Chapter 8: Generating knowledge

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ABOUT THIS CHAPTER

Pharmacy services and practices are performed in several settings and situations and include mainly aspects of drug delivery and information, and communication with several professionals, patients and customers. The general aim must be to improve health and use of medications. For maintaining the current situation and for developing new professional practices and services the values have to be proven. In this chapter we describe the basic features for generating evidence based knowledge, current status and suggestions for improvement where each pharmacist can contribute.

INTRODUCTION

The patient care process is very complicated and generates discrepancies and errors that to a large extent can be prevented and avoided. For a positive outcome of patient care we therefore need a systematic approach to patient care including structures and processes. In modern care we normally have good or excellent structures, including diagnostic tools, medications and educated professionals. The main problem is probably the delivery, the process of care including routines, information, communication, responsibilities etc. Donobedian[1] has described this in detail and this platform can be used to improve the use of medicines. The pharmacist in community and hospital care, in or outside a pharmacy can be the driving force for developing evidence based services based on pharmacy practice research (PPR).

WHAT IS PPR?

Like medical care, nursing care, etc., pharmacy care and therefore PPR consists of core components: the philosophy and definitions, the patient care process, and the practical management system to support the practice. The most important terminology used is listed in box 1.

The concept of clinical pharmacy was initially related to therapeutic drug monitoring (TDM) but developed to various other activities. Pharmaceutical care (PC) was developed to be more focused on the patient outcomes, and medicines management is basically the terminology used for PC in the UK (except Scotland). PC is medicines management, but medicines management is not necessarily PC. Integrated medicines management is seamless PC.[6] Medication therapy management was developed based on PC to be more understandable to non-pharmacists. Medication therapy management is a service or group of services that optimise therapeutic outcomes for individual patients and include medication therapy reviews, pharmacotherapy consults, anticoagulation management, health and wellness programmes and many other clinical services. Very recently Pharmaceutical Care Network Europe (PCNE) updated the definition of PC to: "Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimise medicines use and improve health outcomes".[7] For all these services the fundamentals are to help patients, directly or via other care givers, to get the best benefits from their medications by actively managing drug therapy and by identifying, preventing and resolving drug related problems (DRPs). This should also be the fundamentals and general aim for PPR.

RELEVANT OBJECTIVES FOR PPR

In all clinical research, addressing patient outcome is crucial. This could be related to clinical, economic or humanistic outcomes, as described by the economic, clinical, and humanistic outcomes (ECHO) model.[8] This model provides a theoretical framework for identifying, collecting and using outcomes data to assess the value of and causal relationships between disease, health outcomes and decisions about medical care interventions (eg, treatment with pharmaceutical products and services). This integrated approach provides a theoretical basis for considering potential trade-offs among economic, clinical and humanistic variables in optimising the allocation of healthcare resources. In PPR clinical outcomes could be related to survival, general or specific health status, consumption of healthcare, etc. This outcome is also related to economic outcomes and could be integrated in health economic models and used to calculate values, especially if health related quality of life aspects can be used. Humanistic outcomes in PPR are normally biased since a service to a patient is hard to assess in a blind trial. Nevertheless, it is important to establish that the patients and also the healthcare professionals are satisfied with a new or extended service.

Often it is not possible to measure ECHO model outcomes of a service. In this case and also when outcomes can be measured, results to establish quality and implementation of the process are important. Process outcomes in PPR can be related to adverse drug events, adherence, discrepancies, error, prescription corrections etc., resulting in patient harm or not. This can be viewed as DRPs.

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Box 1 Terminology used to describe pharmacy practices

Clinical pharmacy (CP) is a health specialty, which describes the activities and the services of the clinical pharmacist to develop and promote the rational and appropriate use of medicinal products and devices.[2]
Pharmaceutical care (PC) is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life.[3]
Medicines management (MM) seeks to maximise health gain through the optimum use of medicines. It encompasses all aspects of medicines use, from the prescribing of medicines through the ways in which medicines are taken or not taken by patients.[4]
Medication therapy management (MTM) describes a broad range of healthcare services provided by pharmacists, the medication experts on the healthcare team.[5]

This is the basis for the concept of PC and involves three major functions on behalf of the patient:[9]

- Identifying potential and actual drug-related problems
- Resolving actual drug-related problems
- Preventing potential drug-related problems

The measurement of drug therapy problems or DRPs could be a very good process measure for PPR in hospital, community care and pharmacy settings. This is also a measure of the quality and efficiency of the intervention and thus the pharmacy service. To further classify DRPs is crucial for PPR, and several systems have been developed and extensively reviewed.[10] The two most widely used classification systems, presented in table 1, are the Cipolle *et al*[9] and the PCNE system.

METHODS IN PPR

According to the Medical Research Council (MRC)[12] in the UK, 'complex interventions are widely used in the health service, in public health practice, and in areas of social policy that have important health consequences'. Conventionally defined as interventions with several interacting components, they present a number of special problems for evaluators, in addition to the practical and methodological difficulties that any successful evaluation must overcome. The MRC has published a document for guidance on the development, evaluation and implementation of complex interventions to improve health. It aims to help researchers to choose appropriate methods, research funders to understand the constraints on evaluation design, and users of evaluation to weigh up the available evidence in the light of the methodological and practical constraints. The document focuses on developing, piloting, evaluating, reporting and implementing a complex intervention and is of great value for PPR.

As described in chapters 3 and 5, study design and methods to decrease bias and confounding are very important to establish a true causal relationship between intervention (including all type of pharmacy services) and outcome. The randomised controlled trial (RCT) is considered the most reliable way to assess the effect of an intervention, but the blinding of patients and evaluators, selection of population (inclusion, exclusion, matching) and data analysis (stratification, mathematic modelling) are also of major importance for establishing the direct and true association.

In the selection between randomised and non-randomised designs, size and timing of effects, likelihood of selection bias, feasibility and acceptability of experimentation, and cost must be considered. A major problem connected to complex intervention like the pharmacy service is randomisation by patient, especially when the pharmacy service is part of a multi-professional or multi-disciplinary patient care team. As described above, a complex intervention needs to be developed and piloted for a long time to establish the responsibilities and process of care. To randomise a patient to control and especially to a specific pharmacy service control, if this service is to be evaluated, is very complicated. There is a risk that the intervention is not compared to previous standard care but to a lower level of care. This is because the pharmacist has taken over responsibilities and activities previously performed by another professional and these will thus not be performed in the control group. In this case the outcome might not reflect an improvement in the intervention group, but instead deterioration in the control group. However, often solutions can be found to the technical and ethical problems associated with randomisation. In the MRC document, case study 4 describes how this can be handled. Other possible experimental designs like cluster randomised trials, stepped wedge designs, preference trials, and N-of-1 designs can be the solution.[12] Analysing the results using a quasi-experimental method such as interrupted time series could also be a way forward.

Table 1 Definition and classification of drug related problems (DRPs) based on the two most used systems

DRP: Cipolle *et al*[9]	DRP: PCNE[11]
An undesired patient experience that involves drug therapy and that actually or potentially interferes with the desired patient outcome	An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes
▶ Need for additional therapy ▶ Unnecessary drug therapy ▶ Wrong drug ▶ Dosage too low ▶ Adverse drug reaction ▶ Dosage too high ▶ Non-compliance	▶ Problems – Treatment effectiveness – Adverse reactions – Treatment costs – Other ▶ Causes – Drug selection – Drug form – Dose selection – Treatment duration – Drug use/administration – Logistics – Patient – Other

PCNE, Pharmaceutical Care Network Europe.

RESULTS (STATUS) OF PPR

Table 2 shows the quantity of publications related to PPR. As shown, there were several systematic reviews related to PPR. The total number of systematic reviews listed, including treatment outcomes and pharmacist, was 61 publications, 22 published during the last 5 years. Of those, only seven in fact were systematic reviews and 11 had a clear focus on pharmacist interventions. In total four publications were systematic reviews of pharmacist interventions focusing on patient outcomes including medication review at hospital,[13] community based weight management, warfarin therapy management, and non-dispensing services in low- and middle-income countries. The latter one was a publication from the Cochrane Database of Systematic Reviews. This is one of 150 reviews performed by the Cochrane Effective Practice and Organisation of Care Group.[14] Some

Table 2 The number of publications related to clinical pharmacy practice research

	Search term	Number of publications	AND controlled	AND randomised	AND systematic (sb) (filter)	AND systematic (sb) AND treatment outcome (MESH)
1	Clinical pharmacy	37 061	5295	4175	2279	305
2	Pharmaceutical care	65 366	3796	2677	2440	294
3	Medicines management	5517	473	334	410	53
4	Medication therapy management	14 041	3099	2268	1123	258
5	1 OR 2 OR 3 OR 4	112 079	11 633	8718	5568	833
6	5 AND pharmacist	12 061	880	645	554	61

This search was performed in PubMed 2014-07-27, using text words if not otherwise stated.

systematic reviews of interest for PPR from this group are given in box 2, and discussed further below.

The scope of this chapter is not to summarise PPR and evidence for various interventions on pharmacists or team based pharmacy services' contribution to ECHO. As presented in table 2, there are thousands of PPR studies and hundreds of reviews. As described previously, the research quality and value of each study must be evaluated carefully to draw conclusions on the causal relationships of different interventions. Table 3 presents two selected systematic reviews on medication review outcomes in hospital. The first was based on RCTs and the other was focused on clinical pharmacist interventions. A systematic review of outpatient pharmacists' non-dispensing roles is also presented in table 3.

IMPROVING PPR

If pharmacists want to be seen as high quality healthcare professionals, their practices and services need to be developed, evaluated and found to be of very high quality and contributing to good health. Their development must be in parallel to the development of healthcare and must be at least as good as other health professionals' service and practice development. And this has to be proven. In the authors' conclusions listed in table 3, it is evident that PPR must focus on better outcome measures and better design, but this is only part of the need to be addressed and improved for the future. Pharmacists need better research skills, and a better research culture is also needed. This has to be started during education and continue during all professional practice as a base for life-long learning and development. It is not only universities and other academic institutions that are responsible for this. Below we discuss this in more detail.

Box 2 Some systematic reviews from the Cochrane Effective Practice and Organisation of Care Group, interesting based on potential benefits from pharmacist activities

- Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs
- Discharge planning from hospital to home
- Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns (see also table 3)
- The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilisation and costs in low- and middle-income countries
- Hospital at home admission avoidance
- Interventions for improving outcomes in patients with multi-morbidity in primary care and community settings
- Medication review in hospitalised patients to reduce morbidity and mortality (see also table 3)

DEVELOPING RESEARCH SKILLS

Many pharmacists want to keep up to date but many of the current methods have been shown not to work. The tried and tested methods of standard lectures, provision of knowledge alone or written information, while remaining the backbone of many professional development programmes, just do not work. [17] Some of this time could be spent gaining research skills and undertaking simple effective research based around the practice environment. There are a number of research skills courses available, providing basic research methodologies with practical experience. It is far easier to learn alongside someone who is involved in research and such collaboration and co-operation can be very fruitful. Developing links with a local school of pharmacy can also usefully lead to involvement in research.

Randomised controlled trials

Many research projects, which sadly would have been far more informative had they been conducted as RCTs, are written up every year. The process of randomisation is not difficult, ethics committee approval is sometimes easier to obtain and most patients do not object to being included in randomised studies provided that the reasons are explained to them.

Systematic review writing

Preparing systematic reviews is an important recognised research activity and the task has only just begun. Pharmacists are ideally placed to participate in such activities but surprisingly few have done so to date. As with other forms of research, the skills are best learnt in collaboration with others and a team approach can probably help produce a sharper and accurate review. The whole process of writing a review can give an appreciation of the work involved and of the importance of thoroughness in seeking to find the true answer to a question.

Joining the Cochrane Collaboration

The Cochrane Collaboration[18] is built on the enthusiasm of individuals who collectively can make a difference. There are currently some 52 registered or proposed collaborative review groups covering virtually the whole of medicine; there is also a group looking at the evidence for effective professional practice. All these groups are open to receive new people who are willing to contribute something to the overall effort of producing, maintaining and disseminating systematic reviews of evidence. It may be an offer to hand search a journal that you regularly receive or it may be to be involved in a review. The

Table 3 Three selected systematic reviews interesting for pharmacy practice research

Title and reference	Results and discussion	Authors' conclusion
Medication review in hospitalised patients to reduce morbidity and mortality Cochrane systematic review (Christensen and Lundh[15]).	A total of 4647 references were identified and five trials (1186 participants) were included. We found no evidence of effect on all-cause mortality and hospital readmissions, but a 36% relative reduction in emergency department contacts. It is uncertain whether medication review reduces mortality or hospital readmissions, but medication review seems to reduce emergency department contacts. However, the cost-effectiveness of this intervention is not known and due to the uncertainty of the estimates of mortality and readmissions and the short follow-up, important treatment effects may have been overlooked. It should be noted that this review has been criticised for choosing inappropriate outcomes. It also reports that medication review is largely ineffective whereas at best there is a lack of evidence either way.	Medication review should preferably be undertaken in the context of clinical trials. High quality trials with long follow-up are needed before medication review should be implemented
Medication reviews by clinical pharmacists at hospitals lead to improved patient outcomes: a systematic review (Graabaek and Kjeldsen[13]).	A total of 836 research papers were identified, and 31 publications were included in the study: 21 descriptive studies and 10 controlled (6 RCT) studies. The pharmacist interventions were well implemented with acceptance rates from 39% to 100%. The 10 controlled studies generally show a positive effect on medication use and costs, satisfaction with the service and positive as well as insignificant effects on health service use. Several outcomes were statistically insignificant, but these were predominantly associated with low sample sizes or low acceptance rates	Future research should be designed using rigorous design, large sample sizes and includes comparable outcome measures for patient health outcomes
Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. Cochrane systematic reviews (Nkansah[16]).	A total of 43 studies were included; 36 were interventions targeting patients and 7 were targeting health professionals. One study showed a significant improvement in systolic blood pressure for patients receiving medication management from a pharmacist compared to usual care from a physician. Five studies evaluating process of care outcomes, pharmacist services reduced the incidence of therapeutic duplication and decreased the total number of medications prescribed. Twenty-nine of 36 studies reported clinical and humanistic outcomes. Pharmacist interventions resulted in improvement in most clinical outcomes, although these improvements were not always statistically significant. Eight studies reported patient quality of life outcomes; three studies showed improvement in at least three subdomains. Two of seven studies demonstrated a clear statistically significant improvement in prescribing patterns. Most included studies supported the role of pharmacists in medication/therapeutic management, patient counselling, and providing health professional education with the goal of improving patient process of care and clinical outcomes, and of educational outreach visits on physician prescribing patterns.	A standardised approach to measure and report clinical, humanistic, and process outcomes for future RCT evaluating the impact of outpatient pharmacists is needed. Heterogeneity in study comparison groups, outcomes, and measures makes it challenging to make generalised statements regarding the impact of pharmacists in specific settings, disease states, and patient populations

RCT, randomised controlled trial.

collaboration is a supportive environment in which to develop new skills and sharpen old ones. Details of the review groups and of the nearest Cochrane Centre can be found in the Cochrane Library.

Developing a research culture

The element that continues to be missing within pharmacy practice is an obvious research culture. The incorporation of projects into postgraduate training courses, while producing some interesting though sadly often unpublished material, has not helped to develop a research culture. This is probably due to both a mindset that research is only linked to projects, but also the pressures of service delivery. The medical model has overcome both of these by linking research activity to career progression such that for many clinicians, research activity becomes a way of life. This type of culture change needs to permeate pharmacy.

FOOTNOTES

- Phil Wiffen is editor-in-chief of *EJHP* and also teaches methodology for EBM and systematic reviews.
- Tommy Eriksson is Professor in Clinical Pharmacy, employed at Lund University and Malmö University in Sweden.
- Hao Lu is a clinical pharmacist based at the Beijing United Family Hospital in China.

Competing interests None.

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