

Clinical Pharmacy Services and Evaluation of Medicines Use

The Case of the Swiss Polymedication Check

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Prof. Jörg Schibler

'Care adds quality to life'

Steve Hudson (1952 – 2010)

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M – E – R – C – I !!**

2 ABBREVIATIONS

ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
ADT	Antidiabetic Treatment
AHT	Antihypertensive Therapy
BMQ	Beliefs about Medicines Questionnaire
BP	Blood Pressure
CAS	Certificate of Advanced Studies
COMPARE	COMpute Polypharmacy Adherence RatE
CPS	Clinical Pharmacy Services
CRF	Case Report Form
DPPR	Daily Polypharmacy Possession Ratio
DRP	Drug-Related Problem
EKBB	Ethikkommission beider Basel <i>(German for 'Ethics Committee of Basel')</i>
EKNZ	Ethikkommission Nordwest- und Zentralschweiz <i>(German for 'Ethics Committee of Northwest / Central Switzerland')</i>
evalPMC	EVALuation of the Polymedication Check
FTE	Full Time Equivalent
GP	General Practitioner
GSASA	Schweizer Verein der Amts- und Spitalapotheker <i>(German for 'Swiss Association for Public Health Administration and Hospital Pharmacists')</i>
HbA1c	Haemoglobin A1c
HIV	Human Immunodeficiency Virus
HMG	Heilmittelgesetz <i>(German for 'Federal Act on Medicinal Products and Medical Devices')</i>
HMR	Home Medication Review
IC	Informed Consent
LMT	Lipid Modifying Therapy
LOA	Leistungsorientierte Abgeltung <i>(German for 'Performance-Oriented Remuneration')</i>
MAI	Medication Appropriateness Index

ABBREVIATIONS

MedBG	Medizinalberufegesetz <i>(‘German for ‘Federal Act on University-Medical Professions’)</i>
MMAS	Morisky Medication Adherence Scale
MPR	Medication Possession Ratio
MR	Medication Review
MTM	Medication Therapy Management
MUR	Medicines Use Review
MUR	Medicines Use Review
NHS	National Health Service
NICE	National Institute for Care and Excellence
NMS	New Medicines Service
NSAID	Non-Steroidal Anti-Inflammatory Drugs
OECD	Organisation for Economic Cooperation and Development
OTC	Over The Counter
PCNE	Pharmaceutical Care Network Europe
PCRG	Pharmaceutical Care Research Group
PDC	Proportion of Days Covered
PIM	Potential Inappropriate Medication
PMC	Polymedication Check
SD	Swallowing Difficulties
SSc	Systemic Sclerosis
SWAMECO	SWallowing difficulties with MEdication intake and COping strategies
T-0	Study start evalPMC project, individual for each patient
T-16	Telephone interview 2 evalPMC project
T-2	Telephone interview 1 evalPMC project
T-28	Study end evalPMC project, individual for each patient
QMS	Quality Management System
UK	United Kingdom
WDA	Weekly Dosing Aid
WHO	World Health Organisation
WZW	Wirksamkeit, Zweckmässigkeit, Wirtschaftlichkeit <i>(German for ‘Efficacy, Appropriateness, Economics’)</i>

3 SUMMARY

In view of the demographic changes and the growing proportion of older people, the current healthcare system has to be reconsidered to meet the emerging challenges posed by an increasingly ageing population suffering from several chronic diseases. This polymorbidity often correlates with the continuous use of more than one medicine a day in the general population. This phenomenon is also called ‚polypharmacy‘. Polypharmacy is also known as an independent risk factor for drug-related problems. Common causes for polypharmacy are treatment guidelines, which are usually formulated disease-specific. Due to multimorbidity of a patient, combined use of treatment guidelines may also lead to unnecessary or unfavourable combinations of medicines. According to national and international data, between 4-7% of all the hospital admissions are related to drug-related problems; 30-50% of them could be prevented. Applied to Switzerland, this corresponds to more than 10'000 drug-related hospital admissions per year. Given the increase of chronically ill patients and the lack of medical staff from different disciplines, new models of health care are required to sustain highest patient safety, avoid medication errors, and minimise suffering from drug-related problems. The pharmacist as the expert in drug science and with his broad expertise in patient care can provide a sustainable contribution to face these challenges, especially in outpatients on long-term polypharmacy and resulting need for in-depth counseling.

Lack of adherence as a very specific drug-related problem is the most common cause of the efficacy-effectiveness gap, meaning the gap between therapy efficacy in daily life compared to the effectiveness shown in clinical trials. Adherence to medication regimen is defined as the extent to which patients take medications as prescribed by their health care providers. Thus, the simple statement of the former surgeon general C. Everett Koop "Drugs do not work in patients who do not take them" describes a key issue, especially for outpatient pharmacotherapy. The pharmacist as the last link in the supply chain of a medicine is in the best position to interview the patient about motivation, knowledge, and obstacles for his treatment, and to offer customised support and follow adherence to therapy. Support of adherence to treatment can only succeed if the entire medication is taken into account. Thus, conducting a medication review is the essential first step in any adherence counseling.

SUMMARY

This thesis aimed at giving a general overview over clinical pharmacy services already performed in the Swiss hospital setting and discussing the strengths and limitations of pharmacist-led medication reviews in primary care by evaluating the Swiss Polymedication Check. In addition, specific opportunities for further clarification through pharmacist-led interventions are highlighted in order to select patients at highest needs for future services.

Project A aimed at presenting an overview of existing clinical pharmacy services in the hospital care setting. We performed the first comprehensive survey of clinical pharmacy practice in Switzerland. Our data show considerable regional differences concerning the extent of implementation and pattern of clinical pharmacy services, which points out to the existing crucial gap in seamless care activities. In particular, the regional presence of drug dispensing physicians in the ambulatory care setting seemed to limit the development of clinical pharmacy practice in the corresponding hospitals. Institutions in regions without drug dispensing physicians rather employed pharmacists assigned with clinical activities (n=20, 22% of 135.3 full-time equivalent, FTE) than regions with partial (n=8, 7% of 35.8 FTE) or unrestricted drug dispensing by physicians (n=16, 6% of 68.1 FTE, $p=0.026$). Of hospitals with implemented clinical pharmacy services, 73% had weekly interprofessional ward rounds. In 9%, clinical pharmacists daily reconciled medicines at patient discharge. While interprofessional ward rounds were performed at least periodically, seamless care activities by clinical pharmacists remained insufficiently established.

In order to approach the topic of drug-related problems in patient care from a solution-oriented perspective, the potential of pharmacist-led medication reviews in various settings became a focus of the Pharmaceutical Care Network Europe (PCNE) and was extensively discussed at several meetings and workshops. The following definition for the term 'medication review' has been established and approved by the board of PCNE: 'Medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions.' The PCNE terminology takes into account that the amount of available sources of information defines different types of medication reviews. Specific expertise and skills are required to perform the different types of medication reviews properly. Standardised structures and documentation forms are now needed to achieve appropriate reviews and to translate the findings into an efficient care process. Further, one should also be aware of crucial

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limitations of medication reviews. According to the PCNE definition, medication reviews end in their theoretical process structure with a recommendation for an intervention. Health professionals should therefore be aware of low implementation rates of recommendations resulting in low impact on patient's outcomes whenever no follow-up meeting is achieved to check the sustainability of the advice.

Findings of project A:

- In Switzerland, regional differences in the extent of implementation and pattern of clinical pharmacy services are observed, highlighting a crucial gap in seamless care activities.
- The Pharmaceutical Care Network Europe agreed to a definition for medication reviews and encourages pharmacists to offer pharmaceutical care regardless of the setting.
- Medication reviews offer an excellent opportunity to detect drug-related problems and initiate pharmaceutical care as a contribution within patient care.
- The impact of medication reviews is directly linked to the subsequently provided intervention to solve a detected drug-related problem and to the acceptance rate of this recommendation by the patient and/or the prescriber.

Project B extensively studied the Polymedication Check (PMC), a cognitive and directly remunerated pharmacist-led medication review service in Switzerland. For the first time in the Swiss health care system, a new nationally implemented cognitive service underwent an in-depth evaluation process in daily life setting. Two years after the launch of the service, the Pharmaceutical Care Research Group of the University of Basel initiated an evaluation project (evalPMC) aiming at investigating the impact of the service on medicines use and humanistic outcomes. For this purpose, some theoretical challenges in adherence calculation from refill data had to be considered and various specific outcome measurements had to be developed and piloted. Finally, a randomised controlled trial was conducted in 54 Swiss community pharmacies. Eligible patients used ≥ 4 prescribed medicines over > 3 months. The intervention group received a PMC at study start (T-0) and after 28 weeks (T-28) while the control group received a PMC only at T-28. Primary outcome measure was change in patients' objective adherence, calculated as Medication Possession Ratio (MPR) and Daily Polypharmacy

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Possession Ratio (DPPR), using refill data from the pharmacies and patient information of dosing. Subjective adherence was assessed as secondary outcome by self-report questionnaires (at T-0 and T-28) and telephone interviews (at T-2 and T-16), where participants estimated their overall adherence on a scale from 0-100%.

A total of 450 patients was randomly allocated to intervention (n=218, 48.4%) and control group (n=232, 51.6%). Main addressed DRP during PMC at T-0 was insufficient adherence to at least one medicine (n=69, 26.7%). At T-28, 1020 chronic therapies fulfilled inclusion criteria for MPR calculation, representing 293 of 372 patients (78.8%). Mean MPR and adherence to polypharmacy (DPPR) for both groups were equally high ($MPR_{Int}=88.3$, $SD=19.03$; $MPR_{Cont}=87.5$, $SD=20.75$ ($p=0.811$) and $DPPR_{Int}=88.0$, $SD=13.31$; $DPPR_{Cont}=87.5$, $SD=20.75$ ($p=0.906$), respectively). Mean absolute change of subjective adherence between T-0 and T-2 was +1.03% in the intervention and -0.41% in the control group ($p=0.058$). The number of patients reporting a change of their adherence of more than ± 5 points on a scale 0-100% between T-0 and T-2 was significantly higher in the intervention group ($n_{Improvement}=30$; $n_{Worsening}=14$) than in the control group ($n_{Improvement}=20$; $n_{Worsening}=24$; $p=0.028$). We further evaluated the impact of the intervention on humanistic outcomes, i.e. patients' acceptance of this new service, improved knowledge about their medicines through the intervention, and the availability of a written medication plan. The Polymedication Check increases patient's knowledge of own medicines two weeks after the intervention compared to no medication review. At T-2, the interviewers' ratings of patients' knowledge of medication on a scale from 1 (=poor knowledge) to 10 (=very good knowledge) were significantly higher in the intervention group compared to the control group (Mean_{Int}: 7.4, SD: 1.83 vs Mean_{Cont}: 7.1, SD: 1.87; $p=0.026$). The community pharmacist-led service seems to be highly appreciated by the patients as the majority of 83% of patients judged the counseling by the pharmacist as being helpful for their daily medication management. However, availability of a written medication plan was comparable in both groups (52.5% vs 52.7%, $p > .05$), highlighting room for improvement concerning the patients' management in medicines use.

As a main conclusion of this evaluation study, the current selection criteria for a PMC do not differentiate for patients at highest risk. The promising results of improved adherence and enhanced knowledge in a population with already well-established therapy regimen points at the potential of the service whenever patients at risk are approached. Further, pharmacists failed to implement a weekly dosing aid as a possible optimisation of a patient's self-

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management of medicines use, highlighting the need for additional training of communication skills. Finally, we were also interested in the pharmacists' perspective and their perceptions regarding the new service they could offer. We assessed their arguments in a written survey and a focus group discussion performed shortly after the implementation of the service. In addition, the participating pharmacists from the evalPMC project were asked to fill in an online questionnaire after completing the study. The participants (n=6) of the focus group discussions all stated that recruitment of the very first patient for a PMC was the main barrier for implementing the service in daily practice ('The first is the worst!'). Further, training based on realistic case series from a community pharmacy setting and explicit communication aids were expected to be delivered through the regional or national pharmacists' associations. The evaluation of study pharmacists' perspective was conducted four weeks after study end individually in each study region by voluntary online survey. Out of 59 pharmacists at T-28, a total of 50 (84.7%) completed the survey. Mean estimated time needed to prepare (14min), conduct (30min), and finalise (11min) a PMC was much longer, than proposed by the pharmacists association (pharmaSuisse). However, the pharmacists also stated improved relationship with their patients through the PMC and considered the service as highly important for their professional activity as a pharmacist.

Findings of project B:

- The Polymedication Check underwent an in-depth evaluation process in a prospective randomised controlled trial performed in the German and French part of Switzerland
- No significant impact of the pharmacist-led intervention was shown on objective adherence, while subjective adherence was improved shortly after the intervention.
- In addition, patients' knowledge on medicines was improved by the intervention and patient's acceptance of the service was high.
- The evalPMC project highlighted the need for a re-engineering of the service in order to focus on patients at highest risks for drug-related problems and approach them with tailored interventions.
- Moreover, a follow-up meeting may become an important element in a future service, following the concept of a continuous pharmaceutical care process.
- Pharmacists were highly motivated to perform PMCs once they had overcome the barrier of 'the first is the worst'.

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Project C based on the main conclusion of Project B (need for more tailored interventions to targeted patients) and investigated the potential of the community pharmacy setting to offer the pharmacist's skills purposefully to patients with individual needs. On the one hand, the established routine of community pharmacies the performance of health care campaigns offers opportunities for additional interventions when patients fail to achieve their individual therapy targets, e.g. unreached biomarker values despite the prescription of a medicines therapy. One hundred and six (40.6%) out of 261 patients with antihypertensive therapy were not on target because they violated either the systolic/diastolic (n=62, 23.8%) or the isolated systolic blood pressure (n=44, 16.9%) criterion. Lipid-modifying therapy was prescribed in 122 patients; 38 (31.2%) of them were not on target. Glucose targets were not reached by 8 (27.6%) of 29 patients with antidiabetic treatment. In conclusion, screening detects a considerable proportion of patients (43.8%) who fail to achieve treatment targets despite prescribed therapy. Thus, validated interventions are needed to support community pharmacies in addressing contributing factors to therapy failure.

On the other hand, patient-centred counseling may become more sensitised for specific and underestimated drug-related problems, i.e. swallowing difficulties with medication intake. We therefore developed an in-depth patient self-report questionnaire, which was used in a cohort of patients with systemic sclerosis (SSc) from the European Centre for the Rehabilitation of Scleroderma Rheinfeld, Switzerland, and report new insights on care issues of this population. The final questionnaire consisted of 35 items divided into five sections: complaints, intensity, localisation, coping strategies, and adherence. Eleven out of 43 patients reported current swallowing difficulties with medication intake (prevalence 26%), while 9 (21%) patients reported past swallowing difficulties that had been overcome. Among these 20 patients, self-reported swallowing difficulties were localised mostly in the larynx (43%) and the oesophagus (34%); they were of strong to unbearable intensity (25%), and lead to modification of the dosage form (40%). Knowledge of the pattern of complaints with medication intake, i.e. localisation and intensity, may guide healthcare professionals when choosing the adequate therapy option and enable tailored counseling.

SUMMARY

Findings of project C:

- Existing campaigns performed by community pharmacies offer a wide range for future services aiming at improving therapy efficacy and patient safety.
- Unreached biomarkers despite drug therapy as well as swallowing difficulties with medication intake need further clarification by a health professional to rule out inadequate coping strategies or non-adherence.
- Patient self-reports may guide health professionals in the future when providing tailored counseling, choosing therapy options, or optimising a patient's medication profile.

In conclusion, this thesis showed an increase of the involvement of clinical pharmacists in patient care in Switzerland. Regardless of the setting, the traditional role of pharmacists is currently expanding to a respected contributor and key partner for interprofessional collaboration in patient care. Pharmacists' contributions to patient care are no longer limited to medicines supply only. Multiple opportunities for new services are opening up and their implementation is becoming of crucial importance to tackle the challenges posed by the demographic change and a lack of human and financial resources. In order to overcome internal and external barriers, pharmacists need to assume more responsibility and train their skills in clinical pharmacy practice and interprofessional collaboration. The patients proved to be highly motivated to follow pharmaceutical care models, which is a very promising finding for the development of future services.

4 GENERAL INTRODUCTION

4.1 Medicines use in primary care

Facing demographic realities and as a result an aging population suffering from several chronic diseases, the impact of this polymorbidity often correlates with the continuous use of more than one medicine a day in the general population. This phenomenon, also called 'polypharmacy' has no clear defined cut-off, while the use of more than four or five different drug entities form an established definition.¹ Polypharmacy is also known as an independent risk factor for drug-related problems.² Common causes for polypharmacy are treatment guidelines, which are usually formulated disease-specific. Due to multimorbidity of a patient, combined use of treatment guidelines may also lead to unnecessary or unfavorable combinations. Given the increase of chronically ill patients and the lack of medical staff from different disciplines, new models of health care are required to sustain highest patient safety and avoid medication errors. A recent report has promoted the term 'appropriate polypharmacy', described as 'prescribing for an individual with complex or multiple conditions where medicine use has been optimised and prescribing is in accordance with best evidence'.³ The concept of 'appropriate polypharmacy' recognises that patients can benefit from multiple medications provided that prescribing is evidence based, reflects patients' clinical conditions and considers potential drug interactions. This concept might be promoted in place of existing thresholds that define the term 'polypharmacy' using an arbitrary number of medicines.⁴

According to national and international data, between 4-7% of all hospital admissions are related to drug-related problems; 30-50% of them could be prevented.⁵⁻⁷ Applied to Switzerland, this corresponds to more than 10'000 drug-related hospital admissions per year.⁸ Especially regarding elderly patients on polypharmacy, patients suffering from cognitive impairment or patients taking her medication not as prescribed approximately half of the drug-associated hospital admissions could be avoided in these risk groups.⁶ Avoidable problems usually do not result from individual misconduct, but from suboptimal procedures throughout the medication process. As a result of these risks, the drug-related morbidity is associated with high costs consequences for healthcare systems.⁹⁻¹¹ Situations with a high risk for drug-related problems include events with significant changes in drug therapy or changes in existing diseases, insufficient response to drug therapy, suspected lack of adherence to therapy or medication intake, symptoms of side effects, as well as discharge from the hospital with a change of drug therapy.^{12,13}

4.2 Drug-related problems

A Drug-Related Problem (DRP) is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.¹⁴ In community pharmacies, multiple care issues can be addressed and relevant interventions are feasible. Mehuys et al.¹⁵ listed possible roles for community pharmacists when dealing with older patients with chronic diseases. In addition to drug-drug interactions, non-adherence and deficient knowledge of patients, he also listed practical problems with drug taking such as difficulties with vision 32%, blister opening 12.1%, tablet swallowing 14.8%, tablet splitting 29.7% and distinction between different drug packages 23.4%. All of these drug-related problems are often supposed to be minor, but they might significantly impede the outcomes of a therapy. Potentially Inappropriate Medication (PIM) use in the elderly is very prevalent in Switzerland as well. A recent study revealed lower prevalence rates of PIM use in older managed care patients compared to patients outside a managed care plan (18.6 vs. 21.1%).¹⁶ Hence, irrespectively of belonging to a managed care health plan there is large room for improvement in PIM use.

The Pharmaceutical Care Network Europe (PCNE) developed a classification system aiming at describing DRPs from their effect, including their nature (cause) as well as the intervention to overcome the problems on various levels (e.g. a recommendation to a physician how to solve an observed problem), and the acceptance of this intervention.¹⁷ This classification system originally was developed for a research setting, but unfortunately was not feasible to be implemented in pharmacy practice due to inadequate time expenditure to capture a DRP. Ongoing research aims at developing a tool to support pharmacist in the community setting in documenting their interventions in seamless care and thereby classify underlying drug-related problems as well.¹⁸

4.3 Adherence to medication – an underestimated drug-related problem

The simple statement of the former surgeon general C. Everett Koop "Drugs do not work in patients who do not take them"¹⁹ describes a key issue, especially for outpatient pharmacotherapy. Adherence to medication regimen is generally defined as the extent to which patients take medications as prescribed by their health care providers.¹⁹ The European 'Ascertaining Barriers to Compliance' (ABC) project defined three phases of medication use:

initiation, implementation, and discontinuation.²⁰ Their research has resulted in a new conceptual foundation for a transparent taxonomy, while some research also use primary and secondary non-adherence as another approach to differentiate between initiation and implementation of a therapy. In accordance to their approach, primary non-adherence occurs when a patient does not fill an initial prescription, while secondary non-adherence occurs when a patient discontinues a medication after filling the initial prescription or uses the medicines not as prescribed e.g. incorrect dosing (too high, too low, drug holiday).²¹ Further, distinguishing between intentional non-adherence (e.g. missing or altering doses to suit one's needs) and unintentional non-adherence (forgetting to take medication) may help in understanding and discussing non-adherence.²²

Approximately 25% of patients with different diseases take medication not as prescribed, although the extent of adherence varies between 0-95%.²³ In long-term therapy treatment adherence is on average at 50%.²⁴ Thus, the lack of adherence as a very specific drug-related problem is the most common cause of the efficacy-effectiveness gap,²⁵ meaning the gap between therapy efficacy in daily life compared to the effectiveness shown in clinical trials. Up to 57% (or 269 billion US dollars a year) of the world's total avoidable cost are spent on suboptimal medicine use.²⁶ Risk factors for non-adherence with medication are older age, increasing number of medicines prescribed (especially five or more different medicines taken per day), frequency of dosing regimen (especially 12 or more doses per day), patients' dissatisfaction with prescribers, and multiple prescribers and pharmacies.²⁷

4.4 Understanding non-adherence within patient behaviour models

Taking into account 'that a patient's behaviour is the critical link between a prescribed regimen and treatment outcome',²⁸ the most important factors influencing adherence are patient-behaviour-related. The WHO claims that the understanding of basic behavioural principles and models of behavioural change is the key element to improve adherence - whereas a disease-specific approach is generally of secondary importance.²⁸ Several models of behavioural change provide a conceptual framework for organizing concepts about adherence and other health behaviours. Most prominent, the trans-theoretical information-motivation-behavioural skills model²⁹ outlines three constructs, which are needed for behaviour change: information (i.e. patient has basic knowledge about a medical condition), motivation (i.e., personal attitudes towards adherence behaviour), and behavioural skills (i.e. patient knows specific behavioural

tools or strategies necessary to perform required adherence behaviour). Here, information and motivation interact within each other and have an impact on behavioural skills in order to affect behaviour. Further, the widespread stages-of-change model³⁰ is useful to understand intentional non-adherence and differentiates individuals at different levels of readiness for change. Another specific framework regarding health behaviours was introduced through Meichenbaum & Turk in 1987,³¹ outlining knowledge and skills, beliefs, motivation, and action as the major factors operating on the behaviour change. Conclusively, all of the models encompass patients' knowledge (e.g. didactic provision of generic information) and psychological components (e.g. motivation, beliefs) to explain treatment engagement and adherence.²⁸ Regarding the latter, patients' beliefs are clustered into so-called necessity-beliefs (i.e. perceptions of personal need for treatment) and concerns (i.e. concerns about a range of potential adverse consequences).³² The discussed models have their advantages and disadvantages. Mbuagbaw et al. postulated in 2015 that 'the complexity of adherence behaviour may be beyond the scope of any one single theory. Novel theories are warranted'.³³

4.5 Improving adherence through pharmacist-led interventions

In 2003, the World Health Organization (WHO) highlighted the need for general awareness of healthcare professionals in supporting patients' adherence, especially when therapies concerning fatal diseases as human immunodeficiency virus (HIV) are required.^{28,34} Major efforts were carried out to support patient groups with highest needs for individual care and optimal adherence.³³ However, research evaluating interventions in improving adherence report from low evidence concerning impact on adherence and clinical outcomes.³⁵

One strategy to improve patient' management and empower him in taking his medicines as prescribed is the implementation of a weekly dosing aid in self-management or by repackaging through a community pharmacy. In their systematic review from 2014, Boeni et al. reported a positive effect of drug reminder packaging on adherence and clinical outcomes³⁶ and thereby confirmed a trend observed by Mahtani et al in their Cochrane review in 2011.³⁷ However, both authors highlighted poor reporting and important research gaps i.e. missing humanistic and economic outcomes in the observed studies. Specialised institutions may offer highly complex interprofessional interventions including motivational interviewing, electronic monitoring of drug intake, and continuous follow-up meetings to ensure acceptance and implementation of health professional' recommendation over time.³⁸ Implementation of such complex

interventions in community setting, e.g. the community pharmacies, remained challenging due to different barriers described by Marquis et al. in 2014. They reported four major barriers observed during interviewing participating pharmacists of the program: i) poor communication with patients resulting in insufficient promotion of the programme; ii) insufficient collaboration with physicians; iii) difficulty in integrating the programme into pharmacy organisation; and iv) insufficient pharmacist motivation.³⁹ However, the pharmacist as the last link in the supply chain of a medicine is in the best position to interview the patient about motivation, knowledge, and obstacles for his treatment and to offer customised support and follow adherence to therapy. Support of adherence to treatment can only succeed if the entire medication is taken into account. Therefore, conducting a medication review is the essential first step in any adherence counseling.

4.6 Pharmacist's responsibility in patient care

A worldwide shift in the professional role of pharmacists is observed.⁴⁰ Pharmacists participate increasingly in clinical processes and perform tasks in patient care. This transformation of the profession includes co-responsibility in the achievement of therapeutic success, cost efficiency and avoidance of drug-induced (re) hospitalisations. To describe the future role, the Internationale Pharmaceutische Federation (FIP) published in collaboration with the World Health Organization (WHO) a declaration of "Good Pharmaceutical Practice" in 2011,⁴¹ which assigns the pharmacy an important role in the whole outpatient and inpatient medication process, clearly beyond the traditional responsibility for drug logistics. For the pharmacist four major primary roles have been defined (Box 1).

Box 1 / Roles of the pharmacist defined by the WHO / FIP Declaration 2011

- Role 1: Prepare, obtain, store, secure, distribute, administer, dispense and dispose of medical products.
- Role 2: Provide effective medication therapy management.
- Role 3: Maintain and improve professional performance.
- Role 4: Contribute to improve effectiveness of the health-care system and public health.

These international position statements define an active involvement of pharmacists in the medication management. Key objective is to improve the patient's health by enabling the best possible utilization of drug therapy. This contribution must be based on the needs of each individual. 'Good Pharmacy Practice' requires that an integral part of the pharmacist's contribution be the promotion of rational and economic prescribing and of appropriate use of medicines.⁴¹

4.7 Pharmaceutical care

In the early 1990s, pharmaceutical care was introduced in community pharmacy practice; emphasis was given to providing patient-centred care and cognitive pharmaceutical services⁴². In 2013, the Pharmaceutical Care Network Europe (PCNE) redefined the term as follows: 'Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes'.⁴³ Highlighting the specific pharmaceutical expertise, the definition underlines its complementary worth in patient care together with 'Medical Care' (care provided by physicians) or 'Nursing Care' (care provided by nurses). The use of the terms 'counseling' and 'care' should be clearly differentiated and used carefully. The first competence is for example commonly needed in case of handing over a newly prescribed medication to a patient and represents a regular task in a community pharmacy. Only when pharmaceutical services are repeatedly and continuously provided, does a patient actually undergo care (Figure 1).

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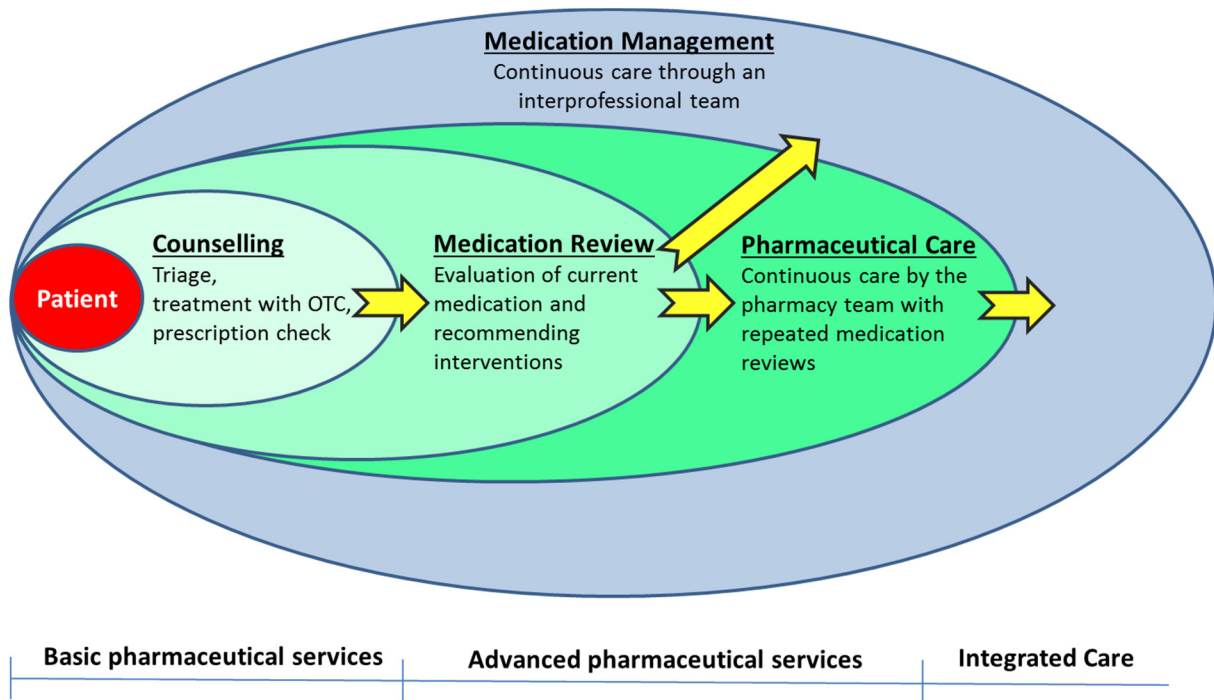


Figure 1 / Framework of pharmaceutical services in patient care

Medication Management (MM) or Medication Therapy Management (MTM) presupposes an interprofessional follow-up patients, e.g. by a pharmacist and the attending physician. In this care setting, seamless communication between involved providers is crucial to ensure patient safety and cost-effective impact. Pharmaceutical care is the pharmacist's contribution to it (Figure 1).⁴³

From a patient's perspective, several changes in care situations, e.g. hospitalisations, readmission at home, transition into assisted living are possible (Figure 2). During admission or discharge process between the care settings, risks of information loss concerning medication therapy and unmet needs can arise. In particular, regarding long-term care, the transition to a nursing home requires a responsible and proactive community pharmacy.

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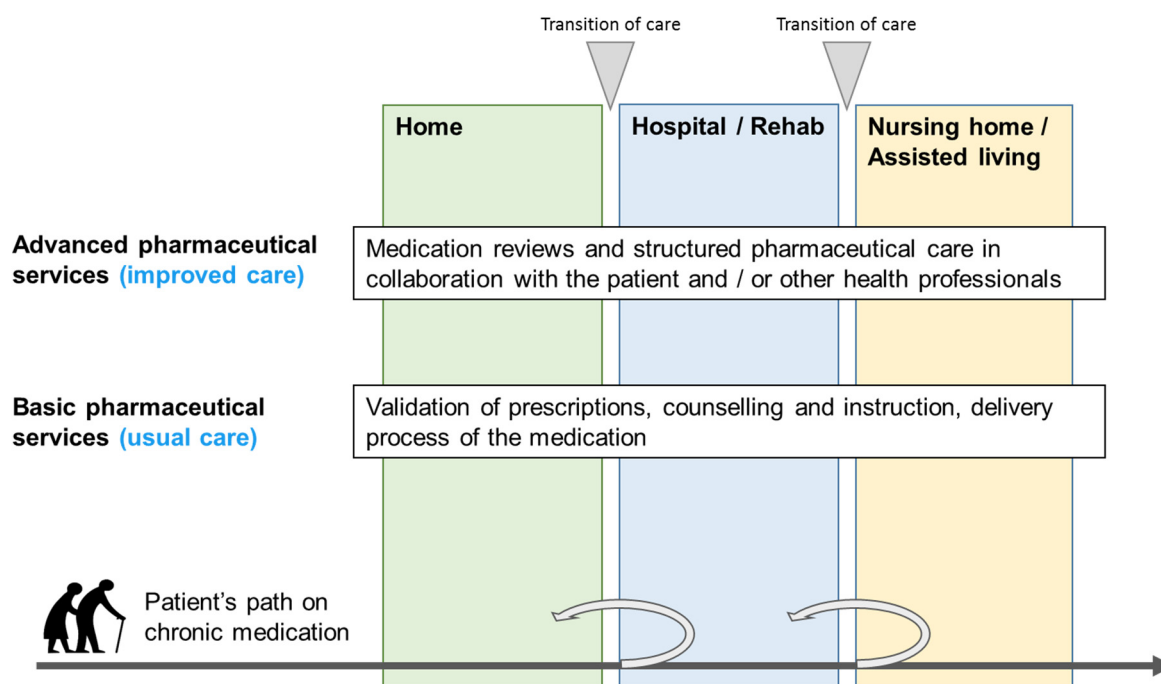


Figure 2 / Continuum of care from a patient's perspective

4.8 Medication review

Following the current PCNE definition, a medication review is 'a structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions.'⁴⁴ Medication reviews should be a routine part of managing the medication therapy.⁴⁵ Three different types can be distinguished, and the terminology follows the available number of information resources (Table 1): simple (I), intermediate (II), and advanced (III) medication reviews.

Table 1 / Proposed typology for medication reviews by the Pharmaceutical Care Network Europe⁴⁵

Type I Simple medication review (only one source of information)	Based on drug history (refill data)
Type II Intermediate medication review (two sources of information)	<p>a) In primary care: Based on drug history AND patient interview</p> <p>b) In secondary care: Based on drug history AND clinical data (diagnoses, lab data etc.)</p>
Type III Advanced medication review (three or more sources of information)	Based on full information from drug history AND patient interview AND clinical data

The analysis in a medication review always includes an inventory of current medication, a history of complaints, their course, the concerns of the patient and the individual needs for support. With respect to the pharmaceutical care process, the medication review is the starting point leading to the suggestion of solutions, the planning and implementation of interventions and ultimately to the evaluation of the outcomes (Figure 3).⁴⁶

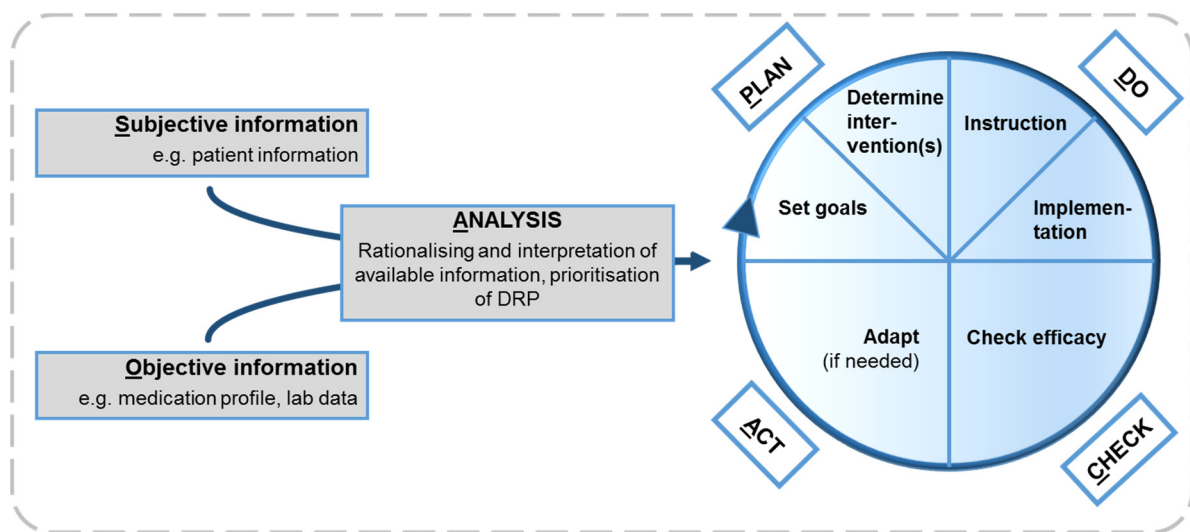


Figure 3 / Proposed process to perform a medication review

Ideally, the recurring analysis is embedded in a continuous care setting, and recommendations are continuously evaluated in accordance with the systematic process of pharmaceutical care.⁴⁷ When lack of adherence to treatment becomes addressed as a common issue in patients on polypharmacy, the pattern of individual behaviour becomes reflected during counseling and tailored helping solutions might be offered as one promising example for this approach. Only by continuous interventions, persistent and effective improvement of adherence to medication can be achieved.

4.9 Patient at risk to suffer from drug-related problems

It is important to identify the patients with the highest need for pharmaceutical care to maximise the existing human resources in the terms of effectiveness and efficiency. One possible approach bases on risk factors, which are used for patient selection (Table 2). Inspired

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by ‚Room for Review‘ 2002⁴⁸ und ‚A Guide to Medication Review‘ 2008⁴⁹, the table differentiates the risks in three main groups: A) the patient at risk, B) the situation at risk, and C) the medication at risk.

Table 2 / Target groups for medication reviews and anticipated challenges

A) Patient at risk	
Age >75 years	<ul style="list-style-type: none"> – Complex medication regimen – Adherence issues – Frailty, fall hazard – Limited access to health services – Repeated hospitalizations (>1/year)
Chronic disease	<ul style="list-style-type: none"> – Long-term medication use mandatory – Changes in chronic condition – New, acute disease – Multimorbidity – Polypharmacy
Life situation	<ul style="list-style-type: none"> – Living alone – Home care / Nursing care – Stressful life stage as a result of external circumstances
Co-morbidities with impact on efficacy of medication	<ul style="list-style-type: none"> – Renal impairment – Liver impairment – Immunosuppression – Psychiatric disease – Physical issues (Swallowing difficulties, Polyarthritis) – Cognitive deficiencies (confusion, dementia)
Self-medication	<ul style="list-style-type: none"> – Use of critical over the counter medication (e.g. Hypericum products, Non-Steroidal Anti-Inflammatory Drugs (NSAID)) – Frequent use of medication mentioned in the Beers-List⁵⁰ – Therapeutic duplication with prescribed therapies
B) Situations at risk	
New prescription	<ul style="list-style-type: none"> – New diagnosis resulting in short or long-time therapy – Manifest adverse drug reaction – Obsolete therapy plan
Transition of care	<ul style="list-style-type: none"> – Initial outpatient contact, e.g. after moving house – Hospital admission – Change between nursing wards – Hospital discharge – Initiation of home care or transfer to nursing care – Change of the family doctor
Complex care situation	<ul style="list-style-type: none"> – Several prescribers – Interdisciplinary care-giving – Interprofessional care-giving

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- | | |
|------------------------------|---|
| Hospital / nursing home stay | <ul style="list-style-type: none">– Medication / nutrition application through feeding tube– Inappropriate medication use through care provider– Long-term prescriptions for antipsychotic drugs, psychotropic drugs, tranquilizers |
|------------------------------|---|

C) Medication at risk

- | | |
|-------------------------------------|---|
| Medication profile and history | <ul style="list-style-type: none">– ≥ 4 medications a day– ≥ 6 single doses a day– ≥ 2 changes in the medication profile within the past 6 months– Recent changes in medication therapy |
| Medication with high risks for DRP | <ul style="list-style-type: none">– Painkillers, especially NSAID– Any kind of anticoagulation– Diuretics– Medicines which require regular monitoring– Drugs with a narrow therapeutic window (e.g. antiepileptics)– Medicines, which are rarely used in respective care area (e.g. oncology products in the nursing home)– Medicines, which in the application can cause problems / risks for the patient (e.g., ready-to-use syringes, inhalers)– Drugs at high risk for interactions– Medicines that require an exceptionally high adherence (e.g. HIV therapeutics, immunosuppressants) |
| Medication associated abnormalities | <ul style="list-style-type: none">– Recent history of falls– Unexpected (over-) reaction to medication therapy– Increased use of on demand medication |

Other conceivable criteria could be economic factors, e.g. patients with high-price medicines therapies, who are suitable for pharmaceutical care even without the listed risk factors in order to maximise their treatment efficiency. The choice of helpful tools to detect drug-related problems is influenced by the available sources of information or by the type of medication review. Often, automated systems are used (e.g. interaction software). In addition, analysis of dispensing records might be a very useful form to become aware of possible adherence issues (e.g. medication profile over time, for example 12 months). Explicit and implicit checklists can be used for in-depth assessment of the appropriateness of a therapy, e.g. an assessment of indicators for drug therapy or its efficiency and safety:⁵¹

Explicit checklists, particularly for geriatric patients, have been developed. They list active compounds that are not suitable for the elderly and thus should – wherever possible – be avoided. These drugs are also called Potentially Inappropriate Medications (PIM).⁵²

- Beers list: Summary of drugs that should be avoided in > 65s in general or should only be considered in older patients with certain diseases (= negative list).⁵⁰

- PRISCUS list: Negative list as the Beers Criteria and thereby specifically adjusted for the elderly population, but with references to possible alternatives and to the German regulation.⁵³
- STOPP / START list: An organ system related listing of typical drug application situations and criteria, within which the removal of a medication or an additional therapy should be considered.⁵⁴

Implicit checklists include key questions, which are answered step by step during the medication review for every medicine within a patient's medication profile. For research purposes, the Medication Appropriateness Index (MAI) was established and accepted as useful. Its ten questions can be used as a manual for the assessment of a single medicine or even the entire profile.⁵⁵

The final question in the evaluation of a medication profile should be carried out regarding indications without treatment, e.g. methotrexate therapy without folic acid substitution. In their study of 2008, Kuijpers et al. reported underprescribing as an increasingly important problem. In their population, the estimated probability of underprescription increased significantly with the number of drugs. Hence, 42.9% of patients with polypharmacy were undertreated, in contrast to 13.5% of patients using four medicines or less (OR 4.8, 95% CI 2.0, 11.2).⁵⁶ However, a change in the number of medicines prescribed as a medicines-related outcome measure is by itself not an indicator of the quality of the medication review.⁵⁷

4.10 Prioritisation of drug-related problems and recommending interventions

In an initial analysis of polypharmacy, several DRPs are usually identified. The prioritisation of problems and the distinction between manifest and potential issues is of crucial importance. If more than one existing DRPs have to be solved during the medication review process, one has to decide, which of the challenges should be tackled first and which one can be postponed. The resulting triage situation requires an immediate estimate of risks for the patient and the evaluation of any alarm symptoms. Problems, which were initially regarded as of lesser importance, need to be documented as well like all others so as not to be forgotten in a follow-up meeting.

Research detected gaps in a pharmacists' performance of detecting DRPs in patients suffering from coronary heart disease when external reviews were conducted in the same patient data. Krska et al. analysed a sample of 169 patient records and identified 1'539 potential issues of which pharmacists identified only an average of 33.8%.⁵⁸ No relationship was found between the proportion of issues noted and potentially relevant factors such as pharmacists' characteristics and their experience of doing reviews. As a limitation of their results, the authors did not report clinical relevance of missed opportunities. This might be discussed as a bias when analysing medication reviews conducted under daily life conditions and corresponding time pressure for health professionals.

4.11 Impact of medication reviews

When investigating the impact of medication reviews, one has to consider that only an implemented advice might have an outcome. In order to perform a cost-effective service, highest implementation rates of accurate advices need to be achieved. Pharmacist should always be able and empowered to check for sustainability of their advice within a follow-up meeting, assuring the patient and/or prescriber took note of their intervention and was able to follow the recommendation. Previous studies showed positive impact of structured interventions to improve adherence provided by pharmacists.^{59,60} But there is still little evidence of effectiveness of community pharmacy interventions. Blendniskopp et al. stated that the value of medication reviews is now generally accepted despite a lack of robust research evidence consistently demonstrating cost or clinical effectiveness compared to traditional care. Medication reviews can be more effectively deployed in the future by targeting and multi-professional involvement.⁶¹

In 2010, Nkansah et al. reviewed a series of international randomised controlled trials which involved a pharmacist delivering services to patients (other than dispensing or compounding pharmaceuticals) using the Cochrane standards for data analysis.⁶² Interventions included patient education, pharmacist telephone advice following home blood pressure monitoring, the monitoring of adverse drug reactions, drug-drug interactions, and adherence assessment. Twenty-nine of the 36 relevant studies selected reported that the pharmacist' intervention led an improvement in most clinical outcomes although the impact was not always statistically significant. Overall, statistically significant improvements occurred in the reduction of systolic and diastolic blood pressure and glycosylated haemoglobin (HbA1c), a reduction in all-cause

mortality in heart failure patients, a reduction of asthma symptoms among asthma patients and a reduction in the incidence of total bleeding in patients on warfarin therapy.

Hatah et al. led a meta-analysis on the impact of pharmacist-led fee-for-services medication reviews; 53 publications meeting their inclusion criteria were analysed.⁴⁶ They reported improvement in medication adherence in a majority of investigated studies (57.9%). Fee-for-service pharmacist-led medication reviews showed positive benefits on patient outcomes e.g. blood pressure and low-density lipoprotein. Interventions that included a clinical review had a significant impact on patient outcomes by attainment of target clinical biomarkers and reduced hospitalization.

4.12 International initiatives in performing medication reviews

Pharmacist-led medication review services are available in several countries such as the United Kingdom (UK) (Medicines Use Review, MUR), United States of America (USA) (Medication Therapy Management, MTM), Australia (Home Medication Review, HMR), Canada (MedsCheck) and New Zealand (Medicines Use Review, MUR).^{46, 63-65} These developments support the efforts of pharmacists to take a more active role in the care of patients. Recent meta-analysis stated that a majority (57.9%) of fee-for-service pharmacist-led medication reviews showed an improvement in medication adherence and showed positive benefits on patient outcomes.⁴⁶

Bulajeva et al. aimed at exploring availability and comprehensiveness of medication review practices in primary care in European countries.⁶⁶ Countries, which reported medication review procedures in community settings (13/25, 15%), most indicated having a type II procedure (11/13 countries, 85%). The authors also report a wide heterogeneity of understandings concerning distinctions of services between the observed countries and their differentiating health care systems. Even though the survey had some contradicting results, it provides insights into the general understanding of medication review practices in different countries. In order to substantiate Bulajeva's survey with specific key elements of existing services, an outline of structured pharmacist-led medication reviews worldwide was accomplished. On September 30, 2015, an empirical web-based search was performed to assess available information in English or German language including its sources, i.e. professional association, or governmental information (Table 3).

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Table 3 / Structured pharmacist-led medication review programs in primary care

Name	Country	PCNE Type	Inclusion criteria	Special feature	Implemented
Home Medication Review (HMR) / Domiciliary Medication Management Review (DMMR)	Australia	2a / 2b	Initiation starts with referral from GP, no specific criteria are defined, consumers may access a HMR when clinically indicated	Interprofessional collaboration with GP mandatory resulting in an individual patient care plan	National
Residential Medication Management Review (RMMR)	Australia	2b	RMMRs are available to current residents on a clinical needs basis		National
MedsCheck	Canada	2a	Chronic condition and prescription for ≥ 3 drugs or diabetes mellitus type 1 or 2	Follow-up review may be applied	National, with regional differences in structure and payment
MedsCheck at home	Canada	2a	Chronic condition and prescription for ≥ 3 drugs and must be unable to present to the pharmacy		Regional (Ontario)
MedsCheck for long term care home residents (MedsCheck LTC)	Canada	2b	Residents of a long-term care home	Reimbursement estimates continuous pharmaceutical care and interprofessional collaboration	Regional (Ontario)
Arzneimitteltherapie-sicherheit in Apotheken (ATHINA)	Germany	2a	Patient with medication in a brown bag	Brown bag method	Regional
Medicines Use Review (MUR)	New Zealand	2a	Patients living independently in the community who have cardiovascular disease, diabetes or respiratory disease plus one risk factor for drug-related problems (list)		National
Polymedication Check (PMC)	Switzerland	2a	Prescription for ≥ 4 drugs for > 3 months)	Possibility to implement a weekly dosing aid for 3 months (reimbursed)	National
Medicines Use Review (MUR)	United Kingdom	2a	It is up to the pharmacist to decide which patients receive this service, but at least 70% of them have to be part of a specific target group. Target groups: Patients with high-risk medicines (diuretics, anticoagulants, NSAIDs), with respiratory disease, at risk of or diagnosed with cardiovascular disease or who were recently discharged from hospital.	Follow-up intervention 'New Medicines Service (NMS)' available	National
Medication Therapy Management (MTM) Program	United States of America	-	Various programs	Various programs	National

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Various guidelines and recommendations exist on how to perform a medication review. As early as in 2002, initiatives from the national prescribing service from UK presented a guide to medication review aiming at reaching the agenda for patients, practitioners and managers.⁴⁸ The authors addressed their call to an interprofessional audience of involved healthcare professionals, i.e. pharmacists, nurses, and general practitioners. This document suggested key principles for the process of medication review:

- All patients should have a chance to raise questions and highlight problems about their medicines.
- Medication review seeks to improve or optimise the impact of treatment of an individual patient.
- A competent person undertakes the review in a systematic way.
- Any medication changes resulting from the review are agreed with the patient.
- The review is documented in the patient's notes.
- The impact of any change is monitored.

Meanwhile, online training programs exist to teach the practitioners on how to perform a medication review.^{67,68} The National Institute for Care and Excellence (NICE) presented a guideline concerning the safe and effective way of optimising a patient's medicines, highlighting the importance of such patient-centred interventions and the need for robust processes within patient care, ideally integrated in an interprofessional setting.⁵⁷ Within their report, medication reviews are just one of several options to improve medication therapy. They recommend carrying out structured medication review for specific groups of people where a clear purpose for the review has previously been identified. They suggest following groups as eligible:

- adults, children and young people taking multiple medicines (polypharmacy)
- adults, children and young people with chronic or long-term conditions
- older people.

By doing so, they recognised that the key focus of the medicines optimisation agenda is to make care person-centred.

In order to meet the emerging need for the exchange of experience with existing services on a scientific level and to encourage networking, PCNE initiated a communication platform called 'PCNE WIKI' in 2015. Aiming at supporting pharmacy practice development, as well as sharing

knowledge, discussing national approaches, and enabling search facility concerning pharmaceutical care and pharmacy practice, the society invites anyone with an interest in the development of pharmacy practice to use the site and to contribute to it.⁶⁹

4.13 Development of clinical pharmacy services in Switzerland

The Swiss health care system is characterised by both liberalism and federalism (Box 1). The environment in which the 1'850 community pharmacies operate for eight Mio inhabitants is fairly competitive: Dispensing physicians, mail order pharmacies, high proportion of about 30% of chain pharmacies, no restrictions to opening new pharmacies and continuous pressure on pharmacists' margins pose distinct problems for the development of clinical pharmacy services provided through community pharmacies. In this context, the Swiss Association of Pharmacists (pharmaSuisse) has adapted international developments and initiated an in-depth reform of the profession.

Box 2 / The Swiss Health Care System

Each person living in Switzerland is obliged to purchase mandatory health insurance from an authorised insurer. They are free to choose their health care physician and have unlimited access to general practitioners and specialists. There is no formal gatekeeping system in place. Almost half of the population (46%) holds a special insurance policy where they receive premium reductions in exchange for agreeing to join one of the 90 existing managed care networks such as Health Maintenance Organisations, family-doctor gatekeeping schemes, Independent Practice Associations, or Preferred Provider Organisations.

The national health care system is individually regulated by the cantons and 26 different systems have to be considered. Notably, in 16 cantons physicians may dispense drugs directly to their patients (dispensing physicians). Ambulatory services are largely provided by physicians operating as independent/single-person practices. In addition, ambulatory services are also provided by outpatient departments of public and private hospitals and by managed-care-style organisations. Similarly, a liberal regulation of medicines supply allows for dispensing physicians, pharmacy chains, mail order pharmacies and supply of some OTC drugs outside of a pharmacy.⁷⁰

When the concept of pharmaceutical care was introduced in Switzerland in the early 1990s, emphasis was given to providing patient-centred care and cognitive services. A postgraduate

education program and mandatory continuous education were launched together with changes to pharmacists' remuneration, which links payments to services delivered and not only to the volumes of medicines dispensed. The current version LOA IV of the remuneration system, introduced in 2010, defines a fee schedule for a total of nine distinct services (Table 4). Among these services, the so-called 'Polymedication Check' (PMC) was newly introduced as the first cognitive service to be delivered independently from the prescriber for patients on ≥ 4 prescribed drugs taken over ≥ 3 months. In addition, current regulation allows repeat prescribing for a maximum of 12 months. Such prescriptions currently constitute nearly 75% of all items dispensed.⁷¹ Hence, Swiss community pharmacies assume very responsible roles in the care of chronic patients.

Table 4 / Services supporting rational and cost-effective drug use provided by Swiss community pharmacies: remuneration in Switzerland and according fees (examples)

Pharmacy service	Description / Activities	Fee (EUR) ^{70,72}
Delivery-Check	Each prescription: check of medication history for interactions and accumulation (including self-medication)	3.00
Drug-Check	Each dispensed item <ul style="list-style-type: none"> • Check for: eventual possibility of repeat dispensing, dosage, limitations, interactions, risk factors, contraindications, misuse • According activities: Patient counseling, eventual contact with prescriber, choice of optimised package size, immediate provision 	4.00
Generic substitution	Pharmacists have been allowed (and are officially invited) to substitute generic drugs for originals with the patient's agreement and when the doctor does not oppose it. Only at first delivery, a fee is available.	40% of the difference to the original
Emergency fee	To cover the extra charges of the pharmacist on emergency, night, and weekend duty, requested per patient and visit	16.00
Supervision of directly observed treatment	When a patient takes drugs in the pharmacy under the pharmacist's supervision (e.g. Opioids, Disulfiram)	10.00
Adherence fee	For preparation of a pill organizer/blister pack for an outpatient with a chronic condition and taking at least 3 different drugs	20.00 / week
Polymedication-Check	For patients on ≥ 4 prescribed drugs taken over ≥ 3 months. If patient agrees, but independently from the prescriber.	45.00

As the increase of multi-morbidities and the simultaneous health workforce shortage of health professionals might worsen the situation, the co-operation of pharmacists and general practitioners holds the potential to provide constructive support in medication management and coordination of care. While efforts are made to re-orient pharmacy practice towards a focus on quality of care, politics allowing doctors to dispense drugs in some Swiss regions work against, and thus provoke unnecessary competition in primary care and complicate coordination among networks of healthcare providers. Regardless of these barriers (or eventually induced by them), the Swiss association of pharmacists (pharmaSuisse) strengthened the efforts in the development of clinical pharmacy services by the following actions:

- the implementation of a quality care program named QMS-Pharmacy (Quality Management System for community pharmacies),
- the launch of different campaigns (e.g. screening for cardiovascular risks, pulmonary diseases i.e. COPD, colorectal cancer, melanoma, microalbuminuria),
- the development of smoking cessation programs,
- and recently by a new integrated service called netCare, a new collaborative health service in primary care.⁷³

4.14 Services for chronic patients through Swiss community pharmacies

In general, patients visit a pharmacy without advance announcement and the pharmacist provides counseling in an ad hoc situation. He reacts to the patient spontaneously and counsels at the counter, without any further preparation. This setting normally does not provide privacy. However, if needed due to the topic or due to insistence by the patient, pharmacists might offer the possibility to switch into a counseling room and facilitate communication. Figure 4 summarises the different services provided by community pharmacies regarding the possible journey of a patient.⁷⁴

GENERAL INTRODUCTION

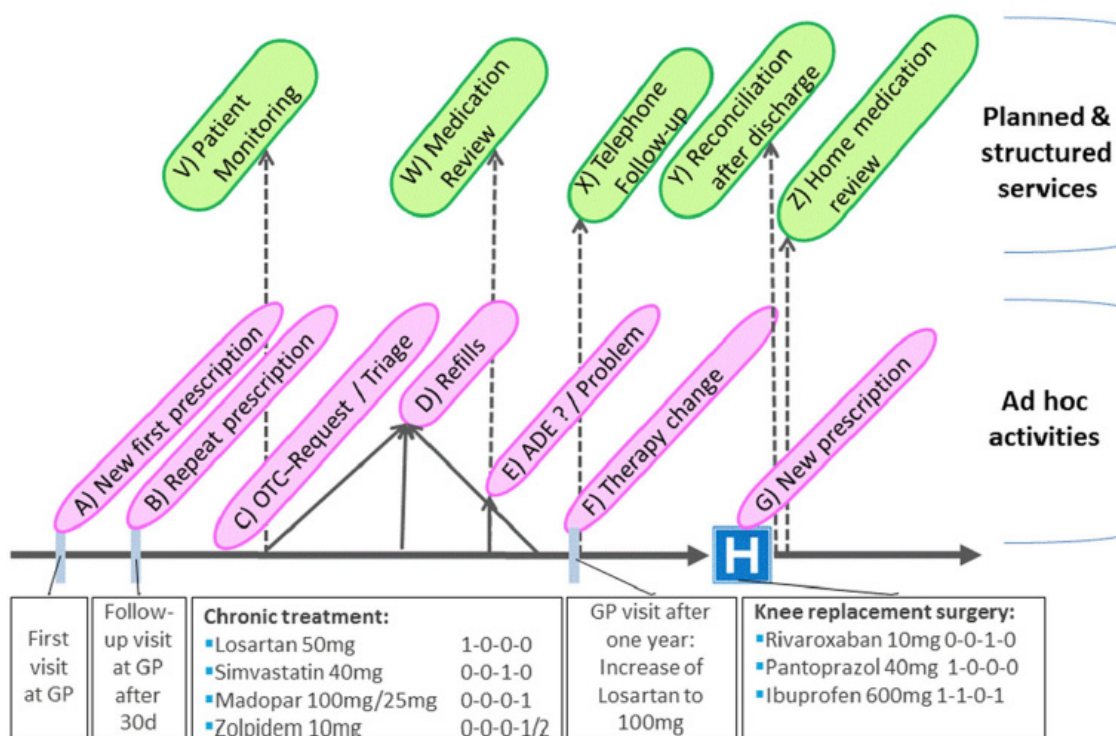


Figure 4 / The journey of a chronic patient with according ad hoc or planned activities of a community pharmacist (OTC=Over the Counter Medicine; ADE=Adverse Drug Event; GP=General Physician; H=hospital)

The patient attends the pharmacy the first time with a new prescription for chronic medication and receives adequate instructions (A). Currently, there is no special service implemented in Switzerland, such as the New Medicines Service (NMS) known in UK.⁷⁵ The newly prescribed medicine is commonly evaluated by the GP after one month; on this occasion, a repeat prescription for up to 12 months can be prescribed (B). Following, the patient will show up regularly to receive a refill in the pharmacy (D), or for a request for OTC medicines to treat minor illnesses (C), or with a particular question (E) concerning a manifest or potential drug-related problem. The patient will see his GP for a renewal of the repeat prescription or for an eventual change (F) of the prior treatment plan only after six months or one year. All these situations might prompt a deepened evaluation of the patient situation. Hereby the ad-hoc counseling evolves to structured pharmaceutical care services. They are mostly planned and can comprise an assessment of patient outcomes (V), a medication review (W) triggered by the questions of the patient or a telephone interview as a follow-up of the therapy change (X). With respect to seamless care, reconciliation of therapies (Y) around a hospital stay represents another very relevant service and for disabled patients even a home medication review after discharge (Z) might be adequate. Currently, Swiss community pharmacists could, in all

situations C-G, perform a polymedication-check and receive remuneration. Therapy monitoring (V) by the pharmacist is not systematically foreseen. Still, measurement of blood pressure, biomarkers for diabetes patients or even lipid values are frequently offered. In general, the patient himself pays these services. However, accredited pharmacies following regular quality controls may perform prescribed testing by use of capillary blood and receive the standard payment for lab testing.

Other services with distinct responsibilities exist, which are not (yet) covered by a specific fee. For example, when a refill prescription is expired, the pharmacist is also allowed to dispense a chronic medicine in advance in order to avoid interruption of the therapy (e.g. dispense of phenytoin for a home resident whose neurologist is on holidays). Moreover, in well-defined situations even dispensing without a prescription is permitted, according to a guideline that clearly specifies the good practice with adequate documentation. Examples are replacement of expired medicine, salbutamol inhaler in case of asthma attack and glycerol trinitrate for angina, etc.

4.15 The Polymedication Check

Targeting individuals and not a population or society as a whole is a key concept of pharmaceutical care that can be viewed as an individualised service of pharmacists delivered to a distinct patient. These services include various contributions of pharmacists in patient-oriented care such as the provision of medication reviews. Since 2010, Swiss community pharmacies can offer a 'Polymedication-Check' (PMC) to patients on ≥ 4 prescribed drugs taken over ≥ 3 months. The PMC is a new cognitive service involving a consultation with a patient in a separate room and taking responsibility for his therapy through interventions and recommendations concerning medication management. Referring to the different types of medication reviews as previously defined, the PMC is identified as an 'intermediate' medication review (Table 1). Information is available from the medication history, which is mandatorily kept in Swiss community pharmacies, and from a structured patient interview. The check focuses on adherence problems, patients' knowledge and handling problems. Pharmacists are instructed to use open questions to detect pharmaceutical care issues and to decide on the need for intervention. However, they must prioritise the problems detected and document them in a very simple way, e.g. if the patient needs counseling (yes/no), has adherence

problems (yes/no), if the pharmacist has to consult with the GP, refer the patient or suggest any other recommendations or interventions. At the end of the interview, the patient signs the documentation form and the pharmacy can charge a fee of CHF 48.60 (45 Euros) to the health insurance. For the first time, Swiss pharmacists are remunerated for actively supporting the care of chronically ill people in terms of monitoring and improving their adherence to ensure therapy efficacy. Such face-to-face medication review provides the opportunity to discuss the patient's values and beliefs in health and his medication, and how medicine taking fits in with the patient's daily life. In this respect, this service represents a new paradigm in pharmacy practice for Swiss community pharmacists.

4.16 Rationale for the thesis

The overall performance of the Swiss health care system is among the best of the countries of the Organization for Economic Cooperation and Development (OECD). The level of patient satisfaction and the life expectancy is one of the highest in the world.⁷⁶ The Swiss population shifts to over-aging; at the same time, the number of healthcare providers declines due to retirement and insufficient recruitment of young professionals resulting in a gap of patient care. Thus, a future challenge will be to overcome this gap. In order to investigate the current and potential pharmacist' contribution to patient care, this thesis aims at giving a general overview over clinical pharmacy services already performed in the Swiss hospital setting and discusses the strengths and limitations of pharmacist-led medication reviews in primary care on the case of the evaluation of the Swiss Polymedication Check. In addition, specific opportunities for further clarification through pharmacist-led interventions are highlighted in order to select patients at highest needs for future services.

5 THESIS OVERVIEW

This thesis consists of three parts, discussing different approaches of the pharmacists' role in patient care (table 5). Narrowing the scope of perspective from a general overview over current clinical pharmacy practice, to in-depth evaluation of a specific service on its impact on patients' behaviour, the thesis will end up with the discussion of two specific approaches for screening individual care issues in the community pharmacy.

Table 5 / Thesis overview: projects A to C with subprojects

Project A *Opportunities for clinical pharmacy service in patient care*

- | | | |
|----|---|---------------|
| A1 | Mapping Clinical Pharmacy Practice in Swiss Hospitals – a Cross Sectional Study | (Publication) |
| A2 | Detecting drug-related problems through pharmacists-led medication reviews | (Work report) |

Project B *Evaluation of the Swiss Polymedication Check*

- | | | |
|----|---|---------------|
| B1 | Development of a method for calculating adherence to polypharmacy from dispensing data records | (Publication) |
| B2 | Proposal of Standardization to Assess Adherence with Medication Records: Methodology Matters | (Publication) |
| B3 | Development of adherence outcome measures | (Work report) |
| B4 | Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy - a prospective randomised controlled trial | (Publication) |
| B5 | Humanistic outcomes and patient acceptance of a pharmacist-led medication review in primary care – a prospective randomised controlled trial | (Publication) |
| B6 | Insights into the pharmacist' perspective | (Work report) |

Project C *Patient-centred screening for care issues in community pharmacies*

- | | | |
|----|---|----------------|
| C1 | Prevalence of unreached cardiometabolic targets among treated patients – sub-analysis of data from a community pharmacy screening campaign in Switzerland | (Short report) |
| C2 | Swallowing difficulties with medication intake assessed with a novel self-report questionnaire in patients with systemic sclerosis – a cross sectional cohort study | (Publication) |

Project A aims at presenting an overview of existing clinical pharmacy services in the hospital care setting. When mapping the pattern of resources for clinical pharmacy practice, the issues within transition of care situations become obvious (A1). We thereby discuss general gaps in patient care, i.e. the involvement of the pharmacist in the discharge process and the lack of communication between hospital and community pharmacists.

To approach the topic of drug-related problems in patient care from a solution-oriented perspective, the possibilities of detecting and handling drug-related problems through pharmacist-led medication reviews in various settings became a focus of the Pharmaceutical Care Network Europe (PCNE) and was extensively discussed at several meetings and workshops (A2).

Project B extensively studies the Polymedication Check (PMC), a cognitive and directly remunerated pharmacist-led service in Switzerland. For the first time in the Swiss health care system, a new nationally implemented cognitive service underwent an in-depth evaluation process in daily life setting. Two years after the launch of the service, the Pharmaceutical Care Research Group of the University of Basel initiated an evaluation project (evalPMC) aiming at investigating the impact of the service on medicines use and humanistic outcomes. For this purpose, some theoretical challenges in adherence calculation from refill data had to be considered (B1 + B2) and various specific outcome measurements had to be developed and piloted (B3). Designed as a randomised controlled trial, the study investigated as a primary outcome the objective adherence calculating the Medication Possession Ratio (MPR) and Daily Polypharmacy Possession Ratio (DPPR) for eligible therapies (B4). Further on, we discussed detected drug-related problems, unplanned visits at the general physician or hospital, and the impact of the intervention on humanistic outcomes, e.g. patients' acceptance of this new service, improved knowledge about their medicines through intervention, and the availability of a written medication plan (B5). Finally, we were also interested in the pharmacists' perspective and their perceptions regarding the new service they could offer. We assessed their arguments in a written survey and a focus group discussion performed shortly after the implementation of the service in community pharmacies, and asked the participating pharmacist from the evalPMC project to fill in an online questionnaire after completing the study (B6).

Project C connects the main conclusion of Project B (need for more tailored interventions to targeted patients) and investigates the potential of the community pharmacy setting to offer the pharmacist's skills purposefully to patients with individual needs. On one hand, the established routine of community pharmacies in performing health care campaigns offers opportunities for additional interventions when patients fail to achieve their individual therapy targets, e.g. unreached biomarker values despite the prescription of a medicines therapy (C1).

On the other hand, patient-centred counseling may become more sensitised for specific and underestimated drug-related problems, i.e. swallowing difficulties with medication intake. When asked, swallowing difficulties are reported by 9-27% of outpatients. They may affect quality of life, lead to hazardous coping strategies (splitting or crushing pills), and reduce adherence to medication regimen. However, health professionals rarely assess swallowing difficulties with medication intake. We therefore developed an in-depth patient self-report questionnaire and named it SWAMECO (SWAllowing difficulties with MEdication intake and COping strategies). We used the questionnaire in a cohort of patients with systemic sclerosis (SSc) and report new insights on care issues of this population (C2).

6 PROJECT A - Opportunities for clinical pharmacy service in patient care

<i>Project</i>	<i>Title</i>	<i>Page</i>
A1	Mapping Clinical Pharmacy Practice in Swiss Hospitals – a Cross Sectional Study	40
A2	Detecting drug-related problems through pharmacists-led medication review	47
APPENDIX		161

6.1 Mapping Clinical Pharmacy Practice in Swiss Hospitals – a Cross Sectional Study
[A1]

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Mapping clinical pharmacy practice in Swiss hospitals: a cross-sectional study

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ABSTRACT

Background Clinical pharmacy activities developed significantly in the last decade. The extent and organisation of these activities in Switzerland remained unknown.

Objectives To map clinical pharmacy services (CPS) provided in Swiss hospitals and to discuss their development focusing on different cultural regions and healthcare systems.

Methods We enrolled all chief hospital pharmacists affiliated with the Swiss Society of Public Health Administration and Hospital Pharmacists (n=47) for an online survey. We asked them to describe the extent and organisation of CPS concerning patient-related, therapy-related or process-related activities, the structural organisation and the available human resources.

Results The survey took place from March to April 2013. It was completed by 44 chief hospital pharmacists (return rate 94%), representing the hospital landscape in Switzerland comprehensively. Thirty-three (75%) hospitals offered regular CPS and seven (16%) planned to do so. Institutions in regions without drug-dispensing physicians rather employed pharmacists assigned with clinical activities (n=20, 22% of 135.3 full-time equivalent (FTE) than regions with partial (n=8, 7% of 35.8 FTE) or unrestricted drug dispensing by physicians (n=16, 6% of 68.1 FTE, p=0.026). Of hospitals with implemented CPS, 73% had weekly interprofessional ward rounds, and in 9.1%, clinical pharmacists daily reconciled medicines at patient discharge.

Conclusions Our data show regional differences in the implementation and pattern of CPS. A significant correlation to drug dispensing by physicians in ambulatory care and human resources provided for CPS was found. While interprofessional ward rounds were performed periodically, seamless care activities by clinical pharmacists remained insufficiently established.

INTRODUCTION

Since the publication of the concept of 'pharmaceutical care' by Hepler and Strand¹ in 1990, great efforts have been made to establish patient-centred pharmaceutical services in outpatient and inpatient settings, especially in the Anglo-Saxon countries.² The pharmacists' contribution is not only limited to drug manufacture and supply, but it expands in taking increasing responsibility for the appropriate drug choice and application. Especially the pharmacist's role in patient care during the hospital stay is highly valuable since the clinical setting and related medication process is recognised as a particularly risky situation.^{3–5} Moreover, the transition from inpatient to outpatient care adds further challenges to patients and health professionals.^{6–8} As a

possible approach to reduce preventable medication errors and correlated harm to the patient, around the world the concept of clinical pharmacy got successfully implemented in the hospital setting with various patient-related services.^{9,10}

Development of structured clinical pharmacy activities in Switzerland

In 2006, the Swiss Society of Public Health Administration and Hospital Pharmacists (GSASA) organised four pioneering workshops to establish the requirements for obtaining the degree of a clinical pharmacist.¹¹ The Swiss Pharmacy Federation approved a structured postgraduate education programme in 2008, leading to the certificate 'Clinical Pharmacy FPH'. In 2011, the GSASA defined clinical pharmacy as "an area of pharmacy aimed at developing and promoting an appropriate, safe and cost-effective use of therapeutic products".¹² According to this definition, the clinical pharmacist is part of a multidisciplinary team and is present on the ward on a daily basis or as a regular consultant for the different services. The activities of clinical pharmacy are organised along three axes:

1. Patient-related axis: To collaborate in patient education and continuity of care to improve medication history, adherence to therapy; transition to the ambulatory setting and education on discharge medication (=seamless care).
2. Treatment-related axis: To analyse drug therapy to optimise and reduce overuse, underuse and misuse of medicines, taking into account the aspects mentioned under (1), to optimise the choice of medication after a risk/benefit analysis and cost-effectiveness; to ensure indications and completeness of treatment; to avoid contraindications according to the pathophysiological state; and to guarantee adaptation and individualisation of treatment.
3. Process-related axis: To consolidate the drug supply chain to ensure that the patient receives the right medication at the right time as prescribed by supporting good prescribing practices, development of guidelines on the preparation and administration of medication; development of treatment guidelines in collaboration with medical and nursing teams in the departments involved; development of computerised decision support systems for the prescription and administration of drugs; and prevention and documentation of adverse drug events on the ward.

These three axes should be completed with the following related activities, which are an integral part of the role of the clinical pharmacist: contribution in continuing education of physicians, nurses

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and pharmacists, as well as in research and development of new services.

Cultural and structural challenges for the development of clinical pharmacy services in Switzerland

Switzerland is characterised by its federalist political system with 26 cantons and its multilingualism (German, French, Italian and Romansh). Since the national healthcare system is independently regulated by the cantons, 26 different systems have to be considered. These heterogeneous conditions can promote innovation as well as create barriers to the development of new healthcare models. Notable for our research is the fact that in 16 cantons of Switzerland, physicians in ambulatory care are allowed to dispense drugs directly to their patients (dispensing physicians). Since lack of collaboration between competitors might be an issue in the development of clinical pharmacy practice, we were interested in the potential interference of this structural factor. Our objectives were to map the clinical pharmacy services provided in Swiss hospitals, to reflect on the aims of the definition and observed realities, and, finally, to discuss the results considering various cultural regions and the peculiarities of different healthcare systems.

METHODS

Online survey

A literature search provided an overview of previously conducted surveys with comparable research questions focusing on clinical pharmacy practice.^{13–18} Based on these findings, general issues and topics were extracted and supplemented by country-specific elements. An expert panel with representatives from the university, postgraduate lecturers and practitioners assessed the comprehensiveness and appropriateness of the survey (content, structure and scope). To ensure a uniform understanding of clinical pharmacy activities, the GSASA definition of clinical pharmacy¹² formed the main reference for this survey. The questionnaire contained 43 items and was phrased in a structured way to describe nature and extent of clinical pharmacy services (patient-related, therapy-related or process-related activities), structural organisation (extent of ward contact) and available human resources (represented as full-time equivalents (FTEs)). Thereby, $FTE_{TotPharm}$ summed up all human resources for pharmacists' activities in the hospital pharmacy while $FTE_{ClinPharm}$ represented resources reserved for clinical pharmacy activities.

Data analysis

The data were transferred in Microsoft Office 2013 Excel and processed for statistical analysis with IBM SPSS Statistics 22. We also used Microsoft Office Excel 2013 and the add-in 'GeoFlow' to visualise our results. Analysis of possible correlations within group and scale variables was provided using the Mann–Whitney U test ($n_{Groups}=2$) or the Kruskal–Wallis test ($n_{Groups}\geq 2$). All tests were performed with a significance level of $\alpha=0.05$.

RESULTS

Conducting the survey

In a cross-sectional study, we enrolled all chief hospital pharmacists ($n=47$) that were affiliated with the GSASA at the index date 1 January 2013 by email. The survey took place from 21 March to 25 April 2013. In the absence of feedback, the contacts were reminded to participate by email or by phone call twice during a period of 3 weeks. The survey was completed by 44 chief hospital pharmacists (return rate 94%).

Institution characteristics

In summary, 6 institutions were affiliated with a university, 21 were independent cantonal and regional hospitals, and 7 were specialised clinics. Furthermore, 10 hospitals were organised in networks. Hospitals were categorised following their characteristics and assigned to the established categories of the Swiss federal statistical office.¹⁹ Overall, all general hospitals with central supply level 1 (university hospitals) employed a pharmacist who could provide insights into their organisation. Likewise, a majority of 80% of general hospitals with central supply level 2 and 52% of general hospitals with primary care level 3 took part in the survey. The coverage decreased in general hospitals with primary care levels 4 and 5, where in 2 of 69 listed institutions a pharmacist was present at least part time and thus surveyed (3%). This trend continued in the psychiatric, rehabilitative facilities and specialty hospitals (4%). In total, 19 trainee placements for the national accredited postgraduate degree in hospital pharmacy were provided by 17 hospitals. Nine institutions offered a total of 13 trainee placements for obtaining the certificate of proficiency in clinical pharmacy.

Extent of clinical pharmacy activities and human resources

The 44 institutions reported a total of 239.2 $FTE_{TotPharm}$ for hospital pharmacists. Of the surveyed hospitals, 33 (75%) already offered permanently implemented clinical pharmacy services ($FTE_{ClinPharm}=35.9$). Another seven (16%) hospitals were planning to introduce appropriate structures. The remaining four (9%) hospitals indicated offering no clinical pharmacy services in the near future. In the French-speaking part of Switzerland (11 institutions), 23.2% of the total hospital pharmacy's human resources were assigned to clinical pharmacy services ($FTE_{ClinPharm}=19.1$; $FTE_{TotPharm}=82.4$). In the German-speaking part (31 institutions), this corresponded to 9.9% ($FTE_{ClinPharm}=14.5$; $FTE_{TotPharm}=146.2$) and in the Italian-speaking part (2 institutions) to 27.4% ($FTE_{ClinPharm}=2.9$; $FTE_{TotPharm}=10.6$). In summary, the clinical pharmacy resources differed significantly over the three language regions ($p=0.032$, figure 1). Median year of establishment for clinical pharmacy services were reported in the French part of Switzerland with 2002 (range: 1989–2010), in the German part with 2007 (range: 1985–2013) and in the Italian part with 2011.

Hospitals in regions without dispensing physicians ($n=20$) revealed significantly more resources available for clinical pharmacy activities (22.0% of $FTE_{TotPharm}=135.25$) compared with regions with limited ($n=8$, 6.7% of $FTE_{TotPharm}=35.8$) or full-dispensing rights for physicians ($n=16$, 6.3% of $FTE_{TotPharm}=68.1$, $p=0.026$), shown in figure 2.

Structural organisation of ward contact

The 33 institutions providing clinical pharmacy services had resources of 222.2 FTE, of which 35.9 were allocated to patient-centred care. In four (12%) of these institutions, pharmacists worked >50% of their time on the ward. Twenty-six (79%) hospitals mentioned part-time activities with patient contact, while three (9%) institutions reported no presence on the wards.

Treatment-related services were more frequent than patient-related activities (figure 3). In 73% of all hospitals with clinical pharmacy services, interdisciplinary ward rounds with pharmacists, nurses and physicians took place weekly. A proportion of 18% of the hospital pharmacists reported weekly involvement of clinical pharmacists in the medication reconciliation process at hospital admission. Meanwhile, pharmacists validated

patients' prescriptions in 9% of institutions at discharge to ambulatory care. Weekly medication reviews according Pharmaceutical Care Network Europe typology²⁰ IIB (medication profile+clinical data) were performed in 42% and type III (medication profile+clinical data+information from physician) in 39% of institutions.

An overview of process-related services revealed ambiguous trends. One-third of all institutions (n=11) maintained a hotline to allow external professionals to ask questions (eg, community pharmacies in case of concern after hospital discharge). A majority of 81% of hospital pharmacies with according services reported daily enquiries from health professionals. Maintaining a hotline for internal professionals was an integral part of the daily routine for 31 out of 33 institutions (94%).

DISCUSSION

To our knowledge, this is the first comprehensive national survey of the clinical pharmacy practice in Switzerland reflecting the practical implementation of a recently introduced theoretical definition. Our data indicated relevant regional differences in the implementation of clinical pharmacy services, while the presence of drug-dispensing physicians seemed to limit the development of clinical pharmacy services.

Characteristics of institutions participating in the survey

All categories of hospitals were represented in the survey. It is surprising that only 47 of 300 listed hospital institutions in Switzerland employed a chief pharmacist. In institutions without GSASA contact information (84%), it may be assumed that no structured clinical pharmacy activities take place since there is no other professional association for hospital or clinical pharmacists in Switzerland.

Interfering factors in the dissemination of clinical pharmacy practice

As a result of the cantonal regulation of the health system in Switzerland, heterogeneous conditions and structures exist and influence the implementation of new disciplines and concepts at the national level. In our study, a significant association between dispensing physicians in ambulatory care and the absence of clinical pharmacy services in hospitals of corresponding regions is shown. In primary care, collaboration between physicians and pharmacists is hampered by this keen competition, which caused multiple public votings with according local altercation between the two professional associations. Apparently this struggle in primary care influenced the collaboration in the institutions. The observed structural differences in drug supply must be clearly evaluated as a disadvantage: hospitals in regions with prevailing dispensing physicians seem to barely tolerate clinical pharmacy activities. This is not favourable in terms of patient safety and cost-effectiveness. A recent study of health insurance data revealed that prescriptions of dispensing physicians show a higher potential for drug-related problems compared with normal prescribing, non-dispensing physicians.²¹ In order to promote the expansion of the interprofessional collaboration, financial disincentives must be discussed critically. Thus, economic competition in primary care affects collaboration in primary care as well as in hospital care and both effects are critical in regard of patient safety.

Clinical pharmacy practice: discussing a definition's theory and observed realities in Swiss hospitals

From a total of 239.2 FTE of pharmacists in Switzerland, around 15% were assigned to the field of clinical pharmacy.

Since the introduction of the certificate 'FPH Clinical Pharmacy', 58 pharmacists had successfully graduated until 2013.²² This may represent a first accomplished step in the right direction, leading to an improved involvement by pharmacists in patient care. However, present resources are insufficient for the adequate coverage of needs. The comprehensive and publicly available supervision by clinical pharmacists at present cannot be guaranteed in Swiss hospitals due to a lack of resources (35.9 FTE_{ClinPharm} in relation to 1.4 million hospitalisations in 2013).²³

Regarding the defined axes of activities, pharmacists' efforts seem to focus on treatment-related and process-related services. In the institutions with clinical pharmacy services, interprofessional ward rounds seemed well established since they took place regularly. Weekly performed treatment recommendations may be also considered as regular. Since they are only performed on selected wards, a large number of drug-related issues endangering patient safety remain unsolved.

The pharmacist's competence in answering medication-related questions to hospital staff seemed to be well established and accepted. However, there were hardly any services enabling external access to valid information about a patient's medication during his hospital stay for community pharmacies and general practitioners. This indicates a huge potential for improvement.

Participation of pharmacists in direct patient-related care was rare, probably due to a lack of resources. A crucial gap was observed in the field of 'seamless care'. Structured discharge management (eg, medication reconciliation) involving a clinical pharmacist was implemented in <10% of the institutions. No institution reported the involvement of a clinical pharmacist in the validation process of a patient's written medication plan (eg, hand over^{24 25}).

Current resources are not sufficient to ensure comprehensive patient care through clinical pharmacists. We propose to discuss the pattern of resource allocation that might have the highest level of efficiency. To demand a maximum of personal resources for all axes of clinical pharmacy activities at once might not be an effective strategy to maximise the clinical pharmacist's impact. For example, an optimised medication process may prevent many interventions at the patient level. Therefore, a reasonable balance between the mentioned axes of activities, that is, direct patient contact, optimising the medication process and development of treatment guidelines, seems more reasonable and might become a topic of further investigation of clinical pharmacists' impact on patient outcome.

Comparing Swiss resources to the international community

Compared with the human resources in North America (FTE_{TotPharm}=17.5 per 100 beds),¹⁸ Swiss hospitals showed a striking neglect of pharmaceutical expertise in hospitals. Compared with data from Europe 2010,¹³ Switzerland offered a similar spread of implemented clinical pharmacy services and corresponding gaps in patient-centred care. Around 40% of European institutions provided regular clinical pharmacy services on the wards. The wide range of reported extent (3.6–79.2%) indicates a heterogeneous distribution of resources, analogous to the situation in Switzerland. The European leader in the field of clinical pharmacy practice was the UK. On average, 90% of National Health Services' institutions carried out daily clinical pharmacy visits on the hospital wards.²⁶ Out of the 30 survey countries, Switzerland ranked on the 20th place right behind the former Yugoslav Republic of Macedonia and just ahead of the Czech Republic.¹³ In particular, the area of transition of care showed to be neglected in Europe:

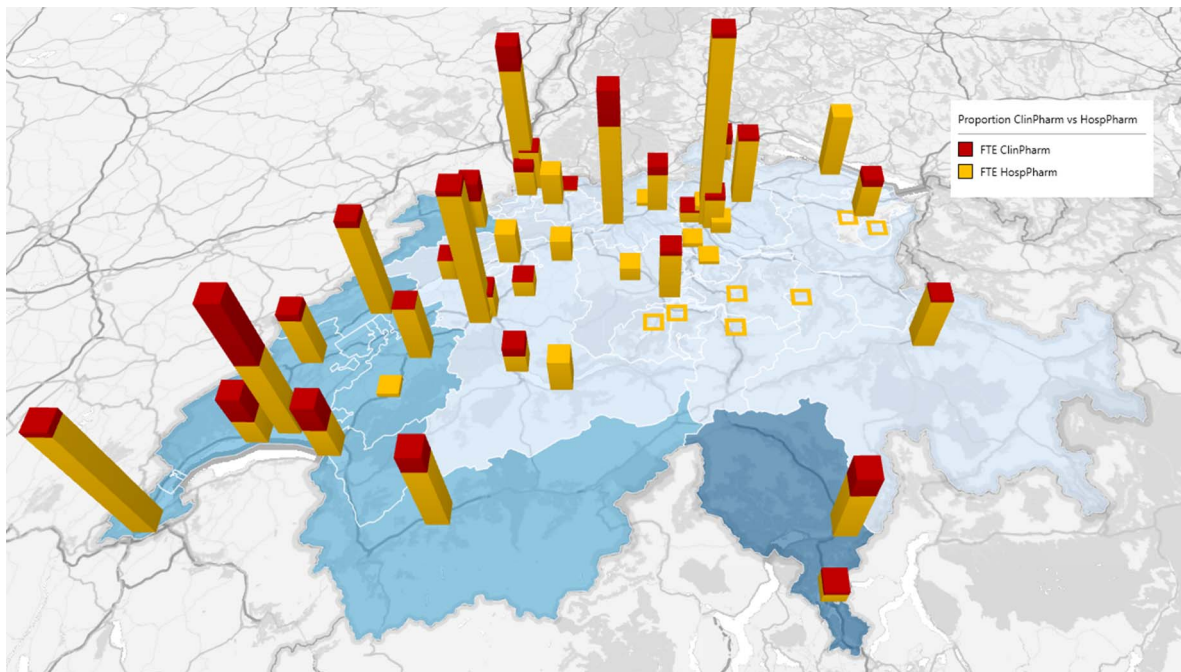


Figure 1 Ratio of clinical pharmacy practice (red) versus other hospital pharmacy activities (yellow) in the different language areas: French (blue), German (light blue) and Italian (dark blue). Hospital networks are represented as one location. Squares without filling represent areas without any pharmacy information. FTE, full-time equivalent.

medication reconciliation supported by a clinical pharmacist took place in only 17% of European institutions upon admission and in 22% at discharge, respectively.¹³ It remained unclear how regularly and frequently these services were provided. In the year 2000, Canada reported seamless care services in 33% of the examined institutions reaching on average 11% of all patients treated (range: 5–50%).¹⁴ In the future, such indicators might become important target values for discussing the impact and extent of the practice of clinical pharmacy, for example,

beds supplied with clinical pharmacy services instead of the total number of an institution's beds provided.

Strengths and limitations

Our study has some strengths. First, the high response rate to the survey of 94% of registered and invited chief pharmacists resulted in a comprehensive overview of the actual clinical pharmacy practices in the institutions contacted. Second, a representative sample of participating institutions was achieved by the

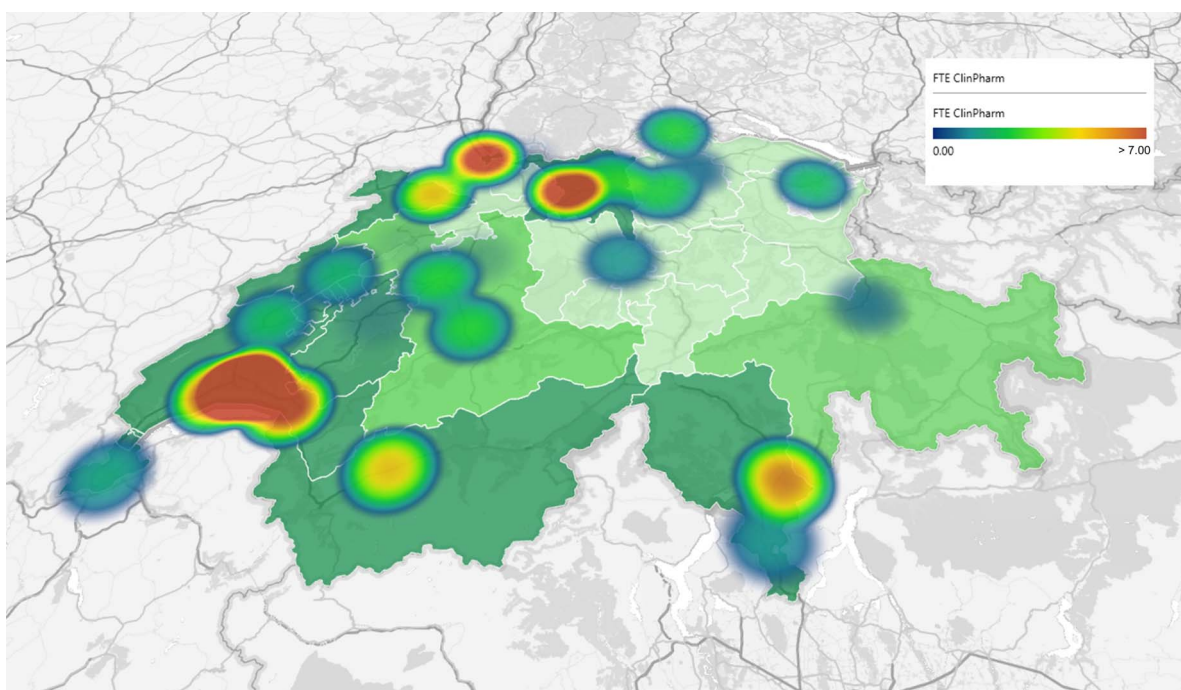


Figure 2 Extent of clinical pharmacy practice (full-time equivalent (FTE)) heat map, blue=low extent, red=high extent) in parts with no (dark green), partial (green) and unrestricted drug-dispensing physicians (light green).

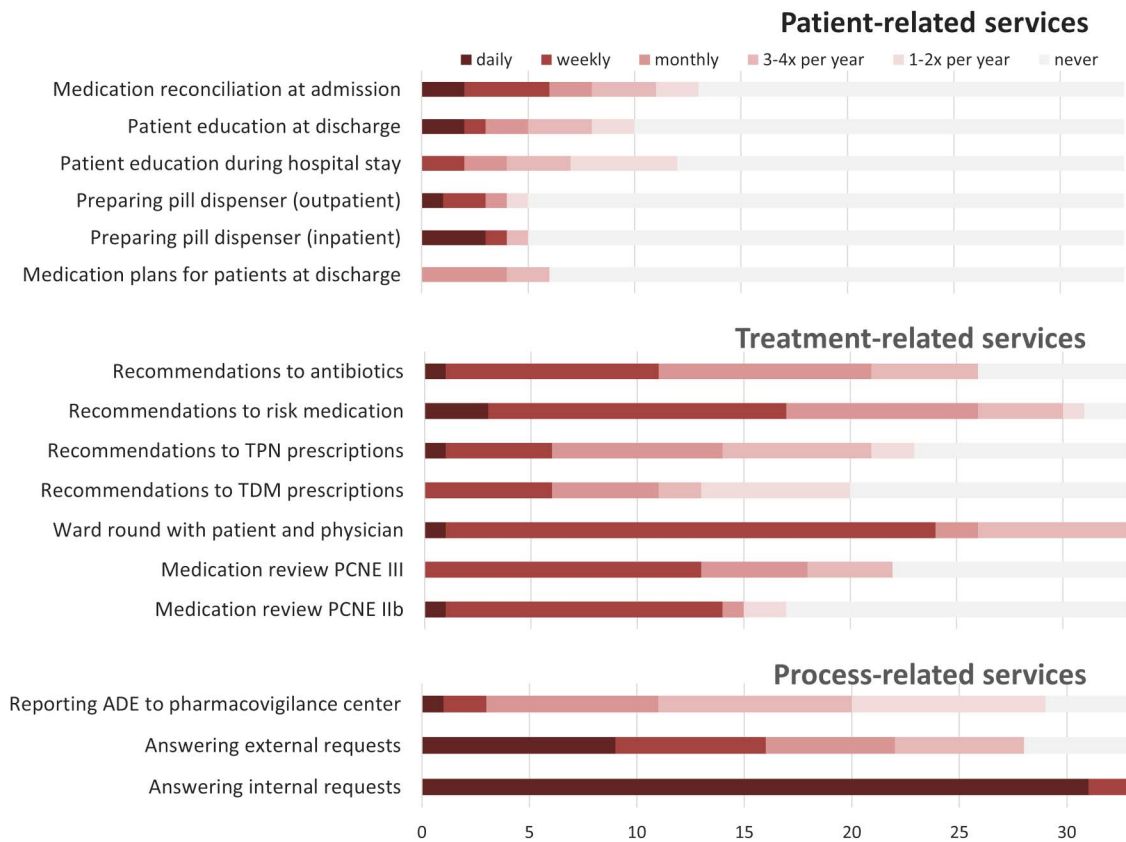


Figure 3 Clinical pharmacy services were structured into (i) patient-related, (ii) treatment-related and (iii) process-related activities. Only responses from the institutions that provide clinical pharmacy activities were taken into account (n=33). ADE, adverse drug event; PCNE, Pharmaceutical Care Network Europe; TDM, therapeutic drug monitoring; TPN, total parenteral nutrition.

survey (all general hospitals with central supply level 1 and 80% of general hospitals with central supply level 2). Third, since the survey took a national approach, we report data from all cultural areas of Switzerland and are able to discuss corresponding patterns of resources and influencing factors on the development of clinical pharmacy services.

The survey was designed as a self-declaration, involving several limitations. First, although the established GSASA definition for clinical pharmacy was implied as a standard reference, different perceptions for practice may persist and could not be validated by the authors. To minimise this effect, we tried to narrow the scope of individual beliefs and personal opinions with explanations and clarifications within the survey. Second, individual institutions reported on services that they have developed and established according to local needs, but that could not be divided into the categories of the survey itself. These results could not be considered in the analysis but should be pursued as an innovation in each case. Third, our results allow no statements as to the quality, efficiency and benefits of provided services on patient outcomes.

CONCLUSION

To our knowledge, this is the first comprehensive national survey of clinical pharmacy practice in Switzerland. Our data show important regional differences in the extent of implementation and pattern of clinical pharmacy services. A striking extent of low dissemination was observed within regions of drug-dispensing physicians in ambulatory care. While interprofessional ward rounds were performed at least periodically in hospitals, which offer clinical pharmacy services, seamless care activities by clinical pharmacists remained insufficiently established.

Key messages

What is already known on this subject

- ▶ The pharmacist's involvement in patient care during the hospital stay appears to be highly valuable since the clinical setting and related medication processes are recognised as particularly risky situations.
- ▶ Around the world, the concept of clinical pharmacy was successfully implemented in the hospital setting with various specific services.

What this study adds

- ▶ This is the first comprehensive survey of clinical pharmacy practice in Switzerland reflecting the practical implementation of a recently introduced theoretical definition.
- ▶ Our data show important regional differences in the extent of implementation and pattern of clinical pharmacy services, highlighting a crucial gap in seamless care activities.
- ▶ In particular, the regional presence of drug-dispensing physicians in the ambulatory care setting seemed to limit the development of clinical pharmacy practice in corresponding hospitals.

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6.2 Detecting drug-related problems through pharmacists-led medication reviews [A2]

Work report

6.2.1 Introduction

The author of this thesis was introduced into the Pharmaceutical Care Network Europe (PCNE) in 2010 and participated over the following years at several working conferences and symposia as a participant, workshop moderator, and finally even as a lecturer. This internal work report summarizes the key-findings of the author's journey within this very inspiring and collaborative international network.

6.2.2 Development of a uniform definition and standard for term 'medication review'

In 2009, PCNE started to discuss a definition and terminology for medication reviews (MR) performed by pharmacists in ambulatory and clinical setting.

At various meetings and workshops, the PCNE definition and terminology of MR was further developed. The first definition of a medication review by PCNE was prepared in a brainstorming in Vimeiro (PT) and discussed 2009 in Geneva (CH): *'A medication review is an evaluation of patient's medicines with the aim of optimizing the outcome of medicine therapy by detecting, solving and preventing drug-related problems'*. Three different types of MR were distinguished. The terminology followed the available number of information resources: I) a simple MR only uses dispensing data from patient history, II) an intermediate MR additionally uses the patient's information from a patient interview, and III) an advanced MR combines dispensing data, patient' information and clinical data.

In 2011, the definition was modified and the main goal of a MR was amended with the term 'managing the risk' (Manchester, UK), highlighting an active role and responsibility of the health

professional with respect to patient safety. In addition, the definition was expanded in such a way that a MR should be part of the medication therapy management.

In 2013 (Berlin, DE) discussions about specific opportunities and limitations in primary or secondary care settings triggered a splitting of the intermediate MR into two subtypes: in primary care, medication history of the pharmacy and patient information is available (2a), while in secondary care, the medication history and clinical information is used (2b). Discussions of the process of performing MR concentrated on the ability of the different types to detect drug therapy problems and patient selection.

In Sliema (Malta, 2014), the discussion about the definition resulted in the addition of the term 'all medicines' including prescribed and OTC and, if accessible, the history. In addition, 'medicines use' was chosen according to the PCNE definition of Pharmaceutical care, which refers to the WHO definition of «responsible use of medicines». This covers effectiveness, quality of life, efficiency, and safety.⁷⁷ Further, it was stated in form of a comment that medication review should be part of the patient's medication management and that PCNE should define the term medication management.

During the 5th PCNE Working Symposium 2016 in Hillerød (DK), a unique consensus method with electronic voting, was used to eventually establish a solid definition of the term 'Medication Review': 'Medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions.'

The PCNE terminology takes into account that the amount of available sources of information defines the type of a MR. Specific expertise and skills are required to perform the different types of MR properly. Standardised structures and documentation forms are now needed to achieve appropriate reviews and to translate the findings into an efficient care process.

6.2.3 Workshop report PCNE Working Symposium 2014, Sliema, Malta

In order to support the European efforts to establish a uniform definition and terminology for medication review, a workshop for the participants at the working symposium 2014 in Sliema (Malta) took place. Markus Messerli and Ms Lea Botermann (PhD Student at the Federal Union of German Associations of Pharmacists (ABDA), Berlin, Germany) performed the moderation of

the workshop, which was chaired by Dr. Saija Leikola. Main topic was to discuss, which DRP could be detected with MR type 2b. Dr. Leikola run in parallel another workshop aimed at establishing a list of DRPs that may be detected within type 1 and 2a medication reviews.

Time schedule was limited to 60 minutes. Through hand voting at the very beginning, participants (n=21) were equally distributed in beginners (n=12) and experienced researchers (n=9). Principal goal of the workshop was to elaborate a list of detectable drug-related problems when MR type 2b or 3 were performed. As a starting point, the moderators used results of the workshop discussion of the previous working conference in Berlin, Germany in 2013.⁷⁸ In a first step, the workshop moderators gave a short overview and assured that the definitions for critical terms used, i.e. pharmaceutical care, drug-related problems, and medication review (including the PCNE typology) were identical. Later, the participants were divided into three smaller groups. They agreed on different settings, in which a pharmacist might be involved and could provide medication reviews PCNE type 2b and/or 3. The discussion revealed five common settings, i.e. community pharmacy, nursing home, hospital, rehabilitation, and assisted living. The groups then focused on the available information and characteristics of each setting. Out of these findings, examples for scenarios of detectable DRPs (Table 6) including their causes (Table 7) were mapped on a flip chart and finally assigned to the PCNE classification for drug-related problems V6.2.¹⁷

Table 6 / Drug-related problems according to PCNE Classification for DRPs (V6.2) that can be detected with medication reviews PCNE type 2b and in addition with type 3; (x) = suspected DRP

		Type 2b	Type 3
<i>P1: Treatment effectiveness</i>			
P1.1	No effect of drug treatment / therapy failure	(x)	x
P1.2	Effect of drug treatment not optimal	(x)	x
P1.3	Wrong effect of drug treatment	(x)	x
P1.4	Untreated indication	x	x
<i>P2: Adverse reactions</i>			
P2.1	Adverse drug event (non-allergic)	(x)	x
P2.2	Adverse drug event (allergic)	(x)	x
P2.3	Toxic adverse drug event	(x)	x
<i>P3: Treatment costs</i>			
P3.1	Drug treatment more costly than necessary	x	x
P3.2	Unnecessary drug treatment	x	x
<i>P4: Others</i>			
P4.1	Patient dissatisfied with therapy		x

PROJECT A - Opportunities for clinical pharmacy service in patient care

Table 7 / Causes for drug-related problems according to PCNE Classification for DRPs (V6.2) that can be detected with medication reviews PCNE type 2b and in addition with type 3; (x) = suspected DRP

		Type 2b	Type 3
<i>C1: Drug selection</i>			
C1.1	Inappropriate drug (incl. contra-indicated drug)	x	x
C1.2	No indication for drug	x	x
C1.3	Inappropriate combination of drugs or drug and food	x	x
C1.4	Inappropriate duplication	x	x
C1.5	Unnoticed indication	x	x
C1.6	Too many drugs for indication	x	x
C1.7	More cost-effective drug available	x	x
C1.8	Synergetic or preventive drug required	x	x
C1.9	New indication presented	x	x
<i>C2: Drug form</i>			
C2.1	Inappropriate drug form	(x)	x
<i>C3: Dose selection</i>			
C3.1	Drug dose too low	x	x
C3.2	Drug dose too high	x	x
C3.3	Dosage regimen not frequent enough	(x)	x
C3.4	Dosage regimen too frequent	(x)	x
C3.5	No therapeutic drug monitoring	x	x
C3.6	Pharmacokinetic problem requiring dose adjustment	x	x
C3.7	Deterioration/improvement of disease requiring dose adj.	x	x
<i>C4: Treatment duration</i>			
C4.1	Duration of treatment too short	(x)	x
C4.2	Duration of treatment too long	(x)	x
<i>C5: Drug use / administration process</i>			
C5.1	Inappropriate timing of administration / dosing intervals	x	x
C5.2	Drug underused / under-administered		x
C5.3	Drug overused / over-administered		x
C5.4	Drug not taken / administered at all		x
C5.5	Wrong drug taken / administered		x
C5.6	Drug abused (unregulated overuse)		x
C5.7	Patient unable to use drug / form as directed		x
<i>C6: Logistics</i>			
C6.1	Prescribed drug not available	x	x
C6.2	Prescribing error (information wrong or missing)	x	x
C6.3	Dispensing error (wrong drug or dose)	x	x
<i>C7: Patient</i>			
C7.1	Patient forgets to take drug	(x)	x
C7.2	Patient uses unnecessary drug		x
C7.3	Patient takes food that interacts		x
C7.4	Patient stored drug inappropriately		x

All groups stated that pharmacists are able to detect various drug-related issues with MR type 2b. Whenever the patient additionally is involved (type 3), more specific individual care can be provided. Hence, no unambiguous pattern or final list for detectable DRPs could be established.

Each setting and type of medication review offers variable opportunities for detecting DRPs. This reflects the wide variety of pharmaceutical care issues. Group discussion revealed that medication reviews need accurate information sources, meaning the data has to be validated before, during or after analysis. In addition, participants agreed that potential DRPs detected within MR type 2b often need further clarification before interventions may be considered, while DRPs detected within MR type 3 allow direct patient contact and therefore direct confirmation of a suspected DRP resulting in a more comprehensive intervention.

6.2.4 Limitations of medication reviews: lesson learned

In 2015, PCNE invited the author to give a lecture during their 9th working symposium at Mechelen (BE). During the preparation of the structured discussion on the effect of medication review in different settings, the author became aware of a crucial limitation: one has to consider that the term 'Medication Review' describes a methodological approach and must not be seen as a completed intervention. A medication review may detect clinical relevant drug-related problems in a first step, but they still need to be solved to have an impact on patient' outcomes. According to the PCNE definition, medication reviews end in their theoretical process structure with a recommendation for an intervention. Thus, this methodological restriction has to be considered whenever different services are compared with each other. The possibility of a pharmacist in performing interventions varies in terms of differences between regional, national or international healthcare systems, different legal competencies regarding settings, and finally personal qualification in knowledge and expertise.

Health professionals should also be aware of low implementation rates of recommendations. One has to be aware that recommending is not performing, and performing is not implementing. Kempen et al. reported in their study implementation rates up to 47% from their interventions (recommending to stop a medication),⁷⁹ highlighting the gap between pharmacists' proposals and prescribers' acceptance of advice. Within a defined risk population, Perera et al. performed a 'medication therapy management' (MTM) program in 2011 and thereby yielded 1,548 pharmacist-initiated medication recommendations faxed to 1,163 prescribers for 1,174 patients in a 5-month period.⁸⁰ The overall prescriber approval rate for these recommendations was 47.2%, 255 (16.5%) recommendations were denied, and 562 (36.3%) had no response. Following the concept of Number Needed to Treat (NNT) as a

commonly known measure to describe the effectiveness of a health-care intervention from an epidemiological perspective, the term 'Number Needed to Review (NNR)' might describe the effectiveness of performed medication reviews. In an ideal setting, the NNR would be 1, representing the average number of reviews needed to be provided to detect a specific clinical relevant drug-related problem that might be solved through an subsequent intervention.⁸¹ Thus, the NNR would be part of the NNT when an intervention based on a performed medication review is described.

7 PROJECT B – Evaluation of the Swiss Polymedication Check

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7.1 Prologue: Theoretical considerations

The Polymedication Check aims at improving a patient's adherence to medication. Therefore, the evaluation study investigated the service's impact on objective and subjective adherence as the primary outcome measures. Since Swiss pharmacies are required by law to document all dispensed medicines, this offers a valid database for individual adherence calculations. Several measures and indices for calculating adherence from dispensing data have been proposed. However, a wide inconsistency in definitions, lack of guidance on methodology, and arbitrary computations hamper this approach.

In order to discuss objective adherence as a primary outcome measure in the evalPMC project, an in-depth methodological discussion took place during the development of the study design. During her master thesis, Adiam Kiflai searched the literature for existing methodological approaches. She then organised an expert panel where the strengths and limitations of the various designs were discussed. Out of this initiative, two co-authored publications resulted:

- one focusing on a method for calculating adherence to polypharmacy from dispensing data records,⁸²
- and another one resulting in a proposal of standardisation to assess adherence with medication records: methodology matters⁸³

In terms of a comprehensive overview of the theoretical considerations regarding the development of outcome measurements for the evalPMC project, both articles are presented in the following part of the thesis. Their implications, i.e. DPPR as a new adherence measure and the proposed reporting standards when medication refill data are used, were of great importance for the evalPMC project.

7.2 A method for calculating adherence to polypharmacy from dispensing data records [B1]

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A method for calculating adherence to polypharmacy from dispensing data records

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Abstract *Background* Several measures for calculating adherence to one medication from dispensing data records have been proposed, but the nomenclature is inconsistent and computations vary. The same measures, like the medication possession ratio (MPR), have been used for multiple medication regimens, and have tended to over- or under-estimate adherence rates. *Objective* To demonstrate the impact of varying elements in MPR to a single medication regimen; to define standards for the estimation of adherence to polypharmacy; to propose a new method for calculating adherence to polypharmacy; to face validate it. *Setting* Face validity of the proposed method. *Method* Variations in the MPR formula were simulated. Standards for the estimation of adherence to polypharmacy were defined. A new method to calculate adherence to polypharmacy was established. Its face validity with three illustrative cases obtained from a pharmacy refill database was assessed. *Main outcome measure* Adherence rate to polypharmacy from refill data records. *Results* MPR to a single medication is operationalized in the numerator and denominator and is influenced by the parameters like observation period, medication gaps, overlap. For polypharmacy, an average MPR is commonly used, which is not accounting for the specificity of multiple medications,

and hence overestimating adherence rate. We propose the daily polypharmacy possession ratio (DPPR) as an index of adherence to polypharmacy. It estimates the proportion of time a patient had medication available for use by considering the presence or absence of multiple medications on each day in the observation period. We calculated possession rates from refill histories over 31 months (January 1, 2011–July 31, 2013) for three illustrative patients. The average MPR estimates were 80 % for a patient with 6 medications/20 refill dates, 90 % for a patient with 4 medications/11 refill dates, and 89 % for a patient with 3 medications/17 refill dates. The corresponding DPPRs were 75, 88 and 99 %, indicating overestimations by 5 and 2 %, and underestimation by 10 %, respectively. *Conclusion* The DPPR accounts for the specificity of polypharmacy including number of medications, medication switching, duplication, overlapping. Research is needed to further confirm the validity of this new index.

Keywords Adherence · Compliance · Daily polypharmacy possession ratio · Medication possession ratio · Pharmacy claims · Polypharmacy · Refill data

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Impact of findings on practice

- The Daily Patient Possession Ratio (DPPR) offers clinicians and researchers a method for estimating adherence to polypharmacy regimens.
- When calculating adherence to polypharmacy, the DPPR avoids the overestimation inherent to using single-medication records.

Introduction

Because a patient's medication-taking behaviour is a prerequisite for evaluating the effectiveness of medications [1] accurate and consistent measurement of adherence is critical. The advance of computerized pharmacy records in developed countries that use medical informatics in their health system enables the assessment of adherence to an index medication based on refill patterns [2]. Several measures for calculating adherence rate from secondary database have been proposed, such as: medication possession ratio (MPR) and related measures of availability; discontinuation/continuation; switching; medication gaps; refill compliance, and retentiveness/turbulence [3]. All have in common that they measure the timeliness of prescription or refills, not actual drug-taking, and use the medication exposure time to estimate adherence. Consequently, the measures quantify the patient's possession of medication and, thus, calculate the highest possible level of medication consumption over a particular time frame. Although there is no gold standard, MPR is the most commonly used measure. It is calculated by dividing the days' supply of a medication dispensed by the number of days in the time interval of interest. Another often used measure is the proportion of days covered (PDC), which represents the proportion of days a patient has a medication available in a given period of time and uses indices truncated at 1.0 [4]. These measures are widely used because dispensing databases contain the necessary elements for calculation: (a) the *quantity dispensed*, which usually is the package size or a multiple of it dispensed at one time; or alternately for dispensing from bulk stock the number of medications supplied at one time; (b) the *prescribed daily dosage*, or the amount of medication to be consumed per day, which is calculated as (pills per dose) \times (dose per day); and (c) the *number of days' supply*, that is, the quantity dispensed divided by the prescribed daily dosage.

Being derived from longitudinal dispensing databases, the MPR and PDC can quantify long-term adherence and associated outcomes. However, five definitions influence the calculation of these measures and explain the variations in results often seen. First, the *observation period*, i.e., the length of the time over which adherence is assessed, may start and end at a specific fill and refill date; on arbitrary start/stop dates that are set as the index or inventory date and are independent from fills and refills; or a combination of a fixed and an arbitrary date. Second, an *initial/terminal gap* between dates of first/last fill and arbitrary start/end dates may be present and can be quantified as a proportion of time without supply. Third, an *interim gap* may exist between refills when prior supply is depleted before refill supply is available. Fourth, the *number of days' supply* dispensed at any fill/refill event may vary and requires adjustments in the calculations. Alternately, and fifth, *overlap* may occur as refill precedes depletion of the quantity from a prior dispensing, and leads to stock piling of

accumulated supply. These five sources of bias may lead to an under- or over-estimation of adherence to a single-medication.

The effects of these five sources of bias are likely to be amplified when adherence to a polypharmacy regimen is estimated using methods for single-medication adherence such as the MPR or, as commonly done, averaging the MPR of each medication in the polypharmacy regimen. Polypharmacy is common due to comorbidities [5], an aging population [6], clinical practice relying on multi-drug combinations [7], or evidence-based guidelines recommending synergistic drug combinations [8]. Polypharmacy is different from regimen complexity, which refers to the number of daily doses for a medication, the presence of non-oral routes of administration, and the need for specific dosing instructions [9]. Because polypharmacy is known to be associated with medication non-adherence [10] because of the greater number of medications that can be missed on a daily basis, the assessment of adherence to the entire polypharmacy regimen is essential. Further, because irregular and inconsistent intake of one or more drugs in a polypharmacy regimen is common and may impact on clinical outcomes, assessment of adherence to polypharmacy is clinically relevant. The few studies that have attempted to calculate adherence to several concurrent medications have averaged the indices obtained for each of the single-medications [11–15]. This method has been shown to overestimate [16] but may also underestimate adherence to polypharmacy regimens.

Aim and objectives

In the absence of an integrated method for assessing adherence to polypharmacy regimens and the estimation errors likely from averaging methods, our aim was to develop a new method for quantifying adherence to polypharmacy regimens. Five objectives applied: (1) to document the estimation bias in single-medication adherence as a function of the sources of variation identified above; (2) to document the estimation bias resulting from averaging single-medication methods to polypharmacy regimens; (3) to specify the standards for calculating an integrated measure of polypharmacy adherence; (4) to define the proposed method for calculating adherence to polypharmacy regimens; and (5) to establish initial face validity of the method by applying to three illustrative cases obtained from the dispensing records of a community pharmacy.

Methods

Estimation bias in single-medication adherence

We constructed a hypothetical refill scenario commonly seen in reimbursement records for medicines for long-term

conditions in order to illustrate the impact of variable elements on the calculations of adherence to single-medication such as hypertension. We selected seven dispensations in analogy to Steiner et al. [14] and calculated several indices. Two different observation periods of 250 days each were used: (1) from the first fill to the last refill date; and (2) over two arbitrary dates. Four calculations were performed:

1. The *proportion of supply between dispensations or adherence in one refill interval* (A_n/B_n), calculated as the days' supply obtained at the beginning of a specific interval divided by the days elapsed before the subsequent fill and expressed as a percentage.
2. The *days without supply between dispensations or gaps in one refill interval* ($G_n = B_n - A_n$), calculated as the days elapsed before the subsequent fill i.e., the number of days between dispensations, minus the days' supply obtained at the beginning of the interval.
3. The *proportion of time with adequate supply or medication possession ratio* ($\sum A_n / \sum B_n$), calculated as the total days' supply obtained over the observation period and across all time intervals divided by the number of days of the observation period and expressed as a percentage.
4. The *proportion of time without adequate supply or gaps over all refill intervals* ($\sum G_n / \sum B_n$), calculated as the total days of gaps (+) or surplus (−) divided by the total days to next dispensation or to end of observation period; that is, the cumulative sum of the number of days between dispensations minus the total days' supply divided by the number of days in the observation period.

Estimation bias in polypharmacy adherence calculated with averaging methods

We again constructed a hypothetical scenario, this one involving 3 medications with a combined 15 refills [17] and an observation period beginning with the initial fill at the start date and ending with the medication review. Medication 1 came in a package size of 14 with seven refills at days 1, 15, 29, 43, 57, 71, 101 and end date at 110 days. Medication 2 came in a package size of 30 with four refills at days 1, 41, 61, 120 and end date at 120 days. Medication 3 came in package size of 60 with four refills at days 1, 31, 51, 101 and end date at 110 days.

Specification of standards

On the basis of the above bias estimation exercises, prior review work, and literature evidence, calculation standards were set to assure uniformity in calculations.

Development of method

A proposed method based on these standards was developed and evaluated for arithmetic accuracy.

Initial assessment of face validity

We applied the method to three illustrative cases varying in the number of medications and refills obtained from the dispensing data records of a community pharmacy in Basel, Switzerland.

Results

Estimation bias in single-medication adherence

Figure 1 depicts the adherence calculations for a patient with a chronic condition with a hypothetical refill scenario of a medication to be taken once daily with 7 dispensations in analogy to Steiner et al. [14]. Table 1 summarizes the calculated adherence rates between each refill event and the next.

Table 2 presents the days without supply between dispensations (or gaps).

Table 3 summarizes the MPR results. The overall possession rates are 108 %/84 % if calculations consider all values without the last refill, and 93 %/87 % if single values are capped at 1.0, underscoring that adherence is underestimated with truncated values.

Table 4 presents the proportion of time without adequate supply (or gaps) over all refill intervals. The proportion of gaps is $-0.08/0.04$ if calculations consider all values and $0.14/0.22$ if negative values are set to zero, thus masking the surplus (negative gaps' value). If accumulated oversupply is assumed to be used when the supply is exhausted and carryover from one interval to the next is allowed, the proportion of time without medication declines from 35 to 25 days, which corresponds to an overall 4 % improvement in supply.

Estimation bias in polypharmacy adherence calculated with averaging methods

Figure 2 graphs the average MPR calculation with a hypothetical scenario of 3 medications with a combined 15 refills. Note that the observation period begins with the first refill at start date "day 1" and runs until the medication review (an arbitrary date). The MPR for medication 1 is $(7 \times 14)/110 = 89 \%$; for medication 2 it is $(4 \times 30)/120 = 100 \%$; and for medication 3 it is $(4 \times 60)/110 = 218 \%$. Hence the average MPR is $[(7 \times 14) + (4 \times 30) + (4 \times 60)]/$

Fig. 1 Scenario of adherence to a single-medication, starting at the first fill (dark, bold line) or an arbitrary date (grey, dotted lines) over an observation period of 250 days (arbitrary end date). R_nX = refill number and quantity dispensed; A_n = number of days' supply; B_n = interval between dispensations; gaps indicate number of days with no medication. Note the arrows from R_2 to R_3 indicate carryover of excess medication from one interval to the next interval

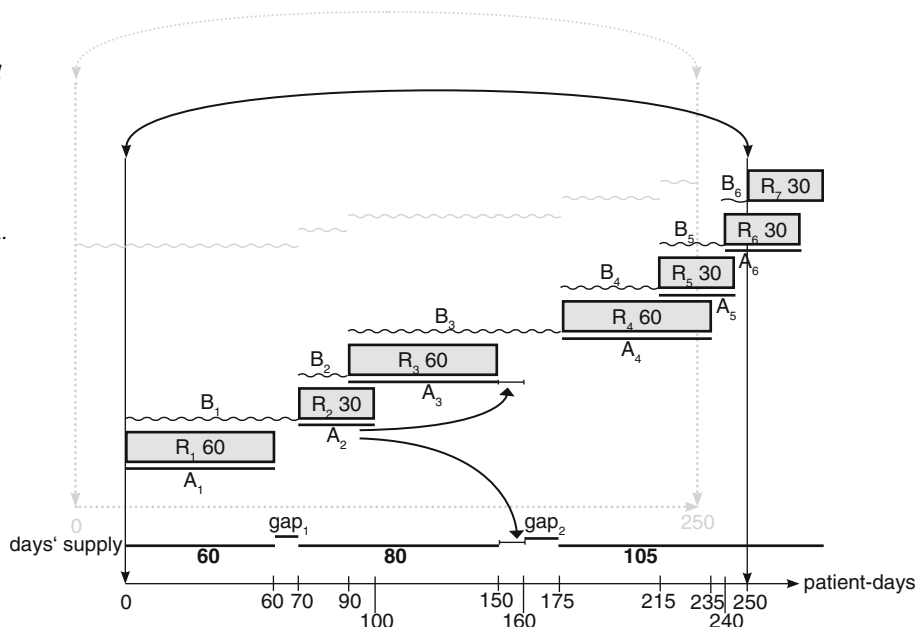


Table 1 Estimates of single-medication adherence between each refill event and the next, for each observation period (starting at a refill date or an arbitrary date)

Refill event	R1	R2	R3	R4	R5	R6
Start at refill date	60/70 (86 %)	30/20 (150 %)	60/85 (71 %)	60/40 (150 %)	30/25 (120 %)	30/10 (300 %)
Start at arbitrary date	60/90 (67 %)	30/20 (150 %)	60/85 (71 %)	60/40 (150 %)	30/15 (200 %)	–

$R(\text{number})$ refers to interval starting at a given refill event and ending at the next refill event; e.g., R_1 is refill event 1 and the interval ends with R_2

Table 2 Days without supply between dispensations (or gaps), for each observation period (starting at a refill date or an arbitrary date)

Refill event	R1	R2	R3	R4	R5	R6
Start at refill date	70–60 (10)	20–30 (–10)	85–60 (25)	40–60 (–20)	25–30 (–5)	10–30 (–20)
And with carry over of oversupply	70–60 (10)	20–20 (0)	85–70 (15)	40–60 (–20)	25–30 (–5)	10–30 (–20)
Start at arbitrary date	90–60 (30)	20–30 (–10)	85–60 (25)	40–60 (–20)	15–30 (–15)	–

A positive value indicates a lack of supply, a negative value indicates a surplus of supply

$(110 + 120 + 110) = 135 \%$, denoting an overconsumption of medication.

Specification of standards

The average MPR calculation does not control for the influence of several medications having been prescribed, across varying schedules, and the expectation that patients adhere to all medications regardless of regimen. Further,

patients rarely refill a medication on exactly the day following the last day of use of the previous dispensing. In addition, because of different package sizes, patients may have refills due on different dates. As a consequence, they adapt their refill obligation to daily duties and schedules and may refill a prescription earlier (overlap of two dispensations, surplus) or later (gap without supply between two dispensations). Thus, apparently excessive or insufficient refill patterns may be misinterpreted as oversupply or lack of medication, when they may represent daily life

Table 3 Medication possession ratio (MPR) calculated over all refill intervals, with or without the last refill, and with single values capped at 1.0, for each observation period (starting at a refill date or an arbitrary date)

Specifications	With last refill	Without last refill	With single values capped at 1.0
Start at refill date	300/250 (120 %)	270/250 (108 %)	(0.86 + 1 + 0.70 + 1 + 1 + 1)/6 (93 %)
Start at arbitrary date	240/250 (96 %)	210/250 (84 %)	(0.67 + 1 + 0.70 + 1 + 1)/5 (87 %)

Table 4 Proportion of time without adequate supply (or gaps) over all refill intervals, with all values or negative values set at zero (no surplus), for each observation period (starting at a refill date or an arbitrary date)

Specifications	With all values	With negative values set at 0 (no surplus)
Start at refill date	(10 - 10 + 25 - 20 - 5 - 20)/250 (-0.08)	(10 + 0 + 25)/250 (0.14)
Start at arbitrary date	(30 - 10 + 25 - 20 - 15)/250 (0.04)	(30 + 0 + 25)/250 (0.22)

Table 5 New definitions proposed of the parameters required to calculate possession rates with refill data

New definitions of the parameters	Pros
Start the observation period at day 1 with the first dispensation	No artificial initial gaps
End the observation period at the last refill date or at the medication review date	No artificial terminal gaps
Exclude any extra doses of the last dispensation beyond the end of the observation period	No artificial oversupply
Allow the carryover of excess medication from one interval to the next interval, yet without retroactive compensation	No artificial oversupply
Exclude patients with two refills or less	No artificial gaps
Consider therapeutic switching ^a as one medication and not as a duplication	No artificial duplication
Consider switching from two medications to one combination pill as therapeutic switching, with the first refill in time determining the index medication substituted by the combination pill	No artificial duplication
Allow generic switching and consider as one medication	No artificial duplication
Consider therapeutic duplication ^b as one medication, with the index medication being the one with the first refill in time	No artificial duplication
Enable changes in dosage according to medical prescription	No artificial oversupply or gap

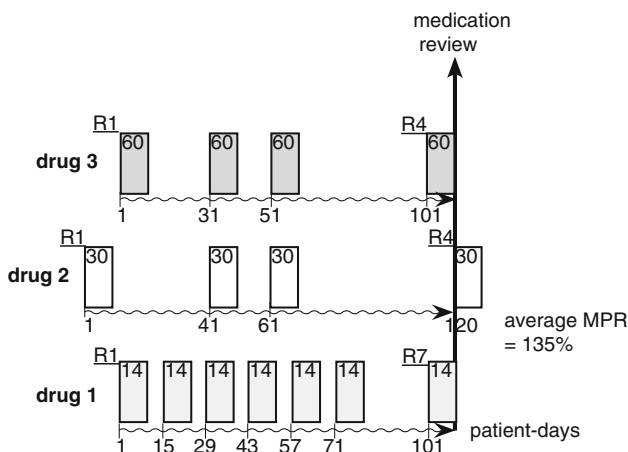


Fig. 2 Scenario of adherence to a combined drug regimen for a patient (with a chronic condition) with a medication to be taken once daily in analogy to [17]. The refills of 3 medications are depicted with 15 dispensations over an observation period defined between the first fill (R1 at day 1, start date) and a medication review (arbitrary end date). *R* refill number; *box with number* quantity dispensed

conditions such as foresight before holidays or using up all medication before the next refill.

We propose new definitions of the parameters needed to calculate medication possession rates with refill data (Table 5). In the numerator, extra doses beyond the end of the observation period should be excluded (no oversupply); therapeutic switching and therapeutic duplication should be

considered as one medication (no duplication), and changes in dosage should be recognised and accounted for. In the denominator, the observation period should start at the first dispensation date, end either at the last refill date or at the medication review date, and cover at least two refills (no gaps). Finally, the carryover of excess medication from one interval to the next interval should be allowed, yet without retroactive compensation.

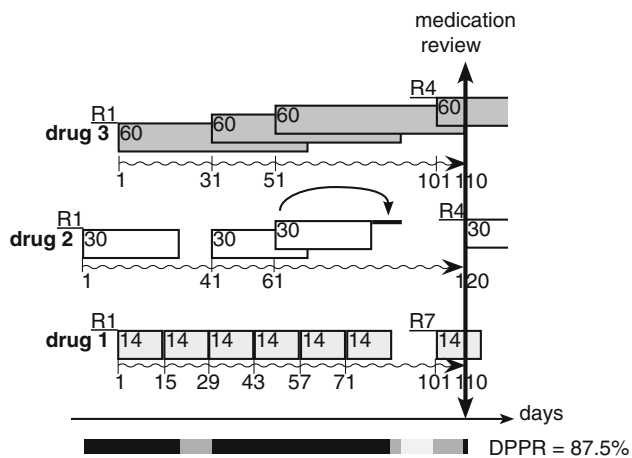


Fig. 3 Calculation of daily polypharmacy possession rate DPPR for 3 medications to be taken once daily, with 15 dispensations over an observation period defined between the first fill (R1 at day 1, start date) and a medication review (end date), same as in Fig. 2. Daily possession is depicted as follow: all medications available (score of 1, black bar), two medications available (score of 2/3, dark grey bar), one medication available (score of 1/3, light grey bar). The arrow indicates carryover of excess medication from one interval to the next interval

New method for calculating adherence to polypharmacy

With these definitions, we posit that the numerator cannot merely be the sum of the days' supply, that each day should be assessed independently, and that the proportion of daily medications on-hand be calculated. We propose as new index the daily polypharmacy possession ratio (DPPR). The method is as follows: Look at each day in the observation period separately, and determine how many medications are available, set a score between 0 (no medication available) and 1 (all medications available) weighted by the number of medications to be taken each day, resulting in daily scores indicating the proportion of medications available for each day. Sum the scores and divide by the number of days in the observation period to obtain the proportion of all medications available for daily use.

Figure 3 shows the calculation of the DPPR for 3 medications to be taken once daily with 15 dispensations over the same observation period as used in Fig. 2. Each daily score can take a value of 1 (all medications available), 2/3 (two medications available), 1/3 (one medication available) or 0 (no medication available). The sum of the daily scores $(10 \times 1/1) + (20 \times 3/3) + (10 \times 2/3) + (54 \times 3/3) + (6 \times 2/3) + (10 \times 1/3) + (9 \times 2/3) + (1 \times 3/3)$ is 104.9. Next $104.9/120 = 87.5\%$ yields the DPPR and represents the weighted percentage of medications available. The accumulated surplus of daily doses is 80 (medication 1). The accumulated number of

days with at least one missing dose is 16 for medication 1 (4.7 %) + 30 for medication 2 (8.8 %) = 46 (13.5 %).

The DPPR requires a “supply diary” for each patient-day. Because overuse or excess prescription of medications cannot be detected with the DPPR, the surplus of daily doses and the total number of missed doses (gaps) during the observation period should be evaluated to complete the description of the observed population.

Initial assessment of face validity

Three patients with polypharmacy using a single community pharmacy in Basel (Switzerland) were selected by the pharmacist who subjectively and clinically identified an adherer, an underadherer and an overadherer. The medication histories between January 1, 2011 and July 31, 2013 were retrieved from the pharmacy database. They include 1 male (M1) and 2 female (F1, F2) patients; aged 72, 78 and 74 years; with 4, 3 and 6 medications daily; and 11, 17, and 20 refill dates over the observation period of 31 months, respectively (Box 1).

The results are presented in Box 1. The MPRs were calculated with the average MPR method and yielded 90 % for patient M1, 89 % for patient F1, and 80 % for patient F2. With the DPPR method and the standards defined above, the DDPDR rates were 88, 99 and 75 %, respectively. The mean numbers of days without supply (gaps) were -10, -1 and -24 %, respectively.

Discussion

The two methods most often used to measure medication adherence from dispensing data records are the MPR and the PDC. However, because of lack of standards and definitions necessary for the parameters used in calculation, the methods described in studies vary widely. As an example, Hess et al. [18] calculated adherence rates ranging from 63.5 to 104.8 % when applying 11 different calculation methods to the same set of pharmacy data. As a consequence, comparing results between studies is often difficult if not impossible. Further, many assumptions are made when adherence rates (i.e., medication consumption) are calculated from secondary databases; e.g., that a person has the medication available on the day of the prescription; that patients consume the medication as prescribed; that patients start taking the medication on the day of dispensation until the supply is exhausted; that medication consumption is consistent throughout the observation period; or that all extra doses accumulated during the observation period are taken by the patient until depleted if refills are

Box 1 Medication histories of three illustrative patients (M1, F1, and F2) between the start date (January 1, 2011) and an arbitrary review date (July 31, 2013), with indication of the prescribed daily dosage (e.g., 1–0–0 stands for one tablet every morning), number of days in the single intervals and in the observation period (total); quantity dispensed at the refill date and total of days' supply (calculated as quantity dispensed divided by the prescribed daily dosage), and total number of days without supply (gaps). Asterisks (*) indicate insufficient supply for the next interval

Patient M1	No days in the interval	Quantity dispensed at the refill date of the medication (prescribed daily dosage)			
		Atorvastatin 20 mg (1–0–0)	Metopropol 25 mg (1–0–0)	Aspirin 100 mg (1–0–0)	Salmeterol 25 µg + fluticason 250 µg (1–0–0)
11.01.11		100	–	90	60*
05.04.11	84	100*	–	196	60*
11.10.11	189	100	100	98	60*
12.01.12	93	100	100	98	60
07.03.12	55	100	100	98	60*
27.06.12	112	0*	0*	0	60
08.08.12	42	100*	100*	98*	120
07.12.12	121	100	100	98	60*
27.02.13	82	100	100	98	60
23.04.13	55	0	0	0	60
14.06.13	52	100	100	98	120
31.07.13	47				
Total	932	900	700	972	780
Total gaps		–96	–23	–18	–238

Calculation: “average MPR” = $[(900 + 700 + 972 + 780)/4]/932 = 90 \%$

DPPR = $[(60 \times 3/3 + 24 \times 2/3) + (60 \times 3/3 + 56 \times 2/3 + 73 \times 1/3) + (60 \times 4/4 + 33 \times 3/4) + 55 \times 4/4 + (65 \times 4/4 + 47 \times 3/4) + (40 \times 4/4 + 2 \times 2/4) + (100 \times 4/4 + 3 \times 2/4 + 18 \times 1/4) + (77 \times 4/4 + 5 \times 3/4) + 55 \times 4/4 + 52 \times 4/4 + 47 \times 4/4]/932 = 88 \%$

Gaps: mean –10 %

Patient F1	No days in the interval	Quantity dispensed at the refill date of the medication (prescribed daily dosage)		
		Metformin 850 mg (1–0–1)	Fosinopril 20 mg (1–0–0)	Glibornurid 25 mg (½–0–½)
18.01.11		100*	98	–
18.03.11	59	100*	98	100
14.05.11	57	100	0	0*
27.06.11	44	100	98	100
12.08.11	46	100	0	0
01.10.11	50	100	98	100
21.11.11	51	100*	0	0*
23.01.12	63	100	98	100
01.03.12	38	100	0	0
16.04.12	46	100	98	100
19.06.12	64	100	0	0
02.08.12	44	200*	98	100*
20.11.12	110	100	98	100
31.12.12	41	100	0	0
19.02.13	50	100	98	100
08.04.13	48	100	0	0
25.05.13	47	100	98	100
16.07.13	52	200	0	100
31.07.13	15			

continued

Patient F1	No days in the interval	Quantity dispensed at the refill date of the medication (prescribed daily dosage)		
		Metformin 850 mg(1–0–1)	Fosinopril 20 mg(1–0–0)	Glibornurid 25 mg(½–0–½)
Total	925	1,000	980	1,000
Total gaps		–22	0	–13

Calculation: “average MPR” = [(500 + 980 + 1,000)/3]/925 = 89 %

DPPR = [(50 × 2/2 + 9 × 1/2) + (50 × 3/3 + 7 × 2/3) + (43 × 3/3 + 1 × 2/3) + 46 × 3/3 + 50 × 3/3 + 51 × 3/3 + (53 × 3/3 + 6 × 2/3 + 4 × 1/3) + 38 × 3/3 + 46 × 3/3 + 64 × 3/3 + 44 × 3/3 + (108 × 3/3 + 2 × 1/3) + 41 × 3/3 + 50 × 3/3 + 48 × 3/3 + 47 × 3/3 + 52 × 3/3 + 15 × 3/3]/925 = 99 %

Gaps: mean –1 %

Patient F2	No days in the interval	Quantity dispensed at the refill date of the medication (prescribed daily dosage)					
		Gliclazid 30 mg (2–0–0)	Sitagliptin 100 mg (1–0–0)	Aspirin 100 mg (1–0–0)	Valsartan 80 mg (1–0–0)	Simvastatin 80 mg (0–0–½)	Gingko-biloba extract (1–0–1)
04.01.11		120	98	–	–	–	–
10.02.11	37	120	196	–	98	100	240
03.05.11	82	0*	0	28*	0*	0	0*
21.06.11	49	120	0	0*	98	0	120
04.08.11	44	240	0	98	0*	0*	0*
18.10.11	75	0	0*	0	196	0*	0*
08.11.11	21	0	98	0*	0	0*	0*
03.12.11	25	0*	0	0*	0	100	120
03.01.12	31	120*	0*	98	0	0	0*
15.03.12	72	120	98	0*	98	0	0*
14.05.12	60	120	0	0*	0	0	0*
04.06.12	21	0	0*	98	0	0*	0*
25.06.12	21	0*	98	0	98	0*	0*
25.08.12	61	120	98	98	0	100	0*
20.10.12	56	240	0*	98	98	0	240
25.01.13	97	120	98	0	0*	0	0*
25.02.13	31	0	0	0*	0*	0*	120
05.04.13	39	120	98	98	0*	0*	0*
13.05.13	38	0*	0	0*	0*	100	0*
13.07.13	61	0*	98	98	98	0	120
31.07.13	18						
Total	939	780	980	714	784	800	480
Total gaps		–159	–66	–186	–204	–223	–497

Calculation: “average MPR” = [(780 + 980 + 714 + 784 + 800 + 480)/6]/939 = 80 %

DPPR = [37 × 2/2 + 82 × 5/5 + (1 × 6/6 + 15 × 5/6 + 12 × 4/6 + 10 × 3/6 + 11 × 2/6) + 44 × 5/6 + (16 × 6/6 + 9 × 5/6 + 29 × 4/6 + 21 × 3/6) + (7 × 4/6 + 14 × 3/6) + (2 × 4/6 + 23 × 3/6) + (15 × 5/6 + 16 × 4/6) + (29 × 6/6 + 13 × 5/6 + 18 × 4/6 + 12 × 3/6) + (26 × 5/6 + 34 × 4/6) + 21 × 4/6 + (16 × 5/6 + 1 × 4/6 + 4 × 3/6) + (18 × 4/6 + 43 × 3/6) + 56 × 5/6 + (79 × 6/6 + 18 × 5/6) + (23 × 6/6 + 2 × 5/6 + 6 × 4/6) + (16 × 5/6 + 12 × 4/6 + 11 × 3/6 + (13 × 4/6 + 25 × 3/6) + (39 × 4/6 + 21 × 3/6 + 1 × 2/6) + 18 × 5/6]/939 = 75 %

Gaps: mean –24 %

not obtained on time or before the next refill [19]. This might explain why some studies specify corrections for values, often without a clear rationale, like setting negative

values to zero [17] or multiplying duration of drug use by factor 1.1 to control for irregular use and early drug dispensation [20].

To enable a more uniform presentation of data and thus improve the consistency and quality of adherence analyses, international experts developed a checklist of key issues on how to perform retrospective analyses of refill medication databases [21]. Unfortunately, the proposed measurements of adherence lack key details and procedures, such as rules to avoid double-counting covered days or handling oversupply. It is evident that accurate calculation of adherence rates from refill data requires standard definitions of the considered time frame, the numerator and denominator, and the management of missing values and/or time periods. A more subtle calculation has been advocated [16] to allow for the comparison of results across studies and the translation to real world practice. With the advance of computerized pharmacy records, some researchers developed computational frameworks to detect such events as medication lapses in refill databases [22]. However, these technical developments are only useful for individual patient information and need further evaluation.

The influence of variable terms on the assessment of adherence to single drug is amplified with multiple drug assessment, especially when the method used is indifferent to the specific settings. A study comparing different calculation methods showed that the use of MPR for more than one medication overestimates adherence, predominantly due to the presence of duplication [4]. Since the “average MPR” does not account for the number of medications, the frequency of medication switching, the duplication, the overlapping, or the unexpected and same-day refills, it can hardly reflect the actual adherence that it was intended to measure. Thus, MPR methods are inadequate for quantifying adherence to polypharmacy regimens.

In this article, we defined new standards for the calculation of possession rates with refill data and proposed a new index, the DPPR. This index considers the presence or absence of multiple medications on each day in the observation period. It quantifies polypharmacy adherence as the percentage of medications daily available. This approach accounts for the specificity of polypharmacy such as the number of medications and frequency of medication switching. It also eliminates duplication and overlapping, the parameters responsible for the general overestimation of adherence. With the three illustrative cases we selected in a community pharmacy over 31 months, we piloted the new method and demonstrated its face validity in daily practice. As predicted, the DPPR values were lower than the average MPR estimates. Thus, we posit that the DPPR is closer to the actual adherence rate than other calculations.

Our approach has several strengths. First, we propose a standardization of the parameters used for calculation. Second, we propose a method that is insensitive to

oversupply and duplication, the two parameters in mathematical calculations that lead to overestimation of adherence rates. Third, the DPPR represents a continuous index of adherence across all subjects rather than a threshold-based index, separating adherent from non-adherent subjects. Moreover, the conversion from continuous data into categorical data as well as the use of cut-points is only recommended when the clinical validity of the specified level of adherence has been demonstrated [21]. To our knowledge, this exists only for oral contraceptives and HIV drugs [23].

Our new index also has limits. First, the DPPR cannot detect oversupply. Thus, we propose to indicate additionally the evaluation of the accumulated surplus (oversupply) and the accumulated days with at least one missing medication (gaps). Second, the DPPR requires a “supply diary” for each patient-day. This may be difficult to generate by computer, mainly because dispensing and recording services may differ across countries. For example, European pharmacies dispense manufactured packagings of varying sizes while US pharmacies have access to bulks and dispense the exact number of units prescribed. The maximum quantity of dispensed drugs is usually 90 days in the Netherlands, with a maximum of 15 days for the first dispensing, while no such restriction exists in Switzerland or Germany, where the first dispensed package can be 100 tablets in size. Finally, calculation with variable dosage schedule (e.g., “take 1 or 2 pills...”) or “as needed” as part of the instructions is not possible and these medications are to be disregarded from the evaluation.

Conclusion

Estimates of adherence to single-medications obtained from MPR-based methods may vary because of differences in calculation methods. This problem is amplified by multiple factors outlined in this article. Because adherence to multiple medications has been assessed with methods developed for single-medication use, results have so far proved divergent. We propose new definitions to standardize the parameters needed to calculate possession rates with secondary databases. We further propose a new method to calculate possession rate with multiple medications that accounts for the specificity of polypharmacy. Studies are needed to validate the new index DPPR, preferably with a national database. Subsequently, defining of a formula and programming of codes for computer-generating the DPPR from dispensing data records should be considered.

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Conflicts of interest None.

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7.3 Proposal of Standardization to Assess Adherence with Medication Records:
Methodology Matters [B2]

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Abstract

Background: Medication adherence is the process by which patients take their medication as prescribed and is an umbrella term that encompasses all aspects of medication use patterns. Ambiguous terminology has emerged to describe a deviation from prescribed regimen, forcing the European ABC Project to define 3 phases of medication use: initiation, implementation, and discontinuation. However, different measures of medication adherence using medication records are currently available that do not always distinguish between these phases. The literature is lacking standardization and operationalization of the assessment methods. **Objective:** To propose a harmonization of standards as well as definitions of distinct measures and their operationalization to quantify adherence to medication from medication records. **Methods:** Group discussions and consensus process among all coauthors. The propositions were generated using the authors' experiences and views in the field of adherence, informed by theory. **Results:** The concepts of adherence measures within the new taxonomy were harmonized, and the standards necessary for the operationalization of adherence measures from medication records are proposed. Besides percentages and time-to values, the addition of a dichotomous value for the reinitiation of treatment is proposed. Methodological issues are listed that should be disclosed in studies on adherence. **Conclusions:** The possible impact of the measures in adherence research is discussed. By doing this, the results of future adherence research should gain in accuracy. Finally, studies will become more transparent, enabling comparison between studies.

Keywords

adherence, medication, standards, measurements, operationalization

Introduction

Medication records are increasingly collected worldwide and available from different sources such as prescribing, dispensing, or reimbursement databases. The ready availability of these records has stimulated widespread use of these data to study patterns of medication use and assess medication adherence in daily clinical practices. Medication records often contain several elements required to calculate the number of days' supply, such as the date of prescribing or dispensing, the quantity dispensed, and the prescribed daily dosage (PDD). Differences in information that is available may exist between Europe and the United States. As an example, the instructions to patients (ie, the daily dosage information, such as, "Take 1 tablet 2 times daily") are rarely contained in US prescription claims. Nevertheless, the US data set might have the days' supply included when the pharmacy staff has access to the dosing instructions and calculates the days' supply with its subsequent entry into the computer processing system. Nevertheless, calculations with medication records represent

a simple approach to determine how much of the prescribed medications are being taken (ie, adherence) and for how long (ie, persistence). These measures have intuitive appeal, and their value in clinical research has been shown.^{1,2} They are objective, noninvasive, and economical for use in large populations because they can be easily derived from data routinely collected for administrative or other purposes. The reported calculations of adherence from medication records are indubitably based on the above-mentioned elements, but specification of standards for these calculations is missing.^{3–5} In the absence of any gold standard, no less than 11 different methods for calculating adherence were identified by Hess et al,⁶

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the most often used being the MPR (medication possession ratio) and the proportion of days covered (PDC).⁷ When applying the 11 different calculation methods to the same set of pharmacy data, Hess et al⁶ obtained adherence rates ranging from 63.5% to 104.8%, demonstrating the dramatic influence of the methods on the computed adherence values. Wilke et al⁸ identified 47 publications with pharmacy claims using 12 different calculation methods. When applied to a simulation with reimbursement data of 113 108 patients, the adherence ranged between 15.7% and 97.0%. In fact, of the 47 publications, only 4 named all the elements that were included in the calculations.⁸ Similarly, Caetano et al³ identified 5 different methods for calculating persistence, which resulted in a wide range of values and interpretations when applied to a hypothetical patient. In some cases, 1 isolated refill beyond the 360 days following treatment start was sufficient to qualify a patient as persistent.⁹ Authors publishing adherence rates mostly omit a description of the operationalization of the assessment methodology⁵—that is, how the adherence measures were calculated. This lack of transparency regarding the operationalization of adherence measures complicates the comparison of adherence results across studies^{6,10,11} and the translation to real-world practice.⁹

In parallel, and almost inevitably, a proliferation of terms emerged in the literature to describe medication use.¹² They all describe a deviant behavior and are often used interchangeably but define different aspects such as seeking medical care, acquiring medication, or deviating from the prescribed therapeutic plan.¹² As a consequence, a European consortium defined a new taxonomy for the umbrella term *adherence to medications*, which is “the process by which patients take their medications as prescribed.”¹² It is divided into 3 quantifiable phases: initiation, implementation, and discontinuation. Persistence represents one aspect of adherence and encompasses the time over which a patient remains on treatment. In this context, standards and definitions are needed to calculate the adherence measures according to the recently proposed taxonomy.¹²

Aims and Objective

The aims were (a) to harmonize the concepts of adherence measures from medication records within the new taxonomy; (b) to propose the standards necessary for the operationalization of these adherence measures; (c) to refine adherence calculation with medication data; and (d) to list the methodological issues that should be disclosed.

Methods

Six researchers with considerable expertise in medication adherence from Switzerland and the Netherlands—2 leading European countries in the integration of adherence measurements from medication records into pharmacy systems—formed a panel in summer 2014. All members were

researchers from academia and involved in governmental projects, and 2 members were doctoral candidates who worked on calculation methods. All are members of ESPACOMP (European Society for Patient Adherence, Compliance and Persistence); 2 are founding members, and 1 a former president. The leadership was taken by a member of the Special Interest Group on Adherence from the European Society of Clinical Pharmacy. Because the lack of standardization of adherence measures is a tenacious problem in adherence research, the panel decided to propose recommendations for future adherence research. A consensual nature of the process based on recent methodological articles^{12,13} and discussion among experts was selected to generate first results in November 2014. Final consensus on the last version was obtained in July 2015. The concepts describing medication use behavior were harmonized; standards were set for the elements related to the (re)fill of a prescription; and the measures were refined, together with their basic calculations capable of quantifying 3 phases of adherence.

Results

Harmonization of Concepts and Proposed Measures Describing Adherence

Because medical records contain variables that are mostly specific to their source—that is, quantity prescribed in prescription records versus quantity dispensed in dispensing records—some variable might be lacking for some calculation. The assumptions for adherence measurements with pharmacy dispensing records are listed in Box 1.

Initiation of the treatment occurs when the patient takes the first dose¹² and represents a dichotomous variable, based on first-fill data. With prescribing and dispensing records at disposal, sometimes, initiation is defined as the time from prescription until the first medication fill¹⁴—that is, a time-to-event variable. To reduce confusion, it should be named time-to-initiation. In any cases, the output is the number of primary nonadherers—that is, patients with a prescription that is not followed by a dispense.

Implementation is achieved when the patient's actual dosing is compared with the prescribed dosing regimen, from initiation until the last dose is taken.¹² For this phase, several measures are proposed.

Discontinuation and persistence are driven by the continuity of medication refilling. Discontinuation occurs when the next due dose is omitted and no more doses are taken thereafter. Discontinuation is, therefore, a dichotomous variable. Persistence describes the time from initiation until last dose¹²—that is, the end of therapy. Persistence is, therefore, a time-to-event variable. The dimension of time is an integral part of both terms.⁴ Exceeding a maximal permissible length without supply (grace period) qualifies for discontinuation or nonpersistence. This maximal gap can range

Box 1. Assumptions Underlying Adherence Measures With Pharmacy Medication Records.

- Medication records are complete, comprehensive, and accurate
- The first intake occurred on the day of the first fill
- The medication is taken as indicated (eg, tablet ingested)
- Lack of a refill equals a medication is not consumed after the oversupply is exhausted
- Medications are not purchased or borrowed from another person or venue
- No unknown treatment interruptions or dosing changes occurred during the observation period

from zero to an infinite number of days. Between those 2 extremes, almost every gap length from 7 to 180 days has been proposed in the literature.¹⁵ Setting the cutoff is equivalent to defining the sensitivity of the measure because the smaller the allowable gap, the higher the number of patients classified as having discontinued or being nonpersistent.¹⁶ A 90-day allowable gap might be adequate to detect true nonpersistence because a study investigating the impact of several gap selections on persistence observed no major change with increasing gap days >90 days.¹⁷ Ultimately, however, the length of the permissible gap should depend on the medication(s)/condition(s) being studied.

Because patients may restart treatment at any point in time, the quantification of *reinitiation* of treatment is proposed as the proportion of patients with a dispensing after the maximal predefined gap length.

Definition of Standards

The definitions of the elements with standards and calculations are summarized in Table 1.

The observation period is defined as the length of time over which the adherence measures are assessed. The period should start at t_1 at the first (re)fill date, with the assumption that the patient starts medication intake that very day. The period should end either at the last refill date t_n or at an arbitrary date t_a (eg, a medication review date; $t_1 + 360$ days). The rationale for such variable end dates is that refills are time-dependent events.

The number of days' supply is defined as the quantity dispensed divided by the PDD. The latter equals the amount of medication to be consumed per day and is calculated with the dosing instruction as Unit(s) per dose \times Dose(s) per day. Changes in dosage regimen according to medical prescription should be accounted for and should be exhaustively described. If the data set does not contain the quantity dispensed as a variable, it should not be used. With data sets that contain PDD as a variable, if the dosing instruction is missing, extrapolation from the following interval (for t_1) or from the previous interval (for all other t) should be allowed. A data set should be excluded if dosing instruction is missing for 2 intervals in a row or if the instruction changed over

Table 1. Definitions of the Elements, With Standards and Calculation.^a

Element	Definition	Standards and Calculation
Start and end points of the observation period	Period starts at t_1 and ends at t_n or t_a	t_1 = date of first (re) fill t_n = date of last refill ^b t_a = arbitrary date ^b
Observation period	Number of days of the entire period ^b	$t_n - t_1$ or $t_a - t_1$
Quantity dispensed	Number of dispensed medication units (eg, tablets)	[quant_disp] ^c
Prescribed daily dosage (PDD)	Amount of units to be consumed per day according to the dosing instructions	PDD = Number of units per dose \times Number of doses per day ^c
Number of days' supply (A_n)	Number of days with medication available	[quant_disp]/[PDD]
Refill interval (B_n)	Number of days between 2 dispensations	(Refill date t_n) - (Refill date t_{n-1})
Oversupply	Number of days' supply accumulated from previous dispensings (stockpile)	If ($A_n > B_n$), then oversupply = ($A_n - B_n$)
Gap	Number of days without medication supply	If ($A_n < B_n$), then gap = ($B_n - A_n$)
Maximal gap length	Number of days of the longest period of time without supply (after taking carryover of oversupply into consideration)	

^aSee Figure 1 for graphical representation.

^ba and n are integral numbers.

^cCan be an integral or a fractional number.

time and is unknown. With data sets that typically do not contain dosage instructions as a variable, noticeable differences may result from assumptions made.¹⁸ Researchers should, thus, explicitly state what assumptions were made to estimate the numbers of days' supply.

Oversupply (or stockpiling) results from overlapping days' supply of subsequent refill intervals and equals accumulated medications. Oversupply should be allowed, with the rationale that patients get supply before they have exhausted their drug supply and in a flexible manner according to their daily activities and duties. It should be carried forward to the next interval (carryover) or at the end of a

period with a gap, with the rationale that this pattern reflects real life—patients exhausting previous supply before starting the new one. Retroactive compensation—that is, the use of an oversupply to compensate a gap that occurred earlier in the dosing history—should be forbidden. Results of a study with hypothetical dispensing patterns suggest that accounting for oversupply in adherence measurement (time-forward approach) performs better than other methods.¹⁰ Oversupply beyond the observation period should not be permitted—that is, extra doses beyond the end of the observation period should be excluded. Oversupply beyond the end date was shown to overestimate adherence measures⁶ by inflating the value of the quantity dispensed.

A gap may exist between refills when prior supply is depleted before refill supply is available. It should be compensated to the extent possible by any existing oversupply from a prior interval. Hospitalization or residence in a long-term care facility may lead to apparent gaps in pharmacy refills and are often interpreted as discontinuation, mostly because they remain unrecognized. If known, the hospitalization period should be subtracted from the denominator, assuming, first, complete adherence to hospital drugs during hospital stay and, second, that patients do not obtain medications at discharge, and with the rationale that the amount of previous medication at the disposal of the patients after discharge is identical to that before hospitalization. A similar approach was used in a study developing an adherence index with inhaled corticosteroid.¹⁹ Unsurprisingly, adjusting for the time a patient was hospitalized by excluding the days of hospitalization marginally influences the adherence rate—that is, the adherence value is approximately 0.5% lower than without accounting for hospitalization days.⁷ If patients use their home medication in the hospital, no adaptation of the calculation is needed.

Switching is defined as one product being initially filled, then a different product in the same therapeutic class being filled at a later point within the observation period, and the initial product no longer filled. Generic switching is defined as switching between products with identical ATC code on level 5 (eg, C03EB01: Lasix 40 mg and Furosemide Actavis 40 mg). In this case, switch is considered as the possession of 2 products one after the other, and carryover is granted under the above-mentioned conditions. Therapeutic switching is defined as 2 different medications—that is, different ATC code on level 5 (eg, A02BC01: Omeprazole 40 mg and A02BC02: Pantoprazole 40 mg; switching within chemical group) or on level 4 (eg, A02BC: proton pump inhibitor and A02BA: H₂-antagonist; switching within pharmacological group). In this case, switch is considered as continuous use, and no overlap is granted—that is, a possible oversupply of one medication should be disregarded, with the rationale that a medical reason forced the physician to change medication (eg, lack of effectiveness, side effects, or intolerance).

Box 2. Issues to Clearly Disclose in Adherence Studies.

1. How was the data sample derived? (reimbursement, dispensing, prescribing data)
2. Was there a minimum number of fills and how was the minimum number of (re)fills defined?
3. Were all or only newly treated patients assessed? What was the definition of a newly treated patient?
4. Which adherence phase was assessed? (initiation, implementation, discontinuation)
5. How long was the observation period and how was it defined? (first vs last refill dates or first vs arbitrary end date)
6. How was the prescribed daily dose defined? (instructions for use, assumptions derived from treatment guidelines)
7. Was a single medication or polypharmacy analyzed?
8. How were hospitalization periods taken into account?
9. Which was the rationale for the use of threshold? (grace period, medication possession ratio)
10. How were missing values handled?
11. How were generic or therapeutic substitution handled?
12. How was dose switching handled?

Mandatory Information in Adherence Studies in Which Medication Records Are Used

To facilitate formal comparison between adherence studies published in the literature, some information should be clearly disclosed (Box 2). The issues are related to the operationalization of the adherence measures, which could dramatically influence the above-mentioned results.

Refinement of Calculation

Implementation is best given by the cumulative proportion of time at which medications are available—that is, in the possession of the patient. For monotherapy, the basic algorithm of the MPR is proposed. It sums the number of days' supply (see calculation below), divided by the number of days in the observation period, multiplied by 100. Some researchers and guidelines include the days' supply for the last prescription dispensed (up to the end of the observation period) in adherence and persistence calculations.²⁰ However, oversupply beyond the observation should be excluded (see above), and the following calculation should be used:

If end date is t_n (last refill date), then the numerator is [(Sum of days' supply) – (Days' supply obtained at t_n)].
If end date is t_a (arbitrary date), then the numerator is [(Sum of days' supply without the last dispensing) + (Days' supply obtained at the last dispensing up to the end date of the period t_a)].

The MPR ranges from 0% to 100%.

For polypharmacy, the basic algorithm of DPPR (daily polypharmacy possession ratio) is proposed. It has been

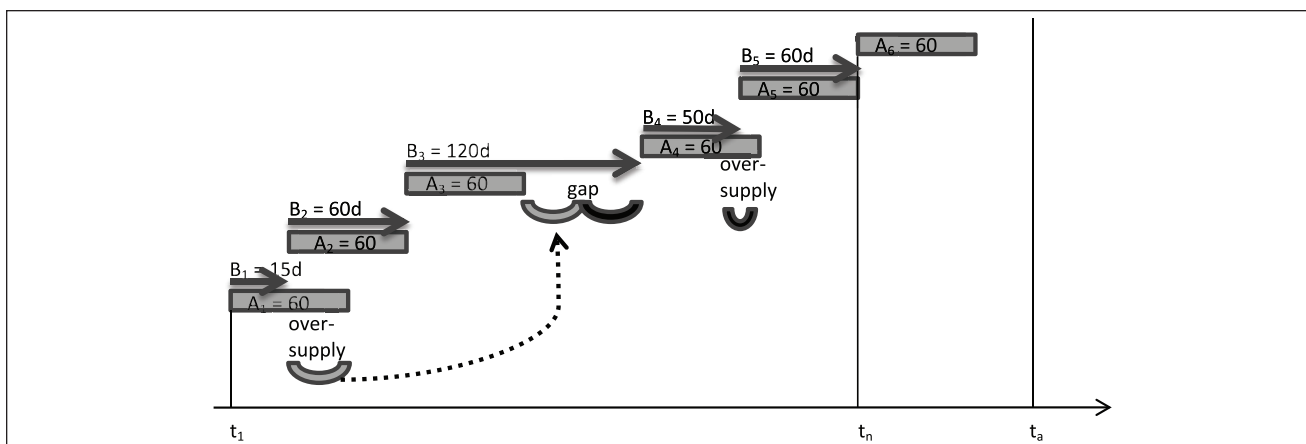


Figure 1. Graphical representation of the elements defined in Table 1. The observation period runs from the start day (t_1 at the first dispensing date) to the end day (t_n at the last dispensing date, or t_a at an arbitrary date); A is the number of days with medication available, and B is the number of days between 2 dispensings. Oversupply obtained from A_1 is carried forward to the next possible interval (arrow) at the end of A_3 , which is likely to occur in the real world. Oversupply obtained from A_4 is disregarded if t_n is the end date and added at the end of A_6 if t_a is the end date.

described elsewhere.¹³ The DPPR does not result from an equation but from the application of a stepwise algorithm. In brief, the number of all medications available is determined for each day separately over the observation period. A score between 0 (no medication available) and 1 (all medications available) is set. To obtain the proportion of all medications available for daily use, one has to sum the scores, divide by the number of days in the observation period, and multiply by 100. The DPPR ranges from 0% to 100%.

The basic algorithm for oversupply is (Number of days' supply A_n) - (Days in the refill interval B_n) if $A_n > B_n$ (Figure 1). The basic algorithm for gap is (Days in the refill interval B_n) - (Number of days' supply A_n) if $A_n < B_n$ (Figure 1). They are calculated simultaneously for each interval and summed up from one interval to the other. Because the use of an oversupply to compensate a gap that occurred earlier in the dosing history is forbidden (retroactive compensation), oversupply always has a value ≥ 0 (negative supply cannot exist).

Implementation is also depicted by the days without sufficient medication supply (gaps). The basic algorithm for the time without supply sums the number of days without supply after each interval (after taking oversupply from previous intervals into consideration; see Figure 1) divided by the number of days of the observation period, multiplied by 100. Last supply dispensed at the end of the observation period should be excluded. The value ranges from 0% to 100%. Because this value does not capture the dynamics of the gaps, further measures are proposed. The maximum gap length is the number of days of the longest period of time without supply (after taking carryover of oversupply into consideration). The mean gap value \pm standard deviation can be an indicator of dispersion.

Discontinuation and Persistence

The maximum period without supply (gap) should be clearly defined. The clinical relevance of stopping therapy should guide the maximal allowed gap. Thus, with drugs with short half-lives or when outcome is linked to short-term drug effects such as cardiovascular or antidiabetic drugs, a shorter gap length can be justified, where patients are considered nonpersistent on the first day on which they would have exhausted their drug supply.²¹ Similarly, shorter gaps might detect clinically meaningful ("true") nonpersistence, for example, for HIV or anticoagulants. After setting the allowable gap length, persistence is best summarized using a Kaplan Meier curve or as a percentage of patients who have discontinued treatment during a defined time period.²² A cutoff at 3 to 6 months could be set to quantify the percentage of early discontinuers.

Reinitiation

Interruption of treatment and its subsequent reintroduction have been investigated, predominantly in HIV patients, where discontinuation(s) of treatment was shown to induce viral resistance^{23,24} and, ultimately, morbidity and mortality.²¹ In these studies, interruption was mostly self-reported²⁵ or was not defined.²⁶ In larger studies analyzing cohorts from the national register, the probability of restarting a therapy with statin was estimated from gaps of different lengths—that is, after reinitiation of treatment.^{27,28} The proportion of patients reinitiating therapy should be calculated by dividing the numbers of patients with a dispensing beyond the end of the allowable maximum gap by the number of patients defined as having discontinued therapy.

Discussion

Standards and their operationalization are proposed to quantify adherence to medication from medication records of various sources within the new taxonomy of the European ABC Group.¹² By doing this, this study builds on previous consensus-based work and links conceptual definitions to operational definitions.

Possession-related measures were selected (MPR for single medication and DPPR for multiple medication) to quantify the implementation phase of adherence because they are easy to calculate and interpret (the higher the value, the higher the medication possession). In addition, by integrating the last medication fill into the denominator, the MPR measures implementation over the time period that the patient was actually using the medication (from first fill to last fill). This deviates from the US standard for performance indicator-based reimbursement, which uses the PDC.²⁹ PDC uses a fixed denominator, often 365 days (based on a calendar year or a year's follow-up). Even more confusing, some researchers used the last medication refill as their end date in PDC calculations, and some others used a fixed end date in their MPR calculations, leading to inconsistencies in the literature. Thus, it could be helpful to use the last fill date exclusively for MPR measures and fixed end date for PDC measures. By doing this, the MPR value would indicate the quality of implementation in a single measure, whereas the PDC would be an indicator of both the quality and the length of implementation during a medication dosing history.

Some researchers have claimed that periods of under- or oversupply of medication may be obscured with possession rates.¹⁵ This might be true because the usual method of calculation used so far does not account for duplication (simultaneous use of multiple agents from the same therapeutic class) and overlapping—the 2 parameters most frequently responsible for the general overestimation of adherence.³⁰ The proposed standards regulate duplication and overlapping and, thus, eliminate major elements that distort calculation results. A special emphasis was set to avoid mathematical equations that would depict impossible situations in the real world, such as including the supply left over beyond the end of the study period. On the other hand, medication oversupply through early refills (ie, stockpiling) is likely to occur in the real world and should be allowed. The most restrictive standard consists of forbidding the use of an oversupply to compensate a gap that occurred earlier in the dosing history (retroactive compensation). The proposed considerations reflect real-world situations because negative supply cannot exist. Patients either have supply (positive value) or they do not (zero value). Consequently, a stepwise algorithm along the intervals instead of an overall equation is needed. This algorithm is clearly more

complicated, but it identifies more precisely periods of time where medication availability was unlikely.

The terms *discontinuation* and *nonpersistence* are used alternately to indicate the end of therapy. Confusion might occur when using nonpersistence as a dichotomous value because persistence is a time-to-event value. Choosing the term *discontinuation* might raise less doubt. Because medication records do not disclose what happens after the last dispense (ie, treatment stop or treatment holiday), uncertainty forces decisions to be made. Defining a cutoff value for the number of days without supply (grace period) beyond which treatment is discontinued—that is, end of therapy—determines nonpersistence. Part of the challenge is to set a limit that avoids misclassification of patients who restart treatment after a period of discontinuation and would otherwise be lost to calculation if the grace period is too small. As a consequence, the assessment of reinitiation is proposed as a further measure in adherence research. By doing this, the cutoff value for discontinuation can still be applied, and prolonged gaps between refills, which may not signify cessation of therapy, will still be detected. It is likely that repetitive stop-and-go patterns have dramatic influence on therapy, and they have seldom been evaluated properly.³¹ With the setting of different cutoff values for discontinuation or nonpersistence, early discontinuers can be assessed, and new fields in adherence research are open for investigation. Generally, the allowable grace period is driven by the time between scheduled refills, and a pharmacological rationale is lacking for the definition of the grace period or the threshold MPR. One study³² defined an allowable interruption gap of 42 days in accordance with a previous clinical trial that reported a potential loss of efficacy of the drug of interest after an interruption of 6 weeks.³³ In most cases, the time between scheduled refills is an order of magnitude longer than the drug's therapeutic effect. Nevertheless, the grace period should depend on the drug forgiveness, which allows larger gaps between scheduled doses without noticeable loss of pharmacological effect. In any case, the search for a universal value set to separate adherence from nonadherence is doomed to failure and can only result in contradictory results.³⁴

To reduce confusion and inconsistency, several terms are excluded from the proposed concepts, such as the *index date*. Although this term has often been used in recent literature as the date of first claim,³⁵ it also indicates the date of a drug-treated event in epidemiological matched cohort studies. Furthermore, the simple measure of refill rates is excluded—that is, a measure based on the number of refills during a specified period of time (flexible or anniversary model)—because the length of time between refills is given no consideration. In addition, the refill rate is implicit in a gap-based measure. The number of refills may nevertheless be a valuable calculation for medications that may be used as needed without detriment to the clinical condition. It may

further be appropriate for medications such as orally inhaled asthma drugs, where information on days' supply may be imprecise.

The way in which raw data are obtained (eg, by pill count; prescribing, dispensing, or administrative data; electronic monitoring of single or multiple medication) determines the content of the database. However, mandatory information for calculations still includes drug name, drug dosage or dosing instructions, quantity of drug dispensed at each (re)fill, and date of each prescription (re)fill. In situations where the database contains the days' supply (as entered by the pharmacist, for example), calculations can be performed when drug name and refill dates are also known. Provided the records are complete, the proposed measures can be calculated indiscriminately with prescribing and dispensing databases. In this regard, it is interesting to see that, increasingly, nationwide personal electronic medicine profiles are stored online for electronic prescribing and electronic monitoring of medicine.³⁶ However, a recent evaluation of the Danish system showed that it was yet unable to accurately detect nonadherence,³⁶ predominantly because of incorrect prescription information and missing dosage information. Experiences from the United States after the introduction of the Medicare Improvements for Patients and Providers Act³⁷ in 2008 showed at least an increased use of e-prescribing in response to the incentive program.³⁸ Today and worldwide, the most accurate database remains the Dutch pharmacy dispensing system. It is worth noting that since January 1, 2014, Dutch physicians are obliged to use e-prescribing, and most of them send the prescription electronically to the pharmacy.

In future, the measures chosen by a researcher should be determined by the overall goals of the study—that is, clinical efficacy trials (eg, MPR of the study drug), selection of ambulatory patients at risk in order to initiate an intervention such as specific counseling (eg, nonpersistence with HIV medication), or conditions for reimbursement (eg, noninitiation). Much more, the study population should determine the cutoff values. As an example, the length of the observation period may vary depending on whether the study population is restricted to new or chronic users of the medications. Finally, because adherence is a complex behavior with several aspects, it cannot be caught in one number. In any case, a careful description of the definitions and operationalization used is crucial if comparisons between studies are to be made.

Strengths and Limitations

This study has several strengths. First, the proposed standards are close to a real-world setting and eliminate overestimation of adherence values. Second, the proposed measures build on the taxonomy established by the European ABC Project and

pursue the work of promoting consistency for different experimental investigations. Third, the proposed measures take full advantage of the information available in many databases, which is not the case for most of the current measures of adherence or persistence.

This study has some limitations. First, as is true of any indirect method of adherence assessment, the proposed measures are unable to confirm ingestion of the dispensed medication. As a consequence, they function as surrogate measures of medication adherence. However, they provide an estimate of the highest possible level of medication possession and, thus, can identify those patients not able to consume the medication in sufficient quantity. In that sense, the measures can be considered to have a high sensitivity. Second, different assumptions must be made, the main one being that all medication will be taken at the days' supply indicated. However, a standardization of the assumptions will lead to comparable estimates of adherence across different studies.

Conclusion

By following the displayed propositions, results of future adherence research should gain in accuracy and in confidence, and results between studies should be comparable. Because the ultimate goal of adherence measurement is to improve patient care, the proposed measures could be used to set flags in electronic databases, based on which health professionals could select appropriate and effective interventions to move into practice. Researchers are invited to discuss this proposition of standards and to communicate their observations. Ultimately, generally approved standards are soon needed along with their operationalization, which could be endorsed by an umbrella society, so that health professionals, researchers, health authorities, and policy makers can make informed choices for the benefit of patients and society.

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7.4 Development of specific adherence measurements for the evalPMC project [B3]

Work report

7.4.1 Computing adherence from theory to practice

Besides the theoretical issues discussed in project B1 +B2, we also faced technical challenges. In order to compute the discussed parameters MPR and DPPR based on individual patient refill data, the so far theoretical algorithm needed to be translated into a feasible application. We were lucky to establish a collaboration with ProPharma Systems AG. Together with their expertise, we developed an application based on Microsoft Visual Basic C++ 2010 and Microsoft Access 2010 and named it COMPARE for COMpute Polypharmacy Adherence RatE. With this application, we were able to export the individual refill data from the different software solutions of the participating pharmacies. The tool then compiled the data in a standardised and computable form. The use of this application for further research projects is regulated within a license agreement between the PCRG and ProPharma Systems AG.

7.4.2 Development and piloting the telephone interviews

In order to develop and pilot the subjective adherence outcome measurements, we conducted a literature research to select validated questionnaires. In collaboration with a clinical psychologist, a comprehensive in-depth patient interview was created. During her master thesis, Ms Véronique Lottaz tested this drafted patient interview with students during their internship in a role-play setting.⁸⁴ Students (n=9) were instructed to answer as a pseudo patient following a fictive patient with polymedication. We defined the ‘beliefs about medicines questionnaire’ (BMQ)^{85,86} and two questions from the German 8-item ‘Morisky Medication Adherence Scale’ (MMAS-8D)⁸⁷ as suitable. In addition, we focused on questions investigating changes caused by the polymedication check. Whenever possible, we choose closed ended

questions, mostly with categorical or Likert scales. Tests with the students showed the 10-item Likert scale as advantageous to a 4-item scale (no anchoring). Students were interviewed face to face with the investigator and occurred problems with wording were subsequently discussed. After adaption, all nine students were interviewed by telephone and interviewer entered data directly in a case-report-form, using Flexiform 2.6.9. The final patient interview contained 58 questions, subdivided in five sections, “medicines use”, “adherence and use of reminder devices”, “visits at GP / hospital”, “beliefs about medicines”, “care provided by pharmacists” (see appendix) . Median duration of one patient interview was 27 minutes (range 18min - 40min). Adherence issues of fictive patients were fully detected in each interview. The patient interview performed with students as pseudo patients proved feasibility, understanding and suitability to assess adherence issues.^{84,88}

7.5 Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy - a prospective randomised controlled trial [B4]

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RESEARCH ARTICLE

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Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy - a prospective randomised controlled trial

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Abstract

Background: In 2010 the 'Polymedication Check' (PMC), a pharmacist-led medication review, was newly introduced to be delivered independently from the prescriber and reimbursed by the Swiss health insurances. This study aimed at evaluating the impact of this new cognitive service focusing on medicines use and patients' adherence in everyday life.

Methods: This randomised controlled trial was conducted in 54 Swiss community pharmacies. Eligible patients used ≥ 4 prescribed medicines over >3 months. The intervention group received a PMC at study start (T-0) and after 28 weeks (T-28) while the control group received only a PMC at T-28.

Primary outcome measure was change in patients' objective adherence, calculated as Medication Possession Ratio (MPR) and Daily Polypharmacy Possession Ratio (DPPR), using refill data from the pharmacies and patient information of dosing.

Subjective adherence was assessed as secondary outcome by self-report questionnaires (at T-0 and T-28) and telephone interviews (at T-2 and T-16), where participants estimated their overall adherence on a scale from 0–100 %.

Results and discussion: A total of 450 patients were randomly allocated to intervention ($N = 218$, 48.4 %) and control group ($N = 232$, 51.6 %). Dropout rate was fairly low and comparable for both groups ($N_{\text{Int}} = 37$ (17.0 %), $N_{\text{Cont}} = 41$ (17.7 %), $p = 0.845$). Main addressed drug-related problem (DRP) during PMC at T-0 was insufficient adherence to at least one medicine ($N = 69$, 26.7 %). At T-28, 1020 chronic therapies fulfilled inclusion criteria for MPR calculation, representing 293 of 372 patients (78.8 %). Mean MPR and adherence to polypharmacy (DPPR) for both groups were equally high ($\text{MPR}_{\text{Int}} = 88.3$, $\text{SD} = 19.03$; $\text{MPR}_{\text{Cont}} = 87.5$, $\text{SD} = 20.75$ ($p = 0.811$) and $\text{DPPR}_{\text{Int}} = 88.0$, $\text{SD} = 13.31$; $\text{DPPR}_{\text{Cont}} = 87.5$, $\text{SD} = 20.75$ ($p = 0.906$), respectively).

Mean absolute change of subjective adherence between T-0 and T-2 was +1.03 % in the intervention and -0.41 % in the control group ($p = 0.058$). The number of patients reporting a change of their adherence of more than ± 5 points on a scale 0–100 % between T-0 and T-2 was significantly higher in the intervention group ($N_{\text{Improvement}} = 30$; $N_{\text{Worsening}} = 14$) than in the control group ($N_{\text{Improvement}} = 20$; $N_{\text{Worsening}} = 24$; $p = 0.028$).

Conclusion: Through the PMC pharmacist were able to identify a significant number of DRPs. Participants showed high baseline objective adherence of 87.5 %, providing little potential for improvement. Hence, no significant increase of objective adherence was observed. However, regarding changes in subjective adherence of more than ± 5 % the PMC showed a positive effect.

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Trial registration: Clinical trial registry database, NCT01739816; first entry on November 27, 2012.

Keywords: Polypharmacy, Community pharmacy, Medication review, Drug-related problems, Adherence to medication, Medicines use, Pharmaceutical care

Background

Increasing complexity of both, the therapy (polypharmacy) and the patient (multimorbidity) raises the risk for drug-related problems with adverse events and medication errors [1, 2]. Avoidable problems usually do not result from individual misconduct, but from suboptimal processes. Drug-related morbidity as a result of these risks is associated with high healthcare costs [3–5]. Situations with a high risk for drug-related problems (DRP) include polypharmacy, significant changes in drug therapy or changes in existing diseases, insufficient response to drug therapy, suspected lack of therapy, symptoms of side effects, as well as discharge from hospital with a change of drug therapy [6, 7]. One approach to reduce the risks for developing DRP is to conduct medication reviews [8–10]. A worldwide shift in the professional role of pharmacists is observed [11]. Pharmacists participate increasingly in clinical processes and perform tasks in patient care. This transformation of the profession includes co-responsibility in the achievement of therapeutic success, cost efficiency and avoidance of drug-induced (re)hospitalisation. Accordingly, the Pharmaceutical Care Network Europe (PCNE) felt the need to redefine pharmaceutical care as “the pharmacist’s contribution to the care of individuals in order to optimise medicines use and improve health outcomes” [12]. In the early 1990s, pharmaceutical care was introduced in community pharmacy practice in Switzerland. Emphasis was given to providing patient-centred care and cognitive services [13]. A postgraduate education program and mandatory continuous education were launched together with changes to pharmacists’ remuneration, which link payments to services delivered and not only to the volumes of medicines dispensed. In 2010, the current remuneration system was introduced, which defines a fee schedule for a total of nine distinct services. Among these services the so called ‘Polymedication Check’ (PMC) was newly introduced as the first cognitive service to be delivered by pharmacists independently of the prescriber for patients on ≥ 4 prescribed drugs taken over ≥ 3 months. In addition, the pharmacist may suggest - among other interventions - to provide the medicines in a weekly dosing aid (WDA) refilled by the pharmacy. Both services, the PMC and the weekly filling of a dosing aid by the pharmacist are reimbursed by the health insurance in the basic insurance. Moreover, the current regulation allows

repeated dispensing of prescribed medicines for a maximum of 12 months. Currently, such prescriptions constitute nearly 75 % of all items dispensed [14]. Hence, Swiss community pharmacies assume very responsible roles in the care of chronic patients.

Adherence and consequences of non-adherence

Approximately 25 % of patients with different diseases do not take their medication as prescribed, although the extent varies between 0–95 % [15]. On average, adherence in long-term therapy is 50 % [16]. Lack of adherence is the most common cause of the efficacy-effectiveness gap [17], defined as the gap between therapy efficacy in daily life compared to the effectiveness shown in clinical trials. Previous studies have shown a positive impact of structured interventions to improve adherence provided by pharmacists [18, 19]. But there is still little evidence related to the effectiveness of interventions performed in community pharmacies. A recent Cochrane review revealed that only a minority of studies with lowest risk of bias (RCT design) improved both adherence and clinical outcomes [20]. However, adherence as an outcome remains challenging to measure because of methodological issues and multifactorial influences [21]. Support of adherence to treatment is only successful if the entire medication is taken into account. Therefore, conducting a medication review is the essential first step in any adherence counseling.

Medication review

According to the current PCNE definition, a medication review is ‘an evaluation of a patient’s medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions.’ [22]. The analysis in a medication review always includes an inventory of current medicines, a history of complaints, their course, a patient’s concerns and individual needs for support. With respect to the pharmaceutical care process [12, 23], the medication review is the starting point leading to the suggestion of solutions, the planning and implementation of interventions and ultimately to the evaluation of the outcomes [24]. Pharmacist-led medication review services are available in several countries such as the United Kingdom (Medicines Use Review, MUR) [25], United States of America (Medication Therapy Management, MTM)

[26, 27], Australia (Home Medication Review, HMR) [28], Canada (MedsCheck) [29, 30], and New Zealand (Medicines Use Review, MUR) [31]. According to a recent meta-analysis, a majority (57.9 %) of fee-for-service pharmacist-led medication reviews improved medication adherence and positively influenced patient outcomes [24].

The Polymedication Check

The Swiss Polymedication Check (PMC) is based on the well-established Medicines Use Review (MUR) from United Kingdom [32, 33]. Information is available from the medication history, which is mandatorily kept in community pharmacies and from a structured patient interview. The Swiss PMC focuses on adherence problems, patients' knowledge and handling problems and is followed by specific interventions or recommendations by the pharmacist. Implementation of such cognitive services provided by a pharmacist is known to be very challenging [34–36]. The same is true for Swiss community pharmacies. Implementation of the PMC is low and after three years only about three checks per pharmacy per year were registered, with a large majority of pharmacies not offering this service. While in 2011 2'534 PMCs were carried out, in 2014 the number of PMCs provided amounted at 6'940 PMCs [37], which is an encouraging trend.

Rationale for the study

In Switzerland, new services remunerated by the basic health insurance require a proof of their efficacy, appropriateness, and economic effectiveness according national criteria [38]. The present study aimed at investigating the impact of the PMC on patients on poly-pharmacy. It was hypothesised that PMC would increase objective and subjective adherence in a community sample.

Methods

Trial design

A prospective, parallel group randomised controlled trial (RCT) design was chosen to evaluate the impact of the PMC. Contemporaneously, an in-depth evaluation of the process and the perspectives of patients and pharmacists was planned to collect information for further development of the service. The study setting considered community pharmacies in a range of representative regions of Switzerland (with and without self-dispensing physicians, city versus country, German-speaking part (D-CH) versus French-speaking part of Switzerland (F-CH)). For each patient the observation period lasted 28 weeks from study start (T-0) until study end (T-28).

Eligibility for study pharmacists

The recruitment of 70 pharmacists was intended; thus, community pharmacies in the cantons Aargau (AG), Basel-Land (BL), Basel-Stadt (BS), Solothurn (SO), Fribourg (FR), Neuchâtel (NE), Genève (GE), Vaud (VD) und Valais (VS) were invited to participate in the study. Basing on the principle of "first in, first served", the ideal recruiting target was 50 pharmacists from the German speaking and 20 from the French speaking part of Switzerland in line with the national proportion of the population. Study pharmacists were required to take part in a study-specific training, and to give written consent regarding the study design as well as a memorandum of understanding through the pharmacy owner to collaborate on the project until the end of study; in addition, they were asked to commit to transfer patient's refill data to the study centre, and to collaborate with either IFAK or OFAC (the two main clearing companies in Switzerland administering the charges between pharmacies and health insurance and therefore also holding the corresponding patient data). The three-hour training session provided by the study centre included an overview over the study, highlighted the need for compliance to the study protocol, and clarified rights and responsibilities of the study pharmacists. No further training on the execution of a PMC was offered as the study aimed at assessing and evaluating current practice.

Screening for eligible patients

In order to avoid selection bias through study pharmacist (e.g. Individual prejudices, preferences), a random sample of 100 potential PMC candidates (age >18, ≥ 4 prescribed drugs for ≥ 3 months) was created for each study pharmacy in collaboration with the two main clearing companies IFAK and OFAC. The latter performed an independent screening for each study pharmacy and listed all patients fulfilling the selection criteria for a PMC. Out of this sample of potential PMC candidates, a random primary sample of 100 was selected by IFAK and OFAC (Fig. 1).

Patient recruitment

The study pharmacist checked this primary sample for exclusion criteria and consecutively invited subsamples of ten patients by a letter to participate in the study. Exclusion criteria for final recruitment were the following: living in a retirement home, prior PMC, receiving weekly dosing aids filled by the pharmacy or another person, cognitive impairment, move or death, insufficient knowledge of written and spoken German or French. In addition, study pharmacists re-checked if a patient met the primary inclusion criteria. The study centre received information on gender, date of birth and the reasons for

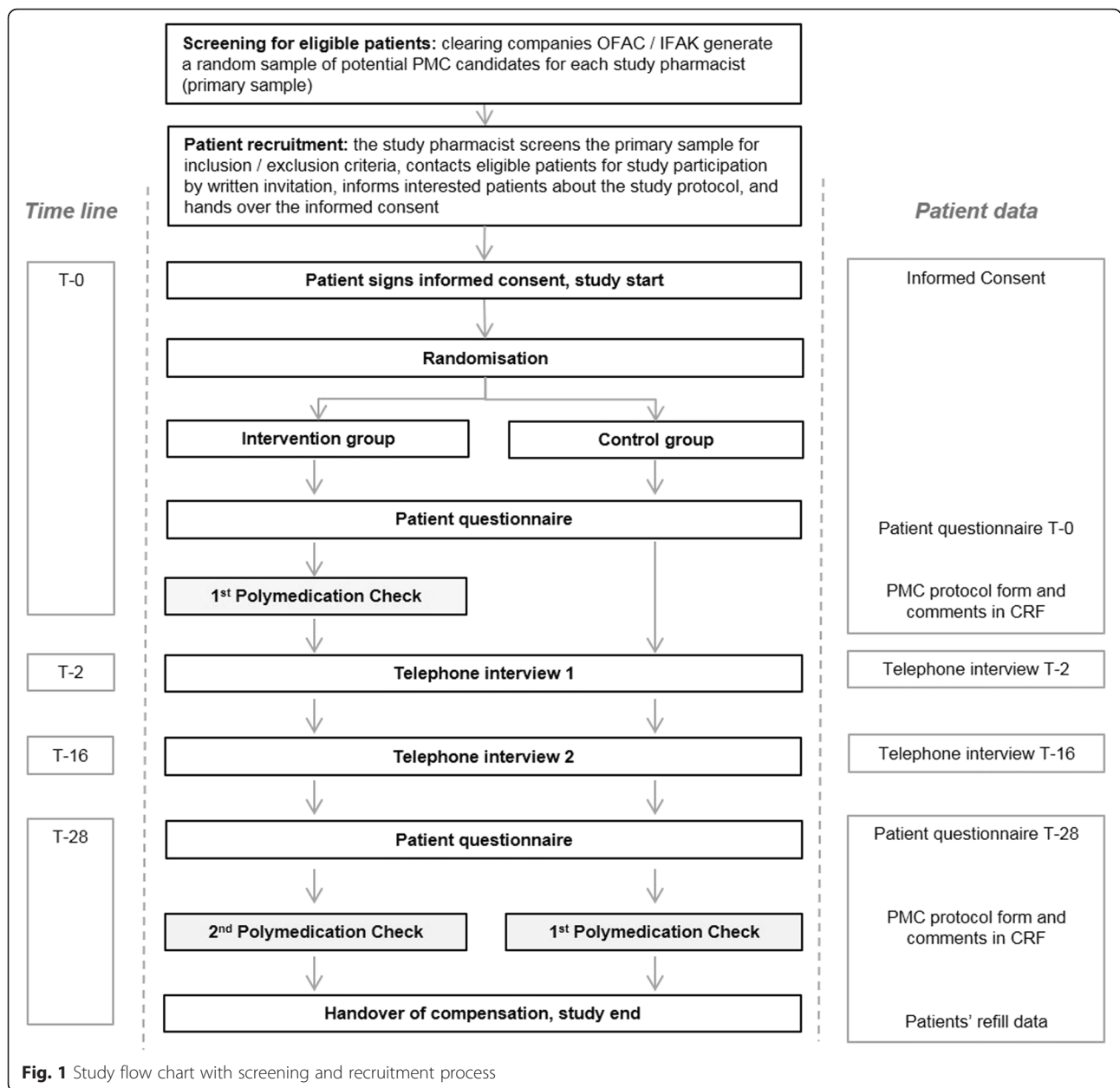


Fig. 1 Study flow chart with screening and recruitment process

exclusion of a patient. If the patient had expressed his interest in the participation, the study pharmacist informed him about the schedule, potential risks, and compensation and handed over the declaration of consent.

Randomisation process

The patients were assigned by 2 x 4 block randomisation into intervention or control group. Initially, each study pharmacist received two blocks containing eight dossiers (four intervention and four control) each packed in sealed and unlabelled envelopes. Once the first

patient had consented, the study pharmacist opened one envelope out of the first block to reveal what arm of the study the patient had been randomised to. Once all eight envelopes of block No. 1 had been assigned, the next block was used. Upon request, further blocks were available.

Structure of the intervention vs usual care

The intervention at T-0 included the execution of a PMC according to the official guidelines. The adapted study PMC protocol was used as assessment form. In a structured face-to-face counselling with the patient, the

study pharmacists screened all medicines currently used. The pharmacists checked for any gaps in knowledge or other pharmaceutical care issues including handling and adherence problems. The interview took place in a separated area. Pharmacists were instructed to use open questions to detect pharmaceutical care issues and to decide if there was need for further investigation. For each medication, the PMC protocol (Additional file 1) required documentation whether the patient knew the reason why he/she took the medicines (yes/no), if he/she needed any counselling (yes/no) or had adherence problems (yes/no). Additionally, handling difficulties were enquired, and the pharmacist documented all resulting interventions such as consultation with the general practitioner (GP), referral of the patient, potential suggestion and implementation of a weekly dose reminder system, or any other recommendations or interventions. Where necessary, an individual patient education and a medication plan could be provided on the basis of the information gained from the interview. None of this follow-up interventions was standardised.

Usual care included no specific intervention and no documentation at T-0. Patients of the control group only received the two self-report questionnaires at study start and study end, and the two telephone interviews. Normal counseling for any new prescription or arising question from the patient was always allowed and guaranteed, so patients from this arm were not restricted from contacting the pharmacist for advice if they wished to do so. If a PMC became indispensable during the study period (e.g. by another pharmacist than the study pharmacist), this patient of the control group was excluded. Overall, the study took seven months for each patient and included two visits at the pharmacy with the completion of questionnaires and participation in two telephone interviews. Patients were able to contact the study centre in case of further interest for the study purposes or any problem with the study process (e.g. missed telephone interview) using a separate telephone hotline available 24 h seven days a week.

Classification of detected drug-related problems and addressed interventions

To classify the addressed drug-related problems and describe the pharmacists' interventions, the GSASA classification tool was used [39]. This instrument comprises five main categories: i) problem, ii) type of problem, iii) cause, iv) intervention, and v) outcome. We adapted the category 'causes' by dividing the section 'Insufficient knowledge of the patient' into three subdomains focussing on patients' individual needs for information about a) safe and effective use of his medicines b) the medicines' potential adverse drug reactions c) his lifestyle, nutrition or empowerment in general. Further

on, we added the category 'More cost-effective therapy available' as the recommendation of generic drugs might be likely triggered throughout a PMC.

Case report forms for study pharmacists

In order to support study pharmacists in their compliance to the study protocol and to ensure coherent data capture, case report forms (CRF) were developed. The study pharmacist documented his interventions or recommendations resulting from PMC, classified the underlying problems according to their urgency (low, medium, high urgency) added any abnormalities or changes in the care of the patient.

PMC protocol form

We used the official documentation form for PMC with minor changes to ease data capture for the purpose of the study (Additional file 1). This assessment form still showed the format of one A4 side. At study end (T-28), in addition to the PMC protocol the study pharmacist documented observed drug-related problems, the frequency of falls, and all changes in therapies since T-0 reported by the patient (dosage change, generic substitution, start/stop, no change). The documentation of these changes was needed to identify eligible therapies for objective adherence calculation.

Patient self-report questionnaires

Patient self-report questionnaires were developed to collect demographic data (age, gender, living situation, education and employment status, smoking status), but also to describe his limitations in executing everyday activities (four items extracted from the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire [40]) and assess his subjective adherence at T-0 and T-28. The patient therefore had to assess his adherence to all his prescribed medicines for the last two weeks using a visual analogue scale (VAS_{AD}) 0–100 mm representing 0 for 'taken none' and 100 for 'taken all my medicines'. Patients were asked to fill in the questionnaires in the pharmacy at T-0 and T-28, seal them in an envelope and return the envelope to the study pharmacist. Thus, the study pharmacists had no knowledge of the responses given by their patients.

Telephone interviews

In collaboration with a clinical psychologist and an economist, two comprehensive in-depth patient telephone interviews were developed aiming at monitoring possible impact of the intervention on patient's knowledge and medicines use. After literature research, the Rob Horne's 'Beliefs about Medicines Questionnaire' [41] and two questions out of the '8-item Morisky Medication Adherence Scale' (German version, 8-MMAS-D)

[42] were defined as suitable to be used as validated questionnaires fulfilling our criteria for telephone interview 1. In addition, we developed new rating questions to report their adherence to their therapy management. Patient had to answer the same question as in the patient questionnaire T-0 to describe their adherence, but in a spoken percentage value. We also chose consistently a 10-item Likert scale. Options ranged from 1 (= 'not at all') to 10 (= 'very much'). The response category 'no answer' was always available. Number of open questions ($N=7$) was limited to ease documentation.

The first telephone interview contained 58 questions, divided into five sections: i) knowledge of their medicines and daily use, ii) subjective adherence estimation/use of reminder devices, iii) visits at general practitioner/hospital, iv) beliefs about medicines questionnaire, v) support by pharmacists. The interview 2 contained 53 questions, divided into the same sections as in the first interview. Compared with the first interview, 18 questions were excluded and 13 new questions were added. The telephone interviews were carried out two (T-2) and 16 weeks (T-16) after study start by clinical psychologists. The interviewers were blinded to the intervention and without any knowledge of the content of the PMC or the patient's questionnaire T-0. A telephone interviewer's coaching and monitoring of compliance with the study protocol was continuously provided by an independent academic psychologist as external expert. A structured interview guide was created using the software program Flexiform 2.6.9 to enable data entry during the interview. Piloting of all study documents and preparation of telephone interviews (recruiting interviewers, briefing and test interviews) were carried out in collaboration with the department of psychology of the University of Basel. All survey instruments were translated into French and retranslated into German to check for differences.

Objective adherence measurement

Objective adherence rates based on refill data of the pharmacies and patient reported dosing regimen. Two methods for objective adherence calculation were used: a) Medication Possession Ratio (MPR) [43], calculated by dividing the days' supply of a medication dispensed by the number of days in the time interval of interest, representing the adherence per each medicine and b) Daily Polypharmacy Possession Ratio (DPPR) [44], the proportion of time a patient had medication available for use by considering the presence or absence of multiple medications on each day in the observation period, representing the adherence per patient with his chronic polypharmacy. In this analysis only medicines were included, of which the patient reported at T-28 a daily use over the whole study period. Only oral drug forms with

definite dosage where considered. Further, a prescription for the medicine had to be redeemed at least once before T-0. Therapies were excluded if prescribed by self-dispensing physicians (cantons BL/SO), changed in dosage during study period, chronic 'on demand therapies' (namely pain killers (ATC N02 and M01A), anxiolytics (ATC N05BA), or magnesium supplements (ATC A12CC). Also creams or drops were excluded from analysis due to imprecise assumption concerning dosing regimen. According to the theoretical calculation for both, the MPR and the DPPR, refill data was exported from the patient's pharmacy. The export included the history of patient's refills from at least 200 days before T-0 and the study period (T0 to T28, 196 days). For each dispensed medicine, the export comprised the date of refill, a product unique identifier number (pharmacode), the drugs' ATC-Code, and the number of packages delivered. Subsequently, the pharmacode was matched with the Swiss index database GALDAT®/pharmINDEX® [45] to add the products' package size (number of tablets) and complemented with the patient reported dosing regimen at T-28 (taken from the PMC protocol of both, intervention and control group). The calculation algorithm started with a look-back loop of 200 days before T-0 taking any packages of medicines postponed to the patient, equalising the fact that the patient was already on therapy before study start. As in previous trials, objective non-adherence was defined as $MPR < 80\%$ [46]. Also for the patient's individualised aggregated measure DPPR, the cut-off for non-adherence was set $< 80\%$.

Subjective adherence measurement

Subjective non-adherence was defined in patient reported questionnaires (T-0 and T-28) as $VAS_{AD} < 100$ m, in telephone interview 1 and 2 as Likert scale < 10 and in telephone interview 2 additionally as $8\text{-MMAS-D} < 6.00$.

Unplanned visits at the general practitioner/hospital

In order to evaluate a negative impact on the health system, patients' unplanned visits at the general practitioner or hospital were assessed within the patient's self-report at T-0 and T-28 and during telephone interview at T-2 and T-16.

Sample size

To determine the required sample size, a power analysis was conducted. In the present study, the null hypothesis is rejected if the primary outcome adherence (as measured by MPR) improves by 5 % through the PMC on an assumed baseline MPR of 60 %. These suggestions were based on experiences from comparable projects [47]. We assumed a standard deviation of 20 % for both groups and used the conventional alpha error of 5 %. To have a statistical power of 80 % we would require 252

patients at T-28 in each group. Assuming a dropout rate of 35 % [48], this would lead to a total sample size of 780 at T-0 (calculated with <http://sampsiz.sourceforge.net>). Thus, we expected from each study pharmacist an enrolment of 10–20 patients. There was no minimal/maximal number for recruited patients per study pharmacist.

Statistical methods

Frequencies were evaluated using the chi-square test, ordinal scales were tested with the non-parametrical Mann-Whitney-*U*-test. The time course of the various endpoints was calculated using a general linear model (GLM) for repeated measurement method. The study groups were recorded as between-subject variable and the course of the corresponding values as within-subject variable in the model. In case of many missing values, individual templates mixed models analysis was chosen as an alternative method. All statistical tests were two-sided with a significance level of 5 %.

Handling missing data

The intention-to-treat analysis included all enrolled subjects, divided into intervention and control groups. Patients were rated as a drop out when they were excluded at their request or when they were no longer available at study end. Reasons for drop out were documented if available. Patients who missed one or both telephone interviews remained in the study.

Ethical approval

The study was approved by the responsible local ethic commission 'Ethikkommission beider Basel (EKBB)' (23.05.2012, registry number EKBB 50/12) as the leading committee for this multicentre study. Following the positive decision from the EKBB, the project was also approved by the local ethics committees of the following cantons: AG/SO (26.11.2012), VS (05.03.2013), VD/NE (12.03.2013), GE (22.03.2013), and FR (25.03.2013). The study was registered with the <https://clinicaltrials.gov/trials> database (NCT 01739816). The fee for providing the PMC was covered by basic health care insurance.

Study pharmacists received a compensation of CHF 150 for participating in the training session and CHF 50 for the delivery of each complete patient data set. Patients were paid CHF 20 for their time spent for the telephone interviews, and as a compensation for obligatory co-payment to the PMC-fee.

Results

Implementation of the study

Patient recruitment was conducted in three stages (BS, BL: July 2012 – February 2013, AG, SO: December 2012 – July 2013, the French speaking cantons (VS, VD, NE, GE, and FR): April 2013 – October 2013) and ended in April 2014 with the last patient completing the study protocol.

Recruitment of study pharmacists and study pharmacies

Of 413 pharmacies invited for participation ($N_{BS/BL} = 110$; $N_{AG/SO} = 135$; $N_{VS/VD/NE/GE/FR} = 168$), 70 pharmacists signed the informed consent and were trained to follow the study protocol. In the end, 64 pharmacists (91.4 %) from 54 different pharmacies took part in the study (Table 1). Pharmacies were more or less evenly distributed between central ($N = 15$, 27.8 %), peripheral ($N = 16$, 29.6 %) and urban settings ($N = 23$, 42.6 %) as well as between being independent ($N = 17$, 31.5 %), belonging to a group ($N = 23$, 42.6 %), and belonging to a chain ($N = 14$, 25.9 %). A majority of 75 % of study pharmacists were women ($N = 48$), mean age was 42.8 years (SD 11.61), mean professional experiences working in a community pharmacy was 14.9 years (SD 10.69), and 27 pharmacists (42.2 %) had post graduate qualification in community pharmacy. The pharmacies showed variation in both size and infrastructure. Virtually all pharmacies were well equipped with a private area for the patients in terms of ensuring privacy from other patients ($N = 51$, 94.4 %). The median consulting area was 7 square meters (Range 1-25 m²).

Patient recruitment

For each pharmacy a random sample of potential candidates was delivered directly to the study pharmacist by

Table 1 Demographics of study population at T-0, divided in language regions German-speaking (D-CH) and French-speaking (F-CH) part of Switzerland. The total sum per study group is highlighted in bold

	Intervention group (N = 218)				Control group (N = 232)				pValue				
	D-CH (n = 146)		F-CH (n = 72)		D-CH (n = 160)		F-CH (n = 72)						
Women (n/%)	76	52.1	42	58.3	118	54.1	78	48.8	47	65.3	125	53.9	0.958
Living alone (n/%)	53	36.3	25	34.7	78	36.5	42	26.3	31	43.1	73	31.9	0.310
Smoker (n/%)	20	13.7	19	26.4	39	18.5	27	16.9	7	9.7	34	15.0	0.335
Age in years (Mean/SD)	66.4	11.38	68.7	11.73	67.2	11.52	67.1	10.80	67.2	13.18	67.1	11.56	0.845
Dash-4 score (Mean/SD)	4.7	1.72	5.3	2.43	4.9	2.01	4.7	1.48	5.3	2.40	4.9	1.83	0.323

IFAC and OFAC. The study pharmacists then consecutively checked samples of ten candidates for inclusion and exclusion criteria and invited the eligible patients. Exclusion criteria are available for 3096 patients as reported by 49 pharmacists (76.6 %) (Fig. 2). The other 15 pharmacists did not report about exclusions. After invitation, a total of 450 patients signed the IC and were randomly allocated to intervention ($N = 218$, 48.4 %) and control group ($N = 232$, 51.6 %) (Fig. 3). Median number of recruited patients per pharmacist was 7 (Range 1–17).

Demographic data of recruited patients

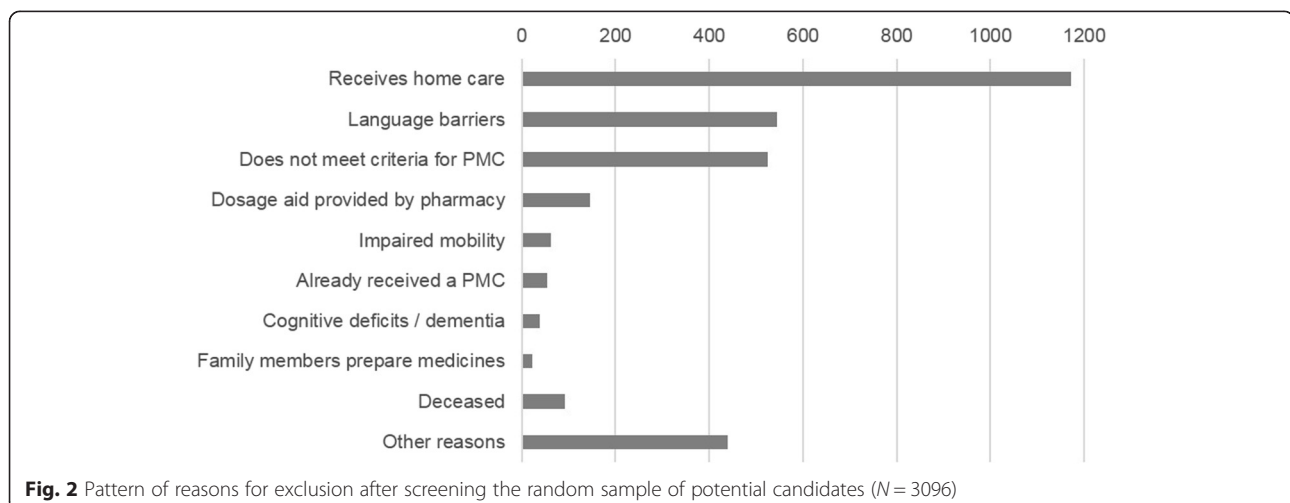
Demographic data of recruited patients ($N = 450$) showed no significant differences between study groups (Table 1). The proportion of women living alone (111 of 243) compared to men (40 of 207) was significantly higher ($p < 0.0001$). Men showed a significantly lower DASH-4 score than women (Men_{DASH-4} = 4.5 (SD 2.09), Women_{DASH-4} = 5.2 (SD 1.60); $p < 0.0001$). No differences between groups observed concerning education and employment (data not shown).

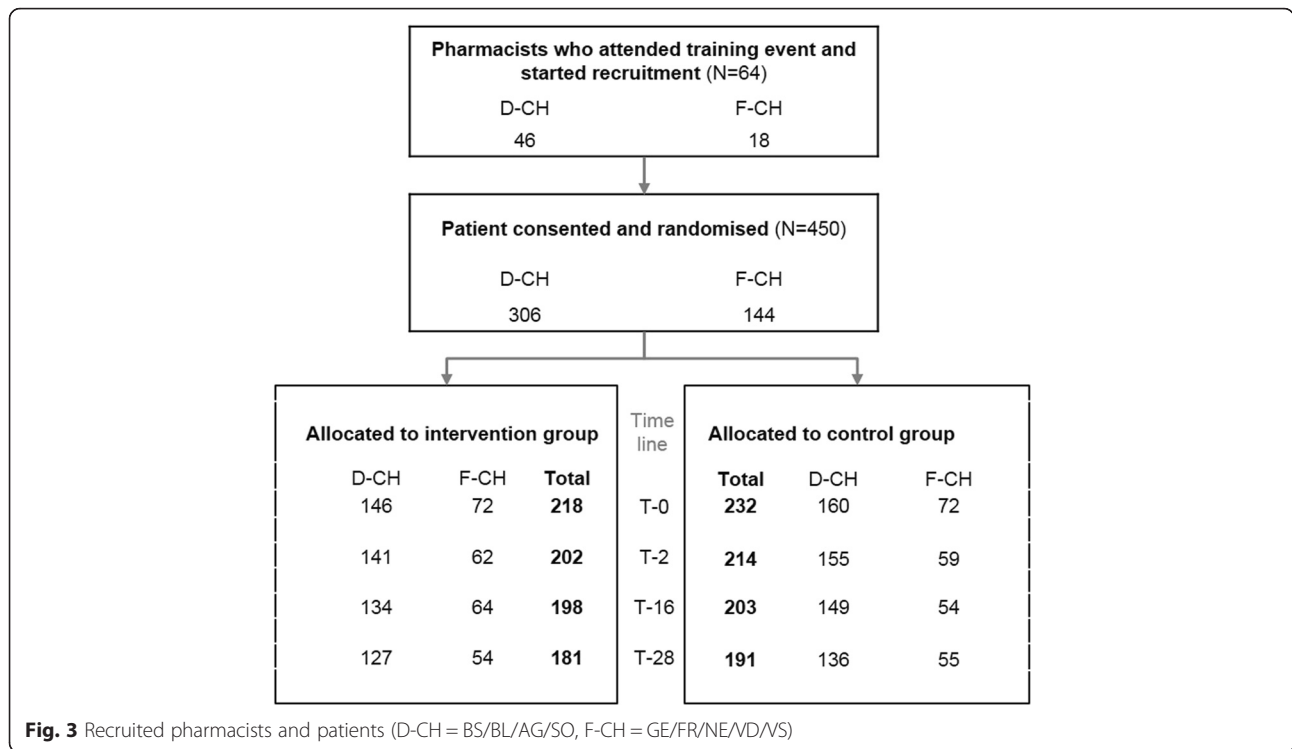
Dropouts

Out of 70 study pharmacists, six (8.6 %) withdrew before recruiting any patient for the study. While four stated that they had under-estimated the time amount to comply with the study protocol, two were no longer interested in the project. Dropout rate of patients was 17.3 % ($N = 78$); the different reasons for dropout are listed in table 2. Only 18 patients (4.0 %) withdrew from the study. The largest single cause for dropout of patients was that five of the 64 pharmacists who began recruiting quit the study (7.8 %), resulting in 17 patients lost in each group.

Intervention

Mean time per PMC was 29.8 min (SD 16.51; Range 5–135 Min). Mean number of chronic medication per patient was 6.8 (SD 2.92; Range 1–19), while 1.9 medicines (SD 2.07; Range 0–12) were prescribed on demand and 0.8 medicines (SD 1.09; Range 0–5) were used as self-medication. A majority ($N = 115$, 52.8 %) revealed to be more time consuming than initial assumptions of the professional association, pharmaSuisse (>25 min). At T-0, study pharmacists reported 258 drug-related problems (1.18 per patient) they had discussed during the PMC. The two main causes of drug-related problems triggering counseling through study pharmacists were a) insufficient adherence to at least one medication of a patient's polypharmacy ($N = 69$, 26.7 %) and b) lack of knowledge about risks or need for further information for safe and effective medicines use ($N = 69$, 26.7 %). The majority of DRPs could be addressed by sole patient counseling (58.9 %). Some pharmacists, however, also intervened by directly changing a patient's care plan in order to optimise the administration of a therapy (15.5 %), adjust the dosage or substitute a therapy (3.9 %) (Table 3). Study pharmacists noted at T-0, that 69 patients in the intervention group (31.5 %) already used a weekly dosing aid (WDA) in their daily medicines management and they recommended the implementation of a WDA for three patients (1.4 %) (Table 4). During the first telephone interview at T-2, 198 patients stated to own a WDA (47.6 %); 173 of them regularly used the aid (41.6 %), while seventeen patients mentioned a sometime use, e.g. during holidays (4.1 %); eight patients did not use the WDA at all (1.9 %). Until the end of the PMC study (T-28), one patient in the intervention group (0.6 %) and four patients of the control group (2.1 %) newly received a WDA as a result of the PMC. When asked at T-2, 74 (42.8 %) of 173 patients, who had originally been





recommended to use a dosing aid, reported that the pharmacy initiated the use of a WDA. Another 54 (31.2 %) bought the WDA themselves, while 20 (11.6 %) received the aid from a hospital. Out of these 173 WDA used at T-2, 158 were independently managed by the patient himself (91.4 %), get refilled by their partner (N = 13, 7.5 %) or another third party (N = 2; 1.1 %). Thereby, men (N = 77) were significantly more often supported by their partners (N = 12) than vice versa (N_{Women} = 94, N_{Support} = 1; p < 0.001).

Table 2 Reasons for patient dropout summed at T-28, N = 78

	Intervention	Control	pValue
<i>Deceased</i>	2	2	
<i>Withdrawal by patient</i>			
- without information	5	7	
- lack of motivation/interest	1	1	
- poor health	0	4	
<i>Pharmacist was unable to collect data</i>			
- not achieved	5	5	
- patient has moved away	3	2	
- patient is in a nursing home	2	0	
- poor health	2	3	
<i>Lost because pharmacist revoke study participation</i>	17	17	
Total n (%)	37 (47.4)	41 (52.6)	0.845

Objective adherence

Out of 2'453 chronic therapies registered in the PMC protocol at T-28, 1'020 (41.6 %) met inclusion criteria for the calculation of their Medication Possession Ratio (MPR) using the defined algorithm (Additional file 2). Sub-analysis of therapies inert to dose adjustments or splitting (and therefore with highest expected validity for calculation of MPR) showed consistent, but no significant trend for improved adherence rates in the intervention group (Table 5). For 212 out of 1'020 therapies (20.8 %) the MPR was < 80 % (intervention N = 96 (19.5 %) and control group N = 116 (22.0 %), p = 0.318). Out of all therapies, the Daily Polypharmacy Possession Ratio (DPPR) was calculated for each individual patient as shown in Table 6 (Additional file 3). Mean DPPR over the whole eligible study population was 87.3 (N = 293, SD = 14.250). In both, intervention and control group, the DPPR in D-CH (mean = 88.38, SD = 14.270) was significantly higher compared to that of F-CH (mean = 84.86, SD = 13.972) (p = 0.01). Both regions showed no significant improvement of DPPR through the intervention (Fig. 4).

Subjective adherence

In addition to objective adherence, we asked participants how they estimated their overall adherence on a scale from 0 to 100 %. The mean absolute change of subjective adherence between T-0 and T-2 was +1.03 % in the intervention and -0.41 % in the control group (p = 0.058) (Table 7). Sub-analysis revealed, that the number

Table 3 Drug-related problems addressed during PMC at T-0 in intervention group (*N* = 258)

	N	%
Drug-related problems		
Potential	149	58
Manifest	109	42
Urgency rated by the study pharmacist		
High	36	14
Medium	113	43
Low	109	43
Recommendation accepted by patient		
Yes	219	85
No	25	10
Unclear	14	5
Causes of pharmacists' interventions		
Insufficient adherence	69	26.7
Patient needs information about safe and effective use of his medicines	50	19.4
Patient needs information about potential medicines' adverse drug reaction	19	7.4
Inappropriate timing or frequency of administration	18	7.0
Under-dosed therapy	15	5.8
Drug-drug/drug-food interaction	14	5.4
Adverse effect	12	4.7
Inappropriate therapy duration	10	3.9
Inappropriate drug administration	9	3.5
Patient needs information about lifestyle, nutrition or empowerment	8	3.1
Not received treatment	7	2.7
More cost-effective therapy available	5	1.9
No concordance with guidelines or contraindication	4	1.6
No dose adjustment because of pathological changes (renal/liver failure)	4	1.6
Not indicated drug or duplication	3	1.2
Incomplete patient documentation	3	1.2
Over-dosed therapy	3	1.2
Prescribed drug not available	2	0.8
Inappropriate monitoring	1	0.4
Not classifiable	2	0.8
Description of pharmacist's interventions		
Counseling of patient, training	152	58.9
Optimisation of administration	40	15.5
Information to other caregivers	24	9.3
Dose adjustment	12	4.7
Substitution of a therapy	10	3.9

Table 3 Drug-related problems addressed during PMC at T-0 in intervention group (*N* = 258) (Continued)

	N	%
Therapy started/restarted	7	2.7
Therapy stopped	7	2.7
Therapy monitoring	3	1.2
Clarification in the patient history	2	0.8
Not classifiable	1	0.4

of patients reporting a change of their adherence of more than ± 5 points on a scale 0-100 % between T-0 and T-2 was significantly higher in the intervention group ($N_{\text{Improvement}} = 30$; $N_{\text{Worsening}} = 14$) compared to the control group ($N_{\text{Improvement}} = 20$; $N_{\text{Worsening}} = 24$) ($p = 0.028$). Table 8 summarises patient self-report of adherence using validated questionnaires. Between the two telephone interviews T-2 and T-16, mean difference between patients' beliefs and concerns about their medicines did not change significantly (Intervention = -0.01 (SD 6.609); Control = $+0.64$, (SD 6.289), $p = 0.697$). At T-16, in total 74 patients had a MMAS-8D score < 6 representing low adherence (intervention $N = 37$ (18.9 %), control $N = 37$ (18.3 %)). Moderate adherence (Scores 6–8) was shown in the intervention group for 83 patients (20.8 %) and in the control group for 89 cases (22.3 %). High adherence was present in 154 patients, 78 from the intervention (39.4 %) and 76 from the control group (37.6 %). No significant difference in adherence between the two groups could be observed ($p = 0.817$).

Use of health care resources by patients and unplanned visits at a general practitioner or hospital

According to the notations in the CRF in 18 cases (8.3 %) out of the 258 DRPs addressed at T-0, the study pharmacist contacted the responsible general practitioner ($N = 17$) or an indicated specialist ($N = 1$) to discuss or inform about issues revealed through the PMC. A phone call was reported in six cases (33.3 %), the other issues were addressed by Fax ($N = 5$, 27.8 %), Email ($N = 1$, 5.6 %), referral letter ($N = 1$, 5.6%), otherwise ($N = 3$, 16.7 %), not specified ($N = 2$, 11.1 %). Four out of 18 physicians did not respond to the pharmacists' initiative (22.2 %). The remaining 14 (77.8 %) gave feedback on

Table 4 Overview of weekly dosing aids in use during study

	Intervention	Control	<i>p</i> Value
T-0 (assessed through pharmacist during PMC)	72 ^a <i>N</i> = 218	-	-
T-2 (assessed through telephone interview)	83 <i>N</i> = 202	90 <i>N</i> = 214	0.838
T-16 (assessed through telephone interview)	90 <i>N</i> = 198	98 <i>N</i> = 203	0.699

^aFrom which three were newly implemented through PMC

Table 5 Objective adherence represented as MPR

	Intervention			Control			pValue
	Mean %	SD	N	Mean %	SD	N	
All therapies	88.3	19.03	493	87.5	20.75	527	0.811
Antiplatelets (B01AC)	91.3	16.24	61	85.4	23.75	64	0.119
Proton pump inhibitors (A02BC)	91.8	13.36	43	87.7	18.27	33	0.493

the addressed issues. Nine fully accepted the pharmacists' recommendations (64.3 %), one partially (7.1 %), and two rejected the recommended intervention (14.3 %). In two cases, the implementation of the recommendations remained unclear (14.3 %). During the study period, patients reported a total of 209 unplanned visits at a general physician or hospital, showing no significant difference between study groups (Table 9). The same was observed for the incidence of falls during the study.

Discussion

Our study presents initial findings on a newly implemented pharmacist-led medication review service, called Polymedication Check (PMC) with respect to impact on patients' adherence. The multicentre parallel group randomised controlled trial was conducted in community pharmacies with very low to moderate experiences in providing medication reviews. This paper presents results from multiple in-depth assessments focusing on patients' adherence and drug-related problems; humanistic outcomes and the patients' as well as pharmacists' perspectives will be dealt with in a second publication.

Study population

Recruitment of study pharmacists posed no problem; all recruited pharmacists attended the required training session. However, experience with providing a PMC proved to be unequal with only 28 % of pharmacists featuring prior experience in conducting >5 PMC and even 34 % with no prior experience at all. Nevertheless, a majority of the study pharmacists who finally started to enrol patients in the project was highly motivated to participate in this evaluation study despite the complexity of the study protocol and their lack of experience with participation in randomised controlled trials. In all regions a

suitable sample of pharmacies was involved into the study. The demographics and characteristics of the participating pharmacies were in line with the total of Swiss pharmacies regarding organisational form of ownership and gender compared to RoKA report 2012 [49] (personal ownership and group (study: 74.1 % vs. RoKA: 69.6 %) or chain (25.9 % vs. 30.4 %), women (75.0 % vs. 80.0 %)). The estimated number of ten patients recruited by each study pharmacist was not reached by most pharmacists (Median 7; Range 1–17) despite up to six months of recruitment period per study region. During the study, six study pharmacies cancelled participation before they started recruiting patients and five more dropped out during the study; as a consequence follow-up of their patients was impossible. Patient dropouts were fairly low (17.3 %), evenly distributed across both study groups and caused by an expected pattern of comprehensible reasons, so there is little concern for a selection bias due to selective dropouts. The reported causes were both rare and typical, such as patients' moving away or being unable to continue due to health reasons.

Impact of the Polymedication Check

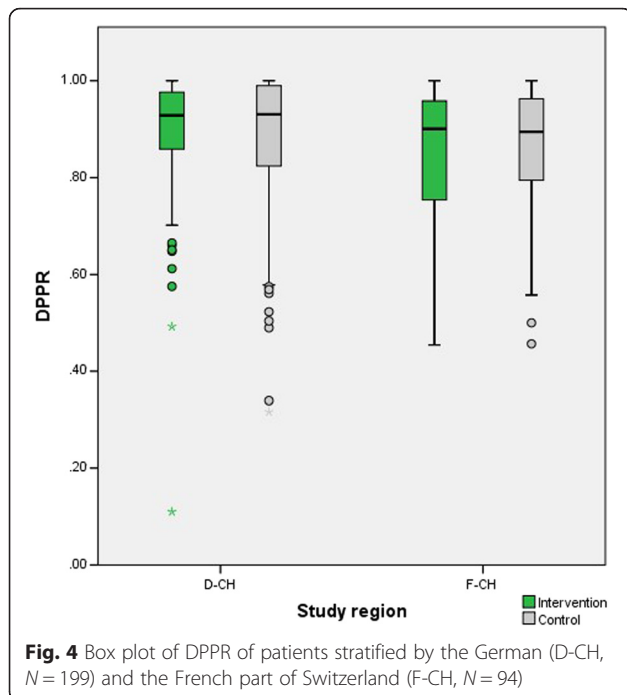
The primary outcome objective adherence showed no significant improvement in the PMC group (mean MPR 88.3 % vs 87.5 % in the control group ($p = 0.811$)).

The adherence in the control population was already at an unexpectedly high rate of 87.5 %, leaving only little room for improvement in the intervention group. This made it nearly impossible to observe the 5 % increase in objective adherence, on which the power calculation was based. Notably, in the intervention group a higher percentage of patients showed more than 5 % increase of subjective adherence compared to the controls. This effect only appeared shortly after the intervention and could not be observed again in the further course of the study.

Our results show that during the PMC non-adherence to medication was the most frequent issue addressed in 26.7 % of PMC cases, followed by a need for information about safe and effective medicines use (19.4 %) or improvement of awareness for risks and adverse effects of therapies (7.4 %). Previous research has shown that adherence counseling was included in only 6.7 % of the reported cases of unspecific pharmacist-patient contacts

Table 6 Objective adherence to polypharmacy represented as DPPR over all patients ($N = 293$)

	Intervention ($N = 146$)		Control ($N = 147$)		pValue
	Mean	SD	Mean	SD	
DPPR (%)	88.0	13.31	87.5	20.75	0.906
Number of medicines eligible for DPPR calculation per patient	3.4	1.68	3.6	1.86	0.425



in usual care [14]. This pattern of detected and discussed drug-related provides an important indication on the impact of the PMC and proves appropriateness of the concept of the PMC regarding its aim at triggering adherence and knowledge issues as topics for individual counseling. The filling of a patient’s medicines into a WDA could be implemented in only very few patients (1.4 %). This unexpected result can be explained with a) the pharmacist judged the patient sufficiently well-organised without a WDA, b) the patient already used a WDA in self-management (which was the case in 42 % of patients in our study) or c) the patients were not willing to delegate the preparation of their medicines to the pharmacist. There is a necessity for guiding a comprehensive assessment of patient needs (self-management of a WDS versus WDA provided by the pharmacy) and differentiating between the active recommendation by the pharmacists and the refusal by the patient. The implementation rate of WDA in patients with chronic polypharmacy revealed in our study, still offers room for

improvement; recent surveys in Canada could show that 75 % of patients in a comparable community sample stated to regularly use a WDA [50]. With respect to the interface between pharmacy and GP, 18 out of the 258 cases of detected and addressed DRPs in the PMC group at T-0, cases triggered a consultation with the patient’s GP (7.0 %), leading in 77.8 % to an interprofessional collaboration and discussion of patients’ DRP with high acceptance rate of pharmacists’ recommendations (71.4 %). Still, considering the recommendations without feedback or acceptance by the GP (N = 8), the overall implementation rate of 44.4 % is comparable to a study of Kempen et al. [51], who reported implementation rates of 42 %. Such low implementation of recommendations will decrease efficacy of any intervention substantially. However, it can be deduced that the pharmacists were able to solve more than 90 % of the patients’ issues independently.

Unlike reported in previous studies [52], no harmful effect of the PMC intervention as reflected by the non-significant group differences in unplanned hospital admissions or in visits to the GP (Table 9) could be observed. This observation is meaningful when looking at the frequency of contacts of pharmacists with the prescriber resulting from a PMC (8.3 %) and considering that only a few of the pharmacists’ recommendations (14.3 %) were rejected. A significant number of DRPs were discovered and solved through study pharmacists providing a PMC (Table 3).

Reasons why we did not detect a significant effect

Overall, the study remained underpowered: The initial estimation of the impact on adherence of the PMC was set on 5 % with a baseline at around 60 %. This assumption was based on the results of other studies from different countries and settings [47]. The unexpected high adherence observed in the control group allowed only little improvement. Thus, a sole increase of the study population, e.g. through an extension of the recruitment period, would remain ineffective. A more effective and internationally accepted approach to enhance the efficacy of medication reviews would be the targeting of patients at risk [9]. The high rate of implemented WDA at T-2 (42 %) (Table 4) indicates an already

Table 7 Subjective rating of adherence during the preceding two weeks

	Intervention		N	Control		pValue	
	Mean %	SD		Mean %	SD		
Patient questionnaire T-0	96.2	8.62	211	96.8	7.05	232	0.204
Telephone interview T-2	97.2	9.31	202	96.4	10.24	213	0.118
Telephone interview T-16	98.5	5.56	198	97.8	7.64	202	0.400
Patient questionnaire T-28	95.5	10.28	178	96.3	9.51	186	0.338

Table 8 Summed scores of validated adherence questionnaires at T-2 and T-16

	Intervention			Control			pValue
	Mean	SD	N	Mean	SD	N	
T-2							
BMQ Beliefs	20.58	4.463	171	20.99	4.301	181	0.328
BMQ Concerns	9.95	4.249	171	10.30	4.949	181	0.726
Difference Beliefs - Concerns	10.64	5.554	171	10.69	6.494	181	0.612
T-16							
BMQ Beliefs	20.66	4.630	188	21.23	3.958	183	0.369
BMQ Concerns	9.89	5.020	188	9.72	4.583	183	0.872
Difference Beliefs - Concerns	10.77	6.360	188	11.51	5.705	183	0.337
MMAS-8D Score ^a	6.85	1.226	198	6.82	1.237	202	0.817

^aMMAS-8D Score: 8 = high adherence, 6–7.75 medium adherence, <6 low adherence

improved patient's self-management mostly initiated through pharmacists before study start. It was a deliberate decision not to focus on patients with specific diseases or drugs in this first evaluation since the service might be offered to every patient meeting the inclusion criteria for a PMC. Since the inclusion criteria were non-specific in terms of risks for non-adherence, it must be assumed, that already well-organised patients with established therapies were included in this study. Further on, patients with the highest need for intervention with manifest non-adherence might not have been motivated to be part of a clinical trial that explicitly aimed at uncovering individual weaknesses in the correct administration of medicines. Experiences with the MUR service from UK resulted in the development of specific interventions for various patient populations, offering to the health care provider a structured and focused flow chart supporting the process of screening for pharmaceutical care issues [53]. Thus, applying more specific criteria in addressing the medication reviews to patients with higher risk for drug-related problems would probably increase the impact of the intervention.

Medication reviews such as the PMC are a screening method aiming at detecting drug-related problems, and the corresponding interventions are unspecific. Thus, in a first step, this service only results in a number of

drug-related problems detected or number of referrals etc. Looking at clinical outcomes, only well planned and monitored interventions can have an impact. The current PMC protocol specifies the provision of a weekly dosing system filled by the pharmacy as its main intervention. This intervention, though known to be effective [54], was offered only to very few patients (1.4 %). All other interventions such as delivery of a medication plan or check of correct use of an asthma device are not foreseen in the protocol and hence could not be evaluated. On the other hand, explicit listing of such predefined interventions on the protocol would probably trigger more frequent provision of such services. So far, the intervention part is insufficiently specified in the current guideline, and especially not well supported by the current PMC protocol.

Strengths

First, the randomised controlled trial design is a distinct strength of this study. Second, the trial was performed under real-life conditions with a representative sample of pharmacists from different regions, including the French-speaking part of Switzerland with differences related to health care (i.e. density of pharmacies,

Table 9 Patient reported unplanned visits at general practitioner or hospital and falls during study period

Unplanned visits ...	Intervention		Control		pValue
	N _{YES}	N _{Total}	N _{YES}	N _{Total}	
... from T-0 -> T-2	14	202	10	214	0.324
... from T-2 -> T-16	50	198	44	203	0.398
... from T-16 -> T-28	46	181	45	191	0.678
Incidence of at least one fall until T-28	31	17.7 %	30	15.9 %	0.638
... thereby injured	17	54.8 %	15	50.0 %	0.705

preferred way of medication supply), cultural and socio-economic factors. Thus, the results of the present study are likely to be highly generalisable. Third, patients' adherence was measured using several validated instruments providing internal validity. Fourth, the in-depth telephone interviews on patient's acceptance and knowledge were performed by trained independent clinical psychologists, blinded to the intervention. Fifth, patients' written self-reports were blinded to the pharmacists; thus a Pygmalion effect could be excluded.

Limitations

First, due to restricted financial means, the study period to investigate the objective adherence was limited to just 28 weeks. With regard to the common package size of 100 tablets for long-term medication, the short study duration offered only two refills to be considered for evaluation of adherence. Newer guidelines suggest follow-up periods of 1–2 years or more to capture long term non-adherence [55]. Second, patients enrolled in clinical trials may be more conscientious than the average patient. During the consent process, patients were told that the purpose of the study was to learn more about their daily medicines use and that their adherence to medication was observed. Thus, all our patients knew they were being monitored, which on the one hand may have led to a higher baseline in self-reported adherence at study start and also during follow-up in both groups of our study patients compared to other patients. The pharmacists on the other hand knew that they were being studied, which may have led them to increase their efforts in delivering pharmaceutical care, notably for both groups. This is known as the Hawthorne effect: a psychological response in which subjects in a research study change their behaviour simply because they are subjects in a study, not because of the research treatment [56]. Thus, the heightened awareness of the patients and also of the pharmacists about the study setting could have influenced the medicines intake for the prospective time. Such influence can only be eliminated through a randomisation at the level of the pharmacy – a procedure posing other problems of bias as well. In order to avoid selection bias by the pharmacists, patients were selected at random solely fulfilling the PMC-criteria and not because of an increased risk or any indicators for manifest non-adherence. Third, because of time constraints and limited resources the recruitment was stopped before the intended number of patients was recruited.

Implications for practice

In line with other authors [9, 55], we recommend to ensure efficiency and efficacy to reconsider and adapt the service on various levels: First, the service should be more tailored to patients at higher risk for drug-related problems, such as patients with respiratory diseases, diagnosed

cardiovascular disease, regularly being prescribed at least four medicines etc. In addition, focusing on patients recently discharged from hospital, or who had changes in their medicines regimen would provide more opportunities to screen for manifest DRPs possibly before the start of a risky treatment. Ideally, these patients would receive a medication review within a very short time (e.g. a few days) after the start and are followed by a follow-up meeting (face-to-face or by telephone call) to check for handling issues and implementations of the recommendations. Second, after detecting the patient at risk for clinical relevant drug-related problems, we recommend to proceed with validated, structured and standardised interventions. This process should allow a follow-up to ensure implementation of pharmacists recommendations (according to the pharmaceutical care process, see also the New Medicines Service from the NHS, UK) [57]. The PMC protocol form should include the documentation of the recommendations or follow-up interventions in a more specific structure. Thus, the current process of the PMC as a service and its protocol need to be re-engineered. Third, pharmacists had no training and supervision when providing the service. An implementation program focusing on the main barriers of the service could still encourage pharmacists to provide PMC in the future. A responsible professional body for coaching and answering frequently asked questions is needed. Qualification and/or accreditation of involved health care providers might be considered to ensure high quality and safe interventions on patient level. Continuing education should be strengthened through systematic integration of PMC cases into practice-oriented teaching. For distinct problems or care issues structured guidance should be developed.

Conclusion

For the first time in the Swiss health care system, a newly implemented cognitive service of community pharmacists underwent an in-depth evaluation process in daily life. The service showed no significant improvement on objective adherence in the observed population. Reasons for not being able to demonstrate significant positive effects are likely to depend on a) an unintentional selection of patients with very high adherence and low risk for drug-related problems causing insufficient power and b) on a low level of experience with providing the PMC among the recruited pharmacists.

However, based on the study results, we conclude that the so called Polymedication Check as a pharmacist-led medication review i) was able to address a significant number of drug-related problems concerning adherence issues and need for knowledge improvement and ii) showed no further financial burden to the Swiss health care system as there was no harm induced and pharmacists' interventions did not cause additional consultations

with other healthcare professionals. Re-engineering of the service should focus on the inclusion criteria to target the patients with highest risk for non-adherence and on the improvement of pharmacists' skills in implementing weekly dosing aids.

Availability of data and materials statement

The datasets concerning the primary outcome and thereby supporting the conclusions are included within the article and its additional files.

Additional files

Additional file 1: Swiss Poly medication Check. (PDF 72 kb)

Additional file 2: Data Medication Possession Ratio (MPR). (XLSX 42 kb)

Additional file 3: Data Daily Polypharmacy Possession Ratio (DPPR). (XLSX 18 kb)

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MMe and KHe conceived the trial design and wrote the ethical proposal and study protocol. NVr helped in developing the measurement tools (namely designing and piloting the telephone interviews) and ensured independent training and support of the involved staff. MMe, as the main investigator, recruited and coordinated the involved study pharmacists and their patients and ensured compliance to the study protocol. MMe and NVr accessed and analysed both the retrieved data. MMe prepared the draft of a first report while EBl, KHe, and NVr contributed to the discussion and reviewed the manuscript. They all agreed to the publication of the final version of the manuscript.

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7.6 Humanistic outcomes and patient acceptance of a pharmacist-led medication review in primary care – a prospective randomised controlled trial [B5]

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7.6.1 Abstract

Background: Since 2010, Swiss pharmacists are encouraged to offer a Polymedication Check (PMC) to their patients, which represents a new cognitive pharmacy service in form of a medication review on patients with ≥ 4 prescribed medicines used over > 3 months.

Objectives: We aimed at investigating the impact of the PMC on patients' knowledge of their medication, their acceptance of pharmacist-led medication review, and the patients' relationship to their pharmacy.

Methods: This randomised controlled trial was conducted in 54 Swiss community pharmacies. Eligible patients used ≥ 4 prescribed medicines over > 3 months. After recruitment, the intervention group underwent a PMC in the pharmacy (T-0) and 28 weeks after T-0 (T-28) while the control group received the PMC not until 28 weeks after study start (T-28). A trained telephone interviewer, blinded to the intervention, interviewed the patients two weeks (T-2) and 16 weeks (T-16) after T-0. Interviewer and patient both rated patient's knowledge of own medicines use. Further, patients reported satisfaction with their pharmacy and appraisal of medication management. The availability of a written medication plan was assessed at T16. Acceptance of the service was measured with patient's self-report questionnaire at T-28.

Results: At T-2 interviewers' ratings of patient's knowledge of own medication were significantly higher in the intervention group compared to the control group (M_{Int} : 7.4, SD: 1.83 vs M_{Cont} : 7.1, SD: 1.87; $p=0.026$). Patient's ratings on knowledge did not differ between groups (M_{Int} : 9.3, SD: 1.22 vs M_{Cont} : 9.2, SD: 1.34; $p=0.350$). At T-16, no difference was found between groups and evaluators. The majority of 83% of patients judged the counseling by the pharmacist as being helpful for their daily medication management. Availability of a written medication plan was comparable in both groups (52.5% vs 52.7%, $p > .05$).

Conclusion: The Polymedication Check increases subjective patient's knowledge of own medicines two weeks after the intervention compared to no medication review. The community pharmacist-led service seems to be highly appreciated by the patients. Still, almost half of the patients on polypharmacy lacked a written medication plan, offering room for improvement concerning the patients' management in medicines use.

Trial registration: Clinical trial registry database www.clinicaltrials.gov NCT01739816; first entry on November 27, 2012.

Keywords: Polypharmacy, Community pharmacy, Medication review, Humanistic outcomes, Patient acceptance, Pharmaceutical care

7.6.2 Introduction

The role of the community pharmacist in primary care has been undergoing change in Switzerland in parallel to international developments: it has become more clinical and patient-oriented. Special services of community pharmacists to older patients taking long-term or multiple medications have been developed.⁷⁴ Since 2010, Swiss pharmacists are allowed to offer their patients a Polymedication Check (PMC), a new cognitive service in form of a medication review with patients using more than three prescribed medicines over a period of at least three months. This reimbursed service aims at detecting drug-related problems in a patients medicines use in daily life and recommending interventions to optimise medicines management in order to prevent negative health outcomes through drug therapy.⁷⁴

In Switzerland, new services remunerated by the basic health insurance require a proof of their efficacy, appropriateness, and economic effectiveness according to national criteria.⁸⁹ As an investigator-initiated project, we aimed at evaluating efficacy and appropriateness of the service by providing a randomised controlled trial in Swiss community pharmacies. We hypothesized that the PMC would increase adherence and improve patient's knowledge about his medication compared to the control group. While another publication of this project reported on the positive impact of the PMC on patients' adherence,⁹⁰ the present article highlights the humanistic outcomes.

Little is known on humanistic outcomes and patient satisfaction of newly implemented pharmacists-led services based on data from randomised controlled trials. Latif et al. investigated improvement of knowledge through medicines use reviews (MUR), a service similar to the Swiss PMC. Thereby they reported that MURs did only slightly increase patients' knowledge and rarely affected medicine use, although some patients felt reassured about their medicines.⁹¹

Similarly, we were interested in investigating the impact of the PMC on patients' knowledge, the acceptance of the service by the patients, the patient satisfaction, and the relationship to their pharmacy, since pharmacists often lack self-confidence about their role within patient centred care and acceptance by their clients.^{92,93} In addition, we aimed at collecting information

on the patients' self-management of medication in order to improve the PMC as a service aiming at optimising patients' medicines use.

7.6.3 Methods

Data was available from a previously described randomised-controlled trial conducted in 54 Swiss community pharmacies.⁹⁰ Eligible patients used ≥ 4 prescribed medicines over >3 months. After recruitment and randomisation, the intervention group received a PMC in the pharmacy (T-0) and another PMC 28 weeks after T0 (T-28) while the control group received a PMC only at T-28 (Figure 5).

7.6.3.1 Outcome measures

Both patient groups filled in self-report questionnaires at study start (T-0) and study end after 28 weeks (T-28). Telephone interviews were carried out 2 weeks (T-2) and 16 weeks (T-16) after T-0 by a trained telephone interviewer (Figure 5). Interviewers were intensively trained (four hours input and two exercise interviews) and regularly supervised by the second author (clinical psychologist). Further detailed description of the development of these measurement instruments is published elsewhere.⁹⁰ The interviews included additional questions that are not reported here. We are convinced that these items are beyond the scope of this present topic and did not influence the presented results.

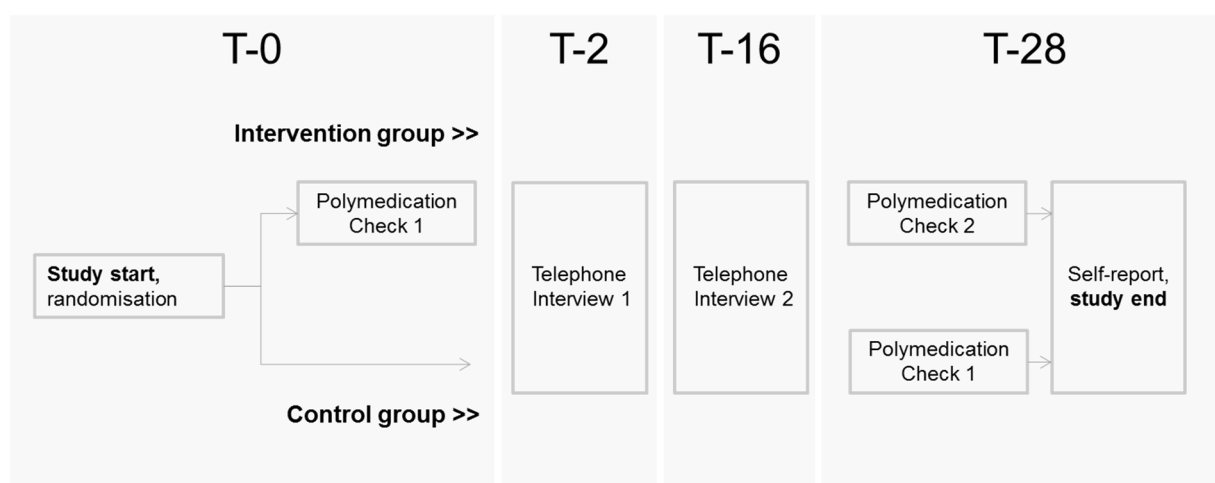


Figure 5 / Study flow chart with relevant outcome measurements

7.6.3.2 Judgement of patient's knowledge of their medicines

At T-2, each patient completed an in-depth telephone interview about his medicine use. For each product that he/she mentioned the interviewer asked 'Do you know why you take this medicine? How often do you take this medicine? When exactly do you take this medicine? Do you have to watch out for anything in particular when dealing with and applying/taking this medicine?'. After the interview, the interviewer rated the knowledge of the use of their medicines on a scale from 1 (=poor knowledge) to 10 (=very good knowledge). Patients also reported their subjective knowledge about the use of their medicines on this scale. Both, patients and telephone interviewer used the identical scale, while patients were not informed about the interviewers' ratings.

7.6.3.3 Patient satisfaction and relationship with study pharmacists

Patients' satisfaction concerning the relationship with the involved study pharmacies and related pharmacist was assessed with six items using a rating scale from 1 to 10 with specific descriptive hints, e.g. 'How satisfied are you with your pharmacy on a scale of 1-10? (1=very dissatisfied; 10=very satisfied)'.

7.6.3.4 Patient appraisal with their medication therapy

Patients' appraisal concerning their medication therapy was assessed with six items using a rating scale from 1 to 10 with specific descriptive hints, e.g. 'How difficult do you find it to administer your medication? (1= very easy; 10 = very difficult)'

7.6.3.5 Availability of a written medication plan

During the telephone interview at T-16, patients reported during the telephone interview, if they were in possession of a written medication plan (yes/no).

7.6.3.6 *Patient' acceptance of the service*

At T-28, patients' reported acceptance of the service with a self-report questionnaire after both groups received a PMC (for the intervention group the second PMC). Patients reported, if they knew the service before they were invited to the study (yes/no), if, from their perspective, the price for the service (CHF 48.60 per PMC) was i) accurate, ii) too high or iii) too low, and if they were able to benefit from the pharmacist' advices provided within the PMC (yes/no). They also rated eight positive and two negative judgments concerning the PMC and the performance of the pharmacist using a 4-point Likert scale (1=disagree, 2=tend to disagree, 3=tend to agree, 4=agree). Ratings ≤ 2 were considered as negative, ratings ≥ 3 as positive statements.

7.6.3.7 *Statistical methods*

Numerical scales are presented as mean and standard deviation (SD). Frequencies were evaluated using the chi-square test. Ordinal scales were tested with the non-parametrical Mann-Whitney-U-test. Analyses for repeated measures with 'time' (T-2 and T-16) and 'rater' (interviewer vs patient) as within-subject factor and 'group' (intervention versus control) as between-subject were used to analyse the main and interaction effects of the intervention on the knowledge of the patient. Statistical tests were performed with a significance alpha-level of 5%.

7.6.3.8 *Ethical approval*

The study was approved by the responsible local ethic commission 'Ethikkommission beider Basel (EKBB)' (23.05.2012, EKBB 50/12) as the leading committee for this multisite study and registered at: www.clinicaltrials.gov trials database (Identifier NCT 01739816).

7.6.4 Results

7.6.4.1 *Judgement of a patient' knowledge of their medicines*

A significant main effect for group (intervention versus control) was found at T-2 (Table 8), revealing that within subject, the intervention group had greater knowledge about their medication at both measure points ($F=5.86$, $p=0.016$). A significant main effect for 'time' showed that both groups increased their knowledge between T-2 and T-16 ($F=45.99$, $p<0.001$).

A significant main effect for the factor ‘rater’ (interviewer vs patient) revealed that the patient estimated their knowledge about medicine higher compared to the ratings of the interviewer (F=435.59, p<0.001). The significant time x rater interaction (interviewer vs patient) indicates that the interviewer rated the patients knowledge at T-16 higher as at T-2 (F=3.99, p=0.046).

Table 8 / Patient’ knowledge concerning medicines use at T-2 and T-16, rated by the interviewer and by the patient.

	Intervention			Control			pValue
	n	Mean	SD	n	Mean	SD	
T-2 Interviewer *	202	7.38	1.850	214	7.11	1.873	0.026
T-2 Patient **	201	9.27	1.223	213	9.21	1.344	0.350
T-16 Interviewer *	198	7.99	1.833	203	7.62	2.096	0.055
T-16 Patient **	198	9.66	0.802	203	9.49	1.178	0.061

* ‘Please rate the patient’ knowledge of the administration of his medication on a scale of 1 to 10. 1=poor knowledge; 10= very good knowledge’; ** ‘If you had to rate your knowledge on a scale of 1 to 10, how sure are you of the administration of your medication?’ 1=poor knowledge; 10= very good knowledge’

7.6.4.2 Patient satisfaction and relationship with study pharmacists

Patient satisfaction with the study pharmacies assessed at T-2 is shown in table 9. Cronbach alpha of this scale was 0.693 in the intervention group and 0.749 in the control group. All six questions on satisfaction with service provision by the community pharmacy show high satisfaction with no significant difference between control and intervention (p >.05).

Table 9 / Patient satisfaction with study pharmacy and judgement about relationship with study pharmacists at T-2 (mean (standard deviation))

	Intervention (n=202)	Control (n=214)	pValue
1. How satisfied are you with your pharmacy on a scale of 1-10? (1=very dissatisfied; 10=very satisfied)	9.61 (0.785)	9.68 (0.681)	0.518
2. Do you generally accept recommendations made to you by your pharmacist? (1=you never accept recommendations; 10=you always accept recommendations)	9.34 (1.256)	9.36 (1.200)	0.891

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3. How competent would you consider your pharmacist, in his/her field of work, on a scale from 1-10? (1=very incompetent in his/her field; 10=very competent in their field)	9.72 (0.677)	9.74 (0.651)	0.768
4. On a scale of 1-10, how satisfied are you with the amount of time your pharmacist has for you? (1=very dissatisfied; 10=very satisfied)	9.71 (0.808)	9.75 (0.600)	0.695
5. On a scale of 1-10, how strongly do you feel your interests to be in good hands with your pharmacist? (1=not in good hands at all; 10=in very good hands)	9.68 (0.762)	9.75 (0.644)	0.366
6. On a scale of 1-10, how much better do you understand your medications and their application after you consulted your pharmacist?(1=not at all better; 10=much better)	9.19 (1.851)	9.15 (1.835)	0.753
Mean	9.57 (0.657)	9.58 (0.701)	0.605

7.6.4.3 Patient appraisal with their medication therapy

Patient' appraisal with their medication management at T-2 is shown in table 10. Cronbach alpha of this scale was 0.031 in the intervention group and -0.078 in the control group. No difference between the groups was observed ($p > .05$).

Table 10 / Patient appraisal with medication therapy at T-2 (Mean and standard deviation are given)

	Intervention (n=202)	Control (n=214)	pValue
1. How satisfied are you on a scale from 1-10 with your daily medication intake (e.g. number of medicines, condition)? (1= very unsatisfied; 10 = very satisfied)	9.12 (1.389)	8.95 (1.563)	0.208
2. How competent do you feel administering your medication? (1 = very incompetent; 10= very competent)	9.33 (1.178)	9.29 (1.492)	0.529
3. How comfortable do you consider administering your medication? (1= very uncomfortable; 10 = very comfortable)	8.23 (2.233)	8.35 (2.204)	0.613
4. How difficult do you find it to administer your medication? (1= very easy; 10 = very difficult)	1.50 (1.259)	1.42 (1.117)	0.965
5. How unappetising do you find taking medication? (1 = delicious; 10 = very unappetising)	2.06 (1.946)	2.08 (1.795)	0.472
6. Do you think that your medication are necessary? (1 = you consider them absolutely unnecessary; 10 = you consider them very important)	9.46 (1.113)	9.39 (1.381)	0.661
Mean	6.58 (0.682)	6.56 (0.652)	0.935

7.6.4.4 Availability of a written medication plan

At T-16, availability of a written medication plan was reported by 104 patients (52.5%) in the intervention group and 107 (52.7%) of the control group. There was not significant group difference ($p>.05$).

7.6.4.5 Patient' acceptance of the service

Of 450 patients enrolled, 372 (82.7%, dropout rate: 17.3%) completed the study. Hundred sixteen patients (31.2%) knew the service before being invited to the study. The price of the service was accepted as appropriate ($n=327$, 87.9%) or too low ($n=13$, 3.8%), while 13 patients (3.8%) stated the cost as too high or did not answer ($n=19$, 5.1%). A majority of 308 patients (83.1%) appraised the counseling by the pharmacist in general as being helpful for their daily medication management. No difference between groups was observed ($p>0.05$). In table 11, the patients' rating of the service is shown after both groups had received at least one PMC.

Table 11 / Statements regarding the PMC rated by all 372 patients at study end after having received at least one PMC (4-point Likert scale; 1=disagree, 2=tend to disagree, 3=tend to agree, 4=agree)

Statement	Mean (SD)
1. The consultation took place in a pleasant atmosphere.	3.97 (0.18)
2. The aims of the PMC were clearly explained to me.	3.93 (0.29)
3. The time spent was worth it for me.	3.78 (0.53)
4. I would recommend the service.	3.83 (0.44)
5. The instructions of the pharmacist helped me in handling my medication.	3.77 (0.60)
6. Thanks to the pharmacist' advice, I do have more confidence in my medication.	3.56 (0.79)
7. The pharmacist had enough time to answer all my questions.	3.96 (0.22)
8. Until today, I felt left with my medication down.	1.51 (0.95)
9. Thanks to the advice, I feel safer than before in the use of my medication.	3.36 (0.95)
10. I had far too little information about my medication.	1.93 (1.10)

When aggregating the results from table 11 (ratings ≤ 2 were considered as negative, ratings ≥ 3 as positive statements), 305 patients (82%) stated improved confidence in their medicines and

289 (78%) reported enhanced security in their medicines use after the PMC. Most patients (n=357, 96%) agreed to recommend the PMC to other patients.

7.6.5 Discussion

We report secondary outcome measures of a randomised controlled trial. The present evaluation of the cognitive pharmacist-led service 'Polymedication Check' (PMC) showed a significantly increased knowledge about medication after the PMC rated by telephone interviewers blinded to the intervention. Both groups reported in both interviews an overall high and constant satisfaction with individual care offered by community pharmacists and a fairly high appraisal of their medication therapy during the study. This important result underscores that pharmacist-led medication reviews neither unsettled the patient in his medicines use nor induced harm as previously postulated by Holland et al.⁹⁴

7.6.5.1 Improved knowledge on medicines use

The PMC positively influenced patient's knowledge on his/her medicine use. Patients seem to know more about their medication use after the intervention compared to controls. This finding may be explained by the observed pattern of addressed drug-related problems during the intervention at T-0. In 27% of cases, the need for further information on safe and effective use of medicines or potential adverse drug reactions represented a cause for further recommendations by the study pharmacist.⁹⁰ While Grymonpre et al. did not show any impact on patients knowledge through a pharmaceutical care model,⁹⁵ Ryan et al. concluded within their Cochrane review that pharmaceutical care services (consultation between pharmacist and patient to resolve medicines problems, develop a care plan and provide follow-up) were affected with positive effects on adherence and knowledge.⁹⁶

Interestingly, we found a discrepancy in subjective knowledge on medication use between external ratings (interviewers) and self-ratings knowledge (patients). This might indicate an overestimation of capabilities by the patients comparable to subjective adherence ratings.^{97,98} The 'one question fits all' approach (e.g. 'Do you know how to use your medicines?') represents a first step for a loose detection of individual issues with medication intake, but needs further in-depth assessment. This should include evaluating patients' knowledge on 'why', 'how often', and 'when exactly' they take their medicines in order to provide individualised patient

education to address these knowledge gaps. In this context, further research might investigate sensitivity and specificity in detecting critical gaps in patients' knowledge about their medicines.

Within this context, we discuss the improvement of knowledge in both groups between T-2 and T-16 with the possibility of confounding by interviewing the patients at T-2. When answering detailed questions about every medication, both groups reflected in-depth their knowledge concerning medicines use, what might could have influenced the measurement at T-16. Implicitly, the impact of the intervention on the outcome 'knowledge' has to be assumed reliable and valid at T-2 only.

7.6.5.2 High acceptance of pharmacists' interventions

While pharmacists reported on their being uncertain about their role in patient-centred care and on the lack of self-confidence,⁹³ simplifications of therapy plans and improvement of knowledge as a result of the PMC provided by pharmacists were highly appreciated by the patients. Further, patients agreed on the price to the PMC. This very positive feedback is a valuable argument in favour of the new service. However, only 31.2% of the patients knew of the possibility of this pharmacist-led service before the start of the study, which indicates a huge gap in communication of new services to the target population two years after implementation. While the pharmacists' willingness to provide the service remains unclear, legal barriers impede any public announcement of new services as advertisement of remunerated health care services is legally forbidden in Switzerland.

7.6.5.3 Room for improvement of patients' medication management

The fact that 47% of patients stated having no written medication plan to organise their complex medication schedule raises the question of the responsibility and points at the need to provide such an important tool. A written medication plan, which is accepted and understood by any individual patient, would probably empower him in his daily medicines management and is highly recommended by current guidelines when optimising a patient' medicines.⁵⁷ Since in Switzerland, pharmacists are obliged by legal regulations to keep records of all dispensed medication, they are in an excellent position to initiate a written overview and validate its actuality in collaboration with the corresponding general physician. Such initiatives are currently being developed in Germany.⁹⁹ Unfortunately, in the current PMC guidelines and

protocol form, this issue is missing and delivery of such a medication plan is not yet part of the service. However, delivery of such a medication plan should be part of interprofessional patient care. Therefore, the development of this specific intervention should involve all stakeholder within the process, namely the patients, the pharmacists, the physicians, and the perspective of a nursing home or hospital. Further, such services clearly need reimbursement provided by the health insurance companies.

7.6.5.4 Implications for practice

Patient satisfaction with pharmacies and the acceptance of this new medication review service will probably motivate Swiss pharmacists to provide the PMC further to patients on polypharmacy. However, the given eligibility criteria for receiving a PMC (self-management of ≥ 3 medicines over a period of at least 3 months) did not differentiate for patients at highest risk or needs. Nevertheless, patients strongly recommended the service to other people in comparable situations, highlighting the need for targeting patient care.

Further evaluation and development of this service should follow a validated process as proposed by Craig et al.¹⁰⁰ In order to allocate human and financial resources in a highest cost-effectiveness ratio, re-engineering of the service should be considered e.g. by revising the selection process for patients qualifying for a PMC with a pre-screening for obvious adherence issues using individual medication records^{82,83,101} or specific validated questions triggering hints for non-adherence to medication.⁸⁷ Similarly, the eligibility criteria for the comparable Medicines Use Review (MUR) service in UK were changed as well six years after its implementation, adding specific target groups to the intervention' focus.¹⁰² This proposal is aligned with recent recommendations of the National Health Institute of Excellence (NICE), which highlights the importance of medicines optimisation, approaching patients at highest risks for medicines-related problems or patients with special needs e.g. people with physical problems such as arthritis or inability to swallow.⁵⁷

In addition, a follow-up meeting shortly after the intervention should be implemented in the process. Such extension of the service would help to ensure adequate implementation of recommendations provided during the PMC and hereby respect the concept of continuity in the provision of pharmaceutical care.^{43,47} The observed high accessibility of patients by telephone two weeks after the study start (416 of 450 patients, 92.4%) offers a highly

interesting approach for a short intervention in terms of a pharmacist-led recall on individual adherence targets.

Based on patients' overestimation of their knowledge about the correct use of their medication observed within our study, we further propose to investigate pharmacists' techniques to identify knowledge gaps during patient counseling. Pharmacists should be aware of this knowledge gap and should be taught specific communication techniques for patient education. Thus, we ultimately call for specific training for pharmacists in order to approach patients' knowledge issues efficiently when providing pharmaceutical care.

7.6.5.5 Strengths

First, the randomised controlled trial design is a distinct strength of this study. Second, the trial was performed under real-life conditions with a representative sample of pharmacies from the German and French part of Switzerland. Thus, the results of the present study are likely to be highly generalizable. Third, the development of the telephone interview-measurement tools were performed in a collaborative, interprofessional approach. Fourth, well trained and supervised interviewers, blinded to the intervention, performed the in-depth telephone interviews on patient's acceptance and knowledge. Fifth, patients' written self-reports were blinded to the pharmacists; thus a Pygmalion effect could be avoided.

7.6.5.6 Limitations

First, patients enrolled in clinical trials may be more conscientious than a more general population. Second, during the consent process, patients were told that the purpose of the study was to learn more about their daily medicines use. Thus, all our patients knew they were monitored, which may have led to a higher baseline in self-reported knowledge about their medicines in both groups. The pharmacists on the other hand knew that they were being studied, which might have increased their efforts in delivering pharmaceutical care, notably also for both groups, also known as the Hawthorne effect.¹⁰³

7.6.6 Conclusion

The Polymedication Check (PMC) as an intermediate medication review offers an ideal starting point for in-depth counseling and providing pharmaceutical care. Independently rated knowledge on a patient's medicines use by an external interviewer indicates a positive impact of the PMC observed two weeks after intervention. The community pharmacist-led intervention was highly appreciated by the patients, as a majority appraised the counselling as helpful for their daily medication management. They further would recommend the service to other patients and were willing to pay for it. However, the given eligibility criteria for receiving a PMC did not differentiate for patients at highest risk or needs, implying the demand for adaptations concerning the screening process of the service. In addition, almost half of the patients on polypharmacy lacked a written medication plan, offering room for improvement with regard to the patients' self-management in medicines use.

Authors' contribution: MMe and KHe conceived the trial design and wrote the ethical proposal and study protocol. NVr helped in developing the measurement tools (namely designing, piloting, and supervising the telephone interviews) and ensured independent training and support of the involved staff. MMe recruited and coordinated the involved study pharmacists and their patients and ensured compliance to study protocol as the main investigator. MMe and NVr accessed and analysed both the retrieved data. MMe prepared the draft of a first report while KHe and NVr contributed to the discussion and reviewed the manuscript. They all approved to the publication of the final version.

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Declaration of interests: The authors declare that they have no competing interests, neither financial nor non-financial.

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7.7 Insights into the pharmacists' perspective [B6]

Work report

7.7.1 Introduction

Implementation of new services has to be considered as a crucial step in the translation of knowledge from research to practice.¹⁰⁴ As recommended by Feletto et al., sophisticated planning and performance monitoring systems are required to effectively implement new services and sustain their delivery, supported by changes to infrastructure and staff mix.¹⁰⁵ However, in the case of the Polymedication Check little efforts were made to integrate the service into the pharmacist's daily practice. As neither the pharmacists' association nor the health insurance companies were interested to support implementation research, the PCRG initiated some small evaluation approaches on their own and tried to catch at least a glimpse of the pharmacist's perspective in order to understand facilitators and barriers better for the development of future services development.

7.7.2 Polymedication-Check - A new challenge for Swiss community pharmacists

Half a year after the PMC was introduced to the Swiss community pharmacists, David De Pretto evaluated within his master thesis the very first experiences from the pharmacist's perspective. A paper questionnaire-based survey was sent to 280 pharmacists from the German part of Switzerland (BS / BL / AG and to all pharmacies from the Toppharm group). From 280 pharmacies enrolled, 143 (51.5%) returned the questionnaire. Thirty-five (24.5%) of them stated to be sceptic regarding the PMC and were not motivated to implement the service in their pharmacy, while 108 (75.5%) rated the service positively. Out of them, 51 (47.2%) already were PMC-providers, while 57 (52.8%) did not offer it, yet. The positive group named time

resources (n=105, 76.6%,) and human resources (n=98, 71.5%) as main barriers for offering a PMC. The sceptics within the pharmacists argued that the patients were not willing to pay for this service (n=25, 71.5%).

Out of 143 pharmacies answering the survey, 15 were interested in participating on a focus group discussion. Finally, six pharmacist joined a meeting on 12th April 2011. The participants all stated that recruitment of the very first patient for a PMC was the main barrier for implementing the service in daily practice (*'The first is the worst!'*). Further, training based on realistic case series from a community pharmacy setting and explicit communication aids were expected to be delivered through the regional or national pharmacists' associations.

7.7.3 Pharmacists' perception - results from the evaluation project

During the evalPMC project, the participating study pharmacists were invited to fill in a questionnaire concerning their perspective of the PMC as newly introduced service in Swiss community pharmacies. The survey was carried out online and anonymously after completion of the study using the software Flexiform 2.6.9. The evaluation of pharmacists' perspective was conducted four weeks after study end individually in each study region by voluntary online survey. Out of 59 pharmacists at T-28, a total of 50 (84.7%) completed the survey. Their estimation of time needed to prepare, conduct, and finalise a PMC is shown in table 12. The time needed to follow additional study protocols according to CRFs was not taken into account.

Table 12 / Pharmacists' estimations of time needed for a PMC [min] (n=50)

	Mean	SD	Min / Max
Preparation	13.8	10.86	2 / 60
Conducting	29.5	10.57	15 / 60
Finalising	10.6	6.11	5 / 30

Study pharmacists reported a high improvement in the relationship with the patient and they considered the PMC as a very important service (Table 13).

Table 13 / Pharmacists' estimations about the PMC as a service (n=50)

	Median	(Range)
How has your personal relationship with patients changed because of providing PMCs? *	5	(3-5)
How important do you consider the PMC service for pharmacists? **	4	(2-4)

* 5-point-likert-scale: 1=worsened, 3=no change, 5=improved;

** 4-point-likert-scale: 1=totally unimportant, 4=very important

At study start, pharmacists' experiences in conducting medication reviews were low for 72 % of study pharmacists. They stated having provided less than five PMC before study start.⁹⁰ The wide range of time needed to prepare a PMC among pharmacists indicates heterogeneous strategies used on how to perform the service in practice. The findings concerning time consumption in preparation and finalising a PMC highlight the need for further professional training and/or higher remuneration, since the pharmacists' association did not consider this extra time when negotiating reimbursement with the health insurance companies.

7.7.4 Sub-analysis of the current remuneration fee for the PMC

During her postgraduate education course in health economy, Ms Marlen Schneider analysed the data from the evalPMC project regarding cost coverage ratio of the current remuneration of the PMC.¹⁰⁶ She provided a full cost calculation based on the time a PMC takes a pharmacist (30-35 min). She considered expenses of pharmacy staff, operational costs (i.e. private counseling area) and material costs of a standard pharmacy based on ROKA data.¹⁰⁷ She concluded that the service causes the pharmacy costs of CHF 73.05, indicating a difference of CHF 24.45 (+ 50.3%) to the current reimbursement of CHF 48.60. Thereby we need to consider that time needed for preparation and finalising the service were not taken in account. According to the health insurance act, compensations should be economically, indicating the need for further negotiations with health insurance companies.

8 PROJECT C – Screening for pharmaceutical care issues in community pharmacies

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- 8.1 Prevalence of unreached cardiometabolic targets among treated patients – sub analysis of data from a community pharmacy screening campaign in Switzerland [C1]

Short report

(unpublished)

Based on a poster presentation at the 7th working conference of the Pharmaceutical Care Network Europe, Manchester, United Kingdom, March 23-26, 2011

8.1.1 Abstract

Title: Prevalence of unmet cardiometabolic targets among treated patients – sub-analysis of data from a community pharmacy screening campaign in Switzerland

Aim of study: Screening for cardiometabolic risk factors provided by community pharmacies attract also patients already treated for cardiovascular risks. A previous retrospective analysis of data from 4380 subjects demonstrated that one third of patients with prescribed medicines for antihypertensive (AHT) and lipid modifying therapy (LMT) did not reach their biomarker targets as defined by guidelines. This prospective study aimed at confirming the results of the pilot study based on data that was collected within a refined screening campaign with standardised measuring methods and specific training of pharmacists.

Method: In a screening campaign for cardiometabolic risk factors, blood chemistry, blood pressure (BP), waist circumference, drug therapy and physical activity were assessed in Swiss pharmacies arranged in the group TopPharm in April 2010.

“Not on target” was defined as having a BP $\geq 140/90$ mmHg (systolic/diastolic BP), or ≥ 150 mmHg (isolated systolic BP) for patients with a prescription for AHT, LDL-C > 3.4 mmol/l for patients with LMT, fasting glucose ≥ 8.0 mmol/l for subjects with antidiabetic treatment (ADT) or if WC was > 88 cm for women or > 102 cm for men.

Results: From a total of 1'347 screened subjects, 329 (24.4%) were eligible because they had a prescription for either AHT, LMT, ADT or any combination. Increased WC was evident in 183 (= 55.6%). Of 261 patients with AHT, 106 (40.6%) were not on target because they violated either the systolic/diastolic (n=62, 23.8%) or the isolated systolic BP (n=44, 16.9%) criterion. LMT was prescribed in 122 patients, of which 38 (31.2%) were not on target. Glucose targets were not reached by 8 (27.6%) of 29 patients with ADT.

Conclusion: In conclusion, screening detects an important proportion of patients (43.8%) who despite prescribed therapy fail to achieve treatment targets. Thus, validated interventions are needed to support community pharmacies in addressing contributing factors to therapy failure, such as non-compliance, unfavourable lifestyle, drug interactions, improper dosing.

8.1.2 Introduction

Screening for cardiometabolic risk factors provided by community pharmacies attract also patients already treated for cardiovascular risks. A previous retrospective sub-analysis of data from 4380 patients demonstrated that one third of patients with prescribed medicines for antihypertensive and lipid modifying therapy did not reach their biomarker targets as defined by guidelines.¹⁰⁸ As data on drug therapy of screened pharmacy customers was only one additional item of the protocol, conclusion of this sub analysis was hampered by missing data and by doubts about the quality of this additional data assessment. Therefore, we adapted our protocol and added a mandatory section on medical history and drug treatment.

8.1.3 Methods

Screening for metabolic syndrome and cardiovascular risks was performed within the scope of a campaign performed by a group of 98 independent community pharmacies during April 2010 in the German speaking part of Switzerland. Collected data included all information needed for individual cardiovascular risk assessment based on the PROCAM-score and the assessment of risk for metabolic syndrome.¹⁰⁹ The screening protocol was developed by the Pharmaceutical Care Research Group, based on a former screening protocol but with more specific questions and a refined structure. Notably, the new screening protocol comprised three mandatory sections:

- under treatment for cardiovascular disease and/or diabetes (yes / no)
- history of stroke and / or insult and / or transient ischemic attack (yes / no)
- drug treatment for antihypertensive therapy (AHT), antidiabetic therapy (ADT) and lipid modifying therapy (LMT), aspirin, other (checkboxes and free text for product names)

In a mandatory one-day course, pharmacists were trained and guidelines for triage were distributed. Advertisement was published in the customers magazine and in shopping windows. All customers aged ≥ 18 years were approached. There were no additional inclusion criteria for screening and no selection criteria for analysis.

All screening protocols were scanned by an automated form processing software (Teleform®; Cardiff Software Inc., USA) and analysed with SPSS V18.

Patients with a prescription for either AHT, LMT, ADT, or combined therapy were analysed with respect to the corresponding biomarker (e.g. blood pressure for AHT). Patients were grouped into „on target“ and „not on target“ based on the following cut-offs.^{109,110}

- Blood pressure (BP) ≥ 140 and/or 90 mmHg (systolic/diastolic BP), in diabetic patients ≥ 135 and/or 85 mmHg
- Low-density lipoprotein cholesterol (LDL-C) ≥ 3.4 mmol/l
- Fasting blood glucose (FBG) ≥ 7.2 mmol/l

Waist circumference was taken as another risk factor.¹¹⁰ A waist circumference ≥ 88 cm for women and WC ≥ 102 cm for men was defined as optimisable and involved appropriate counseling. Furthermore, we screened for patients with risk for metabolic syndrome¹¹¹ and medium to high risk using the PROCAM score, corrected by a factor 0.7 for adaptation to Switzerland.¹¹²

8.1.4 Results

From a total of 1'347 screened subjects, 329 (24.4%) were eligible because they had a prescription for either AHT, LMT, ADT or any combination. Of 261 patients with AHT, 161 (61.7%) were not on target because they violated their individual systolic / diastolic BP criterion. LMT was prescribed in 122 patients, of which 38 (31.2%) were not on target. Glucose targets were not reached by 14 (48.3%) of 29 patients with ADT. Out of 68 patients with combined drug therapy, 14 (20.6%) failed in reaching two of their target outcomes.

Increased waist circumference was evident in 188 of 329 patients under therapy (57.1%). Of the 198 patients „not on target“, 120 (60.6%) showed heightened waist circumference.

Out of 913 subjects without any therapy 220 (24.1%) were newly identified with either a risk for metabolic syndrome (n = 168, 76.4%) and / or >medium risk (PROCAM score 10-20%, n = 80, 36.4%), and / or high risk (PROCAM score >20%, n = 13, 5.9%).

8.1.5 Discussion

BP, FBG, and LDL-C are established surrogate outcomes of AHT, ADT and LMT. A gap between measured biomarker levels and target values according to guidelines indicates suboptimal therapy effectiveness.

In our study, biomarker targets for AHT, ADT or LMT remained unreached in more than half of the therapies. Similar extent of therapy failure in primary care is well known¹¹² but up to now, responsibility for improved achievement of target values was mainly attributed to medical care.

Our study highlights important opportunities for pharmaceutical care. Assessment of a minimal set of biomarkers in community pharmacies is feasible either for screening of asymptomatic subjects or for monitoring treated patients.

Further research needs to address the impact of pharmacist's interventions on improved target achievement, mainly through adherence support and life-style optimization. In particular, obesity in 60% of patients not reaching biomarker targets calls for action. Obviously, such interventions need a close collaboration with physicians.

8.1.6 Conclusion

In conclusion, screening campaigns unintentionally attract an important proportion of patients who fail to achieve treatment targets despite prescribed therapy. Thus, in addition to interventions for patients newly identified to be at risk for cardiovascular disease validated interventions are needed to support community pharmacies in addressing contributing factors to therapy failure, such as non-adherence, unfavourable lifestyle, drug interactions, and improper dosing.

8.2 Swallowing difficulties with medication intake assessed with a novel self-report questionnaire in patients with systemic sclerosis – a cross sectional cohort study [C2]

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8.2.1 Abstract

Objectives: To assess swallowing difficulties (SD) with medication intake in patients suffering from systemic sclerosis (SSc) with a novel self-report questionnaire.

Design and setting: Based on a systematic literature review, we developed a self-report questionnaire and approved it by an expert panel. Subsequently, we sent the questionnaire by post mail to SSc patients of the European Centre for the Rehabilitation of Scleroderma Rheinfeld, Switzerland.

Participants: Patients were eligible if diagnosed for SSc, treated at the centre, and of age ≥ 18 years at study start.

Main outcome measures: Prevalence and pattern of SD with medication intake, including localisation and intensity of complaints.

Results: The questionnaire consisted of 35 items divided into the five sections complaints, intensity, localisation, coping strategies, and adherence. Of the 64 SSc patients eligible in May 2014, 43 (67%) returned the questionnaire. Eleven patients reported current SD with medication intake (prevalence 26%), while nine (21%) patients reported past SD that had been overcome. Among these 20 patients, self-reported swallowing difficulties were localised mostly in the larynx (43%) and the oesophagus (34%), were of strong to unbearable intensity (25%), and lead to modification of the dosage form (40%). Adherence was poor for 13 (30%) of all patients but was not related to SD ($p=0.262$).

Conclusion: Knowledge of the pattern of complaints with medication intake, i.e. localisation and intensity, may guide healthcare professionals when choosing the adequate therapy option and enable tailored counseling.

Trial registration: Clinical trial registry database <https://clinicaltrials.gov/> (Identifier: NCT02105818; first entry on March 28, 2014).

8.2.2 'What this paper adds'

What is already known on this subject?

- Swallowing difficulties with medication intake is frequent in ambulatory patients.
- Assessment tools focus on deglutition disorders with food and liquids and not on medication intake.
- Systemic sclerosis (SSc) is a rare multisystem autoimmune disease and patients are prone to develop swallowing difficulties.

What this study adds:

- We developed a novel self-report questionnaire to assess swallowing difficulties with medication intake.
- A heterogeneous pattern of complaints including localisation and intensity was assessed in a homogeneous population.
- An unprecedented comprehensive insight into the medicines use in everyday life of SSc patients was achieved.

8.2.3 'Strengths and limitations of the approach'

Strengths of this study

- Based on a systematic literature search a patient self-report questionnaire assessing swallowing difficulties with medication intake was developed.
- Face validity of the initial questionnaire involved professional experts as well as patients.
- The use of a visual-analogue-scale to indicate intensity and a human profile to indicate the localisation of complaints ensured that answers were provided independently of language and health literacy.
- First validations of the questionnaire were performed in patients suffering from systemic sclerosis, a highly specific population prone to develop swallowing difficulties.

Limitations of this study

- We did not confirm the patient reported outcomes with clinical diagnosis of the swallowing process or of gastrointestinal disorders.
- Since systemic sclerosis is a rare disease, the investigated cohort provided a limited number of patients.

8.2.4 Introduction

Swallowing is a complex physiological process. Causes for interferences with this process are manifold and include pathophysiological changes in anatomical structures (e.g. gastro-oesophageal reflux disease) or detectable dysfunction of the swallowing process (e.g. sarcopenia). A somatoform disorder of the upper gastrointestinal tract (globe syndrome) is suspected when no organic cause can be found.^{113,114} Solid oral dosage forms are widely used for therapeutic purposes in ambulatory care. Swallowing difficulties are a highly specific drug-related problem and are reported by 9-27% of patients.^{115,116} Such problems may affect the patient's quality of life, lead to hazardous coping strategies (splitting or crushing pills) and reduce adherence to medication regimens.¹¹⁵

Several questionnaires assessing dysphagia (i.e. swallowing problems) in general are available in literature¹¹⁷ but very few instruments detect swallowing difficulties with medication. Available questionnaires were primarily developed for research purposes and are too comprehensive to be used in practice by healthcare professionals.¹¹⁸ Reports mention poor linkage between patients' complaints and diagnostic findings.^{119,120} We hypothesise that the 'one single question fits all' approach (e.g., 'Do you suffer from swallowing difficulties when taking your medication?') represents a first step for a loose detection of individual issues with medication intake, but needs further in-depth assessment to guide a healthcare professional when choosing therapy options or optimising a patient's medicines. We therefore developed a novel self-report questionnaire assessing swallowing difficulties with medication intake and conducted pilot testing on patients with systemic sclerosis (SSc).

Systemic sclerosis (SSc) is a rare multisystem autoimmune disease with a prevalence of 1-10 cases per 100'000 individuals in Europe.¹²¹ Due to vascular remodelling, inflammatory reaction and abnormal fibroblast activation, systemic fibrosis leads to impaired circulation and fibrosis in skin and multiple inner organs. SSc is a chronic, often progressive disease of high morbidity and mortality. Organ failure might also include the gastrointestinal tract.¹²² Progressive worsening of the disease leads often to swallowing problems with food, liquids¹²³ and probably medicines. A common co-morbidity of patients suffering from SSc is sicca syndrome, which may also affect the swallowing process.^{124,125} Since SSc cannot be cured yet, treatment of organ manifestations remains the main therapeutic strategy usually involving oral medications.¹²⁶ Patient education, psychological support, and highly specialised physical therapy are essential to the management of SSc. The European Centre for the Rehabilitation of SSc in Rheinfelden,

Switzerland, serves the trinational region's one million residents and offers specialised care for patients suffering from SSc.

8.2.5 Methods

8.2.5.1 Systematic literature search and article eligibility

The objective of the search was to retrieve validated questionnaires that assessed swallowing difficulties with medication intake. The databases PubMed, CINAHL, and Embase were searched the 29th March 2014 according to the PRISMA statement,^{127,128} publication date before February 2014, without language restrictions, and with the keywords *deglutition disorders OR swallowing difficult*, drug dosage form*, interview* OR questionnaire**. The identified abstracts were screened for eligibility according the following inclusion criteria: i) human population ii) swallowing difficulties with medication intake assessed in a systematic and structured form as an outcome measure (e.g. interview guide), iii) full text publication in English or German language. The full-texts were then screened again for eligibility by two researchers. Discordance was resolved by consensus.

8.2.5.2 Development of the questionnaire

Items from the questionnaires retrieved from literature search were summarised, rephrased, and compiled into a patient self-report questionnaire. We termed the questionnaire SWAMECO for SWAllowing difficulties with MEdication intake and COping strategies. Face validation was performed with a panel of 11 experts (4 patients, 4 pharmacists, 2 speech-language pathologists, and one professor in pharmaceutical care). Positive statements on sections, content relevance, intelligibility, comprehensibility, impact on the patient's privacy, and length of a first draft were graded from 1 (totally disagree) to 4 (totally agree). The higher the value, the more positive the judgement.

8.2.5.3 Study design, sample, and recruitment

The cross-sectional cohort study took place at the European Centre for the Rehabilitation of Scleroderma, Rheinfelden, Switzerland. All patients fulfilling the new classification criteria for systemic sclerosis,¹²⁹ currently being treated at the centre and of age ≥ 18 years were eligible.

Diagnosis of dysphagia was established neither by radiographic assessment nor with a standardised bolus of water with which to take medication.

Eligible patients were invited by letter in March 2014 to participate in the study. They received a written overview of the study including purpose, an informed consent form (including consent to publish data), a SWAMECO self-report questionnaire and a demographics sheet (including confounding factors that may influence swallowing difficulties i.e., tobacco and alcohol consumption, unplanned weight loss (as sign of gastrointestinal manifestation in SSc), and diagnosed pneumonia in the past 6 months). The participants were asked to complete and return the informed consent form, the questionnaire, and the demographics form within 4 weeks.

8.2.5.4 Reporting standards and data analysis

The authors followed the STROBE reporting standards for observational studies. Patient characteristics and answers of face validity are presented as percentages or means with standard deviation. Chi-square test was used to compare group variables. P-values <0.05 were considered significant. Statistical analysis was conducted using SPSS Statistics Version 22 (IBM Corp, Armonk, NY, USA).

8.2.6 Results

8.2.6.1 Systematic literature search

A total of 47 articles were identified (Figure 6). After screening of titles and abstracts, 41 articles were excluded from further analysis (Table 14). The remaining six articles (Table 15) all reported results from observational studies with low level of evidence according to GRADE.¹³⁰ Four articles contained specific questionnaires.^{115,116,118,131} None of them was designed as a self-report form.

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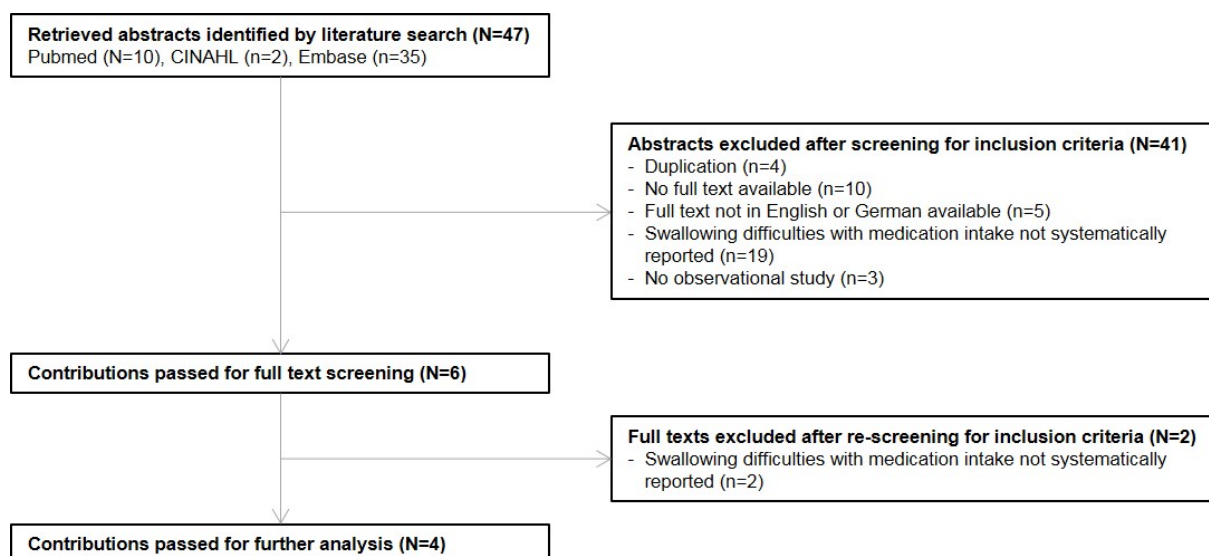


Figure 6 / Flow chart of systematic literature search

Table 14 / Excluded articles from the systematic literature search on swallowing difficulties with medication intake, published before February 2014 (n=37, without duplications). First author, year of publication, title and journal are given in alphabetical order.

First author	Year	Title	Journal
Aitichou M	2012	Crushing pills, an easy practice of an old problem? Evaluation of crushing practices in a geriatric long term care unit	Int J Clin Pharm
Andersen O	1995	[Problems when swallowing tablets. A questionnaire study from general practice] <i>Article in Norwegian</i>	Tidsskr Nor Laegeforen
Baker R	2010	Clinical results from a randomized, double-blind, dose-ranging study of pantoprazole in children aged 1 through 5 years with symptomatic histologic or erosive esophagitis	Clin Pediatr
Dabade TS	2009	Proton pump inhibitor compliance does not impact GERD symptom resolution	Gastroenterology
Fallon A	2011	An analysis of the impact of xerostomia on the quality of life of head and neck cancer patients receiving radiotherapy	Radiother Oncol
Fockens P	2010	Prospective randomized controlled trial of an injectable esophageal prosthesis versus a sham procedure for endoscopic treatment of gastroesophageal reflux disease.	Surg Endosc
Gawron AJ	2013	Esophageal Hypervigilance: A Construct for Reflux and Dysphagia Symptoms Based on Patient Reported Outcomes	Gastroenterology
Go J	2013	Problems with swallowing pills commonly relates to properties like size	Gastroenterology
Gonçalves MI	2008	Speech-language and hearing complaints of children and adolescents with brain tumors	Pediatr Blood Cancer

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Hanawa T	2012	[Questionnaire survey of air extruded jelly dosage form (I) - oral condition of elder patients and applicability of air extruded jelly formulation -] <i>Article in Japanese</i>	Yakugaku Zasshi
Hanssens Y	2006	Improving oral medicine administration in patients with swallowing problems and feeding tubes	Ann Pharmacother
Iwase S	2012	The clinical use of Kampo medicines (traditional Japanese herbal treatments) for controlling cancer patients' symptoms in Japan: a national cross-sectional survey	BMC Complement Altern Med
Kalf H	2013	Swallowing disorders in Parkinson's disease: As frequent and severe as you think?	Dysphagia
Kalf J	2011	Difficulty with pill swallowing in Parkinson's disease	Dysphagia
Kalf J	2011	Pathophysiology of diurnal drooling in Parkinson's disease	Mov Disord
Lazebnik LB	2010	[Gastroesophageal reflux disease in the elderly patients: epidemiology, clinical features, therapy] <i>Article in Russian</i>	Eksp Gastroenterol Klin
Lucia M	2010	Analysis of pharyngeal phase of swallowing hard gelatine pills in asymptomatic adults	Dysphagia
Martinez de Haro LF	2008	[Outpatient monitoring of oesophageal pH with a catheter-free pH-meter (Bravo System). A Study of tolerance, safety and efficacy] <i>Article in Spanish</i>	Cir Esp
Marton I	2011	Evaluation of oral mucositis in children receiving intensive chemotherapy using proms questionnaire	Pediatr Blood Cancer
Mayadev AS	2008	The amyotrophic lateral sclerosis center: a model of multidisciplinary management	Phys Med Rehabil Clin N Am
McNally D	2012	Randomised, double-blind, placebo-controlled study of a single dose of an amylmetacresol/2,4-dichlorobenzyl alcohol plus lidocaine lozenge or a hexylresorcinol lozenge for the treatment of acute sore throat due to upper respiratory tract infection	J Pharm Pharm Sci
Moreto M	2013	Treatment of achalasia by injection of sclerosant substances: a long-term report	Dig Dis Sci
Nishimura N	2012	Prospective evaluation of incidence and severity of oral mucositis induced by conventional chemotherapy in solid tumors and malignant lymphomas	Support Care Cancer
Nito T	2013	Surgical management of intractable aspiration	Dysphagia
Obasan AA	2012	Assessment of compliance to treatment among ambulatory asthmatic patients in a secondary health care facility in Nigeria	Int J Pharm Sci Res
Ogata I	2008	[Some problems for dosage form based on questionnaire surveying compliance in patients taking tamsulosin hydrochloride] <i>Article in Japanese</i>	Yakugaku Zasshi
Payot V	2011	Prevalence of patients' difficulties in swallowing solid oral dosage forms	Int J Clin Pharm
Peterson KA	2010	Comparison of esomeprazole to aerosolized, swallowed fluticasone for eosinophilic esophagitis	Dig Dis Sci

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Sakellariou V	2013	Medication swallowing difficulties reported by adults with idiopathic Parkinson's disease and oropharyngeal dysphagia	Dysphagia
Sasaki CT	2013	Comments on selected recent dysphagia literature	Dysphagia
Seo H	2011	Longitudinal changes of the swallowing process in subacute stroke patients with aspiration	Dysphagia
Simons AJ	2013	Munich dysphagia test-Parkinson's disease (MDT-PD): A new clinical questionnaire for early assessment of dysphagia in Parkinson's disease	Dysphagia
Thinrungron N	2012	Alginate accelerates healing of post-endoscopic variceal ligation ulcers: A randomized-controlled trial	Gastrointest Endosc
Truter I	2012	An approach to dyspepsia for the pharmacist	SA Pharmaceutical Journal
Valenza V	2009	Role of oro-pharyngo-oesophageal scintigraphy in the evaluation of swallowing disorders in patients with myotonic dystrophy type 1 (DM1)	Medizinische Genetik
Verin E	2011	Submental sensitive transcutaneous electrical stimulation (SSTES) at home in neurogenic oropharyngeal dysphagia: a pilot study	Ann Phys Rehabil Med
Zibetti M	2014	Levodopa/carbidopa intestinal gel infusion in advanced Parkinson's disease: a 7-year experience	Eur J Neurol

Table 15 / Articles selected from the systematic literature research on swallowing difficulties with medication intake, published before February 2014. First author, year of publication, title and journal are given in alphabetical order. Articles in bold systematically investigated swallowing disorders and were selected to develop the SWAMECO questionnaire. A short summary is indicated in brackets.

<i>First author</i>	<i>Year</i>	<i>Title</i>	<i>Journal</i>
Kelly J	2010	Patients with dysphagia: experiences of taking medication (Open dialogue with patients exploring 3 questions: What problems do you have taking your medicines? How do you deal with any problems you have when taking medicines? What advice have you been given about coping with your swallowing problems?)	J Adv Nurs
Márquez-Contreras E	2008	Pharmacological compliance and acceptability of lansoprazole orally disintegrating tablets in primary care	Curr Med Res Opin
Marquis J	2013	Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies (Questionnaire with 16 questions in 7 dimensions: current number of daily oral prescribed medicines, demographics, swallowing difficulties, coping strategies for overcoming difficulties, impact on medication adherence and on daily functioning, perception of state of health, whether patients had notified their difficulties to their physician and pharmacist)	Int J Clin Pharm

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Mehuys E	2012	Medication management among home-dwelling older patients with chronic diseases: possible roles for community pharmacists	J Nutr Health Aging
Schiele JT	2013	Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms (Questionnaire with 32 questions in 5 major topics: demographics, medication intake habits, presence of diseases, attitude towards medication intake, coping strategies for overcoming difficulties)	Eur J Clin Pharmacol
Wright D	2002	Medication administration in nursing homes (Questionnaire for nurses with the sections: guidance on completion, respondent details, nursing home population demographics, extent of swallowing difficulties, methods used to overcome swallowing difficulties, experience of overcoming swallowing difficulties, opinions on the ease of changing medication)	Nurs Stand

8.2.6.2 Development of the questionnaire

The existing categories ‘complaints’ and ‘coping strategies’ from the retrieved questionnaires were expanded with the new sections ‘localisation’ and ‘intensity’. The initial version of the questionnaire contained 32 items fitting on four pages as a DIN A4 double-sided colour printed brochure.

Face validity was given with a mean overall agreement of 3.7 (Table 16). The experts agreed with all items (no deletion), proposed 27 changes in the wording or the layout, 2 changes in the scales (adding the category 'no answer' for 2 items), and suggested the separation of 1 item in 2 single items, the addition of 1 free text item, and the inclusion of ‘choking’ as a single item.

Table 16 / Expert judgement on the SWAMECO questionnaire (n=11) by scoring from 1 (totally disagree) to 4 (totally agree). One answer is missing.

Positive statement to judge on	Number of answers	Mean (Standard deviation)
The handling of the questionnaire is clear and logical for me	11	3.7 (0.45)
The questions are formulated in a generally understandable way	11	3.8 (0.39)
The questions are formulated precisely	11	3.5 (0.50)

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The questions have not violated my privacy	10	3.7 (0.64)
The response scales offer all options for my answer	11	3.6 (0.48)
The typeface is legible	11	3.8 (0.39)
The time value of 15 minutes for completing the questionnaire is appropriate	11	3.6 (0.78)

All changes were implemented. The final questionnaire contained 35 items (Table 17) and was re-designed as a DIN A3 landscape format and folded, to be provided as a double-sided colour-printed brochure.

Table 17 / Sections, number of items and type of response scales of the SWAMECO questionnaire

Section	Number of items	Response scales
Complaints	15	Dichotomous (y/n) / 4-point Likert (1=totally agree; 4=totally disagree)
Intensity	1	Visual analogue (scale 0-10 cm, 0=no complaints; 10=unbearable complaints)
Localization	1	Visual analogue (human profile)
Coping strategies	10	Dichotomous (y/n) / Open questions with free text and pre-structured single items
Adherence (MMAS-8D)	8	Dichotomous (y/n) / 5-point Likert

Item 1 asked for current oral medication intake (yes/no). The presence of swallowing difficulties with intake of liquid (item 2), food (item 3) and medication (item 4) was evaluated on a 3-point Likert scale (1=current; 2=past; 3=never suffered from swallowing difficulties). Complaints (items 5-14) were rated on a 4-point Likert scale (1=totally agree; 4=totally disagree) and contained four items related to the sicca syndrome^{132,133} (item 6: “I have a dry mouth during daytime”). Intensity of the complaints (item 15) was rated on a visual analogue scale (VAS; 0/laughing smiley=no complaints; 10/weeping smiley=unbearable complaints). A drawing of the upper human body from head to stomach (item 16) was divided in four segments according to the physiological swallowing process¹³⁴ i.e. oral preparatory stage (mouth), oral propulsive stage (throat), pharyngeal stage (pharynx), oesophageal stage (oesophagus). Patients placed a cross to mark the localisation of their complaints at the corresponding site. Item 17 assessed involved medicines (product name, dosage, and intake interval). Position of the head while swallowing medication (item 18) was asked with three predefined answers (chin toward chest; head straight ahead; head straight back). Since the chin-tuck technique, i.e. to put chin down,

changes pharyngeal dimensions through postural manoeuvre, it is recommended by speech specialists to move the bolus anterior in patients with dysphagia.¹³⁵ Thus, we considered this technique as appropriate for patients reporting swallowing difficulties. Coping strategies were reported by answering open questions with free text options or predefined answers (items 19-20) and closed questions with dichotomous options (items 21-27). The eight validated German questions on adherence to medication (Morisky Medication Adherence Scale MMAS-8D)¹³⁶ completed the SWAMECO questionnaire. A sum score below 6 indicates non-adherence.

8.2.6.3 Cohort study

From the 64 eligible patients, 43 (67%) returned the questionnaire, 35 (81%) of them within 3 weeks. Mean age was 54.6 years (standard deviation 12.23), the majority were female (n=36, 84%) and Swiss (n=32), 10 were Germans, and one was Austrian.

Fully completed questionnaires were obtained from 28 patients (65%). Of 46 missing data, 17 (37%) concerned an item with a block of responses (*'Taking oral medication triggers i) a choking, ii) a cough, iii) nausea, iv) tightness while swallowing.'*). In 10 (22%) cases, questions with a free text option were left unanswered, i.e., i) *'Describe how you feel the discomfort of swallowing medication(s).'* ii) *'Which of your medication(s) cause swallowing difficulties?'*

Current swallowing difficulties were reported by 11 patients (26%) and past difficulties by 9 (21%) patients. Two patients left the question on swallowing difficulties with medication intake unanswered (missing data), but answered the question on swallowing difficulties with food or liquids in the negative. Thus, they were assigned to the group without complaints with medication intake for further analysis. Presence of possible confounding factors (tobacco and alcohol consumption, unplanned weight loss) was not correlated to swallowing difficulties with medication intake (data not shown).

Appropriate swallowing technique i.e., the chin-tuck technique, was mentioned in 4 (9%) cases. Patients with current complaints tilted their head backwards as frequent as patients with past or no difficulties (5/11, 45% vs 11/29, 38%; 3 missing; p=0.467). All 43 patients reported to support their medication intake with a sip of water, and 11 patients had to choke regularly (26%). Non-adherence (MMAS-8D<6) was present in 30% of all patients and did not correlate with current swallowing difficulties (5/11, 46% vs 8/28, 29%; 4 missing values; p=0.262).

8.2.6.4 Pattern of difficulties with swallowing medications

Of 20 patients with current or past self-reported swallowing difficulties with medication intake, 19 (95%) marked their complaints on the human profile (Figure 7) with a total of 35 locations and a median number of marks per patient of 2 (range 1-4). Most marks were placed at the pharynx (n=15; 43%) and oesophagus (n=12; 34%). Five marks were placed outside the gastrointestinal tract.

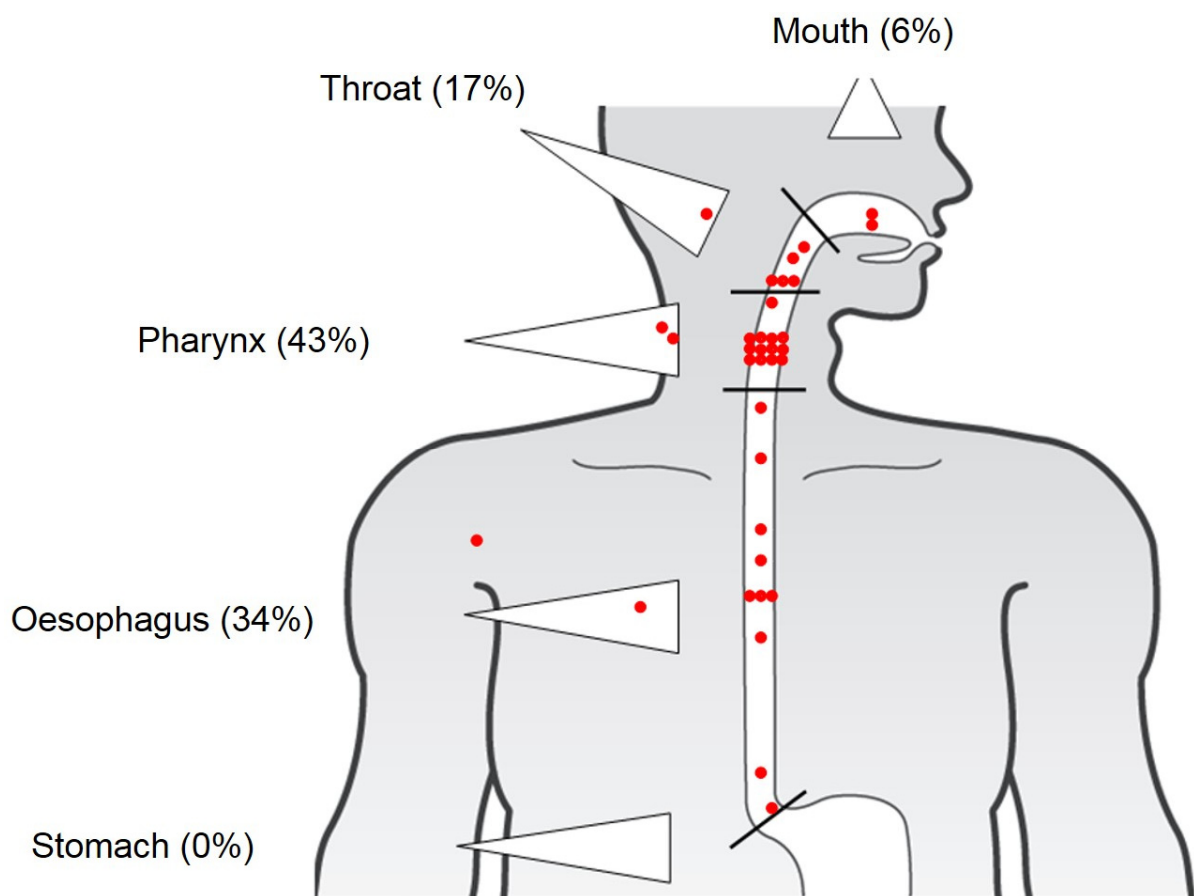


Figure 7 / Localisation of patient's reported swallowing difficulties with medication intake (35 marks provided by 19 patients). The segments correspond to the stages of the physiological swallowing process i.e., oral preparatory stage (mouth), oral propulsive stage (throat), pharyngeal stage (pharynx), and oesophageal stage (oesophagus).

The 20 patients indicated the intensity of complaints with a median of 4.4 (range 0.8 to 9.4). After repartition in tertiles, the intensity was low for 6 (30%) patients, moderate for 9 (45%) patients, and strong for 5 (25%) patients. All patients but one (19 patients; 95%) reported pills or capsules stuck in the throat and could mostly name them (Table 4). In 9 of 23 (39%)

medicines involved, available drug form alternatives could have been recommended by a healthcare professional (Table 18) according to the summaries of product characteristics currently in use in Switzerland.¹³⁷

Table 18 / Active pharmaceutical ingredient, form and frequency of medication reported to cause swallowing difficulties (n=21) and available drug form alternatives according the Swiss summaries of product characteristics.

Active pharmaceutical ingredient	Drug form	Mentioned	Therapeutic group	Alternative drug form available?	Crushing possible?
Prescription drugs (n=14):					
Acetylsalicylic acid (low dose)	Tablet	1x	Antiplatelet	Yes	-
Amlodipine	Tablet	2x	Calcium channel blocker	No	Yes
Dutasteride / Tamsulosin	Capsule	1x	Urologic	No	No ⁺
Esomeprazole	Tablet	1x	Proton pump inhibitor	No	No [*]
Levothyroxine	Tablet	2x	Thyroid hormone	No	Yes
Nifedipine	Tablet	1x	Calcium channel blocker	No	No ^{**}
Omeprazole	Capsule	1x	Proton pump inhibitor	No	No ⁺⁺
Pantoprazole	Tablet	1x	Proton pump inhibitor	Yes	-
Prednisolone	Tablet	1x	Glucocorticoid	No	Yes
Pregabalin	Capsule	1x	Antiepileptic	No	No ⁺
Ranitidine	Tablet	1x	H2 receptor antagonist	Yes	-
Sulfamethoxazole / Trimethoprim	Tablet	1x	Antibiotic	Yes	-
Tadalafil	Tablet	1x	PDE 5 receptor inhibitor	No	Yes
Valsartan / Amlodipine / Hydrochlorothiazide	Tablet	1x	Calcium channel blocker / Diuretic	No	Yes
Self-medication (n=3):					
Acetylsalicylic acid (high dose)	Tablet	2x	Analgesic	Yes	-
Ibuprofen	Tablet	2x	Analgesic	Yes	-
Paracetamol (Acetaminophen)	Tablet	1x	Analgesic	Yes	-
Nutritional supplements (n=4):					
Fish oil	Capsule	1x	-	No	No ⁺
Vitamin C	Tablet	2x	-	Yes	-
Unspecified herbal drug	Tablet	2x	-	Unknown	-
Unspecified enzyme product	Capsule	1x	-	Unknown	-

^{*} No crushing, only floating for suspension possible; ^{**} No crushing recommended due to photosensitivity; ⁺ Opening of capsule possible; ⁺⁺ Opening of capsule but no crushing of pellets possible, only floating for suspension possible

The most frequent complaints related to sicca syndrome were ocular and nasal dryness (80%), dry mouth during daytime (80%), the need to drink water for better speaking (70%), and burning sensations (35%). Four patients (20%) were afraid of taking their medication because of the complaints. Half of the patient (n=10) had been worried about their swallowing difficulties during the past 4 weeks (Figure 8).

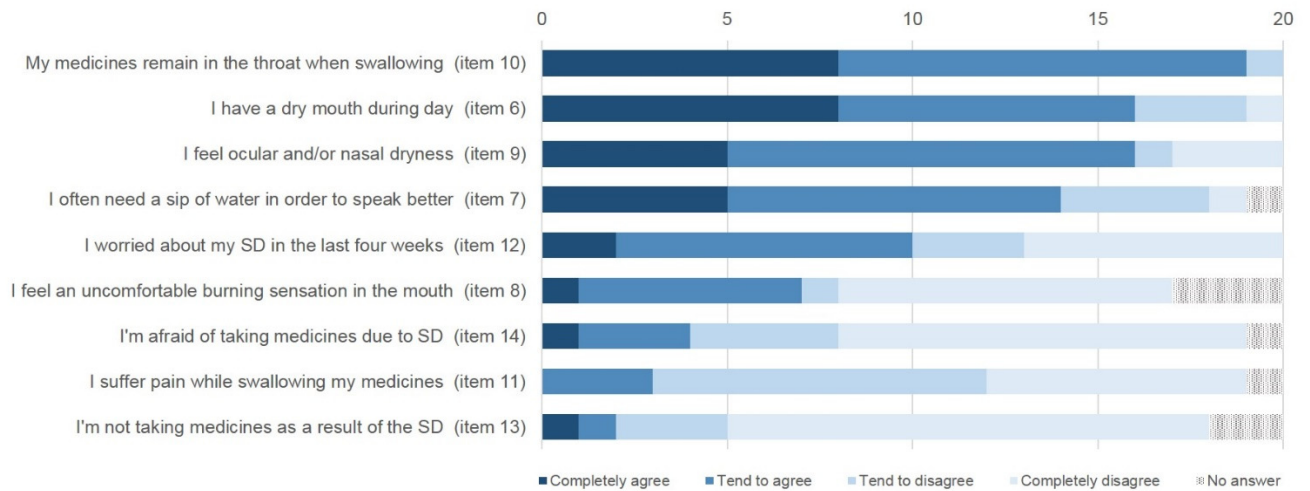


Figure 8 / Answers of the 20 patients who reported swallowing difficulties (SD) concerning general complaints associated with deglutition disorders. The darker the bar, the higher the burden

Coping strategies were reported by 10 patients who modified the dosage form (n=8; 40%) or stopped medication (n=2; 10%). Modification resulted in splitting tablets (n=8; 100%), opening capsules (n=4, 50%), dissolving medication in liquids (n=2; 25%) or crushing pills (n=1; 13%). Only one patient consulted a healthcare professional before applying the coping strategy.

8.2.7 Discussion

We used published questions assessing swallowing difficulties with medication, amended them, and developed a self-report questionnaire. Face validity confirmed the completeness, clarity and appropriateness of the tool. The use of a VAS with smileys to indicate intensity and of a human profile to indicate the localisation of complaints ensured that answers are provided independently of language and health literacy. The self-report structure provides a snap shot of a patient's experience with medication intake and their swallowing difficulties. Simultaneously, it avoids time pressure, because a self-report questionnaire might be filled in advance of a consultation. Further, by using patient's self-competencies to assess a subjective problem, conceivable communication difficulties become circumvented.

8.2.7.1 Prevalence of swallowing difficulties in patients with systemic sclerosis

An unprecedented comprehensive insight into the medicines use in everyday life of SSc patients was achieved. In total, difficulties with swallowing medication concerned as much as 46% of the surveyed patients at some point in time. The self-reported prevalence rate of current swallowing difficulties in this population was high (26%) and in the upper range of studies performed in a more general population,^{115,116} while the rate of past difficulties (21%) was somewhat lower and indicative for sustained complaints. This may be explained by the progressive nature of SSc disease that results in continuous suffering. These results highlight the need for a greater awareness of healthcare professionals on swallowing difficulties in this population.

8.2.7.2 Localisation and intensity of swallowing difficulties with medication intake

In contrast to others,^{115,116} the SWAMECO self-report questionnaire was able to detect a heterogeneous pattern of complaints. On one hand, the human profile allows the patient to indicate precisely the localisation of the complaints. On the other hand, a number from 0-10 from a psychometric response scale is able to quantify the subjectivity of the intensity of complaints.

Previous studies demonstrated that the ability of patients to self-localise dysphagia symptoms is weak,¹¹⁹ especially in those with oesophageal problems¹²⁰ such as SSc patients. This conclusion was generally drawn from a poor correlation between localisation of patients' complaints and objective findings. Other reports similarly indicate that the level of symptoms (i.e., the intensity) is not reliable for predicting the location of the responsible lesion¹³⁸. Inversely, many functional abnormalities can be found with radiographic evaluation or videofluoroscopy that are unrelated to the patients' symptoms.¹²⁰ In summary, symptom referral varies between patients and can hardly be used as diagnostic tool. Regardless their correlation to diagnostic findings, subjective complaints should guide healthcare professionals when choosing the adequate therapy. The SWAMECO questionnaire may support healthcare professionals when assessing the prevalence, localisation and intensity of complaints with medication swallowing. In analogy to pain scales, intensity remains an important marker of patient's burden with medication intake and enables tailored interventions to overcome hazardous coping strategies.

8.2.7.3 *Symptoms referring to sicca syndrome*

Since patients suffering from SSc often develop sicca syndrome,¹³⁹ we added specific items covering xerostomia and ocular or nasal dryness. The corresponding high response to these complaints (80%) confirm the appropriateness of the SWAMECO questionnaire to catch these symptoms. The questionnaire can represent a starting point for deeper medical clarification and initiation of individual counseling.

8.2.7.4 *Coping strategies to overcome swallowing difficulties with medication*

In our study, coping strategies used by patients i.e., opening capsules or crushing pills without informing healthcare providers, are of great concerns. Recent studies revealed that patients are often not aware of safety issues when they modify medication dosage forms.¹⁴⁰ In our survey, patients were asked to report their coping strategies in a free text format. The healthcare provider might use this individual information for further clarification or counseling e.g., by performing an in-depth medicines use review focusing on coping strategies in daily use and empower the patient with recommendations for safe and appropriate medication use. However, pharmacists and physicians rarely question patients about swallowing difficulties, and very few professionals systematically ask patients about this specific drug-related problem¹¹⁵. Since healthcare professionals claim lack of time and personal resources, new screening tools such as the SWAMECO may reduce the workload and involve patients at an early stage.

Even if all patients reported administration of water to ease the swallowing process, the amount of liquid remained unclear and might be critical. Schiele et al. observed that 40.7% of all patients in their study took their medicines with less than half a glass of water.¹¹⁶ Similarly, the swallowing technique of the medication-water bolus showed potential for improvement regarding the low proportion of patients (9%) with head tilted forwards, the strategy regarded as best practice.¹⁴¹ The use of the SWAMECO questionnaire may uncover some individual practices that might jeopardise the treatment's outcome.

In our survey, the majority of medications reported for causing swallowing difficulties were essential therapeutic medications for the treatment of SSc (calcium channel blocker / PDE5 receptor inhibitor) or for the prevention and treatment of gastro-oesophageal reflux disease (proton pump inhibitor / H2 receptor antagonists). For many of the involved products, available

drug form alternatives could have been recommended. Continuous and appropriate use of the medicines is mandatory to slow down the progression of the disease. Consequently, any factor that may influence their efficacy needs the attention of the involved healthcare providers.

8.2.7.5 Adherence to medication

Self-reported non-adherence was indicated by one third of our patients. Compared to other diseases with similar characteristics such as noticeable symptoms, chronicity, and evolution with degradation, our result is much lower than the 91% of outpatients with rheumatoid arthritis¹⁴², or the 91% of elderly patients with asthma who indicated non-adherence with the same method of measurement i.e. Morisky questions.¹⁴³ We expected a higher proportion of non-adherent patients when reporting current swallowing difficulties. As the participating patients were rather young, with full cognitive capabilities and highly motivated to take their medicines as prescribed, we can hypothesise that the observed overall higher adherence to medication results from care an intense care and self-empowerment provided by the specialised centre. It remains unclear whether the pattern of swallowing difficulties with medication intake in a more general population would be similar.

8.2.7.6 Strengths and limitations

Our study has several strengths. First, face validity of the initial questionnaire involved as well professional experts as patients who commented predominantly the wording of individual items. They made a significant contribution to the comprehensiveness of the questions and thus, to the acceptance of the questionnaire and the feasibility of the study. This may explain the high response rate of 67% without the use of any reminders. Similarly, the patient-oriented language may explain that the majority of missing values concerned personal items. Patients deliberately refused to answer, rather than they failed to because of understanding difficulties. Second, the surveyed population suffers from a very rare disease and obtains specialised care in the rehabilitation centre. Thus, we investigated heterogeneous symptoms in a highly homogenous population in regards to the underlying disease. Consequently, our questionnaire may be seen as able to catch all symptoms of swallowing disorders.

We acknowledge some limitations. First, our results are patient reported outcomes and thus, subjective information. We did not confirm the findings with clinical diagnosis of the swallowing

process or of gastrointestinal disorders. Consequently, a correlation between the reported swallowing difficulties and a clinical implication is not possible. Meanwhile, causes of swallowing difficulties must be carefully queried. The SWAMECO questionnaire remains inconclusive on the cause of the symptoms, but offers initial opportunity for further, targeted investigations. Any disruption or impairment in patient's medicines use needs a clarification by a healthcare professional to ensure patient safety and long-term adherence. Therefore, no detailed diagnosis is needed to address swallowing difficulties with medication intake during patient counseling. Second, since SSc is a rare disease, the investigated cohort provided a limited number of patients. However, the European Centre for the Rehabilitation of Scleroderma Rheinfelden is a leading centre in the German-speaking region of Europe and takes care of a considerable number of SSc patients. Further studies might investigate a larger cohort in a more general population.

8.2.8 Conclusion

Through self-report questionnaires, patients can efficiently provide individual information that can be used for relevant counseling and tailored interventions. We developed the first self-report questionnaire assessing swallowing difficulties with medication intake. Pilot testing of the SWAMECO questionnaire in patients with SSc, a highly specific population prone to develop swallowing difficulties, proved feasibility and acceptance of patients. Prevalence of swallowing difficulties with medication intake in the investigated population was remarkably high. Reported localisation and intensity of complaints as well as uncovered potentially hazardous coping strategies indicated the need for in-depth counseling by healthcare professionals. Validation of the SWAMECO self-report questionnaire should be continued in the general population, including evaluation of its complementary value in patient care.

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Competing interest statement: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the

submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Authors' contributions: RAs and MMe performed the literature search. As main investigators, MMe and IAr conceived the trial design and wrote the ethical proposal as well as the study protocol. Thereby, they were supported by RAs. MBu and KHe helped in developing the measurement tools and ensured a balanced expert panel thanks to their professional network. In his role as director of the European Centre for the Rehabilitation of Scleroderma, MBu recruited patients and ensured compliance with study protocol. MMe and RAs accessed and analysed the retrieved data. MMe and IAr prepared the first draft of the manuscript. MBu, RAs, and KHe contributed to the discussion and reviewed the manuscript. They all approved the final version to be published.

Ethical approval and trial registration: The study was approved by the local ethics committee (EKNZ 2014-013) and registered in the international clinical trial registry platform www.clinicaltrials.gov (NCT02105818, first entry March 28, 2014).

Data access statement: All authors had full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement: Participants gave informed consent for data sharing. Patient level data are available from the corresponding author.

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Transparency statement: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Funding: There was no funding of this project (investigator-initiated study).

9 GENERAL DISCUSSION

This thesis aimed at giving a general overview over clinical pharmacy services already performed in the Swiss hospital setting and discussing the strengths and limitations of pharmacist-led medication reviews in primary care by evaluating the Swiss Polymedication Check. In addition, specific opportunities for further clarification through pharmacist-led interventions are highlighted in order to select patients at highest needs for future services.

9.1 Project A - Opportunities for clinical pharmacy service in patient care

To our knowledge, we performed the first representative survey among all Swiss hospitals to describe the pattern of resources of clinical pharmacists and corresponding services five years after establishing a national definition of clinical pharmacy. It may be interesting to the international audience that in certain regions of Switzerland physicians are allowed to dispense drugs themselves directly. Therefore, we were interested in differences in the provision of clinical pharmacy practice between these regions compared to those where pharmacies are exclusively dispensing medicine, investigating a major disrupting factor for interprofessional collaboration. While mapping clinical pharmacy practices in Swiss hospital, we also reported an obvious communication gap between ambulatory and stationary care – even within the same profession i.e. the hospital and the community pharmacists. To closer link hospital and community pharmacists, collaborative initiatives for postgraduate education i.e. acceptance of the recently established Certificate of Advanced Studies (CAS) in clinical pharmacy as a postgraduate program for both disciplines might become an interesting approach.

Transitions of care imply changes in the level, location, or providers of care. Community pharmacies are very often the first of all the healthcare providers involved after hospital discharge. Medication reconciliation is widely recommended to avoid unintentional discrepancies between patients' medications across transitions in care.¹⁴⁴ Reconciliation of therapies is much more than a puzzle game. When reconciliation is seen as the starting point for a structured pharmaceutical care service and is bundled with interventions aimed at improving care transitions post-discharge, health care utilisation may be reduced.¹⁴⁴ Further, Mulhem et al. observed 24-48 hours after discharge non-adherence in 20% of the patients.¹⁴⁵ Thus, a close follow-up is important and a simple telephone follow-up could be easily performed. However, when approaching potentially non-adherent patients, challenging

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problems can arise. Examples are counseling on how to proceed when one or two doses of a drug are missed, how to restart therapy after a drug-holiday, and information on the risk of rebound effects when medication is immediately stopped. The basics of clinical pharmacy knowledge and skills are essential also for community pharmacists to address all these issues. Moreover, specific knowledge is needed in order to perform clinical services for an individual patient. In fact, community pharmacists providing cognitive services (e.g. motivational interviewing) are in need of much more training in clinical pharmacy issues related to patient care in this specific population to become adequately skilled.

The issue of lack of communication between settings has also been part within a recent evaluation provided by the Swiss foundation for patient safety. In their survey, they report a lack of information transfer between community pharmacies and hospitals from the community pharmacists' perspective. Although community pharmacists were willing to share data (given that the legal requirements are met i.e. data protection, patient's privacy), they regularly had been contacted from a hospital in only 4% of cases to support a patient's best possible medication history.¹⁴⁶

Our survey also showed that at patient's discharge into ambulatory care medication prescriptions were validated in only 9% of cases by a hospital pharmacist. In both, the outpatient (3%) and the inpatient setting (9%), the daily provision of medicines in a dosing aid seems to be an activity rarely associated with the active participation of a clinical pharmacist until today. Since in Switzerland increasingly hospitals evaluate a cooperation with community pharmacies and offer their patients a first counseling and medication within their discharge process in an in-house pharmacy, new perspectives for the collaboration between settings are opening up. Calvert et al. reported improved adherence and higher persistence rates through collaboration over settings for patients with coronary artery disease.¹⁴⁷ Adherence to beta-blockers, expressed as proportion of days covered (PDC), was significantly higher in intervention versus control group (71% vs 49%, respectively, $P=0.03$). The PMC as an established pharmacist-led cognitive service offers an ideal starting point for in-depth reconciliation in the community setting. Thereby, seamless care between settings could be improved, given a sufficient implementation rate of performed PMCs as well as adequate clinical knowledge, and experience of the pharmacists in detecting relevant drug-related problems and recommending interventions. The observed gaps in seamless care at admission or discharge of hospitals have led to a national program named 'PROGRESS!',¹⁴⁸ which aims at

improving patient safety through structured medication reconciliation at transitions in the hospital.

As discussed within the work report A2, any type of medication review may detect a relevant number of DRPs independently the setting. However, the impact of medication reviews on patient outcomes is directly related to the subsequently performed intervention and the acceptance rate of the pharmacist's advice by the patient and/or the prescriber.

9.2 Project B - Evaluation of the Swiss Polymedication Check

In Switzerland repeat prescribing for a maximum of 12 months is allowed and such prescriptions currently constitute nearly 75% of all items dispensed.¹⁴⁹ Hence, community pharmacists assume very responsible roles in the care of chronic patients. The recently introduced Polymedication Check is therefore a very important activity. More research, especially on the implementation and the introduction of new remunerated services (such as specific medication review after hospital discharge, telephone follow-up after changes of the therapy plan) is much desired.

As Swiss pharmacists are allowed to start a drug reminder system after such a Polymedication Check, delivery of a dose dispensing service poses multiple issues that are typically part of clinical pharmacy services. Often the therapy plan requires an adaption to fit the predefined options of a pill box, and not all medicines can be dispensed due to stability problems.¹⁵⁰

First evaluations of the PMC service showed that simplifications in therapy plans and improvement of knowledge provided by pharmacists are highly appreciated.¹⁵¹ Patients need well-founded answers. An example is the frequent question on best timing of medication intake. As polypharmacy has developed over a long period of time in each patient, the review of the intake schedule becomes essential and altering the timing of intake may improve therapeutic outcomes. While some medicines need to be taken separately (e.g. Bisphosphonate, L-Thyroxin), most chronic medication can be taken at the same time, preferably in the morning and avoiding doses to be taken at lunch. Thus, when performing medication use reviews, knowledge of disease and chrono-pharmacology is important. Pharmacists have to take note of the pharmacokinetic properties and the «forgiveness of

drugs» to optimise therapeutic coverage and to cope with risks of non-adherence. Skills in disease management are important and chronotherapy is now also an emerging concept.¹⁵²

Implementation of such cognitive services provided by a pharmacist is known to be very challenging.¹⁵³ The same is true for Swiss community pharmacies. The implementation of the PMC is low. After three years, only about three checks per pharmacy per year were registered, with a large majority of pharmacies not offering this service. Focus group discussions revealed the following explanations as barriers to provide PMC: 'no time', 'not my responsibility', 'patients do not understand the service' and 'service already included in validation of prescription'.¹⁵⁴ Pharmacists, however, also showed that pharmacists became highly motivated after first experiences, thus 'the first is the worst'.

9.2.1 Outline of the professional framework to provide the study project

In order to ease the implementation of such a new service, change management processes should have been considered from the very first beginning. The pharmacists' society saw no need for more than theoretical education about the goal and aims of the PMC and the technical handling of the protocol form. No accreditation or qualification was regarded necessary to provide a PMC and only few practical trainings were offered to support pharmacists in their new role.

This evalPMC project was proposed as an investigator-initiated evaluation project by the Pharmaceutical Care Research Group without any intention to comprehensively proof the concept of efficacy, appropriateness and economics, according the national 'WZW' criteria. Later, negotiations with the representatives of the health insurance companies within the so called 'LOA Fonds' followed. However, sponsoring of this research only took place by the professional association. The health insurance companies seemed to be moderately interested to support an evaluation study aiming at the identification of opportunities for improvement of the service. Thus, the present study was designed for specific research purposes only. The reported data are not able to provide final and comprehensive proof of efficacy, appropriateness and economic effectiveness of the service as it may be required for the 'WZW' assessment.¹⁵⁵ Nevertheless, the achieved insights through the evaluation project now offer rational data for further development and improvement of the service.

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Our primary outcome of the evaluation study was a change in patient's adherence to medications. Based on reporting from previously performed projects, we hypothesised a much lower adherence rate than finally observed. Taitel et al. investigated face-to-face patient counseling sessions with a pharmacist that addressed patient barriers to adherence.¹⁵⁶ After 12 months, the intervention group showed a MPR of 61.8% (CI, 54.5%-69.2%) and the comparison group had a MPR of 56.9% (CI, 49.5%-64.3%) with a significant difference of 4.9% between groups ($P < 0.01$). Meanwhile, a systematic literature review and meta-analysis of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories, reported an average combined adherence outcome of 60.2% in control groups.¹⁵⁷ In contrast to these findings, our control showed an average MPR of 87.5%, illustrating the already high baseline adherence and little potential for improvement.

9.2.2 Comparable evaluation programs from UK

Difficulties of objective evaluation of pharmaceutical services under daily-life conditions is also of concern in other studies. In 2006, Clifford et al. recruited patients over 75 years, receiving a first prescription for a newly prescribed medicine for a long-term condition. A pharmacist from a centralised telephone service contacted the patients after two weeks to discuss their medication-related needs.¹⁵⁸ When patients were followed-up after four weeks by a researcher, there was significantly less non-adherence in the intervention group compared to the control group. Based on these findings, the so-called 'New Medicines Service' (NMS) was introduced in 2011. Comparable research from UK recently presented data on adherence improvement due to this pharmacists-led intervention for newly prescribed medicines. In parallel to the evalPMC project, the University of Nottingham conducted an in-depth evaluation of the NMS from 2013-2015, using a comparable study design to ours.¹⁵⁹ The authors performed their evaluation study in 46 community pharmacies in England, including 504 participants. Ten weeks after intervention, 378 of the patients were still taking the initial medicine, 61% (95% CI 54% to 67%) and 71% (95% CI 64% to 77%) patients were adherent in the normal practice and NMS arms, respectively ($p=0.04$ for difference). The authors assessed adherence using one single question ('People often miss taking doses of their medicines, for a

wide range of reasons. Have you missed any doses of your new medicine, or changed when you take it?'), and in addition applied the MMAS questionnaire. In their first research report they discussed the fact that the observed positive trend was not seen within the first recall by the investigation team.¹⁶⁰ Nevertheless, they eventually published only the data assessed 10 weeks after the intervention by telephone interview, but not that assessed 6 weeks after intervention.¹⁶¹ This selection now was criticised by Joseph Bush,¹⁶² as he claimed the reporting of all primary outcomes as announced in their method paper.¹⁵⁹ This publication bias may be discussed as a limitation regarding the meaningfulness of their study. However, regardless of this issue we learned that evaluation of a service in a heterogeneous population provides major difficulties when only limited patients and resources are available. Nevertheless, evaluation research is of great importance since it allows a rational discussion for re-engineering a service.

Policymakers prefer quick and meaningful results to waiting for randomised controlled trials. Stakeholder of health insurance companies, government, and the pharmacist' association need to learn that evaluation research does not aim to confirm a proposed concept or providing highest impact on clinical outcomes, exclusively. Rather, evaluation research offers a rational discussion on how to improve an investigated service, and has to be considered as a continuous quality process.

9.2.3 Implications for pharmacy practice

As a major key finding of our evaluation project, we may assume the structure of the PMC as a success. A respectable number of DRPs was detected during patient interviews although we investigated a highly motivated and organised population. However, the quality of the routinely performed PMC may be limited due to the lack of available clinical information: the patient's disease state, any information about the status of drug-eliminating organs such as the kidney and liver, or the results of blood tests are generally not routinely available to the Swiss community pharmacist. This gap can be overcome when promising eHealth programs and when data standards are implemented on a national level and the patient becomes administrator of his own health data and shares it with involved health professionals, i.e. his pharmacist.

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The pharmacist-led intervention was highly appreciated by patients and recommendations showed a high acceptance rate. Re-engineering of the service should focus on a more efficient screening for patients at highest risk for drug-related problems and provide a bundle of standardised interventions, i.e. interview guides with algorithms to support pharmacists. Kempen et al. analysed in a large-scale implementation study of Dutch community pharmacies 4,579 clinical medication reviews conducted in patients suffering from coronary heart disease.⁷⁹ On average, 2.9 (SD 2.1) DRPs per review were identified while we reported 1.2 DRPs per patient in the evalPMC study. Compared to our service, Dutch pharmacists focused exclusively on a single patient population at risk and probably might have had access to more objective patient information since the intervention is described as a clinical medication review.

Taking note of the heterogeneous population qualifying for a PMC according to the current selection criteria, another decision making step, i.e. triage, is needed to ensure that the pharmacist only approaches patients at highest risk for DRP and/or needs (Figure 9).

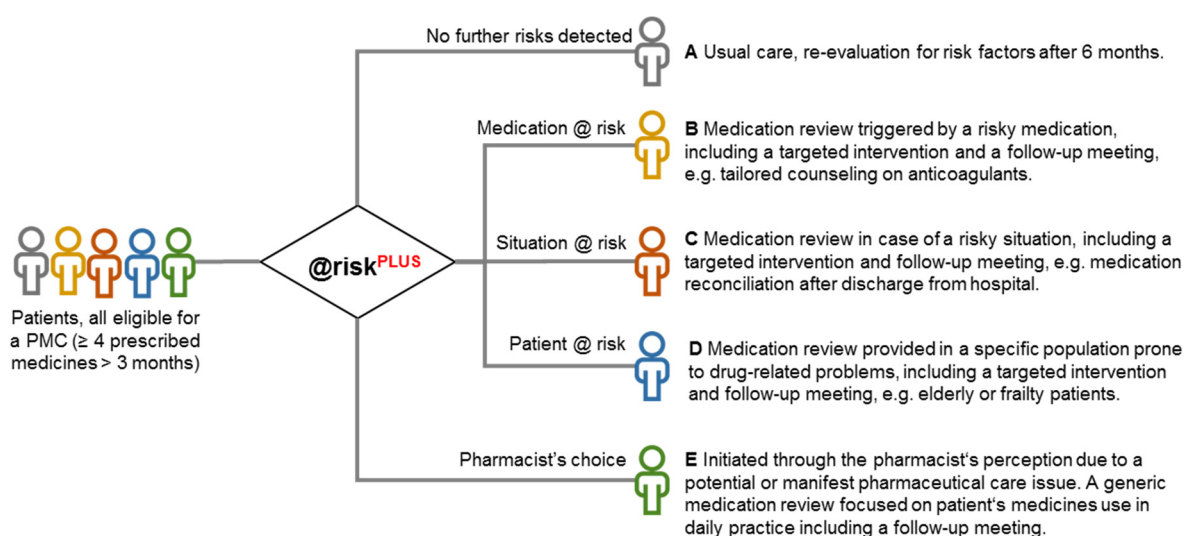


Figure 9 / Proposal for a targeted selection process leading to specific and tailored interventions

In order to respect the already well-organised patients without any further risks for drug-related problems, option A is needed. Thereby a re-evaluation of risk factors should be considered within half a year. Option B-D might be defined using explicit criteria from literature, e.g. regarding risk associated medication according the PRICSUS list,⁵³ or the beers criteria.⁵⁰ Option E reflects the need for an ad-hoc intervention in case a detected issue not listed as a

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criterion in scenario B-D but with need for further structured clarification, e.g. a patient with concerns about his medicines, swallowing difficulties with medication intake, or unreachd biomarkers despite an ongoing drug therapy.

Further, our algorithm using dispensing records to identify patients with poor adherence may also be implemented in software solutions to guide pharmacists in patient care. Mabotuwana et al. developed a generic computational framework that can be used to formulate and query criteria around issues of adherence to long-term medication based on practice electronic medical records¹⁰¹ while other initiatives focus on medicines overuse in order to save money, i.e. the Swiss injury insurance.¹⁶³ Still, adherence as an outcome measure remains challenging to describe due to methodological issues as described in chapter B1 + B2 and due to multifactorial influences.¹⁶⁴

However, the implementation rate of weekly dosing aids within the evalPMC project was low with 1.4% of newly introduced devices by study pharmacists. This issue has to be discussed as a major factor for not having improved patients' adherence even though the already discussed high baseline. Little is known concerning pharmacists' perceptions and barriers towards recommendations of such aids. Communication training should be considered to support counseling with rational and practical arguments for implementing WDAs in patient' daily life. Pharmacists need to foster practical training in performing patient-oriented interventions and taking responsibility in clinical decision-making. This should include interprofessional collaboration and independent supervision ensuring highest possible quality of the service and patient safety. The complexity of the PMC regarding its multistage intervention was not recognised as a challenge for its implementation. The Swiss pharmacists' association overestimated its acceptance by the pharmacists and offered neither guidance with written guidelines or practical training based on case studies, nor external supervision for pharmacist within their new role.

Another observation might offer new opportunities for service development. During the evalPMC project, patients were easily accessible by telephone. Therefore, a follow-up meeting (or a new service) can also be conducted by telephone and does not necessarily have to take place face to face in a pharmacy. Lyons et al. recently reported significantly improved medication adherence in patients with long-term conditions thanks to telephone intervention, led by a pharmacist and tailored to the individual's needs.¹⁶⁵

We claim the structure of the PMC as a robust construct in terms of approved feasibility in daily practice and high acceptance by the patients. Initiatives, initiated through local pharmacists' associations or conglomerates of pharmacies, might take advantage of individual needs and their network in interprofessional collaboration, or approach patients at risk as performed in UK reported by Livingstone et al in 2009.¹⁶⁶

Within the original aim of a PMC, there was the idea of formulating individual adherence targets in order to empower the patient and offer a re-evaluation of achieved targets after half a year in a follow-up meeting. From the scientific perspective, this aim was not investigated, so far, but might become an important outcome measure for further projects, since patient involvement is known to be an important factor for long-term success.¹⁶⁷

9.3 Project C - Screening for pharmaceutical care issues in community pharmacies

In order to discuss the need for a pharmacist's choice option within eligibility criteria for remunerated services (Figure 9), we investigated two scenarios where established competencies of a pharmacist may be used to initiate patient-centred care.

Screening programs in pharmacies offer opportunities to detect patients at risk for a specific disease or issue. Due to our sub-analysis of screening records, we recognise also a need for a structured intervention whenever patients do not reach their previously set therapy targets. Assessing lab tests, i.e. blood glucose measurement and lipid profile are well-established standard services in a majority of pharmacies. Whenever lab results do not fit with a patient's or clinician's expectation, further clarification is of crucial importance to ensure health outcomes. A medication review screening for primary or secondary adherence, under prescribing, or life style issues should always be part of the in-depth assessment.

Patients in the evalPMC project reported in the second telephone interview in 12.7% of cases current swallowing difficulties with medication intake. Pharmacists are in an excellent position to assess such issues actively within a patient-centred care assessment. Our SWAMECO self-report questionnaire uses the patient's capabilities of describing individual needs and complaints and subsequently offers a basis for tailored counseling and individual interventions. Barenholtz et al. suggested already in 2003 that a self-administered questionnaire might be used in an older adult population to identify patients potentially at increased risk of MRPs

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followed by a medication review.¹⁶⁸ Langford et al. adapted this questionnaire and reported a proportion of 14% of patients with identified drug-related problems when their self-administrated 5-item risk assessment was used. The referral rate was approximately 3 times higher with the medication risk assessment questionnaire as a screening tool than with traditional methods.¹⁶⁹

Our questionnaire was able to detect a heterogeneous pattern for localisation and intensity of complaints. In-depth description of swallowing difficulties revealed concrete aspects for further clarification or counseling by physicians or pharmacists. When issues are detected, the pharmacist initiates a PMC during which he might recommend alternative drug forms, improve swallowing technique, change inappropriate coping strategies, and discuss adherence issues if present. Thus, the SWAMECO questionnaire may efficiently guide healthcare professionals in daily practice when choosing patient-centred therapy options or optimising a patient's medicines profile.

10 CONCLUSION

In Switzerland, the involvement of clinical pharmacists in patient care is rising. Regardless the setting, the traditional role of pharmacists currently is expanded to a respected contributor and key partner for interprofessional collaboration in patient care. This is reflected by recent political considerations, resulting in adaptations of the Swiss legislation in 2016: the pharmacist becomes accepted as a medical health professional in primary care and now faces the challenge (and opportunity) to perform his new competencies, e.g. to diagnose and treat simple diseases and contribute within pharmacist-led vaccination programs.¹⁷⁰ In order to monitor this process and evaluate first experiences within newly implemented structured services, this thesis aimed at contributing to the discussion on various levels.

Project A highlighted the existing clinical pharmacy services from the hospital perspective. The pharmacist's competence in answering medication-related questions to hospital staff seemed to be well established and accepted. Remarkably, interprofessional ward rounds were performed periodically in hospitals, which offer clinical pharmacy services. However, there were hardly any services enabling external access to valid information about a patient's medication during his hospital stay for community pharmacies and general practitioners. Further, a crucial gap was observed in the field of seamless care. No institution reported the involvement of a pharmacist in the validation process of a patient's written medication plan at discharge from hospital. This indicates a huge potential for improvement. Pharmacists provide the needed skills for performing medication reviews, i.e. medication reconciliation. They are in an excellent position to contribute within the seamless care process. However, due to limited human and financial resources, hospitals lack involved clinical pharmacists in this process. Nevertheless, the empowerment of patients and providing support to their self-management in medicines use might become an important activity for both, the community and the hospital pharmacist. Meanwhile, the Pharmaceutical Care Network Europe agreed to a definition for medication reviews and encourages pharmacists to offer pharmaceutical care regardless of the setting. Medication reviews offer an excellent opportunity to detect drug-related problems and initiate pharmaceutical care as a contribution within patient care. However, the impact of medication reviews is directly linked to the subsequently provided intervention to solve a detected drug-related problem and to the acceptance rate of this recommendation by the patient and/or the prescriber.

CONCLUSION

Project B confirmed the Polymedication Check (PMC) as a promising new service while its impact remained low due to issues within the selection criteria. The evaluation of the PMC showed low impact on patient's adherence and highlighted the need for re-engineering. We recommend targeting patients in a more selective approach and fostering the pharmacist's intervention regarding support of adherence through implementation of dosing aids. However, patients' knowledge on medicines was improved by the intervention and patient's acceptance of the service was high. In addition, patients seemed to be highly motivated to contribute in a pharmaceutical care model. This may encourage pharmacists in approaching them more often and establishing a strong 'pharmacists – patient' relationship. Nevertheless, inducing the paradigm change in patient-centred care through pharmaceutical care seems to be more challenging than expected by the pharmacists' association and health insurance companies. In order to achieve this change, pharmacists claimed the need for specific training, structured guidance, and supervision during the implementation process. Therefore, strengthening of evaluation research on a local, as well as a national and international level is essential to develop, implement and continuously improve clinically oriented services provided by community pharmacists.

Project C exemplified two potential domains for pharmacist-led interventions based on already existing resources, i.e. public health prevention campaigns, or by involving the patient in a needs assessment. When patients do not achieve individual treatment targets (e.g. biomarkers), further clarification for potential drug-related problems are needed. In order to provide tailored counseling, the use of patient self-report assessments might become more important, e.g. in order to detect drug-related problems or individual patient's needs. Self-reported issues, i.e. swallowing difficulties with medication intake may guide a health professional in addressing hazardous coping strategies or offering alternative drug forms. The PMC as one possible intervention offers an excellent means to in-depth assessing appropriate medicines use, detecting adherence issues, and recommending interventions.

Pharmacists' contributions to patient care are no longer limited to medicines supply only. Offering multiple opportunities for new services, the present situation of lacking human and financial resources also remains challenging. Nevertheless, in order to overcome internal and external barriers, pharmacists need to take more responsibility within patient-centred care and train their skills in clinical pharmacy practice and interprofessional collaboration. The patients proved to be highly motivated to follow pharmaceutical care models. This is a very promising

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finding for the development of future services. Likewise, political decisions create an interesting basis for establishing innovative health care models. The pharmacists need to prove their willingness to offer their expertise now. Finally, yet most important, the health care system should benefit from this willingness toward participation right away. Regarding the support of this change management, the pharmacists' association and the interprofessional collaborators i.e. physicians, as well as the health insurance companies and political stakeholders are called upon to take on their responsibility in establishing integrated care models that primarily focus on a patient's needs and take highest advantage of the various competencies of involved health professionals.

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12 APPENDIX THESIS

The following appendix is limited to the main documents used within the various projects. For further information including all measurement instruments or raw data, send a request to the author.

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APPENDIX THESIS

12.1 Project A

12.1.1 Online questionnaire for the GSASA survey

Preview only: real form can vary slightly - Nur Vorschau: echtes Formular kann geringfügig anders aussehen

Mapping Clinical Pharmacy Practice in Switzerland 2013

ATTENTION: The introductory text will not show up in pagged forms. For this case use an info field as first form field.

Teil 1 - Erhebung der Stammdaten des Spitals

Mit dieser Umfrage soll einerseits der heutige Stand der klinisch-pharmazeutischen Tätigkeiten innerhalb der Schweizer Spitäler erfasst werden. Weiter soll das Hilfsmittel zur Dokumentation von klinisch-pharmazeutischen Interventionen der GSASA erstmalig national ausgewertet werden. Wir möchten uns an dieser Stelle herzlich für Ihre Angaben bedanken.

Bitte füllen Sie die Umfrage auch dann aus, wenn Sie zum heutigen Stand keine klinisch-pharmazeutischen Aktivitäten ausweisen und/ oder das GSASA-Dokumentations-Tool nicht nutzen.

WICHTIG: Wir setzen voraus, dass diese Umfrage von der verantwortlichen Person für den Fachbereich 'Klinische Pharmazie' ausgefüllt wird. Sollte keine entsprechende Person nominiert sein, bitten wir darum, dass die Leitung der Spitalapotheke die Fragen beantwortet. Das Ausfüllen des Fragebogens nimmt im Mittel 20 Minuten in Anspruch.

Für Fragen steht Ihnen Markus Messerli gerne zur Verfügung [Office 061 267 15 29, Email markus.messerli@unibas.ch].

Bitte speichern Sie sämtliche Bereiche nach dem Ausfüllen der Fragen ab und stellen Sie uns den Fragebogen am Ende mit 'Senden' zu (Button oben rechts). So stellen Sie sicher, dass Ihre Angaben ausgewertet werden können.

1. Name der Institution [ⓧ]

2. Ort [ⓧ]

3. Postleitzahl [ⓧ] (1000 ... 9999)

4. Art der Einrichtung [ⓧ]

- Universitätsspital
- Kantonsspital
- Regionalspital mit Notfallstation
- Regionalspital ohne Notfallstation
- Privatspital
- Rehabilitationsspital/-zentrum
- Psychiatrische Klinik
- Spitalverbund / -netzwerk*
- Andere Klinikform:

* falls als Spitalnetzwerk/-verbund organisiert...

... beschreiben Sie bitte dessen Struktur und Umfang. Verwenden Sie dazu wenn immer möglich die Kategorien aus Frage 4. Beziehen Sie sich bitte im Weiteren Verlauf des Fragebogens auf die Einrichtung(en), welche von Ihrer Apothekeneinheit betreut wird. Sollten Sie mehrere Häuser mit mehreren Einheiten betreiben, so ist für jede Einrichtung ein Fragebogen auszufüllen.

5. Struktur und Umfang des Spitalnetzwerk/-verbund:

6. Anzahl Betten: [ⓧ]

7. Bildet Ihre Institution Assistenzärzte aus (= Ausbildungskrankenhaus)? [ⓧ]

- Ja Nein

8. Anzahl Vollzeitstellen 'Apotheker/innen' als Zahl: [ⓧ]

Zum Beispiel:

1. Apothekern 100% + 1 Apotheker 80% = 180 Stellenprocente = 1.8 Vollzeitstellen

9. Wie viele Apotheker/innen werden mit diesen Stellenprozenten beschäftigt? [ⓧ]

10. Anzahl Vollzeitstellen 'Pharma-AssistentInnen' als Zahl: [ⓧ]

11. Wie viele Pharma-AssistentInnen werden mit diesen Stellenprozenten beschäftigt? [ⓧ]

12. Wie viele der beschäftigten Apotheker/innen führen den Fachtitel 'FPH Spitalpharmazie'? [ⓧ]

13. Wie viele der beschäftigten Apotheker/innen führen das Zertifikat 'FPH Klinische Pharmazie'? [ⓧ]

14. Wie viele der beschäftigten Apotheker/innen führen sowohl den Fachtitel 'FPH Spitalpharmazie', als auch das Zertifikat 'Klinische Pharmazie'? [ⓧ]

15. Werden Ausbildungsplätze für den Fachtitel 'FPH Spitalpharmazie' angeboten? [ⓧ]

- Ja Nein

16. Falls 'JA': Wie viele?

17. Werden Ausbildungsplätze für das Zertifikat 'FPH Klinische Pharmazie' angeboten? [ⓧ]

- Ja Nein

18. Falls 'JA': Wie viele?

19. Wie ist die pharmazeutischen Kompetenz innerhalb des Spitalbetriebs vernetzt? [ⓧ]

	Ja - leiende Funktion	Ja - teilnehmende Funktion	Nein - keine Vertretung	Auf Anfrage	Nicht vorhanden
Spitalleitung	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Arzneimittelkommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Aus- und Weiterbildungskommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hygienekommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Antimicrobial Stewardship	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
CIRS-Kommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Qualitätskommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Ernährungskommission	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Palliativ Care	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patientenschulung (z.B. Ernährung / Diabetes)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

20. Anderes:

21. Bietet die Apotheke regelmässig (min. 1x / Jahr) interne Weiterbildungskurse für PFLEGENDE an? Ja Nein

22. Bietet die Apotheke regelmässig (min. 1x / Jahr) interne Weiterbildungskurse für die ARZTESCHAFT an? Ja Nein

23. Welche der folgenden Dokumente unterliegen in Erstellung und Pflege der pharmazeutischen Kompetenz?

	Ja	Nein	Nicht vorhanden	k.A.
Sortimentsliste InHouse	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Inkompatibilität von i.v.-Lösungen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Mörserbarkeit / Suspensierbarkeit von Medikamenten	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Berechnungstabellen für individuelle Dosierungen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verordnungshilfen für TPN	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verordnungshilfen für Onkologie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Unterlagen zur Abgabe an Patienten	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

24. Wie werden folgende Patientendaten elektronisch administriert?

	keine elektronische Erfassung in Planung angedacht	keine elektronische Erfassung in Planung	teilweise elektronische Erfassung	vollständige elektronische Erfassung	weiss nicht
Patientenanamnese mit ICD-10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patientenanamnese ohne ICD-10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vitalparameter	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verordnung der Medikamente	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Abgabe der Medikamente	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verkaufsbericht Ärzte	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verkaufsbericht Pflege	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Verkaufsbericht Konsil (z.B. Empfehlung KlinPharm)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Laboresultate	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

25. Sind der Apotheke die elektronisch erfassten Patientendaten zugänglich?

- Ja - Zugang vollständig gewährleistet
- Nein - Zugang nicht gewährleistet
- Teilweise. Zugänglich sind:

Seitenabbruch --- Teil 2 - Dienstleistungen der Klinischen Pharmazie

26. Werden in Ihrem Betrieb klinisch-pharmazeutische Dienstleistungen angeboten?

- Ja
- Nein, aber in Planung
- Nein

Die Befragung hat die von der GSASA formulierte Definition für 'Klinische Pharmazie' als Basis:

„Die klinische Pharmazie ist jener Teilbereich der Pharmazie, der die Entwicklung und Förderung einer angemessenen, sicheren und ökonomischen Anwendung von Arzneimitteln zum Ziel hat.“

Im Spital versteht man unter „klinischer Pharmazie“ die patientenorientierten pharmazeutischen Tätigkeiten auf den Pflegeabteilungen in interdisziplinärer Zusammenarbeit mit den anderen Fachpersonen.“ (V.1, 11/2011)

Falls JA -> Bitte ALLE der folgenden Fragen beantworten. Danke!

Falls NEIN -> Bitte diese Seite unten speichern und mit Bereich 3 fortfahren. Danke!

27. Wie viele der Apotheken-Stellenprozentage stehen für den Bereich 'Klinische Pharmazie' zur Verfügung?

28. Wie sind die Dienstleistungsangebote des Bereichs 'Klinische Pharmazie' organisiert?

- Ohne Präsenz zur Patientenstation
- Teilweise mit Präsenz zur Patientenstation
- >50% der Arbeitszeit erfolgt auf der Patientenstation

29. Seit wann ist der Bereich 'Klinische Pharmazie' etabliert (Jahr als Zahl, z.B. '2002')?

30. Werden Pharma-Assistentinnen in den Bereich 'Klinische Pharmazie' miteinbezogen? Ja Nein

31. Falls 'JA': Was sind dabei ihre Aufgaben?

Wie häufig bieten Sie folgende Leistungen an (bezogen auf die letzten 12 Monate)?

Wir möchten die Dienstleistungsbereiche der Übersicht halber in drei Kategorien mit jeweils unterschiedlichem Fokus aufteilen. Erläuterung / Abgrenzungen zu den verschiedenen Dienstleistungen sind mittels Zahlenreferenz weiter unten einsehbar.

32. Patientenorientierte Dienstleistungen

	täglich	wöchentlich	monatlich	3-4x pro Jahr	1-2x pro Jahr	nie
Visite auf Station mit Mappex	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Visite auf Station mit Arzt & Mappex	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Visite auf Station mit Arzt am Patientenbett	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patientenschulung während dem Aufenthalt	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patientenschulung beim Austritt	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

33. Behandlungsorientierte Dienstleistungen

	täglich	wöchentlich	monatlich	3-4x pro Jahr	1-2x pro Jahr	nie
Anamnese der Eintrittsmedikation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Empfehlungen zu TDM-Verordnungen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Empfehlungen zu TPN-Verordnungen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Empfehlungen zu Verordnungen von Risikomedikamenten [1]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Empfehlungen zu Verordnungen von Antibiotika	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Empfehlungen zur Austrittsverordnung	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

34. Prozessorientierte Dienstleistungen

	täglich	wöchentlich	monatlich	3-4x pro Jahr	1-2x pro Jahr	nie
Beantworten von internen Anfragen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Beantworten von externen Anfragen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
UAW-Meldung an Pharmacovigilanz-Zentrum	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Erstellung von Therapieplan für Austrittsverordnung z.H. des Patienten	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bereitstellen der Medikamente mit Tagesdispenser [stationär]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bereitstellen der Medikamente mit Tagesdispenser [ambulant]	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

[1] hier liegt der Fokus auf Wirkstoffen mit enger therapeutischer Breite und/oder kritischem Interaktionspotential. Ein Risikomedikament wäre demnach zum Beispiel Methotrexat.

35. Weitere Dienstleistungen, welche nicht aufgeführt sind:

36. Welche Fachbereiche werden klinisch-pharmazeutisch bedient?

Regelmässig / nach Plan	Bei Bedarf / Anfrage	Keine Zusammenarbeit	Kein Fachbereich in unserem Betrieb
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Intensiv Medizin	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Innere Medizin	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Dermatologie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Orthopädie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Chirurgie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Genatrie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rehabilitation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Onkologie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Pädiatrie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Gynäkologie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Psychiatrie	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Ambulante Patienten	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

37. Können Sie kurz schildern, wie die Zusammenarbeit in einem oder mehreren Bereichen zustande gekommen ist?

38. Bieten Sie eine Hotline für externe klinisch-pharmazeutische Anfragen von MEDIZINALPERSONEN an?

- Ja Nein

39. Bieten Sie eine Hotline für externe klinisch-pharmazeutische Anfragen von PATIENTEN an?

- Ja Nein

40. Bemerkungen zur Erfassung der klinisch-pharmazeutischen Dienstleistungen

Seitenumbruch ... **Teil 3 - Akzeptanz und Rahmenbedingungen in der klinischen Pharmazie**

41. Bitte nehmen Sie zu folgenden Aussagen Stellung:

	Stimme überhaupt nicht zu	Stimme eher nicht zu	Stimme eher zu	Stimme voll und ganz zu	Keine Äusserung
Bezogen auf die letzten fünf Jahre hat die Akzeptanz innerhalb der Ärzteschaft -was den Fachbereich 'Klinische Pharmazie' anbelangt- zugenommen.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Ärzte schätzen unsere Empfehlungen und setzen diese um.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Ich werde über die Umsetzung unserer Empfehlungen informiert.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Das FPH Zertifikat 'Klinische Pharmazie' sollte zu einem 'Master' bzw. 'Fachittel FPH' aufgewertet werden.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Das Weiterbildungsangebot der GSASA im Bereich 'Klinische Pharmazie' ist ausreichend.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Mein Betrieb stellt genügend personelle Ressourcen für den Fachbereich 'Klinische Pharmazie' zur Verfügung.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Wir würden in unserem Betrieb gerne mehr klinische Pharmazie anbieten	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

42. Werden in Ihrem Betrieb Forschungsprojekte mit klinisch-pharmazeutischen Hintergrund bearbeitet?

- Ja Nein

43. Falls 'JA': Können Sie in Stichworten umschreiben, worin der Fokus liegt?

Seitenumbruch ... **Teil 4 - 'Dokumentation klinisch-pharmazeutischer Aktivitäten'**

44. Wie dokumentieren Sie ihre klinisch-pharmazeutischen Tätigkeiten hauptsächlich?

- Keine strukturierte Dokumentation
- Internes Dokumentationssystem (eigene Datenbank)
- GSASA-Dokumentation, papierbasiert
- GSASA-Dokumentation, elektronisch
- ABDA Datenbank
- Anderes standardisiertes Tool:

12.2 Project B

12.2.1 Ethical approval evalPMC EKBB 50/12 (Lead committee, study region BS/BL)

Beschlussmitteilung der Ethikkommission beider Basel

Die Ethikkommission beider Basel hat an ihrer Sitzung vom 21. Februar 2012 (in der Zusammensetzung, wie sie auf Seite 2 wiedergegeben ist) das nachstehende Forschungsprojekt eingehend begutachtet:

Titel des Forschungsprojektes

Ref.Nr: EK 50/12

Evaluation "Poly Medikations-Check" - eine neue apothekenbasierte Dienstleistung mit Fokus auf Compliance und die Medikamentenabwendung im Alltag. Eine prospektive, randomisiert-kontrollierte Studie in Schweizer Offizin-Apotheken

Pfiterin

Name, Vorname, Titel: Herbsberger, Kurt, Prof. Dr. sc. nat.
 Funktion: Prof. Pharmaceutical Care, Uni Basel
 Adresse: Pharmazentrum, Klingelbergstr. 50, 4056 Basel

Die Ethikkommission stützt ihre Beurteilung auf die Unterlagen, wie sie im beiliegenden Antrag auf Begutachtung vom 06. Februar 2012 abschliessend aufgezählt sind.

X normales Verfahren vereinfachtes Verfahren Nachbegutachtung

Die Ethikkommission kommt zu folgendem **Beschluss**:

- X **A positiv** (siehe Seite 2ff)
- B positiv mit Bemerkungen** (siehe Seite 2ff)
- C mit Auflage** (siehe Seite 2ff)

- D negativ (mit Begründung und Erläuterung für die Neubeurteilung)** (siehe Seite 2ff)
- E Nicht-Eintreten (mit Begründung)** (siehe Seite 2ff)

Der Beschluss gilt auch für die im "Antrag auf Begutachtung" gemeldeten weiteren Pfiterinnen im Zuständigkeitsbereich der Ethikkommission.

Pro Memoria, Pflichten des/der verantwortlichen Pfiterin

Gepuffte Produkte und Vergleichsprodukte (Arzneimittel und Medizinprodukte) müssen - zur Sicherstellung der Qualität und der Sicherheit - fachgerecht hergestellt, evaluiert und eingesetzt werden.

Meldspflicht bei:

- a) schwerwiegenden unerwünschten Ereignissen (serious adverse events) unverzüglich
 - b) neuen Erkenntnissen, die während des Versuchs verfügbar werden und die Sicherheit der Versuchspersonen sowie die Weiterführung des Versuchs beeinflussen können
 - c) Änderung des Protokolls (Versuchsplans)
 - d) Ende oder Abbruch der Studie
- Zwischenbericht: einmahl pro Jahr
 Meinungs- oder Bewilligungspflicht von Studien bei Swissmedic bzw. anderen Bundes- oder kantonalen Behörden - sofern erforderlich (bei sponsorisierten Studien ist dies die Pflicht des Sponsors)
 Schlussbericht

Für die Ethikkommission:

Ort, Datum: Basel, 23. Mai 2012 Name(n): Prof. A. P. Perruchoud
 Prof. M. Kranzlin

Unterschrift(en):



Ref. Nr. EK 50/12

Seite 2

Zusammensetzung der Ethikkommission

Die Ethikkommission tagte in der nachfolgend erwähnten Zusammensetzung und war damit beschlussfähig (Art. 32 der Verordnung über klinische Versuche mit Heilmitteln vom 17. 10. 2001)

Name, Vorname	Berufliche Stellung / Titel	m	f	ja	nein
Prof. A. P. Perruchoud	Präsident der EKBB	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Fr. Dr. phil. S. Mendelwitsch	Fachpsychologin, Reha, Rheinfelden	<input type="checkbox"/>	X	X	<input type="checkbox"/>
Fr. Dr. A. Koelz	FMH Nephrologie, Praxis, Dornach	<input type="checkbox"/>	X	X	<input type="checkbox"/>
Prof. T. Girard	FMH Anästhesie, US Basel	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Prof. V. Valderatano	Chefarzt Orthopädie, US Basel	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Dr. H. Hartmann	MAE Toxikologe	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Frau E. Seeburger	Study Nurse, Dept. Anästhesie USB	<input type="checkbox"/>	X	X	<input type="checkbox"/>
Pfr. J. Merz	Spitalsseelsorger, US Basel	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Hr. lic. iur. P. Burkli	Assistent, Juristische Fakultät, Basel	X	<input type="checkbox"/>	X	<input type="checkbox"/>
Dr. Th. Fabbro	Statistiker, CTU USB	X	<input type="checkbox"/>	X	<input type="checkbox"/>

Empfehlungen

(erweiterbar)

Aufgaben

• Die initialen Auflagen der EKBB (siehe Schreiben vom 23. Februar 2012) wurden erfüllt. (erweiterbar)

Bemerkungen

- Die EKBB hat die nachfolgend erwähnten Dokumente zur oben genannten Studie zustimmend zur Kenntnis genommen und genehmigt:
 - Studienprotokoll - Version 2 vom 03. Mai 2012
 - Patienteninformation und Einverständniserklärung - Version vom 28. April 2012
 - Erlaubung an die Patienten - Version vom 10. April 2012
 - CRFs - jeweils Version vom 03. Mai 2012
 - Versicherungszertifikat vom 29. März 2012.
- Die EKBB bestätigt, dass sie nach GCP-ICH-Richtlinien arbeitet. (erweiterbar)

APPENDIX THESIS

12.2.2 Patient information and informed consent evalPMC

PATIENTEN-INFORMATION zur Studie „Evaluation Polymedikations-Check – Medikamentenanwendung im Alltag“

Sehr geehrte Dame,
Sehr geehrter Herr

Sie erhalten seit mindestens drei Monaten vier oder mehr Medikamente vom Arzt verordnet. Ihre Apotheke beteiligt sich an einem nationalen Forschungsprojekt, in welchem die Betreuung von Patienten mit mehreren Medikamenten im Alltag untersucht wird.

Wir laden Sie ein, an dieser Studie teilzunehmen. Sie wird im Rahmen der geltenden Gesetze und international anerkannten Grundsätzen durchgeführt und wurde von der Ethikkommission beider Basel geprüft und bewilligt (EKBB 50/12).

Allgemeine Informationen zur Studie: Die Studie „Medikamentenanwendung im Alltag“ wird in öffentlichen Apotheken in Kantonen der Nordwestschweiz und der Romandie durchgeführt. Total werden 800 Patienten in 70 Studienapotheken teilnehmen können. Die Studie wird vom Schweizerischen Apothekerverband, pharmaSuisse, finanziert. Organisation und Koordination erfolgen durch die Universität Basel.

Ziele der Studie: Ziel der Studie ist, die Anwendung von Medikamenten im Alltag zu untersuchen. Um die Patienten zukünftig noch besser beraten zu können, interessieren uns alle Ihre Schwierigkeiten, Probleme und Ihre Wünsche an eine begleitende Unterstützung während der Therapie. Zudem soll diese Studie den Nutzen eines vertieften Beratungsgesprächs mit Ihrem Apotheker/Ihrer Apothekerin (den sogenannten ‚Polymedikations-Check‘) untersuchen.

Ablauf der Studie: Wenn Sie sich zur Teilnahme an der Studie einverstanden erklären, wird Ihnen mitgeteilt, ob Sie entweder der Gruppe A oder der Gruppe B zugeteilt wurden

- Beide Gruppen A und B werden durch die Universität Basel zur Arzneimittel-Anwendung im Alltag befragt.
- Patienten in Gruppe A werden zusätzlich zu Beginn der Studie ein ca. 30 minütiges Beratungsgespräch zum ‚Medikamenten-Alltag‘ mit dem/der Apotheker/in (einen sogenannten ‚Polymedikations-Check‘) durchführen. Bei Patienten in Gruppe B findet dieses Beratungsgespräch 7 Monate später statt.

Die zufällige Einteilung in eine der beiden gleich grossen Gruppen ist die einzige Möglichkeit, um herauszufinden, ob ein strukturiertes Beratungsgespräch mit Ihrem Apotheker / Ihrer Apothekerin Vorteile bringt.

Die Zuteilung wird von der Studienkoordination zufällig und unabhängig von der Anzahl oder Art Ihrer Medikamente getroffen. In jedem Fall erhalten Sie Ihre verordneten Medikamente weiterhin wie gewohnt durch Ihre Apotheke. Alle Patienten haben die gleiche Chance, in die eine oder andere Gruppe eingeteilt zu werden.

Ablauf der Studie: mit der Unterzeichnung der Einverständniserklärung beginnt die Studie. Sie werden zu verschiedenen Zeitpunkten Fragen zu Ihrer Person, Ihrem Medikamentenalltag und Ihrer Betreuung durch die Apotheke beantworten. Dabei gibt es keine richtigen oder falschen Antworten – nur Ihre Meinung und Ihr Eindruck sind für uns wichtig.

Heute	<ul style="list-style-type: none">• Befragung in der Apotheke: Sie beantworten Fragen zu Ihrer Person und der Anwendung Ihrer Medikamente im Alltag.• Gruppeneinteilung: Im Anschluss an diese schriftliche Befragung werden Sie einer Gruppe zugeteilt. Bei Studienteilnehmer/innen der Gruppe A findet sogleich der Polymedikations-Check mit dem/der Studienapotheker/in statt.
In zwei Wochen	1. Telefoninterview: die Universität Basel wird Sie telefonisch kontaktieren und mit Ihnen ein Interview führen. Dieses wird circa 30 Minuten dauern.
In vier Monaten	2. Telefoninterview: die Universität Basel wird Sie telefonisch kontaktieren und mit Ihnen ein Interview führen. Dieses wird circa 20 Minuten dauern.
In sieben Monaten	Befragung in der Apotheke am Ende der Studie: Beide Gruppen A und B führen mit Ihrem Apotheker/Ihrer Apothekerin einen Polymedikations-Check durch.

Weitere Datenerhebungen: Ihre Apotheke wird dem Studienzentrum die Daten Ihrer Medikamentenbezüge in anonymisierter Form übermitteln. Dies rückwirkend über den Zeitraum von sieben Monate vor der Einwilligung zur Studienteilnahme, sowie sieben Monate ab Einwilligung zur Studienteilnahme.

Es werden zu keinem Zeitpunkt: Blutproben entnommen oder Laboruntersuchungen durchgeführt.

Welchen Nutzen können Sie möglicherweise von diesem Projekt haben? Sie werden in jedem Fall mit den bestmöglichen Methoden behandelt und wie bisher von Ihrer Apotheke betreut. Zusätzlich könnten Sie von dem Beratungsgespräch mit dem/der Studienapotheker/in (Polymedikations-Check) und dem daraus bisher nicht sicher dokumentierten Vorteil gegenüber der klassischen Begleitung profitieren. Dank Ihrer Studienteilnahme können die Ergebnisse auch anderen Personen zugutekommen.

Entschädigung: Ihren Aufwand für die Teilnahme an dieser Studie (Besuche in der Apotheke/Telefoninterviews) können wir mit CHF 20.- in Form von Reka-Checks entschädigen.

Mögliche Risiken und Unannehmlichkeiten durch die Studie: Risiken im Zusammenhang mit dem Polymedikations-Check sind keine zu erwarten. Das Beantworten der Fragen in der Apotheke und am Telefon wird Zeit in Anspruch nehmen. Es steht Ihnen frei, auf für Sie unangenehme Fragen keine Antwort zu geben.

Sollten aufgrund der Beratung Rückfragen oder Abklärungen mit einem Arzt nötig werden, so erfolgen diese in jedem Fall stets mit Ihrer Einwilligung.

Kosten: Die Medikamente werden Ihrer Krankenkasse verrechnet. Die Kosten für den Polymedikations-Check werden ebenfalls regulär über Ihre Krankenkasse abgerechnet.

Alternative Behandlungsmöglichkeiten: Unabhängig von Ihrer Zuteilung in eine der beiden Gruppen werden Sie weiterhin sämtliche Möglichkeiten haben, den Service ihrer Apotheke in Anspruch zu nehmen.

Freiwilligkeit der Teilnahme und Rücktritt: Ihre Teilnahme an der Studie ist freiwillig. Sie können Ihr Einverständnis zu jedem Zeitpunkt zurückziehen, ohne dass Sie einen bestimmten Grund dafür angeben müssen oder Nachteile für Ihre weitere Behandlung zu erwarten haben. Das gleiche gilt, wenn Sie auf die Teilnahme an dieser Studie verzichten.

Versicherungsschutz: Für Schäden, die Sie im Rahmen dieser Studie durch die Beratung erleiden sollten, sind die Studienapotheken durch eine Police des Studienzentrums versichert.

Vertraulichkeit der Daten: In dieser Studie werden persönliche Daten von Ihnen erfasst. Diese Daten werden anonymisiert. Sie sind nur Fachleuten zur wissenschaftlichen Auswertung zugänglich. Ebenso kann die Ethikkommission beider Basel Einsicht in die Originaldaten nehmen. Sämtliche Daten werden dabei immer strikt vertraulich behandelt. Ihr Name wird in keiner Weise in Berichten oder Veröffentlichungen, die aus der Studie hervorgehen, publiziert.

Kontaktpersonen: Falls Sie im Zusammenhang mit dieser Studie Fragen haben oder irgendwelche gesundheitliche Schwierigkeiten auftreten, so wenden Sie sich an Ihre/n betreuende/n Apotheker/in, Ihren behandelnden Arzt oder an folgende Kontaktpersonen. Diese werden Ihnen weiterhelfen:

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24h-Studienhotline: 079 / 104 35 62

SCHRIFTLICHE EINVERSTÄNDNISERKLÄRUNG DES PATIENTEN zur Teilnahme an der Studie „Evaluation Polymedikations-Check – Medikamenten- anwendung im Alltag“ (Studiennummer EKBB 50/12; Studienort: Basel-Land / Basel-Stadt)

- Ich wurde vom unterzeichnenden Apotheker ausführlich mündlich und schriftlich über die oben beschriebene Studie informiert und habe die Patienteninformation gelesen und verstanden. Alle meine Fragen wurden mir zufriedenstellend beantwortet.
- Ich hatte genügend Zeit, um meine Entscheidung zu treffen.
- Mit meiner Unterschrift bestätige ich meine Einwilligung zur freiwilligen Teilnahme. Ich kann meine Zustimmung jederzeit ohne Angabe von Gründen und ohne für mich daraus entstehende Nachteile für meine weitere Behandlung zurückziehen.
- Ich bin damit einverstanden, dass wissenschaftliches Personal des Departementes Pharmazie der Universität Basel oder der Studienapotheke im Zusammenhang mit dieser Studie Einsicht in meine medizinischen Daten nehmen darf.
- Eine Kopie der schriftlichen Patienteninformation und der Einverständniserklärung habe ich erhalten.

Name des Patienten / der Patientin in Druckschrift:	Geburtsdatum:	Geschlecht: <input type="checkbox"/> weiblich <input type="checkbox"/> männlich
Ort, Datum:	Unterschrift des Patienten / der Patientin:	
Telefonnummer:	ID Patient Wird von Studienapotheke ausgefüllt	

Bestätigung der/des Studienapotheker/in: Hiermit bestätige ich, dass ich diesem Patienten / dieser Patientin Wesen, Bedeutung und Tragweite der Studie erläutert habe. Ich versichere, alle im Zusammenhang mit dieser Studie stehenden Verpflichtungen zu erfüllen. Sollte ich zu irgendeinem Zeitpunkt während der Durchführung der Studie von Aspekten erfahren, welche die Bereitschaft des Patienten / der Patientin zur Teilnahme an der Studie beeinflussen könnten, werde ich ihn / sie umgehend darüber informieren.

Name der aufklärenden Studienapothekerin / des aufklärenden Studienapothekers	Stempel der Studienapotheke
Ort, Datum:	Unterschrift der aufklärenden Studienapothekerin / des aufklärenden Studienapothekers

12.2.3 PMC protocol form T-0

Pat.-ID: _____	Geburtsdatum: ____ / ____ / _____	Geschlecht <input type="checkbox"/> männlich <input type="checkbox"/> weiblich
----------------	-----------------------------------	--

Der Patient/die Patientin nimmt zurzeit täglich 4 oder mehr Medikamente auf ärztliche Verordnung und über mind. 3 Monate ein

1. Check Zeit Beginn: ____ . ____ Uhr

	Ärztlich verordnete Medikamente (dieser Check basiert auf Informationen vom Patienten und/oder aus der Dokumentation der Apotheke)	Abklärung Bedarf für Beratung zur Anwendung dieses Medikamentes			Vergessen Sie manchmal dieses Medikament zu nehmen?	Beratung durch Apotheke nötig?	Kommentar <small>Fortsetzung auf Rückseite</small>
		Wissen, wie [Dosisintervall]	Wissen, weshalb	Wissen, wie lange			
1	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
2	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
3	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
4	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
5	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
6	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
7	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
8	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
9	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
10	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	

Selbstmedikation: Ja Nein

A	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
B	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	
C	Name/ Stärke / Galenische Form neu ? <input type="checkbox"/>	____ - ____ - ____	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	<input type="checkbox"/> Bei Bedarf <input type="checkbox"/> Befristet <input type="checkbox"/> Dauertherapie	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	Ja <input type="checkbox"/> Nein <input type="checkbox"/>	

2. Beratung

Dokumentation von Massnahmen mit Verweis auf obige Therapie

3. Medikamentenmanagement

Patient qualifiziert für Wochendosiersystem (WDS). Er nutzt bereits neu seit dem PMC ein WDS, Auffüllen erfolgt selbständig durch die Apotheke.

Patient benötigt kein Wochendosiersystem

Patient ist einverstanden

Ja Nein

Ja Nein

4. Weiterführende Massnahmen

Information an
 Rücksprache mit
 Weiterleitung des Patienten an _____ Arzt

Andere Massnahmen nach PMC

[.....]

Patient ist einverstanden

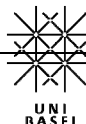
Ja Nein

Ja Nein

Datum: ____ / ____ / ____ Zeit Ende: ____ . ____ Uhr

Stempel Apotheke /Unterschrift Apotheker/in:

Unterschrift Patient/in: _____



12.2.4 PMC protocol form T-28

Der Patient/die Patientin nimmt zurzeit täglich 4 oder mehr Medikamente auf ärztliche Verordnung und über mind. 3 Monate ein

Table with 10 rows for medication management, including columns for name, strength, form, duration, knowledge, and consultation needs.

Section for self-medication (Selbstmedikation) with a grid for Ja/Nein responses.

Section 2: Berating (Beratung) - Documentation of massnahmen with Verweis auf obige Therapie.

Section 3: Medikamentenmanagement - Patient informed, WDS system, and patient consent.

Section 1: Dokumentation von Therapieänderungen innerhalb der letzten sieben Monate.

Main table for therapy changes with columns for start date, pharmacy, type of change, old dosage, success, and reason for change.

Section 4: Hinweise auf arzneimittelbezogene Probleme (Hints) - Patient safety and medication issues.



12.2.5 Telephone interview guide T-2

Preview only: real form can vary slightly - Nur Vorschau: echtes Formular kann geringfügig anders aussehen

Telefoninterview 1 [BS-BL]

Die folgenden Daten bitte vor dem Telefongespräch eintragen:

Patientencode:

Datum (TT.MM.JJJJ)

Visum Interviewer:

Einleitung
Guten Tag Herr/Frau _____, mein Name ist _____, ich arbeite für die Universität Basel.

(Pause zur Begrüssung)

Ich rufe Sie an wegen der Studie zur "Medikamenten-Anwendung im Alltag". Sie haben am _____ in der Apotheke _____ angegeben, dass Sie an dieser Studie teilnehmen möchten. Erinnern Sie sich?

Ich möchte Ihnen nun einige Fragen zum Alltag mit Ihren Medikamenten stellen. Wir behandeln Ihre Angaben natürlich vertraulich. Ihre Antworten werden in einem Formular mit einem Zahlencode erfasst. So bleiben alle Ihre Antworten anonym. Ihr Apotheker und Ihr behandelnder Arzt haben zudem KEINEN Zugriff auf diese Daten.

Ist das so in Ordnung für Sie?

Sie können das Interview natürlich jederzeit unterbrechen oder abbrechen, und Sie können auch einzelne Antworten verweigern.

Das Interview dauert etwa 30 Minuten. Möchten Sie vorher noch kurz etwas erledigen oder wollen wir gleich beginnen? Sie dürfen vorab die Packungen der Medikamente, die Sie täglich einnehmen, holen gehen. So wird es einfacher, die ersten Fragen zu beantworten.

In welcher Sprache möchten Sie die Befragung durchführen? In Hochdeutsch oder lieber in Schweizerdeutsch?

- Hochdeutsch
- Schweizerdeutsch

Startzeitpunkt festhalten (HH.MM):

Das Interview hat fünf Bereiche und nun möchte ich mit dem ersten Bereich anfangen.

(Bereich 1)

Zunächst möchte ich Ihnen einige Fragen zu Ihren Medikamenten stellen.

1. Wie viele Medikamente wenden Sie derzeit UNGEFÄHR an?

2. Ich möchte jetzt gerne alle Ihre Medikamente einzeln mit Ihnen durchgehen.

Können Sie mir eines Ihrer Medikamente nennen? (Falls zögernd) Sie können die Medikamente auch holen gehen.

Medikament 1

Wie oft wenden Sie dieses Medikament an? (Anzahl mal pro Woche/jeden Tag)

- 1x täglich
- Mehrmals täglich
- Wöchentlich
- Monatlich
- Nach Bedarf
- Nach spezieller Verordnung
- Weiss es nicht
- Anderes:

Wann genau, zu welchem Tageszeitpunkt, wenden Sie dieses Medikament an?

- Morgens
- Mittags
- Abends
- Zur Nacht
- Bei Bedarf
- Weiss es nicht
- Anderes:

Was denken Sie, weshalb müssen Sie dieses Medikament anwenden?

ACHTUNG

Die folgende Frage erst im zweiten Durchgang stellen:

Spezielles in der Anwendung oder Probleme mit der Einnahme

Nun möchte ich noch mehr über die Anwendung dieser Medikamente in Ihrem Alltag erfahren.

Die Anwendung beinhaltet: [langsam vorlesen] die Entnahme aus der Packung, das Bereitstellen, allfällige Zubereitung und Einnahme oder Verabreichung. Ich wiederhole die von Ihnen erwähnten Medikamente.

Müssen Sie bei der Anwendung und Handhabung von X auf etwas Spezielles achten?

Zum Beispiel...

zum Einnahmezeitpunkt, ob nüchtern oder nicht, Vorsichtsmassnahmen betreffend Autofahren oder ähnliches.

Medikament 2

Wie oft wenden Sie dieses Medikament an? (Anzahl mal pro Woche/jeden Tag)

- Mittags
- Abends
- Zur Nacht
- Bei Bedarf
- Weiss es nicht
- Anderes:

Was denken Sie, weshalb müssen Sie dieses Medikament anwenden?

ACHTUNG

Die folgende Frage erst im zweiten Durchgang stellen.

Müssen Sie bei der Anwendung von X auf etwas Spezielles achten?

Bemerkungen zu Bereich 1

3. Spezielles in der Anwendung oder Handhabung mit der Anwendung

Nun möchte ich noch mehr über die Anwendung dieser Medikamente in Ihrem Alltag erfahren.

Die Anwendung beinhaltet: [langsam vorlesen] die Entnahme aus der Packung, das Bereitstellen allfällige Zubereitung und Einnahme oder Verabreichung. Ich wiederhole die von Ihnen erwähnten Medikamente.

(Jetzt wieder nach oben zu den Medikamenten scrollen, Medikamente nennen und die übersprungene Anwendungsfrage stellen)

ACHTUNG KEIN INTERVIEW

Einschätzung von Interviewer/In:

4. Wie sicher erscheint der Patient/ die Patientin in Bezug auf das Wissen über seine / ihre Medikamente?

1 = sehr unsicher, 10 = sehr sicher ¹

- 1 2 3 4 5 6 7 8 9 10

Seitenumbruch --- Fortsetzung Bereich 1

Überleitung

Nun haben wir sehr detailliert über Ihre Medikamente gesprochen. Jetzt folgen einige allgemeine Fragen zu den Medikamenten.

5. Denken Sie, dass Sie gut Bescheid wissen, wie Sie Ihre Medikamente anwenden und worauf Sie achten müssen?

(Zeit lassen für eine generelle Antwort.)

Wenn Sie das auf einer Skala von 1-10 angeben müssen, wie sicher fühlen Sie sich? 1 heisst sehr unsicher, 10 sehr sicher.

- 1 1 2 3 4 5 6 7 8 9 10 Keine Antwort

6. Wieder auf einer Skala von 1-10, wie gross schätzen Sie den zeitlichen Aufwand für das Anwenden der Medikamente? 1 bedeutet sehr klein, 10 sehr gross.

Zur Anwendung gehören die Entnahme aus der Packung, das Bereitstellen, allfällige Zubereitungen und die Einnahme oder Verabreichung.

- 1 1 2 3 4 5 6 7 8 9 10 Keine Antwort

Bemerkungen zu Bereich 1

Seitenumbruch --- Bereich 2

Wir möchten in dieser Befragung von Ihren Erfahrungen im täglichen Umgang mit Ihren Medikamenten lernen.

Dabei möchten wir festhalten, dass es auf die folgenden Fragen keine richtige oder falsche Antwort gibt - nur Ihre Erfahrung zählt. Ihre Angaben werden anonym und vertraulich behandelt werden. Weder Ihr/e Arzt/In, noch Ihr/e ApothekerIn werden von diesen persönlichen Antworten erfahren.

7. Denken Sie an alle vom Arzt verordneten Medikamente.

Schätzen Sie in Prozent, wie viele der Medikamente Sie seit Beginn der Studie wie verordnet anwenden können.

Ein Beispiel: Wenn Sie die Hälfte Ihrer Medikamente wie verordnet anwenden könnten, wäre Ihre Antwort '50'. Wenn sie weniger als die Hälfte wie verordnet angewendet haben, so liegt die Antwort zwischen 0 und 50, wenn Sie mehr als die Hälfte wie vom Arzt verschrieben angewendet haben, so wird Ihre Schätzung zwischen 50 und 100 liegen.

1

8. (Falls Antwort < 100%): Wenden Sie dann jeweils eines, mehrere oder alle Medikamente nicht wie verordnet an?

- Eines
- Mehrere
- Alle
- Anderes:

9. (Falls Antwort < 100%): Welcher Anwendungszeitpunkt ist für Sie am schwierigsten wie vorgesehen einzuhalten?

- Morgens
- Mittags
- Abends
- Zur Nacht
- Anderes:

10. Denken Sie an die Zeit vor 4 Wochen zurück. (z.B. das war Ende Juni)

Schätzen Sie in Prozent, wie viele der Medikamente Sie vor 4 Wochen wie verordnet anwenden konnten.

9. Denken Sie an die nächsten 4 Wochen (z.B. das wird Ende August sein)

Schätzen Sie in Prozent, wie viele der Medikamente Sie in 4 Wochen wie verordnet anwenden werden können.

Nun folgen einige Fragen, die sich auf Ihre heutige Situation beziehen.

Es geht nicht darum, ob die Medikamente wirken, sondern nur, wie komfortabel die Anwendung für Sie ist.

10. Wie zufrieden sind Sie mit dem Therapieplan auf einer Skala von 1-10?

Wie gesagt, es geht nicht um die Wirkung, sondern darum, wie viele Medikamente Sie zu welchen Bedingungen einnehmen müssen.

1 heisst, dass Sie sehr unzufrieden sind, 10 dass Sie sehr zufrieden sind.

1 2 3 4 5 6 7 8 9 10 Keine Antwort

11. Wie kompetent fühlen Sie sich die Medikamente anzuwenden? 1 = sehr inkompetent, 10 = sehr kompetent.

1 2 3 4 5 6 7 8 9 10 Keine Antwort

12. Wie angenehm finden Sie es die Medikamente anzuwenden? 1 = sehr unangenehm, 10 = sehr angenehm

1 2 3 4 5 6 7 8 9 10 Keine Antwort

13. Wie schwierig finden Sie es die Medikamente anzuwenden? 1 = sehr leicht, 10 = sehr schwierig

1 2 3 4 5 6 7 8 9 10 Keine Antwort

14. Wie eklig finden Sie es die Medikamente anzuwenden? 1 = sehr appetitlich, 10 = sehr eklig

1 2 3 4 5 6 7 8 9 10 Keine Antwort

15. Denken Sie, dass die Medikamente nötig sind? 1 bedeutet, Sie halten die Medikamente für sehr unnötig, 10 bedeutet, Sie halten sie für sehr nötig.

1 2 3 4 5 6 7 8 9 10 Keine Antwort

Überleitung

Es folgen nun einige Fragen zu Hilfen, die Sie von anderen Personen erhalten oder die Sie selbstständig nutzen.

16. Haben Sie eine Hilfe zur rechtzeitigen Anwendung Ihrer Medikamente?

(Wenn Patient unsicher: Haben Sie zum Beispiel eine Erinnerungshilfe?)

- Ja
- Nein
- Anderes:

17. Falls Ja, welche Art Hilfe haben Sie zur rechtzeitigen Einnahme Ihrer Medikamente?

18. Haben Sie zum Beispiel eine Dosierbox?

Das ist eine Pillenbox, welche Patienten die rechtzeitige Medikamenteneinnahme erleichtert.

(Weiteren Namen sind: Medikamentenspenser, Tabletendose, Tablettenbox, Tablettdispenser, Medikamentenbox, Azrnelkassette, Pillendose, Pilmate, Medikamentenschieber oder Medikamentenschieber.)

- Ja
- Nein
- Anderes:

(Falls ja:) Benutzen Sie diese Dosierbox?

- Ja
- Nein
- Anderes:

19. (Falls Ja:) Von wem haben Sie diese Dosierbox bekommen?

20. (Falls Ja:) Wann haben Sie diese bekommen?

21. (Falls Ja:) Wer füllt die Medikamente in der Dosierbox nach?

22. Nehmen Sie zur Anwendung Ihrer Medikamente Hilfe durch eine andere Person in Anspruch? Zum Beispiel beim Eincremen von Salben oder beim Herausdrücken der Pillen aus der Verpackung? ¹

- Ja
- Nein
- Anderes:

23. Falls Ja, von wem erhalten Sie diese Hilfe?

24. Wie gross ist Ihr aktueller Bedarf nach (zusätzlicher) Hilfe für die Anwendung der Medikamente?

1 bedeutet, dass Sie heute gut zurecht kommen, 10 dass Sie noch mehr Hilfe brauchen würden.

¹

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
- Keine Antwort

25. Wie vergesslich bezüglich der Anwendung Ihrer Medikamente schätzen Sie sich, auf einer Skala von 1-10, ein? 1 = absolut nicht vergesslich, 10 = sehr vergesslich ¹

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
- Keine Antwort

26. Haben Sie Probleme beim Schlucken von Medikamenten? ¹

- Ja
- Nein
- Anderes:

Bemerkungen zu Bereich 2

Seitenumbruch --- Bereich 3

Wir nun schon über die Hälfte des Interviews hinter uns. Ich möchte Ihnen als nächstes einige Fragen zur BERATUNG für die Medikamenten-Anwendung stellen.

27. Haben Sie je von einer Fachperson eine Beratung zu Ihren Medikamenten erhalten? ¹

- Ja
- Nein
- Anderes:

28. Falls Ja, von wem?

Gab es sonst noch andere Personen oder Instanzen, die Sie beraten haben? (erste 3 Antworten werden erfasst)

Beratung 1

Beratung 2

Beratung 3

Es folgen jetzt wieder einige Fragen mit Skalen von 1-10.

29. (Falls Ja:) Wie fachlich kompetent empfanden Sie die Beratung?

Fachlich kompetent heisst, dass die Person genügend Wissen über Ihre Medikamente und deren Anwendung hat.

1 = fachlich sehr inkompetent, 10 = fachlich sehr kompetent

	1	2	3	4	5	6	7	8	9	10	Keine Antwort
Beratung 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

30. (Falls Ja:) Wie verständlich fanden Sie die Beratung?

Haben Sie verstanden was der Berater/die Beraterin sagte?

1 = sehr schlecht verständlich, 10 = sehr gut verständlich

	1	2	3	4	5	6	7	8	9	10	Keine Antwort
Beratung 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

31. (Falls ja:) Wie zufrieden sind Sie mit der Beratung? 1 = sehr unzufrieden, 10 = sehr zufrieden

	1	2	3	4	5	6	7	8	9	10	Keine Antwort
Beratung 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

32. (Falls ja:) Wie zufrieden sind Sie mit der Zeit, die man sich genommen hat, um Sie zu beraten? 1 = sehr unzufrieden, 10 = sehr zufrieden

	1	2	3	4	5	6	7	8	9	10	Keine Antwort
Beratung 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

33. (Falls ja:) Hat Ihnen die Beratung geholfen? 1 = Nein, die Beratung war sehr nutzlos, 10 = Ja, sie war sehr hilfreich

	1	2	3	4	5	6	7	8	9	10	Keine Antwort
Beratung 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Beratung 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

34. (Falls ja:) Was war hilfreich und was war nicht hilfreich an der Beratung?

Hilfreich:

Nicht hilfreich:

35. Denken Sie, dass Sie momentan noch weitere Beratung brauchen könnten? ¹

- Ja
- Nein
- Anderes:

36. Falls Ja, von wem und was erwarten Sie von einer solchen Beratung?

Bemerkungen zu Bereich 3

Seitenumbruch --- Bereich 4

Im vierten Teil des Interviews geht es um die letzten Arzt- oder Spitalbesuche.

Versuchen Sie, so genau wie möglich zu antworten. Wenn Sie sich aber zum Beispiel nicht mehr ganz genau an ein Datum erinnern können, ist das nicht tragisch.

37. Gab es in den letzten zwei Wochen (= seit dem Studienbeginn in der Apotheke) einen ungeplanten Besuch beim Arzt? ¹

- Ja
- Nein
- Anderes:

38. (Falls Ja:)

Wann erfolgte der Besuch?

Bei wem?

Aus welchem Grund?

39. Wann war Ihr letzter geplanter Besuch bei folgenden Ärzten (= mit Termin vorvereinbart)?

	Letzte Woche	Vor 2 Wochen	Vor 3 Wochen	Vor 4 Wochen	Vor mehr als 4 Wochen	Kein Bedarf	Weiss es nicht	Keine Antwort
Hausarzt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Spezialist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Spital	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weiss nicht	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

40. Gab es in den letzten zwei Wochen (= seit Studienbeginn in der Apotheke) Änderungen in Ihrem Medikamentenplan? ¹

- Ja
- Nein
- Anderes:

41. Ist in den nächsten drei Monaten ein Arztbesuch geplant?

- Ja
- Nein
- Anderes:

42. Falls Ja, wann und bei wem?

	In den nächsten 2 Wochen	Nächsten Monat	In den nächsten 3 Monaten	Weiss nicht	Keine Antwort
Hausarzt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Spezialist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Spital	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weiss nicht	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Keine Antwort	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

43. Ist in den nächsten drei Monaten ein Spitalaufenthalt geplant?

- Ja
- Nein
- Anderes:

44. Falls Ja, wann und bei wem? (Klinik, ev. Abteilung)

45. Was ist Ihr gesundheitliches Hauptleiden?

46. Wie störend ist dieses Hauptleiden für Sie im Alltag auf einer Skala von 1-10? 1 = absolut nicht störend, 10 = sehr störend

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
- Keine Antwort

47. Gerne möchte ich mehr über Ihre PERSÖNLICHE ÜBERZEUGUNG in Bezug auf die Medikamente, die Sie aufgrund Ihrer Krankheit einnehmen, erfahren.

Ich werde Ihnen zehn Aussagen vorlesen. Bitte geben Sie mir jeweils an, wie stark diese Aussagen für Sie zutreffen.

Wir erfassen Ihre Antworten in diesem Fall nicht mit Zahlen, sondern bieten Ihnen folgenden Antwortmöglichkeiten an:

Sie können einer Aussage **voll und ganz** [Pause] **eher oder eher nicht** [Pause] **ganz und gar nicht** [Pause] oder **weder noch** zustimmen.

Ich kann diese Antwortmöglichkeiten bei den einzelnen Aussagen gerne nochmals wiederholen für Sie.

Die erste Aussage wäre...

	Stimme voll und ganz zu	Stimme eher zu	Weder noch	Stimme eher nicht zu	Stimme überhaupt nicht zu	Keine Antwort
Meine derzeitige Gesundheit hängt von meinen Medikamenten ab. (Regelanweisung: Antwortmöglichkeiten nochmals aufzählen) Es bereitet mir Sorgen, Medikamente nehmen zu müssen.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Mein Leben, so wie ich es jetzt führe, wäre ohne meine Medikamente nicht möglich.

Ohne meine Medikamente wäre ich sehr krank.

Manchmal mache ich mir Sorgen, wegen der langfristigen Auswirkungen meiner Medikamente.

Meine Medikamente sind mir ein Rätsel.

Meine zukünftige Gesundheit hängt von meinen Medikamenten ab.

Meine Medikamente stören mein Leben.

Manchmal mache ich mir Sorgen, von meinen Medikamenten zu abhängig zu werden.

Meine Medikamente schützen mich davor, dass es mir schlecht geht.

Bemerkungen zu Bereich 4

Seitenumbruch --- Bereich 5

Wir sind jetzt schon fast fertig mit dem Interview.

Ich möchte Ihnen nur noch einige Fragen zu Ihrer Apotheke stellen.

48. Wie viele unterschiedliche Apotheken haben Sie in den letzten 12 Monaten besucht?

49. Haben Sie eine Stammapotheke?

- Ja
- Nein
- Anderes:

Wo beziehen Sie Ihre Medikamente mehrheitlich? (Antwortoptionen vorlesen, Mehrfachnennungen möglich)

- In meiner Stammapotheke (= ärztliches Rezept wird eingelöst)
- In mehreren Apotheken (= ärztliches Rezept wird eingelöst)
- Von einem Arzt (= Direktabgabe durch den Arzt/Ärztin)
- Durch den Versandhandel (= die Medikamente kommen mit der Post)
- Anderes:

Es folgen nun nochmals einige Fragen mit Antworten auf einer Skala von 1-10.

Ich werde wiederum bei jeder Fragen erwarhen, für was die Zahlen stehen. Die folgenden Fragen beziehen sich auf die Apotheke, die Sie angefragt hat, an dieser Studie teilzunehmen.

Wie bei allen anderen Fragen, werden auch hier alle Ihre Antworten anonym erfasst und sind für Ihre Apotheke und den Apotheker / die Apothekerin NICHT einsehbar.

50. Wie zufrieden sind Sie mit Ihrer Apotheke auf einer Skala von 1-10? 1 = sehr unzufrieden, 10 = sehr zufrieden ¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

51. Wenn Ihnen Ihr Apotheker einen Rat gibt, befolgen Sie ihn in der Regel? 1 heisst, sie befolgen den Rat nie, 10 heisst, Sie befolgen ihn immer. ¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

52. Wie fachlich kompetent schätzen Sie Ihren Apotheker/Ihre Apothekerin auf einer Skala von 1-10 ein?

Fachlich kompetent heisst, dass die Person genügend Wissen über Ihre Medikamente und deren Anwendung hat.

1 = fachlich sehr inkompetent, 10 = fachlich sehr kompetent

¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

53. Wie zufrieden sind Sie mit der Zeit, die Ihr Apotheker für Sie aufwendet? 1 = sehr unzufrieden, 10 = sehr zufrieden ¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

54. Wie sehr haben sie das Gefühl, mit Ihren Anliegen bei Ihrem Apotheker / Ihrer Apothekerin gut aufgehoben zu sein? 1 = sehr schlecht aufgehoben, 10 = sehr gut aufgehoben ¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

55. Wie sehr verstehen Sie Ihre Medikamente und deren Anwendung besser, nachdem Sie bei Ihrem Apotheker, Ihrer Apothekerin gewesen sind? 1 = absolut nicht besser, 10 = sehr viel besser ¹

1 2 3 4 5 6 7 8 9 10 Keine Antwort

Bemerkungen zu Bereich 4

Seitenumbruch --- Abschluss

Wir sind nun am Schluss der Befragung angekommen.
Ganz herzlichen Dank!

Haben Sie noch Anmerkungen zum Interview, oder haben Sie noch Fragen?

Endzeitpunkt festhalten: ¹

Ich werde Sie in 4 Monaten wieder anrufen und Sie bitten nochmal an einem Telefoninterview für diese Studie teilzunehmen.

Das Interview wird dann etwas kürzer sein.

Kann ich Sie in 4 Monaten unter der gleichen Nummer erreichen? ¹

Ja Nein

Wenn nein, neue Telefonnummer:

Zu welcher Tageszeit werde ich sie am besten erreichen können für diese Befragung in 4 Monaten?

Ich möchte Ihnen nochmals ganz herzlich für Ihre Teilnahme an der Studie danken.

Bei Fragen zu Ihren Medikamenten können Sie sich jederzeit bei Ihrem Apotheker / Ihrer Apothekerin melden.

Nun möchte ich mich von Ihnen verabschieden. Ich wünsche Ihnen noch einen schönen Tag/Abend!

Abschicken

Zurücksetzen

Vorschau schliessen

FlexiForm 2.6.9, Disclaimer - © 2005-2012 URZ NIKT

12.3 Project C

12.3.1 Ethical approval SWAMECO EKNZ 2014-013

Seite 2

Beschlussmitteilung der Ethikkommission Nordwest- und Zentralschweiz

Die Ethikkommission Nordwest- und Zentralschweiz hat das nachstehende Forschungsprojekt anlässlich der Ausschuss-Sitzung vom 08. Januar 2014 (in der Zusammensetzung, wie sie auf Seite 2 wiedergegeben ist) eingehend begutachtet:

Ref.Nr. EKNZ. 2014-013

Titel des Forschungsprojektes

Schluckbeschwerden und Medikamentencompliance bei Sklerodermiepatienten: Entwicklung, Pilotierung und Validierung eines Self-Assessment Fragebogens

Prüfer/in

Name, Vorname, Titel: PD Dr. med. Michael Busan
 Funktion: Leitender Arzt/Reha Rheinfelden
 Adresse: Saffnerstrasse 98, 4310 Rheinfelden

Die Ethikkommission stützt ihre Beurteilung auf die Unterlagen, wie sie in den beiliegenden "Anträgen auf Begutachtung" vom 13. Dezember 2013 abschliessend aufgezählt sind.

normales Verfahren vereinfachtes Verfahren Nachbegutachtung

Die Ethikkommission kommt zu folgendem **Beschluss**:

A positiv (siehe Seite 2ff)
 B positiv mit Bemerkungen (siehe Seite 2ff)
 C mit Auflage (siehe Seite 2ff)

Nachbegutachtung durch Ethikkommission notwendig

schriftliche Mitteilung an Ethikkommission ausstehend

D negativ (mit Begründung und Erläuterung für die Neubeurteilung) (siehe Seite 2ff)
 E Nicht-Eintreten (mit Begründung) (siehe Seite 2ff)

Der Beschluss gilt auch für die im "Antrag auf Begutachtung" gemeldeten weiteren Prüfer/innen im Zuständigkeitsbereich der Ethikkommission.


Pro Memoria: Pflichten des/der verantwortlichen Prüfers/in
 Geprüfte Produkte und Vergleichsprodukte (Arzneimittel und Medizinprodukte) müssen - zur Sicherstellung der Qualität und der Sicherheit - fachgerecht hergestellt, evaluiert und eingesetzt werden.

Meldepflicht bei:

- a) schwerwiegenden unerwünschten Ereignissen (serious adverse events) unverzüglich
- b) neuen Erkenntnissen, die während des Versuchs verfügbar werden und die Sicherheit der Versuchspersonen sowie die Weiterführung des Versuchs beeinträchtigen können
- c) Änderung des Protokolls (Versuchspplans)
- d) Ende oder Abbruch der Studie

Zwischenbericht einmal pro Jahr
 Meldeungs- oder Bewilligungspflicht von Studien bei Swissmedic bzw. anderen Bundes- oder kantonalen Behörden - sofern erforderlich (bei sponsorisierten Studien ist dies die Pflicht des Sponsors)
 Schlussbericht:

Für die Ethikkommission:
 Ort, Datum, Basel, 11. Januar 2014 Name(N): Prof. A. P. Perruchoud
 Dr. M. Schäfer

Unterschrift(en): 

Seite 2

Ref. Nr. EKNZ: 2014-013

Zusammensetzung der Ethikkommission

Die Ethikkommission tagte in der nachfolgend erwähnten Zusammensetzung und war damit beschlussfähig (Art. 32 der Verordnung über klinische Versuche mit Heilmitteln vom 17. 10. 2011)

Name, Vorname	Berufliche Stellung / Titel	m	f	ja	nein
Prof. A. P. Perruchoud	Präsident der EKNZ	X		X	
Dr. M. Schäfer	Vizepräsident der EKNZ	X		X	
Prof. G. Schubiger	Vizepräsident der EK93	X		X	
Prof. M. Kärlin	Ausschuss-Mitglied der EKNZ	X			X
Prof. T. Körne	Ausschuss-Mitglied der EKNZ	X		X	
Dr. Iur. J. Müller	Ausschuss-Mitglied der EKNZ	X			X

Empfehlungen

(erweiterbar)

Aufgabe:

- Die EKNZ erwartet die Nachreichung des Curriculum vitae des Studienleiters. (erweiterbar)

Bemerkungen

- Die EKNZ bestätigt, dass sie nach GCP-ICH-Richtlinien arbeitet. (erweiterbar)

Basistformular zur Einreichung eines biomedizinischen Forschungsprojektes
eingereicht bei der EKBB beider Basel am 13.12.2013

Titel des eingereichten Forschungsprojektes gemäss Protokoll
Schluckbeschwerden und Medikamentencompliance bei Sklerodermiapatienten: Entwicklung, Fiktion und Validierung eines Self-Assessment Fragebogens

1. Meldung
 Weitere Meldung
Ref. Nr. EK: Ref. Nr. SwsmrmedBAG:

Prüfer/in (verantwortlicher Prüfer/in im Zuständigkeitsbereich der EK)
Name, Vorname, Titel: PD Dr. Michael Buser
Funktion: Leitender Arzt Rheuma Rheumaten
Adresse: Sallmattstrasse 98, 4310 Rietwil
Tel.: 051 836 32 33 Fax: 061 836 53 53 E-Mail: M.Buser@aha-rl.ch
 weitere Mitarbeiter/innen (gemäss beiliegender Liste)

Koordinierender Prüfer/in in der Schweiz (bei Multizenterprojekten)
Name, Vorname, Titel:
Funktion:
Adresse:
Tel.: Fax: E-Mail:

Leitende Ethikkommission (bei Multizenterprojekten gem. AGEK-Konzept (www.swissethics.ch))
Kantonale Ethikkommission:
Präsident/Sekretär:
Adresse: Fax: E-Mail:
Tel.:

Sponsor
Firma / Institution: Universal Basel, Pharmaceutical Care Research Group
Verantwortliche Person in der Schweiz: Prof. Kurt E. Hersberger
Adresse: Klingelbergstr. 50, 4056 BS
Tel.: 061 2557 14 28 Fax: 061 267 14 28 E-Mail: kurt.hersberger@unibas.ch

1. Finanzierungsquelle (falls nicht identisch mit Sponsor)
Firma / Institution:
Adresse:
Kontaktperson: Fax: E-Mail:
Tel.:

Weitere Finanzierungsquellen
Firma / Institution:
Adresse:
Kontaktperson: Fax: E-Mail:
Tel.:

Tel.: Fax: E-Mail:
Firma / Institution:
Adresse:
Kontaktperson: Fax: E-Mail:
Tel.:

CRO (Auftragforschungsinstitut)
Name:
Adresse:
Kontaktperson: Fax: E-Mail:
Tel.:

Art des Forschungsprojektes
 Arzneimittel, Phase: I II III IV
 Medizinprodukte, zertifiziert: Ja nein
 Radiopharmazeutika
 Blutprodukte
 Inmunologische Produkte
 Strahlentherapie
 Gerontologische Studien
 Andere, nämlich:

Transplantation
 Grundlagenforschung
 Epidemiologie
 Personendatenstudien
 Osteoporose, Physiotherapie,
Pflegevorschüben
 Forschung an Embryonen (in vitro)
 Pathologie
 Psychotherapiestudien

Versuchspräparate
(Wirkstoffe und Markenname/n)
In

Vergleichspräparate
(Wirkstoffe und Markenname/n)
In

Forschungsprojekt in Stichworten
Entfallt hier, Stene Zusammenfassung des Studienprotokolls gemäss Vorlage (www.swissethics.ch) unter Checklisten/1.111111

Welches sind Ihre ethischen Überlegungen, die die Durchführung dieses Versuchs rechtfertigen?
Befragung von Sklerodermiapatienten mit Schluckbeschwerden mittels Fragebogen, um Ihre pharmazeutische Betreuung zu optimieren.

Vorgesehene Anzahl Versuchspersonen
In der Schweiz: weltweit:
Im Zuständigkeitsbereich der EK: 80

Teilnahme von besonders schutzbedürftigen Versuchspersonen

ja, nämlich gesunde Versuchspersonen Minderjährige
 ja, nämlich Insassen von Institutionen Urteilsunfähige oder Einmündige
 Notfälle Terminale Patienten
 Andere:

Vorgesehene Anzahl Versuchsorte im Zuständigkeitsbereich der EK

X 1 mehrere (gemäss beiliegender Liste)

Weitere Kantone, in denen das Forschungsprojekt durchgeführt wird

<input checked="" type="checkbox"/> AG	<input type="checkbox"/> AI	<input type="checkbox"/> AR	<input type="checkbox"/> BE	<input type="checkbox"/> BL	<input type="checkbox"/> BS	<input type="checkbox"/> FR
<input type="checkbox"/> GE	<input type="checkbox"/> GL	<input type="checkbox"/> GR	<input type="checkbox"/> JU	<input type="checkbox"/> LU	<input type="checkbox"/> NE	<input type="checkbox"/> NW
<input type="checkbox"/> OW	<input type="checkbox"/> SG	<input type="checkbox"/> SH	<input type="checkbox"/> SO	<input type="checkbox"/> SZ	<input type="checkbox"/> TG	<input type="checkbox"/> TI
<input type="checkbox"/> UR	<input type="checkbox"/> VD	<input type="checkbox"/> VS	<input type="checkbox"/> ZG	<input type="checkbox"/> ZH		

Weitere Länder, in denen das Forschungsprojekt durchgeführt wird

FL andere, nämlich: Deutschland, Österreich (Wohnort der Patienten) keine

Dauer des Forschungsprojekts

vorgesehener Beginn des Forschungsprojekts (Rekrutierung der ersten Versuchsperson): Jan 2014
 vorgesehene Ende des Forschungsprojekts (letzte Versuchsperson, letzte Visite): Dec 2014

Wurde oder wird dieses Forschungsprojekt bereits durch andere Ethikkommissionen in der Schweiz beurteilt?

ja, bitte (Ersch.)entschied(e) belegen nein
 pendelt, nämlich bei:

Mit dem Begleitschreiben werden folgende Unterlagen beigelegt:

<input checked="" type="checkbox"/> Dattens und unterschriebenes Basisformular	<input checked="" type="checkbox"/> Dattens und unterschriebenes Protokoll des Forschungsprojekts:	<input type="checkbox"/> Originalversion vom 13.12.2013	<input type="checkbox"/> Protokoll	<input type="checkbox"/> Amendment (datiert + unterschrieben) Nr. _____ vom _____	<input type="checkbox"/> Letzte Version des datierten und unterschriebenen Protokolls (inkl. Amendments) vom _____	<input type="checkbox"/> Zusammenfassung des Protokolls in allgemeinverständlicher Sprache	<input type="checkbox"/> Information bezüglich Rekrutierung der Versuchspersonen (inkl. Inseratelexte und Abfragelexte vom _____, vorgesehene Medien (namentlich auflühren))	<input checked="" type="checkbox"/> Information für Versuchspersonen	<input checked="" type="checkbox"/> X auf Deutsch vom 13.12.2013	<input type="checkbox"/> auf Französisch vom _____	<input type="checkbox"/> auf Italienisch vom _____	<input type="checkbox"/> in anderen Sprachen: _____ vom _____	<input type="checkbox"/> Einwilligungserklärung für Versuchspersonen	<input checked="" type="checkbox"/> X auf Deutsch vom 13.12.2013	<input type="checkbox"/> auf Französisch vom _____	<input type="checkbox"/> auf Italienisch vom _____	<input type="checkbox"/> in anderen Sprachen: _____ vom _____	<input type="checkbox"/> Ausmass und Art der Entschädigung für Versuchspersonen	<input type="checkbox"/> Ausmass und Art der Entschädigung für Prüfer/innen	<input type="checkbox"/> Amt Versuchs-ort gültige(r) Versicherungsaussweise/-liche vom _____	<input type="checkbox"/> Bestätigung des Sponsors bezüglich Schadensdeckung vom _____	<input type="checkbox"/> Bestätigung der (für die Schweiz bezeichneten Person, welche sich bereit erkl. art, die Pflichten gemäss Art. 7 Abs. 3 Vklm. in der Schweiz zu übernehmen vom _____	<input type="checkbox"/> Verträge, die zwischen dem Sponsor und dem Prüfer oder zwischen einem Auftragsforschungsinstitut (CRO, Call Center) und dem Sponsor oder dem Prüfer abge-schlossen wurden	<input type="checkbox"/> Darlehen und unterschriebenes CV des/der Prüfers/in und CVs der Co-Prüfer/innen	<input type="checkbox"/> Liste weiterer Prüfer/innen an Versuchs-orten im Zuständigkeitsbereich der EK, Stand _____ vom _____	<input checked="" type="checkbox"/> X Liste weiterer Mitarbeiter/innen im Zuständigkeitsbereich der EK, Stand vom _____	<input type="checkbox"/> U.S. 12.2013	<input type="checkbox"/> Wissenschaftliche Literatur	<input type="checkbox"/> Wissenschaftliche Literatur	<input type="checkbox"/> Wissenschaftliche Literatur	<input type="checkbox"/> (Ersch.)entschied(e) anderer Ethikkommissionen	<input type="checkbox"/> Andere Dokumente je nach Art des Versuchs (z.B. für Medizinprodukte, Gentherapie-Versuche):
--	--	---	------------------------------------	---	--	--	--	--	--	--	--	---	--	--	--	--	---	---	---	--	---	--	--	--	---	---	---------------------------------------	--	--	--	---	--

Datum: 13.12.13

Unterschrift des/der Verantwortlichen Prüfers/in: 

Von der Ethikkommission auszufüllen, sofern die Dokumente im Ertscheiderbrief der EK nicht auf-führt werden

Die Ethikkommission bestätigt, alle oben aufgeführten Dokumente erhalten und geprüft zu haben. Für die Ethikkommission:

Name + Vorname, Funktion: Irina Oberli
 Sekretariat Ethikkommission
 Hohenstrasse 53
 CH-4056 Basel

Datum: 11. Jan. 2014

Unterschrift: 

12.3.2 Patient information and informed consent SWAMECO

TEILNEHMERINNEN- / TEILNEHMERINFORMATION zur Hauptstudie „Schluckbeschwerden und Medikamenteneinnahme“

[EKNZ 2014-013]

Sehr geehrter Teilnehmer, sehr geehrte Teilnehmerin

Wir fragen Sie an, ob Sie an einer Studie teilnehmen möchten, weil Sie ein Patient / eine Patientin mit Sklerodermie sind, der / die in der Reha Rheinfelden (Schweiz) behandelt wird. **Das Ziel dieser Studie ist es, mit einem Fragebogen die Häufigkeit und das Ausmass von Schluckbeschwerden bei der Einnahme von Medikamenten bei Patienten mit Sklerodermie zu erfassen, sowie deren Konsequenzen für den Alltag zu untersuchen.**

Zur Studie werden alle Sklerodermiepatienten der Reha Rheinfelden eingeladen einen Fragebogen auszufüllen – **unabhängig, ob Schluckbeschwerden vorhanden sind oder nicht.** Alle Angaben werden anonymisiert erfasst, sodass kein Rückschluss auf Ihre Person möglich ist. Die Studie wird im Rahmen der geltenden Gesetze und international anerkannten Grundsätzen durchgeführt und wurde von der Ethikkommission Nord- und Zentralschweiz geprüft und bewilligt.

Ihre Teilnahme an dieser Studie ist freiwillig. Wenn Sie nicht an dieser Studie teilnehmen wollen, haben Sie keine Nachteile für Ihre medizinische Betreuung zu erwarten. Das gleiche gilt, wenn Sie Ihre einmal gegebene Einwilligung zu einem späteren Zeitpunkt widerrufen. Diese Möglichkeit haben Sie jederzeit. Einen allfälligen Widerruf Ihrer Einwilligung bzw. den Rücktritt von der Studie müssen Sie nicht begründen.

Ablauf der Studie

Wenn Sie sich zur Teilnahme an der Studie einverstanden erklären, bitten wir Sie die beiliegende Einverständniserklärung auszufüllen und in das beiliegende, blau markierte Couvert zu legen und abzuschicken. Wenn Sie nicht an der Studie teilnehmen möchten, steht es Ihnen frei, die erhaltenen Unterlagen zu entsorgen.

Füllen Sie weiter den Fragebogen zu allfälligen Schluckbeschwerden mit der Einnahme von Medikamenten und persönlichen Angaben aus. **Bei den Angaben zu Schluckbeschwerden gibt es keine richtigen oder falschen Antworten - nur Ihre Meinung und Ihr Eindruck sind für uns wichtig.** Alle Angaben werden ausschliesslich in anonymisierter Form für die Studie verwendet und nicht an Dritte weitergegeben. Das Ausfüllen des Fragebogens dauert ca. 15 Minuten. Wenn Sie die Fragebogen ausgefüllt haben, legen Sie bitte beide Dokumente in das beiliegende gelbe Couvert und stellen es via Postweg dem Studienzentrum zu.

Wir bitten Sie, sämtliche Studienunterlagen bis zum **24. April 2014** abzuschicken.

Nutzen: Dank Ihrer Studienteilnahme könnten in Zukunft Patienten / Patientinnen mit Schluckbeschwerden gezielter beraten und betreut werden.

Bitte wenden!

Risiken und Unannehmlichkeiten: Im Zusammenhang mit dem Ausfüllen des Fragebogens sind keine Risiken zu erwarten. Es werden für diese Studie zu keinem Zeitpunkt Blutproben entnommen oder Laboruntersuchungen durchgeführt. Sollten aufgrund der Antworten Rückfragen oder Abklärungen mit einem Arzt nötig werden, so erfolgen diese in jedem Fall stets mit Ihrer Einwilligung.

Bei Zufallsbefunden aus Ihren Antworten (z.B. eine potentielle Nebenwirkung Ihrer Medikamente), die zur Verhinderung, Feststellung und Behandlung bestehender oder künftig zu erwartender Krankheiten beitragen können, haben Sie die Wahl: a) Sie möchten über diese Befunde direkt informiert werden, b) Sie möchten nicht informiert werden, oder c) Sie überlassen die Entscheidung Ihrem behandelnden Arzt (siehe Beilage ‚Einverständniserklärung‘).

Vertraulichkeit der Daten: In dieser Studie werden persönliche Daten von Ihnen erfasst. Diese Daten werden verschlüsselt, d.h. mit einem Code versehen. Dieser Code wird im Studienzentrum verschlossen und getrennt von anderen Daten aufbewahrt. Den wissenschaftlichen Fachleuten sind nur verschlüsselte Daten zur Auswertung zugänglich. Im Rahmen von Inspektionen können die Mitglieder der zuständigen Behörden und Ethikkommissionen Einsicht in Ihre nicht codierte Originaldaten nehmen. Während der ganzen Studie und bei den erwähnten Kontrollen wird die Vertraulichkeit strikt gewahrt.

Ihr Name wird in keiner Weise in Berichten oder Veröffentlichungen, die aus der Studie hervorgehen, veröffentlicht. Verantwortlich für die Einhaltung der nationalen und internationalen Richtlinien zum Datenschutz ist die Pharmaceutical Care Research Group (Universität Basel).

Kosten: Weder Ihnen, noch ihrer Krankenkasse entstehen im Zusammenhang mit Ihrer Teilnahme zusätzliche Kosten. Damit Ihr Aufwand für die Teilnahme und die Frankatur für die Rücksendung vergütet.

Entschädigung: Für die Teilnahme an dieser Studie erhalten Sie CHF 10.- (Reka-Checks), welche Ihnen nach Beendigung der Studie per Post zugestellt werden.

Versicherungsschutz: Für Schäden, die Sie im Rahmen dieser Studie erleiden sollten, ist die Reha Rheinfelden durch eine Haftpflichtpolice versichert.

Kontaktpersonen: Bei Unklarheiten, die während der Studie oder nach deren Abschluss auftreten, können Sie sich jederzeit an die untenstehende Kontaktperson wenden:

Studienkoordination

Markus Messerli, MSc
Leitender Apotheker Reha Rheinfelden Doktorand an
der Universität Basel
Tel.: 061 / 267 15 29
eMail: markus.messerli@unibas.ch

Prüfarzt

PD Dr. med. Michael Buslau
Leitender Arzt Reha Rheinfelden
Tel.: 061 / 836 52 35
eMail: m.buslau@reha-rhf.ch

Diese Patienteninformationen dürfen Sie gerne behalten.

SCHRIFTLICHE EINVERSTÄNDNISERKLÄRUNG DES PATIENTEN / DER PATIENTIN ZUR TEILNAHME AN EINER KLINISCHEN STUDIE

Bitte lesen Sie dieses Formular sorgfältig durch und wenden Sie sich an das Studienzentrum, wenn Sie etwas nicht verstehen oder wissen möchten: Markus Messerli, Universität Basel, 061 / 267 15 29 oder 079 / 751 18 72.

Nummer der Studie	EKNZ 2014-013
Titel der Studie	Schluckbeschwerden und Medikamenteneinnahme bei Sklerodermiepatienten
Sponsor (Studienkoordination)	Pharmaceutical Care Research Group, Universität Basel, Prof. Kurt Hersberger Klingelbergstrasse 50, CH-4056 Basel
Ort der Studie	Reha Rheinfelden, Salinenstrasse 98, CH-4310 Rheinfelden
Studienkoordination	Pharmaceutical Care Research Group, Universität Basel, Markus Messerli Klingelbergstrasse 50, CH-4056 Basel
Studien ID	
Patient / Patientin	<input type="checkbox"/> männlich <input type="checkbox"/> weiblich
Name und Vorname
Adresse [Strasse / PLZ / Ort]
Geburtsdatum / / (Tag. / Monat / Jahr)
Telefonnummer (inkl. Vorwahl)

- Ich habe die zur oben genannten Studie abgegebene schriftliche Patienteninformation gelesen und verstanden. Meine Fragen im Zusammenhang mit der Teilnahme an dieser Studie sind mir zufriedenstellend beantwortet worden. Ich kann die schriftliche Patienteninformation behalten.
- Ich hatte genügend Zeit, um meine Entscheidung zu treffen.
- Bei Zufallsbefunden möchte ich **a)** direkt informiert werden **b)** nicht informiert werden **c)** die Entscheidung dem behandelnden Arzt überlassen.
- Ich weiss, dass meine persönlichen Daten in anonymisierter Form an die Universität Basel zu Forschungszwecken weitergegeben werden. Ich bin einverstanden, dass die zuständigen Fachleute der zuständigen Ethikkommission zu Prüf- und Kontrollzwecken Einsicht in meine Originaldaten nehmen dürfen, jedoch unter strikter Einhaltung der Vertraulichkeit.
- Ich nehme an dieser Studie freiwillig teil. Ich kann jederzeit und ohne Angabe von Gründen meine Zustimmung zur Teilnahme widerrufen, ohne dass mir deswegen Nachteile bei der weiteren medizinischen Betreuung entstehen.
- Im Interesse meiner Gesundheit kann mich der Prüfer jederzeit von der Studie ausschliessen.

Ort, Datum	Unterschrift der Patientin / des Patienten
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Bestätigung der Studienkoordination: Hiermit bestätige ich, dass ich diesem Patienten / dieser Patientin Wesen, Bedeutung und Tragweite der Studie schriftlich erläutert habe. Ich versichere, alle im Zusammenhang mit dieser Studie stehenden Verpflichtungen zu erfüllen. Sollte ich zu irgendeinem Zeitpunkt während der Durchführung der Studie von Aspekten erfahren, welche die Bereitschaft des Patienten / der Patientin zur Teilnahme an der Studie beeinflussen könnten, werde ich ihn / sie umgehend darüber informieren.

Rheinfelden, den 7. April 2014	Unterschrift Studienkoordination
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12.3.3 Patient baseline information questionnaire SWAMECO

Stammdaten ‚Schluckbeschwerden und Medikamenteneinnahme‘ [EKNZ 2014-013]

Sehr geehrter Teilnehmer, sehr geehrte Teilnehmerin

Bitte füllen Sie diesen Fragebogen zu Ihrer Person aus. Dieser hilft uns bei der Auswertung des Fragebogens zu ihren Schluckbeschwerden. Alle Angaben werden anonymisiert ausgewertet und vertraulich behandelt.

ID: _____	Jahrgang: _____	Geschlecht: <input type="radio"/> weiblich <input type="radio"/> männlich
-----------	-----------------	--

1	In welchem Land wohnen Sie?	<input type="radio"/> Schweiz <input type="radio"/> Frankreich <input type="radio"/> anderes: _____	<input type="radio"/> Deutschland <input type="radio"/> Österreich
2	Wann wurde bei Ihnen die Diagnose Sklerodermie gestellt?	____ / ____ [mm / jjjj, z.B. 10 / 2008]	
3	Ihre Körpergrösse und -gewicht	Grösse: _____ cm	Gewicht: _____ kg
4	Kam es in den letzten 6 Monaten zu einem ungeplanten Gewichtsverlust ?	<input type="radio"/> Nein	<input type="radio"/> Ja, circa _____ kg

Studien haben gezeigt, dass Rauchen oder Konsumieren von Alkohol Einfluss auf die Entwicklung von Schluckbeschwerden haben können. Dieses Risiko möchten wir näher untersuchen.

5	Rauchen Sie Tabakwaren ?	<input type="radio"/> Nein, niemals <input type="radio"/> Nein, ich bin Ex-Raucher	<input type="radio"/> Ja, täglich <input type="radio"/> Ja, nicht täglich
		,Niemals‘ bedeutet: noch nie oder weniger als 100 Zigaretten im Leben geraucht.	
6	Nehmen Sie alkoholische Getränke zu sich?	<input type="radio"/> Nein	<input type="radio"/> Ja, circa: _____ Einheiten pro Woche Eine Einheit bedeutet eine 3.3 dl Büchse bzw. eine Stange Bier, 1 dl Wein, 4 cl Schnaps oder ein Mischgetränk mit 4 cl Schnaps
7	Wurde bei Ihnen in den letzten 6 Monaten eine Lungenentzündung diagnostiziert?	<input type="radio"/> Nein	<input type="radio"/> Ja, _____ Mal (e)

Sie sind nun am Ende des Fragebogens angelangt. **Besten Dank für Ihre Teilnahme!** Retournieren Sie nun bitte den Fragebogen und die weiteren Studienunterlagen in dem beiliegenden Antwortcouvert an das Studienzentrum der Universität Basel.

APPENDIX THESIS

12.3.4 Patient self-report questionnaire SWAMECO

Pharmaceutical Care Research Group
Department of Pharmaceutical Sciences
Klingelbergstrasse 50, CH-4056 Basel

Markus Messerli
MSc pharm, PhD Student
Studienzentrum SWAMECO

Phone +41 (0)61 267 15 29
Fax +41 (0)61 267 14 28
eMail markus.messerli@unibas.ch
Web pharmacare.unibas.ch

Fragebogen ‚Schluckbeschwerden und Medikamenteneinnahme‘ [EKNZ 2014-013]

Sehr geehrte Studienteilnehmerin, sehr geehrter Studienteilnehmer

Der vorliegende Fragebogen wurde entwickelt, um Schluckbeschwerden bei der Einnahme von Medikamenten zu erfassen und zu erfahren, wie mit diesen umgegangen wird. Durch Resultate der Befragung soll es in Zukunft möglich sein, Schluckbeschwerden bei Patienten früher zu erkennen und damit die Lebensqualität und Sicherheit von Patienten zu erhöhen.

Schluckbeschwerden werden individuell unterschiedlich empfunden. Es gibt deshalb keine richtigen oder falschen Antworten. Sämtliche Angaben werden anonymisiert ausgewertet und lassen keine Rückschlüsse auf Ihre Person zu. Der Fragebogen umfasst 35 Fragen auf vier Seiten und wird rund 15 Minuten Ihrer Zeit in Anspruch nehmen. Die Fragen sind zumeist so gestellt, dass Sie das Zutreffende ankreuzen können. **Falls nicht anders erwähnt, bewerten Sie bitte jede Frage nur mit einem Kreuz. Bitte beantworten Sie alle für Sie relevanten Fragen.**

Wenn Sie den Fragebogen fertig ausgefüllt haben, retournieren Sie diesen bitte in dem beiliegenden Antwortcouvert an das Studienteam der Universität Basel.

Besten Dank für Ihre Teilnahme!

Angaben zu Ihrer Person

ID: _____	Jahrgang: _____	Geschlecht: <input type="checkbox"/> weiblich <input type="checkbox"/> männlich
------------------	------------------------	---



		Ja	Nein
1	Nehmen Sie zum heutigen Zeitpunkt mindestens ein Medikament ein, welches Sie schlucken müssen?	<input type="checkbox"/>	<input type="checkbox"/>

Haben Sie Schluckbeschwerden...		Ja, zur Zeit	Ja, in der Vergangenheit	Nein, noch nie
2	... beim Trinken ?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	... beim Essen ?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	... bei der Einnahme von Medikamenten ?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- falls Sie **eine der Fragen 2-4** mit ‚Ja‘ beantworten, fahren Sie bitte mit **Frage 5** auf Seite 2 fort.
- falls Sie die Fragen **alle mit ‚Nein‘** beantworten, fahren Sie bitte mit **Frage 18** auf Seite 3 fort.

Bitte nehmen Sie zu den folgenden Aussagen Stellung:

		Trifft voll zu	Trifft eher zu	Trifft eher nicht zu	Trifft nicht zu	Keine Angabe
5	Das Einnehmen von Medikamenten löst oder löste bei mir... .. aus.					
5.1	... ein Würgen ...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.2	... einen Hustenreiz ...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.3	... Übelkeit ...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.4	... ein Engegefühl während dem Schlucken ...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	Ich habe tagsüber einen trockenen Mund.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7	Ich muss öfters einen Schluck Wasser zu Hilfe nehmen, um besser Sprechen zu können.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8	Ich habe ein unangenehmes Brennen in meinem Mund.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9	Meine Augen und Nasenschleimhäute fühlen sich ausgetrocknet an.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10	Ich habe das Gefühl, die Medikamente bleiben beim Schlucken im Hals stecken.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11	Das Schlucken von Medikamenten verursacht Schmerzen.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12	Ich habe mir in den letzten vier Wochen Sorgen wegen meinen Schluckbeschwerden gemacht.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13	Ich nehme manchmal ein Medikament absichtlich nicht ein, weil die Einnahme mir Beschwerden bereitet.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14	Ich habe als Folge meiner Schluckbeschwerden Angst vor der nächsten Medikamenteneinnahme.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

15	<p>Denken Sie an die Medikamenteneinnahme, die Ihnen am meisten Beschwerden bereitet oder bereitet hat. Markieren Sie mit einem Strich oder Kreuz in der untenstehenden Linie zwischen 0 und 10, wie stark diese Beschwerden sind oder waren:</p> <p style="text-align: center;">0 10</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  (0 = keine Beschwerden) </div> <div style="text-align: center;">  (10 = unerträgliche Beschwerden) </div> </div>
----	---

Markieren Sie mit einem Kreuz in der Abbildung, wo Sie Beschwerden beim Schlucken von Medikamenten haben oder hatten.

Beschreiben Sie, wie sich diese anfühlen
(z.B. Kapsel bleibt kleben, Schmerz, Hustenreiz, ...)

(Mehrere Kreuze und Antworten sind möglich)

17 Welche(s) Ihrer Medikamente lösen oder lösten diese Schluckbeschwerden aus?
(bitte den **Produktenamen** und die **Dosierung** angeben, z.B. Aspirin Cardio 100mg 1x morgens 1 Tablette)

		Kopf leicht nach vorne geneigt	Kopf waagrecht	Kopf leicht nach hinten geneigt
18	Wie würden Sie ihre Kopfposition beim Schlucken von Medikamenten beschreiben?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

		Ja	Nein	Keine Angabe
19	Verändern Sie manchmal die Form ihrer Medikamente, um die Einnahme zu vereinfachen?	<input type="checkbox"/> Weiter mit Frage 20	<input type="checkbox"/> Weiter mit Frage 22	<input type="checkbox"/> Weiter mit Frage 22

20 Bitte beschreiben Sie, wie das Medikament dabei verändert wird (mehrere Antworten sind möglich):

Teilen von Tabletten **Öffnen** von Kapseln **Kauen** von Tabletten

Zerkleinern/Mörsern von Tabletten **Auflösen** von Tabletten in einer Flüssigkeit

Andere Strategie, nämlich:

.....

Bitte beschreiben Sie ihre eigene Strategie in Stichworten

		Ja	Nein	Keine Angabe
21	Haben Sie je einen Arzt oder Apotheker um Rat gefragt, bevor Sie die Form des Medikaments verändert haben?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

		Ja	Nein
22	Hat Ihre Ärztin / Ihr Arzt Sie je nach Schluckbeschwerden befragt?	<input type="checkbox"/>	<input type="checkbox"/>
23	Hat Ihre Apothekerin / Ihr Apotheker Sie je nach Schluckbeschwerden befragt?	<input type="checkbox"/>	<input type="checkbox"/>
24	Hat Ihnen Ihr Arzt oder Apotheker bereits einmal eine andere Einnahmeform (Sirup, Lösung, kleinere Tabletten) an Stelle der bisherigen Tabletten / Kapseln angeboten?	<input type="checkbox"/>	<input type="checkbox"/>
25	Essen Sie zur Einnahme von Medikamenten etwas (z.B. Joghurt)?	<input type="checkbox"/>	<input type="checkbox"/>
26	Trinken Sie zur Einnahme von Medikamenten etwas (z.B. Wasser)?	<input type="checkbox"/>	<input type="checkbox"/>
27	Verschlucken Sie sich manchmal bei der Einnahme von Medikamenten?	<input type="checkbox"/>	<input type="checkbox"/>

Es folgen nun einige Fragen zum Alltag mit Ihren Medikamenten:

		Ja	Nein
28	Vergessen Sie manchmal Ihre Medikamente zu nehmen?	<input type="checkbox"/>	<input type="checkbox"/>
29	Manchmal wird ein Medikament nicht genommen und zwar aus einem anderen Grund als Vergesslichkeit. Wenn Sie an die letzten 2 Wochen denken, gab es Tage, an welchen Sie Ihre Medikamente nicht genommen haben?	<input type="checkbox"/>	<input type="checkbox"/>
30	Haben Sie jemals die Einnahme Ihrer Medikamente verringert oder gestoppt ohne Ihren Arzt / Ihre Ärztin zu informieren, weil Sie sich schlechter fühlten nach der Einnahme?	<input type="checkbox"/>	<input type="checkbox"/>
31	Wenn Sie reisen oder Ihr Zuhause verlassen, vergessen Sie manchmal ihre Medikamente mitzunehmen?	<input type="checkbox"/>	<input type="checkbox"/>
32	Haben Sie ihre Medikamente gestern genommen?	<input type="checkbox"/>	<input type="checkbox"/>
33	Wenn Sie das Gefühl haben, dass Ihre Krankheit unter Kontrolle ist, hören Sie manchmal mit der Einnahme Ihrer Medikamente auf?	<input type="checkbox"/>	<input type="checkbox"/>
34	Jeden Tag Medikamente zu nehmen empfinden viele Personen als lästig. Fühlen Sie sich manchmal schikaniert, wenn Sie den Therapieplan für Ihre Krankheit genauestens einhalten müssen?	<input type="checkbox"/>	<input type="checkbox"/>

35	Wie oft haben Sie Mühe, sich an die Einnahme aller ihrer Medikamente zu erinnern?	Nie / selten <input type="checkbox"/>	Hin und wieder <input type="checkbox"/>	Manchmal <input type="checkbox"/>	Fast immer <input type="checkbox"/>	Immer <input type="checkbox"/>
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Sie sind nun am Ende des Fragebogens angelangt. **Besten Dank für Ihre Teilnahme!**

Retournieren Sie nun bitte den Fragebogen und die weiteren Studienunterlagen in dem beiliegenden Antwortcouvert an das Studienzentrum der Universität Basel.

13 APPENDIX AUTHOR

13.1 Curriculum vitae

Personalien

Name	Messerli	Geb. Datum	11. Juli 1981
Vorname	Markus	Zivilstand	Ledig
Adresse	Bettingerstrasse 7	Bürgerort	Rüeggisberg, BE
PLZ	CH 4125 Riehen, BS		

Sprachen

Muttersprache	Deutsch
Fremdsprachen	Englisch (Wort/Schrift), Französisch (Wort/Schrift), Italienisch (Wort)

Mittel- und Hochschulen

1992 - 2000	Gymnasium Bäumlhof, Basel <i>Abschluss: Matura Typ D, Neusprachen</i>
2001 - 2006	Studium der Pharmazeutischen Wissenschaften , Universität Basel Diplomarbeit im Bereich der Klinischen Pharmakologie in Zusammenarbeit mit der Firma Vitaplant AG, Witterswil (Prof. U. Drewe / Dr. M. Kreuter / Dr. K. Berger) <i>Titel: Etablierung pharmakologischer Untersuchungsmodelle zur Bestimmung antidiabetischer Aktivität verschiedener Pflanzenextrakte in vitro</i> Assistenzjahr in der Breite-Apotheke AG, Basel (Leitung: Dr. Andreas Rüegg) 2006 Prüfungserfolg Staatsexamen ‚eidg. dipl. Apotheker‘ bzw. ‚MSc pharm‘
2010 – 2016	Dissertation , Pharmaceutical Care Research Group, Universität Basel <i>Titel: Clinical Pharmacy Services and Evaluation of Medicines Use - the Case of the Swiss Polymedication Check</i> (Supervisor: Prof. Kurt E. Hersberger) <ul style="list-style-type: none"> – Studienleiter ‘Evaluation Polymedication Check - a randomised controlled trial (evalPMC)’ [NCT01739816], ‘Swallowing difficulties with medication intake and coping strategies in patients with systemic sclerosis (SWAMECO)’ [NCT02105818] – Assistenz im Rahmen von Lehr- und Weiterbildungsveranstaltungen, Entwickeln und Betreuen von Masterarbeiten, Prüfungsexperte ‚OSCE Staatsexamen‘

Berufliche Tätigkeiten

2006 – 2007	Flugplatz Apotheke , Basel	<i>Offizin-Apotheker</i>
2006 – 2007	Vitaplant , Witterswil	<i>Wissenschaftlicher Mitarbeiter</i>
2005 – 2009	Breite-Apotheke , Basel	<i>Offizin-Apotheker</i>

APPENDIX AUTHOR

- Stellvertretung der Geschäftsleitung im Tagesbetrieb
- Betreuung Alters- / Pflegeheim in pharmazeutischen Belangen
- Auszubildner angehender Apotheker/innen während dem Assistenzjahr

2008 – dato **Reha Rheinfelden, Rheinfelden** *Leitender Apotheker*

- Fachtechnische Verantwortung für den Umgang mit Arzneimitteln im Betrieb
- Aufbau und Leitung des Fachbereichs ‚Klinische Pharmazie‘
- Vigilanz-Verantwortlicher der Klinik gegenüber Swissmedic

2016 – dato **Apotheke Hersberger, Basel** *Offizin-Apotheker*

- Stellvertretung der Geschäftsleitung im Tagesbetrieb
- Betreuung Alters- / Pflegeheim in pharmazeutischen Belangen
- Initiation ‚Kompetenzerweiterung Klinische Ernährung‘

Weiterbildungen

2012 **SVEB-Zertifikat**, nach ‚eduQua‘-Vorgaben

- Zertifikat des Schweizerischen Verbandes für Weiterbildung
- Kompetenznachweis, um im eigenen Fachbereich Lernveranstaltungen mit Erwachsenen im Rahmen vorgegebener Konzepte, Lehrpläne und Lehrmittel vorzubereiten, durchzuführen und auszuwerten.

2011 – 2014 **Fähigkeitsausweis FPH Impfen und Blutentnahme**
Teilnahme am Pilotprojekt zur Entwicklung des heutigen Fähigkeitsausweises

2010 – 2014 **Fähigkeitsausweis FPH Klinische Pharmazie**
Ausbildungsort: Bruderholzspital Basel, Betreuung durch Frau Andrea Studer und Herr Dr. Markus Lampert
Titel Zertifikatsarbeit: *Klinische Pharmazie in Schweizer Spitälern 2013 - Eine Übersicht zu Ressourcen, Praxis und Leistungen*

Nebenberufliche Tätigkeiten / Engagements

2003 – 2004 **Präsidium Fachgruppe Pharmazie**, Universität Basel
Koordinieren der Vereinsaktivitäten, Organisieren und Betreuen div. Grossanlässe

2008 – 2010 **Vorstand IG Phytotherapie**
Vorstandsmitglied der IG Phytotherapie

2012 – dato **Verhandlungsdelegation pharmaSuisse LOA**
Delegationsmitglied von pharmaSuisse bei Tarifverhandlungen mit den Krankenversicherern hinsichtlich dem Vertragswerk zur Leistungsorientierten Abgeltung der Offizin-Apotheken (LOA V) z.H. des Bundesamts für Gesundheit.

2015 – dato **Arbeitsgruppe Klinische Ernährung GSASA**

Gründungsmitglied der Arbeitsgruppe innerhalb der Gesellschaft Schweizer Amts- und Spitalapotheker (GSASA), persönliches Hauptinteresse ‚Verabreichung von Medikamenten via Sonde‘

Freizeitaktivitäten

- 2006 - dato **J+S Experte „Lagersport / Trekking“**
- Experte im Sportfach „Lagersport / Trekking“, Sicherheitsaktivität „Bergtrekking“
 - Coaching von Jugendorganisationen in Lagerplanung und Abteilungsbetrieb, Projektleitung m+ (kantonaler ThinkTank mit Fokus ‚Mitgliederentwicklung‘), Ausbildung des nationalen Kurskaders in Zusammenarbeit mit der Fachleitung J+S, Projektbetreuung (Konzeptionierung / Buchhaltung / Controlling / Public Relations)
- 2008 - dato **Bergsport**
- Alpinwandern, Bergsteigen, Skitouren – Hauptsache hoch hinaus!
 - Mitglied SAC und AACB, Mitglied Hüttenkommission Biferten
- 2013 - dato **Imkerei**
- Betreuung von acht Völker in CH Kasten am Riehener Schlipf (BS)
 - It’s more than honey!

13.2 Publication list

Publications in international scientific, peer-reviewed journals

A method for calculating adherence to polypharmacy from dispensing data records; *Isabelle Arnet, Ivo Abraham, Markus Messerli, Kurt E Hersberger; International Journal of Clinical Pharmacy. 2014 Feb;36(1):192-201*

Proposal of standardization to assess adherence with medication records – methodology matters; *Isabelle Arnet, Marcel J. Kooy, Markus Messerli, Kurt E. Hersberger, Eibert R. Heerdink, Marcel Bouvy, Ann Pharmacother. 2016 May;50(5):360-8. doi: 10.1177/1060028016634106. Epub 2016 Feb 25*

Mapping clinical pharmacy practice in Swiss hospitals – a cross sectional study; *Markus Messerli, Karen Maes, Kurt E. Hersberger, Markus L. Lampert; European Journal of Hospital Pharmacy; doi:10.1136/ejhpharm-2015-000868; Epub 2016 Feb 26*

Development of clinical pharmacy in Switzerland - involvement of community pharmacists in care for older patients; *Kurt E. Hersberger, Markus Messerli; Drugs Aging. 2016 Mar;33(3):205-11. doi: 10.1007/s40266-016-0353-6. Review.*

Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy - a prospective randomised controlled trial; *Markus Messerli, Noortje Vriends, Eva Blozik, Kurt E. Hersberger; BMC Health Serv Res. 2016 Apr 23;16(1):145. doi: 10.1186/s12913-016-1384-8.*

Swallowing difficulties with medication intake assessed with a novel self-report questionnaire in patients with systemic sclerosis – a cross sectional cohort study; *Markus Messerli, Rebecca Aschwanden, Michael Buslau, Kurt E Hersberger, Isabelle Arnet; BMJ Open; submitted on May 13, 2016*

Humanistic outcomes and patient acceptance of a pharmacist-led medication review in primary care – a randomised controlled trial; *Markus Messerli, Noortje Vriends, Kurt E. Hersberger; BMC Health Serv Res; submitted on May 24, 2016*

The Challenge of Behaviour Change: A Meta-Analysis on the Efficacy of Psychological Interventions for Enhancing Adherence to Antiretroviral Therapy in HIV; *Cosima Locher, Markus Messerli, Jens Gaab, Heike Gerger; Psychological bulletin; in preparation*

Scientific position papers

Position Paper on the PCNE definition of Medication Review 2016; *Nina Griese, Kurt Hersberger, Markus Messerli, Saja Leikola, Nejc Horvath, Foppe van Mil, Mitja Kos; submitted to the board of PCNE in May 2016.*

Publications in national health care professional's journals

Herausforderung «Polymedikations-Check»; Markus Messerli, David De Pretto, Kurt E. Hersberger; *pharmaJournal* 16, 08/2012

Bessere Compliance dank Polymedikations-Check; Markus Messerli, Kurt E. Hersberger; *Care Management - Zeitschrift für Integrierte Versorgung, Qualität und eHealth*. 04/2012; 5(2):10-12.

Verabreichung von Medikamenten per Sonde – Grundlagen und Übungen, Markus Messerli, *i.m@il-offizin* Nr.11+12, 2013

Gleichgewichtsprobleme in der Rehabilitation – ein interaktiver und komplexer Fall; Christopher Müssig, Markus Messerli; *Swiss Medical Forum*. 08/2014; 14(35):645–646.

Das Globussyndrom; Markus Messerli; *i.m@il-offizin* Nr.17, 2014

Spitalapotheker beteiligen sich vermehrt an klinischen Prozessen; Markus Messerli, Markus Lampert; *H+ Hospital Forum Competence*, 09/2014

Methotrexat: Risikopotential und pharmazeutische Betreuung; Markus Messerli; *i.m@il-offizin* Nr.20, 2014

Blue, pink, purple – Farbenfrohe Urinanalyse; Rouhlat Kamo, Stephan Griessbach, Markus Messerli; *Swiss Medical Forum*; 02/2015; 15(7):161-163

Herausforderung Polymedikations Check; Markus Messerli, *i.m@il-offizin* Nr.20, 2015

Publications in manuals or themes folders

Medication Review - Medikationsanalyse; Markus Messerli; 46 Seiten; Themenheft *pharmActual*;05/2014

Medikationsanalyse in der Offizinpharmazie; Markus Messerli, Kurt E Hersberger, Jeanette Dommer, 20 Seiten, Themenbeitrag *pharManuel* 2016

Grundlagen der Medikationsanalyse; Kurt Hersberger, Markus Messerli, Nina Griese-Mammen; *Lehrbuch Klinische Pharmazie Jaehde et al.*; 4. Auflage, submitted 2015

Poster presentations

Prevalence of unreached cardiometabolic targets among treated patients – subanalysis of data from a community pharmacy screening campaign in Switzerland; Markus Messerli, Fabienne Böni, Philipp Walter, Kurt E Hersberger; *7th Working Conference of the Pharmaceutical Care Network Europe 2011, Manchester, United Kingdom*

Polymedication-Check – First experiences with a new reimbursed cognitive service; *Messerli Markus, De Pretto David, Kurt E Hersberger; 40th European Symposium on Clinical Pharmacy 2011, Dublin, Ireland*

Polymedication Check – A new challenge for Swiss community pharmacists; *Markus Messerli; David De Pretto, Kurt Hersberger; 1st Swiss Pharmacist Congress GSASA / pharmaSuisse 2011, Interlaken, Switzerland*

Development of outcome measures to investigate intermediate medication reviews provided in Swiss community pharmacies; *Markus Messerli, Véronique Lottaz, Noortje Vriends, Matthias Schwenkglens, Kurt E. Hersberger; Centennial Congress of Pharmacy and Pharmaceutical Sciences FIP 2012 Amsterdam, Netherlands*

Collaborative development of outcome measures to investigate intermediate medication reviews provided in community pharmacies; *Markus Messerli, Véronique Lottaz, Noortje Vriends, Matthias Schwenkglens, Kurt E. Hersberger; PCNE Working Conference 2013, Berlin, Germany*

Clinical Pharmacy Practice in Swiss Hospitals 2013; *Markus Messerli, Karen Maes, Kurt E. Hersberger, Markus L. Lampert; Journées Franco-Suisses de Pharmacie Hospitalière 2013, Montreux, Switzerland*

Evaluation of the implementation of a classification system for pharmaceutical interventions; *Karen Maes, Amanda Gaufrond, Markus Messerli, Kurt E. Hersberger, Markus Lampert; 42nd ESCP Symposium on Clinical Pharmacy 2013, Prague, Czech Republic*

Development of the PCNE standards for medication reviews; *Markus Messerli, Kurt E. Hersberger; PCNE Working Symposium 2014, Sliema, Malta*

Patient's perspective of the Polymedication-Check - Results from a randomised controlled trial in Swiss community pharmacies; *Markus Messerli, Kurt E. Hersberger; 2nd Swiss Pharmacist Congress GSASA / pharmaSuisse 2014, Interlaken, Switzerland*

Validation of a novel self-report questionnaire to assess swallowing difficulties with medication intake in patients with systemic sclerosis; *Markus Messerli, Rebecca Aschwanden, Michael Buslau, Kurt E Hersberger, Isabelle Arnet; 43rd ESCP Symposium on Clinical Pharmacy 2014, Copenhagen, Denmark*

Self-reported prevalence, localization and intensity of swallowing difficulties with medication intake in patients with systemic sclerosis - a cross-sectional cohort study; *Markus Messerli, Rebecca Aschwanden, Michael Buslau, Kurt E Hersberger, Isabelle Arnet; 83. Jahresversammlung der Gesellschaft für Allgemeine Innere Medizin 2015, SGIM, Basel, Switzerland*

Scientific lectures

The impact of medication review – does it work? Structured discussion with opponent on the effect of medication review in different settings; *Markus Messerli; 9th PCNE Working Conference, 6 February 2015, Mechelen, Belgium*

Medication review in Swiss community pharmacies – a randomized controlled trial; *Markus Messerli, Kurt E. Hersberger; Annual Research Meeting Department of Pharmaceutical Sciences University of Basel; 10 February 2016, Basel, Switzerland*

Oral presentations

Polymedication Check – A new challenge for Swiss community pharmacists; *Markus Messerli; David DePretto, Kurt Hersberger; 1st Swiss Pharmacist Congress GSASA / pharmaSuisse 2011, Interlaken, Switzerland*

Polymedication-Check – Assessing the impact of community pharmacy based medication review; *Markus Messerli, Véronique Lottaz, Noortje Vriends, Kurt E. Hersberger; 3rd PCNE Medication Review Symposium 2012, Leuven, Belgium*

Evaluation „Polymedikations-Check - Eine randomisiert-kontrollierte Studie in Schweizer Offizin-Apotheken; *Markus Messerli; Förderinitiative Pharmazeutische Betreuung Deutschland 2013, Berlin, Germany*

Validation of a novel self-report questionnaire to assess swallowing difficulties with medication intake in patients with systemic sclerosis; *Markus Messerli, Rebecca Aschwanden, Michael Buslau, Kurt E Hersberger, Isabelle Arnet; 43rd ESCP Symposium on Clinical Pharmacy 2014, Copenhagen, Denmark*

Medication reviews in Swiss community pharmacies – lessons learned from evaluation of the Polymedication Check and suggestions for development of new service delivery models, *Kurt E Hersberger, Markus Messerli, 1ère rencontre nationale des sciences pharmaceutiques cliniques 2015, Lausanne, Switzerland*

Workshop moderation

Herr S., UAW Arzneimittelexanthem; *Markus Messerli; Fallbeispiel GSASA-Workshop Klinische Pharmazie 2012, Baden, Switzerland*

Performing medication reviews in primary care – improve your competences; *Markus Messerli, Kurt E. Hersberger; 42nd ESCP Symposium on Clinical Pharmacy 2013, Prague, Czech Republic*

The PCNE-DRP classification for experienced users; *Markus Messerli, Samuel Allemann; PCNE Working Symposium 2014, Sliema, Malta*

APPENDIX AUTHOR

Drug-related problems and medication review: Which DRP can be detected with MR level 2b; *Markus Messerli, Lea Botermann; PCNE Working Symposium 2014, Sliema, Malta*

Nahtlose Betreuung: Fallbeispiele; *Markus Lampert, Markus Messerli, Karen Maes; 2nd Swiss Pharmacist Congress GSASA / pharmaSuisse 2014, Interlaken, Switzerland*

Entscheide Dich – Anwendung Deiner Kompetenzen im Entscheidungsspiel; *Markus Messerli, Corina Metaxas, Karen Maes, Dominik Stämpfli, Samuel Allemann, Michael Fretz; Forum Pharmazie 2015; Basel, Switzerland*

'To vaccinate or not to vaccinate – that's the question! A debate' *Markus Messerli, Pharmaseminar 2015, Luzern Schwarzenberg, Switzerland*

Medikamentengabe via Sonde; *Markus Messerli; 6. Januar 2016; Fallkolloquium Klinische Pharmazie; Advanced Studies University of Basel, Switzerland*

Varia

Klinische Pharmazie in Schweizer Spitälern 2013 - Eine Übersicht zu Ressourcen, Praxis und Leistungen; *Markus Messerli; Zertifikationsarbeit Fähigkeitsausweis FPH Klinische Pharmazie 2014*

Herausforderung für Patient und Betreuungsumfeld; *Markus Messerli; Kolumne Rheinfelden medical; Neue Fricktaler Zeitung, 08.04.2015*

Schlussbericht Evaluation Polymedication Check; *Markus Messerli, Noortje Vriends, Eva Blozik, Kurt E. Hersberger; z.H. Schweizerischer Apothekerverband (pharmaSuisse), den Vertretungen der Krankenversicherer (santésuisse / curafutura) und dem Bundesamt für Gesundheit (BAG) 15.05.2015*

Completed Reviewer Assignments: 6x BMC Health Services Research, 1x BMJ