.C. Palozzo, B.L. Zamengo

Colorectal cancer is one of the most common visceral cancer in U.S., in both incidence and fatality rate, as described in literature[1'2]. A current management cohort study is ongoing to evaluate the incidence, the fatality rate, the therapeutical trends, the number and days and costs of hospitalisation, the prescription coats of the out-patients in the ULSS, (Local Health District), n. 16 of Veneto Region.
Between 1991 and 1998, 312 patients, (139 males and 173 females) were diagnosed of colorectal tumor, with a mean value of hospitalised patients around 10 per 100.000 people per year and an overall cost of over 20,000 million Lira. In most cases 70,8% patients were hospitalised once, the 20,2% was hospitalised twice and the rest 9% at least three times or more. Up to January 1997, 179 patients (83 males and 96 females) were still alive: among them 11 were less than 50 years old, 72 were 51-70 years old and 96 older than 70. The percentage of survivors was 52,4%, 62,1% and 94,8% respectively, in the three groups of age. For better studying the characteristics of outpatients who had a previous hospitalisation for colorectal cancer, a one year period was chosen: during 1997, 42 patients were hospitalised for diagnosis of colorectal carcinoma, of them 34 patients were hospitalised only one time and the rest at least two or three times. The prescriptions of these outpatients by their general practitioners didn't show any specific therapeutical trend beside that they received mainly gastrointestinal system and pain-killer drugs. The several and different types of prescribed drugs doesn't let the opportunity to find out a drug based therapy to identify outpatients with colorectal carcinoma.

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Servizio Farmaceutico Azienda ULSS 16, Regione Veneto, Via Berchet 10, 35131 Padova, Italy

24 DIGOXIN USE IN CONGESTIVE HEART FAILURE: PHARMACOEPIDEMIOLOGICAL STUDY

A.M. Grion, M.C. Giron, A.C. Palozzo, B.L. Zamengo

Congestive heart failure (CHF) is a major cause of morbidity and mortality in the U.S. and its prevalence is increasing, particularly among the elderly. CHF is diagnosed in 10% of the population by age of 75 and is the most common reason for hospitalisation in patients over 65 years of age[1] **.** The rising incidence may be attributed to improved survival among acute myocardial infarction patients and to the ageing population. Since both these trends are likely to continue, CHF is becoming an important health problem. A pharmacoepidemiological study was performed to investigate the prevalence of CHF in the USSL n. 16 (Local Health District) of Veneto Region, Patients were identified on the basis of:

1. cardiac glycosides prescriptions as therapeutical drug by itself or combined with other cardiovascular drugs, such as ACE inhibitors, diuretics,nitrates, inotropic agents etc.;
2. rate of hospitalisation for CHF.

Over a period of one year (1996), in our community a total number of 11.322 outpatients (2.9% of total population) were treated with digoxin by itself or associated with other drugs. Among them 1.399 were less than 64 years old, 4.672 were between 65-79 years old, ad 5.251 were equal or over 80 years old, In the past two years (1995 and 1996), only 1.030 patients (9,1% of the 11.322 patients) have been hospitalised for CHF: the prevalence of hospitalisation increased with age, (6.7%, 7.7% and 10.9% in the three groups, respectively), and it was higher in males than in females, (9.8% vs 8.7%). The number of hospitalised people per year was similar and accounted for an annual estimated cost of nearly 7,300 million Lira.
From these data digoxin seems to be over prescribed compared to the number of hospitalisations ad the prescribed drugs, all included in the National Formulary, for the expected patients with CHF, accounted for more than 1,000 million Lira per year.

1. Clin.Cardiol. 1993; 16: 380-390

Servizio Farmaceutico, Azienda ULSS 16 del Veneto, Via Berchet 10, 35131 Padova, Italy

25 LICENSED DRUGS IN THE TREATMENT OF CHILDHOOD FEVER IN ITALY

A. Addis, P. Vivarelli, M. Bonati

Introduction: In paediatric practice, drug prescribing often does not comply with an evidence based medicine approach. As fever is a common illness in childhood, antipyretic drug use is widespread. The objective of our study was to investigate how many and which types of antipyretic drugs are labelled for use in children in Italy.

Methods: All antipyretic drugs marketed in Italy were identified according to the Anatomical Therapeutic Chemical Classification index (N02B ad M01B). Indications and dosages have been retrieved using the Italian Directory of Medicines and Manufacturers.

Results: For 13 antipyretic molecules, we found 104 trade names and 211 different formulations. After the exclusion of all compounds with multiple ingredients (29% of all formulations), we identified 73 (49%) formulations with no indication for use in children, 26 (17%) contraindicated and 50 (34%) formulations with dosage indications for infants or children. Four antipyretic agents (ibuprofen, naproxen, diclofenac, propifenazone) have no formulations with labels for use in children in Italy. Antipyretic which are not commonly used for children elsewhere (e.g., nimesulide), are marketed with a indication for paediatric use.

Discussion: Our analysis shows how antipyretic drugs commonly used in other countries have no indications for use in childhood in Italy (e.g., ibuprofen). A large number of formulations of antipyretic drugs are not licensed or have no indications for use children. In Italy it is cause for concern that the licensing authority and pharmaceutical companies have not evaluated antipyretic drugs that are used extensively in children.

Conclusion: Pharmaceutical companies, pharmacists, prescribers and regulatory authorities should work together to improve pharmaceutical care in children.

Regional Drug Information (C.R.I.F.), Laboratory for Mother and Child Health, Istituto di Ricerche Farmacologiche "Mario Negri"' Milano, Italy

26 BREAST OVER BOTTLE: THE CONFLICT OF INTERESTS

P. Vivarelli*, M. Brunetti, A. Addis*, M. Bonati***

Introduction: The benefits of human milk over artificial formulas may persist beyond infancy, and are clearly established and widely recognised in both the industrialised and developing world. The duration of breastfeeding remains short regardless of whether the WHO international code for marketing breast milk substitutes is adopted or not, raising some economic considerations.

Methods: In Italy we reviewed the official 1998 National Therapeutic Formulary for registered infant milk formulas, manufacturers and prices.

Results: Thirteen manufacturers market 144 preparations with 74 brand names (111 ad 71 respectively for powdered milk). Taking into account the most widely used (ad registered) substitutes, we focused our analysis on starting (38) and carry on (27) powdered formula "for all babies". Size of preparations range from 200-2000 g for both types (median 550 and 700 g, respectively), whereas the price was higher for starting (37-67 Ital. Lire/g; median 58; 1 UK pound=2,784 Ital. Lire) than carry-on formulas (26-60 Ital. Lire/g; median 48). A linear relationship was found between price and size of formula preparation but it is important to underline that comparable packs (for contents and amount) showed a average variation in price of 10 Ital. Lire/g, corresponding to 4,000-20,000 Ital. Lire/pack.

Discussion: To quantify the effect of those differences on family economies, we use regression analysis and age related nutritional milk needs (from 2.43 kg during the first month of life to 2.17 kg/month after the fifth) to estimate the cost of formula feeding a infant in the first year of life. Estimates range from 1.04-1.62 million Ital. Lire depending on whether one uses the 200 g or 2 kg package. Since the average monthly income of an Italian family is 3.5 million Ital. Lire, and half this for 20% of families, at least 3-5% of the net family income may be necessary to feed an infant with formula. Taking that the Italian incidence of live-born babies as 530,000/year it is straightforward to calculate that the national expenditure for "standard" (not soy, premature, anti-reflux, etc.) formula may range from 553 to $857x10^9$ Ital. Lire, once again depending on the package size.

Conclusions: Permanent education and recall efforts for the population - including physicians - could raise the incidence and duration of breastfeeding, and oppose initiatives by infant formula manufacturers that regularly breach the code. Manufacturers' interests conflict with those of the majority of mothers and their children, and the cost of purchasing formula can be presented as a further saving and a convincing tactic for promotion breastfeeding,

* Laboratory for Mother ad Child Health, Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milano, Italy.
** Laboratory of Health Services Research.

27 SHORT VERSUS LONG THERM PROPHYLAXIS WITH CEFTAZIDIME IN PATIENTS WITH SURGICAL COLECISTECTOMY: CLINICAL AND PHARMACOECONOMIC OUTCOMES

G. Liuzzo, F. Saglimbene, M. Castiglione

The prophylaxis treatment in antibiotic therapy is very reality on the basis of clinical and economic reasons.
The objective of this study was to evaluated two groups of patients with two prophylaxis regimens: Short therm versus Long therm prophylaxis - STP vs/ LTP - from clinical and economic point of view.
38 patients with surgical colecistectomy were randomised 1:1 to STP or LTP with ceftazidime 1 gr. im administred 1 hour before surgical intervention, 5 and 12 hrs. after, in STP group, versus 1 gr. im bid for each day during the follow up on surgery, in LTP group. The following outcomes were evaluated:
- days necessary for the medication;
- score of surgical wound;
- temperature;
- hospital recovery days;
- number of days who the physicians were involved;
- number of days who the nurses were involved;
- economic outcomes: costs of two treatments regarding the use of ceftazidime;

The two treatments show statistical similar results of:
- number of days necessary for the medication;
- score of surgical days;
- temperature;
- statistical important different results about:
- number of recovery days: 104 in STP vs/ 174 in LTP;
- costs of pharmacological treatment with ceftazidime: group in STP:400 $ for each patient; group in LW; 2.500 $ for each patient (+ 710 %).

Conclusion: The treatment with ceftazidime 1 gr. im in STP in patients with surgical colecistectomy is greater advantageous than in LTP, from clinical and economic point of view - + 70 % of recovery days in LTP vs. STP ; + 710 % of direct costs of pharmacological treatment with ceftazidime in LTP vs. STP.
Similar outcomes on the two treatments:
- score of surgical wound;
- temperature;
- number of days who physicians and nurses ware involved.

28 THE ARNO PROJECT: A POPULATION ORIENTED DATA BASE FOR DRUG UTILIZATION IN ITALY

M. de Rosa*, G. Tognoni**
For ARNO working group

Introduction: Since 1988, we set up a system with the purpose of collecting and monitoring data on drug prescriptions by providing advanced computer and informatics resources to the Local Health Units,

Objectives: The system has been activated with the purpose of providing a friendly and efficient interface between a "core facility", where data are concentrated and a powerful elaboration capacity is assured, and the Local Health structures where the data of General Practitioner's prescriptions are collected for reimbursement, in order to build a comprehensive drug utilisation Data Base.

Materials and methods: The system has been conceived to combine an highly sophisticated central computational capacity, which allows all types of handling and statistical analyses of the huge masses of data derived not only from the database on prescription, but from many databases linked together (population, vital statistics health and social indicators, drugs information, to implement a flexible system that enables to analyse the data from different point of view. The system, monthly updated, is distributed through the network (Internet) and the authorised users can access to the database. A working group with the co-ordination of the Cineca-Inter university Computing Center has been establish to co-ordinate the collaboration of the Local Health Units, the Italian Society of Hospital Pharmacy (SIFO), and the Laboratories of Clinical Pharmacology and Epidemiology of the Istituto di Ricerche Farmacologiche Mario Negro. The main strength of the Arno project is its "epidemiological" orientation. Many efforts have been made with Date Quality to have a reliable population oriented database which assures a high degree of confidence to both general and stratified analyses. The drug utilisation data are expressed as number of Defined Daily Doses (DDD), boxes and expenditure related to 1000 inhabitants.

Results: The main findings of the first general, will be used to document the methodological stenght of this large Data Base which allows the real-time monitor of 4 millions inhabitants - 20 millions of prescriptions - 16 Local Health Units of North Italy, during year 1997, as they are prescribed by 3500 General Practitioners and 400 Paediatricians.
Specific attention is been given to the variability of the prescriptions patterns across gender and age strata

Conclusions and perspectives: A comprehensive database of drug prescriptions can be seen as an important point of departure for exploration of new area of epidemiological research (case control studies, chronic cohorts), and development of surveillance projects.

* CINECA - Vie Magnanelli 6/3 40033 Casalecchio (BO) Italy
** 1st. Mario Negri V.1e Eritrea 20157 Milano Italy

29 DIABETES MELLITUS PHARMACOEPIDEMIOLOGY APPROACH TO COMPLICATIONS THROUGH CASE-CONTROL METHODOLOGY

A. Ferrarese*, M. De Rosa, G. Monesi***, G. Tognoni******

Introduction: The Arno Data Base which includes prescriptions in general practice, has been used to provide a pharmacoepidemiology profile on treatment of diabetes in routine conditions of care. The study is based on a protocol by a group of Diabetologists who wanted to improve care practice thanks to an interdisciplinary and clinical epidemiological approach (GIVID).

Objectives: 1. To assess the prevalence of drug-treated diabetes, through the identification of the patients treated with Insulin and Oral Antidiabetics; 2. To analyse concurrent treatments such as indicators of comorbidity and diabetic pathology complications; 3. To produce data to implement programs for continuing education for both Diabetologists and General Practitioners.

Materials and methods: The study includes the population of 9 Local Health Units of Veneto in the North-East of Italy (1,873,827 inhabitants) participating to the ARNO Project who received prescription medications free of charge, as part of the national Health care program (SSN), during 1996. The cohort of patients were identified by prescriptions for insulin and oral antidiabetica (more than 4 boxes/year). The selection of controls to examine the concurrent therapies (meant to check Diabetes complications) was done under the design of a "case control" study, controls were identified among the patients who had taken Antiabetic drugs; their number was twice the number of cases, with same gender, age, and general practitioner. Statistical analyses was performed to compare the proportions of patients with and without diabetics. The drug utilisation data are expressed as number of defined daily doses (DDD), related to 1,000 patients.

Results: A population of 40.439 patients was recruited, it shows a prevalence of drug-treated Diabetes of 2.2%. The 86.6% of patients is treated with Oral Antidiabetic (alone or together with insuline) while the 13.4% is treated with insuline only, consistently with the expected portions of NIDDM and IDDM. From the analysis of the concurrent therapies in the 40-64 year-old class, these results come out:
- The consumption of Cardiovascular agents (which show micro and macroangiopathic complications) is double in diabetics patients (especially for ACE-inhibitors, Calcium channel blockers and Diuretics which cover about 60% of the whole area, while Beta blocking agents are equally prescribed among cases and controls).
- Diabetic women are prescribed total a higher amount of drugs than men (171,923 DDD/1000 patients vs. 152,138) and a higher exposure to drugs for cardiovascular problems.
- A comparison with the female control population shows a higher exposure of diabetic women to Psychotropic drugs and a considerably lower consumption use of Sexual Hormones.

Conclusions and perspectives: Drug utilisation data can contribute to describe the epidemiology of drug-treated diabetes and its complications in a real caring context, and can promote dialogue between Diabetic Centers and Primary Health Care Services. In this sense, the cooperative (multidisciplinary) use of available data-base can lead to:
- Identify cohorts of patients depending from each Family Doctor to start local working groups;
- Carry out population studies especially aimed at critical patients;
- Complete drug exposure data with test strips consumption, in order to study the self-monitoring compliance.

These date can represent an useful interface with Public Authorities and Patients' Associations for defining health care strategy and planning activities.

* Farmacia Ospedaliera - Osp. Civile 45100 Rovigo Italy,
****** CINECA - Via Magnanelli 6/3 40033 Casalecchio (BO) Italy,
******* Diabetologia - Osp. Civile 45100 Rovigo Italy,
******** 1st Mario Negro V.1e Eritren 20157 Milano Italy.

30 UPDATING THE NATIONAL LIST OF REIMBURSED DRUGS (NLRD) IN AN ERA OF LIMITED RESOURCES

S. Shani, S.H. Klang, B. Haran, J. Shemer

The National Health Insurance Law was implemented in Israel in 1995. The law states that each citizen is entitled to receive health care treatments of established quality. The NLRD was defined as the 1994 formulary of the largest sick fund in Israel. All drugs included in this list must be reimbursed by the different sick funds. From 1995 to 1997, the NLRD was updated only once since the Ministry of Finance allocated no financial resources for this purpose, although numerous new molecules have been registered. The Pharmacoeconomics Unit in the Pharmaceutical Administration at the Ministry of Health set up a mechanism for updating the NLRD by evaluating clinical, epidemiological and economic data. Every six months, the Pharmacoeconomics Unit screens all the new registered drugs in that lime period for breakthrough products. Breakthrough products are drugs with significant clinical efficacy compared to current therapies for the same disease-state, or drugs which are indicated for the treatment of diseases for which no drug therapy is currently available. The Pharmacoeconomics Unit then sets priorities according to the available clinical data from the literature together with applications from physicians politicians and patients' interest groups. Subsequently, the number of potential users for each drug is estimated, and an economic evaluation is made: A cost minimisation analysis is carried out in order to assess the coat of including each drug in the NLRD. For selected drugs at the top of the proposed list, a cost benefit analysis is carried out in order to determine the money saving potential. The above procedure leads to the creation of a list of drugs considered for inclusion in the NLRD ranked according to their clinical and economic performance. When a certain budget is allocated for updating the NLRD, the decision-maker uses the proposed list as a basis for deciding which drugs will be included in the NLRD. In December 1997, after a considerable public outcry, the Ministry of Finance allocated NIS 150 million for updating the NLRD, Since the proposed list was existent, the Minister of Health was able to sign the order for the addition of several drugs to the NLRD within a week.

Ministry of Health, Jerusalem, Israel.

31 A SYSTEMATIC APPROACH TO NEW DRUG DEVELOPMENTS: MONITORING THE USE OF THE ATYPICAL ANTIPSYCHOTIC OLANZAPINE

A. Gilchrist *, M. Taylor **, K. Drury, P. Murray

The emergence of a new range of psychotropic drugs, which carry both significant clinical and cost implications, presents a challenge to mental health care. Evidence based practice implies that objective rational information should ideally govern prescribing. Edinburgh Healthcare Trust identified the need for a systematic evaluation of new drugs. Olanzapine is one of several new psychotropic drugs with potentially significant cost implications due to its widespread use.

This study armed to implement a systematic evaluation of olanzapine prescribing and impact within the Trust. The objectives were to identify the population for whom olanzapine was selected, and monitor treatment outcome to influence future prescribing of olanzapine.

A newly devised standardised assessment instrument which included demographic and clinical items was completed by the prescribing clinician following a structured decision to initiate olanzapine. The newly devised clinical assessment instrument used a linear analogue scale with referenced anchor points and included the clinical global impression scale, as well as an estimate of the positive and negative symptoms of schizophrenia, adverse events and quality of life. The inter-rater reliability of this scale will be demonstrated. After six months of treatment each patient on olanzapine will be reviewed by the same prescribing clinician using the same clinical assessment instrument in order to determine if any change has occurred.

Preliminary results at baseline are reported here. 42 patients initiated on olanzapine therapy have been recruited and assessed from 5 January to 20 May 1998 (age range = 16-69 years). Patients comprised: acute psychiatry inpatients, 19; outpatients, 18; learning disabilities, 2; old age psychiatry, 2; continuing care inpatients, 1. Starting dose of olanzapine ranged from 5 to 25mg daily. 22 patients were initiated on 10mg daily (= recommended starting dose). Reasons for initiating olanzapine therapy as indicated in the structured patient assessment represent some of the patient selection criteria as follows: 7 patients had experienced intolerable extrapyramidal side effects from traditional antipsychotic drugs; 6 had schizophrenia in whom minimising side effects from the outset of treatment was a priority; 1 had marked negative symptoms; 6 had refractory schizophrenia; 3 for other reasons; 17 had a combination of 2 of these reasons and 2 had a combination of 3 of these reasons. Ideally, atypical antipsychotics should not be prescribed concurrently with other antipsychotics. 14 patients were also receiving other antipsychotic medicines. 11 were receiving one other antipsychotic, 2 were receiving 2 others and 1 was receiving 3 others.

The efficacy of the new antipsychotics such as olanzapine has been established in worldwide trials. However the issue of cost efficiency remains to be settled. Evaluation of therapy in clinical practice using this method will provide a locally valid perspective on patterns of use, including monotherapy versus polypharmacy, efficacy and tolerability. It will enable future prescribing of the drug to be based on the evidence of continuously generated local data.

*Department of Pharmacy & ** Department of Psychiatry, Edinburgh Healthcare Trust, Royal Edinburgh Hospital, Edinburgh EH1O 5HF, Lothian Pharmacy Practice Unit/University of Strathclyde, UK.

POSTER DISCUSSION FORUMS

1 EFFICACY AND SAFETY OF SERTRALINE VERSUS CLOMIPRAMINE IN PATIENTS WITH MODERATE TO SEVERE DEPRESSION: A RANDOMISED, OPEN LABEL, PARALLELGROUP, CONTROLLED CLINICAL TRIAL

F. Batel Marques*, A. Vaz Serra,, N. Cobrado*, M.M. Caramona***

Purpose: to comparatively evaluate the efficacy and safety of sertraline and clomipramine in patients with moderate to severe depression.

Methods: A multi-centre, randomised, open label, parallel-group, comparative study of sertraline with clomipramine was conducted in psychiatric outpatients. Male and female patients aged between 18 and 65 years with the diagnosis of moderate to severe major depression according to DSM-III criteria and a score ≥ 18 in the first 17 items of the HAM/D (Hamilton rating scale for depression) were recruited. Follow-up evaluations were performed at 2, 4 and 8 weeks. Initial daily doses of 50 mg of both sertraline and clomipramine were administered. Efficacy was comparatively evaluated by changes in HAM/D and CGI (clinical global impression) scores while outcome measures for safety included frequency of side effects and number of dropouts due to adverse drug effects. Statistical analysis was carried out using parametric and non-parametric tests according to the study protocol. Significance for differences was set at 0.05 level.

Results: 119 patients were recruited and randomised (58 on the sertraline group and 61 on the clomipramine group). There were no significant differences on baseline scores for the HAM/D and CGI. At the end of the study HAM/D scores decreased 66% for the sertraline group and 55% for the clomipramine group ($p<0.05$). Similarly CGI scores decreased 58% and 46% for the sertraline and clomipramine groups, respectively ($p<0.05$). Dropouts due to side-effects were 11 in the clomipramine group and 4 in the sertraline group ($p>0.05$). A total of 27 patients in the sertraline group experienced, at least, one side effect, while side effects were present in 46 patients of the clomipramine group ($p<0.05$).

Discussion and conclusions: The present study confirmed the better safety profile of sertraline when compared to clomipramine for the selected indications, which is consistent with previous trials. However, differences in efficacy were not documented. This results provided evidence for a more favourable efficacy profile of sertraline in managing patients with moderate to severe depression, when compared with clomipramine,

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* Laboratory of Pharmacology School of Pharmacy,
** Department and Psychiatry University Hospital and School of Medicine, Largo de D. Diniz, 3000 Coimbra Portugal. Fax No + 351 39835139, Tel no + 351 39834301

2 ONLY HALF OF PATIENTS FREE OF GASTRIC ANTI-SECRETORY DRUGS AFTER HELICOBACTER PYLORI ERADICATION TREATMENT

H-F. Kwint*/*, P.A.G.M. De Smet**/***, L.G. Biesma***, J. Riezebos***, S.E.B. Werkman***, B.M.E.R. Steffens*****

Introduction: Treatment strategies aimed at eradicating Helicobacter pylon have shown positive results in the management of duodenal ulcer disease and gastritis. Triple- and quadruple-regimens lead to cure rates of 85 to 95 % in randomised clinical trials. Whether these rates can be extended to patients treated in general clinical practice remains to be verified. Not all these patients will have confirmed disease. Because of the side effects of the different regimens drug compliance in general practice could also be less.

Aim: This study investigates the use of anti-secretory drugs 6 to 12 months after Helicobacter eradication treatment as an indirect indicator for success of the treatment.
Method: In a retroprospective study the use of gastric anti-secretory drugs six to twelve months after Helicobacter treatment was assessed. In 4 different community pharmacies 105 patients were selected which received Helicobacter eradication treatment between April 1995 and April 1997. The medication histories of these patients were analysed.

Results: Only 46 % of the patients was free of anti-secretory drugs six to twelve months after Helicobacter treatment. 25 % incidentally (< 0.5 dose unit a day) used anti-secretory drugs and 29 % did this chronically (>0.5 dose unit a day).

Discussion: The low 'cure rate' in comparison with randomised controlled trials may be attributable to different factors. Firstly, it has to be established whether Helicobacter was successfully eradicated in the patients using incidentally or chronically anti-secretory drugs 6 tot 12 months after treatment. For example, lack of medication compliance of Helicobacter treatment could cause unsuccessful eradication. Secondly, indication of anti-secretory drugs before and after treatment has to be asked. Eradication helps prevent ulcer recurrence in patients with duodenal or gastric ulcers but its value is less clear with other causes of dyspepsia. Also gastric complaints could have a different character after treatment. To answer these questions questionnaires of the patients using anti-secretory drugs 6 to 12 months after Helicobacter treatment will be send to their general practitioners. At the moment a randomised clinical trial is carried out in 15 community pharmacies to assess if extensive information and motivation by the pharmacist of patients with Helicobacter treatment can improve medication compliance and reduce use of anti-secretory drugs 6 to 12 months after treatment.
Conclusion: This study shows that Helicobacter pylori eradication treatment lead to only 46 % patients free of gastric anti-secretory drugs 6 to 12 months after treatment.

* Stevenshof institute for Research, Theda Mansholtstraat 5b 2331 JE Leiden, The Netherlands,
E-mail: sir@stevenshof.nl (correspondence),
** Scientific Institute Dutch Pharmacists, KNMP, The Hague
*** SIR Pharmacy Practice Masterclass

3 NEPHROTOXICITY OF AMPHOTERICIN B IN LIPID EMULSION: A RANDOMISED, CONTROLLED STUDY IN NEUTROPENIC PATIENTS

A.l. Martinez*, A. Novo, F. Puigventos*, O. Delgado*, J. Bargay**. J. Gines*, M.V. Alvarez*, J. Besalduch**, J. Serra***

Objectives: To evaluate the differences in renal tolerance to amphotericin B administered in 5% dextrose in water [group A] compared to amphotericin B administered in a lipid emulsion (Intralipid 20 %®) [group B].

Methods: Prospective, controlled, randomised, open study comparing the two treatments protocols in 20 haematological neutropenic patients with fever of unknown origin despite empiric antibiotic therapy. All patients start amphotericin B at 10-20 mg/24h and the doses was increased in a few days to 0,5 mg/Kg/24h. During treatment we registered serum creatinine, serum urea, potassium supplements and concomitant nephrotoxic drugs administered.

Results: 9 patient were included in group A and 11 in group B. No differences in initial serum urea and creatinine and in duration of concomitant nephrotoxic drugs administered were detected. The comparison of initial versus final serum creatinine in group A (0,86 mg/dL vs 0,97 mg/dL) and in group B (1,03 mg/dL vs 1,33 mg/dL) didn't presented statistical differences. Also no differences in the initial versus final serum urea, in the potassium supplements and in the efficacy of the treatment were observed.

Discussion: Five clinical trials comparing both modalities of amphotericin B administration, concluded that amphotericin B in Intralipid was less nephrotoxicity than control. The day doses administered to our patients (0,5mg/Kg/day), lower than mentioned studies (range 0,71-1,31 mg/kg/day) could explain the results.

Conclusions: At the doses of 0,5 mg/Kg/day, the administration of amphotericin B presented good renal tolerance in both groups. No differences were observed in the parameters of renal function of patients treated with amphotericin B in lipid emulsion and in dextrose 5 % in water.

* Pharmacy Department,
** Haematology Department. Son Dureta Hospital. C/Andrea Doria 55, 07014-Palma de Mallorca, Balearic Island, Spain

4 COST-BENEFIT ANALYSIS OF A NATIONWIDE INFANT IMMUNISATION PROGRAMME AGAINST HEPATITIS A IN AN AREA OF INTERMEDIATE ENDEMICITY

G.M. Ginsberg, P.E. Slater*, D. Shouval**

The availability of safe and effective Hepatitis A vaccines prompts an evaluation of a nationwide infant vaccination campaign as a supplement to strategies aimed at specific at-risk groups such as travellers and military personnel. This paper estimates the costs and benefits for a nationwide infant immunisation programme against Hepatitis A for the period from 1997 - 2014 in Israel, an area of intermediate endemicity. The model is also extended to provide estimates of benefit-cost ratios a selection of other countries covering a wide range of endemicity levels. A policy of aiming to immunise all one year olds in Israel from 1997—2014 would for a cost of $61.9 million (plus $20 million in terms of lost work and transport costs) to the health services and $83.9 million to society, reduce the number of cases of Hepatitis A during the next 45 years from 505,000 to 223,000. This would reduce national expenditures by $128.4 million in health service resources alone, $84.2 million in averted work absences and transport costs in addition to a further $22.4 million in averted premature mortality costs. The health service, direct benefit and social benefit to cost ratios are 2.07/1, 2.53/1 and 2.80/1 respectively.
The adoption of a nationwide infant HAV immunisation policy in Israel appears to be not only medically but also economically justifiable.

Medical Technology Assessment Division and
* Department of Epidemiology Ministry of Health, Ben Tbai 2, Jerusalem, Israel.
** Liver Unit, Hadassah Hospital, Ein Kerem, Jerusalem, Israel.

5 EVIDENCE BASED PHARMACEUTICAL CARE OF HYPERTENSIONE: AN ITALIAN EXPERIMENT

E. Marrazzo, L. Ferraro*

Introduction: The pharmaceutical expenditure of Azienda U.S.L 1 (Local Health Office 1) of Turin for 1997 was approximately 67 billion lire, 25% of which (17 billion lire) goes to pharmaceuticals for treating hypertension. Considering the prevalence of hypertension in the adult population and the incidence of antihypertensives on the total expenditure for pharmaceuticals it has been decided to use the compulsory training courses, which the Azienda U.S.L. 1 has been holding for General Practitioners (GPs) for years. This decision was made based on the need to promote a more rational use of these drugs in order to control hypertension according to the international guidelines.

Objective: The objective of this paper is to evaluate to what degree a training program can modify the prescription-writing profiles of the doctors involved, is order to plan, if necessary, further initiatives.

Materials and methods: The course was broken down into three sessions attended by 78 GPs, 34% of the doctors under contract with the Azienda U.S.L. 1 (232), During the course various problems related so hypertension were discussed: the proper way to measure blood pressure, diagnosing hypertension, drug and nondrug therapy. etc. Moreover, a pharmacist gave a lecture illustrating data on the prescription and cost of antihypertensives. All the prescriptions written by the 78 GPs who had participated in the course for the previous and subsequent months were analysed and divided in therapeutic groups following ATC classification: C02 Antihypertensives, C03 Diuretics, C07 Beta blocking agents, C08 Calcium channel blockers, C09 Agents acting on the renin-angiotensin system. Comparisons were made: 1) among therapeutic groups and 2) among single active principles. The indicators used were: the number of pieces prescribed and their price.

Results: At present the preliminary results for the two months (March and November 1997) are available. The cost of antihypertensives in both months made op 23% of the total. The therapeutic groups most used were the same for both months: *C09 Agents* acting *on the renin-angiotensin system (*— 42% of the total number of pieces and —50% of the total expenditure for that category) and *CO8 Calcium channel blockers, (*- 28% of the total number of pieces and —31% of the expenditure in that category) in conflict with the provisions of the guidelines. Nonetheless, in November 1997, the prescription of beta blocking agents (+ 2%) and diuretics (+ 7%) were higher than in March 1997. The prescriptions for ACE-inhibitors (+ 5%) and calcium channel blockers (+ 1%) also increased, though to a leaner degree. Using the same methodology and indicators, all the single active principles, divided into therapeutic groups, were taken into consideration. The largest number of prescriptions were written for enalapril and enalapril + hydrochlorothiazide. Losartan, a drug brought onto the market in 1997, is increasing in the number of pieces prescribed by approximately 30%.

Conclusions: Though a few positive signs can be seen by this preliminary analysis of only two months (more prescriptions of diuretics and beta blocking agents), it should be considered that what occurs in two months is not indicative of the yearly trend of a phenomenon. Moreover, for a chronic pathology such as hypertension, it is probable that the adoption of the guidelines reflects the acceptance of new patients assigned to doctors, rather than a change in therapies already established and perhaps well tolerated. We shall see if the outcome of the other months confirms these preliminary results.

Drug information Centre, Azienda USL 1 Torino, Via S. Francesco da Paola 31, 10123 Torino, Italy
* U.O.A. Farmaceutica Territoriale ASL 4 Torino, Lungodora Savona 26, 10152 Torino, Italy

6 INTRAVENOUS IMMUNOGLOBULIN USE

Vallès R., Gorchs M., Garcia M.

Introduction: In recent years, the usage at intravenous immunoglobulin (IVIG) has increased progressively. IVIG are labelled in Spain for use in various primary immunodeficiencies HIV infection during childhood, multiple myeloma, chronic lymphocytic leukemia, bone marrow transplantation, idopathic thrombocytopenic purpura, Kawasaki syndrome and Guillan - Barre syndrome. Furthermore, their efficacy in dermatomyositis, multifocal motor neuropathy and chronic inflamatory demyelinating polyneuropathy has been established in controlled clinical trials. However, the information available on other uses, such as Lambert - Eaton myasthenic syndrome and myasthenia gravis, is provided only by preliminary results from controlled studies, open-label trials and case reports and the response was variable. With this wide range of indications and because IVIG area a very expensive product of human plasma, we thought it necessary to review the use of IVIG and the evidences supporting their efficacy.

Aim: The objective of this study was to analyse the use of IVIG in our hospital and to evaluate if the indications were supported by the medical literature.

Methods: The indications, dosage and data of the patients who received IVIG from April 1997 to March 1998 were collected. We also reviewed the information available on the indications and efficacy of IVIG.

Results: Seventy-five patients were treated with IVIG during the study period. Of the patients, forty-seven were children with a mean age of 5,43 years (min. o and max. 24 years) and the indications were primary immunodeficiencies (24 patiens/47: 51%), HIV infection (17/47: 36%), and the other six patients had neonatal sepsis, lymphoblastic leukemia, idiopathic thrombocytopenic purpura, Guillain-Barre syndrome. Kawasaki syndrome and nephrotic syndrome. The adults patients, with a mean age of 55.5 years (min. 23 and max. 82 years), received IVIG for: primary immunodeficiencies (8/28: 28.5%), idiopathic thrombocytopenic purpura (7/28: 25%), chronic demyelinating neuropathy (4/28: 14.3%), and other indications, one case each, were dermatomyositis chronic lymphocytic leukemia, immunoblastic lymphoma, myasthenia gravis, multiple myeloma, polymyositis, Lambert-Eaton myasthenic syndrome, Guillain-Barre syndrome and pure red cell aplasia.

Conclusion: Only in the case of nephrotic syndrome evidence did not support IVIG use, but the efficacy in some other indications has not been established in controlled clinical trials.

Department of Pharmacy, Corporacio Sanitaria del Parc Taulli, Parc Tauli s/n, 08208 Sabadell, Spain

7 PREVALENCE AND NATURE OF SELF-MEDICATION REQUESTS IN COMMUNITY PHARMACIES OF CENTRAL PORTUGAL

F. Batel Marques, N. Cabrado, M. Caramona

Self-medication is a component of the individual management of the health/disease process and must not be neglected as an important part of community pharmacy practice. The recently approved European guideline on the switching procedure of the legal status of medicinal products for human use, from prescription to non-prescription, clearly points out the role of community pharmacists as important advisers in promoting responsible self-medication.
This study was aimed at characterising the prevalence and the nature of self-medication related requests in community pharmacies.
A cross-sectional study in 21 community pharmacies (10 typically urban, 11 typically rural) located within the Portuguese Central Health Authority area was carried out during one complete working day at each pharmacy. According to the study protocol requests for pharmacy services were classified in "self-medication requests" and "non-self-medication requests". Self-medication requests were typified, according to their nature, as the acquisition of medicines without medical prescription (products not classified as medicines for human use were not included in this study) and not asking for any advice, or the presentation of signals/symptoms and/or requesting any advice from pharmacy personal. Statistical analysis was produced by using *Chi-square* (to compare prevalence), significance for dependencies being set at a 5% level. Results are, whenever applicable, expressed as mean ± S.D.
A total of 2053 clients (1369 - 66.7% - from urban pharmacies) were identified during the study period, corresponding to an average of 98 ± 65 clients per day and per pharmacy (137 ± 58 in urban pharmacies). Self-medication requests were present in 33% and in 29% of the clients attending urban and rural pharmacies, respectively ($p>0.05$). Of a total of 649 self-medication related requests, 580 (89%) were made by the straight acquisition of a medicinal product without asking for any advice, whilst in 69 (11%) of the cases any advice was requested. The last represented 9.7% of self-medication related requests in urban pharmacies and 12.7% in rural pharmacies ($p>0.05$).
Self-medication was found to represent nearly one third of the motives for requesting community pharmacy services regardless of the socio-geographical location therefore being a generalised phenomenon across the society. The vast majority of requests corresponded to the acquisition of self-selected medicines without asking for pharmacist's advice. This was the case in both urban and rural pharmacies. For community pharmacy practice these results strongly suggest the need for a more active intervention if the safe use of non-prescription medicines and responsible self-medication habits are to be promoted. Moreover, and in the light of a high prevalence of self-medication attitudes amongst pharmacy clients, professional interventions seem to be of potential favourable impact in maintaining and promoting public health.

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Laboratory of Pharmacology, School of Pharmacy, University of Coimbra, Largo de D. Diniz, 3000 Coimbra, Portugal. Fax: +351 39835139, Tel: +351 39834301

8 GUIDELINES POLICIES AND PROCEDURES FOR HANDLING CYTOTOXIC DRUGS IN THE PHARMACY

E. Mizrahi

The vast number of cytotoxic agents in use today and the ever increasing number of chemotherapeutic protocols created the need for the use of a handy, concise, and a guiding directive to assist the pharmacists in performing their tasks.
In order to facilitate the acquisition of regularly needed information by the pharmacists who practice in the cytotoxic unit and to establish a uniform practice within the unit, guidelines for practice were written.
The commonly used cytotoxic agents in the medical center were addressed as to their storage, reconstitution, dilution, expiration dates, maximal doses, and their use within the context of the commonly used protocols in the medical center. Guidelines for safety, for doing various tasks, and for the work flow in the pharmacy cytotoxic unit were established and written down to assist and direct the pharmacists and the pharmacy technicians perform in a safe, easily achieved, and a uniform manner. These guidelines have been helping the practising pharmacy staff in the cytotoxic unit of Sheba Medical Center in Israel, and are presented as a suggested guidelines model.
These guidelines writing task was part of the pharmacist work and was made possible by the pharmacy director who realised the need for the compilation of the data and allocated the time for its development.

Department of pharmacy, Cytotoxic unit, Sheba Medical Center, Ramat Gan, Israel

9 GENTAMICIN KINETIC PROFILE OF NEONATES IN AN INTENSIVE CARE UNIT

Rocha M.J., Almeida A.M., Leitao F., Santos J., Falcao A.C., Caramona M.M.

Gentamicin is an aminoglycoside antibiotic frequently used to treat gram-negative bacillary infections and suspected sepsis in neonates. Obstetrical risk factors and disease procedures required for the management of critically ill neonates are associated with an increased risk of infections. Although dosage schedules have been established for premature and term infants, in order to obtain appropriate gentamicin serum concentrations, toxic levels are common in this age group. The risk of toxicity or poor efficacy is further increased because of the wide inter-patient variability in the pharmacokinetic parameters of gentamicin, depending on the stage of maturity of the new born. The aim of the present work was to assess the gentamicin kinetic profile in these patients in order to improve our specific dosage regimens. The study involved 40 infants of 31.4±4.9 weeks of age (mean±SD), weighing 1.7±1.0 kg and treated with standard doses of gentamicin (3.8±1.2 mg/kg/day). All of them presented two gentamicin concentrations (peak and trough levels) obtained as part of the clinical routine procedure of our intensive care unit. Demographic and clinical data were retrospectively collected in the sequence of the existing protocol that was implemented in order to prevent toxic and/or sub-therapeutic gentamicin concentrations. The kinetic analysis was done assuming a one-compartmental open model with zero-order absorption (IV perfusion) and first-order elimination. The pharmacokinetic parameters determination was done by nonlinear regression performed with the most popular clinical pharmacokinetic software package used in our country PKS ®, Abbon Diagnostics). The obtained results showed the final estimates for both clearance (CL = 0.59±0.26; CV = 45%) and volume of distribution (Vd = 0.40±0.10; CV = 26%). Bearing in mind the demographic characteristics, the obtained estimates for CL and Vd seemed to be similar to those described by other authors. This observation is relevant for us in order to allow better "a priori" and "a posteriori" dosage schedules and could be used to develop the clinical pharmacokinetics service implementation in our hospital. Finally, this information must be complemented by the fact that trough levels above 2 µg/mL (potentially toxic concentrations) were observed in 45.5% of our study population, which can be changed in the future by the clinical application of our work.

Laboratory of Pharmacology, Faculty of Pharmacy, University of Coimbra, 3000 Coimbra, Portugal.
E-mail: acfalcao@cygnus.ci.uc.pt

10 THEOPHYLLINE, STEROIDS AND GOLD: AN ANTIASTHMA PHARMACOKINETIC COCKTAIL

Falcão A.C., Rocha M.J., Castel-Branco M.M., Mano A.J., Almeida A.M., Caramona M.M.

Theophylhine has been used for several decades in the treatment of asthma and remains the most widely prescribed antiasthma drug worldwide. In recent years, however, with the appreciation of the importance of inflammation in the pathogenesis of asthma and the consequent use of therapeutic alternatives (mainly the steroids and ß$_2$-agonists), the use of theophylhine in industrialised countries has declined. Nevertheless, long term administration of oral corticosteroids in patients with asthma may be associated with serious side effects and non-steroidal antiinflammatory drugs, including gold salts, have been shown to reduce the need for systemic corticosteroid treatment. In the present work we studied the kinetic profile of theophylhine administered concomitantly with methylprednisolone (steroid compound) and auranofin (oral gold) by analysing the relationship between doses and observed and predicted concentrations of theophylhine in six adult patients. The kinetic analysis was done by using two different commercial software packages, the PKS (Abbott Diagnostics) and the CAPCIL (SIMKIN Inc./courtesy of Dade-Behring), assuming a one-compartment open model with first-order absorption (k_a for PKS=0.5 h^{-1}; K_a for CAPCIL=O.3 h^{-1}) and first-order elimination (CL, $t_1/_2$ and V_4 by default for each program). The measured and predicted theophylhine concentrations were used to calculate percentage prediction errors:

%PE = [(predicted conc. — measured conc.)/measured conc.] x 100

A linear regression analysis was also carried out for the observed concentrations and those predicted by each method (PKS versus CAPCIL). The obtained results showed a bias in the observed versus predicted concentrations indicating persistent over-predicted theophylhine levels (results expressed as median and interquartile range; %PE for PKS = 56.9 [36.8-114.5]; %PE for CAPCIL = 32.6 [14.1-91.2]). The regression analysis between observed versus predicted concentrations confirm the same tendency showing an intercept significantly different from zero for both cases (PKS and CAPCIL). Additionally, it must be emphasised that all serum theophylhine concentrations were positioned below the accepted therapeutic window for this drug (10-20 mg/L). In conclusion: 1) both PKS and CAPCIL fail to predict the theophylhine concentrations based exclusively on their population pharmacokinetic parameters by default; 2) theophylline concentrations were lower than expected with obvious implications on its efficacy and emphasised the importance of therapeutic drug monitoring for this kind of drug/patients; 3) we can speculate about a possible interaction between theophylline and auranofin because the decrease in theophylline concentrations was greater than that supposed by the concomitant steroid utilisation (plus 25% on theophylhine clearance).

Laboratory of Pharmacology, Faculty of Pharmacy, University of Coimbra, 3000 Coimbra, Portugal.
E-mail: acfalcao@cygnus.ci.uc.pt

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11 PHARMACOKINETICS OF CYCLOSPORINE A IN PAEDIATRIC PATIENTS

J. Cardenete, M.A. Marngues*. R. Tomas, R. Moreira, I. Badell, M. Torrent**, J. Bonal**

The objective of the study was to analyse the pharmacokinetic behaviour of cyclosporine A (CPA) in paediatric patients undergoing allogeneic bone marrow transplantation (BMT) and to evaluate the utility of a pharmacokinetic study performed before bone marrow infusion. The pharmacokinetic study was used to individualise the CPA dosage in order to achieve therapeutic levels as soon as possible.
The study population consisted of 35 consecutive hematology patients scheduled for an allogeneic BMT between September 1991 and February 1998. Ten days before BMT a single IV CPA dose of 3mg/Kg was given to the patients over a 2h infusion. Eight blood samples were collected from each patient. Whole-blood CPA levels were determined by specific fluorescence polarisation inmunoassay (TDx®). For the pharmacokinetic characterisation, a two-compartment open model was fitted to the concentration-time data of each patient by nonlinear regression analysis (Adapt PC collection). This information was used to design the individual CPA dosage.
The desired CPA trough levels were 100-200 ng/mL.

Results:

Age (years)	ID(mg/Kg/d)	Vc(L/Kg)	Cl(L/h/Kg)	$T1/2_g$(h)
7±4	6.0±2.0	0.886±0.593	0.557±0.262	3.8±3.8

ID:IV initial dose;Vc:volume of distribution (central compartment); Cl:clearance; $T1/2_g$:Beta half life.

An important interindividual variability was found in all pharmacokinetic parameters. The highest variability was observed in half-life, having a coefficient of variation of 100%. There was an inverse relationship between age and CPA clearance. Consequently, the younger children have higher CPA dosage requirements. The pharmacokinetic study performed before BMT worked well in predicting the individual CPA requirements. Most of the patients achieved levels within the therapeutic range 24 h after starting the recommended ID.

* Department of pharmacy, Hospital de Sant Pau, Sant Antoni MªClaret, 167,06025, Barcelona, Spain.
** Department of paediatric, Hospital de Sant Pau, Sant Antoni Mª Claret, 167.08025, Barcelona, Spain.

12 TWO SAMPLES AUC ESTIMATION FOR MONITORING CYCLOSPORIN-A (CsA) FOLLOWING KIDNEY AND BONE MARROW TRANSPLANT

M.E. Araujo-Pereira*, L.M. Pereira/***, J.G. Morais*****

In recent years several authors have been proposing a therapeutic drug monitoring strategy for CsA based on the estimation of steady-state AUC with very few data points collected over a given dosing interval. This was indeed a recommendation emerged from the 5th International Congress of Therapeutic Drug Monitoring and Clinical Toxicology in Vancouver 1997. Those abbreviated AUC estimates have been tested in clinical settings and seem to bring numerous advantages over a complete, stressful and costly 8 to 10 blood samples based AUC determination. Our study expanded this rationale to the usage of CsA in kidney (KT) and bone marrow transplanted (BMT) patients using only two concentration-time points optimally placed in the 12 hours dosing interval. 35 patients submitted to BMT were treated with either intravenous CsA or oral CsA microemulsion (Neoral ®), and 32 KT patients were given orally either conventional CsA or CsA microemulsion. Totally, 84 data sets were analysed consisting of complete plasma concentrations versus time profiles and respective AUC's estimated either by a trapezoidal or a log-trapezoidal rule. Subsequently, a stepwise multiple linear regression procedure was conducted using the plasma concentrations as independent and identically distributed predictors of the previously calculated AUC's. The goal was to identify the least possible combination of predictors, including an independent term whenever needed, capable of adequately estimate AUC. The necessary statistics were used to assess the underlying assumptions, such as autocorrelation, as well the goodness of fit criteria. Typical equations were obtained as follows,

	IV	Oral
KT	-	$AUC=712+2.59\ C_{2h}+5.38\ C_{6h}$ $R^2=0.94$
BMT	$AUC=-15+3.58\ C_{2h}+7.94\ C_{8h}$ $R^2=0.97$	$AUC=-9+3.19\ C_{2h}+6.81\ C_{6h}$ $R^2=0.99$

These expressions provide good predictability, are very easily implemented and reduce significantly the waste associated with an intensive blood sampling strategy. Furthermore, in many cases through concentrations alone are useless for CsA dosing adjustment and this methodology may essentially with a similar effort provide a much accurate alternative.

* Servicos Farmaceuticos Hospital de Sta. Maria, Av. Egas Moniz, 1600 Lisbon, Portugal
** UFEB - Pharmacotherapy, Epidemiology and Biopharmaceutics Unit. Instituto Superior de ciencias da Saude - Sul, Quinta da Granja, 2825 Monte de Caparica, Portugal
*** Faculdade de Farmacia Universidade de Lisboa, Av. Forcas Armadas 1600 Lisbon, Portugal

13 BOOTSTRAPING VALIDATION OF THE ABREVIATED AUC ESTIMATION

L.M. Pereira*/*, M.E. Araujo-Pereira**, J.G. Morais*****

Recently, several reports have surfaced in the literature proposing the estimation of the area under the curve (AUC) using only a few concentration-time data points by means of multiple linear regression, rather than using the full data set classically required by numerical integration procedures, such as the trapezoidal rule. However, no report has been published yet validating that technique in formal statistical terms. Being an inference problem transposed to a time series framework, a number of underlying assumptions are implicit whether or not they are addressed by the end users. The reason why good correlation coefficients may be encountered between three, two or even one concentrations and the overall AUC is more of an information theory and maximum likelihood nature, than of a regression type. Predictability is definitely a different issue than good correlation or goodness of fit. Therefore, the objective of this study was to make use of a bootstrapping sampling technique in order to generate equally plausible pseudo-patients and their respective steady-state drug levels. Several data sets could thus be generated with different error structures. For each of those amplified samples the exact AUC was calculated as well as different abbreviated
estimates obtained by stepwise multivariate linear regression. Linear models were selected on the basis of their adjusted R^2 and power statistic. Finally several matrixes resulted with the variances and covariances for all the estimates, and bias and precision were determined for each model.

	CV=5%			CV=20%			CV=40%		
	AUC_2	AUC_3	AUC_4	AUC_2	AUC_3	AUC_4	AUC_2	AUC_3	AUC_4
MPE(%)	0.026	-0.06	-0.01	1.1	0.59	0.62	5.1	-2.4	1.6
RMSE(%)	4.0	4.3	4.2	9.5	6.7	6.1	45	35	27

CV=Coefficient of variation for bootstrapping seed, AUC indices=number of predictor concentration points. MPE = Mean prediction error, RMSE = Root mean square error

As a conclusion it became apparent that the abbreviated methodology for estimating AUC is heavily dependent on the variability for each covariate (concentration), or in other words, the intraindividual variability. The findings confirmed the appropriateness of the applications so far encountered in the literature for this methodology, namely for less noisy drugs in terms of their concentration versus time profiles, irrespective of their patient to patient variability. Also the application of the so-called limited sampling model for the estimation of AUC's in bioequivalence studies is subject to the same caveats aforementioned. In all cases caution should be taken in characterising the variability patterns of each drug, for instance using bootstrapping sampling.

* UFNEB — Pharmacotherapy, Nutrition and Biopharmaceutics Unit, Instituto Superior de Ciencias da Saude - Sul,
Quinta da Granja, 2825 Monte de Caparica, Portugal
** Servicos Farmaceuticos, Hospital de Sta. Maria, Av. Egas Moniz, 1600 Lisbon, Portugal
*** Faculdade de Farmacia, Universidade de Lisboa, Av. Fomas Armadas 1600 Lisbon, Portugal

14 THE EVIDENCE BASE MEDICINE AND THE LOCAL ETHICAL COMMTITEE ACTIVITIES IN AN ITALIAN UNIVERSITY HOSPITAL

R. Di Pasquale, M. Dell'Aera, R. Trombetta, M. Lattarulo

Introduction:. The application, assessment and analysis of controlled clinical trials and the presence of pharmacist in the Ethical Committee delineate a new scenario where the pharmacist is increasingly involved in clinical pharmacy activities.

Aims: 1) To assess the qualitative (study design) and quantitative aspects of clinical trials approved in the course of two years activity by the local Ethical Committee. 2) To create a computerised records system of the studies assessed.

Materials and methods: The data were input in a data base in which the drug studied, the disease, the study design, the number of cases enrolled, etc. . . , were recorded for each trial.
The analyses were made using the EPIINFO program The quantitative data, i.e. frequency of studies of given drugs and disease, were also studied. The data on the methodological quality of the studies were obtained by cross-analysis of the experimental phases (I,II,III,IV) with the multicentre and/or randomised nature of the trials, and use of placebo or drugs as controls.

Results: Over two years of activity, the Ethical Committee met 21 times and 186 trials were approved: 175 experimental protocols were assessed (some protocols were presented in several hospitals). The drug categories most studied were: antimicrobial agents (19%), followed by cardivascular drugs (17%). The most commonly experimented drugs were the piperacillintazobactam association, azitromycin. cefepime, picotamide and interferon beta. The diseases most studied were hypertension (22 studies), followed by respiratory infectious (17 studies). Clinical studies were found to be predominantly multicentric (165 of 186). Controlled, randomised trials accounted for 148 studies, vs 22 non randomised. Most studies were conducted comparing standard drugs with new drugs (122 of 186). The study populations were mainly adults (142 studies), followed by the elderly (24 studies) and lastly children (7 studies). The study design most frequently called for enrolment of 200 to 400 patients (79 studies). followed by 400 to 600 (42 studies).

Discussion: The data show that few new drugs were studied. Interferon beta us an exception, bearing in mind its promising results in relapsing-remitting type multiple sclerosis. The other drug studies do not tend to a true advancement of knowledge but rather to extensions of indications or, more often, the study of "me-too" molecules, as shown by their use in diseases like hypertension and respiratory infections. Overall analysis of the data points out that the study protocols are well designed and conducted, as evinced by the data on mono/multicentric and/or randomised trials but that the scientific utility of the data obtained in these studies is not always high.

Pharmacy Service, University Hospital of Bari, P.zza G. Cesare, 11, 701124 Bari, Italy
E-mail: farmacia@cimedoc.uniba.it

15 DOCUMENTING PHARMACEUTICAL CARE IN COMMUNITY PHARMACY

K. van der Graaf*, L. de Jong-van den Berg, H. de Gier*****

Introduction: Electronical documentation of Pharmaceutical Care (PC) activities has been introduced in about 250 community pharmacies, since its introduction in 1995 (De Gier, 1996). Management of drug related problems has become daily practice, as an integrated part of computerised processing of patients and prescriptions by using the Pharmacon ®-system. An evaluation of PC activities in planning practice research is needed.

Aim: The primary objective of this pilot-study was to describe the application of the Electronical Pharmaceutical Dossier (EPD), in particular to answer the following questions:

- What procedures are being used by pharmacy staff in documenting patient consultations and interventions?
- What are the patient characteristics of patients involved in PC documentation (risk groups, disease oriented, any patient with drug related problem)?
- What is the response of patients to documentation of PC oriented activities in their pharmacy and interventions based on this registration?

A secondary objective was the development of a method to analyse the EPD registrations. In other words: how useful are structured text files and code systems in practice research?

Methods: A retrospective, descriptive evaluation of a random sample of 100 EPD's per pharmacy will be carried out in 10 community pharmacies. All available data, such as medication histories, drug use profiles and registrations of drug related problems and subsequent interventions will be analysed based on a total period of six months. Patients' responses to interventions will be documented based on a questionnaire survey by the pharmacists involved in the pilot-study.

Results: The feasibility of the research methods will be presented based on the evaluation of 100 EPD's in one pharmacy during the period October 1997 - April 1998.

Discussion: The proposed methods will be used in the 10 pharmacies in order to evaluate documentation of PC activities in 1,000 EPD's. After this pilot-study the research methods will be applied in a larger survey including 25 community pharmacies and 150 general practitioners. Patients will be recruited after the start of medication to treat asthma, migraine, hyperlipidaemia, or diabetes mellitus type II. The collaborative use of protocols and documentation systems to achieve the integrated care with pharmaceuticals will be compared with the 'traditional' practice of pharmaceutical dispensing, in which the team approach and documentation are lacking.

* Apotheek 'De Drie Stellingen', P.O. Box 122, 8430 AC Oosterwolde, The Netherlands.
** Department of Social Pharmacy and Pharmacoepidemiology, Faculty of Pharmacy, University of Groningen,
Ant. Deusinglaan 2, 9713 AW Groningen,The Netherlands.
*** Health Base Foundation, Randhoeve 225, 3995 GA Houten, The Netherlands,

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16 IMPACT OF A CLINICAL PHARMACIST ON DRUG THERAPY IN A DEPARTMENT OF INTERNAL MEDICINE

A. Hammerman, R. Rotem, N. Meidan, A. Porat

Several studies have documented the impact of clinical pharmacy services on patient care and drug costs in hospital wards. However in Israel, where most hospitals do not provide such services, until now it has not been tested whether they are beneficial in the local health care setting

Objectives: To determine whether a clinical pharmacist's activity in an internal medicine department of a medical center in Israel leads to changes in quality of drug utilisation and costs.

Methods: During the first three months of the clinical pharmacist's work all interventions and consultations given in the department were documented. The effect of' these interventions on the costs of drug therapy was calculated by measuring the change in drug acquisition costs during the study period and during the three preceding months in this department as well as in the other five internal medicine departments of the hospital, in which there were no clinical pharmacy services.

Results: During the study period the pharmacist joined 44 clinical rounds in which he documented 40 consultations as a response to physician requests for drug information and 42 interventions on his own initiative. The pharmacist's recommendations were accepted in 38 of the 42 cases (90%). In 10 cases the pharmacist's initiative to improve the quality of drug therapy led to an increase in drug acquisition costs. However, during the study period, the overall drug costs in the department went down 12.6% relative to the three preceding months, while during the same period the drug costs in she other internal medicine departments went down 2.2%.

Conclusions: The results of this study conform with many other studies that show that clinical pharmacists have a beneficial impact on the quality of drug therapy and on cost savings in the hospital. For these reasons, the clinical pharmacist is shown to have a crucial role in the department medical staff.

The Soroka University medical Center, Beer Sheva, Israel.

17 DOES MONITORING OF THE DIGOXIN LEVEL SERVE AS AN ESSENTIAL TOOL IN THE OPTIMISATION OF THERAPY?

E. Blum*, H. Mayan, A. Hoffman***

Digoxin is a widely used medication for the treatment of supraventricular arrhythmias and congestive heart failure. It has a narrow therapeutic-to-toxic ratio (0.8-2 ng/ml) which, if not maintained, can lead to life-threatening adverse reactions including heart blockage, ventricular tachycardia and death. Since many (patho)physiological factors affect digoxin blood concentration it is essential to achieve individualised optimisation of therapy. Unfortunately, the commonly used radioimmunoassay assay has specificity problems that make the results unreliable in certain cases. The necessity of digoxin blood monitoring and the proper utilization of this tool were examined in a prospective study conducted at the "Sheba Medical Center". To assess the importance of digoxin blood levels monitoring, the indications for ordering the assay were characterised, the cases of digoxin blood levels above 2 ng/ml were evaluated, and the degree to which the medical staff used the results to improve therapy were recorded and analysed. Data were collected from the medical charts of 86 patients. It was found that the assay was ordered as a routine procedure for any patient receiving digoxin. It was clinically unnecessary in 73% of the cases!! Furthermore, in most cases (31%) the medical staff paid no attention to the results. In characterising the cases of toxicity, it was found that most of the toxicity cases resulted from drug interactions and/or renal insufficiency. These cases could have been identified beforehand by a clinical pharmacist or an alert medical staff (even without the digoxin assay). In conclusion, the outcome suggests that the medical team did not adequately use the digoxin concentration data to optimise therapy. On the other hand, this data can be clinically helpful when interpreted with respect to the entire clinical situation. The uncritical use of blood level data should be avoided while an educated intervention by a clinical pharmacist can assist the medical staff to use these assays in a rational, safe and economical manner.

* School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel.
** Dept. of Medicine E, Sheba Medical Center, Tel Hashomer. Israel.

18 EVALUATION OF THE USEFULNESS AND UTILISATION OF DRUG INFORMATION PROVIDED TO THE CLINICIAN BY THE DOCTORLINE SERVICE.

Mele A., Albano M., Di Pasquale R., Vasaturo T. ,Nobili A., Macaria G.L.

Introduction: Several articles concerning information in clinical practice have been recently published. The application of Shaughnessy's formula for evaluating the usefulness of different kinds of information source has been evaluated in a pilot study.

Objectives: To test the applicability of this formula as a method for evaluating and rating the usefulness of the information provided to the clinician by a medical information service (DOCTORline).

Methods: Based on the Shaughnessy definition the usefulness of each information provided results as follows (Usefulness of medical information = Relevance x Validity / Work): *Relevance* - for each query an increasing score is attributed according to A) the frequency of the problem arising, and B) the level of direct applicability of the information requested to an ongoing clinical case (Relevance = A+B). *Validity* - for each information provided an increasing score will be attributed as a function of the scientific value and the type of documentation used; "critical appraisal" criteria of literature evaluation will be used. *Work* - an increasing score system is attributed as the product of the factors A) time spent to produce the information; B) resources, both human and technological, utilised for obtaining the information (Work = A x B). Each factor of the Shaughnessy formula was rated according to a 5 point scale, the final score ranging from a minimum value of 0.2 to a maximum of 25. The formula was then tested on a sample of 80 consecutive requests for drug information received by the DOCTORline service between July and August 1997.

Results: Mean values of relevance, validity and work were, respectively, 3.1 (± 0.8), 3.2 (± 1.3) and 3.2 (± 1.5). No correlation was found between the factors (relevance vs validity r=0. 10; relevance vs work r=0.03; validity vs work r=-0.08). Mean value of the usefulness of information given in reply to the 80 queries was 4.8 (± 5).

Conclusions: Despite the limited amount of information analysed and certain problems encountered in the standardisation of the mode of using the score system of the three formula factors, the application of the Shaughnessy formula was found to the very useful for monitoring and controlling the quality of a clinical information service. On there bases, at the beginning of May a new study has been started to assess the usefulness of a larger sample (200) of queries.

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ASFE - Associazione per lo Sviluppo della Ricerca in farmacoEpidemiologia.Viale Certosa 148 - 20156 Milan, Italy

19 GROUP DECISION-MAKING AT THE FORMULARY COMMITTEE: SELECTION AND ECONOMIC EVALUATION OF MEDICAL DEVICES METHODOLOGICAL ISSUES FOR DAILY PRACTICE

Applications using the PHARMA DECISION® software

P.A. Kenigsberg*, the Pharma Decision users group

Surprisingly, economic evaluation of medical devices has attracted little academic interest, although expenditures for medical devices often equal drug expenditures in many hospital pharmacy budgets.

As few, if any, comparative trials are usually available, elements of information are usually limited to a comparative analysis of technical characteristics from suppliers documentation and quantitative needs from the care units.

In order to assess cost-effectiveness (or value for money) when comparing medical devices, a general and simple methodology has been developed and tested with the PHARMA DECISION users group.

For many devices, it is the medical intervention, not the medical device itself, that improves health. Therefore, we propose that effectiveness criteria for medical devices may be measured not only in the perspective of the patient, but also in the perspective of the medical, nursing or technical staff.

Effectiveness can be assessed by using either evidence-based, technical characteristics of devices or subjective preferences from the care unit teams. Subjective preferences will reflect expert opinion when little evidence is available. Preference analysis, based on multi attribute utilities assessment, will reflect the attributes of devices that appear most useful to the users in real practice. Documented needs from the users can then be used as selection criteria by the Formularly Committee.

Evidence-based and subjective elements, cost and effectiveness remain clearly separated at all steps of the procedure, in order to facilitate the dialogue between the pharmacist and the group of users.

A comparison of up to 10 different devices can be graphically displayed on the PHARMA DECISION® cost-effectiveness decision matrix.

This synthetic view of all the dimensions of device evaluation facilitates group decision-making upon mutually agreed terms.

* Manager, Operational Pharma Economics, Pharmacia & Upjohn, BP 210, F-78051 St Quentin en Yvelines Cedex, France.

20 SAFETY OF USE FOR SINGLE-USE MEDICAL DEVICES COLLECTION, ANALYSIS AND REPORT OF EVENTS

A 1 7-month retrospective study at Assistance Publique des Hopitaux de Marseille

M. Lambert, N. Ausias, S. Pradeau-Bernardini

Assistance Publique des Hopitaux de Marseille is a 4000-bed, teaching hospital, localised on 4 distinct sites. Expenditures for medical devices represent 50% of the total pharmacy budget (of which 20% concern single-use devices).

Rapid evolution of technologies and operating procedures is leading to increasing invasiveness of medical devices and potential risk. In a teaching hospital where staff or students turnover is very high, it is important to maintain a continuous information on the proper use of the 3500 active references used in the hospital.

Since January 15th 1996, French Hospital Pharmacists have a legal obligation to declare any incident or alteration of characteristics and / or performances of medical devices.

We have surveyed 106 device-related events over a period of 17 months. Spontaneously declared events were collected manually on specific event report forms. The 4 different sites provided the same contribution as to the number of declarations. Medicine provided 40% of declared events, ICU 25%, paediatrics 20%, surgery 11%. We found that most of the incidents concern the less invasive devices (classes I and IIA as defined by EC Directive 93/42), which are the most widely used references. Declared events originated respectively from nurses (65% of the cases) and from physicians (30%).

As soon as an event is declared, we inform the supplier, who conducts an investigation in the concerned hospital department. Observed causes of incidents concern faulty manufacturing in 50% of the cases. The other 50% of incidents can be attributed to lack of information, education, resistance to change and device misuse.

We have been using the Pharma Decision vigilance logbook for the follow—up and consolidation of the different stages of event instruction. We found the software useful in reporting information back to the care units. As central purchasers, we intend to use data collected in the vigilance database to refine our device selection criteria in hospital tenders.

Assistance Publique des Hopitaux de Marseille, Department of Pharmacy, Central Purchasing Center, 80 rue Brochier, 13354 Marseille, France.

21 HOME SERVICE PROGRAM FOR ONCOLOGY PATIENTS IN CONTINUOS INFUSION USING ELASTOMERIC INFUSOR

M. Gambera*, I. Aiello*, D. Fagnani, M.M. De Rosa***

A home service program for oncology patients using elastomeric infusor filled in the centralised laboratory for oncology preparations of the hospital pharmacy department for all type of patients, day-hospital, ambulatory and in-patients was started. The aim of the present research is to assess the compatibility and stability of oncology therapies and to evaluate some publications on similar experiences *(1, 2, 3)*. The protocols used are 5-FU continuous infusion for the treatment of the colon carcinoma or the methastatic stomach malignancies *(4, 5)* and VAD - Vincristine, Adriamicyn and Desametason - for the second line treatment of multiple myeloma *(6)*.
The results permitted to reduce hospitalisation time with improved quality of life for oncology patients, lower coat of the treatments achieved by managing the therapy only in day-hospital giving the same quality in terms of safety for the patients and efficacy of the treatment.
The elastomeric infusor used have proved to be easy to handle, inexpensive and able to minimize hospitalisation for the patients. This project has strengthened the very good co-operation existing between oncologists, pharmacists and nurses, reduced the risks for the staff and enhanced the quality of the service offered to the community.

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Hospital Pharmacy Azienda Ospedaliera "Ospedale di Vimercate", Via Cesare Battisti 23, 20059 Vimercate (MI) Italy, fax no +39 039 6654688, phone no +39 039 6654601
* Pharmacy Service
** Oncology Division Medicina II°

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M.L. Aiezza, M. Cammarota, A. Gallo, E. Piscitelli, **A. Nicchia**, Italy

35. *Compatibility studies of two different formulation of methotrexate in PVC infusion bags*
A.M. Goglio, F.S. Robustelli della Cuna, E. Strocchi, G. Magistrali, R. Pannuli, **M. Crispi**, P. Politi, C.M. Camaggi, Italy

Clinical Pharmacokinetics

36. *Assessment of intra-individual variability on the theophylline kinetic profile in critically ill patients*
A.C. Falcao, A.M. Almeida, M.M. Castel-Branco, **M.M. Caramona**, Portugal

37. *Cyclosporine therapeutic monitoring - evaluation of the mFPIA AxSYM ® compared to mFPIA TDxFLx TM*
G. Fidalgo, **M.E. Pereira**, Portugal

38. *Therapeutic drug monitoring of methotrexate in all and osteosarcoma patients*
A.P. Carrondo, **M.E. Pereira**, Portugal

39. *Artificial neural networks (ANN) for population pharmacokinetic analysis*
M.A. Soares, **L.M. Pereira**, Portugal

40. *Theophylline absorption modeling from a sustained release formulation by a noncompartmental approach*
A.P. Carrondo, **L.M. Pereira**, Portugal

41. *Population analysis of gentamicin in burn patients*
A.P. Carrondo, M.O. Rodrigues, M.A. Soares, L.M. Pereira, Portugal

Design of Clinical Trials

42. *Supply of quinacrine for an institutional clinical trial*
B. Lehmann, A. Tibi, M. Stachowicz-Richard, P. Prognon, D. Pradeau, France

43. *Management of clinical trials in paediatric patients: specificity of antiepileptic drugs*
S. Mairesse, S. Abrioux, I. Chauveau, S. Pravot, P. Meunier, J. Grassin, France

44. *A health-care setting as promotor of a clinical trial, solving problems related to the manufacturing and management of study drugs*
N. Viratelle, S. Abrioux, **C. Grebeaux**, S. Bretagnol, J. Grassin, France

45. *Quality of life assessment in palliative care: which measure?*
N. Pratheepawanit, **M.S. Salek**, D.K. Luscombe, I.G. Finlay, United Kingdom

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46. *Importance of a clinical pharmacist support on the antiretroviral therapy adherence*
A. Carmona, S. Grau, H. Knobel, M. Marin, E. Salas, A. Del Villar, D. Campany, Spain

47. *Problem solving in pharmaceutical care: methodological issues for daily practice*
P.A. Kenigsberg, France

48. *Information drug workshop in psychiatric care*
M-L. Biscay, France

49. *The development of the pharmaceutical care in Ukraine*
T. Kalynyuk, I. Zarooma, I. Kaminnyj, Ukraine

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50. *Prospective evaluation of artificial nutrition through a computer-assisted program*
M.J. Martinez, M.T. Inaraja, V. del Campo, I. Castro, S. Pellicer, Spain

51. *The management of domiciliary artificial nutrition (DAN): development of a new model*
M. Corti, M. Ghiringhelli, H. La Russa, A. Luoni, O. Ruffato, **G. Monina**, Italy

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52. *Drug information centres in Denmark*
K.F. Bach, A. Arnberg, Denmark

53. *Evidence based medicine and formularies*
R. Moscogiuri, G. Console, Italy

54. *Drugdex-Italia project: the active participation of the hospital pharmacists*
C. De Marino, A. Venturelli, L. Zeuli, S. Cozzolino, G. Bacis, M.L. Farina, G. Macario, Italy

55. *The quick-rescue and general medicine doctor: «synergy» of pharmaco-vigilance*
R. Salotti, **L. Fabrizio**, Italy

Evaluation of Medical Devices and Medical Procedures

56. *Evaluation of two disposables infusion devices for home chemotherapy*
M-D. Belles. M-D, Castera, F-J. Abad, A. Marco, F. Meseguer, H. Garces, M-L. Lapuerta, M-L. Gimenez, Spain

57. *Cost analysis of allogeneic bone marrow transplantation*
F. Bailly-Salins, **M-C Woronoff-Lemsi**, E. Deconinck, M. Jacquet, J-Y. Cahn, France

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58. *Credit for learning - an innovation in continuing education of pharmacists in the United Kingdom*
A.M. Brown, R. Mitchell, United Kingdom