Dear reader,

In January 1999, the Pharmaceutical Care Network Europe (PCNE) together with the Danish College of Pharmacy Practice, Pharmakon, organised a working conference during which the outcomes of pharmaceutical care were the core topic. Participating were a mixture of researchers in the field of outcome assessment and practising pharmacists from 18 different countries, including some from outside Europe.

The aim of the working-conference was:

- to contribute to the development of validated outcomes instruments to measure the impact of pharmaceutical care on patients and the health care system;
- to contribute to the above by means of defining, constructing and developing validation methods for instruments which are capable of assessing those outcomes properly.

During the conference there were a number of excellent presentations, each dealing with constructing, validating and using instruments and questionnaires. There was also a networking market where the participants got a chance to share their research with others. But the emphasis of the conference was on the working groups, in which instruments for assessing the impact of pharmaceutical care were constructed.

The main way of proceeding in the workshops (which lasted 14 hours in total and were on average attended by 10 people) was a very logical one:

a discussion on the exact content and nature of the outcome to be measured;

- a discussion on the dimensions of the outcome
- a discussion on how changes in each dimension could be measured and where the data should be collected
- then a possible instrument was constructed and compared with the existing ones (if any)
- and finally the validation of the instrument was discussed and prepared.

In this proceedings you will find the results of the conference: the scope of the outcomes under discussion, the full text of the presentations (including the introductory lectures for the workshops), the abstracts for the networking market and the material produced by the workshops.

You are welcome to use whatever you would like. However, we would appreciate if you would inform us of the fact that you are using our material, and possibly we could co-operate in the procedure of completing and validating the instruments.

We are very grateful to the participants for putting a huge effort into making the working conference a success, but would also like to thank the Danish Pharmaceutical Association, Glaxo Wellcome, Federal Union of German Association of Pharmacists (ABDA), and the Royal Dutch Association for the Advancement of Pharmacy (KNMP) for their financial support. We would also like to thank Pharmakon for providing the perfect settings and conference secretary Helle Tømming for her work.

Foppe van Mil

on behalf of the organising committee:
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MEASURING OUTCOMES IN PHARMACEUTICAL CARE

Lecture by Mary Tully, School of Pharmacy and Pharmaceutical Sciences, University of Manchester, UK

In a lecture of this length, it is not possible to give anything other than a very brief overview of the issues surrounding pharmaceutical care and outcomes measurement. Separate overviews of these areas are given, followed by a discussion of the measurement of the outcomes of pharmaceutical care itself. Finally, there are some recommendations for research in this area. Hopefully, this will set the scene for the remainder of the conference.

Overview of Pharmaceutical Care

There are several definitions used for the term 'pharmaceutical care', but two are most commonly quoted. These are "the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve the patient's quality of life[1]" and "a practice in which the practitioner takes responsibility for the patient's drug-related needs and is held accountable for this commitment[2]". The pharmaceutical care process goes beyond providing information to patients or dispensing the correct medication. It can best to be considered as a cyclical process. Within this, the pharmacist assesses the patient, plans therapy and care, evaluates the impact of that therapy and care and then follows up whether or not the assessment and plans needed to be re-assessed and updated[2]. This has also been described as a process concerned with the initiation of therapy (or the therapeutic plan), monitoring therapy (deciding upon which information to collect, when and implementing this) and managing therapy (where the pharmacist revises the plans and its objectives, based upon the monitoring data)[3].

It is essential when considering the concept of pharmaceutical care to appreciate that the measurement of outcomes are an essential part of its implementation. The first definition makes this explicit. However, it should also be included in the second definition. To be

held accountable implies that the results, i.e. the 'outcome', of your practice will be compared to a previously agreed level of service that should have been provided. The desired outcomes of pharmaceutical care are cure for disease, elimination or reduction of symptoms, arresting or slowing of the disease process and prevention of disease or symptoms[1]. Although the measurement of outcomes can clearly be used in the assessment of the cure or the prevention of disease, it is in the impact of pharmaceutical care on symptoms or disease processes that outcomes assessment becomes really important. Here, no cure or prevention is possible and therefore the severity of disease and how it affects the patient is crucial. Measured longitudinally over time, this can provide essential data on the effect of care.

Overview of Outcomes and Outcomes Measurement

Donabedian was one of the first people to specifically use the term outcome when assessing health care, specifically the quality of that care[4]. He used the tripartite descriptions of structure, process and outcome in describing health care activities. Structure is the organisational framework for the activities, such as the number of wards or the number of pharmacists in a hospital. Process is the activities themselves, for example a patient counselling service. Outcome is the impact of the activities in relation to individuals or communities, such as improved health and productivity of the population. Structure and process are relatively easy parameters to measure. Until the past decade, it appeared that many health care providers considered that if these were adequate monitored and funded, a good outcome (i.e. a quality service) was automatically ensured[5]. Outcome assessment was limited to mortality and morbidity rates and financial accounting, data that were easily or routinely available.

In the context of health care, the term outcome has a specialist meaning, where the health of the patient is the outcome of interest. Donabedian considered an outcome to be "a change in patients' current and future health status that can be attributed to antecedent health care[6]." Jenkinson stated that this could be assessed "in terms

of mortality, morbidity, physiological measures and, increasing, more subjective patient-based assessments of health[7]."
Mortality is a very blunt instrument to be used as a health outcome measure. Death can be far-removed in time from the intervention and mortality statistics ignore the existence of health states considered 'worse than death' (such as persistent vegetative states). In addition, graduations of this outcome are not possible. Reported symptoms and conditions are commonly measured outcomes, but seldom take account of health from the *patient's* prospective rather than from the clinician's prospective. This has been elegantly described in 1991 as "what matters in the twentieth century is how the patient feels, rather than how doctors think they ought to feel on the basis of clinical measurements[8]". As a result, health status measures, which assess wider aspects of health such as well being and social functioning, have become more widely used, especially for research purposes. Measurement of health gives richer and more pertinent data about the patients, compared with clinical examinations or laboratory tests, which tell very little about what the disease means to the sufferer[9].

In the literature on outcomes, there are many similarities in the definitions given of concepts such as health status, health-related quality of life or quality of life. At different times, some authors have described the same measures using various titles[9,10], adding to the confusion. Generic outcome measures, such as the SF-36[11], can be used in any disease state but are, by necessity, very general in what they measure. Disease specific outcome measures, such as the Arthritis Impact Measurements Scale[12], are intended for use for specific disease and include more specific assessments than is possible for generic measurements. However, they cannot be used to compare different disease states. Domain or dimension specific outcome measures, such as the McGill Pain Questionnaire[13], are even more narrow in what they measure and could be used in addition to generic outcome measures. Patient-centred outcome measures are very different to the previous measures, which were all pre-defined questionnaires. The patient centred measures, such as the Patient

Generated Index[14], allow the individual to include items in the instrument that are personal to them (such as playing cards).

Outcome measures must be robust and suitable for the use for which they are intended. They should be valid (i.e. measure what they are supposed to measure), reliable (i.e. measure in reproducible way), sensitive to change (i.e. detect change over time), practical (e.g. not over burden the patient), and appropriate to for the use intended to (e.g. contained questions about the symptoms that are expected to change).

However outcomes assessment is not easy - that is why structure and process assessment has been so commonly used instead. The lack of common definitions has already been discussed. There can be great difficulties in separating the effects of health care from other influences (such as the influence of help with housework when convalescing) or in isolating the effect of one health care component (such as a pharmacist's intervention) from all others. The relevant outcome may be infrequent, such as in studies to prevent specific adverse drug events, or there may be a long delay to reach the specific outcome, such as in the prevention of stroke. As a result, the use of intermediate endpoints is common. However, the link between the intermediate and final outcome must be well investigated, as has been the case with BP measurement and prevention of stroke[15].

Pharmaceutical Care and Outcomes

Outcome measurement could be used for the assessment of the pharmaceutical care of either individuals or groups, but are most commonly used for the later. They can be used to describe the patient's overall health state, detect previously unidentified problems, improve the prediction of such problems, set treatment goals, monitor treatment response or disease progression and improve professional-patient communication. The use of outcome measures for group comparison is relevant to research and audit in pharmacy practice. The instruments can be used to eliminate poor or unnecessary practice, promote good practice, develop means to evaluate new

services, increase the accountability of such services and empower patients, involving them in service evaluation and planning.
There has been one recent review of literature assessing the outcomes of pharmaceutical care[16]. However, it is also pertinent to consider other recent reviews of the outcomes of pharmaceutical services in general[17-19]. The review of pharmaceutical care[16] only considered studies that demonstrated the patient-pharmacist relationship and where desired outcomes were established with the patient, drug related problems were identified, drug therapy recommendations were made (to the patient or doctor), and monitoring, follow-up and documentation of the pharmacists' activities were done. Bero and colleagues[17], in a review for the Cochrane Collaboration examined the effect of expanding outpatient pharmacists roles on health service utilisation, costs and patient outcomes. They included studies that fulfilled specified methodological quality criteria (as is usual with Cochrane reviews), that compared pharmacy services with either no intervention or with other professionals, and which evaluated services (other than dispensing) delivered in outpatient settings only. Holdford and Smith[18] examined how published research demonstrated the impact of pharmaceutical services on health care outcomes. They included studies that evaluated pharmacy-based services in the USA and where the effect of the service was assessed using economic, clinical or humanistic measures. The review by Tully and Seston[19] aimed to assess the impact of pharmacist reviewing or monitoring long-term prescribing in ambulatory care or community practice. We included studies conducted in outpatient clinics, primary care clinics, nursing or residential homes or community pharmacy. Pharmacists had to be actively involved in medication monitoring or review of the treatment of individual patients. The studies that were included assessed patient outcomes, service costs or specified processed measures and there had to have been comparison to concurrent or historical controls.

Examples of studies that had used outcome measurements to assess pharmaceutical care are those by Lobas and colleagues and Jaber and colleagues[20,21]. The first of the studies aimed to measure

the effect of pharmacists in a family practice clinic on drug therapy and the quality of patient care[20]. The authors used a before-after study design following 184 patients over 14 months. The outcome measures that they used were health status (using a subjective assessment by independent researchers as to whether the patient's disease state had changed from baseline) and cost avoidance. The second aimed to determine the impact in an outpatient clinic of a pharmaceutical care model for patients with non-insulin-dependent diabetes mellitus[21]. They used a randomised-controlled trial to follow 39 patients over four months. They used a mixture of intermediate and patient outcomes, such as renal function, blood pressure measurements, number of hospitalisations and health status (using the Health Status Questionnaire).

The findings of these four reviews can be divided into methodological and outcome measurement findings. The authors of these reviews found that descriptive research was common and that randomised controlled groups were rarely used. Such a study design is important when trying to prove the attribution of the intervention that is being assessed. There was a lack of methodological rigour in the studies, e.g. no independent assessments of the services were conducted, and with the same individual provided the service often doing the assessment. Methodological details were seldom reported, thus making it extremely difficult to replicate services that were found to be effective. Similarly, the source of costing and the perspective taken were seldom reported. Poor quality statistical analyses were also often found.

Very few studies conducted any assessment of outcomes or used outcome measures. In my own work[19], we initially screened over 4,000 citations, looked at copies of 250 articles but only included 49 studies in the final document. Many were rejected because only process measures were used. Clinical or so-called economic measurements were most commonly reported, with health status measurements being found in only three of the 49 papers included in our reviews. 'Economic' studies mostly only reported acquisition costs, not relating them to the patient outcome, as would be expected

in a proper economic assessment. More worryingly, measures were sometimes used without the presentation of evidence of their validity or reliability.

Recommendations

The authors of the above reviews made recommendations for future studies that evaluate pharmaceutical care and pharmaceutical services. Standard operational definitions must be prepared and used, so that readers clearly understand what is meant when terms such as 'pharmaceutical care' or 'patient counselling' are used. Research methods must be rigorous and appropriate for the hypotheses being tested. Consistent and valid methods for data collection are essential and the outcome measures used must be valid, reliable and sensitive to change. Researchers need to include full details of the service provided in their papers, with clear descriptions of the practice setting and the patient demographics. The relationship between structure, process and outcome must be rigorously evaluated and there must be clear differentiation between these measurements. Pharmacy practice researchers must become familiar with the concept that outcomes measurement refers to the assessment of the patient's health and not to other aspects of pharmacy services such as patient knowledge. Links between intermediate and final outcomes must be rigorously established.

There are several gaps in the research base that must be filled. There is a need for more studies conducted in community pharmacies and for proper economic analyses. Most of the studies included in the above reviews were from the USA. The reproducibility of these results in pharmacy services in the rest of the world must be assessed. Kenny and colleagues[16] suggested the need for an international research network for pharmaceutical care research. Hopefully, this conference will see the development of just such a network.

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MEASURING MEDICATION COMPLIANCE – HOW CAN IT BE DONE?

Lecture by John Urquhart, Maastricht University; Maastricht, The Netherlands.

First it is useful to define what is meant by "compliance", to avoid confusion. A useful taxonomy of ambulatory pharmacotherapy is a logical starting point. Ambulatory pharmacotherapy has 3 phases, as Aristotle conceived for the drama: a beginning, a middle, and an end.

Beginning: "acceptance"
The beginning is the patient's acceptance (or not) of the recommended plan of treatment, given the diagnosis and other aspects of the patient's medical situation. "Acceptance" is a term descriptive of the first phase. It is inherently dichotomous, i.e., a yes or no matter. This phase calls for the best in communicational skills among involved caregivers, to be sure that the patient is properly informed about the choices and their foreseeable consequences. An occasional, indecisive patient may start and quickly stop, then restart, which deviates from a strictly dichotomous process. Such deviations from the ideal require operational definitions when one seeks to analyze data from a pharmaco-epidemiologic perspective, but those details do not negate the basically dichotomous character of acceptance.

Middle: "execution of the treatment plan"
The middle is the patient's execution of the prescribed regimen of treatment. It is useful to note that, while we are here discussing pharmacotherapy, some prescribed regimens involve exercise or diet, which change the details but not the concept of what we are discussing. Limiting our attention to prescribed drug regimens, we see that a properly prescribed drug regimen specifies a quantity of drug to be taken at either defined intervals (e.g., q6h) or frequency (e.g., BID). In statistical terms, the prescribed drug regimen specifies

a time-series of events. The quality of execution of the drug regimen can be expressed as "the extent to which the actual dosing history corresponds to the prescribed regimen", which is also the definition of the term "compliance" (1). Because the execution of the prescribed regimen is an on-going process, with a wide range of possibilities for deviation of the actual from the prescribed, "compliance" is not dichotomous but continuous, with a wide spectrum of possible values, until the patient comes to the …

End: "discontinuation"
Treatment eventually stops, either because of professional advice or the patient's decision. Some patients may discontinue and, sometime later, start a second cycle of treatment … or was it a long drug holiday occurring within a single cycle of treatment? Subject to this relatively minor ambiguity, discontinuation is, like acceptance, inherently dichotomous. In any case, our focus here is on "compliance" as defined above.

Blanket term
A useful blanket term for all three phases is "adherence", defined as "following professional recommendations for treatment".
…… *So?*
The foregoing may resolve the long-running debate in which some claim to find evidence for authoritarianism in the term 'compliance', but not in the term 'adherence'. My 25-years in this field have not yet enabled me to discern this difference, but perhaps I am insensitive. I do recognize that many, though still too few, drugs have sound scientific evidence to support the claim that their recommended regimens are optimal. Thus, a well-substantiated drug regimen has the authority of science behind it, which does not mean that it has to be presented to the patient in an authoritarian manner, but it does set limits on the individualization of regimens. For example, there are many circumstances in which it would be far more convenient if the last-taken dose of a low-estrogen oral contraceptive maintained blockade of ovulation for several days, but 36 hours is the present

view of the limit (2), and no amount of caring or sensitivity to patients' needs can make it otherwise.
Also, as we are beginning to recognize, all drug regimens have limits within which one can reasonably expect the drug to provide full therapeutic benefits, and beyond which those benefits decline. This idea gains quantitative expression in the parameter "forgiveness", defined as the post-dose duration of therapeutic drug action minus the recommended interval between doses (3).

The combined oral contraceptives were the first products to be analyzed in this manner, by means of a special protocol, in which placebo pills were, with suitable controls and blinding, substituted for actives in women who had had prior tubal ligations, in order to learn how soon the blockade of pituitary gonadotropin release ended and the ovulating surge of pituitary gonadotropin release occurred (2). Five such studies, reviewed in (2), indicate that the post-dose duration of pituitary blockade can be as short as 36 hours in some women, so that became the basis for labeling recommendations in the UK. The FDA was uncharacteristically less risk-averse than their British counterparts, and set the limit in the US labeling at 48 hours. In any case, the nominal degree of forgiveness, using the UK value, is 36 - 24 = 12 hours, which is not a very wide margin for error in dose timing. If a patient skips her morning pill and does not have the opportunity to take the omitted pill until after midnight, she has reached a point at which the risk of breakthrough ovulation is rising. The labeling informs her when and for how long to use back-up barrier contraception, and how to phase back into correct dosing at convenient times. Thus, the oral contraceptive labeling is a model for all chronic-use pharmaceuticals.

What about 'concordance'?

A British working party recently proposed that we should adopt the term 'concordance' (4), with implications that empowered patients could negotiate customized regimens with sympathetic caregivers. The timing limits defined for the combined oral contraceptives shows that there are inevitably limits on how far one can deviate from the

recommended regimen. These limits are drug specific: the values for the oral contraceptives are not generalizable to other pharmaceuticals, each of which has its own pharmacokinetic and pharmacodynamic characteristics that determine the limits on dose-timing consistent with full safety and effectiveness. Clinical pharmacologists thus have their work cut out for them to provide such information for each of the major chronic-use pharmaceuticals.

The British working party also made much of the importance of patient empowerment to facilitate adherence. Certainly a well-informed, confident patient is best equipped to make judgments about 'acceptance' or 'discontinuation', but the middle phase, 'regimen execution', is quite a different matter. One only has to look at the quality of regimen execution by knowledgeable physicians who self-prescribe, to see that empowerment and technical knowledge do not guarantee good quality of execution of the prescribed regimen (5).

Clearly defined terminology is essential, but clarity has not been a conspicuous feature of previous discussions about terminology for this field, mainly because acceptance, regimen execution, and discontinuation are usually not differentiated and discussed as separate phenomena. I would not object to switching to 'concordance' in place of 'adherence' as a blanket term for the three phases of ambulatory pharmacotherapy, but there is no evident benefit to changing. We do, however, need a term for "the extent to which the actual dosing history corresponds to the prescribed regimen". If "compliance" really does offend too many people, perhaps we could call it by its Welsh-like acronym, TETWTADHCTTPR, pronounced "tetwa tad hicked purr". If indeed "tetwtadhcttpr" is deemed less authoritarian or unfeeling than "compliance", perhaps we should adopt it. There is, however, one last constraint on the nomenclature to recognize, and that is the classification used by the Index Medicus of the US National Library of Medicine for indexing: regardless of whether you use the term 'adherence' or 'concordance', they index your published work under

‘compliance’. It remains to be seen what they would do with ‘tetwtadhcttpr’.

The measurement challenge

Now that we have a precise definition of 'compliance', we turn to the problem of its measurement. The definition indicates that we need to find a method to compile the dosing histories of ambulatory patients, which means the times when doses were taken, and the quantity of medicine taken at those recorded times. Having, by one means or another gotten a reliable dosing history, we can then reckon "compliance" from the comparison of the actual and the prescribed dosing histories. So the measurement problem comes down to the question of how to obtain a reliable dosing history. In concept, at least, the simplest approach is…

Asking the patient

… but that is easier said than done. Taking the medicine is, or should be, a routine in one's daily life, occupying usually less than half a minute per prescribed dose, out of the day's 1440 minutes. Both its routine nature and the small fraction of the day it represents conspire to make the act of dosing easily forgettable. Most people have had the experience of taking the medicine, and then an hour or two later wondering whether the medicine had been taken. A more difficult question to answer reliably is: did I take the medicine a week ago last Thursday? These and other difficulties impose natural limits on the reliability of dosing histories of those patients who are prepared to be fully candid about the quality of their execution of the prescribed regimen. With those patients who cannot or will not be candid, histories are essentially meaningless.

This last point touches on a major problem in this field, which is that many patients are reluctant to admit to their physician or other caregiver that they have not followed the regimen correctly. This prevalent feeling leads to a form of dissembling for which the term 'little white lie' (LWL) is apt, for it should not be confused with a basic lack of co-operation. This LWL behavioral phenomenon has many manifestations, which have the effect of invalidating pre-electronic methods of compiling dosing histories.

A vivid example is provided with the method of returned tablet/capsule counts. Patients are asked to return their drug packages at the next scheduled visit, as is usually done in clinical trials, but many discard all or nearly all untaken medicines (6-10). This pill-dumping phenomenon is most vividly seen in the results of this method when patients have been dispensed 50%, 100%, or more medicine than needed for correct dosing throughout the interval between scheduled visits (11).

Another example of the LWL phenomenon was provided by a big public opinion survey in the Munich area about a decade ago, done by a German opinion-polling firm. They asked about 2000 people, all of whom had at one time or another been prescribed a drug, if they always followed correctly the doctor's instructions. About three-quarters said 'no'. Then they were asked if they had told the doctor of their deviation from his/her instructions, and only about 5% said 'yes'. Then they were asked if they thought the doctor should be informed about their deviations from the instructions, and the vast majority said 'yes'. Then they were asked if an electron-ically monitored medicine bottle would be an acceptable way for the doctor to learn of deviations, and the vast majority said 'yes'. This result epitomizes the situation: mistakes are common but rarely admitted; common sense indicates that the doctor should know about them, but the patient does not want to be the messenger; automatic delivery of the message is acceptable and even desirable (12).

The clinical importance of LWL-motivated behavior is revealed by recent work of Prof. Hans R. Brunner and his colleagues at the hypertension center of the University Hospital in Lausanne, Switzerland. They have found that half of hyper-tensive patients about to have their drug treatment escalated because of nonresponse at a lower level in the stepped-care sequence are, in fact, clinically unrecognized noncompliers (13). This shocking finding illustrates both the pervasiveness of poor compliance and the poor quality of its recognition on clinical grounds.

Patient diaries are another way of 'asking the patient', and provide another illustration of the "little white lie". Henry Milgrom, an

asthma researcher in Denver, has published a stunning graphic, which shows parallel chronologies of electronically recorded and diary recorded doses of inhaled drug. With inhaled steroids, many diary entries were recorded during long intervals between electronically recorded doses (14). As Milgrom points out, these are pediatric patients, so the LWL is presented to the doctor with parental collusion. Patients and their families prefer to accept consequences of undertreated disease than to hear their doctor's reaction to a candid dosing history.

Measuring drug levels in plasma

Many believe that the measurement of drug concentrations in plasma is an objective way to assess compliance, but for most drugs it only takes a day or so of correct dosing to bring drug levels into the accepted therapeutic concentration range. This rapid response is a consequence of the relatively short plasma half-lives of most drugs: it takes about 4 times the plasma half-life to bring the plasma level into steady-state, but correct dosing during only two half-lives prior to the time of measurement will suffice to provide a drug level that implies good compliance. One of the many manifestations of the LWL is a phenomenon called 'white-coat compliance', which is correct dosing, or maybe even an extra dose or two, in the day or so prior to a scheduled visit. This seeming objectivity of drug level data washes up on the rocks of the LWL. Some drugs have plasma half-lives of many days, e.g., fluoxetine, digitoxin, amiodarone, and a few others, so their concentrations plasma could give a fair indication of their intake, subject to other considerations noted below.

Low-dose phenobarbital marker

Morgan Feely, Tom Pullar, and their colleagues in Leeds have used low-dose phenobarbital as a chemical marker to estimate aggregate drug intake (15). They incorporate 2 mg of phenobarbital into the usual doses of drugs used for therapeutic purposes. This amount of phenobarbital is too little to have discernible biological effects, but is large enough to be measurable in plasma. The plasma half-life of

phenobarbital is sufficiently long that a single-point measurement of its concentration in plasma gives a reliable indication of aggregate drug intake over an approximately two-week period. This method works well because the inter- and intra-subject variability in the pharmacokinetic clearance of phenobarbital is sufficiently low that one has only to stratify patients by age in order to have satisfactory measures of drug intake from this method. Marker concentrations at the low end of the normal range pose an interpretative problem, for they could represent either high-end clearance values or a degree of partial compliance. By policy, Feely and Pullar classify these patients as being satisfactory compliers with high clearance values.

Marker data do not, however, indicate anything about dose timing, which is important information for management efforts to improve compliance (16). It is essential that marker-containing drug be the only source of drug available to the patient, and of course that there be no other source of phenobarbital in the patient's life. The phenobarbital marker method does not lend itself to the monitoring of multiple, concomitantly prescribed medicines. Despite these limitations, the phenobarbital marker provides a direct method that can give a reliable indicator of aggregate drug intake over a 2-week period from assay of a single plasma sample.

Electronic monitoring

Electronic monitoring is an indirect method, for it relies on electronic time-stamping of maneuvers made with the package in which drug is dispensed. Electronic monitoring does not prove drug intake, but shows dose timing.

During the decade since its introduction, electronic monitoring has gained the status of being the gold standard method for compiling drug dosing histories, from which compliance can be determined. The formal term for the method is "electronic medication event monitoring". A "medication event" is a set of maneuvers made with a drug package that are necessary to remove a dose of drug. Microswitches or optical sensors that have been integrated into the package can detect these maneuvers, which vary from one type of

package to another. The switch and sensor actions are analyzed by appropriate microcircuitry, time-stamped, and stored in memory for subsequent analysis. Time-stamping is a simple but powerful maneuver, because it can readily be made both irrevocable and immutable.

The first electronic monitor was an eyedrop dispenser that recorded time and date whenever the dispenser was inverted with the cap removed, which pair of occurrences define a 'medication event' (17). The maneuver of inverting the dispenser with the cap removed does not indicate where the eyedrop went, but it is impossible to remove an eyedrop from the dispenser unless it is inverted with the cap removed. Thus, the finding that the scheduled dosing time has passed without the occurrence of the medication event constitutes proof that the medicine was not taken, unless, of course, the patient has a second source of medicine in an unmonitored package. So, sole reliance on the monitored package is a pre-condition for reliable data.

Solid dosage form containers are monitored with respect to the time of occurrence of the cycle of opening and closing of the package: the medication event is the pair of events, opening and then closing. Similarly, the actuation of a metered-dose inhaler is the medication event that is time-stamped for inhalational drugs.

In each case, one must make an assumption about the quantity of drug removed and that the removed drug went where it was supposed to go. Obviously, the measurement will be misleading if the patient willfully executes the medication event and then fails, for whatever reason, to take the medicine. That may happen on occasion by accident, but as a systematic behavior it is restricted to a very small minority of willfully uncooperative patients. Time-stamping forces the patient who would create a false record of good compliance to perform the necessary maneuvers with the monitored package on schedule, every day, for weeks or months. Such behavior, while not impossible, completely transcends the LWL attitude and enters a domain of overtly fraudulent behavior that is, while not nonexistent, distinctly unusual. Such patients would be misclassified as drug nonresponders.

Despite its indirect nature, electronic monitoring provides, with few exceptions, reliable data on drug intake in ambulatory patients. There are several reasons why this simple method works so well. First, the detection of microswitch actions is inherently reliable, so medication events are correctly detected. Second, the main error that patients make is to neglect to take scheduled doses, so the time for dosing passes without occurrence of the medication event. Third, it is in the natural course of events that ingestion or application of the medicine promptly follows the medication event; there will, to be sure, be occasions on which something happens to interrupt this natural sequence, but the probability is low because the entire act of self-medication takes less than a minute to accomplish. Fourth, to overcome the logic of medication event monitoring in compiling a false record of good compliance requires a degree of fanaticism that completely transcends the simple maneuvers that create false records of good compliance under the rubric of the LWL. Fifth, concerns that patients take something other than the recommended number of doses appear to be much exaggerated. To be sure, an occasional patient will misunderstand the dosing instructions, but for the vast majority of regimens the recommendation is to take one unit of medicine (tablet, capsule, drop, "puff") at each scheduled dosing-time.

What about multiple medications?

There are two approaches with presently available monitored packages. One is to look at the various medications the patient is prescribed and pick the one for monitoring that, if not taken correctly, is most likely to get the patient into major difficulty soonest. For example, in the multi-medicine regimen for managing congestive heart failure, the diuretic has that primacy, so, if resources are limited, the logical choice is to monitor the diuretic. A second approach is based on evidence that compliance with multiple, synchronously-taken medicines is very tightly coupled: if the patient takes one medicine, he/she almost invariably takes them all; conversely, if he/she skips the dose of one medicine, he/she skips the

others as well (18). Thus, even if no single medicine has evident primacy, the monitoring of one of several synchronously taken medicines can be expected to give reliable data on them all. Looking ahead, of course, one can anticipate that an electronically monitored, multidrug dose-organizer will be sooner or later be available.

In planning to monitor a single agent in a multi-drug regimen, one will encounter some patients who are insistent upon using a dose organizer, and object to monitored, vial-type packages, because it disrupts their routine. My advice to investigators or caregivers who encounter this objection is to allow the patient to continue to use the familiar organizer and classify the patient *a priori* as fully compliant. I do this on the premise that anyone with such a well-developed routine for taking medicines has a very high likelihood of consistently taking the medicine per the prescribed regimen.

Similarity of compliance patterns across diseases, drugs, prognoses, symptoms

One of the most striking findings to emerge from the past decade of use of electronic monitoring methods has been that the range and distribution of deviations from prescribed drug regimens are so similar across qualitatively very different disease and treatment situations (3,6-11,14,18-20). This finding calls into question many frequently-repeated, unsupported notions about patient compliance that still echo from the pre-electronic era. Chief among these no longer supportable "sayings" is that noncompliance is the consequence of some unsatisfactory aspect of the patient's response to treatment – side-effects, dosing frequency, disappointing clinical course, early recovery, delayed recovery, and so forth. As in other areas of medicine, the advent of reliable measurements brings new, sometimes initially unwelcome perspectives, as speculations and theorizing from the past prove to be untenable in light of sound data.

Economics of electronic monitoring

Recent advances in manufacturing technology have brought the cost of electronic monitoring of solid oral dosage forms down to the range

where a monitor with a 2-year functional lifetime has a cost equivalent to about 6 weeks of treatment with recently-introduced, chronic-use pharmaceuticals. Against that cost, one must assess the value of the information derived from monitoring.

A compelling situation is hypertension treatment. Recent findings from Prof. H.R. Brunner's group in Lausanne indicate that clinically unrecognized noncompliance is responsible for half the escalations of treatment from step-1 to step-2 in the standard "stepped care" scheme for managing hypertension. Typically, this escalation occurs from low-priced, multisource beta blockers and thiazide diuretics, to premium-priced, single-source agents. Thus, the cost of treatment jumps from ca. 15 US cents per day to $1.50 or more per day, i.e., an annualized escalation in treatment cost from ca. $60 to ca. $600. Given a cost of electronic monitoring of ca. $100, we can estimate the economic impact of monitoring, on the following assumptions.

Let us assume for the monitored group that a monitor is provided to every patient who would otherwise be automatically escalated from step-1 to step-2, and that there is no re-use of monitors. We also assume that all those with initially uncontrolled blood pressures who are identified by monitoring as non-compliers remain on step-1 treatment and are satisfactorily managed. We make no assumptions about the unmonitored patients who proceed to step-2, except that they do not return to step-1; some may in fact escalate to step-3, but that further increases their treatment cost and makes the estimated difference larger. At the end of a year's experience with the conventional, no-monitoring approach versus the monitoring approach, we have the following cost comparison for treating 100 patients:

Unmonitored		***Monitored***	
Monitor cost:	0	Monitor cost:	10000
Drug cost:	$60000	Drug cost : 50@$60	3000
	50@600	30000	
TOTAL	$60000		$43000

Thus, the projection is a first-year cost savings of 28%. The break-even point is reached during the 4th month. During the second year, and beyond, the cost savings rise to 45%. Obviously, a key factor in both arms is the success of managing poorly compliant patients. One has to see the extent to which ongoing monitoring is needed in some of the patients for purposes of maintaining satisfactory compliance, and indirect costs thereof. There probably are some efficiencies possible in the deployment of monitors, plus learning-curve effects, that could add to the savings. Note that this economic model is simplified by the assumption that 100 patients are clustered just at the point of imminent escalation as the year begins, whereas in reality patients come to the switch point one at a time throughout the year.

Of course, this is only part of the problem created by hypertension. The biggest problem in hypertension management today is created by early discontinuation of treatment, which plays a key role in the disappointing epidemiology of hypertension treatment: fewer than 30% of patients with hypertension are adequately managed, as shown in one survey after another in the western countries, notwithstanding their differences in organization and financing of medical care. The dynamics of early discontinuation are not well understood, though the phenomenon has been very carefully documented by Judith Jones and her colleagues (21). It is difficult to escape the conclusion that a key factor in early discontinuation is that patients receive relatively little encouragement to continue taking the medicine. One of the attractive developments in recent years has been ambulatory blood pressure monitoring (ABPM) and self-monitoring of blood pressure, as a way to engage patients more closely in the treatment process. An intriguing finding, published a few years ago by Vetter's group in Zurich (22), but little heeded at the time, was that the benefits of ABPM on blood pressure control were mediated through its effect to improve drug regimen compliance. A very important question, now practical to ask, is: will the new focus that electronic monitoring brings to the process of regimen execution result in better quality of blood pressure management and lower rates of early discontinuation?

If indeed, astute use of electronic monitoring can postpone discontinuation, then there is a strong economic case to be made to pharmaceutical manufacturers for supporting monitoring of premium-priced antihypertensive drugs. One could maintain a 2-year program of electronic monitoring at today's costs for ca. $50/year. If monitoring succeeds in adding 2 years of continued treatment with a $600/year pharmaceutical, of which the manufacturer's gross margin is ca. $500, we have a $100 investment to net $1000 in margin flow. I leave it to the pharmacists in the audience to consider how their investment in time in this kind of program could be adequately compensated, either through its favorable impact on their sales or via some kind of manufacturer-sponsored program supported by the program's effects on sales and margin-flow. If something along these lines were to prove cost-effective in the management of hypertension, one might reasonably expect similar economics in the management of other chronic diseases.

Medical benefits

The case has been made and confirmed again and again during the past 30 years that it is better to treat than not to treat hypertension, and better to treat hypertension effectively rather than ineffectively. The contribution to this process that can be made by economical, reliable compliance monitoring lies in its ability to do the following:

(a) avoid needless escalation of treatment,
(b) maintain continuity of blood pressure control through continuity of correct dosing,
(c) prevent early discontinuation by maintaining the patient's direct involvement in the quality of the treatment process.

We are just at the threshold, after a decade of use of electronic monitoring as a high-cost research tool, of seeing its entry into routine care as an economical management tool. The foregoing 3 points will require many studies in many settings before they gain universal acceptance, though, taken at face value, they are hardly revolutionary or visionary constructs. They already have deep roots in

basic principles of clinical pharmacology and of human motivation, plus common sense.

Is compliance an outcome?

Some say so, but what does that actually mean? One of the pioneers of compliance research, Stefan Norell, puts it well: *"... the aim of 'improving' compliance is not to achieve perfect agreement between behavior and prescription, but to increase compliance only to the level where the outcome of treatment is improved. In practice, however, this level is often unknown ..." (23).*

I think it is more useful to regard compliance as a measure of the quality of drug regimen execution, and to regard drug regimen execution as the driving force in pharmacotherapy. Without the medicine being taken at all there is no pharmacotherapy. When the medicine is taken in an unsatisfactory manner, far removed from the prescribed regimen, the consequences are likely to be a suboptimal mix of beneficial and adverse effects. Naturally if the recommended drug regimen is itself substantially suboptimal, which sometimes is the case, then one may be able to deduce a more nearly optimal regimen from the clinical correlates of the various dosing patterns that patients execute.

Safety evaluation

In safety evaluation, the usual patterns of patient compliance are such that only about a third of patients have unrelenting, per-prescription exposure to the medicine, and thus this third may be the only subgroup who are exposed to the full toxic potential of the drug. Another third of patients have intermittent short lapses in dosing that may avoid some mechanisms of toxicity, simply because the occasional lapse in drug exposure and drug action allows time for cellular repair mechanisms to work. Yet another third of patient have intermittent drug holidays, which trigger rebound or recurrent first-dose effects, which may be special sources of hazard, and/or longer periods of time for cellular repair mechanisms to work. In the conventional approach, which is to ignore compliance and average

data from all patients, exposure-dependent risks are underestimated in those actually at risk and mis-attributed to those not at risk.

Why are some drug regimens suboptimal?

The main reason is that many drug regimens are set solely on pharmacokinetic criteria, on the assumption that drug actions disappear as the concentration of drug falls to levels judged too low to exert therapeutic action. This assumption is true for some drugs, but not others, exemplified by the best-selling drug in the history of the pharmaceutical industry, omeprazole. It has a plasma half-life of 30-60 minutes, but a post-dose duration of action (inhibition of gastric acid secretion) of 3-5 days (24). This discrepancy between its pharmacokinetics (PK) and its pharmacodynamics was fortunately detected early in its development, otherwise it might have been abandoned because of a perceived need for dosing every several hours to maintain omeprazole levels in plasma.

In contrast, when cimetidine was being developed, its regimen was set originally on purely PK grounds, with 4 times daily dosing based on its plasma half-life of ca. 3 hours. When ranitidine came into the market with originally a twice-daily regimen, cimetidine was immediately at a competitive disadvantage. That disadvantage worsened when it was discovered that ranitidine could be dosed once daily at bedtime with no loss of efficacy. Eventually it was learned that cimetidine could be given twice daily, and then later it was learned that it, too, could be given once daily at bedtime without loss of effectiveness. In the long interval needed to prove that point, however, the competitive disadvantage took its toll. The final insult was that cimetidine's total daily dose fell from 1200 mg to 800 mg with the use of the once-daily regimen, which mean a one-third fall in revenues. Thus, errors in setting drug regimens can be very costly.

One of the hopes for systematic use of compliance monitoring during drug development is that the data will allow us to analyze the clinical correlates of substantial underdosing by those patients who comply poorly with the selected regimen. If those clinical correlates

suggest that full benefits occur despite underdosing, it would give early warning that the selected regimen was set too high.

Variability in drug response

A conspicuous feature of most drugs is the extent of variability in the magnitude of their actions. In 1991, Carl Peck and the late John Harter sought to model the sources of variance in drug response, using theophylline as an example because of its well-understood clinical pharmacology (25). They pointed out that giving the 'standard' dose of theophylline to the 'ideal' patient results in a range of action that has a coefficient of variation of about 80%. This degree of variability is akin to an elevator in a 20-story building that, when '10' is pushed, is likely to go to any floor between 3 and 17. Such behavior in an elevator would lead to its immediate shutdown for repairs, but comparable variability in the actions of theophylline is simply accepted. The analysis done by Peck and Harter showed how the different sources of variability in drug response interact, and that variable patient compliance rivals pharmacokinetics as the leading source of variability. There has been subsequent controversy over the values chosen by Peck and Harter, particularly their analysis of the role played by pharmacodynamics (26,27), but there has been no real challenge to the notion that variable patient compliance is a leading source of variability in drug response.

Variability in drug response impacts unfavorably on perceptions of product value, simply because of the inherent uncertainty in outcomes of use of such products. All other things being equal, prescribers prefer low-variability, predictable drugs, just as they prefer low-variability, predictable automobiles and other consumer products.

How can we summarize the clinical consequences of variable compliance?

Several generalizations are possible. The first is to say that the clinical consequences of variable compliance depend on the drug, the nature and severity of the disease for which the drug has been

prescribed, and whatever co-morbidities the patient may have and their severities. If the drug is crucial managing the disease, then compliance will, subject to the drug's forgiveness, play a crucial role in the progress of the disease. For example, a patient with stage 3 or 4 congestive heart failure is critically dependent upon correct use of the prescribed diuretic in order to maintain salt and water balance, and deviations from the prescribed regimen that would have little adverse impact in stage 1 or 2 heart failure can result in acute cardiac decompensation, and an urgent need for intensive corrective steps that require hospitalization. In general, the "sicker" the patient, the less is the latitude for suboptimal treatment, of which omitted doses of medically crucial medicines are one component. To continue with the above example, the same patient with stage 3 or 4 congestive heart failure could omit prescribed doses of laxative with the only consequence being some discomfort consequent to constipation – which is not to say that we can ignore the issue, for an added element of discomfort can further complicate an already deteriorating medical situation. Nevertheless, if the patient were presenting in the emergency room from the combined effects of three days' omission of the diuretic and the laxative, the medical priority is clearly to rid the patient of 2 kilos of acutely retained fluid, and deal later with the 2 kilos of feces in the colon. If the patient's heart failure is complicated by chronic obstructive pulmonary disease, then the margin for error in diuretic-based management of salt and water balance is even narrower than indicated above.

Each therapeutic situation has its own dynamics, in which prescribed drugs of various kinds interact in various ways. It constitutes a form of a "therapeutics IQ test" to consider how suboptimal compliance with prescribed regimens, which is a common occurrence, is impacting in commonly occurring clinical situations. In general, the most common form of noncompliance is underdosing, the clinical consequences of which tend to mimic worsening of the underlying disease(s), which in many situations is the natural course of events. To disentangle these we need reliable measurements of patients' preceding dosing histories. Having such

data will inevitably bring into the forefront of clinical judgment the logical question 'nonresponder or noncomplier?'. Thus far, most of the published estimates of the clinical impact of noncompliance have focused on the consequences of overdosing, which, though far less frequent than underdosing, tends to have a distinctive clinical signature, thus facilitating its correct recognition.

Prospect

The prospect is that the ability to measure compliance reliably and economically brings this important variable in ambulatory care into the sunlight. There, noncompliance can be managed based on objective data, and improved, along the promising lines indicated by Cramer and Rosenheck (16). Furthermore, medical decisions can be made on the basis of a firm understanding of the underlying dynamics of poor response. The logical goal is to use dose and drug escalation when they are pharmacologically indicated, and to recognize and attack poor compliance, guided by reliable measurements, when inadequate dosing is the basis for poor response to rational drug therapy.

Acknowledgments

I am indebted to many colleagues who have helped to develop this story, which has been two decades in the making, and continues to unfold in new and fascinating ways. Prof. Hans R. Brunner has recently identified and performed crucial experiments that reveal the hitherto unsuspected extent to which clinically unrecognized noncompliance confounds stepped-care management of hypertension, and, by implication, the pharmacotherapy of other chronic diseases. Joyce Cramer has developed, more than any other single investigator, an immense amount of insight and practical information about noncompliance and its clinical correlates, and, most recently, has led the way in showing how objective measurements of dose timing play a key role as a management tool in successful efforts to improve compliance. Gerhard Levy, Carl Peck, Lewis Sheiner, and Terry Blaschke have provided running commentaries on pharmacometric

aspects of variable drug exposure, and are helping their clinical pharmacological colleagues to recognize that the study of variable compliance is not just a behaviorists' backwater, but a series of vivid natural experiments that can inform clinical pharmacology generally, and the clinical pharmacology of specific drugs, specifically. Bradley Efron, Joerg Hasford, Els Goetghebeur, and Donald Rubin have, in quite different ways, helped educate me in the statistical aspects of the clinical covariates of variable compliance. Erik de Klerk and I have had many enlightening discussions about how to analyze and interpret drug dosing histories. Finally, my long-time partner, Dr. Jean-Michel Métry has inspired, instigated, or fomented hundreds of studies using electronic monitoring, involving over 2 million patient days of monitored dosing; without all that experimental work to draw upon, this field would be only a minor branch of theoretical biology.

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ASSESSING AND TRANSLATING INSTRUMENTS (OVERVIEW)

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Assessing, Translating and Validating Instruments

objectives and concepts
choosing a health outcome instrument
translating and validating instruments
methodological problems ans some examples

Objectives and concepts

HEALTH

A state of optimal physical, mental and social well-being and not merely the absence of disease or informity (WHO, 1946)

CLINICAL STATUS

Signs, symptoms, diagnostic categories, biochemical and psysiological conditions (ERGHO, 1997)

Objectives and concepts

FUNCTIONAL STATUS

The ability of a person to perform and adapt to his/her environment, measured both objectively and subjectively over a period of time (VAN WEEL, 1993)

HEALTH STATUS

The defined well-being of a person in terms of physical, mental, and social condition or function (ERGHO, 1997)

Objectives and concepts

QUALITY OF LIFE

QoL, rather than being a description of patients' health status, is a reflection of the way that patients perceive and react to their health status and to other, nonmedical aspects of lives (GILL & FEINSTEIN, 1994)

Choosing a Health Outcome Instrument

- *Match an instrument to your needs*
- *What is your aim? Do you want to describe, to compare or to evaluate health outcomes?*
- *Condition specific, dimension specific or generic instruments?*
- *Health measurements is essentially evaluative or subjective rather objective*

Development of cross-cultural applicable health status and outcome measures

3 APPROACHES:

sequential

parallel

simultaneous

Translating and Validating Instruments

Definition of Concepts

Original Questionnaire - Source Language Version

Forward Translations

Reconciled Version - Target Language Version

Translating and Validating Instruments

Reconciled Version - Target Language Version

Backward Translation(s)

Comparison between Back and Source Versions

Modified Target Language Version

Translating and Validating Instruments

Modified Target Language Version

Cognitive Debriefing

Final Target Language Version

Validation Tests

Translating and Validating Instruments

RELIABILITY

test-retest
split-half
internal consistency

VALIDITY

content validity - face validity
construct validity - convergent/divergent validity
criterion validity - concurrent/predictive validity

Translating and Validating Instruments

RELIABILITY

INTERPRETABILITY

BURDEN

CONSTRUCTING INSTRUMENTS: THE EXAMPLE OF HEALTH RELATED QUALITY OF LIFE

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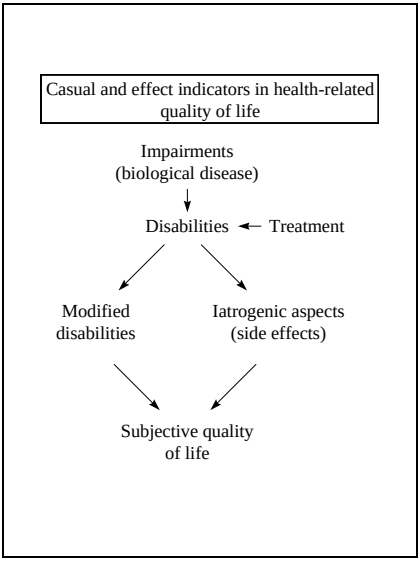


WHO HEALTH 21
Quality of life indicators

- Monitoring and evaluation health policy in the first place
- Short questionnaire, ten items or less
- Easy to score and interpret, single score
- Unidimensional
- Use in general population
- Suitable for cross-national measurements

Indeks medicus

Heading	Year
Rating scales (psychopathology)	1969
Compliance	1975
Quality of life	1977

Quality of life instruments

- Patient friendly
- Positive and negative well-being
- Short and strictly operational
- Strict translation procedures
- Strict validation procedures
- Standardization on 0 - 100 scales

Health related quality of life

1. Multi dimensional concept (health)
   - somatic well-being
   - social well-being
   - mental well-being

2. Subjective concept
   - self rating scales
   - an indeks or a profile

1. Control of disease
   - symptoms
   - compliance
   - side effects

2. Patient as person
   - independce
   - occupation
   - self-care
   - quality of life

3. Interpersonal relations
   - family
   - others
   - social function (role)

4. Caregiver
   - family burden

Psychological General Well-Being Schedule

Total score range from 0 to 110 with higher scores indication better well-being

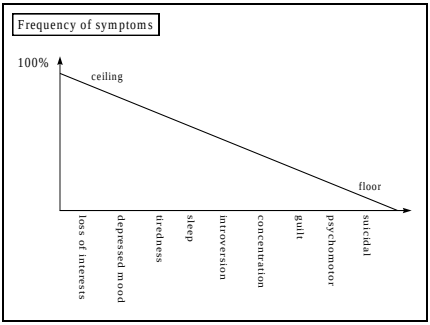
		Percent scale
Normal values:	82 ± 16	75%
Major depression (recovered):	81 ± 18	74%
Panic disorder (recovered):	75 ± 23	68%

Difference between recovered major depression and panic patients on SCL-90 was phobia ($p \leq 0.05$)

From Børup & Unden (1994)

Quality of life and depression
Two-stage evaluation

First stage PGWB/WHO POSITIVE WELL-BEING	Second stage MAJOR DEPRESSION (CD-10) INVENTORY NEGATIVE WELL-BEING
1. In good spirirts	1. In low spirits
2. Active and vigorous	2. Lack of energy
3. Interested in things	3. Lack of interest
4. Fresh and rested	4. Sleep disturbances
5. Calm and relaxed	5. Restless/subdued
	6. Difficulty in concentrating
	7. Lacking self-confidence
	8. Guilt feelings
	9. Suicidal thoughts
	10. Decreased/increased appetite



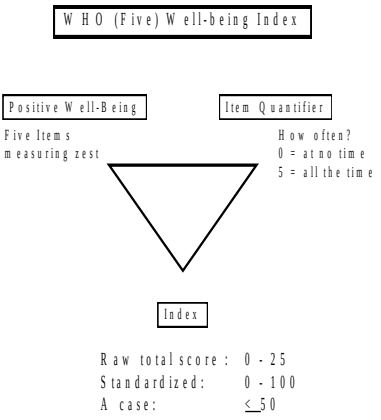
Psychological General Well-being Schedule (PGWB)

Administration:	Patients	(10 minutes)
Components:	- Anxiety	(5 items)
	- Depression	(3 items)
	- Positive well-being	(4 items)
	- Self-control	(3 items)
	- Vitality	(3 items)
	- General health	(3 items)
	- Time experience	(1 item)
Scaling:	Each item rated from 0 to 5 (bipolar)	
Scoring	Normal standards	

WHO Well-being Questionnaire

World Health Organisation, European Quarter
Copenhagen, Denmark

First version:	28-item scale with reference to the Zung scale and Psychological General Well-Being Scale
Second version:	22-item scale (Bradley version)
Third version:	10-item (WHO-Ten-WBQ)
Fourth version:	5 item (Bech 1996) Guelfi et al (1997) Heun et al (1998)



WHO (PGBW) Five

Rasch Analysis
in Danish Population Study

PGBW (WHO) Five Scale

The five statements below refer to how you have been feeling in the past two weeks. Just put a tick in the box ☐ which is closest to how you are feeling

		All of the time	Most of the time	More than half of the time	Less than half of the time	Some of the time	At no time
1.	I feel cheerful and in good spirits	☐	☐	☐	☐	☐	☐
2.	I feel calm and relaxed	☐	☐	☐	☐	☐	☐
3.	I feel active and vigorous	☐	☐	☐	☐	☐	☐
4.	I wake up feeling fresh and rested	☐	☐	☐	☐	☐	☐
5.	My daily life is filled with things that interest me	☐	☐	☐	☐	☐	☐

Danish Population Study
(N=1082)

WHO Five in PGWB version
Mean: 72.3 ± 15.3

Cut-off score 50 versus major depression

sensitivity: 0.93
specificity: 0.87

The psychometric triangle (after Bech 1996) for the scientific analysis of rating scales

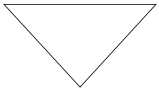
Internal validity

A: internal consistency
•Cronbach's alpha
•Item total coefficient (Likert)
•Factor analysis

B: homogeneity
•Loevinger-Mokken coefficient
•Latent structure analysis

Test-retest reliability

Spearman correlation coefficient



External validity

•Responsiveness (sensitivity to measure change during treatment)
•Goal of treatment (standardization)
•Prediction of relapse
•Prediction of compliance
•Case identifier

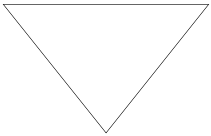
Validity of Patients Self-Assessments

- Consistency: Item structure analysis
- Applicability: Percentage of complete items
- Cronbach's alpha not sufficient
- Loevinger's coefficient of homogenity is sufficient
- Responsiveness: Sensitivity to measure change during treatment
- Less severe disorders, e.g. anxiety
- Continuation or maintenance treatment

Assessing the dimension of severity

Internal validity
- content
- construct

Reliability



External validity
- prediction of treatment response
- discrimination of treatment efficacy

External Validity of QoL Data

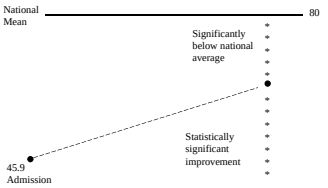
- Outcome trial: Efficacy, safety, QoL
- Prediction of relapse
- Prediction of dropping out (compliance
- Early onset of action
- Goal of treatment
- Case identifier (depressive syndrome)

SF-36

Responsiveness or senditiviy to change in major depression (N=94)

Subscales	Baseline	Follow-up
Physical functioning	86.3	85.7
Role functioning	56.4	72.6*
Bodily pain	69.7	69.9
General health	61.8	67.5
Vitality	46.4	60.5*
Social functioning	68.1	82.2*
Role emotional	46.6	73.7*
Mental health	51.9	67.3*

Ware JE et al
Ware JE et al



Cost-effectiveness analysis

Costs: US$
Direct: medical (medicine, hospitalization etc.)
non-medical (care givers)

Indirect: medical (comorbidity, travelling)
non-medical (loss of working hours)

Effectiveness:	Rating scale scores
Efficiency:	Reduction in symptoms
Social function:	ADL, or other social adjustment behaviour
Quality of Life:	Subjective well-being or satisfaction with treatment

Item analysis of quality of life instruments
in depression and schizophrenia
(Pukrop R, Steinmeyer EM. Pharmacopsychiat 1997; 30: 208)

Instruments:

Sickness Impact Profile (SIP)
- Short-Form 36 (SF-36)
- Psychological General Well-Being (PGWB)

Nottingham Health Profile (NHP)
Mood Questionnaire (FB)
Activities of Daily Living (ADL)
Lancaster Quality of Life Profile (LQLP)
Satisfaction Scale (SS)
Welzel-Lohnen Coloured Scales (WKCS)

Conclusion of facet theoretic model:

A general quality of life dimension
covering positive and negative well-being

APPLYING OUTCOME MEASUREMENTS IN RESEARCH PRACTICE (ABSTRACT)

James C. McElnay, Pharmacy Practice Research Group, School of Pharmacy, The Queen's University of Belfast, Northern Ireland

Pharmaceutical care as described by Hepler and Strand[1] or a variant thereof, has been accepted by most national pharmacy associations in developed countries as a developmental goal for both the community and hospital sector. To date, however, there has been a lack of good research evidence that pharmaceutical care provision leads to improved patient outcomes and less still that it is cost-effective. This is partly due to the expense involved in performing large, well designed trials and the difficulty in getting the full co-operation of practitioners in their execution. When promising research data are available, there is the additional difficulty of getting new services incorporated into routine practice, with the associated increase in remuneration for new pharmacy services.

One of the major shortcomings from a research perspective is relative lack of robust, validated outcome measurement tools. Clinical outcome measures, e.g. peak expiratory flow rate and biochemical markers in blood, can generally be predicted from purely clinical research studies. Methods for the evaluation of non-clinical outcomes, for example, disease specific health-related quality of life, medication management parameters (e.g. patient compliance with medication regimens, GP adherence to pharmacist recommendations), financial outcomes and patient/practitioner satisfaction with new practice models, are at a less advanced stage of development. Many published works within the pharmaceutical care area have experimental designs that are not robust enough to give confidence in the results presented.

A number of ground rules should be adhered to in the design of research programmes to evaluate the impact of extended pharmaceutical services. These include: do not overburden participants (practitioners and/or patients) with too many outcome

measurements; always perform pilot work to test methodology; train practitioners in outcome measurements; select previously validated outcome measures where possible; define hypothesis at start of study rather than "trawling" data for $p<0.05$ values; ensure sample size is large enough to detect statistical differences between control and intervention groups. The performance of large, well designed trials is expensive and they should not be embarked upon without sufficient resource, both from a financial perspective and from the perspective of availability of expertise, e.g. support from statisticians, economists, communication experts and psychologists, depending on the study itself and local requirements.

The above issues will be addresses in the lecture and will be illustrated by completed and ongoing research work performed by the Pharmacy Practice Research Group at The Queen's University of Belfast. Studies presented will include community pharmacy based projects (individualised smoking cessation programme; pharmaceutical care of the elderly), projects at the interface between hospital and community practice (pharmaceutical care of elderly CHF patients; programme for *H*. pylori eradication) and within the hospital setting (management of community acquired pneumonia).

The need for further national and international collaboration in research programmes will also be addressed.

Reference:

1. Am. J. Hosp. Pharm., 47, 533-42, 1990

WORKSHOP REPORT I+II: ASSESSING PATIENT SATISFACTION AND HEALTH STATUS

Chaired by Hanne Herborg and Linda McKeigan

Introduction

The workshop was chaired by Hanne Herborg and Linda McKeigan and dealt with the satisfaction of patients. Satisfaction depends heavily on expectations and therefore was defined as the evaluation by the patient of the provided care. Six domains, influencing satisfaction, were identified being: (1) technical competence of the care giver, (2) disease management, (3) interpersonal relationships, (4) communication, (5) accessibility of the pharmacist and (6) pharmacy environment. The group will continue its work through focus groups with patients and pharmacists, and then make a draft for the instrument. No construction work has been done on health status instruments, but some thoughts concerning its measurement were formulated

Structure of workshop

1. **Content and nature of the outcome**
   Patient satisfaction - the patient's evaluation of his/her pharmaceutical care
2. **Domains and subdomains**
   see Appendix I
3. **Recommendation for measuring changes in the domain**
   - Measure pre and post pharmaceutical care and
   - Measure in a concurrent control group
4. **Presentation of instrument - Patient Satisfaction with Pharmaceutical Care**
   Core instrument of generic items (first draft attached)
5. **Conditions for use**

- Purpose - to compare pharmaceutical care to traditional pharmacy services
- Setting - community pharmacy
- Population - adults

Mode of administration - self-administered

6. Plan for instrument development and validation

6.1 Run focus groups with patients and pharmacists who have had experience with pharmaceutical care, as well as with patients who have not experienced pharmaceutical care, to identify service attributes important to pharmaceutical care and to patient satisfaction with that care

6.2 Refine the first draft, i.e., remove redundant items, modify wording to improve clarity, add items to represent missing components, select one response scale, consider adding a "not applicable" category of response
- in particular, include components addressing potential causes of dissatisfaction; information gathering by the pharmacist; problem identification by the pharmacist; pharmacist advice regarding side effect management; patient confidence in medications, medication taking abilities, and coping mechanisms; fees for pharmaceutical care services

6.3 Preliminary testing - to establish face validity with patients, pharmacists, physicians, payors, administrators and to assess respondent comprehension and burden

6.4 Pilot test - after revisions from preliminary tests, administer to 30 patients to assess the wording of items and to examine response distributions and descriptive statistics for skewness and variability of responses

6.5 Validity testing to confirm domain structure
- in 200 patients who have been recipients of pharmaceutical care
- recommend pre and post testing so that the instrument is tested in patients who have experienced pharmaceutical care

and those who have not
- conduct tests to confirm validity of summated rating scales for each hypothesized dimension i.e., factor analysis, Cronbach's alpha, item analyses
- determine test-retest reliability by administering at an interval of 2-4 weeks

6.6 Translate instrument into other languages (and cultures)
- using recommended procedures

6.7 Use in evaluative studies of pharmaceutical care and accumulate evidence of construct validity

7 Identified key issues

- Items can be developed using a bottom-up or top-down approach. Bottom-up entails a brainstorming exercise to identify components and by groupings these to determine domains; top-down entails determining the overall structure of domains and subdomains, then identifying components. We believe that both are required.

- Generation of items by researchers is speculative as far as representing the patient's point of view and the salient aspects of pharmaceutical care. Therefore, both patients and pharmacy practitioners with experience in pharmaceutical care should be involved in the process of identifying important attributes of pharmaceutical care from their different perspectives. This should be done using qualitative research methods such as focus groups and interviews

- It is unlikely that any one instrument will be applicable in all cultures and health care systems

- Choice of response scale - although an excellent/poor response scale may be psychometrically superior, the phrasing of items for this type of scale is difficult. Phrasing of items is easier with an agree/disagree response scale; however, this type of response scale is vulnerable to a bias known as Acquiescence Response Bias which must be controlled through balanced

wording of items and special statistical techniques

8. **Participants in development and validation process**
   - Interested members of PCNE
   - Europharm Forum

9. **Restrictions or recommendations on instrument use**
   NA at this point in time

Report, Assessing Health Status

1. Workshop Process

An abbreviated approach was taken to this portion of the workshop because of time limitations. A state of the art lecture was given by one of the workshop leaders and then group members participated in a critical appraisal discussion of two studies using health status measures, one successfully and the other unsuccessfully. From this discussion, key issues were identified in the use of health status measures in pharmaceutical care research.

2. Workshop Output

Key issues in assessing health status outcome in studies of pharmaceutical care - see final slide in PCNE.ppt file (oral report given at the conclusion of the conference)

Patient Satisfaction with Pharmaceutical Care - First Draft of the Questionnaire

This draft of the questionnaire is the product of the efforts of two separate groups which generated items for a generic and a disease-specific instrument respectively. After reviewing the two sets of items group members decided that they were not sufficiently different to warrant different questionnaires and the items were pooled to create the beginnings of one questionnaire; however, the merged questionnaire contains two different response scales as well as some redundant items. These have been identified as issues which must be addressed before use. Instrument domains are indicated with

subheadings. These would not appear in the final questionnaire. Also, the items would be randomly ordered.

Please rate each of the following aspects of your pharmacy service as: Excellent, Very Good, Good, Fair, or Poor.

Technical Competence

1. How well my pharmacist works with my doctor.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

2. My pharmacist's knowledge of diseases and drugs.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

3. The pharmacist's advice on my disease and my medicines.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

4. The quality of the pharmacist's recommendations about my medicines

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

Therapeutic Relationship

1. The trust I have in my pharmacist

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

2. The comfort I have in approaching my pharmacist

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

3. My pharmacist's interest in my health

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

4. My pharmacist's willingness to listen to me.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

5. The opportunity to ask my pharmacist all the questions I want to ask.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

6. The pharmacist's ability to understand my problems.

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

7. The amount of time my pharmacist spends with me

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

Communication

A. Dialogue

1. **The pharmacist's ability to explain how my medicine is working.**

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

2. **The pharmacist's ability to improve my understanding of my disease.**

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

3. **The pharmacist's ability to listen to problems I have with my medicines.**

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

4. The quality of the information that my pharmacist has given me.

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

5. The usefulness of the information given to me by my pharmacist.

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

Environmental Factors

1. My overall impression of the pharmacy

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

2. The privacy of my consultation with the pharmacist.

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

3. The opening hours of the pharmacy

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

4. The location of the pharmacy

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

5 The amount of time I have to wait at the pharmacy.

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

General Satisfaction

1. The overall quality of the service from the pharmacy

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

2. The quality of my consultations with the pharmacist

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

Disease Management (Disease Specific)

1 How well my pharmacist taught me to use my inhaler(s) [or other device].

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

2 The teaching I received from my pharmacist about how to monitor my condition [e.g., measure the air flow in my lungs].

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

3 The directions I got from the pharmacist about how to change my drug dose according to my air flow measures.

Excellent Very good Good Fair Poor

☐ ☐ ☐ ☐ ☐

For the next set of items, please indicate how much you agree or disagree with each of the following statements about your pharmacy services by ticking the appropriate answer on the scale.

Therapeutic Relationships

1. I can always trust my pharmacist

Strongly Disagree Disagree Not sure Agree Strongly Agree

☐ ☐ ☐ ☐ ☐

2. I am uncomfortable when my pharmacist calls my physician about my medicines.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

3. The pharmacist listens to my concerns about my health.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

4. The pharmacist understands my health needs.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

5. The pharmacist cares about me.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

6. The pharmacist is always ready to solve problems I am having with my medicines.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

<u>Communication</u>

B. Information

1 The leaflets that the pharmacist gives me are easy to understand.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

2 The leaflets that the pharmacist gives me are useful.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

3 My pharmacist provides me with information tailored to my needs.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

4 I do not know how to take my medications.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

Accessibility of the Pharmacist

A. Private Consultation

1. I don't ask the pharmacist questions because of lack of privacy in the pharmacy.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

2. I am happy when the pharmacist offers to speak with me privately.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

3. There is a separate space for me to speak privately with the pharmacist.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

4. It is easy to make an appointment with the pharmacist when I need to.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

B. Pharmacist Time

1. The pharmacist devotes enough time to me.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

2. I often have to wait too long to see the pharmacist.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

3. I usually get to see the pharmacist without waiting.

Strongly Disagree ☐ Disagree ☐ Not sure ☐ Agree ☐ Strongly Agree ☐

General

1. I would recommend this pharmacy to my family and friends.

Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
☐	☐	☐	☐	☐

APPENDIX I

Structure of the patient satisfaction questionnaire

Global - 3 items
Dimensions - components
Sub-dimensions - components

1.0 Technical Competence (i=4)	pharmacist's knowledge, advice / recommendations, working relationship with doctor
2.0 Disease Management (i=3)	training in self-monitoring and dosage adjustment
3.0 Interpersonal Relationships (i=13)	trust, comfort, amount of time with pharmacist; opportunity to ask questions; pharmacist's interest in me, willingness to listen, understanding of my needs, caring, readiness to solve problems
4.0 Communication	quality, usefulness of information; tailored information; useful and easy to understand leaflets
4.1 Information (i=4)	
4.2 Dialogue (i=5)	ability to explain the medicine, improve understanding of disease, to listen to problems, knowledge of medicine
5.0 Accessibility of the Pharmacist	
5.1 Private Consultation (i=4)	privacy, ease of appointment

5.2 Pharmacist Time (i=3)	enough time with the pharmacist, waiting time
6.0 Pharmacy Environment (i=5)	overall impression, opening hours, location

WORKSHOP III, ASSESING KNOWLEDGE AND ATTITUDE TOWARDS MEDICINE

Chaired by Marion Schaefer and Frank Verheyen

Introduction

This workshop dealt with the patients' knowledge and attitude towards medicines. The instrument should uncover elements explaining certain behaviour. In this field the patients' individual variables like age, education and social status are of uttermost importance. The concept of knowledge with regard to pharmaceutical care was split into three levels being:

- essential knowledge (to be able to follow the instructions of use)
- basic knowledge (to understand why a medicine has to be used)
- extended knowledge (to understand how the treatment works)

Three domains for attitude were identified, mainly in the field of behavioural sciences: (1) individual self-perception, (2) general philosophy and beliefs about medicines and (3) influence of environment (e.g. social acceptance of disease).

This group started to construct a questionnaire and has submitted a validation plan.

A) Report: Attitude

1. What is the exact content and nature of the outcomes, which we wish to measure?

The questionnaire is to collect and assess information about patients' underlying attitudes towards medicines. As these attitudes may have an influence on patients' behaviour and concordance pharmacists should use this knowledge to support the individualised counselling.

The questionnaire allows comparison of patient attitudes on the international, national, and pharmacy level as well as reflecting changes over time.

The approach chosen considers psychological as well as sociological models but provides a new concept of attitudes towards

medicines within the context of Pharmaceutical Care. Special emphasis was given to the patient's perspective.

2. What are the domains and sub-domains of the instrument?

1. Individual self-perception

- importance of a disease for one's life
- effect on daily life
- self perceived knowledge of the disease
- self efficacy and competence
- internal locus of control

2. General philosophy and beliefs about medicines

- self perceived knowledge of drug therapy
- opinion on certain "classes" of medicines
- expectations with regard to the effect of medicines
- desire for instant relief from symptoms
- perceived cost - benefit ratio of treatment
- medicines considered as helpful or harmful

3. Environment

- social acceptance of the disease
- accessibility to the health care system
- trust in health care professionals
- influence by family and friends, media and experts
- external locus of control

3. How can changes in each domain be measured?

A five point Likert Scale is used for evaluating the selected items ranging from „strongly agree (1)" and „agree (2)" via „no opinion (3)" to „disagree (4)" and strongly „disagree (5)". As some of the items bear neither a favourable nor unfavourable connotation it is not yet possible to postulate the optimal score for each domains. This might be possible after the validation process.

4. Presentation of the constructed instrument

Pre-test
Pharmaceutical Care Network Europe
- Attitudes Towards Medicines Questionnaire -
(PCNE-ATMQ)

Dear Patient,

Code:.....

Thank you very much for your willingness to fill out this questionnaire. You will be part of a European wide scientific project called the „PCNE-ATM Questionnaire“ (Pharmaceutical Care Network Europe - Attitudes Towards Medicines Questionnaire). This questionnaire has been developed by an international working group who investigates what people think about their medicines and illnesses. To create a useful tool we need your opinion on this questionnaire so that we will be able to determine whether the questions are understandable and whether it is feasible to administer such a questionnaire in a community pharmacy:

Please rate **all** statements. Afterwards, your pharmacist will discuss them with you.

The questionnaire comprises statements you need to score on a rating scale. This rating scale allows you to express your opinion regarding the statement by: **strongly** agreeing or **strongly** disagreeing, **agreeing** or **disagreeing** or having **no opinion** at all.

Please mark what spontaneously „pops up“ in your mind when you read the statement.

Example: If you **agree** with a statement mark:

Strongly agree	Agree	No opinion	Disagree	Strongly disagree
☐	☒	☐	☐	☐

This is not a test of knowledge and there is no right or wrong. We only need to know your personal opinion. Your answers will be treated highly confidential and we will neither record your name nor your address.

Thank you very much for your help.

PCNE - ATM Questionnaire

1 It is important for me that a medicine immediately relieves my symptoms

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

2 If I need further information I ask my doctor

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

3 I do not have any problems with taking my medicines in front of others

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

4 I am already seriously ill

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

5 I do not have easy access to a pharmacy

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

6 I know how to take my medicines

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

7 I would like other people to pay more attention to my illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

8 Medicines rarely solve my health problems

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

9 I am afraid to become too dependent on my medicines

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

10 Some of my medicines are too expensive for their effect

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

11 I believe in natural remedies

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

12 I avoid speaking about my illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

13 I sometimes think about not having my medicine dispensed because it costs too much

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

14 If I need further information I ask my pharmacist

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

15 I feel rejected because of my illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

16 I believe I am receiving the best treatment possible

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

17 I am satisfied with the service I get when I am ill

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

18 I usually follow my pharmacist's advice

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

19 I can contribute to improving my health

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

20 Other people do not accept me because of my illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

21 I am able to control my symptoms

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

22 It is easy to get an appointment with my doctor

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

23 I am concerned about my health

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

24 I am not worried about possible side effects of my medicines

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

25 I have to wait too long for specialist treatment

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

26 I do not have enough information about the medicines I use

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

27 The support of family and friends help me to cope with my disease

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

28 I am afraid of being unable to work/seek work because of my illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

29 I usually follow my doctor's advice

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

30 I am afraid that my illness(es) will shorten my life

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

31 I trust the advice I get from my doctor

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

32 I find the advice of family and friends about medicines useful

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

33 I feel that my illness(es) will not restrict me doing my daily activities

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

34 Medicines usually make me feel better when I am ill

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

35 I can manage my illness on my own

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

37 I would take medicines if they improved my performance

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

38 I prefer chemical medicines to natural remedies

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

39 I feel I can tell my doctor anything

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

40 I feel that my illness(es) will not allow me to have a full and active life

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

41 I am afraid of becoming seriously ill

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

42 I sometimes decide to buy a medicine because I have read about it in a magazine

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

43 I sometimes do not get the service I need

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

44 I trust the advice I get from my pharmacist

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

45 Since I have been ill other people pay more attention to me

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

46 I am able to follow the doctor's instructions

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

47 It takes too long for some medicines to work

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

48 I do not like taking medicines to prevent illness

Strongly agree ☐ Agree ☐ No opinion ☐ Disagree ☐ Strongly disagree ☐

Thank for rating all these statements. To permit a useful interpretation we would like you to provide some demographic data:

Gender Female ☐ Male ☐
Age: _____ Years

What is the highest level of formal education you have completed?

No qualification ☐
GCSE/O-level ☐
A-level ☐
Degree ☐
Postgraduate ☐

Are your currently using any prescribed medicine?
Yes ☐ No ☐

Are your currently using any self purchased medicine?
Yes ☐ No ☐

How would you describe your health?
Very good ☐ Good ☐ Fair ☐ Poor ☐

5. Conditions for use in testing and practical setting.

The questionnaire has been developed to be used for research as well as for practice. It should be self-administered in the pharmacy. If the patient has any questions he or she can ask the pharmacist for advice. Then privacy should be ensured.

The construction of the questionnaire as a module system with interfaces to other instruments enables researchers or pharmacists to extend it according to their focus and range of interest. The Assessment of the patient by the pharmacist should be completed with regard to:

- Knowledge about health/drugs (interface to knowledge instruments)
- Compliance (interface to compliance testing instruments)
- History of drug-related problems (interface to DRP-instruments)
- General satisfaction with services (interface to satisfaction instruments)
- Ability to cope with health problems (interface to coping instruments)

6. Plan for validation of the instrument

As the questionnaire is intended to be used on an international level all members of the working group were asked to pursue the validation of the questionnaire in the various countries. So far, PCNE-members from Spain, Belgium, Switzerland and Germany agreed to contribute to the validation of the project.

Plan:

1. Developing guidelines for pre-testing the questionnaire (For detailed information see: Appendix 1)
2. Translation of the instrument
3. Qualitative Pre-test (approx. 12-15 patient)
   Objective: Test for usefulness and comprehensibility.
   Measures: Structured pharmacist-patient interview
   Itemanalysis (Item-Difficulty Index, Item-Discrimination Coefficient)
4. Quantitative Pre-test (approx. 50 patients)
   Objective: Establishing validity and reliability of the instrument
   Measures: Statistical analysis (e.g. factor analysis, cluster analysis, tests for internal consistency)

7. Identified key issues

The identified key issues lead to the formulation of the above mentioned domains and items.

8. Who will be involved in the validation of the instrument?

a. Development and co-ordination of the project: Prof. Dr. Marion Schaefer, Katrin Muehlbauer RPh, Dr. Frank Verheyen
b. Co-ordination of implementation:
   Switzerland (Contact: Dr. Kurt Hersberger)
   Spain (Contact: Flor Alvarez de Toledo)
   Belgium (Contact: Christiane Hendrickx)
   Germany (Contact: Katrin Muehlbauer)
   The pre-tests will be carried out by community pharmacists

9. What restrictions or recommendations need to be attached to the instrument in a general recommendation document?

As attitudes in the medicine use process are individual concepts and fulfil different functions it is not possible to define a „gold-standard". Therefore some of the items can be seen as additional information the pharmacist needs to assess the patient's attitude. To conclude whether these information hinder or improve the rational drug use might not yet be possible to determine. Further investigations seem necessary to reveal which items or combinations of items provide the most useful insights into patient's attitudes.

International Pretest PCNE-ATM-Questionnaire

Dear colleagues,
finally, we come up with more details regarding our commitment to coordinate and organise the qualitative pretest for the PCNE-ATM-questionnaire as discussed during the PCNE Working Conference in Hilleroed in January. Enclosed you will find:

- a patient's version of the PCNE-ATMQ,
- an interviewer's version (IV) of the PCNE-ATMQ, and
- an information letter/guidelines for the interviewer (pharmacist) explaining how to follow through the pretest.

Schedule and inclusion criteria

In order to get significant results we need at least a total of 12-15 patients per country.
The pretest can be done by one or more pharmacies as long as the total of patients is reached. The interviewing process should be completed by a pharmacist, only.
Please let us know by 3-31-1999 whether you were successful in recruiting a pharmacy and whether you/ your country is going to participate in the pretest. Below is a schedule how the project should ideally move on.

Schedule of the pretest

February/March- 31- 1999	April/Mai 1999
Pharmacy recruitment: 1 or more	• Translation of PCNE-ATMQ (both versions), translation of the information letter and guidelines for the interviewer, ideally by PCNE-member
June 1999	July/August 1999
Official beginning of pretest phase: • 12-15 patients per country, • patient recruitment by the pharmacy itself	1) Evaluation of the questionnaires by each **PCNE-member.** (Guidelines for evaluation will follow

1) Duties PCNE-member: explains duties to interviewer (see enclosures!) **2) Duties interviewer:** • interviews patients, • collects data (hence correct patient code!) • sends data back to **PCNE-member**	from Frank and Katrin.) 2) PCNE-member sends back a **summary of the evaluation** to Frank and Katrin. **3) Future idea/plan for 1999 or longer:** In case of positive results and general interest a quantitative, international pretest can be done and aspects like itemanalysis, validity, and reliability could be evaluated

We strongly hope that your motivation to take part in the project has not changed yet and that our suggestions how to follow through the procedure meet your ideas and fit into your working schedule.

If you have any other ideas how to do so or if you have any questions regarding our project please contact us. Best regards and looking forward to hearing from you.

Frank Verheyen, PhD
(Pharmacist)

Katrin Mühlbauer, RPh,
(Pharmacist)

Dear interviewer,
we are pleased that you will actively contribute to a European wide project called the Pharmaceutical Care Network Europe-Attitude Towards Medicine Questionnaire (PCNE-ATMQ) and we thank you very much in advance for your cooperation. Currently there are 14 members from different European countries involved in this working group who mainly exists of pharmacists.

Before going into more details regarding the above mentioned project we would briefly like to introduce what Pharmaceutical Care Network Europe (PCNE) is about.

The organisation was founded in 1994 with the aim to continously develop pharmacy focusing on pharmaceutical care services throughout Europe.
In addition, PCNE also cooperates with the EUROPHARM- Forum (WHO), another professional organisation dealing with the implementation of pharmaceutical care projects into pharmacy practice.

But now back to the project.

Goal of the project
The PCNE-ATM -questionnaire has been developed from an international working group during a Pharmaceutical Care Network Europe (PCNE) Workshop Conference at beginning of this year and the goal is to investigate what people think about their medicines and illnesses.

Pretest
Every newly developed questionnaire needs to be tested for usefullness and comprehensibility for research or practice.A pretest is the first step to assess the tool for the above mentioned criteria and you are asked to hand out this questionnaire to 12-15 patients willing to participate.

/ **Important steps to make the project a success:**

/ **1). Criteria for patient selection:**
You can select:

- any kind of patient i.e. being healthy, or having a chronic or transient illness
- is older than 18 years and
- is literate and proficient in the nation's language and
- oriented to self, place, and time

/ **2) What to do with the patient:**
Explain the patient briefly:

- what the goal of the project is, and
- that his opinion is important
- Explain the patient that he needs to fill out the questionnaire **by himself**

It is important that you do not help him answer the questions or influence him on how to answer. However, if you see that the patient is in doubt what to answer, stress that we just would like to know what he thinks.

- **Time to fill out will take approximately 10-15 minutes**

/ **3) What to do next:**

Once the patient has finished you need to go over **every single question WITH him/her** discussing where (s)he had problems in answering: e.g. (p=patient):

- p did not understand the wording
- p did not know what to answer, could not rate the statement
- p became angry, sad, etc.
- p felt insecure, incomfortable in answering, was hesitating
- the statement was not applicabel for p
- p thought the statement was too intimate
- p thought the questionnaire was too time consuming
- **This will take another 30 minutes**

/ **4) Interviewer's version (IV)**

The interviewer's version is a copy of the patient's questionnaire.
/ **HENCE!** Transfer the **patient's code number** of the patient's questionnaire to the interviewer's version.
Record the patient's responses according to the prepared item(s) in the IV or document your own opinion, comments, etc. under „other".

/ 5**) And finally - you are done!** ☺

Thank you very much for your help and cooperation!

PCNE-ATQM - Interviewer's Version (IV)

Note! All the questions are to be answered by ticking a box in the following check-box:

Patient did not understand the wording ☐	Patient did not know what to answer ☐	Patient became angry, sad etc ☐	Patient felt unsure, uncomfortable in answering, was hesitating ☐	Statement was not applicable for patient ☐
Patient thought the statement was too intitmate ☐	Patient though the question was too time consuming ☐	**Other:**		

In the final questionnaire it is recommended to put the check-box after each question, but in the proceedings we will only show the questions.

1	It is important for me that a medicine immediately relieves my symptoms
2	If I need further information I ask my doctor
3	I do not have any problems with taking my medicines in front of others
4	I am already seriously ill
5	I do not have easy access to a pharmacy
6	I know how to take my medicines
7	I would like other people to pay more attention to my illness
8	Medicines rarely solve my health problems
9	I am afraid to become too dependent on my medicines
10	Some of my medicines are too expensive for their effect
11	I believe in natural remedies
12	I avoid speaking about my illness
13	I sometimes think about not having my medicine dispensed because it costs too much
14	If I need further information I ask my pharmacist
15	I feel rejected because of my illness
16	I believe I am receiving the best treatment possible
17	I am satisfied with the service I get when I am ill
18	I usually follow my pharmacist's advice
19	I can contribute to improving my health
20	Other people do not accept me because of my illness
21	I am able to control my symptoms
22	It is easy to get an appointment with my doctor
23	I am concerned about my health
24	I am not worried about possible side effects of my medicines
25	I have to wait too long for specialist treatment
26	I do not have enough information about the medicines I use
27	The support of family and friends help me to cope with my disease
28	I am afraid of being unable to work/seek work because of my illness

29	I usually follow my doctor's advice
30	I am afraid that my illness(es) will shorten my life
31	I trust the advice I get from my doctor
32	I find the advice of family and friends about medicines useful
33	I feel that my illness(es) will not restrict me doing my daily activities
34	Medicines usually make me feel better when I am ill
35	I can manage my illness on my own
37	I would take medicines if they improved my performance
38	I prefer chemical medicines to natural remedies
39	I feel I can tell my doctor anything
40	I feel that my illness(es) will not allow me to have a full and active life
41	I am afraid of becoming seriously ill
42	I sometimes decide to buy a medicine because I have read about it in a magazine
43	I sometimes do not get the service I need
44	I trust the advice I get from my pharmacist
45	Since I have been ill other people pay more attention to me
46	I am able to follow the doctor's instructions
47	It takes too long for some medicines to work
48	I do not like taking medicines to prevent illness

B) Workshop report: Knowledge

Due to the limited time frame it was not possible to develop a questionnaire to measure patients' knowledge. We rather used the remaining time to outline recommendations for the development of knowledge questionnaires:

The PCNE Recommendations for developing knowledge questionnaires

Patients need a certain amount of knowledge about their medicines and the way they are used to make sure that they gain an optimal benefit from their treatment. Knowledge questionnaires should focus on disease specific rather than general issues. It should also be

considered that the concept of the „informed patient“ is differently seen in the various countries.

A knowledge questionnaire is used to measure whether an intervention like Pharmaceutical Care has led to an improved understanding of the disease as well as the treatment. (Interface to outcome measurement)

Steps to be taken to develop a knowledge questionnaire

1. **Define the knowledge needed to ensure optimal drug use according to**

™ essential knowledge (to be able to follow the instructions of use)
™ basic knowledge (to understand why a medicine has to be used)
™ extended knowledge (to understand how the treatment works)

2. **Define the knowledge needed to ensure optimal drug use according to**

™ the disease itself
™ the medicines used to treat the disease
™ the desired outcomes of the treatment (e.g. lowering blood pressure)

Administration of the Knowledge Questionnaire

Identify the patient’s level of knowledge with regard to

™ self perceived knowledge about a certain disease and treatment
™ the main source of information/knowledge the patient refers to
™ the willingness to seek more information (information needs)
™ Note: This sort of information can be used as independent variables when the outcome of the intervention is measured and interpreted in research
It is also useful to optimise advise giving in practice.

Possible Questions to be asked in the different categories

Disease

Essential:	symptoms of the disease
Basic:	possible cause of the disease
Extended:	prevalence, prevention

Medicines

Essential:	routes of administration
Basic:	serious side effects
Extended:	management of adapted use

Outcomes

Essential:	target of the treatment
Basic:	measurement of the treatment outcomes
Extended:	evaluation the treatment outcomes

Additional Note

The questions mentioned before are examples that have to be expended dependent on the nature of the disease and the medicines involved treating it.