

# Use of medicines by the elderly

## The role of pharmacy in promoting adherence

2018



International  
Pharmaceutical  
Federation

## Colophon

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# Contents

Foreword .....	3
Acknowledgements .....	4
Executive summary .....	5
<b>1 Introduction .....</b>	<b>7</b>
1.1 Background.....	7
1.2 Aims and purpose of this report.....	8
1.3 Scope and definitions.....	8
1.4 Methods.....	9
1.5 Structure of this report.....	10
1.6 References .....	10
<b>2 Adherence and non-adherence .....</b>	<b>11</b>
2.1 A context for the use of medicines in the elderly.....	11
2.1.1 Overview .....	11
2.1.2 A sequence of encounters and events .....	11
2.1.3 Characteristics of elderly patients .....	12
2.1.4 “Intentional” and “non-intentional” non-adherence and shared decision-making in health care ..	13
2.1.5 Adherence to medication in specific disease states .....	14
2.2 Roles and responsibilities of pharmacy.....	14
2.3 Measures of adherence.....	16
2.4 References .....	16
<b>3 Options for enhancing adherence.....</b>	<b>18</b>
3.1 Preamble.....	18
3.2 Initiatives at the health system level .....	18
3.3 Education and training of health professionals .....	19
3.4 Counselling and education of patients and their carers .....	20
3.4.1 Overview .....	20
3.4.2 Specific health conditions .....	21
3.4.3 Patient participation .....	23
3.4.4 Follow-up counselling and education.....	23
3.4.5 Telephone counselling .....	24
3.4.6 Physical space for pharmacy consultations.....	24
3.5 The role of carers .....	25
3.6 Polypharmacy, complex regimens, and medication reviews .....	25
3.7 Packaging, dose administration aids and reminder systems .....	26
3.8 Conclusion .....	27
3.9 References .....	27
<b>4 Current initiatives to promote adherence.....</b>	<b>30</b>
4.1 Data compilation .....	30
4.2 Recognition and commitment .....	30
4.3 Targeting the needs of the elderly .....	30
4.4 Current pharmacy programmes and services.....	30
4.4.1 Dose administration aids.....	30
4.4.2 Reminders .....	31
4.4.3 Staged supply .....	31
4.4.4 Counselling and provision of cognitive pharmaceutical services .....	31
4.5 Promoting adherence for specific conditions and medicines .....	32
4.6 Training of pharmacists about adherence.....	32

4.7 Funding of pharmacy services .....	32
4.8 Initiatives in individual countries .....	33
4.8.1 Australia.....	33
4.8.2 Belgium .....	34
4.8.3 Denmark .....	35
4.8.4 Ireland.....	36
4.8.5 The Netherlands .....	37
4.8.6 Singapore .....	37
4.8.7 Spain.....	38
4.8.8 Switzerland.....	39
4.9 References .....	40
<b>5 Effective pharmacy interventions.....</b>	<b>41</b>
5.1 Implications of this review.....	41
5.2 Methodological issues in evaluating interventions.....	42
5.2.1 Overview .....	42
5.2.2 Heterogeneity of potential research subjects.....	42
5.2.3 Selection of participants and selection bias .....	43
5.2.4 Heterogeneity of interventions.....	43
5.2.5 Lack of standardisation in the measurement or classification of adherence .....	43
5.2.6 Possible methodological solutions.....	43
5.3 A formulation of interventions to improve adherence.....	44
5.4 References .....	45
<b>Appendix 1: Literature search.....</b>	<b>46</b>
<b>Appendix 2. Survey form .....</b>	<b>47</b>

# Foreword

By the President of the International Pharmaceutical Federation (FIP)

Population ageing and the consequent increase in the number of people on multiple medicines for long-term conditions create a need for the development of targeted services to improve care at the community level and **to enhance patients' quality of life**. Enabling people to live a longer and better life should be the overarching goal of every health system. Health professionals, patients and the broader community must work together to achieve this goal.

In 2003, the World Health Organization (WHO) published a report on adherence to therapies for patients with chronic conditions. Analysis of the data collected in several studies, in both developed and developing countries, led to the conclusion that the lack of adherence to therapy is a cross-cutting issue, with about 50% of patients not taking their medicines as prescribed.

The International Pharmaceutical Federation (FIP) is committed to improving global health by closing gaps in the development, distribution, dispensing and responsible use of medicines. Poor adherence to therapy in chronic conditions is associated with worse health outcomes and increased health costs. This report aims to identify and describe pharmacy interventions and programmes that lead to improvements in medication adherence by the elderly, and to review available information on their effectiveness.

The results of the literature search and case studies included here show that pharmacists can have a positive effect on adherence through the provision of a range of services, particularly in the community pharmacy setting. However, we also note that minimal financial reimbursement is currently offered to pharmacy to provide such services. In many jurisdictions, remuneration systems are completely lacking.

In order to ensure the sustainability of services to promote adherence, specific remuneration systems should be in place. The investment would lead to improved realising of services, improved resource allocation for services, and better documentation of the services provided and their consequences for patients' health outcomes. Resource allocation should support not only interventions that generate the best possible health outcomes in accordance with individual and community preferences, but also those that generate economic advantages, minimise waste and create new employment opportunities.

FIP firmly believes that interventions aimed at improving adherence to therapy represent a good return on **investment. This is in line with the WHO's findings in the cited report, where it concludes that "increasing the effectiveness of interventions to improve adherence to therapy can have a far greater impact on the health of the population than any improvement in specific medical treatments"**.

This report stands as proof that pharmacists worldwide are already contributing to this goal, and are engaged in supporting elderly patients in a variety of ways. We trust this publication may further inspire policymakers, professional organisations, educational institutions and our fellow pharmacists to consolidate and expand their role in improving adherence to treatments by elderly patients, leading towards more sustainable health systems, longer lives and increased well-being.

Dr Carmen Peña

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The content of this report has been produced independently by the authors, editors and case-study contributors.

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## Executive summary

Non-adherence to medications is a significant cause of therapeutic failure and a major worldwide public health problem. The consequences of non-adherence are greater in older people because they often require multiple medicines for chronic conditions with comorbidities, and they often have greater difficulty managing their medications because of declining cognitive function, memory, mobility and manual dexterity. The increasing numbers of older people compounds the problem of non-adherence at the population level and creates a pressing need for effective strategies to promote adherence.

This report reviews existing knowledge on such strategies, and specifically identifies pharmacy programmes and interventions that are likely to be effective. Its preparation comprised (i) a narrative review of published literature, and (ii) a compilation of case studies and other information supplied by member organisations of the International Pharmaceutical Federation on relevant interventions and programmes to improve medication adherence in their respective countries, particularly those targeting the elderly.

Although the problem of adherence has been recognised and described since ancient times, and although a large body of evaluative research has been undertaken on a wide range of interventions, no consolidated set of solutions has emerged. This is partly due to the difficulties of conducting research on adherence. Some of these difficulties are inherent to the complexity and variability of the sequence of events that starts with a recognition of the need for a medicine and ends with the actual taking of the medicine. Other difficulties relate to the measurement of adherence and the need to rely on indicators of variable validity. These indicators are used inconsistently, and definitions of thresholds of appropriate or acceptable levels of adherence also vary.

Pharmacy has a prominent position in this sequence of events and has an essential role in promoting and **monitoring adherence**. **Pharmacists' pivotal contributions encompass education and counselling** of patients and their carers<sup>1</sup>, providing dose administration aids, dispensing medicines, generating reminders to take medicines and to refill prescriptions, and following patients to identify and resolve difficulties with medicines use. However, despite its major role in the provision of medicines, pharmacy is somewhat isolated from the other health professions involved in the management of patients. This isolation, which reflects health system and funding structures as well as professional differences, limits the scope of interventions that could improve adherence if the health professionals involved were able to work together in a more integrated way.

Although strong evidence for the effectiveness of specific initiatives to promote adherence is scarce, such evidence as is available supports the following interventions:

- New medicine services, comprising education and counselling of patients by pharmacists when newly prescribed medicines are dispensed, with follow-up face-to-face and telephone counselling sessions over the subsequent weeks.
- Review, education and counselling of patients and carers by pharmacists when repeat medicines are dispensed, with continuing reinforcement when the delivery of a dose requires a specific manoeuvre, for example, the use of inhaled medicines.
- The provision of dose administration aids that facilitate taking the correct dose at the correct time.
- Systems for reminding patients to take their medicines as prescribed.
- Simplification of medication regimens by managing polypharmacy, including the reconciliation of medicines introduced by different prescribers or in different care settings, and reducing the frequency of dosing.

Given the number of potential intervention points from diagnosis through to dispensing and taking of a medicine, it is perhaps not surprising that multiple interventions are often shown to have relatively greater effect than singular interventions.

Three overlapping elements are essential in all of these interventions.

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<sup>1</sup> For the purposes of this report, a carer has been defined as a person who provides care, assistance and support to another person for the management of her or his medical condition, including medication taking. The carer refers to parents, adult children, spouses, partners or other family members.

The first is effective communication with the patient and carer by all members of the healthcare team. Effective communication includes: (i) engaging the patient (and carer, where applicable) in the decision-making process about treatments and choices in medications; (ii) **assessing the patient's cognitive status and level of health literacy**, and guiding the discussion to ensure that he or she can engage in this decision-making process; (iii) establishing and sustaining links between members of the healthcare team, especially doctors, nurses and pharmacists, so that pharmacists have access to all relevant clinical information; (iv) enabling pharmacy to fulfil its pivotal role to enhance understanding of the therapeutic plan and dispel any ill-founded concepts that might lead to intentional non-adherence; (v) making use of contemporary communication technology for follow-up contacts with patients (or carers); and (vi) implementing pharmacy-led services to support patients taking new medicines.

The second element is to make it as easy as possible for older patients to take their medicines correctly. This entails: (i) keeping medication regimens as simple as possible from the outset; (ii) reviewing medication regimens (for example, by means of home medication reviews conducted by pharmacists) to identify and manage polypharmacy; (iii) providing dose administration aids that help patients (or carers) to take the right medicine in the right dose at the right time, and to keep track of what they have or have not taken; (iv) enabling family members to support the patient in adhering to his or her medication regimen; and (v) providing reminders, both to take medicines and to obtain and fill repeat prescriptions.

The third element is to sustain the effort. None of the interventions described above is self-sustaining, and **adherence can only improve on an ongoing basis with continued input to the patient's needs by (i) repeating messages whenever the opportunity arises** (for example, when prescriptions are being refilled), (ii) repeatedly enquiring whether taking the medicine is causing any problems, and addressing any problems that emerge, preferably in consultation with the prescriber, and (iii) observing dose administration techniques on an ongoing regular basis, and making corrections where necessary (for example, with inhaled medicines).

Most of these approaches apply to patients of all ages, particularly adults. However, as noted above, the elderly are large users of medicines, their medication regimens are often complex, and the presence of cognitive decline adds to the challenge. Mild or early cognitive decline may be unnoticed by health professionals in brief encounters. All health professionals, notably including pharmacists, should be given training and possibly other support so that they do not miss signs of cognitive decline in patients, and can **take account of patients' impairments in their communications, advice and actions**.

# 1 Introduction

## 1.1 Background

Adherence to medication is a significant challenge for people of all ages, especially older people. Non-adherence has major clinical and economic consequences. The clinical consequences depend on the type of condition for which a medicine is used, the efficacy of the medicine for the condition, the extent of non-adherence, and the medicine's pharmacological properties. The economic consequences are due to problems that would have been prevented by correct use of medicines, and the adverse outcomes lead to additional use of health services and hospital admissions. Unused dispensed medicines are often wasted, and substitute medicines could be more expensive and/or less efficacious. Worldwide, non-adherence represents an annual avoidable cost of approximately USD 269bn — approximately 4.6% of the world's total health expenditure.<sup>1</sup>

As the numbers of older people are increasing in many countries, both developed and developing,<sup>2</sup> the consequences of non-adherence are likely to increase. Complex chronic conditions and multiple comorbidities are prevalent in older people, requiring the ongoing use of multiple medicines, often with complex timing and dosing regimens. Older people often have greater difficulty managing their medicines because of declining cognitive function, memory, mobility and manual dexterity.

The 2015 Global Burden of Disease Study<sup>3</sup> lists acute and chronic diseases that account for the greatest burden in people aged 65-plus. According to evidence and accepted practice, most of these conditions are amenable to treatment, modification, prevention or palliation by pharmaceuticals. The conditions that account for the largest number of disability-adjusted life-years (DALYs) lost worldwide among people aged 65-plus are:

- Ischaemic heart disease
- Stroke
- Chronic obstructive pulmonary disease
- Diabetes mellitus
- Sense-organ disease (such as glaucoma)

Other important contributors to the burden of disease in this age range are:

- Back and neck pain
- Lower respiratory infections
- Chronic kidney disease
- Hypertensive heart disease
- Alzheimer's disease
- Lung cancer

Adherence — defined in more detail below — refers to the correct use of a medicine. Adherence requires the engagement of patients and those who might benefit from taking medicines for preventive reasons. Engagement means trust and mutual respect between patient and health professional; an understanding by the health professional of the patient's concerns, wishes, motivations and expectations; and a common setting of goals for prevention and/or therapy.<sup>4</sup>

Health professionals must recognise that non-adherence may be unintentional (due, for example, to forgetfulness or difficulty with the management of medication regimens) or intentional (resulting from the patient's unwillingness or incapacity to fill a prescription, or unwillingness to start or continue taking a medicine as recommended by a health professional).

As Charles Everett Koop, then Surgeon General of the United States, declared more than 30 years ago, "Medicines don't work in patients who don't take them".<sup>5</sup> Koop's epigram and the critical importance of patient engagement are foundational themes of this report.

## 1.2 Aims and purpose of this report

The aim of this report is to identify and describe pharmacy interventions and programmes that lead to improvements in medication adherence by the elderly, and to review available information on their effectiveness.

The report was commissioned by the International Pharmaceutical Federation (FIP). FIP and its member organisations intend to use the report in determining how to advise governments and other agencies on the role of pharmacy in promoting medication adherence by the elderly.

This project has been conceived in the epidemiological context of the increasing prominence of chronic disease and related risk factors in both developed and developing countries, as the reference to the 2015 Global Burden of Disease Study above shows.<sup>3</sup> Medicines, and self-management using medicines, are essential in the management of all these conditions. The development and implementation of interventions, programmes and policies to ensure the appropriate and correct use of medicines are, therefore, critical challenges in health care.

## 1.3 Scope and definitions

This report identifies, describes and evaluates pharmacy interventions and programmes that are intended to enhance medication adherence by the elderly. It is confined to factors affecting the use of medicines as prescribed or professionally recommended. It does not seek to evaluate the quality of medical assessment leading to prevention or therapy that may include medicines, or to assess whether medicines are prescribed correctly.

The expression “pharmacy interventions and programmes” refers to services undertaken by pharmacists, or programmes undertaken by, or on behalf of and identified with, the pharmacy profession. These include:

- Interventions delivered exclusively by pharmacists, as well as multi-professional services involving pharmacists
- Services targeting individual patients as well as those targeting communities or populations
- Services for improving medication adherence that are specific to the elderly, and services that are not specific to the elderly but that could reasonably be applied to the elderly
- Services involving personal carers of older people (e.g., family members)
- Services that may have multiple outcomes, of which medication adherence by the elderly is one

This report concentrates on pharmacy services that can be, or have been, implemented in practice. It also covers factors that facilitate and factors that hinder or impede implementation. Interventions that have only been used in a research context are not covered. Where available, economic data are provided; and where such detail is available, the costs of service delivery and remuneration arrangements for those providing pharmacy services are examined.

**The term “carer” has been defined as a person who provides care, assistance and support to another person for the management of her or his medical condition, including medication taking. The carer refers to parents, adult children, spouses, partners or other family members.**

The term “medicine” refers to allopathic medicines — pharmacologically active substances with recognised indications in the treatment or prevention of disease or symptoms. The report does not cover complementary, traditional or naturopathic medicines. It is mostly confined to medicines that are ordinarily administered by **the patient or the patient’s personal carer (orally, via the respiratory tract, topically, or via a self-administered injection kit)**. Medicines that require a technically skilled health professional for administration are mostly excluded.

The report examines pharmacy services that have general application in medication adherence, as well as services that are relevant to particular conditions, particular types of medicine, and patients with specific

characteristics. It encompasses medicines used across the spectrum of health care — for prevention, curative therapy, disease modification and symptom relief, as well as in palliative care. Prevention spans primary disease prevention, the prevention of exacerbation or relapse, and the prevention of complications.

“Medication adherence” is defined as “the extent to which a patient’s medication-taking behaviour and/or execution of lifestyle changes corresponds with agreed recommendations from a healthcare provider”.<sup>6</sup> Thus adherence refers to the use of medicines in accordance with a specified regimen, which may be:

- a regimen prescribed or explicitly recommended by a treating health professional, or
- the use of a non-prescription medicine explicitly recommended by a treating health professional in accordance with a regimen specified by the health professional or the medicine’s manufacturer, or in professionally recognised guidelines.

“Elderly” is not specifically defined for the purpose of this report. In general usage, those aged over 65 years are often labelled elderly. The review covers materials that refer to “the elderly” or “elderly people”, whether or not these terms are defined.

“Effectiveness” refers to the achievement of (i) desired levels of adherence, (ii) desired preventive or therapeutic outcomes that are reasonably attributable to a given intervention or programme, or (iii) a combination of (i) and (ii).

The report gives priority to pharmacy services for which published descriptions and evidence of effectiveness are available. It also covers services for which evidence of effectiveness is available but unpublished. Interventions and programmes that have been implemented but not evaluated are given lower priority.

Where possible, the analysis identifies components of interventions and programmes that might account for their outcomes, and the report will list criteria that agencies could use in choosing services to be funded and/or promoted. Commonalities among effective interventions or programmes, or among their salient components, are examined to assist in this choice.

## 1.4 Methods

The project comprised three stages.

Stage I comprised a literature review with the following steps:

- a. Literature searches using a range of appropriate electronic databases of published literature, including PubMed, Medline and Google Scholar. Search terms are listed in Appendix A.
- b. “Snowball” searching using the reference lists within identified publications.
- c. Identification of relevant grey literature, particularly on measures undertaken by FIP member organisations to enhance medication adherence.
- d. Definition of criteria for selection of relevant articles.
- e. Selection of relevant articles.
- f. Appraisal and narrative review of selected articles.

Stage I concentrated on articles written in English.

Stage II comprised a critical compilation of case studies and other information provided by members of FIP on relevant interventions and programmes to improve medication adherence in their respective countries. These statements were solicited by means of a template prepared by the authors of this report and distributed by FIP. The template is included in Appendix B.

Stage III comprised preparation of a draft report for submission to the FIP Executive Committee, and subsequent preparation of a final report taking into account the feedback received.

## 1.5 Structure of this report

This report has five chapters, including this chapter.

Chapter 2 explores adherence and non-adherence from conceptual and practical perspectives. It expands on the definition given in section 1.3 above, and examines the distinction between intentional and non-intentional non-adherence. It identifies barriers to adherence and further emphasises the importance of **patients' engagement in prevention or treatment programmes**. It also provides a taxonomy of adherence, reviews issues relating to specific diseases and classes of medicines, and outlines methods of measuring adherence and its effects, with particular reference to the use of medicines by the elderly.

Chapter 3 concentrates on factors affecting adherence, and describes patient- and system-based strategies for facilitating adherence in the elderly. It examines evidence on the role of pharmacists in monitoring, supporting and fostering adherence, both as individual health professionals and as members of multidisciplinary teams.

Chapter 4 describes pharmacy interventions and programmes to enhance adherence to medication by the elderly, using information supplied by FIP member organisations, as indicated in Part III of the Methods section (see Section 1.4 above).

Chapter 5 synthesises the findings from Chapters 3 and 4 and links them with the principles introduced in Chapter 2. It reviews the methods used in studies evaluating interventions designed to improve, and comments on methodological opportunities and limitations. It then summarises potentially effective approaches to the management of non-adherence.

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## 2 Adherence and non-adherence

### 2.1 A context for the use of medicines in the elderly

#### 2.1.1 Overview

The development of interventions to improve adherence depends on understanding what motivates people to adhere to prescribed regimens and why non-adherence occurs.

This chapter explores these essential elements. It examines the decisions and events that occur between identifying the need for treatment and the act of taking a medicine, and describes how these decisions and events might influence adherence. It outlines the characteristics of elderly patients and highlights those that affect adherence and those likely to be modifiable.

#### 2.1.2 A sequence of encounters and events

In examining opportunities to enhance adherence, it is helpful to consider a sequence beginning with an individual's health problem and ending with that individual's use of a prescribed or recommended medicine according to a specified regimen. Participants in the sequence are:

- The person who uses or might use the medicine, referred to in this report as “the patient”;
- The patient's carer (if there is a carer), who could be a partner, a family member, some other personal attendant, or a health professional, often a nurse;
- The health professional(s) with overall responsibility for the patient's clinical management — usually a medical practitioner, sometimes a nurse or an allied health practitioner, and sometimes a team;
- One or more pharmacists who have a pivotal role because of their expertise in medication management.

This sequence can be described in six phases. These are more or less consecutive, but they may overlap.

The first phase comprises diagnosis, formulation of a treatment plan, and prescription. An individual is diagnosed as having a disease, a syndrome or an injury, or as being likely to benefit from a preventive intervention. On the basis of the diagnosis and the patient's wishes, a treatment plan is formulated, and this may or may not include medicines. If the patient needs a medicine, an appropriate medicine is selected and prescribed. The diagnosis and the treatment decision are usually the responsibility of a health practitioner other than a pharmacist, although in some jurisdictions, pharmacists with certified advanced practice competence may also initiate and/or modify treatment with prescription medicines. In the contemporary healthcare paradigm, decisions about treatment are shared with the patient.

The second phase comprises a decision to act (or not to act) on the diagnosis and prescription. This decision rests with the patient, but may be delegated to or assumed by a carer (if present). Several factors may affect the decision to act, including the patient's (and/or carer's) wishes and beliefs, and his or her intellectual and emotional engagement with the health problem and motivation to do something about it. Other important factors are memory (e.g., remembering to fill a prescription), access to supply, and the cost of the medicine and the patient's ability to afford it. The outcome is that the patient (or carer) may decide to act, that is, take the prescription to a supplier, or decide not to act, or neglect the decision.

The third phase is the supply and distribution of the medicine. Supply depends on the manufacture and/or importation of medicines, and distribution may be done by manufacturers, importers or wholesaler agencies. The distributor stores medicines and physically delivers them to the dispenser, who is usually a pharmacist.

The fourth phase is dispensing. This may be the first opportunity in the sequence for a pharmacist to interact with the patient. The pharmacist oversees the storage of necessary quantities of medicines in a dispensary, interprets the prescription, selects the specified medicine from the dispensary, and dispenses it to the patient. The dispensing process is a critically significant professional service in health care, and is examined further in section 2.2 below.

The fifth phase is initiation — **the patient, possibly under a carer's guidance, starts taking the new medicine.** The expectation is that this initiation step will be pursued correctly, but several factors may influence the **patient's adherence to the prescribed regimen.** The initiation phase is foundational and possibly influential: if the patient initially perceives the medicine to be disagreeable (because it is difficult or unpleasant to take, or causes side effects), he or she might be reluctant to continue taking it. **Patients' medicine-taking behaviour** may reflect expectations based on projection rather than the experience of taking the medicine. They may take a lower dose than recommended in order to assess the effects of the medicine or detect side effects, or they may take a higher dose, seeking a quicker or more intense effect. Both are forms of non-adherence.

The sixth phase is persistence, wherein the patient continues to take the medicine, with or without following the prescribed dose, timing, dose interval, duration, and other directions (such as before, with, or after food). **Many factors influence persistence, including the patient's reaction to the initiation phase, the patient's and/or carer's motivation and memory, the ease of dosing, the ease of taking the medicine, the continuing availability of the medicine, the consistency or variability of the product — including appearance and packaging — and the effect of reminders or prompts.**

In principle, these six phases are sequential in a temporal sense, but in practice, they do overlap. The manner in which the steps in one phase are executed inevitably influences what happens in subsequent phases. For example, the quality of the communication between the prescriber and the patient about the diagnosis and the prescription can have a great influence on the decision to act, initiation, and persistence, and memory can affect the decision to act, the initiation phase and the persistence phase.

The six phases have the following implications.

- The use of medicines entails several decisions, actions and interactions. Viewed comprehensively, it is complex, and pharmacy is in a pivotal position in the sequence.
- The interactions involve different elements of the health system. At the very least, they involve a patient (with or without a carer), a diagnostician/treatment planner/prescriber, a manufacturer/supplier/distributor, and a pharmacist. They also involve regulatory, quality control and funding mechanisms, which precede the sequence outlined above but define many of the processes in the sequence. The effective use of medicines, especially the ongoing use of medicines for chronic conditions, requires interactions between elements that are not necessarily well connected in most health systems and lack natural pathways of communication.
- Where an ongoing need for a medicine exists, as typically occurs for patients with chronic conditions, the phases will be repeated each time a repeat prescription is issued. In this situation, the first phase will concentrate on monitoring and reassessment rather than primary diagnosis. The initiation (fifth) phase will mostly be omitted, unless the medication regimen is changed or the physical properties of the medicine change, which may occur if the brand of the medicine is changed or the manufacturer alters packaging or the medicine's appearance, colour or other characteristics.
- Many of the processes that make up each phase are potentially modifiable. This creates multiple opportunities to improve adherence. As noted above, pharmacy is in a pivotal position in the sequence, so pharmacy interventions to improve adherence have the greatest potential to be effective.
- Given the complexity of the sequence, it seems likely that multiple interventions, or multi-faceted interventions, will have the greatest effect on adherence.

### 2.1.3 Characteristics of elderly patients

In the first half of the 20<sup>th</sup> century, increases in life expectancy were due mainly to decreases in infant and childhood mortality. Since 1960, however, the extended life span has been increasingly attributable to

declining mortality among people aged over 60 years. This has created a growing population of older people in most developed countries and, subsequently, an increasing prevalence of the afflictions of ageing and diminished physiological performance.<sup>1</sup> These generate a self-perpetuating cycle of loss of function, disease and disability. As the cycle continues, multiple morbidities accumulate, leading to the use of multiple medicines, with resultant drug interactions. Polypharmacy thus often exacerbates the cycle, and distorted pharmacodynamics due to diminished physiological performance further complicate the picture.

Commonly occurring health states in the elderly are sensory impairment (deterioration of hearing and eyesight), cognitive impairment (leading to deterioration of memory, and confusion), musculoskeletal deterioration, and impairment of motor coordination and balance. Common cardiovascular, respiratory, neurodegenerative and musculoskeletal disorders accelerate the loss of function, and are themselves complicated by the progressive loss of function.

Disability often leads to erratic use of medicines, or non-adherence. Specific manifestations range from inappropriate decision-making about the use of medicines to forgetfulness, and to loss of manual dexterity for the handling of tablets, capsules and the packaging in which they are delivered.

However, the extent of a person's actual disability reflects the interaction of two distinct phenomena: (i) the individual's intrinsic level of function, and (ii) the characteristics of the environment in which the individual functions.<sup>2</sup> The environment is modifiable, and modifications have the potential to improve adherence. In this context, the "environment" encompasses not only the space in which a person lives, but also the objects within that space, access to and availability of professional services such as pharmacy, and support provided by others.

An important feature of declining cognition is that the deterioration is often not apparent to an observer until it is quite advanced. Specific testing is often needed to elicit the signs of cognitive impairment and dementia in the early stages, and sometimes even in the intermediate stages. Health professionals who may have relatively brief encounters with patients may not detect the extent of impairment, and may therefore fail to **make provision for the patient's deficit**. With regard to adherence, it follows that health professionals should receive specific training in approaching older patients who may be affected by cognitive decline and neurodegeneration. Clearly this should apply to pharmacists in their dispensing, counselling and follow-up roles.

#### 2.1.4 "Intentional" and "non-intentional" non-adherence and shared decision-making in health care

As noted in Chapter 1, adherence is defined as "**the extent to which a patient's medicine-taking behaviour and/or execution of lifestyle changes corresponds with agreed recommendations from a healthcare provider**".<sup>3</sup> Regardless of whether it is intentional or non-intentional, non-adherence may result in a patient omitting a medicine altogether, or taking it differently from prescribed instructions with regard to dose, timing, intervals and/or duration. It may affect one or more medicines in a treatment plan.

"Non-intentional" non-adherence occurs when a patient does not adhere to a medication regimen for reasons that are not under his or her control, that is, the patient does not follow the agreed recommendations, but has not made a conscious decision to reject these recommendations.<sup>4</sup> The reasons could be extrinsic to the patient (for example, interrupted supply of a medicine), intrinsic (for example, due to memory impairment), or a combination of extrinsic and intrinsic (for example, the packaging of the medicine is confusing for a patient with some cognitive impairment, or the labelling is indistinct for a patient with poor eyesight, or the package structure is not accessible for a patient with reduced manual dexterity).

"Intentional" non-adherence implies a deliberate or conscious decision not to follow the healthcare provider's recommendations. A useful definition is "an active decision on the part of patients to forgo (discontinue, skip or alter) prescribed therapy".<sup>4</sup>

It is important to note that intentional non-adherence implies a desire on the part of a patient not to take the medicine as prescribed. A patient may desire to adhere but be unable to do so because the medicine is

unaffordable. In a literal sense, this is an example of non-intentional non-adherence, but in the sense that the patient is making an explicit decision not to use a prescription, it could be called intentional.

A more complex notion is encapsulated in the “Necessity-Concerns Framework”, proposed by Horne *et al.*<sup>5</sup> They argue that a patient balances “implicit judgment of personal need for treatment (necessity beliefs) against concerns about possible adverse consequences”. In a meta-analysis of 94 studies, they reported that “higher adherence was associated with stronger perceptions of necessity of treatment”. Adherent patients were approximately 75% more likely than non-adherent patients to strongly believe that they needed the treatment, and adherent patients were half as likely as non-adherent patients to have concerns about their treatment). The meta-analysis further showed that these relationships were independent of the country in which each study was done and the measure of adherence used.

The “Necessity-Concerns Framework” provides a vehicle for shared decision-making in health care. Traditionally, the relationship between patients and health professionals, especially doctors, has been paternalistic, with health professionals setting the agenda and applying their values in making treatment decisions. Over the past two decades, however, patients have demanded a more mutualistic relationship, in which **“the agenda is negotiated; the patient’s values are explored; and the [health professional] takes an advisory role regarding the patient’s goals and decisions”**.<sup>6</sup> The notion of shared decision-making has been taken up enthusiastically in North America and many European countries,<sup>7</sup> and the notion of an advisory role is certainly compatible with the ethos of community pharmacy practice. Its implementation for elderly patients with cognitive impairment is obviously constrained. However, among those whose cognitive capacity is retained, **shared decision-making is likely to enhance patients’ autonomy and self-efficacy, that is, patients’ motivation and ability to assess and control their environment, make appropriate decisions relating to their well-being, and implement these decisions.** Shared decision-making may involve not only the patient but also the patient’s carer.

### 2.1.5 Adherence to medication in specific disease states

The importance of adherence differs for different medicines and disease states. Many (but not all) empirical studies define an acceptable level of adherence, such as taking the correct medicines correctly over 80% of doses.<sup>8</sup>

However, for medicines that have a critical prophylactic or physiological action, missing even a single dose **may increase the risk of an acute event or an exacerbation of the patient’s condition**, and missing one dose could lead to a pattern of missed doses and consequent failure of therapy. Inhaled respiratory medicines for asthma and chronic obstructive pulmonary disease are an important case in point. Punctilious adherence to recommended therapy is critical for the efficacy of these medicines, and adherence refers not only to the right dose and frequency but also to a consistently correct inhaler technique.<sup>9</sup>

In other situations, missing a single dose is not likely to be an important concern. However, patients who are attuned to accurate adherence may become anxious when they realise that they have missed a dose, and it may be helpful for these patients to be able to seek advice from a pharmacist or the prescriber. Such encounters can be used to reinforce the importance of adherence.

## 2.2 Roles and responsibilities of pharmacy

In most countries, community pharmacy operates in a retail business context, physically, organisationally and financially separate from the health professionals who are licensed to prescribe medicines. The majority of prescribers are registered medical practitioners; others include registered nurses, pharmacists and optometrists. The range of medicines that authorised health professionals may prescribe is defined by the scope of practice for which they are registered. In rural and remote areas where other health professionals may be scarce, nurses are often required, and given necessary authority, to assume the role of prescriber.

Randomised trials of pharmacist prescribing have involved physician and pharmacist collaboration<sup>10</sup> or community pharmacist and nurse teams.<sup>11</sup> The studies followed blood pressure measurements in patients with hypertension or patients with diabetes who had elevated blood pressure. The intervention groups that involved pharmacist prescribing showed greater reductions in blood pressure than the control groups. Pharmacist prescribing required special authorisations.

Although they are licensed to prescribe within a limited pharmacopoeia in some locations, **pharmacists'** main role in the sequence outlined in section 2.1.2 above is to dispense prescribed medicines. The management and process of dispensing itself has several components. These are listed below, and discussed further in Chapter 3.

- Ensuring that the pharmacy contains or has access to the requisite medicines, and that they are stored correctly, are within expiry dates, and comply with regulatory conditions.
- Receiving the prescription, delivered either by hand (usually by the patient or carer) or electronically.
- Interpreting the prescription, with reference to the named medicine, the formulation, the strength or **concentration, the quantity to be dispensed, and the prescriber's specifications as to dose, frequency, and any instructions for taking the medicine.**
- Checking that these parameters are consistent with the listing of the medicine.
- **Checking that the prescription is consistent with what the pharmacist knows of the patient's recent regimen, with regard to dose, brand specification, formulation and presentation.**
- Checking for interactions with other medicines that the patient is taking.
- Labelling the packaging of the medicine, or repackaging it in a dose administration aid format with other medicines that the patient is taking.
- Explaining to the patient and/or carer the use of the medicine and its effects and common side effects (especially those of "red-flag" significance), and the arrangements for obtaining further quantities before the dispensed quantity has been fully consumed.
- Answering any questions from the patient and/or carer.

Thus, in dispensing, the pharmacist has an opportunity to communicate directly with the patient and/or carer, **and can thereby both assess the patient's needs and wishes** and provide timely education; this has been shown to enhance adherence (see section 3.4). **The patient's characteristics and wishes are important** determinants of what is actually dispensed. Will the patient be confused by brand substitution or a change in the appearance of a medicine that he or she has previously taken? Does the patient have a preference for tablets or capsules? Is the patient visually impaired, necessitating large-print labels? Does the patient have musculoskeletal impairments causing difficulty in opening packaging? In response to such questions, the pharmacist may or may not have flexibility in choosing the product that is to be dispensed. For example, the pharmacist may be able to choose between a proprietary or generic product, and between different brands that vary in their packaging.

Adherence is reinforced by effective communication between the prescriber and the patient, and between the pharmacist and the patient (or carer) at the time of dispensing of the medicine. It is evident that a poor relationship between the prescriber and the patient adversely affects adherence,<sup>12</sup> and that health professionals can favourably influence the degree of adherence.<sup>13</sup> The intensity and content of the communication is likely to be different if the patient is taking a medicine for the first time, as distinct from a repeat prescription. It is notable, however, that the pharmacist often does not have access to even basic clinical information on the patient relevant to the prescription, such as the diagnosis and co-morbidities, and may not have information on other medicines prescribed unless they were dispensed in the same pharmacy system. It is also notable that the pharmacist and the prescriber do not routinely communicate, other than **through the medium of the written prescription. These factors limit the scope of the pharmacist's counselling role.**

Universal health records (or e-health records) and pharmaceutical records provide a mechanism for improving adherence and promoting medication safety by giving pharmacists comprehensive access to individual **patients' medication information.** Their development was pioneered in France in 2007. French public health law provided the legal basis for establishment of the "Dossier Pharmaceutique" (DP), which lists all the medicines dispensed to the patient in any participating French community pharmacy in the previous four

months, including over-the-counter medicines. Every pharmacy is required to offer this service, but the DP is only created once a patient has consented. Patients may withdraw consent at any time.

The data are collected at the point of dispensing and stored in a centralised secure server. Only pharmacists and the professionals legally entitled to dispense medicines have access to the data. By May 2014, 22,297 French community pharmacies — almost 99% of all French community pharmacies — operated the DP and around 32 million pharmaceutical records had been created.<sup>14</sup>

## 2.3 Measures of adherence

Estimation of adherence is important. Failure to determine whether, or to what extent, a patient is adhering to a prescribed regimen may result in an assumption that an effective medicine is ineffective. Prescribers may then make unnecessary changes, including potentially dangerous increases in dosing level or frequency.<sup>15</sup>

In principle, adherence can be measured or monitored either directly or indirectly.

Direct methods involve measuring levels of the drug or a metabolite in tissues or body fluids (usually blood, urine or saliva). These methods are valid, but only for those drugs or metabolites that can feasibly be assayed. Assays are inevitably invasive, may be costly, and provide only limited information about a pattern of adherence, usually reflecting only recent use of a medicine.<sup>15</sup>

Indirect methods include the following:

- The use of prescription databases to calculate various indicators based on time periods between the refilling of prescriptions. Several such indicators have been specified.<sup>15</sup>
- The use of electronic medication packaging devices. These are designed both to monitor adherence and to remind patients to take the next dose. They are discussed further in section 3.7.
- “Pill counts”. These involve periodic inspections of packaging to ascertain the numbers of tablets or capsules removed and assumed to have been consumed.
- **Patients’ self-reports, or carers’ reports, compiled through** personal interviews, diaries, questionnaires, or online. Patients and their carers may have different perceptions or observations on the extent of adherence.<sup>12</sup>

Most of the methods of measuring adherence are more appropriate for research or evaluation studies than for routine monitoring and promotion of adherence. Researchers use a variety of methods and indicators, and no standardised approach to the measurement of adherence exists. As a consequence, it is often impossible to compare the findings of different studies and synthesise their results in systematic reviews, and meta-analyses are not feasible.<sup>8</sup>

However, practical information on an individual patient’s adherence pattern can often be elicited by the prescriber or the pharmacist. Where a patient has a good relationship with his or her prescriber and/or pharmacist, a carefully considered sequence of questions can lead to an informative discussion that reveals gaps in adherence and potentially identifies resolvable medication issues.<sup>16</sup>

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## 3 Options for enhancing adherence

### 3.1 Preamble

A wide range of methods have been used to enhance adherence. The main methods can be grouped as follows:

- Policies and regulations at the health system level, developed with the intention of ensuring that populations have affordable access to necessary medicines of high quality, with appropriate support for administration and adherence.
- Education and training of health professionals, particularly those with responsibility for prescribing medicines, dispensing medicines, and following up patients with ongoing needs for medicines.
- Counselling and education of patients, and their carers, on the rationale of their treatment, and matters relating to medicines and medication regimens; this typically occurs at the time of dispensing, especially for new medicines, but may also occur when a repeat prescription is filled.
- Follow-up after initial dispensing, either by face-to-face consultations or by telephone, or by inspecting dose administration aids. This reinforces adherence and provides an opportunity to enquire about drug-related problems.
- Reducing the adherence burden, either during formal medicine reviews or in follow-up discussions. This may involve “de-prescribing” to reduce polypharmacy (multiple medicines — prescribed or over-the-counter), altering dose schedules, altering preparations and presentation to facilitate medicine use, and managing drug-related problems.
- Packaging and dose administration aids. These both make taking medicine easier and serve as reminder systems, thereby facilitating adherence. They may also enable health professionals to monitor individual patients’ medicines use.
- Systems to facilitate repeat prescriptions and supply for ongoing medicines use.

These approaches have been used both singly and in various combinations.

### 3.2 Initiatives at the health system level

In almost all jurisdictions, pharmacy forms part of the complex system of functions and structures that make up a health system. A detailed review of health system initiatives that relate to pharmacy is beyond the scope of this report. However, it is noteworthy that pharmacy has a major input into health policy, regulation, its own and **other health professions’ compliance with regulations, and cost control mechanisms**. In general, the primary aims of pharmaceutical policy at health system level are to support a reliable supply of high-quality medicines deemed necessary for the population served, and to control costs to governments, health services and consumers.

In many health systems, the regulatory framework extends to promoting the quality use of medicines, and promoting adherence is a key element of this.<sup>1</sup> In addition, through vigilance over the quality of medicines supplied to patients, pharmacy helps to prevent the sale and use of substandard and falsified medicines, which are reported to be particularly prevalent in low- and middle-income countries.<sup>2</sup>

At national and even supra-national level, pharmacy has a track record of advocacy in highlighting the human and economic costs of non-adherence and proposing policy and funding arrangements designed to enhance adherence. In a comprehensive frame, an example is the Quality Use of Medicines programme in Australia,<sup>1</sup> which has ensured that national resources are allocated to a broad range of ongoing activities, some of which are outlined in Chapter 4. In a more specific frame, pharmacy has had a leading part in multi-professional advocacy relating to the management of asthma and chronic obstructive pulmonary disease, notably advocacy to “put non-adherence to inhaled respiratory medication higher on the policy agenda” in Europe.<sup>3</sup>

At regional and local levels, community pharmacy makes a major contribution to primary care, although its potential as a major primary care agency is certainly not fully realised. The barrier is the lack of health system

integration that often sets different health professionals apart rather than enabling them to work together on the needs of the patient. Sustaining this barrier is a tension between medical practitioners and pharmacists. Doctors tend not to recognise that pharmacy could make a major contribution to patient care, while pharmacists perceive that doctors are “unreceptive to pharmacy initiatives”.<sup>4</sup>

The promotion of adherence is sometimes a by-product of regulatory elements that are intended primarily to serve other aims. For example, many regulatory authorities impose controls on who may prescribe a particular medicine, the indications for which it may be prescribed, the quantity that may be dispensed, and the number of repeat prescriptions that can be issued without requiring a patient to undergo clinical review. These controls are primarily intended to ensure safe and appropriate use of medicines and limit costs, but they could also assist in promoting adherence by creating therapeutic conditions that engage patients and allow those responsible for dispensing to participate actively in the sequence outlined in section 2.1.2. Importantly, they provide an imperative for collecting and monitoring data on prescriptions and dispensing, thereby creating a mechanism for monitoring adherence at the population level.<sup>5</sup>

With safety as an aim, regulatory mechanisms in many jurisdictions define presentation, packaging and labelling requirements. As discussed in section 3.7 both the presentation of medicines, their packaging and the clarity of labels on bottles, boxes and blister packs have great potential to influence adherence.

Mechanisms for controlling cost are important in enhancing adherence, although — perhaps surprisingly — cost has less of an effect on adherence in the elderly and those with long-term health conditions than others. In an Australian national sample survey conducted in 2016–17, participants were asked, “Since last year, has there been any time [you] delayed getting or did not get prescribed medication because of the cost?”. Overall, 7.3% of respondents answered “yes”. However, fewer of those aged 65-plus years answered “yes” — the proportions ranged from 6.5% to 10.4% in those aged 15–64, and from 2.0 to 2.8% in those aged 65-plus. In addition, fewer of those with long-term health conditions said “yes” — 4.5% of those with long-term health conditions, versus 8.9% of others.<sup>6</sup> A systematic review and meta-analysis showed, in publicly insured populations with a mean age of 72 years, there was a significant increase in non-adherence to medicines for which a co-payment was required.<sup>7</sup>

### 3.3 Education and training of health professionals

Intuitively, it seems likely that health professionals involved in the sequence outlined in section 2.1.2, notably pharmacists, would be more effective in promoting adherence in elderly patients if their education programmes covered the problems of adherence and techniques for advocacy.<sup>8</sup> While modern university pharmacy curricula vary in their design and structure, they invariably address the three foundational domains of learning that have prevailed for several decades: the cognitive domain, covering mental skills and knowledge; the affective domain, referring to attitudes; and the psychomotor domain, encompassing manual and physical skills.<sup>9</sup>

In general, pharmacy curricula at both undergraduate and graduate levels include lectures, tutorials and demonstrations on taking a patient’s medication history. Students have opportunities to gain first-hand experience in taking a history that covers the actions and interactions of both prescribed and over-the-counter medicines, as well as adverse drug reactions and allergic reactions.

However, pharmacy students are not usually trained to take a medical history, which is one of the major skills taught to medical students. Inter-professional learning involving both medical and pharmacy students would give both groups the experience of taking a medical history and a medication history.

Undergraduate and graduate-entry pharmacy curricula also cover education and training in the principles of counselling and patient education relating to medication use and adherence, both in general and in connection with a wide range of specific health conditions.

Specific training for counselling and patient education is usually undertaken as a postgraduate course or as part of a continuing professional development course outside the framework of a degree programme. While published evaluations of pharmacy interventions to promote adherence sometimes mention pharmacist

training, detailed information on pharmacist training is seldom provided. Notably, however, some quite detailed information is provided in reports on new medicine services, home medication reviews and targeted services for specific conditions such as hypertension.

An example of pharmacist training to provide targeted services is examined in an Australian study, which provided detail on a training programme preparing pharmacists to deliver services that targeted medication adherence for hypertension management. This study reported that pharmacists' capacity and confidence improved. However, adherence per se and patient outcomes were not assessed. Social learning theory formed the theoretical foundation of the training programme, which comprised provision of a manual of self-directed pre-reading, lectures, workshops, case studies, and competency assessment covering the application of knowledge and clinical skills.<sup>10</sup>

Evaluation of specific training for previously qualified pharmacists has focused on specific conditions, particularly hypertension. Evaluation outcomes include pharmacists' satisfaction with training, adherence and health outcomes such as changes in blood pressure.

With regard to health outcomes, a randomised controlled trial<sup>11</sup> of "enhanced pharmacist care" provided by pharmacists credentialed to prescribe antihypertensive medication showed beneficial effects on patients' systolic blood pressure; the patients were rural residents but not specifically in the elderly age range.<sup>12</sup>

## 3.4 Counselling and education of patients and their carers

### 3.4.1 Overview

Ultimately, patients themselves determine whether, or how consistently, they follow "agreed recommendations from a healthcare provider" on medicines use, and their behaviour is greatly influenced by a partner, carer or other family members if present. It follows that any opportunity to provide counselling and education to patients and those around them has great potential to improve their own understanding of, and engagement with, the management of their health conditions.

Explanation and discussion at the time of dispensing new prescriptions and refills (repeats) are natural and universally recognised responsibilities of pharmacy. During a pharmacy consultation, the pharmacist may:<sup>13</sup>

- Ask the patient to discuss his or her concerns, beliefs and preferences about medicines
- Assess medication adherence
- Assess use of medicines delivery and monitoring devices, and provide education and guidance as necessary
- Attempt to resolve any identified medication-related issues
- Discuss management of the health condition
- Discuss lifestyle factors that might affect medicines use and health status, e.g., smoking, alcohol consumption
- Discuss any difficulties in obtaining, using and storing medicines
- Discuss the presentation of the medicine and whether a change (e.g., from tablets to liquid) might be helpful
- Obtain a history of over-the-counter or non-prescription medicine use, including complementary medicines, and discuss any potential side effects and interactions
- Create a medication profile and develop an action plan for any actions arising from the consultation
- Provide written information (e.g., patient information leaflets) as appropriate
- Review any available clinical measurements that might reflect adherence (e.g., serum HbA1C and blood glucose levels for people with diabetes)

The first point — asking the patient to discuss his or her concerns, beliefs and preferences — elevates the patient from a passive role to one of a partnership with the prescriber and dispenser. The partnership is based on **two-way communications rather than projecting the patient as a passive recipient of health professionals' advice and decision-making**. This negotiated approach is part of concordance and can lead to better adherence to medication. Suggested interventions to promote the partnership have included encouraging patients, by means of advertisements, to ask their pharmacist questions. However, interventions targeting pharmacists proved to have a greater positive effect on adherence than those targeting patients. These interventions involved the provision of structured interviews or question protocols to assist pharmacists in determining the nature of patients' medication-related problems in connection with conditions such as asthma, COPD and hypertension.<sup>14</sup>

### 3.4.2 Specific health conditions

Various models of counselling and education have been evaluated, mostly in relation to specific medical conditions or groups of conditions. The following are some illustrative examples.

#### Alzheimer's disease

A Japanese study evaluated a pharmacy-led service to improve adherence to donepezil therapy by providing **information for patients and their families about Alzheimer's disease and the significance of consistent pharmacotherapy**. Patients were referred to the service by their primary care physician. The consulting pharmacist was supplied with clinical and functional data about each participating patient, and then met with the patient and family members. Education covered information on how to store and take the medicine and the actions of donepezil, including latency in the manifestations of its effects, the nature of its effects in improving symptoms and/or delaying progression, and the benefits for carers. A second pharmacist consultation was scheduled four weeks after the first. All donepezil users were enrolled in a non-concurrent comparison of patients who commenced the medication before and after the service was introduced. The one-year donepezil persistence rate among the patients who used the service was 73%, compared with 49% among those who did not.<sup>15</sup>

#### Asthma and chronic obstructive pulmonary disease

In the context of asthma and COPD, adherence means not only taking or using prescribed medicines, but also following the correct technique for using inhalers. The inhaler adds complexity to improving adherence in the management of asthma and COPD. A systematic review of errors in inhaler use found that inhaler technique was incorrect in almost one-third of more than 59,500 observed tests of technique described in 144 published articles, and that the prevalence of incorrect inhaler technique had not improved appreciably over a 40-year period.<sup>16</sup> The authors suggest that patients may have received insufficient instruction with observation by the instructor, and they reiterate the accepted components of patient education — careful instruction with demonstration and observation, repeated tuition, individual matching of inhaler and patient (possibly choosing among breath-actuated, dry powder and metered-dose inhalers), video instructions, computer assistance and written material. The systematic review did not focus on any particular age range, other than analysing separately for children, and did not highlight the role of pharmacy in the suggested patient education. However, it is clear that the problem would apply across adult age ranges and possibly more so in the elderly, and that pharmacists dispensing inhalers should provide education on, and monitor, inhaler technique. As noted in section 2.1.5, advocacy to put non-adherence to inhaled respiratory medication higher on the policy agenda has received attention in the European Union.<sup>3</sup>

#### Cardiovascular disease

A qualitative study exploring pharmacists' involvement in supporting patients with cardiovascular disease highlighted **pharmacists' perceptions that the scope of their practice encompassed advising patients about their conditions, lifestyle modifications and disease or risk-factor control as well counselling about medicines and adherence**. The majority of the 21 participating community pharmacists considered that they had sufficient knowledge about cardiovascular disease to do this effectively. However, those who offered a higher level of care expressed interest in the possibility of specialisation and credentialing for pharmacy professional services in cardiovascular disease.<sup>4</sup> In the elderly, cardiovascular disease is often associated with cognitive

impairment and, as noted in section 2.1.3, cognitive impairment is often unrecognised. For example, a study of 251 older, outpatient US veterans with heart failure found a surprisingly high prevalence of unrecognised cognitive impairment (58%), and that cognitive impairment was significantly associated with poorer medication adherence.<sup>17</sup> This points to a particular need for pharmacists to consider cognitive impairment in the provision of counselling and education to patients, and the value of involvement of patients' carers.

## Depression

Patients taking antidepressant medicines have a high incidence of non-adherence problems, and pharmacist counselling has the potential to promote adherence. A study of pharmacist counselling practices used simulated patients in three scenarios: a patient, hesitant to begin treatment, receiving an antidepressant for the first time; a patient perceiving lack of effect two weeks after commencing an antidepressant; and a patient wanting to discontinue an antidepressant after three months because of improvement. The study concluded that, while pharmacists provided information on the risks and benefits, their coverage of adherence-related issues was incomplete.<sup>18</sup>

## Diabetes mellitus type 2

A 2015 systematic review of adherence to oral antidiabetic agents and insulin identified 52 studies that met inclusion criteria. Overall, the results were inconsistent, with some comparable interventions producing contrary results for comparably measured adherence outcomes — for example, interventions including continuous education and reinforcing text messages based on patients' blood glucose levels, and pharmacist-delivered care plans.<sup>19</sup> In view of the relatively high prevalence of non-adherence to antidiabetic medication and the importance of controlling diabetes, detailed written guidance is available for pharmacists providing support to patients with diabetes.<sup>13</sup>

## Hypertension

A pre-post evaluation of a rural community pharmacy intervention to improve adherence to antihypertensive blood pressure medication was conducted in Montana, USA. The study showed an increase in adherence from 73% to 89%. The intervention consisted of brief consultations and the provision of standard educational materials. The participating pharmacies received specific programme funding to provide the intervention, synchronise prescriptions across prescribers and provide feedback to physicians.<sup>20</sup>

## Immune-mediated inflammatory disorders

A systematic review of interventions to improve adherence in patients with immune-mediated disorders included studies of adult outpatients with psoriasis and psoriatic arthritis, Crohn's disease, ulcerative colitis, rheumatoid arthritis, spondyloarthritis, and multiple sclerosis. A total of 1,538 citations were identified and, of these, 15 studies met inclusion criteria. The interventions reported in these studies comprised the following: (i) educational interventions, covering knowledge of the disease, the mechanisms of action, benefits and side effects of the prescribed medicines, and the consequences of non-adherence; (ii) behavioural interventions, promoting and/or reinforcing adherence by means such as reminders and motivational interviewing; (iii) cognitive behavioural interventions, designed to alter thought or behavioural patterns to support adherence; and (iv) multi-component interventions, combining any of (i) to (iii). Overall, the results suggested that multi-component interventions were effective in improving adherence in most of the conditions considered.<sup>21</sup>

## Osteoporosis

The potential to prevent osteoporosis-related morbidity and mortality by means of pharmacotherapy has been recognised for more than two decades.<sup>22</sup> A focus group study of patients with osteoporosis concentrated on patients' experience with physicians, but reported that factors affecting adherence to osteoporosis pharmacotherapy included a lack of knowledge about osteoporosis and difficulty with medicines or failure to remember to take them. Some of the suggested solutions, which included dose administration aids and education by health professionals other than doctors, are undoubtedly within the scope of the dispensing pharmacist's practice.<sup>23</sup> A systematic review highlighted the need for pharmacists to be involved in counselling patients on the optimal duration of therapy and the significance of following "drug holiday" recommendations from clinical practice guidelines, with monitoring and reassessment for reinitiation of therapy.<sup>24</sup>

### 3.4.3 Patient participation

In general, educational interventions are designed to increase patients' self-efficacy and understanding of their condition and their medicines. The effectiveness of patient education is likely to be enhanced if patients are given the opportunity to participate in their own treatment and management decisions, and through self-monitoring.

A recent systematic review of interventions to improve adherence among patients aged >65 years with cognitive impairment and living in the community identified two studies evaluating educational interventions. The interventions included the provision of oral, written or visual information, or a combination.<sup>25</sup> Both studies showed that educational programmes were associated with significant improvements in adherence.<sup>15,26</sup>

Patient education is mostly provided via spoken communication between the prescriber and/or the dispenser and the patient, often supplemented with written materials. Other communication formats, and multimedia formats that use more than one format, have been extensively evaluated. These include the combination of (i) text, still graphics, and photographs or diagrams, (ii) video and animation formats, and (iii) audio. The potential advantages of using multiple media in patient education programmes are as follows:

- Patients with low levels of literacy are likely to find multimedia formats more accessible than conventional spoken or written delivery.<sup>27</sup>
- Where there is a perceived or known language barrier, multimedia materials can be translated more readily than finding satisfactory interpreter services for one-to-one consultations.
- Information can be taken in at the patient's preferred pace, unlike spoken communication.
- Information can be repeated as needed.
- Contemporary information and communication technology platforms that can be used to deliver patient education are portable and/or can be driven by the internet, enabling patients and their carers to have access when and where they require, and at low cost.
- Information can be tailored or personalised to be relevant to the particular needs of individual patients.

Despite these potential advantages, a systematic review of multimedia interventions found no difference in the effect on adherence between multimedia education and usual care or no education. This was based on moderate-quality evidence from the two studies (involving 4,552 subjects) that examined adherence as an outcome, out of the 24 studies that met the inclusion criteria of the systematic review. Although the 24 studies focused on educational initiatives, the interventions that they assessed included other components, such as counselling, cognitive behavioural therapy, and other forms of support, and the effect of multimedia education on outcomes could not be separated from the effects of these other components. Overall, insufficient information was provided on the variability and quality of the interventions, and the data could not be pooled because of the high level of heterogeneity in the comparators used and the outcomes measured.<sup>28</sup>

### 3.4.4 Follow-up counselling and education

As well as at the time of dispensing, pharmacy-based counselling and education may occur in the context of follow-up. An example is the New Medicine Service (NMS) intervention, which has been introduced in England,<sup>29</sup> and reproduced in Ireland<sup>30</sup> (see Chapter 4) and, more recently, Norway.<sup>31</sup> In England, the NMS intervention begins when a patient takes a prescription to a community pharmacy for a medicine that he or she has not previously taken. It comprises two follow-up encounters, either face-to-face or by telephone, with the pharmacist, respectively 7–14 and 21–35 days after the medicine was dispensed. The aim of each encounter is to find out whether the patient is experiencing any difficulties with the medicine, manage these appropriately and promote adherence. A formal cost-effectiveness evaluation showed that the NMS intervention improved adherence compared with normal practice, and that this “translated into increased health gain at reduced cost”.<sup>29</sup>

### 3.4.5 Telephone counselling

Pharmacist telephone counselling offers a potentially efficient way of delivering advice on adherence, particularly for follow-up consultations. Telephone counselling has been used to support both patients and carers. As with all counselling services, training is required, and it is important for those delivering telephone counselling to be aware that the “body-language” dimension is absent.

In a Hong Kong trial of pharmacist phone counselling (versus “usual care”), non-adherent stable patients on five or more chronic medicines were randomised to receive an intervention consisting of six to eight 15-minute pharmacist phone calls over two years. The age range of subjects was 34–96 years, with a mean of 71 years. The phone calls took place at the middle of the period between clinic visits. In each phone call, the pharmacist **asked about the patient’s treatment regimen and clarified misconceptions about it, answered questions about side effects, reinforced the importance of adherence to medication and other elements of the treatment regimen, and promoted healthy behaviours.** More than half of those randomised became adherent following screening, with no further intervention. In the intervention group, a greater proportion of baseline non-adherent patients became adherent, and a greater proportion of baseline adherent patients remained adherent. High adherence scores were associated with a significantly reduced mortality. The authors concluded that the important aspect of the intervention was the fact that it provided periodic reinforcement, and that this had an effect in promoting persistence with treatment.<sup>32</sup>

A brief pharmacist telephone intervention specifically addressed barriers to adherence among elderly non-adherent patients with hypertension and diabetes mellitus taking angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Subjects were on a US Medicare Advantage health plan, and this enabled compilation and analysis of diagnostic, prescription and dispensing data. The pharmacist at the health plan followed a standard script which was tailored to include an introduction, an alert to patients that their medicines refill was overdue, and targeted questions to identify barriers to medication adherence. The pharmacist then provided recommendations for managing the issues identified. Most phone call conversations were three to five **minutes long. The pharmacist could also call the patients’ physicians or pharmacies to resolve identified problems.** Over a six-month period following the intervention, patients who received the intervention had significantly better adherence, as measured by standard indicators, although **both intervention and control groups’ adherence levels remained suboptimal.** The commonest barriers to adherence were memory and “doctor issues”, such as difficulty scheduling appointments.<sup>33</sup>

The importance of providing support for carers of patients with significant cognitive impairment or dementia has been widely acknowledged.<sup>34</sup> A protocol has been prepared for a systematic review of telephone interventions delivered by health professionals for educating and psychosocially supporting informal carers of adult patients.<sup>35</sup> This is discussed further in section 3.5 below.

### 3.4.6 Physical space for pharmacy consultations

Several publications have drawn attention to the importance of physical space and privacy within pharmacy premises so that pharmacists, patients and their carers can have confidential, undisturbed consultations. For example, the Pharmaceutical Society of Australia guidelines for the delivery of medication adherence services<sup>13</sup> stipulate that the area should be:

- Physically separated from the retail pharmacy area to provide privacy and confidentiality, and to prevent the patient and the pharmacist from being overheard by others
- Furnished such that the pharmacist and the patient can both be seated, and large enough for this, and for any equipment and documentation that might be needed
- Marked as a private consulting area.

In some countries, such as Portugal, the existence of a private consultation area is mandatory by law.

## 3.5 The role of carers

The presence of carers living with patients has been shown to improve adherence for patients with cognitive impairment, including those with mild cognitive impairment. However, the presence of a carer rarely occurs in the absence of other factors that are also likely to influence adherence. Consequently, the benefit attributable to the presence of the carer may be difficult to discern.<sup>36</sup>

In many instances, care-giving falls to family members and other ‘informal’ carers, that is those who are not paid for care-giving. The physical, social, emotional and financial burden on informal carers is substantial, and it is argued that support from a professional counsellor or peer can mitigate this burden. The telephone is clearly a convenient medium to provide support for carers, especially where a carer is housebound with a patient.<sup>34</sup>

A systematic review of studies using telehealth interventions designed to improve family carers’ health outcomes identified 4,205 articles, of which 65 met inclusion criteria. Of these, 33 articles referred to family carers of adult and older patients. Technologies included video, Internet, telephone and telemetry/ remote monitoring. Interventions delivered through these technologies included education, consultation and decision support, psychosocial support, cognitive behavioural therapy, training in problem-solving, social support, monitoring, and clinical care delivery. In 62 of the 65 articles, carer outcomes were reported as having improved. The outcomes included enhanced psychological health (less anxiety, depression, stress, burden, irritation and isolation), improved caregiving knowledge and skills, better quality of life, and improved social support and social functioning.<sup>37</sup>

## 3.6 Polypharmacy, complex regimens, and medication reviews

Polypharmacy — often reported as meaning the use of five or more medicines<sup>38</sup> — is common among older people living in the community. Both intuition and research evidence<sup>39</sup> suggest that multiple prescribed medicines and a complex medication regimen adversely affect adherence. Adherence has been found to be inversely proportional to the frequency of dose.<sup>40</sup> Multiple medicines tend to be associated with comorbidities, and the presence of comorbid diseases may independently impair adherence.<sup>36</sup> Polypharmacy can, in some circumstances, be an expression of overdiagnosis, which “occurs when a diagnosis is ‘correct’ according to current professional standards but when the diagnosis or associated treatment has a low probability of benefiting the person diagnosed”.<sup>41</sup> Overdiagnosis is increasingly recognised in contemporary health care.

According to a published protocol, a systematic review of interventions for improving adherence in older adults prescribed multiple medicines is in progress.<sup>42</sup> An earlier systematic review of pharmaceutical care found that three approaches were successful: regular scheduled patient follow-up combined with the use of a multi-compartment dose administration aid; group education combined with individualised medication cards; and medication review by pharmacists, concentrating on regimen simplification.<sup>43</sup>

A powerful approach to the resolution of polypharmacy is the medication review, which may be conducted at the pharmacy or the home (or nursing home) of an older patient with chronic conditions. The Pharmaceutical Care Network Europe has produced a classification of types of medication review according to their coverage. Four types are described:<sup>44</sup>

- Type 1: A simple medication review based on medical history information available in the pharmacy. This may reveal drug interactions, some side effects, unusual dosages and some adherence issues.
- Type 2A: An intermediate medication review based on information obtained directly from the patient, including the medication history. In addition to the findings from a Type 1 review, this may reveal drug-food interactions, effectiveness issues, side effects, and problems with over-the-counter drugs.

- Type 2B: An intermediate medication review based on information obtained also from the general practitioner. Additional information may be obtained about indications for medicines used, and drugs taken without indications.
- Type 3: An advanced medication review based on medication history, patient information and clinical information. Further additional information may be obtained about dosage issues.

Medication reviews are demonstrably effective,<sup>45,46</sup> but they often pose logistical difficulties. Home medication reviews, in particular, are time-consuming for pharmacists, and divert them from their dispensing workload. Remuneration arrangements are often cumbersome or inadequate. Medication reviews are likely to be most effective when a good working relationship exists between the pharmacist and the patient's physician. Consent is needed, and this may be difficult to obtain from a patient who is cognitively impaired. Nevertheless, when these logistical problems can be overcome, medication reviews provide a very good mechanism for managing polypharmacy.

### 3.7 Packaging, dose administration aids and reminder systems

Blister strips — sheets of plastic with pockets or blisters that contain tablets or capsules, sealed with a thin sheet of aluminium<sup>47</sup> — have been in widespread use for some decades. On some blister strips, each blister is labelled with the day of the week. This form of packaging serves as a simple dose administration aid and is especially helpful for the use of medicines that rely on adherence to daily dosing, such as oral anticoagulants.

For patients who are committed to taking their medicines, they help intuitively to prevent missing individual doses, and provide a simple answer to the often-asked question, “Have I taken my pills today or not?”. Repackaging tablets and capsules into a multi-compartment device has been a popular and reliable method of assisting patients who are required to take multiple medicines and multiple doses each day.<sup>48</sup> The device contains all the tablets and capsules needed for each time of day, for each day of the week. The pharmacist dispenses medicines in the device, which is sealed to prevent spillage or the mixing-up of the items in it. Community pharmacists generally support the use of multi-compartment devices, but consider that they may not be an appropriate mechanism for promoting adherence where a patient's medication regimen may change, or where a patient wants to have an active involvement in his or her therapy.<sup>49</sup> Of course, such devices can only be used for solid preparations in tablet or capsule form.

Recent evaluations have concentrated on electronic dose administration aids, defined as “electronic adherence-promoting devices integrated into the packaging of a prescription medication”. A variety of such devices have been invented. Some of these incorporate reminder systems comprising audible or visual prompts, others actually dispense medicines to be taken according to the prescribed dosing schedule, and yet others send alerts to carers or healthcare professionals if doses are missed<sup>50</sup> using software systems for various devices, such as mobile phones and computers. The efficacy of information systems (not specifically medication alert systems) that send alerts to a health professional has been studied in elderly patients. Patients and carers were motivated to use these systems, but the professionals who received the alerts were often insufficiently responsive to resolve in a timely fashion the matters that patients brought to their attention.<sup>51</sup>

Evaluations of electronic devices have generally been equivocal, and this may reflect the diversity of clinical contexts in which they are deployed. In a systematic review,<sup>52</sup> 32 randomised trials and five non-randomised studies of a broad range of electronic devices were examined. The devices all had the following features: they recorded dosing events; they stored records of adherence; they provided audiovisual reminders to take medicines; they had digital displays; and they provided real-time monitoring and feedback on adherence. Overall, the findings did not uphold their effectiveness. The studies reviewed were of variable quality, and the effects of the devices on adherence were also very variable.

Robotics offers the possibility of integrating the functions of existing devices, which invariably focus on a single aspect of medication use, such as providing reminders. Recently, a device has been developed to manage all aspects of medicines use for older home-care patients on long-term medication. At set dosing

times, the device issues a spoken reminder message, an audible signal, a light signal, and a text display. The patient is thus prompted to press a button on the front of the device, which then delivers a sachet containing the required medicines. If the patient misses a sachet, the device sends an alarm signal to the home-care centre, and a staff member from the centre can then intervene. The alarm remains activated until the problem that triggered it is resolved. Unused doses are moved into a locked compartment if not used within a predetermined time. The device records data on sachets dispensed or not used, is secure and tamper-proof, and records attempts at tampering. A pilot study has shown the device to be acceptable to motivated patients and home-care service staff, and to have particular potential value for older people living alone. Following the pilot study, improvements were made to ensure the device's safety and improve its reliability.<sup>53</sup>

## 3.8 Conclusion

Overall, especially in the elderly, with or without a carer involved, no single intervention has been shown to overcome non-adherence. It is apparent, however, that good communication between pharmacist and patient will reduce non-adherence. Modified mechanical and electronic dose administrations aids can be helpful for some but not all patients. They are likely to have the greatest potential benefit for those patients with forgetfulness and confusion associated with taking medicines in unintentional non-adherence. Improving communication between all those **involved in the patient's care**, accompanied by continuing learning and teaching, will be the most rewarding approach, and likely to reduce the prevalence of non-adherence.

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## 4 Current initiatives to promote adherence

### 4.1 Data compilation

As noted in section 1.4, some FIP member organisations provided information on relevant interventions and programmes to improve medication adherence in their respective countries. To provide the information, respondents completed a questionnaire prepared by the authors of this report. The questionnaire template is included in Appendix B. Responses were received from organisations in Australia, Belgium, Denmark, Ireland, the Netherlands, Singapore, Spain and Switzerland.

This chapter provides an overview of the responses (sections 4.2–4.7) and a summary description of the initiatives in each country (subsections in section 4.8).

### 4.2 Recognition and commitment

It was clear that the organisations representing pharmacy professionals in all the respondents' countries recognised the importance of adherence from the perspective of individual patients. They also recognised the high prevalence of non-adherence and its consequences, not only for individual patients but also for carers, prescribers, pharmacists, other health professionals and the community as a whole. Where cost estimates of non-adherence were made, the costs were substantial. Worldwide, non-adherence was reported to account for 57% of the "total avoidable cost due to suboptimal medicine use", and for 4.6% of total health expenditure.<sup>1</sup>

In each of the respondents' countries, significant initiatives had been undertaken to promote adherence, and most countries had a track record of appreciable investment to support multiple interventions. The interventions were variously at the policy level, the community level and the individual patient level, and depended heavily on the pharmacy profession. Many of the interventions that they described were not focused exclusively on adherence — rather, adherence was one of a range of intended outcomes.

Most of the interventions listed were directed at patients with a broad range of conditions, but several were designed only to contribute to the management of one or a small number of specific conditions, notably asthma, COPD, hypertension, and vascular disease requiring lipid-lowering medicines.

### 4.3 Targeting the needs of the elderly

Strong evidence exists to show that older people need, and are prescribed, more medicines than younger people, and that the prevalence of non-adherence is higher in the elderly, due mainly to the difficulties faced by older people in obtaining and managing their medicines. While many of the initiatives described by the respondents did not specifically target the elderly, they mostly proposed solutions relevant to the elderly. Where the elderly were specifically identified, the term "elderly" was generally taken as referring to people over the age of 65 years.

### 4.4 Current pharmacy programmes and services

#### 4.4.1 Dose administration aids

Interventions involving the use of dose administration aids were frequently reported. The provision of dose administration aids was evidently on the initiative of the pharmacist in discussion with the patient and/or carer, rather than on the instruction of the prescriber. Dose administration aids were mostly made up at the community pharmacy level; in one instance (Denmark), a national programme had been introduced to support

automated systems for producing the packaging. In some jurisdictions (for example, Australia), formal guidelines on pharmacy processes for producing dose administration aids were available.

Most of the national programmes that included the provision of dose administration aids appeared to provide solutions consisting of the preparation and provision of medicines in packaging that was based on the times when the medicines should be taken. However, a few programmes, namely the Swiss initiatives and the Spanish *Adhiérete* initiative, also added electronic systems, such as electronic dose dispensers.

#### 4.4.2 Reminders

Pharmacists often provided medication reminders, most commonly by telephone (increasingly using cell or mobile phones) or by e-mail. Mobile phone reminders were used especially for patients taking multiple medicines over prolonged periods.

#### 4.4.3 Staged supply

Some jurisdictions, notably Australia, had dispensing rules that allowed pharmacists to supply medicines to patients in periodic instalments with a limited number of doses, thereby creating a mechanism by which pharmacists could actively oversee medication adherence. Specific dispensing rules had also been created to allow pharmacists to maintain the supply of medicines if a patient ran out of doses and had not been able to obtain a repeat prescription in time, a process known as continued dispensing.

#### 4.4.4 Counselling and provision of cognitive pharmaceutical services

Pharmacist counselling services were the most frequently reported initiatives designed to promote adherence. Counselling took place both at the time of dispensing new and continuing medicines and subsequently for follow-up. Counselling by pharmacists should be considered at two levels: (i) the advice that pharmacists traditionally give when dispensing a medicine; and (ii) cognitive services above and beyond this advice. Specific programmes to enhance counselling refer to the latter.

While prescribers provided information about diagnoses and treatment plans, pharmacists usually took responsibility for counselling patients and carers regarding their medicines. Particular efforts were made when new medicines were introduced, and significant national programmes to support the introduction of new medicines were in operation in some jurisdictions (see sections 4.5, 4.8.3 and 4.8.4 below). These programmes had been subjected to evaluations, and evidence suggested that they resulted in significantly improved adherence.

Pharmacists also took responsibility for discussing changes in medication with patients and carers. These changes could involve adding or removing medicines from a regimen, changes in the dose or frequency prescribed, and changes in medicine brands or manufacturers, with the consequence that the dispensed tablets or capsules appeared unfamiliar to patients. In situations where the pharmacist was uncertain about a prescription or the patient or carer raised concerns with the pharmacist about a prescription, the programmes made provision for involvement of the prescriber in the discussion.

Motivational interviewing was an important element in the cognitive services. In general, the objectives of **motivational interviewing were to discuss patients' concerns about medicines, help them to manage any side effects, and explain the importance of adherence.**

Several respondents reported on the conduct of home medicine reviews in their respective jurisdictions. Home medicine reviews provided an opportunity for pharmacists to investigate problems that patients encounter with their medicines, and to suggest ways of managing polypharmacy, drug interactions and related complications. Such reviews also provided an opportunity to assess the usage of over-the-counter (non-prescription) medicines and alternative medicines, and to consider whether or not these might interact with **patients' prescribed** medicines. However, despite their potential benefits, some major barriers of time and logistics militated against their frequent use. Home medicine reviews were either initiated by the prescriber or required the involvement and endorsement of the prescriber.

## 4.5 Promoting adherence for specific conditions and medicines

While many of the pharmacy initiatives were designed to promote adherence across a wide range of conditions and for a wide range of types of medicines, others had been developed for the management of specific conditions or groups of conditions.

For example, pharmacists in Denmark conducted programmes to instruct patients in the correct use of inhalers to deliver medicines for asthma and COPD, and to monitor and promote their correct use on an ongoing basis. Community pharmacists in Belgium formed the nucleus of multidisciplinary groups of health professionals aiming to promote adherence to programmes and medication for osteoporosis. Swiss pharmacists participate in inter-professional programmes for chronic conditions, specifically HIV, multiple sclerosis, type 2 diabetes mellitus, metabolic syndrome, and for patients taking oral cancer drugs. The efforts of Spanish pharmacists were also directed at asthma and COPD, as well as hypertension.

The New Medicine Service (NMS), targeting patients of all ages who were taking newly prescribed medicines on a long-term basis, was introduced in England in 2011 and pilot-tested in Ireland in 2017. In the NMS, pharmacists conducted a structured education and adherence programme for patients with a newly diagnosed chronic disease. The conditions and medicines covered in the Irish NMS are listed in section 4.8.4.

The Danish Ministry of Health also mandates that pharmacies provide a New Medicine Service, introduced in 2016. The Danish NMS consists of two consultations with a pharmacist, each typically taking about 10 minutes. The first consultation, in the pharmacy, is usually held on the day when the new medicine is first dispensed, and the second is scheduled for three to four weeks later, and can be held at the pharmacy or over the telephone.

## 4.6 Training of pharmacists about adherence

The curricula of degree programmes for pharmacists invariably cover adherence and related topics, usually under a heading such as “clinical training”. This encompasses basic clinical sciences and the management of patients and their medicines. **A major component of the latter comprises training in how to take a patient’s drug or medication history, covering prescribed, over-the-counter and alternative medicines, and a history of allergy or abnormal reactions to medicines.**

For qualified pharmacists, most adherence-promoting initiatives did not require specific training or credentialing. The main exception was the training, initial supervised experience and credentialing needed in order to be authorised to carry out home medication reviews.

## 4.7 Funding of pharmacy services

In most instances, funding of pharmacy services to promote adherence was provided by governments, often from a global health budget. The funding was often provided on a fee-for-service basis.

In some jurisdictions, pharmacists could charge a modest fee, separate from the general dispensing fee, for specific services, including the dispensing of medicines in a dose administration pack.

Some additional funding was provided through individual pharmacy associations, and occasionally through grants from the pharmaceutical industry for specific programmes.

## 4.8 Initiatives in individual countries

### 4.8.1 Australia

The Pharmaceutical Society of Australia (PSA) has produced best-practice guidance for the delivery of medication adherence services. These services have been incorporated in a five-year agreement between the Australian Government and the Pharmacy Guild of Australia, a national professional organisation that supports pharmacy owners and is recognised in legislation. The present agreement covers the period 2015–20, and specific measures for the delivery of medication adherence services came into effect in 2017: dose administration aids, staged supply, continued dispensing, collaborative clinical pharmacy services and home medication review. A new agreement is negotiated every five years; the 2015–20 agreement is the Sixth Community Pharmacy Agreement.

#### Dose administration aids

The PSA has produced guidelines to assist pharmacists in the provision of dose administration aid services.<sup>2</sup> As described in sections 3.5 and 4.4, a dose administration aid is a device that can be used as a part of a coordinated approach to medication management. Its purpose is to ensure that patients receive the correct medicine at the correct time, in the correct dose, and in a safe and hygienic manner.

As noted in section 3.7, dose administration aids can be used for any solid medicines in tablet or capsule form. The Australian dose administration aid guidelines refer to patients of all ages, although most recipients are likely to be older. Under the Sixth Community Pharmacy Agreement, data evaluating the use of dose administration aids focus on processes of medicines delivery and on healthcare costs, but not patient outcomes. While (as mentioned) comprehensive guidelines have been produced to assist pharmacists and pharmacy students receive training on the provision of dose administration aids in the course of their broader training on dispensing, there is no specific training or credentialing relating to dose administration aids.

#### Staged supply

Staged supply — the process by which pharmacists supply medicines to patients in periodic instalments that contain less than the required or prescribed quantity — is also a national initiative supported under the Sixth Community Pharmacy Agreement. Staged supply can be used for all conditions, but is likely to be applied to drugs of abuse. The evaluation of staged supply is part of the Sixth Community Pharmacy Agreement.

#### Continued dispensing

Continued dispensing refers to the supply of an eligible medicine to a patient where there is an immediate need for that medicine, and it is not practical to obtain a prescription. The supply is contingent upon the medicine having been previously prescribed, the therapy is stable, and there has been prior clinical review by the prescriber, who supports continuing medication. Continued dispensing is supported under the Sixth Community Pharmacy Agreement, and can potentially be used for a wide range of conditions, types of medicines and age groups. No specific data are collected on the continued dispensing or its effects on adherence.

#### Collaborative clinical pharmacy services

MedsCheck and Diabetes MedsCheck are structured, collaborative clinical pharmacy services that take place in the pharmacy. They involve a review of medicines that a patient is using, a face-to-face consultation with a pharmacist, a medication profile for each patient, an action plan and a follow-up consultation.

Each MedsCheck focuses on education and self-management, and aims to identify medication-related problems (including but not confined to non-adherence), improve effective use of medicines and provide education about medicines, their best use and storage.<sup>3</sup>

Each Diabetes MedsCheck focuses on medicines for type 2 diabetes, the use of monitoring devices, education, self-management and adherence to diabetes therapy. The aim is to optimise the patient's use of medicines and monitoring devices for diabetes, improve blood glucose control and reduce the risk of developing complications. It is targeted at patients who are unable to gain timely access to other diabetes education or health services in their community. During a MedsCheck consultation, the pharmacist may refer a patient to other appropriate clinical services such as dose administration aids and staged supply.

To be eligible to obtain payments for MedsChecks and Diabetes MedsChecks, a pharmacy must deliver the services in accordance with all rules outlined in the Sixth Community Pharmacy Agreement. To be eligible, patients must not have received a similar service in the preceding 12 months, they must be living at home in the community, and they must be taking five or more prescription medicines, or have had a recent significant medical event or a new diagnosis that would affect the diagnosis, or be taking medicines with a high risk of adverse effects. Pharmacists must be approved to be a service provider, and can claim fees for up to 20 services in any calendar month.

### Home medication reviews

A home medication review is a comprehensive clinical review of a patient's medicines in his or her own home by an accredited pharmacist, on referral from the patient's general practitioner. The aim is to identify, prevent and resolve actual or potential medication-related problems, and optimise pharmacotherapy. In addition to direct benefits for the patient, the service provides information for health professionals involved in the patient's care, improves health professionals' knowledge and understanding of medicines and promotes cooperative relationships between members of the healthcare team.

Home medication reviews are available only to patients who live in a community setting, who are at increased risk of experiencing medication misadventure, and whose general practitioner confirms a clinical need and that the patient will benefit from the review.

In order to undertake home medication reviews, pharmacists must be credentialed by the Australian Association of Consultant Pharmacy, which is the major credentialing body for professional pharmacy cognitive services, or they must pass a test to be recognised as a Certified Geriatric Pharmacist under the auspices of the Society of Hospital Pharmacists.

## 4.8.2 Belgium

The Belgian Pharmaceutical Association has provided information on two initiatives: a three-month study known as ICAROS – the Impact of Community Pharmacy Intervention on Medicine Use and Adherence Rates in Patients with Osteoporosis — conducted in 2016; and an ongoing national initiative known as Family Pharmacist.

### ICAROS

The aim of ICAROS was to evaluate the feasibility of community pharmacy intervention for patients with osteoporosis, examining the quality of pharmacotherapy and adherence. The study involved 105 community pharmacists (of whom 80 completed the study), and it targeted ambulatory patients who had used at least one osteoporosis drug in the preceding 12 months. The drugs comprised bisphosphonate, strontium ranelate, denosumab, selective oestrogen-receptor modulators and teriparatide. Before the intervention, pharmacists received training in communication skills, an information package and access to a web tool. In the intervention, each participating patient had a one-on-one counselling session with a pharmacist, covering their use of the osteoporosis drug as well as calcium and vitamin D, and any drug-related problems. Pharmacists recorded data on the patient's adherence and drug-related problems and provided advice, and had a follow-up contact with the patient four to eight weeks later to ask whether their advice had been taken and whether the drug-related problems had been solved. The study reported positively on the acceptability of the intervention to both pharmacists and patients, although the patient participation rate was less than 60%.

## Family Pharmacist

In this new national Family Pharmacist programme, pharmacists monitor the medicines used by chronically ill patients and provide advice on their **correct use**. **The pharmacist also ensures that the patient's medication plan is correct and up-to-date**, and that it is accessible to other members of the healthcare team, particularly the family physician. Family pharmacists are required to register all dispensed drugs systematically in the **patient's local and shared pharmaceutical record**. Each time a patient visits the pharmacy, the information on both prescribed and over-the-counter medicines is checked, consolidated, corrected if necessary, and provided to the patient.

The Family Pharmacist programme began in 2017 and is envisaged as an ongoing initiative. It is conducted under the auspices of the pharmacy professional associations and the National Institute for Health & Disability Insurance, which provides the funding. No specific credentialing is required for participating pharmacists.

### 4.8.3 Denmark

The Association of Danish Pharmacies has identified four initiatives relevant to adherence: New Medicine Service; Inhalation Technique Assessment Service; Multi-Dose Dispensed Medicines; and Medication Review.

#### New Medicine Service

Patients are recruited into the national New Medicine Service by the pharmacist or through referral by the general practitioner. The service, which was inaugurated in 2016, consists of two confidential consultations, the first at the time when the patient collects a new medicine for a newly diagnosed chronic disease. The second consultation is held three to four weeks later and may either be face-to-face or by telephone. In the course of the consultations, the pharmacist sorts out drug-related problems and concerns, discusses opportunities to improve the way the medicine is taken, and provides additional information about the condition and the medicine.

The New Medicine Service is specified under Danish pharmacy legislation and pharmacists are obliged to deliver it. It is funded through an agreement between the Association of Danish Pharmacies and the Ministry of Health, and is free of charge for the patient. No specific credentialing is required.

#### Inhalation Technique Assessment Service

The Inhalation Technique Assessment Service, which began in 2006, is designed for people with asthma and COPD, who are instructed in and have a demonstration of inhalation technique. While the service targets first-time users, it is also available for multiple users. The patient receives advice on how to prepare the inhaler, how to hold it, how to inhale, how to close the inhaler and store it, the use of multiple doses, and mouth washing. Pharmacy staff document the advice given to each patient on a registration form. If necessary, **the demonstration and the assessment of the patient's technique are repeated until the patient can use the inhaler confidently and correctly**. The patient is referred to a doctor if he or she has persisting problems in using an inhaler, or does not respond to the inhaled medication.

The service is conducted under an agreement between the Association of Danish Pharmacies and the Ministry of Health. It is funded by the Danish Government, and is free of charge to the patient. Pharmacists are paid on a fee-for-service basis.

There is no formal training for the service, **and the requisite skills are part of the pharmacist's expected competencies**. However, pharmacists providing the service must be credentialed. This is based on a multiple-choice examination and documentation of five instances of delivering the service.

The service has been evaluated and shown to be acceptable and effective.<sup>4</sup>

## Multi-dose dispensed medicines

Under legislation passed in 2001, Danish pharmacists are required to supply drugs in automated dose packs. This has been identified as being of particular value for older patients. “Dose-pack” pharmacies are accredited by the Danish Medicines Agency, and this accreditation includes permission to install dispensing machinery that automatically makes up dose packs. A qualitative study conducted in 2008 concluded thus: “The general impression from the analysis is that automated dose dispensing in . . . primary care . . . is a technology with good, potential opportunities to improve the medication of weak patients in particular, but that there are risks involved and many potential obstacles.”<sup>5</sup> Dose dispensing fees are paid by individual patients, but may be reimbursed if the medicines involved are eligible for reimbursement.

## Medication review

Medication review was introduced in Denmark in 2010, and the Association of Danish Pharmacies has developed the programme including manuals, guidelines and credentialing of pharmacists to perform the reviews. Credentialing is based on written case reports and delivery of five services according to the guidelines. Medication reviews are conducted intermittently on a local basis, and patients or institutions pay for them. Further information is available from:

<https://www.pharmakon.dk/apotek-primaersundhedssektor/forskning/international/>

### 4.8.4 Ireland

The Irish Pharmacy Union has highlighted the example of a New Medicine Service pilot, launched in 2017 (IPU, 2017) and addressing the conditions and medicines listed below.

Hypertension	Thiazides and related diuretics Beta-adrenergic blockers Vasodilator antihypertensives Centrally acting antihypertensives Alpha-adrenoceptor blockers Drugs affecting the renin-angiotensin system Calcium-channel blockers
Antiplatelet/anticoagulant therapy	Oral anticoagulants Antiplatelet drugs
Asthma and COPD	Adrenoceptor agonists Antimuscarinic bronchodilators Theophylline Compound bronchodilator preparations Corticosteroids Cromoglycate and related drugs Leukotriene receptor agonists Phosphodiesterase type 4 inhibitors
Type 2 diabetes mellitus	Insulins (short-, intermediate- and long-acting) Antidiabetic drugs
Chronic pain	Gabapentinoid agents (pregabalin, gabapentin) Tricyclic antidepressants (amitriptyline, nortriptyline) Carbamazepine Duloxetine Opioids Topical lignocaine Topical capsaicin

The NMS is a structured, pharmacist-led intervention, delivered within the community pharmacy, consisting of advice and support on medicine-taking for a newly prescribed medicine for these specific chronic disease

states, delivered within two weeks of commencing the medicine. It was first commissioned in England by the National Health Service in 2011. A 2016 review of the English NMS showed a 10% improvement in adherence to new medicines in the intervention group compared with controls who received normal practice; adherence was defined as missing zero doses over the previous seven days, according to patient report at 10 weeks.<sup>6</sup>

In the Irish pilot programme, patients allocated to the NMS had two interventions: (i) a structured interview with a pharmacist seven to 14 days after a new medicine was first dispensed; and (ii) an assessment by the pharmacist of the new medicine, using the patient's medication record and the Proportion of Days Covered (PDC) scale.<sup>7</sup> The Irish pilot project yielded a 9% improvement in adherence, as measured using the PDC, and the intervention was well accepted by patients and pharmacists.<sup>8</sup>

#### 4.8.5 The Netherlands

The Royal Dutch Pharmacists Association (KNMP) identified two examples of national services to improve adherence: the Medication Monitoring and Optimisation programme and the Telephone Counselling service. A more comprehensive overview of evidence-based interventions is currently being prepared by the Netherlands Institute for Health Services Research (NIVEL) in close collaborations with the Netherlands Patient Federation, Sint Maartenskliniek Nijmegen, and the KNMP. This is due to be released in spring 2019.

##### Medication Monitoring and Optimisation Programme

The Medication Monitoring and Optimisation (MeMo) programme, which was introduced in 2010, specifically targets the elderly. It starts with structured, uniform counselling sessions for patients at the initiation of and follow-up for chronic therapies. This is followed by a continuous phase in which patients' adherence to medication is actively monitored on a monthly basis using standardised search algorithms applied to the pharmacy database. When an instance of discontinuation of a medicine is detected, tailored interventions are invoked to improve adherence and optimise pharmacotherapy.

For patients with osteoporosis, the MeMo programme was associated with a halving of the rate of discontinuation of bisphosphonate therapy after one year from 32% to 16%. For patients on lipid-lowering medicines, the rate of discontinuation after one year dropped from 26% to 14%. Results from the ongoing MeMo asthma/COPD programme promise improvements in therapy control and patients' quality of life, but are as yet unavailable.

The MeMo programme is run entirely by pharmacists, with no specific credentialing required. It is funded from regular dispensing fees.

##### Telephone Counselling Programme

The Telephone Counselling Programme consists of a structured telephone call to each patient seven to 21 days after a new prescription is dispensed. The aim is to improve adherence by providing patients with information, asking about their actual medication intake behaviour, and addressing practical barriers (e.g., side effects) and perceptual barriers (e.g., concerns about medication, or beliefs that they have low necessity).

An evaluation of the programme reported that its effectiveness varied with different classes of drugs. It produced improvements in adherence to renin-angiotensin system inhibitors, lipid-lowering drugs and bisphosphonates, but not in adherence to antidepressants.<sup>9</sup> The programme was run only on a local research basis.

#### 4.8.6 Singapore

Various initiatives that promote adherence and other components of quality medicines use were reported from Singapore. These are outlined below.

## Medication Management Service

The Medication Management Service comprises a face-to-face pharmacist interview with each patient, involving a comprehensive medication reconciliation and review. It particularly targets patients who obtain medicines from more than one doctor, take five or more long-term medicines, have a new and/or complex medication regimen, or have questions or problems with their medicines. The interview is designed to ascertain actual doses taken, any untreated symptoms and adverse drug reactions. Patients also receive education on disease and medication management. The medicines list is updated in the medical electronic database and a copy is given to the patient and his or her carer. If necessary, the information is discussed with prescribers.

The service has been provided since 2006. It is available in most pharmacies, polyclinics and departments of public health. It is not funded, but patients may be charged a fee. Pharmacists' training to provide the service takes place "in house", and includes the principles and management of chronic diseases.

A specialist Medication Management Service was introduced in Singapore General Hospital in 2012 to provide medication support for patients with chronic kidney disease and on dialysis, particularly those with drug-related problems. It involves teams comprising three nephrologists, a pharmacist, a renal care coordinator, a nurse clinician and clinical assistants. The pharmacist carries out a comprehensive medication review and provides counselling, and reports to the attending nephrologist with a reconciled medicines list and any recommendations to resolve drug-related problems. Participating pharmacists are specifically trained for this role, covering topics on haemodialysis, chronic kidney disease and its complications, and medication therapy management.<sup>10</sup>

## Aged Care Transition (ACTION) Programme, Medication Review Service

The ACTION programme, initiated by the Singapore Government to improve post-discharge outcomes of elderly patients, aims to facilitate patients' transition from hospital to their home, and to improve medicines use.

The programme includes a home-based medication review service. Pharmacists undertaking home-based reviews must have had at least one year of experience in the Medication Management Service. In addition, they must undergo a six-week training programme conducted by a pharmacist experienced in home-based medication reviews, and must conduct reviews under supervision before being allowed to work independently.<sup>11</sup>

### 4.8.7 Spain

Two initiatives from Spain, the AdherenciaMED Project and the Adhiérete programme, are outlined below.

#### AdherenciaMED Project

The AdherenciaMED Project aims to develop a comprehensive approach to improving adherence, including strategies and protocols for incorporation into daily pharmacy practice. It focuses on two aspects: (i) the specific training of pharmacists to give support and enhance high-quality interventions, and (ii) the design of a service that could be implemented in the community. It is directed at asthma, COPD and blood pressure control.

A pilot study has been conducted to evaluate the applicability of the programme and to assess the scale of its effects. Subsequently a six-month study began in September 2017 in six Spanish provinces. The outcomes of the study are awaited. If they are favourable, the programme will be extended to other health conditions and other parts of Spain.

## Adhiérete

The primary objective of the Adhiérete programme, which was conducted from 2013 to 2014, was to evaluate adherence to treatment in elderly chronic, poly-medicated, non-complying patients through pharmacy services. Secondary objectives included assessing the cost-effectiveness of the programme **and the patient's** quality of life, detecting drug-related problems and mitigating negative outcomes associated with medicines, assessing the efficacy and effectiveness of e-prescriptions, strengthening relationships between patients, doctors and pharmacists, and assessing the use of communication systems and new technologies in relation to adherence and the quality of prescriptions.

The programme included a randomised trial with 60 community pharmacies and 225 patients. Each community pharmacy recruited five patients, of whom two used personalised dosage systems to support adherence, two used a mobile application, and one used a personalised dose system with an alert. This showed significantly improved adherence to medication in the target group. Results included an increase in adherence to treatments from 35% to 76%, improvement in quality of life, a one-third reduction in drug-related problems, and high levels of patient satisfaction.

### 4.8.8 Switzerland

Four programmes were identified by pharmaSuisse: the polymedication check, begun in 2010; the pharmacy-filled weekly pill organiser, begun in 2004; the inter-professional programme for chronic conditions (SISCare), begun in 2011; and an electronic pill dispenser for polypharmacy (begun in 2014). None of the four programmes is specific to the elderly, but most beneficiaries are elderly.

#### Polymedication check

The polymedication check involves a “Type 2A” review (see section 3.6) in the taxonomy specified by Pharmaceutical Care Network Europe.<sup>12</sup> Eligible patients are those having at least four different medicines covered by health insurance over the previous three months. This review is based on medication history and patient information, and can be done if the patient is able to provide information. It covers both prescribed and over-the-counter medicines, exploring drug interactions, unusual dosages, adherence issues, drug-food interactions, effectiveness issues and side effects. The review is done in pharmacies exclusively by a pharmacist, and there is a maximum of two reviews per patient per year. Pharmacists are paid approximately EUR 40 for each review, and this is covered by Swiss basic health insurance.

#### Pharmacy-filled weekly pill organiser

Under the pharmacy-filled weekly pill organiser initiative, pharmacists prepare weekly pill boxes or blister packs for outpatients who have chronic conditions and who are taking at least three different medicines. The sole intent is to improve adherence. The initiative is not specifically for elderly patients. It can be initiated by **a medical doctor's prescription, or on a pharmacist's suggestion after a polymedication check.** In the latter case, reimbursement is limited to three months; at the end of this period, patients may ask their doctor for a prescription to continue. Pharmacists are paid approximately EUR 18 per week.

#### Inter-professional programme for chronic conditions (SISCare)

SISCare is intended to improve the safety and efficiency of medication regimens. It involves motivational interviewing, adherence monitoring and risk management. It covers HIV, multiple sclerosis, type 2 diabetes mellitus, the use of oral cancer drugs and the metabolic syndrome. SISCare is conducted by the organisation Sispha, a multidisciplinary collaboration of pharmacists and family doctors affiliated with Lausanne University Clinic. Its cost is covered by a dedicated fund from the Swiss basic health insurance.

## Electronic pill dispenser

The electronic pill dispenser is a novel electronic medication supply device designed to support older drug users with polypharmacy. It is also applied in the context of opioid-assisted treatment, substance-use disorders, HIV and psychiatric disorders.<sup>13</sup> The aim is to improve adherence and quality of life. An evaluation study is in progress. The initiative is funded by basic Swiss health insurance and from university funds.

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## 5 Effective pharmacy interventions

### 5.1 Implications of this review

Seven major implications emerge from this review.

First, non-adherence to medication is a persisting and widely recognised problem in the elderly, despite the introduction of many interventions to promote adherence. Non-adherence has a high cost in both human and economic terms.

Second, pharmacy has a prominent position in the sequence of events involved in the use of medicines, and has an essential role in promoting and monitoring adherence. Other than patients, none of the participants in this sequence of events contributes as much to them, or has such a comprehensive view. **Pharmacists' pivotal** contributions encompass education and counselling of patients and their carers, providing and often assembling dose administration aids, dispensing medicines, generating reminders to take medicines and to refill prescriptions, and following patients to identify and resolve difficulties with their use.

Third, despite its central position in the provision of medicines, pharmacy is somewhat isolated from the other health professions involved in the management of patients. There is, for example, little interaction between prescribers, who are usually medical practitioners, and pharmacists. This isolation, which reflects health system and funding structures as well as mutual professional perceptions of disparity, limits the scope of interventions that could improve adherence if the respective contributors were able to work together in a more integrated way.

Fourth, indicators for the measurement of adherence are used inconsistently, and definitions of thresholds of appropriate or acceptable levels of adherence vary. The inconsistencies do not conceal the fact that adherence is a problem in healthcare delivery, but they are sufficiently large to complicate the monitoring of adherence and the evaluation of interventions.

Fifth, there is a large body of descriptive, analytic and evaluative research on adherence. However, much of the research is parochial and, as discussed in section 5.2 below, heterogeneous with regard to research design and the definition and measurement of outcomes. Consequently, to date, relatively few analytic studies have evaluated interventions with sufficient clarity, consistency and rigour to generate valid and transferable conclusions. Several major, well-designed systematic reviews of interventions to improve adherence have been undertaken, but they invariably find too much heterogeneity to permit a confident consolidation of findings.

Sixth, although (following from the fifth point) strong evidence for the effectiveness of specific initiatives to promote adherence is scarce, such evidence as is available supports the following interventions:

- New medicine services, comprising education and counselling of patients by pharmacists when new medicines are dispensed, with follow-up face-to-face and telephone counselling sessions over the subsequent weeks.
- Review, education and counselling of patients and carers by pharmacists when continuing medicines are dispensed, with continuing reinforcement when the delivery of a dose requires a specific manoeuvre, particularly, for example, the use of inhaled medicines.
- The provision of dose administration aids that facilitate taking the correct dose at the correct time.
- Systems for reminding patients to take their medicines as prescribed.
- Simplification of medication regimens by managing polypharmacy and reducing the frequency of dosing.

Given the number of potential intervention points from diagnosis, through to dispensing, and taking of a medicine, it is perhaps not surprising that multiple interventions are often shown to have relatively greater effect than singular interventions.

Seventh, most of the points made above apply to patients of all ages, particularly adults. However, the elderly are large users of medicines and their medication regimens are often complex. The presence of cognitive decline adds to the challenge, and mild or early cognitive decline may be unnoticed by health professionals in brief encounters. Pharmacists should be given training and possibly other support so that they do not miss signs of cognitive decline in patients, and can take account of patients' impairments in their communications, advice and actions.

## 5.2 Methodological issues in evaluating interventions

### 5.2.1 Overview

Research on non-adherence and evaluation of interventions to optimise adherence are beset with methodological challenges. The problem of non-adherence is not new, the opportunities for interventions are legion and, as noted in section 5.1 and elsewhere in this report, the volume of research and evaluation that has been undertaken is large. However, despite this effort, relatively few definitive conclusions have emerged on what to do.

Adherence can be quite tightly monitored and managed within the context of a clinical trial of a newly introduced medicine (or a new indication for a medicine). In this situation, the medication regimen is defined in detailed protocols, resources and energy are available to apply the regimen rigorously, and participants are volunteers, often with enthusiasm to comply with the trial protocol.

However, maintaining rigour and validity in observational studies and clinical trials of interventional programmes (as distinct from drug trials) poses some particular difficulties. These arise from:

- The heterogeneity of potential research subjects and their health states, which gives rise to many potential confounding effects
- The selection of patients or participants for study, which often relies on those willing rather than those selected to participate, giving rise to potential selection biases, lack of external validity (transferability to other groups) and, in some situations, insufficient numbers of participants
- The heterogeneity of interventions, with index interventions often occurring among other concurrent or "background" interventions that might influence adherence, and that are not usually documented as potential confounders
- Imprecise or insufficiently detailed descriptions of interventions, making it impossible to identify components of interventions that account for any apparent effects, and further limiting the potential to transfer or generalise from any apparently successful interventions
- Lack of standardisation and imprecision in the measurement or classification of adherence, leading again to heterogeneity among studies.

### 5.2.2 Heterogeneity of potential research subjects

Older patients represent a broad cross-section of the community in terms of age, fitness and mobility, cognitive capacity and medicines use. Many of the studies cited in this report do not stratify or adjust for these characteristics, and do not necessarily examine their distribution across comparison groups. Given that the study populations are often relatively small, it is unlikely that the characteristics (whether recorded or not) are evenly distributed across comparison groups, even if randomised. This creates the conditions for potential confounding, with the consequent risk of distorting results and conclusions.

### 5.2.3 Selection of participants and selection bias

The selection of patients or participants is a critical element in both the planning and the execution of a piece of evaluative research. Many of the articles cited in this report provide insufficient information on patient selection or the allocation of individuals to comparison groups. Evaluation logic suggests that patients receiving an index intervention should be compared with those not receiving the intervention, or adherent patients should be compared with non-adherent patients. However, recruitment often relies on those willing rather than those selected to participate in a study. These factors give rise to selection bias and limit the external validity of the findings.

### 5.2.4 Heterogeneity of interventions

Many of the articles cited in this report also provide little significant detail on the interventions that they evaluated. Given that many of the interventions apparently comprised an index intervention as one of a number of concurrent activities that might influence adherence and that might vary between comparison groups, it was sometimes difficult to discern the exact nature of the intervention.

Indeed, in their systematic review, Nieuwlaat *et al*<sup>1</sup> noted that none of the reported interventions had common success factors. Complex interventions were generally compared with usual care rather than simple interventions. It was therefore difficult to attribute improvements in adherence and clinical outcomes to particular aspects of an intervention, and to work out how to transfer apparently successful interventions to other settings.

### 5.2.5 Lack of standardisation in the measurement or classification of adherence

Some studies classified patients' medicine-taking behaviour dichotomously as "adherent" or "non-adherent" in relation to a previously recognised threshold, while others used pre-defined indicators to create continuous variables, such as the "proportion of days covered" (PDC) based on the actual and predicted time intervals between prescription refills. Most clinical trials take a PDC of  $\geq 80\%$  as "adherent", but this is variable. The variability means that it can be difficult or impossible to present valid meta-analyses or even to combine findings from two or more studies informally.

The ascertainment of adherence is also heterogeneous across studies. Some studies rely on "direct" estimates, obtained by asking patients about their medication use, or by periodic "pill counts", or by the use of electronic dose administration aids that record the removal of a tablet or capsule from a package. Adherence can also be estimated indirectly by measuring levels of drugs or their metabolites in body fluids, or by measuring physiological phenomena (such as blood pressure in a patient taking antihypertensive medicines). Complex methods of measurement may be possible in research studies such as randomised efficacy trials of medicines, but they are mostly inappropriate in routine clinical practice. Of course, it is essential to assess the validity of an indirect measurement, and it is not always clear that a measured physiological variable is a valid indicator of adherence.

### 5.2.6 Possible methodological solutions

While some useful information has emerged from systematic reviews of interventions to improve adherence, the value of any systematic review depends on the validity and quality of the research that is reviewed. Systematic reviews published in recent years have consistently drawn attention to the methodological weaknesses of both controlled trials and observational studies evaluating these interventions, and all the systematic reviews have concluded that a meta-analysis is impossible because of heterogeneity.

From a methodological perspective, the strongest studies have been randomised controlled trials or observational studies conducted in circumscribed health systems that compile comprehensive data on enrolled patients. For reasons more to do with funding than with patient care, these systems have the capacity

to track patients through most or all of the sequence (see section 3.1) from presentation and diagnosis through dispensing to medicine use, including prescription refills. They can therefore generate reasonably consistent, reliable quantitative data on adherence.

In order to be able to monitor adherence and evaluate new and existing interventions, researchers should consider the following points:

- Specify interventions in detail, listing and describing all the component activities that are included.
- Describe the study sample of patients in detail, noting how the sample was selected, as well as inclusion and exclusion criteria.
- Provide data on response rates at the time of patient recruitment and subsequent follow-up or drop-out rates.
- Define adherence and, as far as possible, encourage researchers on medicines use and adherence to use a small set of indicators so that valid comparisons can be made between studies.
- Collect data on potential confounders such as comorbidities (especially cognitive status) and concurrent treatments, and/or stratify the study sample by such factors as age and sex.

While systematic reviews done to date have provided useful information, further systematic reviews are not warranted until a substantial body of research following the five points above has been published.

## 5.3 A formulation of interventions to improve adherence

The problem of adherence is an ancient one. *Decorum*, one of the works in the Hippocratic corpus dating from the first or second century AD, gives the following advice:

*Keep a watch . . . on the faults of the patients, which often make them lie about the taking of things prescribed. For through not taking disagreeable drinks, purgative or other, they sometimes die.*

After almost two millennia, Haynes *et al*<sup>2</sup> wrote that

*. . . increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.*

Further, Brown and Bussell<sup>3</sup> observed that

*The multifactorial nature of poor medication adherence implies that only a sustained, coordinated effort will ensure optimal medication adherence realisation of the full benefits of current therapies.*

The words “sustained”, “coordinated” and “effort” encapsulate the nature of the main interventions that are consistently or at least repeatedly found to be effective for elderly patients. The significant elements of these interventions are as follows:

- **Effective communication with the patient and carer by all members of the healthcare team.** Effective communication includes: (i) engaging the patient (and carer, where applicable) in the decision-making process about treatments and choices in medications; (ii) **assessing the patient’s** cognitive status and level of health literacy, and guiding the discussion to ensure that the patient can engage in this decision-making process; (iii) establishing and sustaining links between members of the healthcare team, especially doctors, nurses and pharmacists, so that pharmacists have access to all relevant clinical information; (iv) enabling pharmacy to fulfil its pivotal role in patient education and counselling on medicines and adherence, both to enhance understanding of the therapeutic plan and dispel any ill-founded concepts that might lead to intentional non-adherence; (v) making use of contemporary technology, notably mobile phones, for follow-up contacts with patients (or carers) to determine whether patients are taking their medicines correctly and whether there are any difficulties in taking them or with side effects; and (vi) implementing pharmacy-led services to support patients taking new medicines.

- **Making it as easy as possible for older patients to take their medicines correctly.** This entails: (i) keeping medication regimens as simple as possible from the outset; (ii) reviewing medication regimens (for example, by means of home medication reviews conducted by pharmacists) to identify and manage polypharmacy; (iii) providing dose administration aids that help patients (or carers) to take the right medicine in the right dose at the right time, and to keep track of what they have or have not taken; (iv) enabling family members to support the patient in adhering to his or her medication regimen; and (v) providing reminders, both to take medicines and to obtain and fill repeat prescriptions, both possibly triggered by systems that are activated by failure to take a medicine or failure to refill a prescription.
- **Sustaining the effort.** None of the interventions described above is self-sustaining, and adherence can only improve on an ongoing basis without continued input to the patient's needs by: (i) repeating the message whenever the opportunity arises (for example, when prescriptions are being refilled); (ii) repeatedly enquiring whether taking the medicine is causing any problems, and addressing any problems that emerge, preferably in consultation with the prescriber; and (iii) observing dose administration techniques on an ongoing regular basis, and making corrections where necessary (for example, with inhaler technique for patients with asthma or COPD).

As the experience of the past 2,000 years suggests, non-adherence is a persistent problem that no intervention will resolve entirely. Much can be done, however, to promote adherence and minimise non-adherence, thereby optimising therapeutic outcomes.

## 5.4 References

1. Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. The Cochrane Library, 2014; doi: 10.1002/14651858.CD000011.pub4.
2. Haynes RB, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews, 2008;(2):CD000011.
3. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clinic Proceedings 2011;86(4):304–14. doi: 10.4065/mcp.2010.0575.

## Appendix 1: Literature search

The literature search that formed the basis of this report used the following electronic databases, to which access was obtained through the University of Sydney Library:

- Cochrane Library (Database of Systematic Reviews)
- Embase
- Google Scholar
- PubMed – Medline  
Science Direct

The search terms employed are listed below.

### Pharmacist activities:

Adherence  
Adherence training  
Adherence education  
Adherence and elderly  
Adherence and carers and family  
Adherence and spouses/partners  
Pharmacists and adherence

### Adherence and specific disorders:

Adherence and high blood pressure  
Adherence and asthma  
Adherence and chronic obstructive pulmonary disease  
Adherence and inhalers  
Adherence and HIV  
Adherence and cancer drugs  
Adherence and oncology services  
Adherence and demented patients  
Adherence and psychiatric patients

### Adherence and specific activities or situations:

New Medicine Service  
New prescription  
Adherence and electronic devices  
Adherence and remote areas  
Adherence and community-based elderly

In addition to formal literature searching through databases, the references cited in each selected article were scanned, and additional references were thereby found. Ad hoc follow-up searching was also done through the Cochrane Library, Google Scholar and PubMed.

## Appendix 2. Survey form

The following survey template was sent to FIP member organisations. Its purpose was to obtain information about relevant initiatives in the member countries, and case studies. The information obtained is compiled and discussed in Chapter 4.

### National pharmacist interventions and programs to promote adherence to medications in the elderly

As you know, the FIP has commissioned us to prepare a report on pharmacist interventions and programs to promote adherence to medications in the elderly.

As we discussed at the Seoul conference in September, the report will contain information on major relevant initiatives in each country (some of these were discussed during the Seoul meeting).

We now invite you to provide information on examples of pharmacist interventions and programs to promote adherence in the elderly. We would be pleased to know of interventions that specifically target the elderly as well as well as interventions directed at broader age ranges including the elderly.

The headings below are a guide to the types of information that we are seeking.

We will compile responses into a section of the report. We will send a draft of this section to you for review before the whole draft report is submitted to the FIP Board.

We would be most grateful to receive your response by **3 January 2018**. Please e-mail it to Michael – [michael.frommer@sydney.edu.au](mailto:michael.frommer@sydney.edu.au).

Many thanks.

Parisa Aslani  
Tim Chen  
Michael Frommer

**Your name:**

**Your institution or agency and address:**

**Your e-mail address:**

**1. Please outline one or more major examples of pharmacist services or programs that promote adherence to medications in the elderly in your country.**

**2. For each of these examples, please answer the following:**

2.1 Is the initiative entirely focused on adherence, or is adherence one aspect of a broader set of interventions?

- A Focused exclusively on adherence
- B One aspect of a broader set of interventions

If B, please list the other areas at which the intervention is directed:

2.2 Is the initiative specific for a particular disease and/or health condition or group of diseases/health conditions, or is it non-specific?

- A Non-specific
- B Specific

If B, please indicate which disease(s) and/or or health conditions(s)

2.3 Is the initiative specific for a particular medicine or class of medicines, or does it apply to a wide range of types of medicines?

- A Non-specific
- B Specific

If B, please indicate which medicine(s)

2.4. Does the initiative specifically target the elderly, or is it directed at a broad range of age groups?

- A Specifically the elderly
- B Broad range of age groups

3. Please describe the initiative or program.

4. What are the intended outcomes of the initiative or program, and how are these outcomes evaluated?

5. Is the initiative or program delivered on a national scale, or at state/provincial level, or at regional/local level?

6. When did the initiative or program begin?

7. Has the initiative or program ended, or is it still being delivered actively? If it has ended, when did it end?

8. Is the initiative or program intended to be delivered on a continuous basis, or is it run intermittently or cyclically?

9. What is the name of the agency (or agencies) that deliver the initiative or program?

10. How is the initiative or program funded?

11. Is the initiative run exclusively by the pharmacy profession, or is it multidisciplinary? If multidisciplinary, what is the role of pharmacy?

12. How are pharmacists trained and credentialed to deliver the initiative or program?

13. Please list any publications, or reports in the public domain, describing or evaluating the initiative or publication.

14. Please list or attach any media stories that provide additional information.

Other comments or additional information:

*Thank you very much for providing information for the survey.*

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