iSIMPATHY

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Evaluation Report

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Interreg
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Foreword

Populations are ageing and many people over the age of 50 years live with multiple long-term conditions and as a result take multiple medications (otherwise known as polypharmacy). Medication is the single most common healthcare intervention and generates the third highest cost of health expenditure. Studies suggest up to 17% of all unplanned hospital admissions are attributable to medicines related harm.[a,b] The Patient Safety 2030 report suggested that this could be addressed by developing a holistic systematic approach that extends across the professional, cultural, technological and procedural boundaries.[c] Both the European Union (EU) and Organisation for Economic Co-operation and Development (OECD) have recognised the need to reduce harm associated with medication use.

In view of this evidence, the World Health Organisation (WHO) has recognised polypharmacy as a priority area of the third global patient safety challenge, Medication Without Harm.[d,e] Polypharmacy management needs a whole systems approach which optimises the care of people with multiple long-term conditions through maximising benefit of medicines, while reducing the risks of inappropriate polypharmacy.

The SIMPATHY (Stimulating Innovation Management of Polypharmacy and Adherence in The Elderly) consortium explored how healthcare management programmes could be implemented to improve medication safety and prevent patient harm by addressing the inappropriate use of multiple medications. Fundamental to these programmes is the principle that healthcare providers work in partnership with patients to enable shared decision-making regarding medication, which improves patient adherence and medicines related outcomes. The iSIMPATHY project built on this, recognising that the increase in multiple long-term conditions and associated polypharmacy is a problem through the years and not limited to the older person.

This report illustrates the effects of prioritising working together to address inappropriate medication use. Evidence is shared to inform the development of health policies to address the quality, economic and political environment which will support addressing inappropriate medication use over the coming years. Digital technology and Patient Reported Outcome Measures have been the innovations used in this project together with data indicators and multi-professional clinical teams across a range of healthcare settings.

First and foremost, the priority for polypharmacy management must be about the quality and safety of patient care. It is essentially done within the economic resources available and enabled by political support.

[a] Kongkaew C et al. Risk factors for hospital admissions associated with adverse drug events. Pharmacotherapy The Journal of Human Pharmacology and Drug Therapy, 2013; 33(8):827–37

[b] Osanlou R et al. Adverse drug reactions, multimorbidity and polypharmacy: A prospective analysis of one month of medical admissions. BMJ Open, 2022; 12(7), [e055551].

[c] Yu A, Flott K, Chainani N, Fontana G, Darzi A. Patient Safety 2030. London: NIHR Imperial Patient Safety Translational Research Centre; 2016.

[d] World Health Organisation. Medication Without Harm - Global Patient Safety Challenge on Medication Safety. World Health Organization, Geneva, 2017.

[e] Mair A. Medication Safety in Polypharmacy, Third Global Patient Safety Challenge. Rep., World Health Organisation., Geneva, 2019.

We commend the recommendations of this report and call for your support in tackling together the important issues in delivering appropriate management of polypharmacy for our populations.

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Mair A, Kirke C, Scott M, Michael N, Kanan Y, Law S, Scullin C, Fleming G, Hyder Skinner N, Kyle D. iSIMPATHY Evaluation Report, Edinburgh, iSIMPATHY Consortium; 2023.

Note on currency conversion rates: Currency conversions were calculated using xe.com and were correct as of 19/06/2023. https://www.xe.com/currencyconverter/convert/?Amount=1970&From=GBP&To=EUR

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1. Executive summary

Implementing Stimulating Innovation in the Management of Polypharmacy and Adherence Through the Years (iSIMPATHY) was a three-and-a-half-year European Union (EU) funded project and managed by the Special EU Programme Body in Northern Ireland, Scotland and the Republic of Ireland. The project aims were to ensure the most sustainable use of medicines for patients by training pharmacists and other healthcare professionals to deliver person-centred medicines reviews and embedding a shared decision-making approach to managing polypharmacy (the use of multiple medicines).

There are 8.6 million unplanned hospital admissions across Europe each year due to adverse drug events, of which approximately 50% are potentially preventable (Figure 2).

The iSIMPATHY project embedded a multidisciplinary collaborative approach to deliver pharmacist-led, person-centred medicines reviews using the 7-Steps methodology.

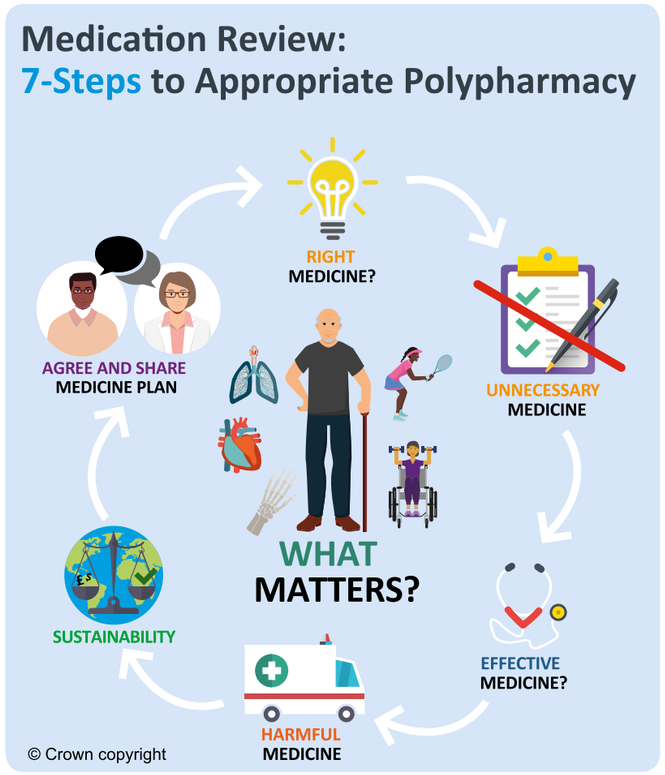


Figure 1: 7-Steps to appropriate polypharmacy, Scottish Polypharmacy Guidance, 2018.

In order to undertake the work, a project team of pharmacists were recruited, and a comprehensive bespoke training programme developed. This programme included the rationale for the 7-Steps approach, the importance of numbers needed to treat (NNT) in this context as well as change methodology and the psychology of interacting with patients. The project sought to evaluate the impact of reviews through assessing the levels of polypharmacy, medicines appropriateness, patient reported outcome measures (PROMs) and pharmacist interventions. This was complemented by qualitative studies with project pharmacists and managers and with a survey of multidisciplinary professionals working with project pharmacists. The project developed a person-centred version of the Medicines Appropriateness Index (PC-MAI), and pharmacist interventions were graded and classified according to the Eadon scale for clinical significance. Robust training and quality assurance (QA) processes standardised the approach across the project.

Reviews were carried out in different settings including hospital in-patient, out-patient and GP practice settings. A total of 6,481 patients participated in iSIMPATHY medicines reviews. The average age of patients reviewed was 72 years and 53% were female. An average of six long-term conditions were recorded per patient. The project pharmacists made an average of 11 interventions per review which included patient education, medicines reconciliation, medication changes and monitoring.

A number of key benefits were obtained by utilising the 7-Steps approach.

Interventions made were graded for clinical significance, with 82% being classified as clinically significant and 968 (4%) potentially preventing major organ failure, adverse drug reactions or incidents of similar clinical importance. Ninety-four per cent of interventions recommended were accepted. The average number of medications reduced from 12 to 11, with 92% of the reviews resulting in more appropriate medication use, therefore decreasing the likelihood of medication-related harm. Inappropriate medications were stopped (i.e. deprescribed), reduced or altered to improve appropriateness.

The changes in number of medications and improvement of appropriateness will minimise medication waste which is important to achieving both climate and sustainability strategies of the three jurisdictions. With respect to health inequalities, the criteria for review means that those from more deprived communities will benefit from reviews at younger ages due to a higher prevalence of multiple long-term conditions.

Patient experience was captured through Patient Reported Outcome Measures (PROMs). Patients reported large improvements in understanding, with over 90% of patients reporting post-review that they fully understood their medicines and potential problems with medicines, compared with 16% pre-review. Patients reported reduced side-effects, 64% pre-review, reducing to 38% post-review. Improvements were also reported in patients' ability to perform their usual activities and in some parameters of medicines adherence. Patients also reported decreased pain, discomfort, anxiety and/or depression following these reviews.

Many patients and carers were very appreciative of the opportunity to engage in reviews and very positive about the experience:

> **"No-one has ever sat down with me and taken time to go through all my medicines with me."**

> **"…huge improvement walked for half an hour this morning used to have to stop every few minutes because of the dizziness."**

Project pharmacists worked within multidisciplinary teams in the different practice settings, and also engaged closely with healthcare professionals across care settings, for example liaising with specialist teams and community pharmacists. All multidisciplinary team survey respondents would welcome continuation of the service provided during the iSIMPATHY project, with high levels of satisfaction

reported with iSIMPATHY and its effects on patients and healthcare professionals. Healthcare professionals felt more empowered in addressing medication-related harm and welcomed the collaborative working with multidisciplinary colleagues:

"ISIMPATHY is one of the most impactful changes in General Practice in 20 years." (GP, Ireland)

"We have definitely made significant changes to medications as a direct result of these reviews and advice." (Consultant, Scotland)

An analysis of the economic costs and benefits associated with polypharmacy reviews was undertaken as part of the iSIMPATHY project, with detail shown in Annex A. The analysis determined that, on average, 100 reviews:

- Cost £7,500 (€8,786) to deliver
- Result in £13,100 (€15,346) direct savings associated with medication changes
- Can be associated with £6,600 (€7,731) indirect savings from avoided adverse drug reaction-related hospital admissions (in-patient costs)
- Avoid an average of £168,800 (€197,800) in medical costs and are associated with a 7.4 Quality-Ajusted Life Year (QALY) gain, using Eadon intervention classification calculations

The total cost reduction from net medication changes alone would more than outweigh the staff cost for the Republic of Ireland and Scotland. With either the bottom-up or top-down approaches to economic analysis, the benefits (cost avoidance) would outweigh the associated direct cost in all three regions.

If comprehensive medicines reviews were provided to all patients aged over 65 years (over 75 years in Northern Ireland), taking five or more medicines in each country the maximum avoidable inpatient cost would be £24.7 million (€28.9 million) for Ireland; £11.0 million (€12.9 million) for Northern Ireland; and £36.0 million (€42.1 million) for Scotland.

The iSIMPATHY model has been demonstrated to be generally applicable in a range of healthcare settings and in different healthcare systems. There has been interest both at EU level and globally to adopt this methodology to address this public health challenge. [1,2] An implementation pack and accredited online training pack is available to facilitate and support scaling. Over the course of this project over 200 healthcare professionals have completed this training, online or in face-to-face sessions, with positive feedback.

This programme has delivered on its key objectives by improving patient outcomes, safety and individual engagement with their medication regimens by fully adopting a "what matters to me" person-centred approach, the 7-Steps process, the clinical guidance of the Scottish polypharmacy guidance and the change methodology as set out in SIMPATHY.

There are significant healthcare resource utilisation benefits as indicated by a positive return on investment of both medication and healthcare costs, together with patient reported improvements.

The approach is scalable by means of the tools and resources developed over the duration of the project and strong support for spread and scale up has been expressed by patients, project pharmacists, policy makers, healthcare professionals and managers.

iSIMPATHY: Impact of comprehensive person-centred medicines reviews

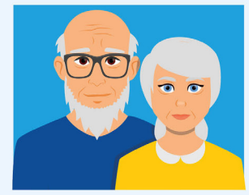
iSIMPATHY

iSIMPATHY embedded a multidisciplinary collaborative approach to deliver pharmacist-led, person-centred medicines reviews using the 7-Steps methodology.

8.6 million unplanned **hospital admissions** each year across Europe due to **adverse drug reactions**

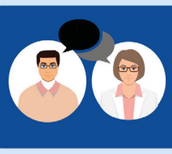
50% of **hospital admissions** due to adverse drug reactions are **preventable**

Over 6400 patients reviewed
- average age **72**
- **53%** female
- average **6** co-morbidities



Average **11 interventions** per review e.g. education, medicine reconciliation, drug changes, monitoring

iSIMPATHY's methodology can be applied across healthcare systems. An implementation pack and accredited online training is available.



"We have definitely made significant changes to medications as a direct result of these reviews and advice." (Consultant, Scotland)

Direct medicines cost savings per review of £131 and potential total of £1688 savings from avoided healthcare resource usage

82% of interventions rated clinically significant.
4% of interventions (968) potentially prevented major organ failure or adverse drug reactions of similar clinical importance

Medication Review:
7-Steps to Appropriate Polypharmacy

Appropriateness of medicine was improved in 92% of reviews

Average reduction of 1 medicine: 12 to 11

Better understanding of medicines, improved adherence and less harm reported in Patient Reported Outcome Measures (PROMs) and average 7.4 Quality-Adjusted Life Years (QALY) gained per 100 patients.

"Before my medication review, I suffered badly with heavy legs and wheezing… after just a few small changes to my tablets I'm now out walking for 30 minutes every morning." (Patient, Ireland)

Scottish Government Riaghaltas na h-Alba
NHS SCOTLAND
moic
HSC Northern Health and Social Care Trust
HSE
Interreg Northern Ireland - Ireland - Scotland
European Regional Development Fund
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2. Introduction and Background

2.1 Introduction

A recent systematic review concluded that preventable medication-related harm remains a frequent and enduring serious problem, causing severe or potentially life-threatening outcomes in over a quarter of all preventable harm cases.[3] Among these inpatient care settings, geriatric care, specialised care settings, intensive care and emergency departments constitute a particular risk.[4] A person-centred approach, to address patient needs, enable self-management and involving patients in decisions has been shown to address up to 15% of harm.[5] Public involvement is also important in changing policy[6] as well as nudge theory to support behaviour change, human factors, and change management for a scalable, sustainable solution to preventable medication-related harm due to inappropriate polypharmacy.

It has been estimated that the global population aged over 65 years will double from 8% in 2010 to 16% in 2050 due to advances in healthcare, education and socio-economic circumstance.[7] During this period, the number of people aged 80 years and above in developing countries is projected to increase by 250%, compared to 71% in developed countries.[8] The most common multiple long-term conditions are non-communicable diseases and will occur 10-15 years earlier in deprived areas than in areas that are more affluent.[9] In Europe, the over 80 years population will triple between 2008 and 2060.[10] However, evidence shows that the average healthy life years (HLY) for EU citizens in 2018 is only 64 years, meaning that many people are living for around twenty years in sub-optimal health. Healthy life years represent approximately 77% and 81% of the total life expectancy for women and men respectively.[11]

Multimorbidity is defined by the World Health Organization as the co-occurrence of two or more chronic medical conditions in one person.[12] Patients with multimorbidity may require medicines to treat each condition, which can lead to polypharmacy. Currently around 50 million EU citizens are estimated to have multimorbidity. Most of them are 65 years and over, and this number is expected to continue to increase.[13] In deprived communities, epidemiological data indicates that multimorbidity increases markedly with age. In a Scottish study, multimorbidity was prevalent in 81.5% of individuals aged 85 years and over, with a mean number of 3.62 morbidities.[14] Ornstein et al. found that the most prevalent chronic conditions in primary care were hypertension (33.5%), hyperlipidemia (33.0%), and depression (18.7%).[15] The presence of multimorbidity is associated with multiple symptoms, impairments and disabilities. This results in a combined negative effect on physical and mental health, which can affect a person's quality of life, limiting daily activities and reducing mobility.[16,17] The need to take multiple medications can be just as problematic, resulting in frequent health care contacts and an increase in the likelihood of medication-related harm.[18] The over 60 population consumes nearly three times more medicines than the general population, but with adherence to long term medication ranging between 25-70%.[19] Polypharmacy and multimorbidity are the two major predictors for experiencing medication-related harm in primary care[20] and among older adults in acute care,[21] with age also associated in the latter. Furthermore, it imposes a large economic burden due to patients' complexity of health care needs and frequent interaction with health services, which may be fragmented, ineffective and incomplete.[22]

The burden of multiple diseases can have a combined effect on physical health, the quality of day-to-day living and mental health. People with multiple long-term conditions utilise twice as much primary care services and are three times as likely to be hospitalised than those without multiple long-term conditions.[23,24]

2.1.1 What is polypharmacy and why is it important to address?

Polypharmacy is the concurrent use of two or more medications. While polypharmacy is often defined as routinely taking a minimum of five medicines,[25] it is being more frequently suggested that the emphasis should be on evidenced-based practice and whether the medicine is appropriate.[26,27] All medication that a patient is using should be considered including prescribed, traditional, herbal preparations and those purchased by the patient without a prescription.

Despite an increase in multimorbidity, most medical research, guidelines, and contractual agreements (such as pay-for-performance initiatives) are focused on the management of single disease states.[28,29] In these patients, individually treating each condition inevitably leads to the use of multiple medications (polypharmacy), the risks and benefits of which are largely unproven and often unpredictable.

It is important to note that polypharmacy is not inappropriate per se, and it is often beneficial as set out in the Scottish Polypharmacy Guide.[26] For example, effective secondary prevention of myocardial infarction requires the use of at least four different classes of drugs (antiplatelets, statins, angiotensin-converting enzyme inhibitors and beta blockers). However, polypharmacy becomes inappropriate when the risks of multiple medications begin to outweigh their potential benefits for the individual patient.

Therefore, appropriate polypharmacy should be considered at every point of initiation of a new treatment for the patient, and when the patient moves across different health care settings. However, the increased risk of harm is not always offset by increased benefits, and for many preventive medicines, such benefits may never be realised due to a shortened life expectancy. The risk of harm is generally higher in older people with multimorbidity than in younger patients due to their reduced ability to clear drugs (e.g. due to kidney and/or hepatic impairment) and increased vulnerability to adverse drug effects (e.g. due to general frailty, drug–drug and/or drug–disease interactions) and medication burden.[31,32,33] Many medications are also prescribed to address the side effects of other medicines and this is often referred to as the prescribing cascade.[34] In many instances this is inappropriate, and needs to be reviewed (e.g. diuretic prescribed for ankle oedema caused by use of amlodipine). It may be appropriate if it is specifically prescribed to prevent harm where a medication is needed, for example, where a proton pump inhibitor is given to prevent gastrointestinal (GI) bleed with non-steroidal anti-inflammatory medications where the use of an NSAID is necessary.

There is mounting evidence that polypharmacy is a public health threat and a major source of unnecessary harm, leading to greater use of health services, hospitalisation, reduced quality of life and substantial financial cost to health-care systems.[35] A study found that those admitted to hospital on potentially inappropriate medication had at least three subsequent readmissions.[36] The incidence of medication-related harm (MRH) associated with hospital readmission was found to be 78 per 1000 discharges with estimated costs to the National Health Service of £396 (€464) million annually, of which £243 (€285) million is potentially preventable.[37]

Studies suggest up to 17% of unplanned hospital admissions in the UK are attributable to medication-related harm and 50% of these are avoidable with 70% of these in elderly patients on multiple medicines. [38,30] If this was extrapolated across the EU, this would result in at least 8.6 million admissions each year (Figure 2). There are, therefore, significant opportunities to reduce this burden by timely and effective interventions.

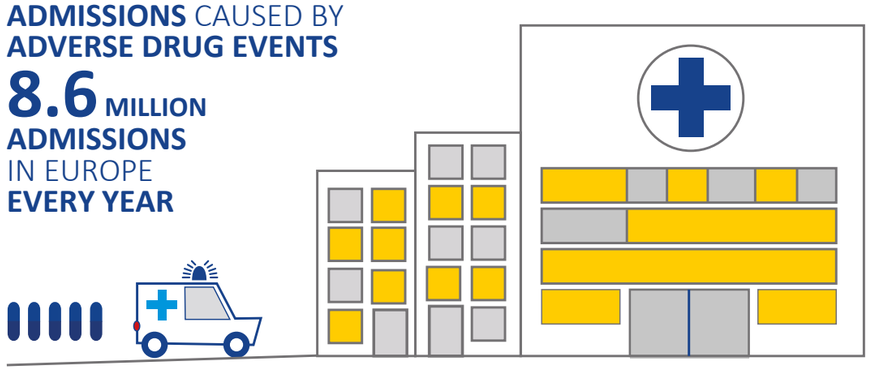


Figure 2: Unplanned admission to hospital in Europe each year due to ADR (produced with permission of SIMPATHY project, Mair et al 2017).

Every day, 750 older people living in the United States (age 65 and older) are hospitalised due to serious side effects from one or more medications.[39] Older people sought medical treatment or visited the emergency room more than 35 million times for adverse drug events, and there were more than 2 million hospital admissions for serious adverse drug events.[40] Over the next ten years, there will be at least 4.6 million hospitalisations of older Americans and 15 times as many outpatient visits for side effects from medications. Similar problems are seen in Canada[41] and the UK.[42]

In 2012, the US Institute for Healthcare Informatics estimated that inappropriate polypharmacy contributes to 4% of the avoidable costs of health care, equating to an expenditure of $18 billion worldwide, and one recommendation was to support pharmacist collaboration with physicians for medication reviews.[43] Similarly, in the UK, it was estimated that there are 237 million medication errors in England over a year long period,[42] and preventable adverse drug reactions were estimated to cost the National Health Service (NHS) £98.5 (€115) million per annum, consume 181,626 bed days, cause 712 deaths and contribute to 1708 deaths during initial hospitalisation.

In view of this evidence, the WHO has recognised polypharmacy as a priority area of the third global patient safety challenge, Medication Without Harm.[44,45] Polypharmacy management needs a whole systems approach which optimises the care of patients with multiple long-term conditions through maximising benefit of medicines, while reducing the risks of inappropriate polypharmacy.

2.1.2 Rationale for interventions used to address polypharmacy in iSIMPATHY

When undertaking a polypharmacy review, a recommended way to assess the appropriateness of a prescription is to take a holistic review of the medication in discussion with the patient or carer so that the patient's life priorities are considered and that an integrated care approach is taken.[46,47] It is important to consider which medications should be targeted and which populations would most benefit from review. Patients with the highest risk of inappropriate polypharmacy are those with the greatest frailty, on the most medicines, and taking high-risk medicines.[48] The most vulnerable patient groups include older patients above the age of 65 years and patients living in care homes, both of whom are susceptible to effects of drug–drug interactions, a higher risk of falls, adverse drug reactions, cognitive impairment, non-adherence, and poor nutritional status.[49,50,51,52] Certain medication classes, including benzodiazepines, antidepressants, antipsychotics, antihypertensives, opioids and diuretics, have been associated with an increased risk of falls, and practitioners should review appropriateness of continued treatment.[53]

When undertaking medication reviews to address polypharmacy, it is important to consider the risks and benefits of treatment in the context of the numbers needed to treat (NNT). Some countries have adopted or recommend a person-centred approach, such as the 7-Steps process in Scotland,[54] where NNTs are considered as part of the process, while other studies targeted addressing potentially inappropriate medicines using explicit tools such as Beers[55] or STOPP/START[56] criteria to identify medicines to target for review.

The EU funded SIMPATHY (Stimulating Innovation Management of Polypharmacy and Adherence in The Elderly) project, explored how healthcare management programmes can be implemented to improve management of polypharmacy across Europe. From the benchmarking exercise, SIMPATHY found that, with the exception of Scotland, there were no effective national programmes to address polypharmacy across the EU. These findings showed that some countries had some programmes run at institutional level or across a health region. Patients were found to want a review of their medication[57] and studies have found that they are willing to deprescribe if trust has been built between the prescriber and the patient.[58]

SIMPATHY identified six key recommendations that were important for institutions and countries to be able to implement programs to address polypharmacy and adherence.[59]

These were:

1. Use a systems approach that has multidisciplinary clinical and policy leadership
2. Nurture a culture that encourages and prioritises the safety and quality of prescribing
3. Ensure that patients are integral to the decisions made about their medicines and are empowered and supported to do so
4. Use data to drive change
5. Adopt an evidenced based approach with a bias towards action
6. Utilise, develop and share tools to support implementation

In NHS Scotland a person-centred programme was introduced for medication reviews to address inappropriate polypharmacy. This programme drew on work from indicators built on the findings of empirical research by Pirmohamed et al. (which identified a list of high-risk medications),[60] the pharmacist-led information technology intervention for medication errors (PINCER trial)[61] and the Data-Driven Quality Improvement in Primary Care (DQIP).[62]

Translation of learning from these safety prescribing programmes in Scotland was achieved by inclusion into national polypharmacy guidance,[63] and by adopting the key recommendations from SIMPATHY and using the 7-Steps process. It is supported by a suite of 69 indicators for the identification of patients most at risk and 17 indicators at a national level to show the improvements in reduction of medication-related harm as a result.[64] The 7-Steps approach starts by matching therapeutic objectives to current life priorities with the patient. This initial discussion guides decision-making in subsequent steps that consider medication need, effectiveness and safety before a therapeutic plan and follow-up strategy are agreed upon. Applying the 7-Steps as part of a holistic medication review has the potential to address all six dimensions of quality in health care: efficacy, safety, efficiency, timeliness, equity and acceptability.[65] The approach is designed to be applied at the point of medication review (to correct inappropriate prescribing) and when initiating new medicines (to prevent inappropriate prescribing). This may result in reducing the dose or stopping (deprescribing) a medication, but this should not be the primary objective of a medication review. Addressing unmet needs may include starting new medication.

iSIMPATHY was a €3.1 million European project funded in the EU INTERREG VA programme, managed by the Special EU Programme Body. Scottish Government, through Effective Prescribing and Therapeutics, was the lead partner, with delivery in Northern Ireland, Scotland and the Republic of Ireland over a period of three and a half years. The project implemented change management and tools developed in Scotland identified within a previous EU funded SIMPATHY project to ensure patient outcomes to medication are optimised, minimising patient harm.[66] With the patient at the centre and involved in the decision-making about their medication, the project aimed to develop new forms of data monitoring and systems modelling to inform a ‘health in all policies’ approach, with a specific focus on health inequalities to address inappropriate polypharmacy. To do this, the project delivered the person-centred 7-Steps polypharmacy review process described above.

2.2 Aims and objectives of the iSIMPATHY intervention

By 2023, the iSIMPATHY project aimed to have transformed the approach to optimisation of medicines in the three project jurisdictions through the delivery of medicine reviews to over 6,000 patients, and in delivering training to 200 GPs, hospital doctors, pharmacists and other healthcare professionals. It has provided a significant contribution towards the embedding of a single approach for appropriate polypharmacy management as well as firmly establishing the value of cross-border working in this field.

The project helped devolved regional and national governments identify opportunities for the strategic alignment of policies affecting key drivers of health and health inequalities across sectors and inform budget allocation decisions. iSIMPATHY has been developed on the basis of a specific understanding of partners' needs, evidence use and policy-making practices to co-produce new models and decision tools for the economic evaluation of health and non-health-sector strategies. This will allow policy makers to identify opportunities for synergistic action, for disinvestment, and to monitor evolving local contexts, including unanticipated changes, to help next-step decision making. The primary and secondary aims of the project are listed below:

Primary aims:

To assess the impact of comprehensive person-centred medication reviews using the 7-Steps methodology on:

- Appropriate polypharmacy
- Clinical interventions made as assessed by Eadon criteria (a tool that assesses clinical significance of the intervention)
- Prescribing appropriateness as assessed by PC-MAI and polypharmacy safety indicators
- Patient Reported Outcome Measures (PROMs)
- Healthcare economics

Secondary aims:

- To develop a training package for healthcare professional use
- To support the professional development of the participating pharmacists
- To assess the perception of the 7-Steps process by a range of healthcare professionals

2.3 Overview and project delivery

2.3.1 Funding and partners

The €3,112,034 budget was funded through the European Union's INTERREG VA Programme, with 85% awarded by the Special European Projects Body (SEUPB), and 15% provided by the project partners' Departments of Health.

iSIMPATHY was managed by corporate partners: the Scottish Government, the Health Service Executive, the Medicines Optimisation Innovation Centre and the SEUPB with delivery partners: NHS Ayrshire and Arran, NHS Highland, NHS Dumfries and Galloway (Scotland), Health Service Executive CHO 1 and CHO 8 (Community Health Organisations) (Republic of Ireland) and the Northern Health and Social Care Trust (Northern Ireland).

2.3.2 Overview of cross-border project interventions

Three new cross-border interventions were achieved by iSIMPATHY through the delivery of a whole-systems approach towards medicines reviews embedding the six key principles from SIMPATHY.

These were achieved by the development and sharing of tools, delivery within different settings, producing guidance to optimise results and influence implementation, and embedding the practice within multidisciplinary teams to ensure sustainable adoption post-project.

Cross-border working has been important in achieving this output. Each jurisdiction started at different stages of maturity in relation to adoption of structured polypharmacy medicines reviews.

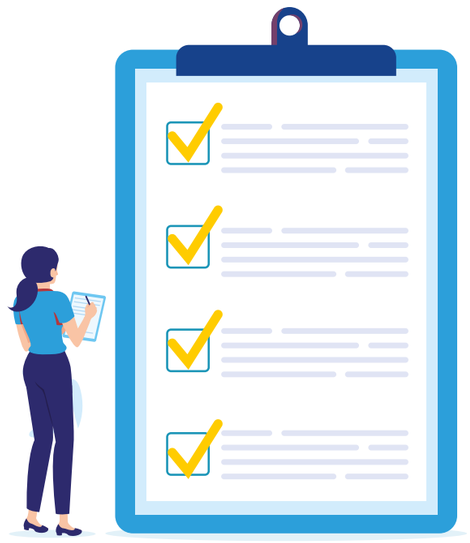
Scotland had already developed tools and processes to implement polypharmacy reviews in primary care. These include change management tools and the Polypharmacy Guidance and mobile app published in 2018. It also had a person-centred process to deliver the reviews, the 7-Steps review process, which places the patient at the centre of interventions. Scotland had also developed case finding indicators to support identification of patients at high risk of medicine harm. New to Scotland was delivery in outpatient and hospital settings which previously had not been able to implement this approach and required additional and focussed support from the project.

Scotland and Northern Ireland have been recognised as two of the leading regions in Europe with four-star reference site status for medicines management under the European Innovation Partnership for Active and Healthy Ageing. Northern Ireland developed the Medicines Optimisation Quality Framework (MOQF)[67] to support health and wellbeing through use of medicines. It supports quality improvement through the consistent delivery of recognised best practice and supports the development of new evidence based best practice. Delivery in the acute setting to date has concentrated on the admission and discharge phases of hospital stay. Unique to Northern Ireland is the use of Scottish tools including the 7-Steps tool during the inpatient phase of the patient's hospital stay.

In the Republic of Ireland (ROI) comprehensive medicines reviews were not systematically resourced or available in primary care prior to the project, outside of research and pilot project settings. Adding dedicated capacity and capability (clinical pharmacists) to the general practice team and delivering 7-Steps reviews with patients was novel to ROI.

Shared and developed tools that are integral to the new intervention

1. The 7-Steps process was adopted across Northern Ireland and the Republic of Ireland. Enabling a standardised holistic approach to the reviews supports implementation and effectiveness and keeps the patient at the centre to ensure that care is centred around what matters to them.
2. The Polypharmacy Guidance provides evidence-based recommendations to ensure effective use of medicines and helps identify individuals at risk of medicine related harm. The Scottish Polypharmacy Manage Medicines app provides accessible clinical guidance and practical tools for patients/ carers and prescribers. The pharmacists within the three areas used this to optimise decision making and enable best practice patient care.
3. Northern Ireland are experienced in the use of the Eadon scale, a tool to measure the impact of clinical interventions on patient care.[68] This is a scale ranging from one to six, where grades four or more indicate a significant intervention resulting in improved standards of patient care. This has been routinely used in Northern Ireland in a number of different settings, and the Northern Ireland team provided training and support to the project on the use and benefits of the tool.[69]
4. As a key enabler to collecting information directly from patients, PROMs were developed by Scottish Government in partnership with Glasgow University and Digital Health and Innovation (DHI). The reporting mechanism took the form of a patient and carer toolkit within the national polypharmacy web and mobile app.[70] The “Questions for my Review” section within this app comprises two sets of questions, designed to gather PROMs before and after a medicines review. These were improved during the project to capture quality of life measures so that QALY could be determined and support the economic analysis.
5. The Medicines Appropriateness Index (MAI) is an example of a tool improved by the project through cross border working. This tool has been widely used in work in Northern Ireland. During the pharmacist training phase, the tool was recognised as requiring updating, and the project team, including the pharmacists and MAI developer Prof Hanlon, improved the tool to ensure that it was person-centred. It has now been relaunched as the Person-Centred Medicines Appropriateness Index (PC-MAI) and is integral to the intervention.
6. Use of change management tools that were developed as part of the SIMPATHY project, specific for management of medication, and the six key recommendations.
7. A training programme for all healthcare professionals on the management of appropriate polypharmacy which has been accredited by the Royal College of Physicians (RCP UK). This can be delivered via e-learning or face to face, supported by a QA process to ensure those delivering the interventions are appropriately trained.



Delivery across different settings to support implementation and test change

The three jurisdictions delivered the medicines reviews within different settings using a standardised approach adapted to suit settings and the local landscape.

- The mix of primary and secondary care (including the outpatient setting) provided learning and support on how to optimise adoption of the guidance within each area.
- Examples of cross border collaboration and learning are:
    - In all clinical settings medical and pharmacy leadership is essential. For example, within GP practices it was important to have strong leadership to support the implementation and adoption. The work can be isolating in GP practices if not integrated within the multidisciplinary team locally.
    - Actively seeking expressions of interest from settings worked better than the service being imposed, which should be accompanied by clear messaging of the benefits and challenges.
    - Within secondary care settings patient engagement is different and needs consideration around the capacity of patients to consent. If they are in hospital, they are likely to need more time for the review and may have more complex needs.
    - Within the outpatient setting, patients were identified by doctors, nurses and healthcare professionals. There was the need for the healthcare professionals to proactively identify patients for review by the pharmacist.

The outcome of the cross border working to develop the evidence-based polypharmacy review interventions is a structured approach with a set of tools and guidance to support implementation at scale.

2.3.3 Project delivery overview

Although pharmacists were employed in all three regions to deliver the reviews, in each region, multidisciplinary teams were involved in the training and planning of implementation. In Scotland and Northern Ireland, the pharmacists were independent prescribers. Pharmacists do not have prescribing rights in Ireland, which meant that prescribing decisions needed to be actioned by a medical prescriber. The study was performed by 10.5 whole time equivalent pharmacists across three regions: Scotland, the Republic of Ireland and Northern Ireland. Scotland and the Republic of Ireland had multiple primary care sites from which patients were drawn, Northern Ireland and Scotland used secondary care sites, and Scotland also used outpatient sites. An additional secondary care site was added in Scotland from September 2022. The project took a change management approach, using KOTTER, PESTEL and SWOT to develop the new iSIMPATHY medication review service.

Patient selection:

The inclusion criteria for admission into the project was determined by whether the patient met one or more of the following criteria as outlined in the Scottish Polypharmacy guidance:

- Taking five or more regular medications (initially, 10 or more medicines, however this was reduced to broaden patient recruitment in some sites)
- Prescribed a high-risk medication
- Approaching the end of their life
- Aged 50 years and over and resident in a care home.

The 7-Steps review process (Figure 3) was applied and any recommendations were summarised and actioned, or presented to the patient's GP to assess and action.

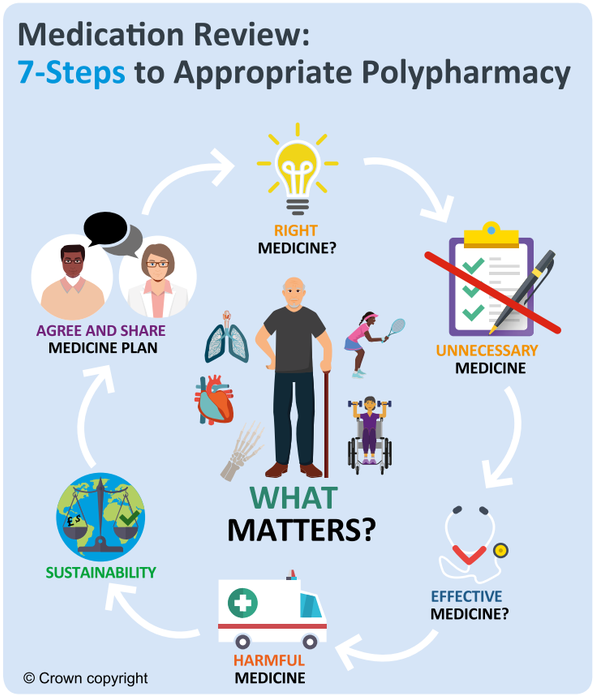


Figure 3: 7-Steps to appropriate polypharmacy, Scottish Polypharmacy Guidance

Pre-review preparation included confirming the medication history, laboratory results and searching relevant information, which was challenging at times and time-consuming. After the initial review, the pharmacist and patient had a follow up appointment, assessing how the changes were received, determining if any other interventions were needed and to address questions and concerns. Pharmacists often liaised with other healthcare professionals including specialist teams and community pharmacists as appropriate.

Scotland

iSIMPATHY medicines reviews in Scotland were delivered by NHS health boards from the SEUPB eligible areas. These were initially NHS Dumfries and Galloway and NHS Highland, then in year three of the project NHS Ayrshire and Arran replaced NHS Highland. In Scotland, reviews were undertaken in three settings: secondary care, out-patient clinics and primary care. As lead partner the Scottish Government had oversight and responsibility for delivery in Scotland, but the operationalisation of the delivery was delegated to the health board directors in line with how services are delivered in Scotland. Patients were identified based on the selection criteria in the Scottish Polypharmacy Guidance 2018.

Republic of Ireland

iSIMPATHY medicines reviews in the Republic of Ireland were carried out in Primary Care. Four pharmacists (3.5 wte) joined one or more general practices across 11 sites in Community Healthcare Organisations (CHO) 1 and 8 (Counties Donegal, Sligo, Leitrim, Cavan, Monaghan and Louth). An additional pharmacist joined the project in the final months. Practices were invited to submit an expression of interest and selected based on the size of the patient population.

The pharmacists worked in the practice and/or remotely, with most reviews being provided via telephone. This was initially due to COVID-19 restrictions and later patient preference, with face-to-face reviews also offered once restrictions had eased. Reviews were provided to practice patients resident in the community and in nursing homes, however limited data was analysed from the latter group due to lack of capacity to consent to data processing. Patients were selected by the pharmacist through running reports and searches, e.g. for numbers of medicines prescribed, presence of particular polypharmacy indicators, or by referral from the GP.

Northern Ireland

iSIMPATHY medicines reviews in Northern Ireland were carried out in the Northern Health and Social Care Trust (NHSCT) catchment area in the acute inpatient hospital setting. The team were largely based on acute wards and selected patients for review. Patients were also referred to the service by nursing, medical and pharmacy staff.

2.3.4 Development of PC-MAI

The Medication Appropriateness Index (MAI) instrument is intended to assess the appropriateness of medications prescribed by a health care provider. To appropriately apply the MAI, both a list of medical problems and medications is required. Medication history information obtained from patients may also be helpful. The original tool assesses the effectiveness of the medication for the patient based on recommendations at a population level, e.g. is it indicated for hypertension in general. In the 7-Steps person-centred methodology, the reviewer is asked to consider whether the medication will benefit the individual patient, thereby adopting a person-centred approach, therefore a Person-Centred MAI, PC-MAI. This is applied with clinical judgment and always with regard to patient preference and life expectancy.

As a result, in collaboration with Professor Hanlon (who developed the original MAI tool),[71] the MAI tool was adapted to develop the Person-Centred MAI, (PC-MAI). Question 2 was modified to get the reviewer to consider individual level benefits and also to review "when required medication." Additional training was provided with worked case examples on the PC-MAI before the reviewers were asked to undertake a quality assurance process with their scoring. The table below shows the questions used as part of the review where each question is given a score, which is then aggregated to provide an overall score. A higher PC-MAI score indicates less appropriate prescribing and/or a low score indicates more appropriate prescribing.

Table 1: Person-Centred Medicines Appropriateness Index (PC-MAI)

Person-Centred Medicines Appropriateness Index (PC-MAI)	Score
Is there an indication for the drug?	
Is the medication effective for the condition in this individual?	
Is the dosage correct?	
Are the directions practical?	
Are there clinically significant drug-drug interactions?	
Are there clinically significant drug-disease/condition interactions?	
Is there unnecessary duplication with other drug(s)?	
Is the duration of therapy acceptable?	
Overall Score	

In order to provide the assurance that each of the reviewers were able to score in a consistent manner using the tools, a similar methodology was used as in the original MAI development. Twenty cases were given to the medication reviewers. They were bench marked against the "gold standard" which was peer reviewed for any discrepancies by an expert clinical team.

2.3.5 Development of Patient Reported Outcome Measures

As a key enabler to collecting information directly from patients, PROMs were developed by Scottish Government in partnership with Digital Health and Innovation (DHI) and the University of Glasgow. The reporting mechanism took the form of a patient and carer toolkit within the national polypharmacy web and mobile app.[70] The "Questions for my Review" section within this app comprises two sets of questions, designed to gather Patient Reported Outcome Measures before and after medicines review.

These questions have been developed through:

- A research study funded by Scottish Government which synthesised existing published evidence on PROMs relevant to polypharmacy, followed by consultation with patients, carers and professionals on key requirements for polypharmacy PROMs.[72]
- A series of patient and professional workshops facilitated by DHI to draft and review questions that would reflect the themes and priorities identified in the research study.
- Incorporation of the EQ-5D-3L instrument to describe and value health status. This will support economic analysis of impact of medicines review on QALYs.[73]

The questionnaires could be completed in four ways:

1. By a patient, who then submits their answers by email to their healthcare professional to provide a person-centred focus to the medicines review.
2. In collaboration by a patient and carer.
3. By a healthcare professional (e.g. practice pharmacist, GP, hospital clinician) asking the patient the questions and filling in the answers on their behalf.
4. By non-clinically trained staff (e.g. community connectors, link workers, care home and care at home workers), supporting the patient to complete the questionnaires.

The completed questionnaires were emailed to the healthcare professional as a record and to provide a person-centred focus for shared decision-making within the medicines review.

2.3.6 Project specific training

A comprehensive training programme was put in place for the project pharmacists covering all requisite aspects including use of specific tools that were required for the project evaluation component.

A multidisciplinary team was put in place to deliver the necessary training plan including pharmacists, doctors and clinical psychologists. A series of five training sessions were held with the key elements and learning outcomes that were entailed described below:

Session	Content
1	What is polypharmacy and why it needs to be addressed; the WHO Medication 'Without Harm Global Patient Safety Challenge'; an introduction to change methodology; the objectives of the project including the context and differences regarding the three jurisdictions.
2	iSIMPATHY methodology based on the key recommendations of SIMPATHY. More detail on change methodology was introduced as well as the Scottish Polypharmacy Guidance and the 7-Steps review process. Worked case study examples were presented to provide practical illustrations and guidance on applying the concepts and tools discussed. Information was also provided on PROMs and the accompanying app, including a demonstration of the app in use and its integration into clinical practice.
3	Effective person-centred consultation, remote consultation skills, triage tips, video consultations, motivational interviewing.
4	Training on the key tools to be used in the project, PC-MAI and the Eadon intervention scale. Training was provided on all the relevant data sets to be collected, including data governance to ensure that a robust comprehensive evaluation could be undertaken.
5	The final session emphasised the significance of change methodology and identifying the factors that facilitate or hinder its implementation in clinical practice. This is essential to change the patient safety culture in practice. Subsequently, project pharmacists presented their findings and insights to the group, fostering peer-to-peer learning and encouraging further discussion.

2.3.7 Development of healthcare professionals e-learning training

In order to equip healthcare professionals including doctors, nurses and pharmacists to undertake comprehensive person-centred medication reviews, a polypharmacy training course was developed, accredited by the Royal College of Physicians (United Kingdom) for three external CPD credits (code 138908). Successful completion of each module's multiple-choice questionnaires will result in a printable certificate including 1 point. The training can be accessed through NHS Education for Scotland at **https://learn.nes.nhs.scot/59670**. The training comprises of three 45 minutes online modules followed by a range of webinars and additional content including pre-module reading.

It focuses on highlighting the public health challenge of polypharmacy, and the urgency to address it to prevent medication-related harm and hospital admissions. The process is a person-centred approach to review appropriate use of medication using the 7-Steps process where shared decision-making is paramount and centred around "What matters to the patient?" and the effective use of medicines.

Module	Content
1. Why should we address polypharmacy?	• Definition and dangers of polypharmacy • Medication adherence • Adverse drug reactions • Criteria for selection for polypharmacy reviews • Short introduction to the 7-Steps medication review process
2. 7-Steps methodology	• The 7-Steps medication review process • Numbers needed to treat (NNTs) • The 7-Steps review process in practice • High risk medicines combinations
3. Change methodology and numbers needed to treat (NNTs)	• Implementing change methodology • Case study example of the 7-Steps in practice • Understanding NNTs

The training modules were developed using the original training provided to the project pharmacists alongside a small multidisciplinary working group. The modules went through a pilot phase with feedback being incorporated into final release.

A polypharmacy medication review workshop was developed for undergraduate pharmacy students based on the 7-Steps model. This was delivered to all final year pharmacy students at both Northern Ireland universities. Feedback from both universities was very positive.

Training sessions were also delivered face-to-face to healthcare professionals in Ireland and in Scotland, following the training modules and assessment as in the online training model.

Shared learning model

A shared learning model was developed as a vehicle to provide ongoing peer support and upskill the pharmacists and healthcare professionals (HCPs) as they progressed through the project utilising case studies for interactive learning. The model had four components: education (delivered by a clinical expert), case presentation, case-based discussion and addressing project challenges/solutions and was delivered in collaboration with Project ECHO NI at monthly virtual sessions, each of 90 minutes duration. Resources were uploaded on Moodle for access retrospectively. The collaborative model was facilitated to provide a safe, supportive space to learn and share where all participants were both teachers and learners. The project team participated in curriculum development to agree topics for the education component. Participants were surveyed at the end of both years one and two to evaluate the model.

2.3.8 Quality Assurance process

In order to achieve robust results a quality assurance (QA) process was designed for the Eadon Intervention Scale and the PC-MAI to ensure the consistent application by the iSIMPATHY pharmacists. Following extensive training the pharmacists independently applied both tools to training cases as described in Figure 4 for the training and case validation phases of the project.

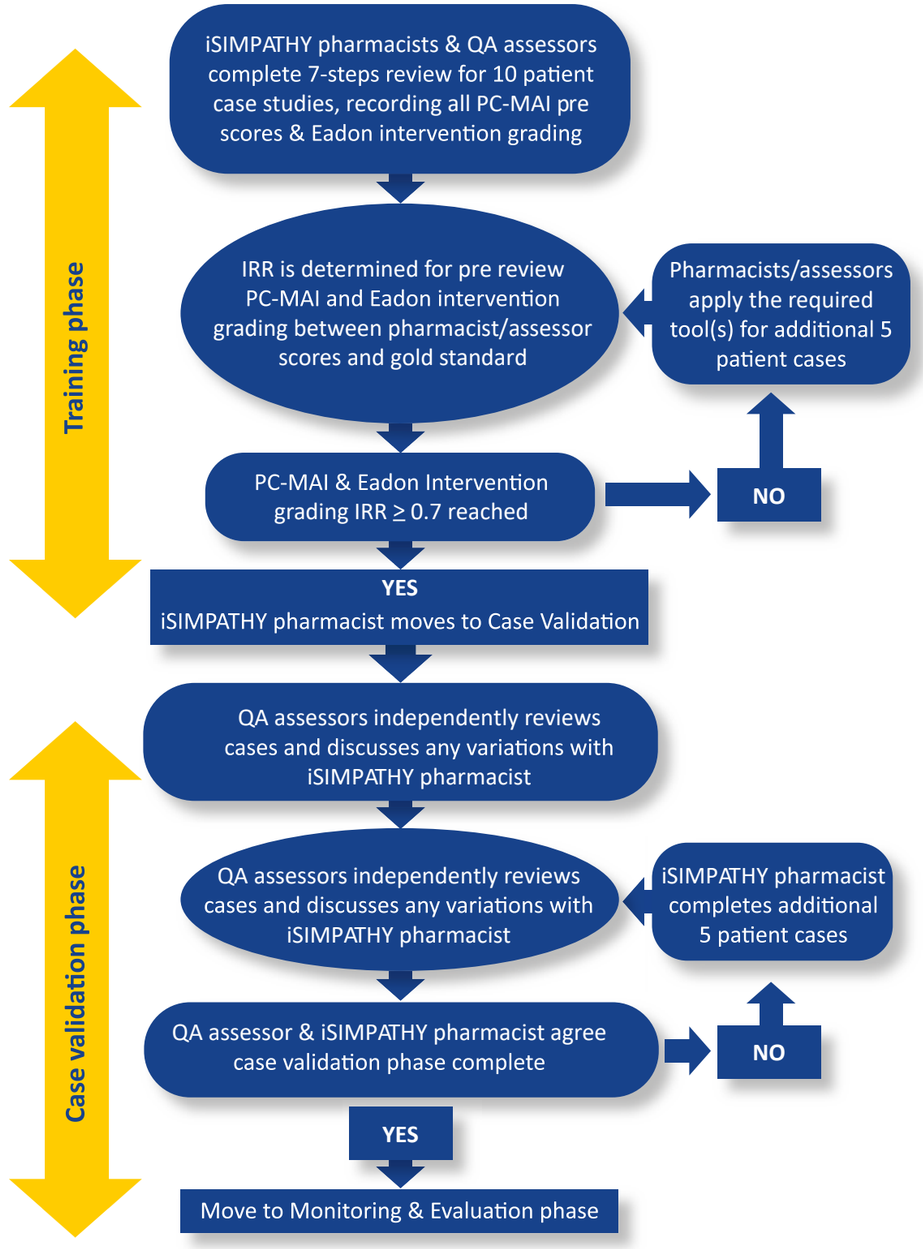


Figure 4: The iSIMPATHY quality assurance process for medication reviewers

On successful completion of the case validation phase, the QA process moved on to the monitoring and evaluation phase of the project. This involved the iSIMPATHY pharmacists providing a full description of Eadon and PC-MAI for 10% of cases. Fifty per cent of these cases underwent QA by the QA assessor who determined the PC-MAI and Eadon scoring independently. Any differences were discussed, and final scores agreed. If wide variation in scoring was identified, relevant pharmacists were supported through further training/mentoring and case discussion as outlined in Figure 5.

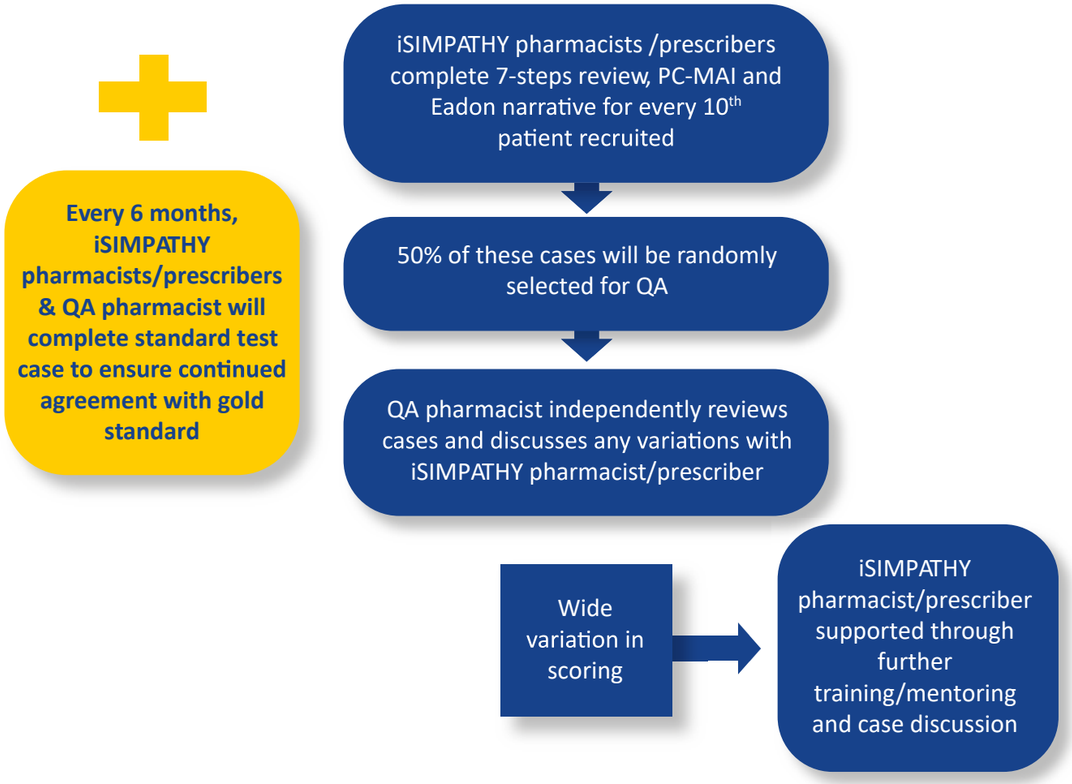


Figure 5: iSIMPATHY quality assurance process (monitoring and evaluation phase)

Inter-rater reliability

In order to provide the assurance that each of the reviewers was able to score in a consistent manner using the tools, a similar methodology was used as in the original MAI development. Twenty cases were given to the medication reviewers.

Gwet's agreement coefficient was used to assess the inter-rater reliability of the project pharmacists rating of MAI and Eadon on the reviews undertaken. Comparisons were made between the project pharmacists as a cohort, and between each pharmacist and a 'benchmark' rating that was derived through consensus between two expert pharmacists and verified by a peer review group of a GP, consultant geriatrician and clinical pharmacist.

The summary PC-MAI statistics (aggregated score for each question for each individual drug) were determined to be problematic in regards to establishing the inter-rater reliability of the cohort. As such the individual questions that make up the index were compared instead. In addition, in order to increase the sensitivity of the coding, 'A' and 'B' responses were treated as separate ratings on a continuum, rather than grouped together as was done in the original MAI studies (where A and B responses were treated as the same response). The results of this new analysis suggested that 5 of the 17 pharmacists had scores that were below the predetermined acceptability threshold of 70% agreement with the benchmark using simple percent agreement, and 1 coder had a score below the acceptable level of reliability against the benchmark using Gwet AC ordinal scale. Gwet AC ordinal scales were higher than simple percent agreement, as Gwet allows for partial agreement to be considered in the comparison (i.e. A is closer to B than A is to C).

Pharmacists appeared to perform better on the Eadon grading in regard to agreement, where only 1 coder out of 15 was below the acceptable agreement threshold against the benchmark using simple percent agreement. However 2 out of 15 pharmacists were below the reliability threshold against the benchmark using Gwet AC. Eadon was calculated using categorical scales.

Additional support was provided for individuals scoring outside the acceptable threshold to improve reliability. On reassessment, all pharmacists scored within the acceptable threshold.

Analysis of the cohort as a whole suggested acceptable levels of reliability between pharmacists (Gwet 0.78 for raw PC-MAI scores, and 0.77 for Eadon grading). These results suggest a sufficiently similar approach to the coding of medicines/interventions across the tools.

3. Methodology

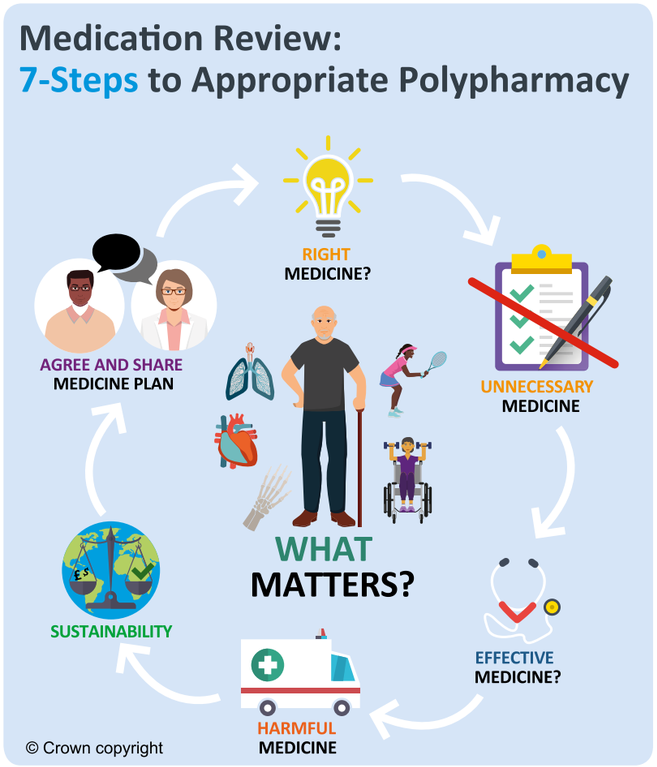


Figure 6: 7-Steps to appropriate polypharmacy, Scottish Polypharmacy Guidance

3.1 Data collection

3.1.1 Core data set from 7-Steps medication reviews

Reviews were undertaken using the 7-Steps review process outlined in Figure 6. From these reviews, data was collected on the outcomes of the review to enable evaluation.

Pharmacists recorded the outcomes of the review and demographic information about the patients using the specification laid out in the minimum core dataset. In addition, approximately 10% of patients had a full drug list recorded and were assessed using the PC-MAI. Information relating to clinical interventions were recorded and graded according to the Eadon criteria. Detail of the dataset can be found in Annex C.

3.1.2 Survey

A mixed methods survey was sent to healthcare professionals who worked directly or indirectly with the iSIMPATHY project pharmacists. Respondents were asked to answer 27 evaluation questions relating to the project as well as two demographic questions in order to ascertain their location and profession. The questions were primarily closed 5-point Likert scale questions, with a few open-ended questions. The survey was created in Questback and was forwarded via project pharmacists and leads to relevant individuals.

3.1.3 Interviews

Semi-structured, in-depth interviews were utilised with pharmacists directly involved in delivering medication reviews. These interviews were conducted digitally through Microsoft Teams, and with a duration of approximately an hour. The interviews were based on a semi-structured interview guide. The interview guide served the purpose of exploring a number of relevant topics in a more systematic and comprehensive way, as well as to keep the multiple interviewers focused on the desired line of questioning in a consistent fashion. The questions in the interview guide were comprised of the core evaluation questions and many associated questions related to the central questions. In order to have the interview data captured more effectively, recording of the interviews was considered an appropriate choice. Interviews were recorded and a “verbatim transcript” of the interview was produced to allow for analysis.

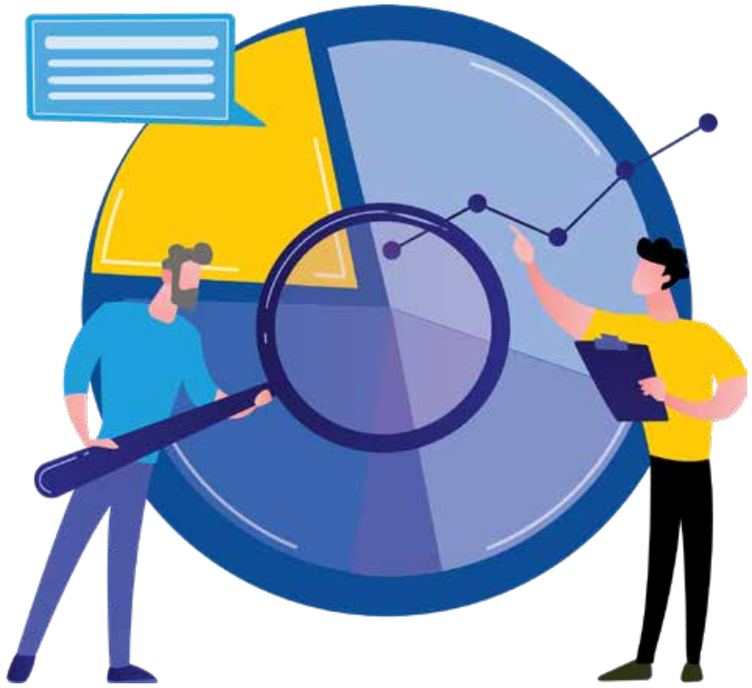
3.1.4 Focus groups

A similar approach was taken with the focus groups. The focus groups were conducted with participants who were more involved in the implementation of iSIMPATHY but did not conduct the medication reviews themselves. Participants were primarily involved in the logistical aspects of the programme’s roll out, operations and management. In these focus groups, participants were interviewed in a discussion setting with semi-structured topic guides in the presence of the session moderator. These discussions lasted around one hour.

3.2 Analysis

Data from the minimum core dataset, as well as data on clinical interventions and their grading were downloaded into Microsoft Excel (Office 365) as well as Statistical Package for the Social Sciences (SPSS 27) for analysis. Descriptive statistics were provided for the data from the minimum core dataset. Continuous data were plotted, explored and tested for normality of distribution. Dependent upon this, a t-test, Mann-Whitney U (unpaired data) or Wilcoxon signed ranks test (paired data) was applied to the data if comparisons between or within groups were required (results were considered significant when the 2-tailed p value was ≤0.05). For group comparisons of 3 or more, an Analysis of Variance (ANOVA) was conducted for normally distributed data and a Kruskal-Wallis test was conducted for non-normally distributed data (results were considered significant when the 2-tailed p value was ≤0.05). Multiple hierarchical linear regressions were conducted, the data was first entered using a backwards stepwise method. Variables that were found to be redundant were removed. The remaining variables were then re-entered using a blockwise entry, with steps being determined by the variable's theoretical justification and/or their contribution to the previous backwards model. The variables were tested for the assumptions of a multiple linear regression. Many variables were found to deviate significantly from linearity, thereby limiting the ability of the results to be generalised beyond the participants directly included within the sample to a wider population.

A deductive thematic analysis approach was taken to the coding and interpretation of the results of the interviews and focus groups. Thematic analysis allowed for the identification of patterns of experiences and attitudes across the participating cohort that could be drawn into the evaluation of the project.



4. Results

- 6,481 patients participated in medicines reviews over the lifetime of the project.
- Data submitted by 13 pharmacists (4 Republic of Ireland, 5 Scotland, 4 Northern Ireland) was analysed relating to the 4,933 reviews (N) completed with full data recorded up to January 2023.
- 3,210 patients consented to their data being used within the evaluation.

4.1 Demographic analysis

- N=4,933
- Age: 72 (mean); 74 (median) (Range 6-101) Number of patients: 3,207
- Gender: Male: 47% (n=2,305). Female: 53% (n=2,614) Number of patients: 4,919

Table 2: Analysis of multimorbidity, interventions and medicines per patient

	Mean
Number of multiple long-term conditions per patient (n=3,193)	5.8
Interventions per patient (including 2 standard interventions) (n=3,192)	10.9
Medicines per patient before review (n=3,192)	11.9
Medicines per patient after review (n=3,191)	11.0

Primary indication for review recorded (n=3,210)

- 3,179 (99%) receiving 5 or more regular medicines
- 130 (4%) approaching end of life
- 1,110 (35%) receiving high risk medicines
- 86 (3%) over 50 years and resident in a care home setting

The data was then analysed by considering socio-economic status and gender for the reviews undertaken across all three regions and then broken down by region.

4.1.1 Socio-economic status

Table 3: Analysis by socio-economic status (n=3,190)

	Socio-economic				
Mean	**Most deprived (n=739)**	**Average (n=2,082)**	**Least deprived (n=369)**	**Mean of study total**	
Age	71.7	72.3	74.2	72.4	Significant difference p<0.001
Number of multiple long-term conditions	6.0	5.7	6.0	5.8	Non-significant difference p=0.85
Number of interventions (including 2 standard interventions)	11.0	11.1	9.5	10.9	Significant difference p<0.001
Number of medicines pre-review	12.4	11.8	11.7	11.9	Significant difference p<0.01
Number of medicines post-review	11.4	10.8	11.2	11.0	Significant difference p<0.001
Pre PC-MAI patient (n=375)	20.4	21.2	16.23	20.4	Non-significant difference p=0.106
Post PC-MAI patient (n=366)	7.9	7.0	3.8	6.8	Significant difference p<0.01

Socio-economic status was not found to be interacting with pre-review PC-MAI scores across the patient groups, suggesting that socio-economic status was not leading to systematic differences in the inappropriateness of the medication the patients were on pre-review. However, there were differences found between the least deprived group and the average group ($p<0.05$). Caution is advised when interpreting these results due to the low sample size of the least deprived group that had a recorded PC-MAI score (n=48).

A significant difference was found for the post-review PC-MAI score ($p<0.01$) suggesting that socio-economic status was interacting with the inappropriateness of the patients' medication post-review, a breakdown of the results by group show that the most and average groups deprivation groups were not significantly different from each other post-review. However the least deprived group was significantly different from both ($p<0.01$) suggesting that although the inappropriateness of the medication the patients were receiving was comparable pre-review, the least deprived group had lower inappropriate prescribing than the other two groups post-review. This indicates that although all groups had a reduction in inappropriate prescribing post-review, the least deprived socio-economic group benefited the most from the process. Once again caution is advised when interpreting these results due to the low sample size of the least deprived group.

4.1.2 Analysis by gender

Table 4: Analysis by gender (n=3,210)

Mean	**Male (n=1,519)**	**Female (n=1,691)**	**Mean of study total**	**Notes**
Age	71.1	73.4	72.4	Significant difference p<0.001
Number of multiple long-term conditions	5.7	6.0	5.8	Significant difference p<0.01
Number of interventions (including 2 standard interventions)	10.6	11.1	10.9	Significant difference p<0.01
Number of medicines pre-review	11.5	12.3	11.9	Significant difference p<0.01
Number of medicines after-review	10.6	11.3	11.0	Significant difference p<0.01
Pre PC-MAI patient (n=375)	19.4	21.1	20.4	Non-significant difference p=0.568
Post PC-MAI patient (n=366)	6.4	7.1	6.8	Non-significant difference p=0.173

Female recipients of reviews were older, had more multimorbidity, and were taking higher numbers of medicines pre-review than males. Females received more interventions, a similar reduction in medicines and remained on more medicines post-review. Appropriateness was similar in males and females pre- and post-review.

4.1.3 Region

Table 5: Analysis of patient data by region (n=3,210)

	Region				Notes
	ROI (n=1,915)	NI (n=614)	SCT (n=681)	Mean of study total	
Age (Mean)	74.5	72.1	66.7	72.4	Significant difference p<0.001
Gender					
Female	53%	58%	46%	53%	
Male	47%	42%	54%	47%	
Deprivation status					
Most deprived	21%	24%	29%	23%	
Average	73%	40%	66%	65%	
Least deprived	6%	36%	5%	12%	
Multiple long-term conditions (mean)	5.7	6.2	5.9	5.8	Significant difference p<0.001
Number of interventions (mean) (including 2 standard interventions)	11.4	9.6	10.6	10.9	Significant difference p<0.001
Number of medicines pre-review (mean)	12.2	12.0	10.9	11.9	Significant difference p<0.001
Number of medicines post-review (mean)	11	12.0	10.0	11.0	Significant difference p<0.001
Pre-review PC-MAI (patient) (Mean) (n=376)	25.4	12.4	12.5	20.4	Significant difference p<0.001
Post-review PC-MAI (patient) (n=367) (mean)	9.3	1.9	3.1	6.8	Significant difference p<0.001

Significant differences were observed in pre-review PC-MAI scores (p<0.001) between regions, with higher levels of inappropriate prescribing identified among the patients reviewed in the Republic of Ireland and lower levels in those reviewed in Northern Ireland and Scotland. Post hoc analysis found that the pre-review PC-MAI scores of Northern Ireland and Scotland did not differ significantly.

A large decrease in inappropriate prescribing was observed for each region. The reduction in the Republic of Ireland was the largest, however post-review PC-MAI scores remained significantly higher in the ROI than in the other regions. Caution is advised when interpreting sub analysis of PC-MAI results due to the low sample size, particularly with Northern Ireland (n=56 pre-review, and 55 post-review). Post hoc analysis found that the post-review PC-MAI scores of Northern Ireland and Scotland did not differ significantly.

4.2 Interventions

The pharmacists categorised their clinical interventions according to Eadon classifications and grading. The interventions were categorised by the problem addressed (Table 6), result of the intervention (Table 7) and grading of the anticipated clinical significance of the intervention (Table 8).

Table 6: Intervention problem category (n=2,623 patients)

Eadon problem category	Count
Drug: interaction, formulation, dose, frequency, time, duration, duplication, indication	10,253
Specific or additional patient education	4,252
Request/review test/investigation/measurement e.g. labs, vital signs, spirometry	4,222
Medicines reconciliation	2,623
Standard patient education	2,623
Referral needed e.g. to another healthcare professional	1,530
Drug/device omitted	937
Other	924
Adherence	659
Side-effect/adverse drug reaction	305
Review patient's own medicines e.g. safety/appropriateness	239
Allergy	117
Formulary change	89
Total	28,773

Table 7: Intervention result category (n=2,622 patients)

Eadon Result Category	Count
Prescription altered (stop)	3,904
Specific or additional patient/carer education	3,588
Requested/reviewed test/investigation/measurement e.g. labs, vital signs, spirometry	3,134
Medicines reconciled (iSIMPATHY intervention)	2,622
Standard patient and/or carer education (iSIMPATHY intervention)	2,622
Information given – healthcare professional	2,341
Prescription altered (start)	1,813
Referral made	1,427
Prescription altered (decrease)	1,345
Information given – patient	1,267
Other	1,205
Prescription endorsed e.g. medication record endorsement	1,134
Prescription unaltered advice accepted *	768
Prescription altered (increase)	563
Unresolved *	511
Prescription unaltered advice NOT accepted *	415
Patient's own medicines reviewed	102
Total	28,761

* Unaltered and unresolved account for 6% of total interventions indicating that 94% of interventions were actioned at the time of data collection.

Table 8: Eadon grading by region (n=2,623)

	Region			
Eadon Grading	**ROI**	**NI**	**SCT**	**Total**
1. Detrimental to patient	0	0	0	0
2. No significance to patient	369 (2%)	1 (0%)	42 (1%)	412 (2%)
3. Significant: does not improve patient care	2,986 (20%)	311 (7%)	581 (14%)	3,878 (17%)
4. Significant: improves patient care *	10,804 (73%)	4,060 (87%)	3,353 (83%)	18,217 (78%)
5. Very significant: prevents a major organ failure or adverse reaction of similar importance + 6. Potentially lifesaving	607 (4%)	282 (6%)	79 (2%)	968 (4%)
Total number of interventions which have an Eadon score	14,766	4,654	4,055	23,475
4. iSIMPATHY interventions	3,098	1,224	924	5,246
Total number of interventions with 2 standard iSIMPATHY grade 4 interventions included.	17,864	5,878	4,979	28,721

4.3. Change in appropriate polypharmacy

4.3.1 Change in number of medicines

Table 9: Change in number of medicines as a result of review

Change in prescribed medicines	Number (%) of patients (n=3191)
Number (%) of patients who had their medicines decreased	1,659 (52%)
Number (%) of patients who had their medicines stay the same	1,113 (35%)
Number (%) of patients who had their medicines increased	419 (13%)

The chart below shows the change in the number of medications across the regions before and after the reviews.

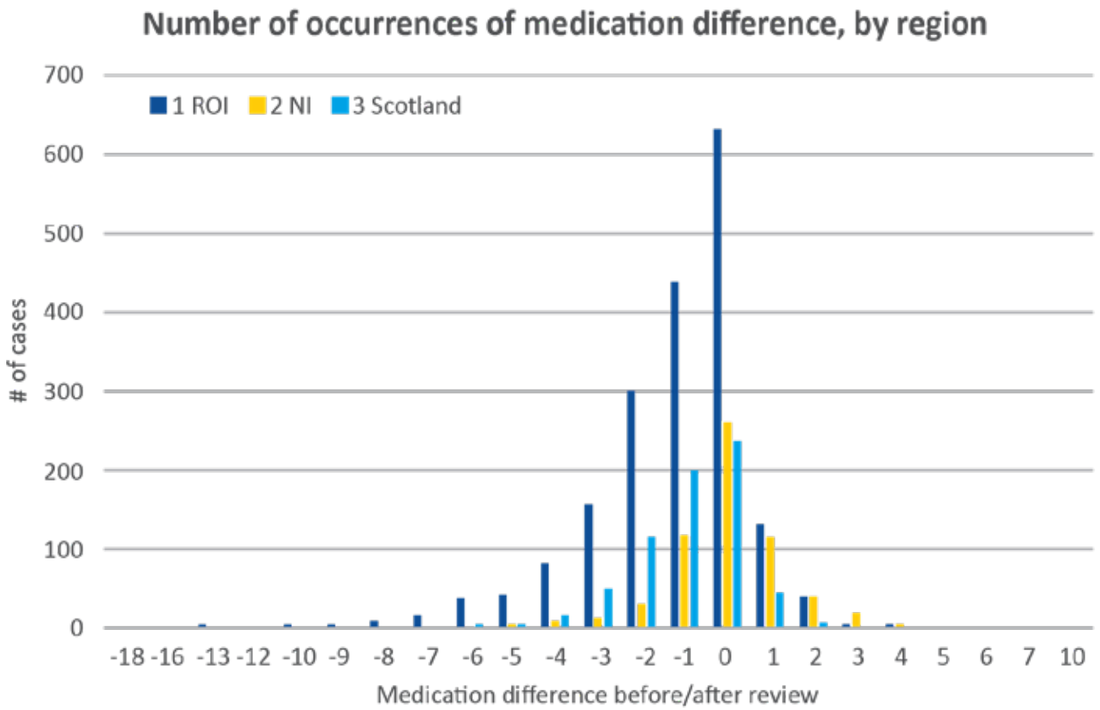


Chart 1: Number of occurrences of medication differences before and after review, by region

4.3.2 PC-MAI

The appropriateness of medications was assessed using PC-MAI.

Paired/listwise comparisons were conducted when there was both a pre- and post-review PC-MAI score for each patient (n=362).

Table 10: Descriptive statistics for patient level PC-MAI comparisons

Descriptive statistics					
	N	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
Pre-review PC-MAI	362	20.6	15.0	0	99
Post-review PC-MAI	362	6.8	8.8	0	66

- There was a mean decrease of 13.8 in PC-MAI rating per patient from pre- to post-review.
- 92% (n=334) of patients had a decrease in PC-MAI scores between pre- and post-review, 8% (n=28) patients had no change in PC-MAI score, no patient had an increase in PC-MAI score from pre- to post-review.

As this data is comparing pre- and post-review outcomes, matched pairs were utilised. This leads to the data having a different number of patients, as well as a different average total than the PC-MAI data in Table 5 which was using unmatched data, as it was a comparison between rather than within groups.

Table 11: Region pre-review PC-MAI (n=362):

Descriptive statistics					
	n	Mean	Std. Deviation	Minimum	Maximum
ROI	228	25.4	15.2	2	99
NI	54	12.4	9.5	0	36
SCT	80	12.5	11.3	0	56

Table 12: Region post-review PC-MAI (n=362):

Descriptive statistics					
	n	Mean	Std. Deviation	Minimum	Maximum
ROI	228	9.3	9.8	0	66
NI	54	1.9	3.2	0	17
SCT	80	3.1	4.6	0	19

4.3.3 Polypharmacy indicators

The core polypharmacy outcome indicators were triggered 1,179 times in 793 patients. These are indicators associated with an increased likelihood of a serious adverse outcome due to medication-related harm that can also be affected by patient or disease factors as identified in the Scottish Government Polypharmacy Guidance.[63] The following categories were identified, using the composite indicators in the guidance:

Table 13: Categories of polypharmacy indicators identified in medicines reviews

Indicator category	Number	%	Most common indicator
Bleeding	324	27.5	Patient on an oral anticoagulant is prescribed an antiplatelet n=116
Falls	304	25.8	Patient without dementia aged 75 years or older is prescribed TWO or more drugs with significant sedating or anticholinergic effects (excluding drugs only used for epilepsy) n=171
Renal	149	12.6	Patient with eGFR q60 and on an ACEI or ARB is prescribed an NSAID n=51
Cardiac	123	10.4	Patient is prescribed a betablocker and has a pulse of <60bpm n=63
Hyperkalaemia	57	4.8	Patient on an ACEI or ARB, potassium sparing diuretic, aliskiren or potassium supplement has hyperkalaemia (last K >5.5 mmol/l) n=23
Hypoglycaemia	48	4.1	Patient aged 65 or older without dementia is on intensive hypoglycaemic therapy and HbA1c is <48 (<6.5%) n=20
Cerebrovascular disease	46	3.9	Patient with AF and CHADSVASC score >=3 is not prescribed an oral anticoagulant n=34
Hypotension (= low blood pressure)	44	3.7	Patient without heart failure is on BP lowering treatment and BP is <110/65mmHg n=23
Hyponatraemia	26	2.2	Patient prescribed a thiazide diuretic has hyponatraemia (i.e. serum Na+ < 130 mmol/l) n=14
Extrapyramidal symptoms	21	1.8	Patient aged 65 years or older is prescribed metoclopramide on repeat n=19
Lactic acidosis	12	1.0	Patient with eGFR<30 is prescribed metformin n=12
Bloods	7	0.6	Patient on an oral corticosteroid is prescribed an NSAID (irrespective of gastroprotection) n=5
Dependency	5	0.4	Patient is prescribed an opioid at an average daily dose equivalent to >180mg morphine per day over the previous 6 months n=4
Hypokalaemia	5	0.4	Patient prescribed a loop diuretic has hypokalaemia (i.e. serum K+ < 3.0 mmol/l) n=3
Neurotoxicity	4	0.3	Patient on lithium is prescribed an NSAID n=4
Respiratory	3	0.3	Patient with asthma requiring treatment is prescribed a non-selective beta-blocker (oral or topical) n=3
Hypercalcaemia	1	0.1	Patient on a thiazide diuretic has hypercalcaemia (i.e., corrected serum calcium > 2.65 mmol/l) n=1

For the 793 reviews where outcome data was recorded, the risk was fully resolved for 77% (n= 891) of polypharmacy indicators, with progress towards resolution in many of the remainder, e.g. decreasing dose with a view to stopping in an appropriate timescale, stopping one sedating/anticholinergic medicine. In some cases, it is not appropriate to address the indicator due to patient factors, e.g. active bleeding preventing prescribing of an anticoagulant.

4.4 Multivariate analysis

Multivariate analysis was undertaken to determine the effect of different factors on the baseline metrics and the outcomes of the review. Output tables can be found in Annex B.

1. What elements contribute most to the number of medicines a patient takes?

Number of multiple long-term conditions is the single biggest predictor of the number of medicines a patient will be taking, explaining 26% of the variance in number of medicines pre-review. Gender, region, and socio-economic status improved the predictive power of the model, but only explained an additional 2% bringing the model to 28%. Age was found to not have any predictive power when the other variables were included in the model.

2. What contributes most to the number of interventions made by the pharmacists?

Number of medicines pre-review was the best predictor of the number of interventions a pharmacist was likely to make, explaining 17% of the variance in number of interventions. When multimorbidity, age, socio-economic status and region were included in the model, the variance explained rose to 20%. Gender wasn't a significant predictor when other variables were included within the model.

When pre-review PC-MAI scores were included in the analysis, only number of medicines pre-review contributed to the model. Pre-review PC-MAI scores accounted for 39% of the variance in number of interventions, when number of medicines pre-review was also included in the analysis this rose to 43% of the variance explained. Including PC-MAI scores reduces the sample size (362 compared to 3190 in the previous paragraph).

3. What contributed most to inappropriate prescribing pre-review?

Number of medicines pre-review was the best predictor of the patients' pre-review PC-MAI score, explaining 35% of the variance. When number of medicines was controlled for, no other variable significantly explained the remaining variance apart from region. When region was included in the model, the two variables accounted for 44% of the variance in a patients' pre-review PC-MAI score.

4. What contributed most to number of medicines post-review?

The number of medicines pre-review is closely correlated with the number of medicines post-review (accounting for 86% of the variance in medicines post). All other factors examined accounted for only an additional 1% of the remaining variance.

5. What contributed most to post-review PC-MAI?

Pre-review PC-MAI scores were the best predictor of post-review PC-MAI scores explaining 48% of the variance in post-review MAI scores. When number of medicines pre- and post-review; number of interventions; region and deprivation were added to the model (no other variable was found to significantly explain the remaining variance), the model's predictive power increased to 59% of the variance.

The multivariate analysis found multiple statistically significant predictors (with multimorbidity, number of medicines pre-review, and PC-MAI pre-review being the most prominent), however in most cases was only able to explain around a third of the variance within the model. This suggests that there are highly influential variables that interact with these outcomes of interest that were not accounted for within the data collected for this study. Future work should look to identify these missing variables and include them alongside the existing identified predictors reported in this study.

4.5 Patient Experience

Patient experience was collected through Patient Reported Outcome Measures (PROMs) questionnaires submitted via the Manage Medicines app or website.

258 pre- and post-review pairs were analysed.

PROMs were submitted from the Republic of Ireland (n=193), Scotland (n=61) and Northern Ireland (n=4)

Northern Ireland experienced delays with information governance and challenges with PROMs completion associated with delivering reviews in the hospital in-patient setting.

Two versions of the PROMs questionnaire were used during the project. The second version was improved to include the EQ-5D-3L questionnaires to enable economic analysis. Earlier data submitted was transposed to the second questionnaire, with data gaps where earlier respondents had not been asked the later questions.

Sample size is reported for each part of the analysis, as numbers differed with fewer patients having completed post-review PROMs questionnaires and submission of incomplete questionnaires.

Throughout this section, * denotes statistically significant difference between pre- and post-review responses ($p<0.05$).

Understanding
Sixteen per cent of respondents felt they had sufficient understanding of the purpose of their medicines pre-review (n=257), rising to 93% post-review (n=245)*.
Thirteen per cent reported they had sufficient understanding of the problems that any of their medicines may cause pre-review (n=258), increasing to 93% post-review (n=246)*.

Views and concerns
Eighty-six per cent of the 257 respondents reported not having had a previous medicines review.
Of those that had (n=35), 23% reported their views and concerns were fully considered, 54% most considered, 20% some considered and 3% not considered in that previous review.

Following the iSIMPATHY review, 41% of 229 respondents reported their views and concerns were fully, 54% most and 6% some considered*. Sixteen people additionally reported that they had not had a medicines review before.

Side effects
Sixty-four per cent of respondents reported that they thought they may be experiencing side effects from their medicines pre-review (n=251), dropping to 38% post-review* (n=249).

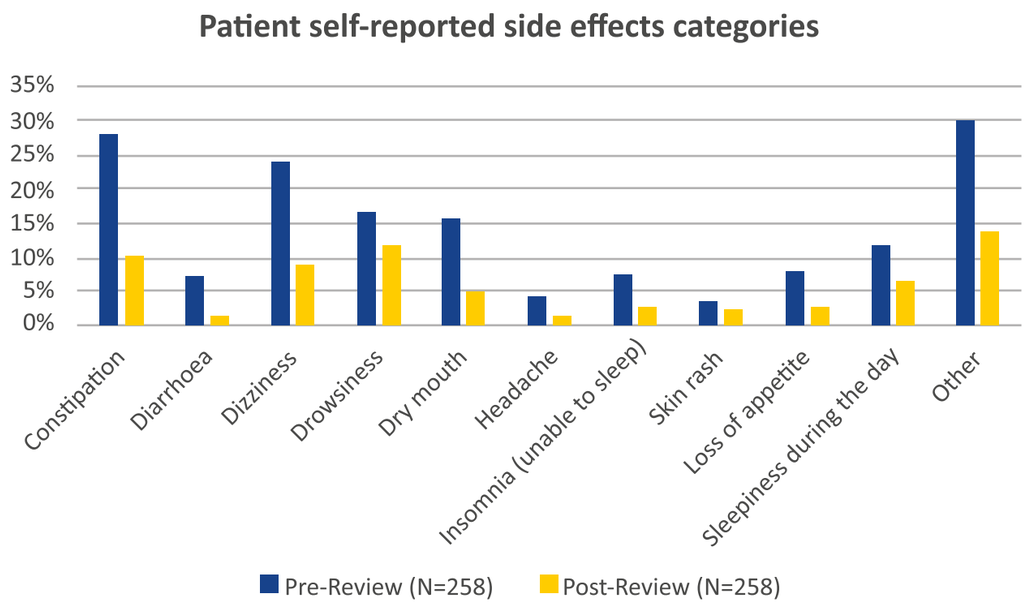


Chart 2: Self-reported side effect categories

"There was a definite improvement in my constipation and shortness of breath. I had no idea that changing my tablets could help with these things".

Adherence
Five questions relating to adherence were asked:

Table 14: Adherence responses

Question	% reporting Yes pre-review	% reporting Yes post-review	% point change
Did you ever forget to take your medicines?	11	0	-11%
Did you ever have problems remembering to take your medicines?	14	1	-13%*
At times when you felt better, did you stop taking one or more of your medicines?	14	1	-13%*
If you felt worse when you took your medicine, did you stop taking it?	22	3	-19%*
Did you ever take more medicines than prescribed, or take medicines for a different purpose than prescribed?	2	0	-2%

Activities of Daily Living (EQ-5D-3L)
Mobility issues were reported by 46% of respondents pre-review (n=124) and 41% post-review (n=115).
77% of respondents stated they had no problems with self-care both pre-review (n=119) and post-review (n=115).

The number of patients who reported that "I have no problem performing my usual activities" rose from 58% pre-review (n=184) to 69% post-review (n=171)*.

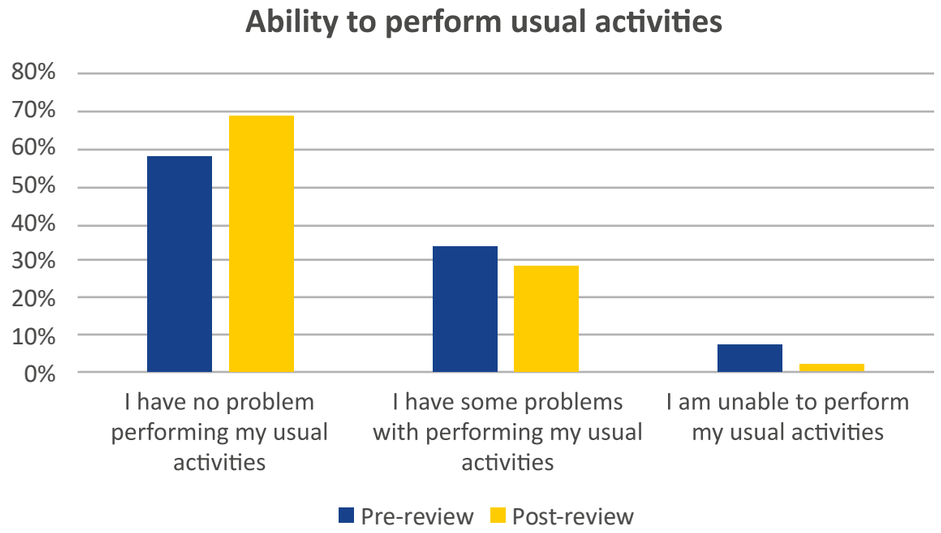


Chart 3: Ability to perform usual activities pre- and post-review

"Went on outing with daughter at weekend. Had turned down offer in previous weeks."

"Feeling well – eating better."

Forty-eight per cent of respondents reported having no pain or discomfort pre-review (n=125), increasing to 56% post-review (n=115)*.

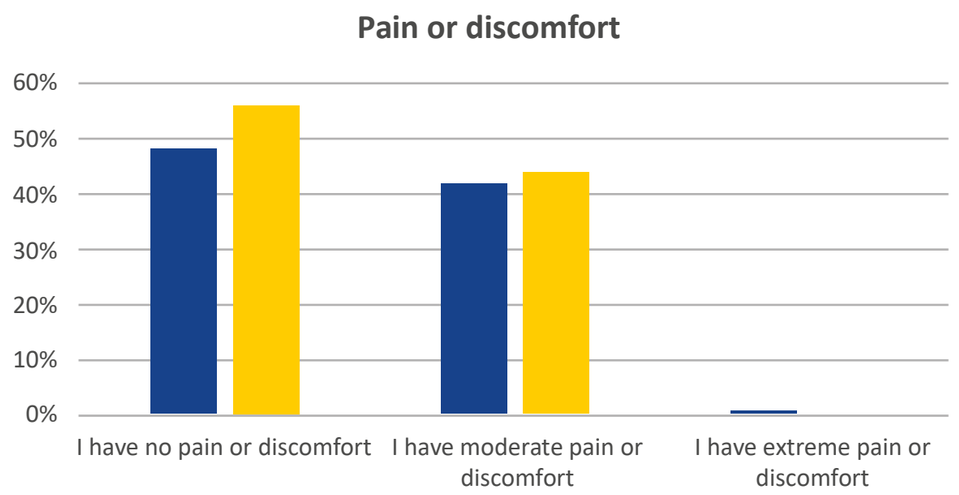


Chart 4: Pain or discomfort pre- and post-review

Sixty-three per cent reported not being anxious or depressed pre-review (n=175), increasing to 73% post-review (n=175)*.

4.6 Health Economic Analysis

The costs and benefits associated with polypharmacy reviews undertaken as part of the iSIMPATHY project were analysed. A brief description of the methodology is provided here, and the detailed report can be found in Annex A. Direct medical costs include staff costs associated with medication reviews (or cases – note that one review/case can include multiple interventions), the net costs associated with medication change (a medication reduction represents a direct saving to the healthcare system), and the savings associated with the avoidance of adverse drug reactions (ADRs). A top-down costing approach was taken, and total costs estimates were extrapolated to national perspectives. Benefits are measured in terms of quality-adjusted life years (QALYs), taking a bottom-up approach based on patient-level data. To illustrate the value of the health gains from iSIMPATHY, we present a range of values, namely from £15,000 to £70,000 per QALY, for the willingness to pay for a QALY. The UK Treasury Green Book recommends a value of £70,000 per QALY, while recent reviews of the literature suggest a range around 0.5 to 1.5 times GDP per capita,[74] implying a value of between £16,500 to £49,356 in the United Kingdom.[75] A further review of stated willingness to pay found a median value internationally below USD 35,000 (2018 prices, equivalent to £26,320 in that year).[76]

Given that iSIMPATHY delivers overall cost savings (Table 15) and generates QALY gains compared to usual care, it is dominant in the health-economic sense.[77] That implies it would pass the NICE threshold of £20,000-£30,000 per QALY and the Irish threshold of approximately €45,000.[79]

The results are presented per 100 reviews undertaken.

- Cost £7,500 (€8,786) to deliver (excluding cost of additional data collection)
- Result in £13,100 (€15,346) savings associated with medication changes
- Net cost reduction from this alone would be around £5,600 (€6,562)
- Reviews can be further associated with avoided inpatient cost of £6,600 (€7,731) from avoided ADR-related hospital admissions
- Using Eadon intervention classification calculations, 100 reviews avoid an average of £168,800 (€197,800) in medical costs and are associated with a 7.4 QALY gain

The different approaches used to estimate avoided admissions and (Eadon) avoided medical cost mean that these are not additive.

With this analysis, the impact of the scale up of the intervention was undertaken.

If comprehensive medicines reviews were provided to all patients aged 65 and over taking 5 or more medicines in each country (75 and over in Northern Ireland), the maximum avoidable inpatient cost would be (per year) £24.7 million (€28.9 million) for the Republic of Ireland; £11.0 million (€12.9 million) for Northern Ireland; and £36.0 million (€42.1 million) for Scotland.

Table 15 summarises key findings per 100 cases in each region. Note, no calculation of net benefit is made here as the different approaches to estimating patient benefit and avoided healthcare costs will overlap. However, setting out the total cost reduction from net medication changes alone would more than outweigh the staff cost for the Republic of Ireland and Scotland. With either the bottom-up or top-down approaches, the benefits (cost avoidance) would outweigh the associated direct cost in all three regions.

Table 15: Summary of costs and benefits per 100 cases

Summary costs, cost avoidance and patient benefits (numbers / '£) for one year per 100 cases in each region	Region				Total / Average
	ROI		NI	Scotland	
Staff cost for 100 cases, excl. data collection		-£12,400 (-€14,526)	-£3,200 (-€3,748)	-£6,700 (-€7,848)	-£7,500 (-€8,785)
Staff cost for 100 cases, incl. data collection		-£13,500 (-€15,812)	-£4,000 (-€4,685)	-£7,900 (-€9,254)	-£8,500 (-€9,956)
Net medication change: total cost reduction / increase (100 cases)		£24,700 (€28,927)	£0	£14,400 (€16,863)	£13,000 (€15,223)
Bottom-up: Eadon score avoided cost, QALY gain					
Total QALY gain (100 cases)		7.0	7.8	8.3	7.4
Monetary equivalent of QALY gain (£ per QALY)	£15,000	£105,000 (€122,955)	£116,900 (€136,890)	£124,500 (€145,790)	£111,200 (€130,215)
	£70,000[1]	£489,800 (€573,854)	£545,600 (€638,923)	£581,200 (€680,646)	£518,900 (€607,686)
Healthcare resource cost avoidance (100 cases)		£172,300 (€201,779)	£176,600 (€206,802)	£146,600 (€171,672)	£168,800 (€197,669)
Top-down: avoided admissions					
ADR admissions avoidable by 100 med reviews		0.9	1.1	0.8	0.9
Inpatient bed days avoidable by 100 med reviews		7.1	9.6	8.3	8.1
Inpatient cost avoidance (100 cases)		£5,900 (€6,909)	£8,100 (€9,485)	£6,100 (€7,143)	£6,600 (€7,729)

[1] The Green Book 2022 gov.uk[80]

The data here clearly illustrates the benefits to the patients and across the whole health and care system of undertaking the reviews.

4.7. Pharmacist Experience

4.7.1 Introduction

This section is based on interviews with 10 iSIMPATHY project pharmacists who worked in the three regions of the project and in both primary and secondary care. It explores their perceptions and experiences around:

- being involved in iSIMPATHY
- the impact of iSIMPATHY on patients
- the impact of iSIMPATHY on professional development and practice

The experience of being involved in iSIMPATHY varied across regions and between individuals. It is important to note that each region delivers healthcare differently, and the role of pharmacists can vary across regions and healthcare settings.

In the Republic of Ireland, pharmacists do not prescribe medication and had not routinely been based in a primary care setting prior to the iSIMPATHY project. There is also a part-private, part-public health system in place. In Northern Ireland, the pharmacists were able to prescribe and were based in a secondary care setting. In Scotland, pharmacists were able to prescribe and were based in both primary and secondary care settings.

4.7.2 Experience of being involved in iSIMPATHY

Communication and support

iSIMPATHY programme

Most pharmacists spoke positively about the communication and support they received from the iSIMPATHY programme. They felt that the regular online meetings were useful. They valued the opportunity to discuss issues and highlight challenges with pharmacists and programme managers from across all three regions.

> **"I've never had a job where it's been so well structured and lines of communication have been so well laid out and very clear."**
> **Pharmacist, secondary care**

Whilst there were regular opportunities for pharmacists to provide feedback, some felt that when issues were raised, they were not responded to or taken seriously. They felt that the approach from programme management was too 'top down' and that problems took too long to reach a resolution. For example, a few pharmacists commented on the time it took for data monitoring processes to become clear and consistent. They noted that discussions around these issues were not held openly in the meetings, which left them feeling disconnected. Two pharmacists noted that they did not receive timely feedback when they enquired about the quality assurance processes.

> **"I felt like there was a complete time in the middle where there was a lag of communication, and that caused disconnect."** **Pharmacist, primary care**

Regional and local
Within each region, pharmacists were positive about the communication and support they received. All felt that they had good local project management support and useful peer networks, both digitally and in-person.

> **"We were very close, our own team...We had a lot of support locally."**
> **Pharmacist, primary care**

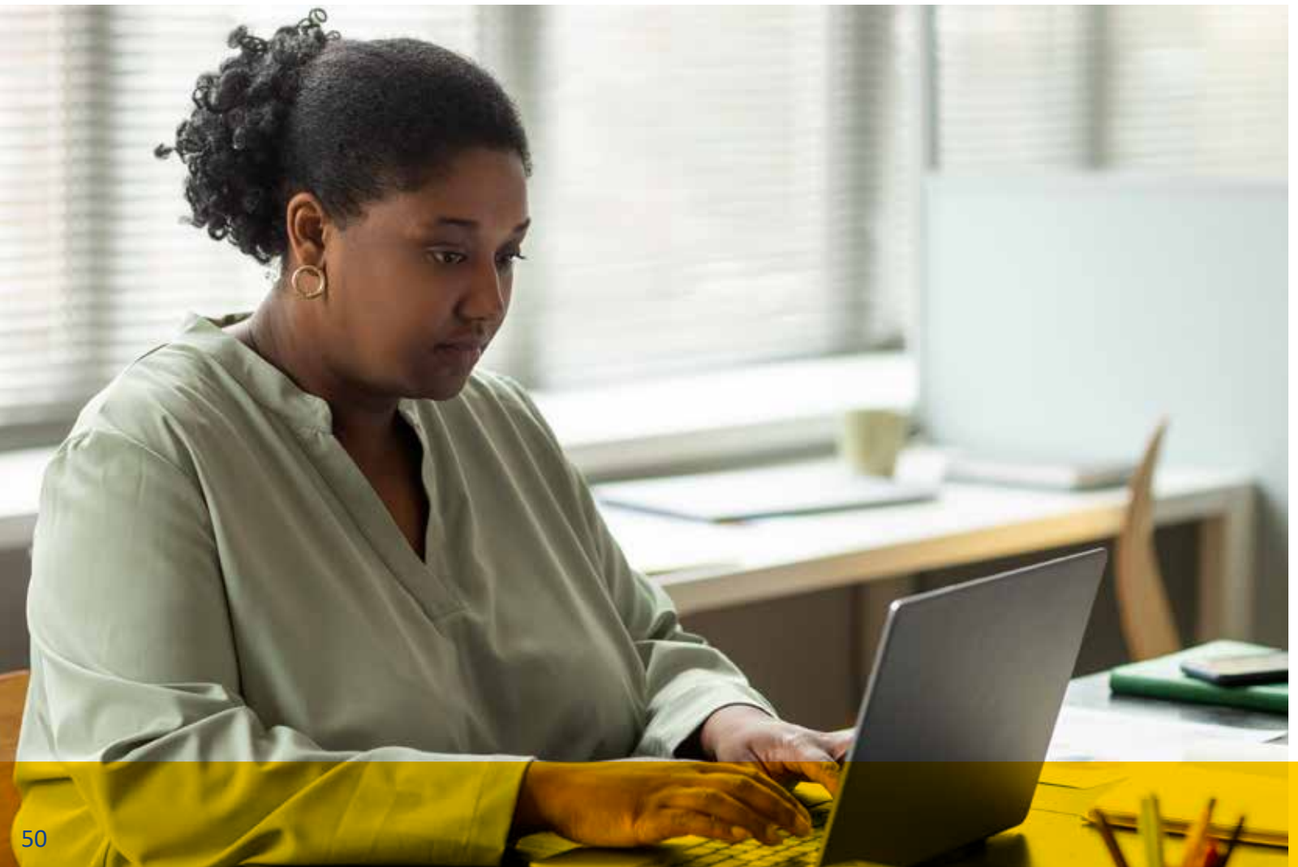
In one secondary care setting, all of the pharmacists worked in the same hospital and the regional project manager was also based on site. This approach worked well and allowed for regular, ongoing, informal communication and support.

One pharmacist noted that they had a mentor in the local area who was involved with the iSIMPATHY project. They found this type of support particularly valuable.

Locally, pharmacists had mixed experiences. Some had a high level of support and buy-in from people in their local team (e.g. GP practice, hospital ward or outpatient clinic). However, others did not initially have a lot of support and worked to establish relationships and lines of communication.

Where pharmacists worked in primary care settings, they were often the only pharmacist in the practice. In the Republic of Ireland, pharmacists are not routinely based in primary care, so there were no established methods or practices.

Identifying patients for a medication review
Overall, pharmacists felt that the selection criteria for the medication reviews was clear. Most pharmacists said that they conducted a 'pre-review' which involved looking over a patient's current medication for eligibility and risk factors.



Pharmacists noted that part way through the project one of the eligibility criteria was changed from patients being on 10 or more medicines to 5 or more medicines. This had been done to support some pharmacists identify patients. This did not significantly change their approach to identifying patients but did make it easier to identify suitable patients for review. Two pharmacists noted that the patients on 10 or more medicines were more complex and benefitted more from the review than those on 5 or more medicines.

Pharmacists had different approaches to identifying and selecting patients, depending on the healthcare setting and the data available to them. Broadly these were:

- searching digital record systems that held data on how many or what type of medication patients were prescribed
- referrals from other healthcare professionals
- opportunistic selection of appropriate patients, who were in the healthcare setting for something other than a medication review

At times, pharmacists also took a targeted approach to identifying patients. For example, working with GPs in a primary care setting to focus on medication reviews for particular cohorts of patients, such as those with diabetes or other long-term health conditions.

Conducting the medication review
All of the pharmacists spoke positively about the process of conducting medication reviews using the 7-Steps method.

Reviews were conducted over the telephone, in-person at clinics, or on hospital wards. As a significant portion of the project was delivered during the COVID-19 pandemic, pharmacists in primary care settings said that most reviews were conducted over the phone.

Pharmacists noted that the 7-Steps method was thorough and provided a useful structure to the review process. Whilst some felt that it was initially a lot of work, all pharmacists agreed that over time, the process became a familiar and innate part of their working practice.

> **"I think the 7-Steps is very good, it's a great framework to do that, to do the review."** **Pharmacist, Primary care**

In particular, pharmacists commented positively on the first part of the review: 'What matters to you?' They felt that this wasn't something they normally focused on or had time to discuss with patients. However, they felt it was key to the review and made sure that discussion was led by patients and their needs, rather than from the perspective of the healthcare professional.

How issues were addressed
The pharmacists involved in iSIMPATHY were a mix of prescribers and non-prescribers. In the Republic of Ireland, pharmacists do not have prescribing rights.

At the outset, there were no standard procedures in place for all pharmacists, regarding how to action changes or issues arising from a medication review. Pharmacists in each region developed their own processes, depending on the setting and their capacity.

Where pharmacists were prescribers, they followed similar processes after conducting a medication review:

1. If the change is within the pharmacist's competency, action the change immediately.
2. If the issue is complex or beyond the pharmacist's competency, discuss with relevant healthcare professionals before making any changes.
3. If the issue is outside the pharmacist's remit, document it and refer onto the appropriate person.

Where pharmacists were not prescribers, they followed broadly the following process:

1. Write a report to the doctor and patient where appropriate summarising recommendations
2. Allocate time in the doctor's schedule to review the recommendations
3. Where possible, follow up to ensure that recommendations were actioned

For pharmacists working in both primary and secondary care sector, these processes seemed to work well. Broadly, pharmacists felt that their recommendations were actioned and issues were resolved for the patient.

Where pharmacists felt there was a safety issue, they prioritised following up these actions until they were addressed.

What worked well

Pharmacists commented on the aspects of delivering iSIMPATHY that they felt worked well. These included:

- having extended time to speak with patients
- a high level of patient engagement
- buy-in from the organisation and colleagues
- communication and peer support
- administrative support
- the opportunity for personal development

Time

All pharmacists commented that having dedicated time for medication reviews was a key success factor.

> **"I think they loved the opportunity just to have somebody to talk to for a wee while. Just somebody to take the time to focus on them and see what really matters to them. I think it was really well received by patients."** **Pharmacist, secondary care**

> **"So they've definitely had a lot more time to talk about issues that they might not have had time to talk about with their doctor unfortunately."** **Pharmacist, primary care**

Patient engagement

All pharmacists said that patients were engaged and keen to take part in a medication review once they understood what it was. They noted that most patients had never experienced this type of in-depth review and welcomed the opportunity to review their medications and be heard.

Buy-in

Some pharmacists commented that they had good backing from their organisation and colleagues at the outset. This was important for establishing and maintaining communication and referral pathways. One pharmacist noted that they had buy-in from senior management, which again, helped to establish the role easily within an existing team.

Two pharmacists noted that demonstrating the value of having an iSIMPATHY pharmacist within the team helped to achieve buy-in and was important in the early stages of the project.

> **"I do think that the GPs really valued our opinion and I do think that they all found the benefit of the reviews and the prescribing practices kind of changed thereafter."** **Pharmacist, primary care**

Communication

Where possible, pharmacists attended multidisciplinary team meetings. This helped ensure that a wide range of healthcare professionals were aware of the iSIMPATHY project. This also helped to establish good relationships with key people, who were able to provide referrals or clinical support.

Peer support

Pharmacists also said that they enjoyed being part of an international project that worked across three different regions. They particularly appreciated the regular communication with other project pharmacists and the access to a range of clinical experts.

Admin support

Where pharmacists had administrative support, this optimised their input and this was greatly appreciated.

Personal development

Pharmacists said that they felt being part of the project, working collaboratively, undertaking training, and conducting reviews using the iSIMPATHY methodology helped improve their clinical knowledge and skills.

"I loved learning so much more clinical information as well…Even just with doing the reviews it just really felt like my clinical knowledge really improved…" Pharmacist, secondary care

What was challenging?
Pharmacists also commented on the areas where they felt they encountered challenges or barriers to delivering the project. These included:

- lack of buy-in from colleagues
- lack of referrals
- data monitoring and collection
- lack of standard operating procedures
- ability to conduct post-review follow-ups
- patient engagement in some regions in primary care
- patient engagement in secondary care

Post-review follow-up
Across all regions and healthcare settings, pharmacists found post-review follow-ups difficult to deliver. Follow-up with patients was not built into the project review process and pharmacists often did not have time to conduct additional follow-up calls. A few pharmacists noted that as follow-ups were not included in the key performance indicator targets, they did not have time to conduct them. Similarly, there was no infrastructure, standard process or administrative support in place to support follow-up discussions.

Despite the challenges in following up with patients, most pharmacists said that they made time to follow-up because they felt it was clinically important, particularly for individuals with more complex cases. A few pharmacists noted that they conducted follow-up calls in their own time, beyond their contracted working hours.

Patient engagement
Pharmacists commented that initially there were challenges reaching patients in primary care, as they had to explain their role and the project. This was particularly challenging in one region, which did not usually have pharmacists based in a primary care setting. Pharmacists also commented that there were cultural barriers that hindered patient engagement, as some patients were reticent to change anything that a doctor had prescribed.

Pharmacists working in secondary care noted that there were challenges conducting medication reviews on the wards, as the focus is often on the immediate presenting acute issue, rather than longer term health issues. It was also not always the most appropriate time to change medicines or to have a discussion about medication, particularly if a patient had recently received difficult news or a poor prognosis.

Suggestions for improvement
In general, pharmacists felt that the principles behind the project were robust and they valued the opportunity to be part of the project. More broadly, most pharmacists felt that their roles would have been easier to implement if there was better awareness and understanding of the role of a pharmacist and the value of an in-depth medication review.

In terms of patient involvement, pharmacists felt this would improve if patients were more aware of the option to have a medication review, and the role that pharmacists have in healthcare provision. They felt that medication reviews could be better promoted to patients through advertising, social media, campaigns, and through other healthcare professionals.

4.7.3 Impact on patients

Patient care
All the pharmacists felt that engaging in a medication review improved the care that patients received. Primarily, they felt this was because the iSIMPATHY method allowed them more time with patients and began with a focus on the patients' priorities. This in turn provided space and freedom to talk to patients about their life holistically and focus on what mattered to them.

"You probably don't appreciate what a difference that question at the beginning can make for the whole review." Pharmacist, primary care

For some, this was a different approach to how they previously engaged with patients, where they often had a focus on outcomes for the organisation, rather than outcomes for the individual.

"I feel like it was all person-centred, whereas maybe before in GP practice…it was more process-centred." Pharmacist, primary care

They found that patients greatly appreciated having time to discuss their issues and were able to open up and speak honestly over the duration of the 30–60-minute review, which they would not have done during a shorter 10–15-minute consultation.

"There's a lot more honesty coming from the patients as well. They feel like they've got time to talk...Tell you what their anxieties are around medications and that sort of thing." Pharmacist, secondary care

Pharmacists commented that more time led to better quality conversations, with a few noting that they used motivational interviewing techniques from the iSIMPATHY training.

"I actually think overall the conversations with the patients are of a much better quality than what I would have experienced before." Pharmacist, secondary care

Defining and achieving realistic goals
Having more time for medication reviews allowed pharmacists to instigate discussions about sensitive issues, or topics that patients might be less inclined to discuss openly e.g. smoking cessation. With time, pharmacists found that patients were able to define a solution for themselves. They felt that this approach was preferable to patients being told what to do, or which behaviours to change.

Similarly, pharmacists felt that patients were more confident about setting goals for themselves because they felt better informed about risks, benefits and adverse reactions of their medication.

> **"Yeah, it's the empowering them with knowledge as well helps them take more care of themselves and encourages them to take their medicines…"**
> **Pharmacist, primary care**

Health and wellbeing
Most pharmacists felt that the iSIMPATHY medication reviews helped to improve patients' health and wellbeing. For most, health and wellbeing were intrinsically connected, and improvements in health usually led to improvements in wellbeing, and vice versa. Overall, they felt that this contributed to improved quality of life.

> **"…I think our approach in that we kind of listen to the patient and take that approach it does help their wellbeing as well as their physical health."** **Pharmacist, secondary care**

Pharmacists felt that improvements in health were achieved because patients were taking fewer medicines, were feeling fewer side effects, or because they had made changes to their diet or lifestyle. They also noted that as their health started to improve in one area, patients were more able and more motivated to make improvements in other areas.

For example, following reviews, patients were keener to reduce or stop smoking, improve their diet or to be more active, and as they did, they began to feel better, and were spurred on to make further positive changes. For some patients, pharmacists said the benefits were felt immediately, and for others, they were gradual and felt more generally in their day-to-day life.

> **"So I think he was maybe on eleven or twelve to start with and we managed to cut it down to three, just because every time he did a wee bit more he felt so much better, so in time everything was improving. So it was his diabetes first and then his blood pressure came down and then his cholesterol came down..."** **Pharmacist, primary care**

Physical activity
Most pharmacists did not feel able to comment on whether or not patients were more physically active as a result of the medication review. However, a few suggested that improved physical activity may have been a subsequent outcome for some patients, as they felt healthier and more confident.

> **"…they're able to do more things or able to get out a bit more or even kind of more confident."** **Pharmacist, primary care**

4.7.4 Autonomy

Most pharmacists felt that patients were more empowered and engaged in decision making following a medication review.

Broadly, they felt this was because patients were better educated through the review and had a clearer understanding of the medicines they were taking, why they were needed, and the possible side effects and potential risks.

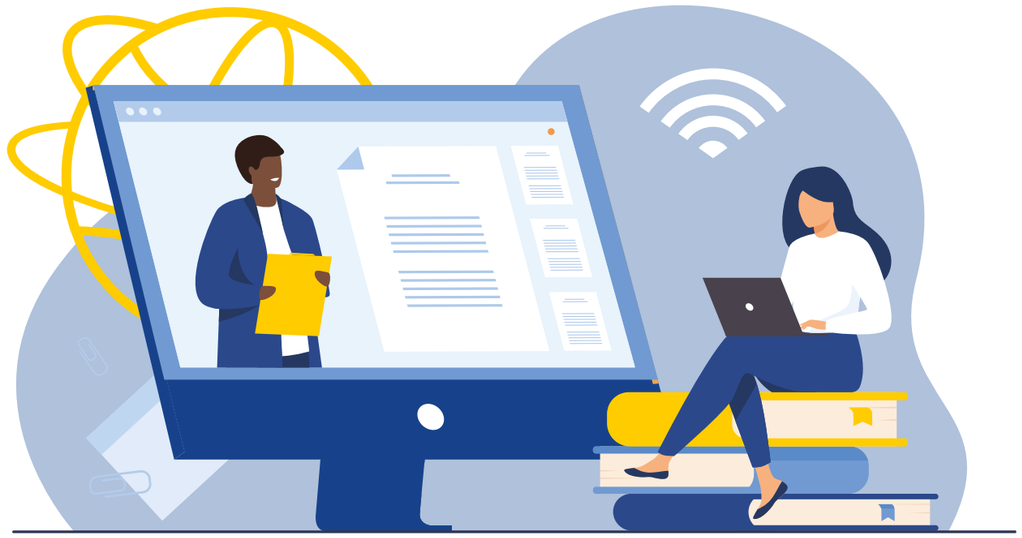
> **"I think it kind of helped improve their understanding of their chronic conditions and why certain medicines were prescribed."** **Pharmacist, secondary care**

Pharmacists commented that going through the medication review process helped patients to see that they had a role to play in making decisions about their healthcare.

> **"It's only the beginning of a shift of mind set around medicine taking and just the whole attitude towards healthcare from paternalism to them being more empowered to be involved."** **Pharmacist, primary care**

4.7.5 Impact on professional development/practice/culture

All the pharmacists spoke very highly of the iSIMPATHY training that they received before and during the project. All felt that the training was relevant, useful and of a high quality. Most said that they had enjoyed taking part in the training.



> **"...the initial training was good, and very clear and easy to understand."**
> **Project Pharmacist**

The ongoing training, which included ECHO sessions were also valued. Most pharmacists especially enjoyed the opportunity to share learning through case study discussions. A total of 13 sessions were delivered over two years. The average number of participants in Year 1 was 16 with 71% attending >7 sessions. At the end of Year 2, 86% of respondents had applied their learning in practice, 88% had increased confidence delivering reviews and 63% agreed the network created a community of support. All participants responded that case-based discussion was an impactful way of learning.

> **"I felt that the training did empower me to conduct the review."** **Pharmacist, primary care**

Most pharmacists commented that the training had helped them to develop their skills, both clinically and generally.

> **"My clinical knowledge is completely... it's completely changed. It's very vast, I see things from a completely different perspective from when I started iSIMPATHY."** **Pharmacist, primary care**

4.7.6 Organisational change

Approach to patient care
Pharmacists felt that there had been a positive change in the overall approach to patient care due to iSIMPATHY. They noted that other pharmacists, nurses and doctors were learning from the iSIMPATHY approach and incorporating some iSIMPATHY methodology into their own practices.

> **"So I definitely think the care has improved for the patients of all the surgeries that I've done the reviews in."** **Pharmacist, primary care**

Pharmacists also said that they had seen improvements in:

- prescribing practices (e.g. approach to tapering)
- inclusion of pharmacists in care plan development
- monitoring of medicines and long-term illness
- recognition of medicine safety and appropriateness
- the language used with patients

> **"I think it definitely promotes a more cohesive way of working between the multidisciplinary team and within pharmacy as well."** **Pharmacist, secondary care**

> **"Yeah, they're looking at the way they're prescribing differently…things that I would have implemented that they're now using the processes going forward."** **Pharmacist, primary care**

Ways of working
In all regions, pharmacists said that their colleagues were able to see the benefit of medication reviews and the iSIMPATHY pharmacist role.

> **"It's kind of showcased what pharmacists can do"** **Pharmacist, primary care**

Looking to the future
Going forward, all pharmacists hoped to continue using the iSIMPATHY methodology as much as possible. Many commented that they felt they would take a more person-centred approach in the future, focusing on the issues that patients identified as priorities.

> **"I think it would work really well in GP practice and my plan is to go back to GP practice and incorporate that into my day to day working."** **Pharmacist, primary care**

Pharmacists said that they hoped to build and maintain relationships with healthcare professionals, to make them more aware of what a pharmacist could offer. A few pharmacists spoke about how they would develop or adapt the iSIMPATHY methodology. One pharmacist suggested it would be helpful to have an online forum for iSIMPATHY pharmacists to continue sharing learning and resources, or to post queries.

> **"I'll try and incorporate the seven steps as much as I can."** **Pharmacist, secondary care**

Pharmacists based in the Republic of Ireland commented that they would like to see the role of pharmacists as prescribers developed in the region, in order to match services offered in Scotland and Northern Ireland.

4.8 Multidisciplinary team experience

This section summarises the views of the wider multidisciplinary team that are involved in the reviews alongside the project pharmacists. This is important to understand as the wider healthcare team are involved in the care of the patients and may have some influence on the decisions making regarding the medication reviews.

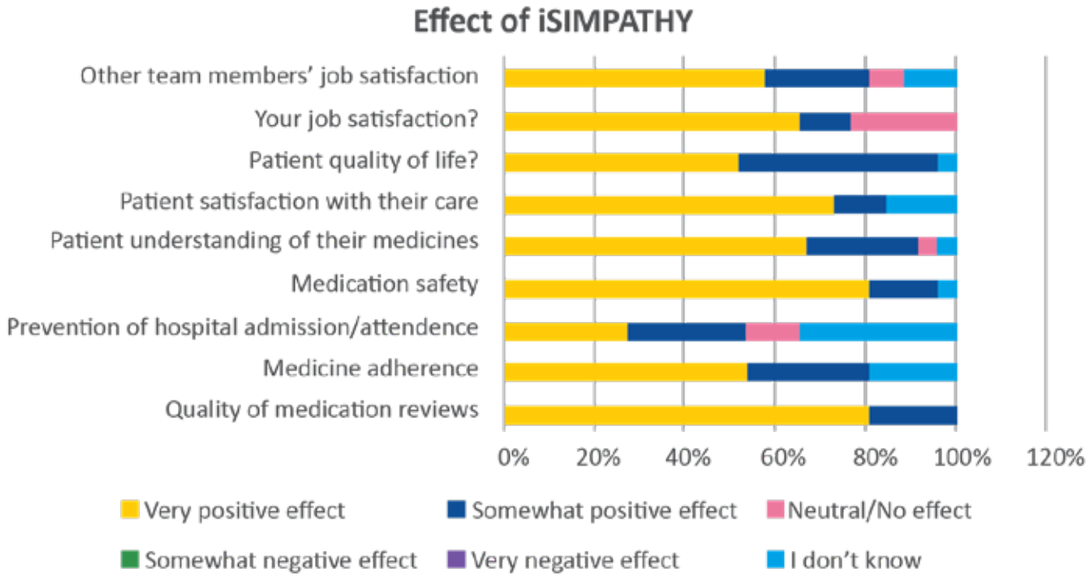


Chart 5: Effect of iSIMPATHY

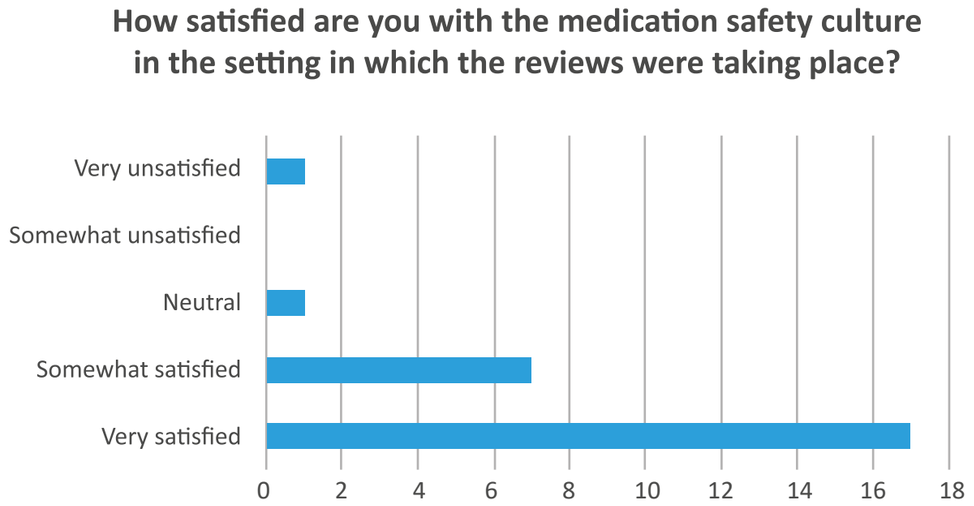


Chart 6: How satisfied are you with the medication safety culture in the setting in which the reviews were taking place?

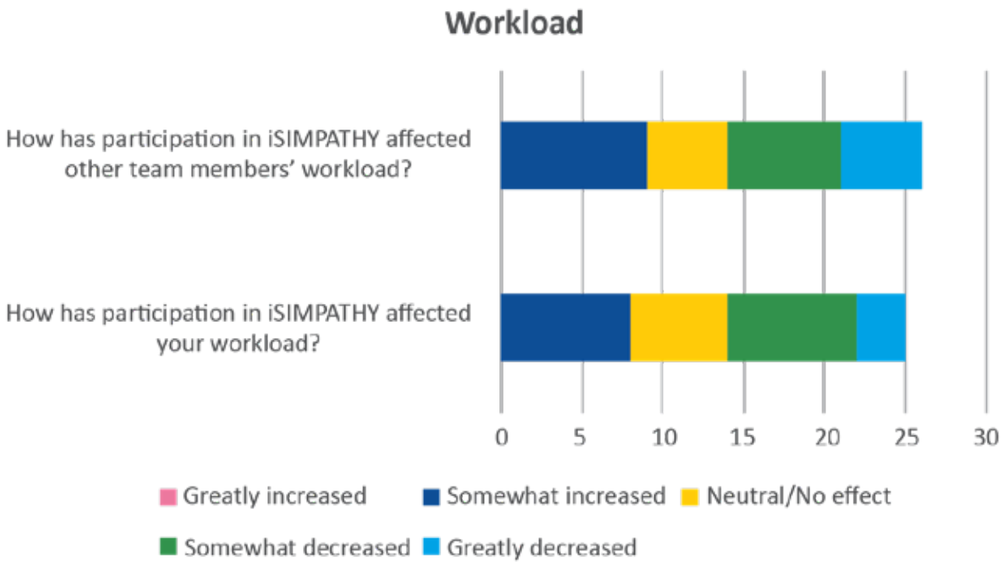


Chart 7: Workload

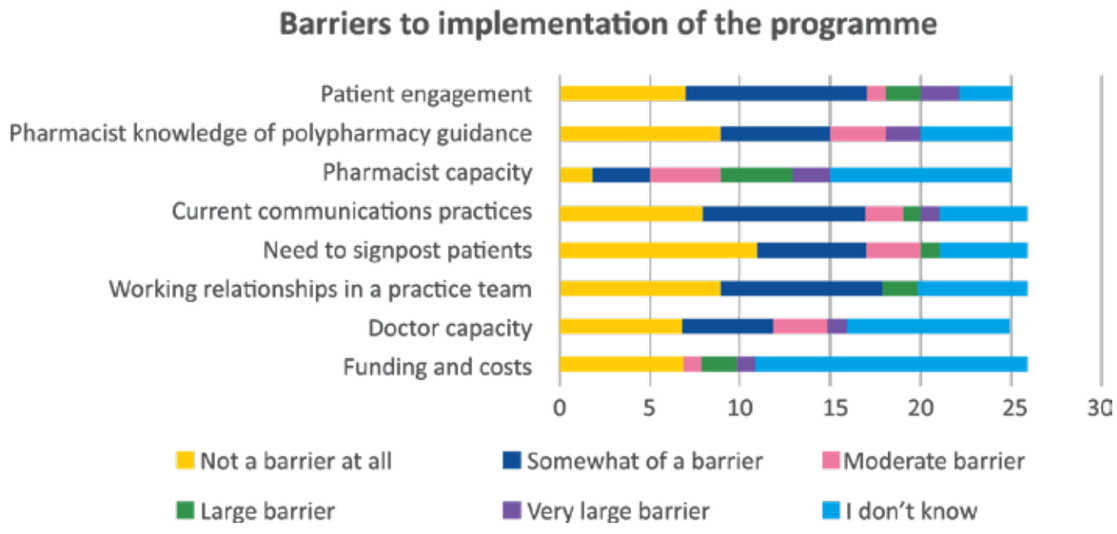


Chart 9: Barriers to implementation of the programme

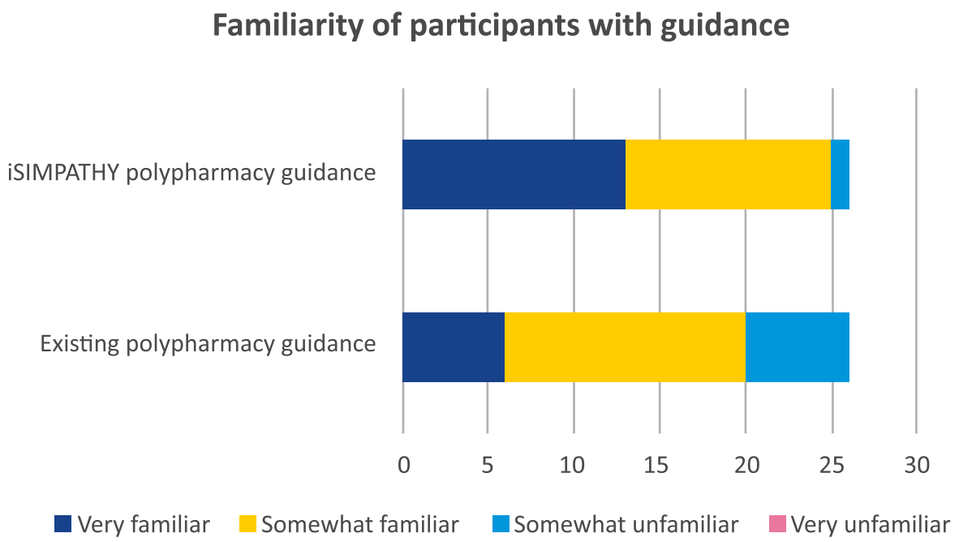


Chart 8: Familiarity of participants with guidance

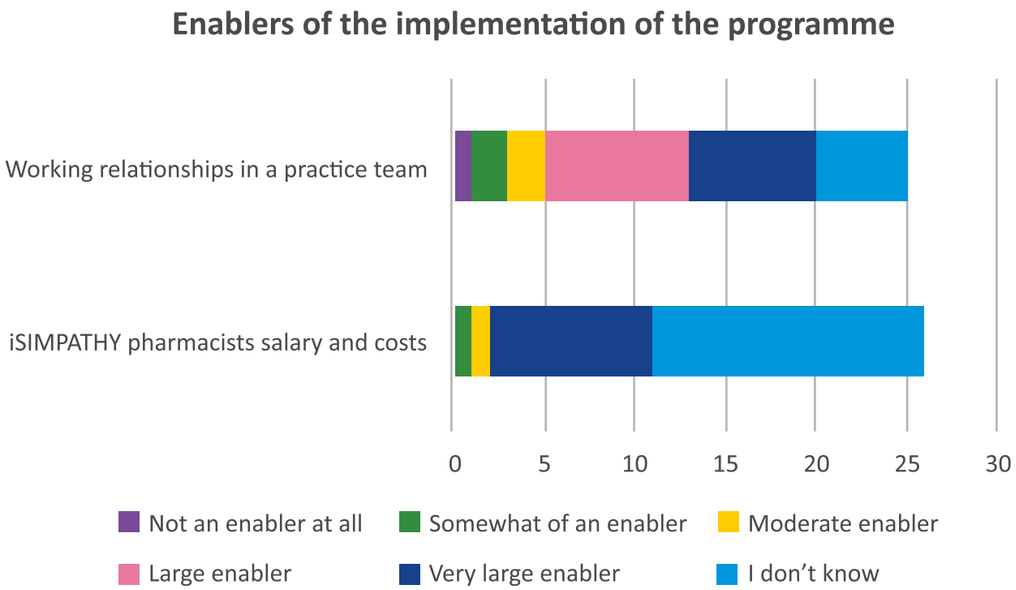


Chart 10: Enablers of the implementation of the programme

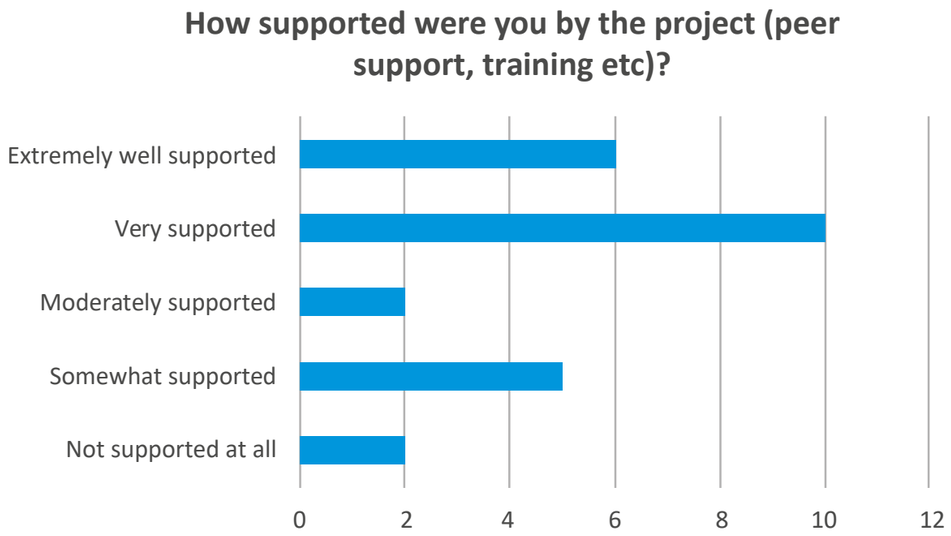


Chart 11: How supported were you by the project (peer support, training etc)?

The most commonly referenced barriers that would most hinder the successful scale up of the iSIMPATHY methodology nationally were:

1. Issues around funding
2. Issues around time management to conduct reviews
3. Issues around current work culture and the need to embrace change

The most commonly referenced enablers that would most contribute to the successful scale up of the iSIMPATHY methodology nationally were:

1. Good communication
2. Availability of necessary funding
3. Support for/engagement with project

The most common training and support needs identified for national scale up were:

1. Knowledge of the role/project
2. MDT communication
3. Miscellaneous

All 25 respondents (100%) would welcome continuation of the service provided during the iSIMPATHY project.

4.9. Management Experience

4.9.1 Involvement with iSIMPATHY

Participants in all three jurisdictions spoke positively about their involvement in the iSIMPATHY project. They felt that there had been significant learning from their involvement in the project. Each jurisdiction met individual challenges, but the consensus was that it was a beneficial experience:

"So yeah, it's been a fantastic project...really utilising pharmacists' talents to the full, and making a huge impact for patient safety."

"I suppose I'm excited about being involved in this project, because I do think that it will be a future service, and it'll be nice to be involved in something that is going to be I hope mainstreamed, and that we all believe that it should be, because it's given such great benefits to I suppose the patients first and foremost."

4.9.2 Benefits of the programme/benefits of conducting medication reviews

Participants discussed many of the positive developments that have come from their involvement in the iSIMPATHY project. Themes included:

- a greater focus on person-centred care and patient safety
- facilitating good working relationships within teams and between professions
- increasing the perceived value of medication reviews in the healthcare system
- high patient interest and uptake of medication reviews
- the project acting as a vehicle for the professional development of the pharmacists involved
- fostering an environment of knowledge transfer and information sharing
- added value of the project on the broader healthcare setting

These themes are further explored below.

4.9.3 Person-centred care/Patient safety

Participants discussed how involvement in the iSIMPATHY project and the utilisation of its methodology contributed to greater person-centred care and patient safety. The main driving force of this improvement was felt to be the thoroughness of the medication reviews conducted by the project pharmacists. In many cases iSIMPATHY reviews were the only medication reviews that a patient would receive. There was a shift in focus on what matters to the patient, through the adoption of the iSIMPATHY methodology. Participants commented that the project pharmacists have embraced this method of conducting medication reviews, and are likely to continue to use this approach even after the project has concluded:

"Yeah, absolutely. You know the methodology allowed the patient to sort of express what their highest concerns were, how the pharmacists and the team could meet those. So, absolutely I think it had a big impact on patient-facing care. And as we said, we talked about like the touchpoint of somebody just explaining to the patient as well. So, I think that cannot be underestimated as well."

"…yeah, it's where they work collaboratively as a team, but being an iSIMPATHY pharmacist was a completely different role where they had that extra time to sit down with the patient, start off with the question, "What matters to you?" You know, it was different. They had more time to do it too."

"I definitely think there was an added value to the pharmacist's role I think that was from both a patient's perspective on their behalf, but also from their own perspective in terms of their own role. You know, to be able to sit down and say, "If I had not spoken to this patient, they may not be here today," is a huge thing"

4.9.4 Working relationships and perceived value of medication reviews in the healthcare system

Participants commented on how the project had a positive effect on the perceived value of medication reviews overall, and of the pharmacists' role in conducting those reviews. Participants mentioned broad improvements, however the most commonly cited example was in relation to the interactions between pharmacists and GPs. Participants discussed how they feel that GPs now seem to have a greater appreciation of the value of medication reviews, and how undertaking reviews can improve medication safety. Participants felt this has led to GPs having a better understanding of the role a pharmacist can play in the practice, and the value this role can bring to patient care.

"… the relationship with GPs, which obviously is the big transformation."

"…they appreciate the capability, the knowledge, the understanding that the pharmacist has and that they bring to this, and are learning from that…so that the GPs then feel that their knowledge and understanding is improved, and that has knock-on benefits for other patients that they're dealing with."

"I mean, I think the GPs now realise like the value of a pharmacist and what a medication review is, a proper medication review. I mean, that's the bottom line."

4.9.5 Professional development; knowledge and information sharing

One of the major benefits of involvement in the iSIMPATHY programme across all three jurisdictions, appears to have been the professional development of the project pharmacists. In each focus group the participants provided multiple examples of how involvement in the programme had fostered skills sets or provided invaluable experience to the pharmacists. Pharmacists were said to have been enthusiastic in regard to their involvement in the project and have become 'leaders in the field', examples were given around how they had been interviewed on local radio, presented at conferences etc. This has fostered a knowledge and information sharing environment amongst the pharmacists.

"again many of the basic pharmacist skills as well as those inter-professional skills, negotiation, maybe a bit of conflict management, maybe even raising concerns, or addressing poor division practice in terms of prescribing. You know, you could all meet those competences as well and it would be a really fertile ground for pharmacists that did wish to develop using this type of approach."

"I think we probably didn't appreciate how much the pharmacists would gain from doing this and I think just benefiting from going through the process and they now say the seven step process is engrained in what they do and they will always use that."

Participants discussed not only the benefits to the participating pharmacists, but also the benefits to the wider colleagues that were indirectly involved in the iSIMPATHY project:

"I suppose what we could say for the pharmacists…have got lots of positive feedback from GPs saying, the pharmacists have done really well with managing that patient because I think what that reflected was the practice had really struggled in the years and hadn't got anywhere. So the pharmacist giving more time to it was really beneficial. So they saw for their patients and their practice the benefit."

"(the project pharmacist) would note down interesting things as (they were) going along and collecting all the information. Certainly (they) would have trained foundation level pharmacists, and (they are) training undergrad students in both the universities in the final year of their degree. You know, so it is definitely embedding those ideas and the seven steps reviews. So, there definitely has been learning within pharmacy groups, and (they) would have trained different groups within the Trust."

The participants also discussed the positive experience the pharmacists involved in the project expressed throughout the course of the project:

"I think they really enjoyed the patient contact and having a lot of patient time compared to some other jobs where if they were doing the pharmacotherapy service it's really... so many tasks to do. I think for them that was the biggest satisfaction they got was actually knowing that they were really making a difference for individual patients which I think is a really positive thing."

"I think for them personally presenting at conferences and going to international conferences again was a really positive thing for them that came out of the project. They've really developed and flourished in this role which has been positive too."

4.9.6 Added value

Participants discussed some of the benefits of their involvement in the programme that went beyond the initial aims of the project. For instance, in the Republic of Ireland, pharmacists were able to highlight discrepancies between medication lists across GP, community and hospital settings. They then approached software companies to try and ensure more cohesion between the lists in order to discern which medication list is most up to date. This was stated to be an important piece of learning from the project that will inform future development.

In Scotland, participants mentioned that their involvement in the programme allowed them to test out a model of care that they otherwise would have struggled to enact, and that the programme had provided wider learning around role and responsibilities within their local healthcare system and what adjustments need to be made to implement this kind of project moving forward.

In Northern Ireland a participant discussed how the work on the iSIMPATHY programme, has informed

their practice in general as well as relating to medicines reviews, and has fed into broader research work on the efficacy and longevity of improvements that are made through medication reviews.

One participant mentioned how the use of numbers needed to treat by the pharmacists was helpful to doctors:

"And I think for maybe more sort of traditional medics or consultants, the focus on number needed to treat or harm was useful in allowing them to get more quantitative in their counselling and in what the pharmacists were telling them and suggesting…..So, those types of things were very helpful to me, it gave me credibility when speaking to the patients and going, "Oh yeah," and also it gives the pharmacists a bit of credibility, and use of data end evidence as well to back up their suggestions."

4.9.7. Challenges/barriers

The participants discussed multiple challenges/barriers that arose during the course of the project.

Recruitment
In the Republic of Ireland a substantial delay was experienced in recruitment of the project manager, resulting in the work package lead trying to fulfil aspects of this role:

"I suppose the other big challenge was we didn't have project management to pull on. We didn't have a kind of structured system to support projects like this."

In Scotland one of the participants described having issues recruiting project pharmacists, which in turn led to a delay in conducting the reviews:

"There was quite a significant delay in the recruitment process which was unfortunate. So it did mean that by the time we interviewed and recruited we were quite late, I suppose, coming to the rest of the iSIMPATHY team. I think that has challenges because obviously people were then joining quite late and having to try and catch up and do the different things."

COVID-19

Across all three jurisdictions participants referenced the COVID-19 pandemic, and the ensuing restrictions as leading to severe challenges for the programme. The pandemic was said to have led to a strain on staff's time and organisational resources.

"We did face significant challenges just because of the environment on doing the polypharmacy reviews. Obviously busy hospital wards, it was still certainly at the start in July when they started there was still no visiting to the hospitals. Again that was quite challenging for doing polypharmacy reviews 'cause you might want to include family members. It was just trying to work through some of that."

Demands of the project/time constraints

Participants referenced the targets for the number of reviews being a challenge, and the issues with trying to meet those targets given the time intensive nature of the medication review process:

"Making the numbers was always a challenge and trying to have a realistic expectation for the staff about what they could actually achieve in the time that was available. And also because there was quite a lot of other demands on their time, they were having to develop presentations which was very good but it just took away from the time that they could actually do the delivering of the actual polypharmacy reviews."

"The other thing was that the number of reviews that were set and the capacity we had to deliver them and the way our model was evolving didn't match. And that became a source of tension within the project."

"I think it is quite time demanding, because there is the pre-work that needs to go in"

Participants made reference to the complexity of the cases that were being selected by or referred to the pharmacists. This increase in complexity resulted in more time being required to prepare and conduct the reviews. This in turn exacerbated tensions around achieving the designated target number of medication reviews.

"…The GP expectation was that the pharmacist would see these patients in, say, 10/15 minutes but actually it was probably taking them half an hour at best, an hour… to really unpack a lot of stuff that was just there. And then once you've unpacked it all, make some decisions with the patient and then see them through."

"When the pharmacist went to do the polypharmacy reviews they were unpicking lots of problems that had been there for a long time and then it was trying to go back."

Ambiguity around roles
The participants described an ambiguity around the role of the pharmacists on the project at some of the project sites:

In the Republic of Ireland the project introduced the primary care pharmacist role for the first time. The initial challenge appears to have been handled well despite the limited roadmap available, as patients, GPs and community pharmacists all adjusted well to the new role.

In Scotland, ambiguities around the roles and responsibilities of the project pharmacists seemed most apparent in primary care settings and with GPs:

"I think there was a mismatch of expectations. But during the process the pharmacists…didn't stay too long, I think the frustrations with how things were worked out led [them] to leave. Although [they] did do a lot of good work."

"The GPs took a view that rather than just receiving advice on polypharmacy reviews they required the pharmacist to follow all the actions and recommendations through with the patients to the end of the process which increased the amount of work significantly for the pharmacists. That was compounded by the fact that there was no longer the space in the practice for the pharmacist, we had IT connection issues and things like that. It was a really, really difficult process."

"We probably should have done better about setting out for GPs what iSIMPATHY is and what iSIMPATHY isn't"

In secondary care settings, the new role was also a challenge at times:

"They had a very specific role so I suppose the big concern when we had pharmacists who would be simply doing project work, particularly in a busy hospital, if they walk onto a ward and somebody sees you're from pharmacy they would inundate you with lots of other questions. Sometimes you would have to deal with them because if it was like a patient safety risk you couldn't not respond to it. But I suppose it was like making the steer very clear, they are project pharmacists, this is what their main role is"

Communication with project
Participants in Scotland and the Republic of Ireland referenced some broader project management related challenges. Once again, these issues stemmed around the targets of the project, but also broader communication issues:

"A lot of the materials weren't actually ready yet. Some of the data collection tools just didn't exist, or they were being built. We ended up probably having to try and retrospectively gather data which is always tricky and much more time consuming than collecting it at the time. So my view would be that there should have been a pilot at very small scale before a lot of this was rolled out because the tools that were rolled out were very good but they came, from our perspective, too late."

"I think, again, part of the problem was we came in quite late so I think all the initial work had previously been done so I know there was a lot of pressure put on the (pharmacists) to actually do the initial case studies. Then they felt they waited quite a long time to get feedback. Then when they started collecting the data there was also then some, I suppose, concern about if they had actually been collecting the data correctly. I think that is always the challenge when you're doing a research project is to ensure consistency of actual data collection and the input of the data so you can utilise the results. I think that was barriers for the staff."

"I don't think the project was necessarily listening to what we were trying to say early on. I think if that had happened we could have restructured but we found ourselves in a process that we couldn't get out of and part of that was because that was the way the grant was given. And you need to do X number of reviews etc. to build up the statistical strength. But if that had been tested earlier in large scale... those things might have been worked out."

Participants also discussed finding one incident with a negative outcome due to deprescribing. They went on to say that pharmacists felt that training didn't cover enough on managing short term risks after stopping medication (e.g. cholesterol medications or aspirin), and that pharmacists needed more than the scheduled 15-minute follow-up in order to manage these patients safely.

Resourcing

Participants discussed logistical issues around finding physical space for pharmacists to be present within GP practices. In the Republic of Ireland this was remedied somewhat with remote access and contacting patients over the phone.

"The other challenge would be getting space within the practice to physically be there. So, we had to overcome that by setting pharmacists up with remote access to GP software, and that took time as well."

Ensuring recommendations are actioned

Participants discussed issues around ensuring that pharmacists' recommendations were actioned. In secondary care settings there was a lack of oversight in regard to whether pharmacists' recommendations were actioned once the patient left secondary care. In primary care settings non-prescribing pharmacists were dependent on GP time and ability to action the reviews recommendations:

"…we were doing it in an acute hospital setting we didn't really get to do the follow up so I think that's been some of the difficulty. Recommendations have been made but because at that point the patient is then transferred to primary care we don't know if the recommendations have been actioned because obviously that's beyond the scope"

"So like we were doing the reviews, but the challenge was to get them actioned on time to make them worthwhile, you know. That was definitely a bit of a challenge within the practices."

Multidisciplinary team working

Some participants generally felt that iSIMPATHY had not fundamentally changed the nature of multidisciplinary working but had built on what was already there. Overall, they witnessed good communication between and within teams during the project:

"I think for us it probably hasn't changed the interdisciplinary working 'cause I think…(the pilot site)…does have a really good multidisciplinary team working. They've also tried... really hard to integrate the services and get services working across before. It's probably just fostered... built on that to help with the communication skills of that. I think there's nothing detrimental about what has happened, I think if anything it's just built on the already existing foundations"

The participants discussed how the iSIMPATHY pharmacists facilitated communication between primary care and community pharmacists, sharing relevant information.

"Yeah, just one of the other aspects I was thinking of there was, there was also facilitation of the iSIMPATHY pharmacists' communication with the community pharmacists, you know. So, that worked actually both ways, in terms of like the iSIMPATHY pharmacist was able to get information on the patient's medication history and, say, what their compliance was like and their adherence, but likewise, the community pharmacist had the positive of somebody in the GP practice that they could relate to in terms of particular patients, or like highlighting patients that they felt needed to be reviewed."

"...actually it worked out really well and there was quite a lot of positive feedback from the community pharmacists."

"I think that the iSIMPATHY pharmacists promoted the role very well. You know, they went out, they spoke to the pharmacy teams, they spoke to the medical teams, and they explained what they were doing, and I think that that open relationship helped certainly."

A few participants mentioned how the work of the iSIMPATHY pharmacist changed some of the nature of the interactions between pharmacists and doctors, with more proactive collaboration:

"It is more sort of proactive, med rec, deprescribing. And medicine ownership in a way, rather than just hoovering up all my mistakes as a doctor, which in my early training kind of I viewed the pharmacists as, you know on the ward. Now the pharmacist is a much more integral partner, coming on ward rounds when they can, inputting their decisions that I would do, "Yeah, actually I wasn't aware of that," or, "Oh yeah, I see that this is important." Rather than just going, "Oh yeah, this hasn't been signed," "This is the wrong dose," or, "We have run out of that."

Next steps

Participants discussed what they would like to see moving forward with iSIMPATHY and medication reviews. These views varied considerably by jurisdiction as they were often in reaction to the local context they had experienced at their respective project sites. Northern Ireland and the Republic of Ireland discussed their desire to seek further funding to continue parts of the work that were undertaken during iSIMPATHY.

> **"Yeah, from my point of view I think this should be business as standard now. Whether you roll it out for every patient, or every patient with over ten medicines or whatever, that is a moot point, but I do think there is a lot of value in at least having it as a service."**

There was an agreement across jurisdictions that the most complex patients were the most likely to benefit from this type of medication review, with patient identification and selection an important consideration moving forward:

> **"I think we need to get some evidence data as to patient selection, because we are not going to be able to do this for everybody, and so if we can stratify our patients on who will really benefit, probably will benefit, and probably won't benefit from an iSIMPATHY approach, then you know we can target limited resources. So, I think that is some of the things that I would say just sort of where iSIMPATHY could go."**

The skill set of the pharmacists was raised as a potential risk factor. In both Scotland and Northern Ireland, participants discussed how the programme benefited from experienced pharmacists and a certain level of confidence they brought, as they were often operating in professionally isolated environments and that less experienced pharmacists may struggle navigating the spaces they may find themselves in.

However, in Northern Ireland some participants felt that certain aspects of the work could be delegated:

> **"Yeah, I don't think a Band 8a needs to be doing all this …a really good Band 6 or average Band 7 could do a lot of this quite satisfactorily. I suppose then if we do it with better electronic systems and better link-up with GPs and primary care, a lot of the sort of mistakes and issues that we are saying may be eliminated and thus we free up pharmacists then to do more sort of what they are trained to actually do towards the sweet spot, rather than clearing up the mistakes, which is unfortunately what they seem to be defaulting to in many places"**

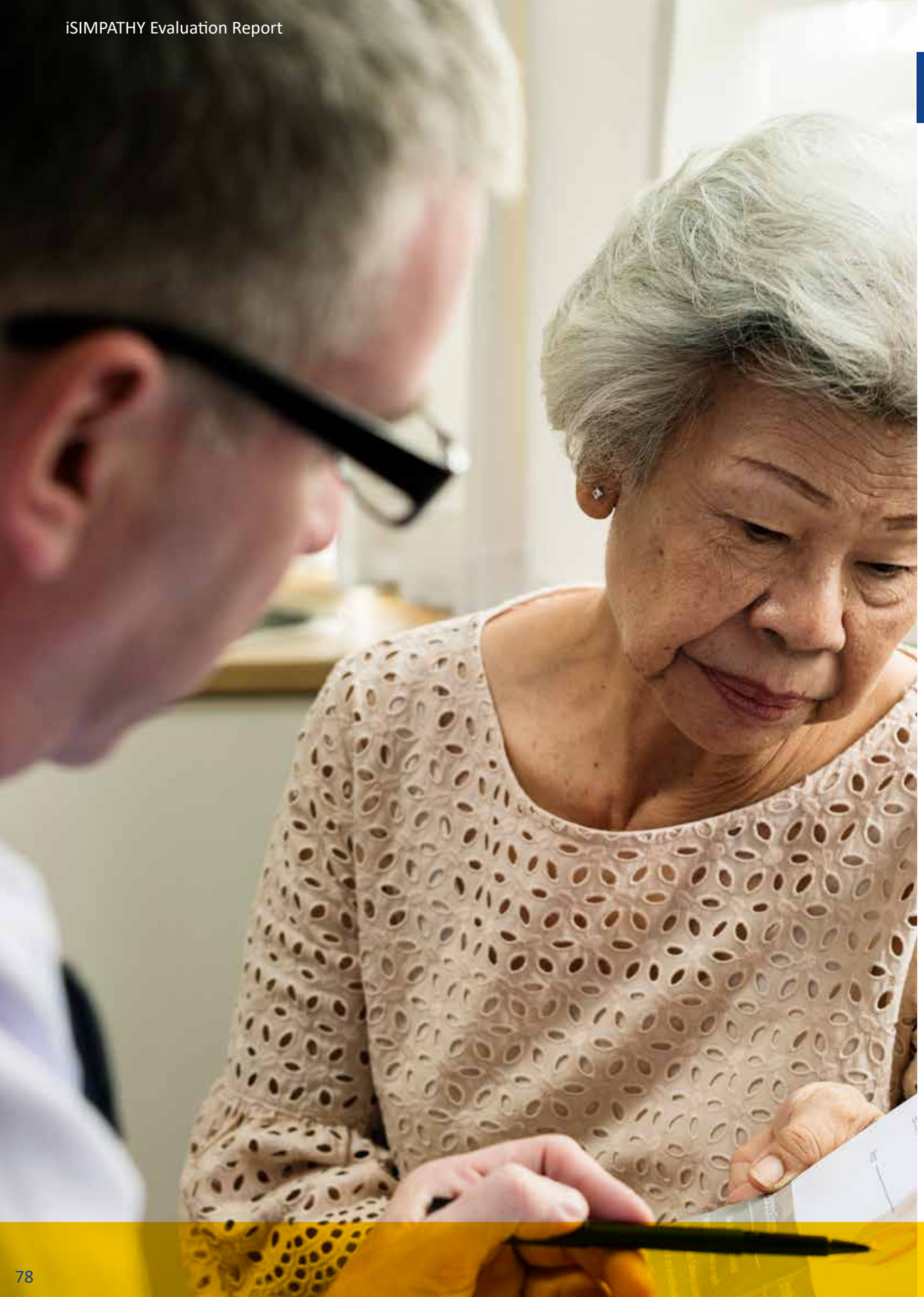
There was a discussion around the need to think about how best to monitor the implementation of the suggestions of the medication reviews. This was particularly pertinent for patients transitioning from secondary to primary care.

Participants in Scotland felt that although there were benefits in conducting medication reviews in secondary care settings, the benefits of the reviews are more pronounced in a primary care setting in that patients can be seen in a more typical environment (as opposed to the acute episode that may have led them to the hospital ward), with potential input from family and carers. This richer context for the reviews was viewed as the preferred model to adopt moving forward.

Participants also mention being sensitive to local context would better position the programme to succeed.

> **"…I think for Scotland it has to fit within the pharmacotherapy service under the general medical services contract, if it doesn't it's constantly butting heads with a process and a flow. It's the right thing to do it's just got to be fitted and better integrated into that model because at the moment for us it's set slightly outside that and that caused a lot of tensions."**

Some participants discussed the need to incorporate senior leaders from the outset in order to ensure appropriate buy-in from the beginning.



5. Discussion

This project was effective in optimising the use of medications in patients with multimorbidity and associated polypharmacy. There has been valuable learning with regards to the introduction of system change in different settings and in terms of development of accredited training materials. These materials were beneficial for the iSIMPATHY pharmacists and are available for healthcare professionals involved in medication prescribing and use.

Patients were selected for review according to inclusion criteria based on the risk stratification and prioritisation set out in the polypharmacy guidance. Most (95%) were on five or more medicines and 35% were on high-risk medicines, i.e. one that when used inappropriately, will have an increased risk of medication-related harm. Polypharmacy and multimorbidity are the two major predictors for experiencing medication-related harm in primary care[80] and among older adults in acute care[81], with age also associated in the latter. Reviews were provided in the care home setting and to those approaching end of life, however, these reviews were under-represented in the submitted data, due to limitations with obtaining consent to data collection and sharing.

Although selection criteria did not restrict reviews to an older population, application of the patient selection criteria resulted in reviews being provided to people with an average age of 72. The profile of people reviewed, and the associated outcomes varied in the three jurisdictions. In the Republic of Ireland and Northern Ireland, the people that were reviewed were older, and more likely to be female, while in Scotland the mean age was lower with more males reviewed. In all three jurisdictions the average socio-economic group was the most common.

This project demonstrated that medication review resulted in improved medication appropriateness, measured using the modified version of the Medicines Appropriateness Index, Person Centred MAI (PC-MAI), developed in conjunction with the MAI developer.

Baseline PC-MAI was associated with the number of medicines pre-review and with the jurisdiction, with lower appropriateness identified in the Republic of Ireland.

The results in this project (mean reduction in PC-MAI of 13.8) are consistent with improvements observed in other pharmacist-led interventions. A Cochrane review found a mean reduction of 6.8 in studies aiming to improve appropriate polypharmacy in older people.[82]

Some of the differences in the pre- and post-review PC-MAI scores were noted between the jurisdictions. It is possible that this may reflect differences in the population distribution, or the difference in application of the selection criteria and settings in which each service was offered. The prior lack of access to clinical pharmacists in GP practices in the Republic of Ireland may be associated with the higher baseline PC-MAI, although patients were also older and prescribed more medicines pre-review than in Scotland. In a small number of cases (8%) there was no improvement in PC-MAI observed following a review; this could be due to the patient's therapy being optimised at baseline and therefore not requiring changes in a review, recommendations not being implemented (due to patient or clinician disagreement) or due to time constraints (recommendation not actioned at the time of data recording).

The average number of medicines prescribed for people participating in reviews decreased from 12 to 11 medicines, due to a combination of medicines stopped, started and doses decreased and increased. Polypharmacy is a risk factor for under-prescribing of appropriate therapies and so medicines optimisation does not necessarily lead to reductions in polypharmacy.[83] Fifty-two per cent of patients saw a decrease in their medication as a result of the review process, with 13% seeing an increase, and 35% staying the same. This mixed picture is what would be expected as the purpose of the structured medication review is to ensure that patients are taking medications appropriate for their conditions and thus not simply to reduce per se but most importantly ensure appropriate polypharmacy for the individual.

The number of medicines pre-review was the greatest predictor of number of medicines post-review, and accounted for the vast majority of the variance in the model. If number of medicines pre-review was excluded from the model, then the number of medicines post-review was most associated with the number of multiple long-term conditions, with a much smaller association with gender, region and socio-economic status.

Patients residing in the least deprived areas were on the lowest numbers of medicines pre-review, their medications were more appropriate compared to the average deprivation group (but not the most deprived group) prior to their review (lower PC-MAI) and they received the lowest number of interventions. Improvement was seen in each socio-economic grouping between pre- and post-review. The members of the least deprived socio-economic group appeared to have benefited more from the review process, as they were found to have significantly less inappropriate prescribing post-review than the other two groups, who had similar levels of inappropriate prescribing post-review. The most and average deprivation groups appeared to have benefited equally from the review process, suggesting that socio-economic status alone is not solely explaining the difference found between the least deprived and other groups post-review.

Multiple interventions were made in each review, most commonly medication changes and patient education. Education and information sharing is core to the 7-Steps approach incorporating “What matters to me”. This resulted in improved understanding and enabled shared decision-making with empowered patients. Multivariate analysis established the number of medicines pre-review as the best predictor of the number of interventions a pharmacist was likely to make.

The vast majority of interventions were Eadon grade 4[84] and above meaning that they were deemed likely to result in a clinically significant improvement to patient care. Nine hundred and sixty-eight (4% of interventions recorded) were rated as preventing major morbidity and organ failure. Notably, none of the interventions made were categorised as being clinically detrimental. Unaltered and unresolved interventions accounted for 6% of the total indicating that 94% of interventions were accepted. This spread of intervention grades observed in this project mirrors the results achieved in other pharmacist-led intervention studies for example in the intermediate care setting.[85]

Polypharmacy indicators are associated with an increased likelihood of a serious adverse outcome, due to medication and/or patient or disease factors.[86] Pharmacists prioritised addressing some of these indicators, in particular those associated with bleeding and falls risks. Risks from polypharmacy indicators were resolved in 77% of cases where they were identified, a high level of efficacy in addressing indicators which are often complex to resolve. In some cases, the risk will have been reduced but not removed (e.g. reducing the number or dose of sedative or anticholinergic medicines) and in some cases, it is not appropriate to address the indicator due to patient factors, e.g. active bleeding preventing prescribing of an anticoagulant.

A person-centred approach is central to the 7-Steps methodology, starting with “What matters to you?” Patient reported outcome measures (PROMs) were used to gain an understanding of this.

A relatively small number of PROMs were received and there was variability in number across the jurisdictions. PROMs measures may therefore not be representative of all project participants. There was a low level of patient engagement with the digital version of PROMs app with regard to their independently uploading the responses and the majority of responses reported were uploaded with support from the pharmacist conducting the review. This may have led to some degree of bias in responses.

The PROMs received indicated improvements in a range of areas including patient understanding, reduced side effects and some aspects of adherence. Some patients reported an improvement in ability to perform usual activities and better ‘activity’, ‘pain/discomfort’ and ‘anxiety/depression’ scores were reported post-review in the EQ-5D-3L measures. This suggests an improvement in health-related quality of life. The following comment highlights the value that patients attached to the review process:

> **“huge improvement walked for half an hour this morning used to have to stop every few minutes because of the dizziness”.**

Two approaches to the health economic evaluation were undertaken.

Using a bottom-up approach, an economic value can be attached to each intervention graded using the Eadon scale. This was based on an original piece of work developed by Karnon et al. but updated to reflect current values.[87]

Based on work conducted by the Scottish Government Polypharmacy Model of Care Group the avoided associated healthcare costs were calculated.[88] A second, top-down approach was based on attributable factors derived from the academic literature and applied to the total admission numbers in the three jurisdictions estimating the maximum total avoided admissions due to Adverse Drug Reactions (ADRs) and consequently associated bed days. Both analyses reported positive findings.

The average total costs avoided from associated healthcare resource utilisation was £168,800 (€197,800) per 100 cases and in addition the QALYs gained was 7.4 per 100 cases.

The results demonstrated that per 100 cases there were 0.9 avoided admissions and 8 days of avoided inpatient costs. If comprehensive medicines reviews were provided to all patients aged 65 and over taking five or more medicines in each country (75+ in Northern Ireland), the maximum avoidable inpatient cost would be £24.7 million (€28.9 million) for the Republic of Ireland; £11.0 million (€12.9 million) for Northern Ireland; and £36.0 million (€42.1 million) for Scotland.

The intervention cost £7,500 (€8,786) to deliver per 100 cases.

It is clear that there are large healthcare resource utilisation benefits to be accrued by the implementation of this structured medication review approach. The total cost reduction from net medication changes alone would more than outweigh the staff cost for the Republic of Ireland and Scotland. With either the bottom-up or top-down approaches to economic analysis, the benefits (cost avoidance) would outweigh the associated direct cost in all three regions. There are clear synergies with the benefits achieved by such pharmacist-led work in other countries.[89,90,91]

When delivering healthcare improvements and improving patient safety, it is important to deliver the quadruple aim,[92] the need to improve patient outcomes, cost effectiveness, patient experience and staff satisfaction. This will also help develop the culture to address medication safety. Determining staff satisfaction was carried out by seeking the views of the project pharmacists and managers in interviews and a survey of the wider multidisciplinary team (MDT).

Qualitative work with the project pharmacists, as well as regional management found widespread positivity with regards to participants' experience with iSIMPATHY. The other HCPs involved in the project also expressed many positive consequences of their involvement in the project, with all those surveyed hoping the project would continue moving forward.

Most notable positive experiences appeared to centre around the shift towards a more person-centred approach to care, and the benefits to the patients that were observed through the adoption of the iSIMPATHY methodology. Indeed, many participants commented on how involvement in the project had permanently influenced how project pharmacists and other healthcare staff would approach patients well beyond their time in the iSIMPATHY programme. The opportunities for professional development that the project afforded those involved, the improved understanding of the value of medication reviews and the role of the pharmacist amongst members of the pharmacists' MDTs, were other advantages noted.

Pharmacists felt both communication and patient selection criteria were clear. They also stated that engaging in such a medicines review service improves the care that patients receive making patients more confident about their medicines and indeed empowering them in this respect. From an organisational perspective the project pharmacists felt that the other HCPs involved could see the value of having this service available as part of overall care.

Despite the challenges of COVID-19, the pharmacists in most cases were able to adapt and deliver the reviews through alternative methods such as telephone review. Pharmacists felt that the implementation would have benefited from more standard operating procedures and project support from the outset, especially where the role was new for the pharmacists. Dedicated time for the reviews was seen as a success factor and welcomed by patients. Pharmacists also reported that the reviews led to other positive patient lifestyle choices such as smoking cessation, or dietary changes that had an impact on their cardiovascular risk. The pharmacists said that patients felt more empowered and engaged in the decision making following a review.

The pharmacists raised issues that were challenging to the implementation of the project and indicated that more support was needed to implement change at practice level. The pharmacists reported that the iSIMPATHY methodology was incorporated into other areas of practice and promoted collaborative ways of working within the multidisciplinary team.

The majority of respondents to the multidisciplinary team survey (primarily GPs and non-project pharmacists) felt that the iSIMPATHY methodology had a positive effect on:

- the quality of the medication review conducted
- patients' adherence to their medicines
- medication safety
- patient knowledge and understanding of their medicines
- patient satisfaction with their care
- patient quality of life

Respondents were satisfied with the medication safety culture in the setting in which the medication reviews took place. They felt that involvement in iSIMPATHY had positively impacted both their and colleagues' job satisfaction and felt well supported by the project. All respondents said they would welcome a continuation of the service delivered by the project. Good communication, availability of necessary funding and support for/engagement with project were the most commonly referenced enablers to successful implementation of the iSIMPATHY programme if it was to be scaled up nationally.

Managers in all three jurisdictions spoke positively about their involvement in the iSIMPATHY programme, noting positive developments including a greater focus on person-centred care and patient safety, good working relationships within teams and between professions, an increase in the perceived value of medication reviews and enhanced professional development and knowledge transfer among the project pharmacists and multidisciplinary teams.

Challenges included recruitment delays, the effect of COVID-19 restrictions and communication between sites and programme leadership. Time pressure to deliver reviews and establishing new project roles were noted to be particularly challenging.

Managers were focussed on the next steps in seeking future expansion of this service, ensuring that resources and delivery would be secured to deliver the most effective medicines review service in the future.

6. Conclusions and next steps

The project delivered on the key areas of improving medication safety via ensuring appropriate prescribing of medications in patients with multimorbidity, improving adherence via enhanced patient knowledge and empowerment. The project illustrated the continual need for the use of change management methodology to support implementation, in particular addressing the barriers and enablers, for example, raising awareness and setting out the urgency in addressing the challenge among patients, the public, wider healthcare teams, policy makers and health and care leadership.

There were cost-savings relating to both medicines changes as well as via minimising medication-related harm. The analysis indicated that there were health benefits of 7.4 QALYs gained per 100 cases, and sustainability benefits via improved patient understanding and adherence to their medications thereby reducing the associated carbon footprint.

The key outcomes and benefits are informing business cases to scale and spread this approach, where investment is required. Work is underway to incorporate the person-centred comprehensive medicines review model used in iSIMPATHY into mainstream use and guidance. Barriers such as competing priorities need to be addressed if medication reviews are to be incorporated into patient pathways. Patient awareness and empowerment to be active participants in the review is crucial, with this service supporting this very successfully.

Publications in more specific detail peer reviewed journals would facilitate adoption of the methodology beyond the three project jurisdictions.

7. Recommendations

The project illustrates the importance of implementing the six key recommendations from the SIMPATHY project. The following would facilitate the implementation of the iSIMPATHY methodology:

- **Ensure the 7-Steps methodology is adopted when reviewing medicines with people with multimorbidity, improving understanding and facilitating shared decision making with empowered patients.**
- **Ensure adequate dedicated pharmacist capacity is available to deliver comprehensive person-centred medicines reviews with those with complex polypharmacy. Steps should be taken to work with policy makers, patients, clinical leaders and finance colleagues to ensure the scale and spread of this methodology into routine practice.**
- **Ensure appropriate capability among those delivering medicines reviews. This is supported by guidance, training and peer and professional support.**
- **Support patient awareness and empowerment to be active participants in the review, informed by patient involvement in the design of the delivery of the service. Where required, adequate support should be provided such that patients can use digital technology e.g. PROMs.**
- **Processes, documentation and supports require development with a lead time before delivery of reviews.**
- **Further work should be undertaken to identify factors which would help prioritise those who would benefit most from a review.**
- **When undertaking scale and spread, further work is required to embed innovation and new technology. This could include the role of AI in predicting those who would benefit most from a review and the use of pharmacogenomics to inform prescribing decisions.**

ANNEX A Health Economic Analysis – Full Report

1. Introduction and Background

This Annex describes the analyses of the economic costs and benefits associated with polypharmacy reviews undertaken as part of the iSIMPATHY project. The project trained healthcare professionals to deliver effective medicine reviews across the three jurisdictions of Northern Ireland (NI), Scotland and the border areas of the Republic of Ireland (ROI) by the end of March 2023.

Methodology for this cost consequence analysis is largely based on preceding work carried out for the earlier SIMPATHY project. Costs considered are healthcare resource costs for healthcare professionals carrying out the reviews, (reduced) medicines cost from net medication changes, and hospital admissions (stays) averted. Possible benefits achieved through medicines reviews and medication optimisation are estimated in the form of Quality Adjusted Life Years (QALYs) gained in a bottom-up approach, and adverse drug reactions (ADRs) averted in an alternative, top-down approach.

Results are presented for the number of cases and interventions recorded in the iSIMPATHY project, and for 100 cases to make individual estimates comparable. Table 16 provides an overview of the number of cases and interventions associated with iSIMPATHY. There can be multiple interventions per case. Note that, only a subset of the total number of recorded cases had interventions recorded. The total number of interventions linked to Eadon scores and the total number of cases with an interventions record (all of which consented) were used to derive an estimate for interventions per case. Each of these cases was also associated with an additional two educational interventions, recorded separately - see section 4.1 for further detail.

Table 16: Overview of number of cases and interventions

Cases / Interventions	ROI	NI	SCO	Total
Total cases in project	2,336	1,485	1,112	4,933
- of which consent given	1,898	613	681	3,192
-- for which we have Eadon scores	1,549	612	462	2,623
Total interventions recorded in project	17,865	4,660	5,834	28,359
- Interventions with Eadon scores	14,766	4,654	4,055	23,476
Interventions per case	9.5	7.6	8.8	9.0
Addn'l general education interventions at Eadon=4[1]	3,098	1,224	924	5,246

[1]2 additional interventions per case, see chapter 5.1

2. Methodology

A bottom-up approach was taken to estimate staff cost associated with reviews, differentiating the different system setups of the three administrations. A unit staff cost per minute of pharmacist time was estimated and applied to the recorded time for reviews. Time taken by pharmacists to record data in the project was recorded separately, and results are shown including and excluding this additional administrative element, as this was arguably more labour intensive for the project than it would be for a regular review.

For ROI, an additional GP fee per review of €17.50 (£16)[93] was added for each case. In NI, all reviews are undertaken by prescribing pharmacists in the hospital setting with GP/doctor input considered to be standard practice and not costed here. In Scotland, reviews are undertaken in both primary and secondary care settings and the average recorded doctor time was included – although not financed by the iSIMPATHY project – rather than a fee per review.

Total results of staff cost therefore only give a broad indication, with regional variation depending on the system setup. It should also be noted that, although these staff costs can be directly attributed to the carrying out of reviews, the estimated time costs are best regarded as opportunity costs where the clinicians' time could have been used otherwise.

Net medication changes are calculated directly from recorded interventions in the project. A central average cost per item is applied to the net changes, based on the latest information available from BNF[94] for Scotland and NI, and from PCRS[95] data for ROI and it is assumed that the average cost per item applies to one prescription for 28 days. Stopping one chronic medication during a review has been costed as delivering savings over a one-year period following the review, with 12 repeats (13 total for one year) also being stopped. This may be a conservative estimate of cost avoidance, where the medication may not otherwise have been dispensed over a number of years. Cost savings to the healthcare system associated with reduced dispensing fees when an item is discontinued have not been included in the economic analysis. These additional savings apply across the three jurisdictions.

To estimate further cost avoidance and health benefits we took two independent approaches.

Approach 1, bottom-up, applied economic values of cost avoidance and QALY gains to the Eadon scores recorded for each intervention[96] as part of iSIMPATHY. Associated economic values are taken from a systematic review of interventions preventing medication errors by the University of Sheffield.[97]

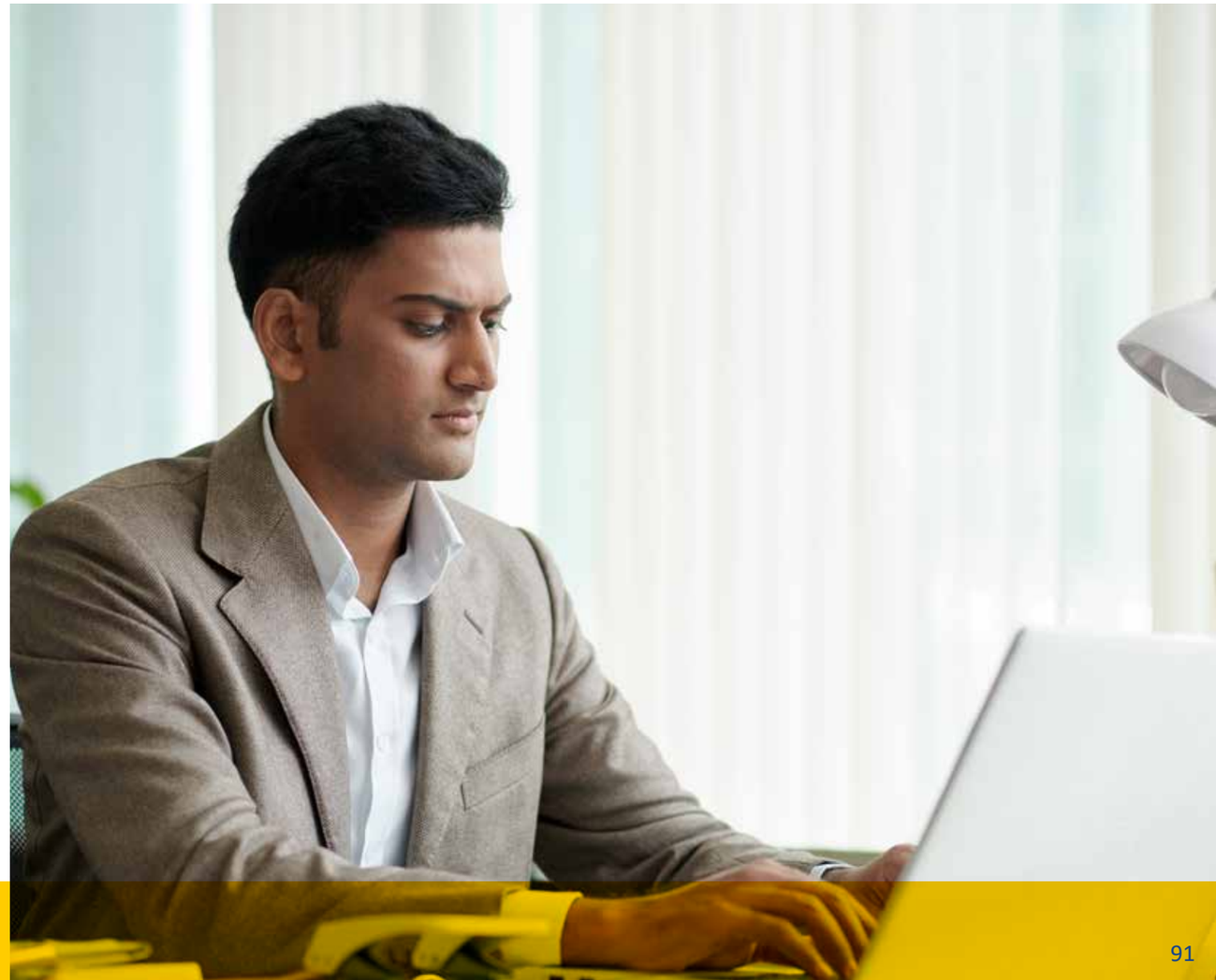
The Sheffield review synthesises previous literature to generate estimates of the costs incurred and QALY loss from a medication error at different levels of severity as defined by Eadon. A range of estimates was derived from two approaches: litigation payments for cases of medication errors resulting in adverse health consequences were attributed to associated QALY loss based on the NICE implied range of value of a QALY of between £20,000 (€23,000) and £30,000 (€35,000) per QALY gained; secondly, estimates of QALY losses were made by assuming a utility decrement for each category and an accompanying duration of effect. These approaches were combined into associated QALY loss ranges and the mid-point used in the Sheffield model[98] (see summary input Table in section 6).

A strong assumption is made here that the inverse of costs incurred and QALY loss from medication error holds true – that is, the avoidance of a medication error will yield the equivalent level of cost avoidance and QALY gain. However, this assumption seems plausible in cases where individuals were able to exercise, sleep and work again due to not being as ill following a medication review. It should also be noted that these benefits are for avoided cost and QALY gain and are therefore not cash releasing.

Note also that an additional two scores reflecting general education during reviews were added per each intervention, scored at Eadon level 4. These were consistently carried out during the project, but not recorded in the data recording system. There is also some scope for variation within the recorded Eadon scale levels, with an observed centring around level 4, however, to counteract this a quality assurance process was put in place for the pharmacists at the outset of the iSIMPATHY project with written instructions and peer sessions in order to achieve standardised Eadon scoring.

For approach 2 on projected benefits, we assessed the potential number of avoidable ADR related hospital admissions using a range of attributable fractions from literature. We apply estimates of the proportion of hospital admissions attributable to ADRs to stratified populations and associated admissions from each country. To this we apply estimates of the proportion of ADRs that are avoidable or potentially avoidable. We applied an estimate that 50% of potentially avoidable ADR admissions would be avoided with an iSIMPATHY medication review, and we include that assumption here to derive the potential productive opportunity (PPO) that could be achieved from ADR-related admissions avoided by medication review.

Although these estimates are not directly linked to the data recorded by iSIMPATHY, the resulting ADR-admissions avoided through medication reviews are extrapolated for the total cases recorded by iSIMPATHY and for 100 cases. Section 4.2 provides further detail on the analysis. All cost data were inflated to 2022 prices using the ONS CPI Health inflation index.[99] More information on input data and assumptions is provided in section 6.



3. Healthcare practitioner and (avoided) net medication change cost

3.1 Staff cost

Tables 17 and 18 show the recorded staff times for reviews and the results for a bottom-up staff costing approach respectively, applying a unit cost per minute to pharmacist time and to GP/doctor time where applicable. For ROI, an additional GP fee per review of €17.50 (£16)[100] was added for each case. In NI, all reviews are undertaken by prescribing pharmacists in the hospital setting with GP/doctor input considered to be standard practice and not costed here.

In Scotland, reviews are undertaken in both primary and secondary care settings and the average recorded doctor time was included – although not financed by the iSIMPATHY project – rather than a fee per review. Added recorded pharmacist time for data collection is identified separately, and results are shown including and excluding this additional administrative element, as this was arguably more labour intensive for the project than it would be for a regular review.

Total results of staff cost only give a broad indication, with regional variation depending on the system setup. Staff posts were directly funded by iSIMPATHY specifically for the purpose of carrying out reviews. In other circumstances, where capacity is available to carry out comprehensive medicines reviews within existing healthcare resources, the estimated time costs are best regarded as opportunity costs where the clinicians' time could have been used otherwise.

Table 25 in Section 6 provides background detail on staff cost assumptions, based on PSSRU[101] and ROI Department of Health Consolidated Salary Scales.[102]

Estimates for total associated staff costs ranged from £3,200 (€3,747) to £13,400 (€15,693) per 100 cases excluding time spent on data collection, with a total average of around £7,500 (€8,786) per 100 cases. Total cost per 100 cases including data collection ranged from £4,800 (€5,620) to £13,500 (€15,810), with a total average of around £8,500 (€9,960).

Table 17: Average staff time recorded

Staff time (minutes)	Region						All	
	ROI		NI		SCO			
	Average per review	CI	Average per review	CI	Average per review	CI	Average per review	CI
Pharmacist time (pre, during, post)	127.7	(124.9,130.5)	46.9	(43.8,50.1)	94.8	(90.3,99.2)	96.0	(93.8,98.1)
Pharmacist data collection time	12.89	(12.5,13.3)	11.59	(10.8,12.4)	17.87	(16.2,19.6)	13.7	(13.3,14.2)
Total pharmacist time[1]	138.5	(135.4,141.5)	51.6	(48.2,55.1)	108.6	(103.3,113.9)	105.6	(103.2,108)
Doctor time[2] (pre, during, post)					1.0	(0.8,1.3)		

[1]total pharmacist time (review and data collection) estimated based on average of number of entries and estimated total minutes

[2]only reported for Scotland, as ROI=fee per review and NI = prescribing pharmacist only

Table 18: Staff cost associated with average review time

Staff cost (£)	Region						Average for all regions	
	ROI		NI		SCO			
	Cost	Confidence Interval	Cost	Confidence Interval	Cost	Confidence Interval	Cost	Confidence Interval
Per case								
Pharmacist time (pre, during, post)[1]	£108	(£106, £110)	£32	(£30, £35)	£66	(£62, £69)	£69	(£66, £71)
Pharmacist data collection time[1]	£11	(£10.6, £11.21)	£8	(£7, £9)	£12	(£11, £14)	£10	(£10, £11)
Total pharmacist time	£119	(£116, £122)	£40	(£38, £43)	£78	(£74, £82)	£79	(£76, £82)
Total GP review fee	£16	(£16, £16)	n/a		n/a		n/a	
Doctor time[2] (pre, during, post)	n/a		n/a		£1.6	(£1.19, £1.89)	n/a	
Total per case, excl. data collection	£124 (€145)	(£122, £126) (€143, €148)	£32 (€37)	(£30, £35) (€35, €41)	£67 (€78)	(£64, £71) (€75, €83)	£75 (€88)	(£72, £77) (€84, €90)
Total for 4,933 cases	£289,700 (€339,340)	(£284,200, £295,300) (€332,844, €345,844)	£48,200 (€56,460)	(£45,000, £51,400) (€52.700, €60,198)	£74,600 (€87,369)	(£70,800, £78,400) (€82,919, €91,828)	£412,600 (€483,244)	(£399,900, £425,200) (€468,425, €498,060)
Number of cases in each region	2,336		1,485		1,112		4,933	
Total for 100 cases in each region, excl. data collection	£12,400 (€14,525)	(£12,200, £12,600) (€14,289, €14,757)	£3,200 (€3,748)	(£3,000, £3,500) (€3,515, €4101)	£6,700 (€7,847)	(£6,400, £7,100) (€7,499, €8,320)	£7,500 (€8,784)	(£7,200, £7,700) (€8,437, €9,023)
Total for 100 cases in each region	£13,500 (€15,814)	(£13,200, £13,800) (€15,459, €16,162)	£4,000 (€4,685)	(£3,800, £4,300) (€4,423, €5,038)	£7,900 (€9,253)	(£7,500, £8,400) (€8,789, €9,843)	£8,500 (€9,950)	(£8,200, £8,800) (€9,608, €10,311)

[1]Band 8a pharmacist/ ROI: Senior Pharmacist mid-point

[2]only reported for Scotland, as ROI=fee per review and NI = prescribing pharmacist only

3.2 Net medication change

Table 19 provides a high-level overview of net medication changes recorded in the three administrative areas. Table 27 in section 6 provides further background detail on net medication differences (increase/ reduction before and after review).

Table 19: Net medication change

Total review cases, net medication change	Region						Totals / Averages	
	ROI		NI		SCO			
	Number	CI	Number	CI	Number	CI	Number	CI
Total cases (incl. interventions record)	1,898		613		681		3,192	
Average # medicines before review	12.2	(12,12.4)	12.0	(11.7,12.4)	10.9	(10.6,11.3)	11.9	(11.7,12.1)
Average # medicines after review	11.0	(10.8,11.2)	12.0	(11.7,12.4)	10.0	(9.7,10.3)	11.0	(10.8,11.1)
Average medication difference	-1.24		0.00		-0.92		-0.93	

Table 20 shows the estimated cost implications when applying average unit costs onto the observed net medication changes. Stopping one chronic medication during a review has been costed as delivering savings over a one-year period following the review, with 12 repeats (13 total for one year) also being stopped.

Whilst ROI and Scotland saw net drug reductions of 1.24 and 0.94 items per review respectively, net change observed for NI close to zero.

Cost implications from net medication changes ranged from zero (no change) for NI to a reduction of £14,700 (€17,226) and £24,700 (€28,945) per 100 cases in Scotland and ROI respectively. The average net reduction across all regions was estimated to be around £13,100 (€15,351) per 100 cases.

Table 20: Average cost per item dispensed

Total review cases, net medication change, associated cost change (£)		Region			Total
		ROI	NI	Scotland	
Per case	Average medication difference per case	-1.24	0.00	-0.94	-0.80
	Average associated cost reduction / increase per case	-£247 (-€289)	£0	-£147 (-€172)	-£131 (-€153)
For 4,933 cases	Cases	2,336	1,485	1,112	4,933
	Net medication difference	-2,897	0	-1,023	-4,588
	Net associated cost reduction / increase	-£576,800 (-€675,844)	£0	-£160 (-€187)	-£736,900 (-€863,471)
Per 100 cases in each region	Cases	100	100	100	100
	Net medication difference	-124	0	-94	-80
	Net associated cost reduction / increase	-£24,700 (-€28,943)	£0	-£14,700 (-€17,224)	-£13,100 (-€15,350)

BNF 2018/19 average cost per item, inflated to 2022 prices, for NI and Scotland

PCRS 2021/22 average cost per item, inflated to 2022 prices, for ROI

assumed 1 new prescription and 12 repeats per item for annual cost (1 per 28 days)

4. Healthcare cost avoidance and patient benefits

4.1 Approach 1: Linking recorded Eadon scores to cost avoidance and QALY gains

Here, we apply economic values of cost avoidance and QALY gains to the Eadon scores recorded for each intervention[103] in a bottom-up approach. Associated economic values are taken from a systematic review of interventions preventing medication errors by the University of Sheffield.[104] See the Methodology section on the underlying derivation of the cost avoidance and QALY values and on assumptions made. Table 29 in section 6 provides background detail on Eadon scores, cost and QALY consequences of intervention.

Quality Adjusted Life Year (QALY)

The NICE definition of a QALY states that a QALY is: "A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health."

Example

Campbell et al (2014) estimate a potentially life-threatening medication error to cause an average loss of 2.7 QALYs. In our assumption that the inverse holds true (described in section 4), an intervention that leads to an Eadon score of 6 (potentially lifesaving) would therefore generate 2.7 QALYs, i.e. the person would benefit from an average 2.7 additional years spent in perfect health (or an equivalent of more years spent in less than perfect health).

Tables 21 and 22 provide the results of approach 1, for 28,721 interventions with Eadon scores linked to cases, and per 100 reviews, both in terms of cost avoidance and QALY gain.

Total avoided costs from avoided associated healthcare resource used were estimated at between £146,600 (€171,757) and £176,600 (€206,898) per 100 cases across the three administrations (total average £168,800 (€197,800).

Total QALYs gained associated with recorded Eadon scores were estimated at between 7.0 and 8.3 QALYs per 100 cases for the three administrations (average 7.4 per 100 cases). (see Table 22 for detail)

Table 21: Avoided healthcare resource cost summary

£	For 28,721 interventions, incl. standard interventions				Per 100 cases				For 4,933 cases			
	Region			Total**	Region			Total**	Region			Total**
	ROI	NI	Scotland		ROI	NI	Scotland		ROI	NI	Scotland	
Eadon 1	£0	£0	£0	£0	£0	£0	£0	£0	£0	£0	£0	£0
Eadon 2	£1,400	£0	£200	£1,500	£100	£0	£0	£100	£4,300	£0	£1,700	£2,900
Eadon 3	£11,000	£1,100	£2,100	£14,300	£700	£200	£500	£500	£35,100	£9,200	£22,900	£26,900
Eadon 4	£1,427,800	£536,500	£443,100	£2,407,400	£92,200	£87,700	£95,900	£91,800	£4,546,900	£4,324,700	£4,731,200	£4,527,500
Addn'l general education interventions at Eadon=4	£409,400	£161,800	£122,100	£693,300	£26,400	£26,400	£26,400	£26,400	£1,303,800	£1,303,800	£1,303,800	£1,303,800
Eadon 5+6*	£819,700	£381,400	£109,800	£1,310,900	£52,900	£62,300	£23,800	£50,000	£2,610,400	£3,074,500	£1,172,200	£2,465,400
Total	**£2,669,200 (€3,124,284)**	**£1,080,900 (€1,265,187)**	**£677,300 (€792,693)**	**£4,427,400 (€5,181,706)**	**£172,300 (€201,655)**	**£176,600 (€206,708)**	**£146,600 (€171,590)**	**£168,800 (€197,800)**	**£8,500,600 (€9,949,694)**	**£8,712,300 (€10,197,482)**	**£7,231,800 (€8,463,853)**	**£8,326,500 (€9,745,052)**

* Eadon scores 6 added to Eadon scores 5 for non-disclosure reasons. Differential costs applied to underlying data

**includes additional cases which were not assigned a deprivation score. Numbers may therefore not add up across scores

Table 22: QALY gain summary

QALYs	For 28,721 interventions				Per 100 cases				For 4,933 cases			
	Region			Total**	Region			Total**	Region			Total**
	ROI	NI	Scotland		ROI	NI	Scotland		ROI	NI	Scotland	
Eadon 1	0	0	0	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Eadon 2	0	0	0	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Eadon 3	0	0	0	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Eadon 4	50	20	20	80	3.1	3.0	3.3	3.1	154.8	147.3	161.1	154.2
Addn'l general education interventions at Eadon=4	10	10	0	20	0.9	0.9	0.9	0.9	44.4	44.4	44.4	44.4
Eadon 5+6*	50	20	20	90	3.0	3.9	4.1	3.4	145.9	192.8	204.1	167.1
Total	**110**	**50**	**40**	**190**	**7.0**	**7.8**	**8.3**	**7.4**	**345.2**	**384.5**	**409.6**	**365.7**

* Eadon scores 6 added to Eadon scores 5 for non-disclosure reasons. Differential QALY scores applied to underlying data

**includes additional cases which were not assigned a deprivation score. Numbers may therefore not add up across scores

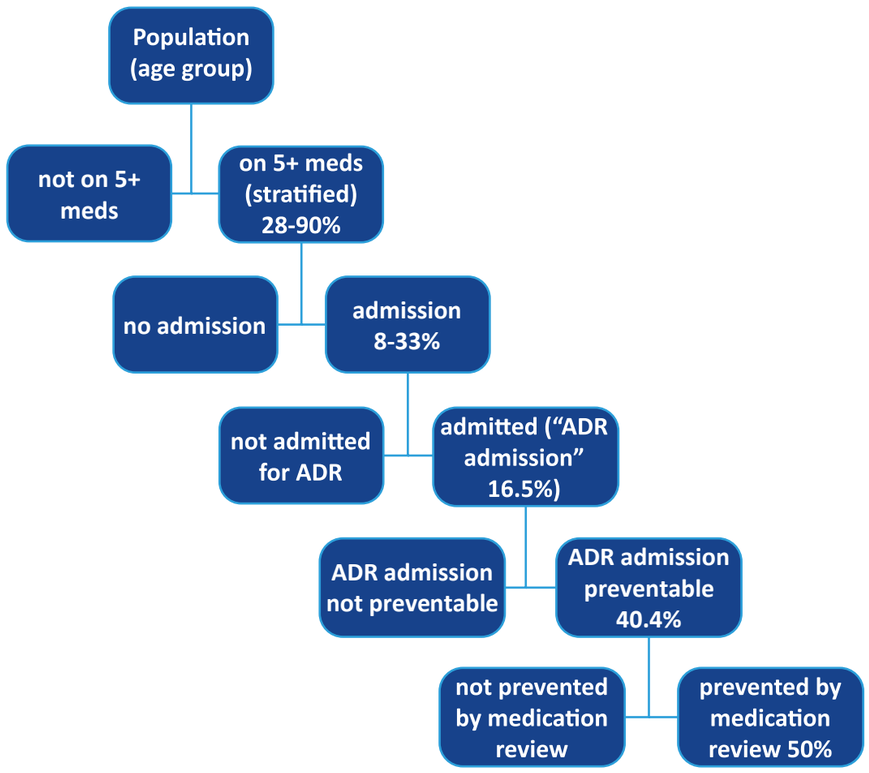
4.2 Approach 2: Theoretical projection of potential avoided admissions

Approach 2 can be seen as a lone-standing case study and it is important to note that it is independent of the reviews undertaken as part of iSIMPATHY, although estimates are projected onto the sample numbers for the iSIMPATHY project. It is a **top-down** approach based on attributable fractions derived from academic literature and applied to total population and total admission numbers in the three administrations and estimates the maximum potential avoided admissions due to ADR and consequential avoided bed days and inpatient cost.

We obtained data on the population sizes for cohorts aged 65+ in ROI and Scotland, and 75+ in NI, numbers of inpatient admissions associated with this age band, and stratified population estimates (for those aged 65+ or 75+ on 5 or more medications, ranging between 55-90% of the total populations) for each of the three jurisdictions. We apply the same proportions of admissions per population (range between 23-33%) to the stratified population estimates to estimate the number of admissions associated with the stratified population.

Osanlou et al (2022)[105] estimate the proportion of hospital admissions attributable to ADRs to be 16.5% of which 40.4% are estimated to be avoidable or possibly avoidable. Not all of the potentially avoidable ADR admissions will be prevented through medicines reviews. We have made the assumption here that around 50% of potentially avoidable hospital admissions linked to ADRs could be avoided following a medicines review.

When applying these assumptions in combination, it is possible to estimate a factor of how many ADR-related hospital admissions for a given population would have taken place but are instead avoided due to a medicines review.
The schematic demonstrates the cascading assumptions applied to a population.



We applied the factor to the estimated number of admissions for the stratified populations to estimate the number of ADR-admissions avoidable by medication review. From this, the maximum total associated avoidable inpatient bed days and associated cost were also estimated.

Table 23 summarises the data and estimates for the three administrations and outlines individual comments on data and assumptions made.

Worked example of the cascade of proportions applied to stratified admissions data:

For a Scottish population of 1,073,900 people aged 65+, the stratified population on 5+ medications was 594,800 (55%). There were 249,700 recorded inpatient admissions for the cohort (23%) and applying that proportion to the stratified cohort gave 138,300 admissions associated with people on 5+ medications. From Osanlou et al (2022), 22,800 (16.5%) of these admissions can be expected to be caused by an ADR, of which 9,200 (40.4%) are avoidable or possibly avoidable. Assuming 50%, 4,600 of these admissions would be avoidable by medication review (3.33% of stratified admissions, or 0.8% avoided admissions in the stratified population).

The population-level estimates were then extrapolated to the iSIMPATHY sample of 4,933 cases and to 100 cases, assuming that these samples would have been taken from the same stratified population. Results are shown in Table 24. The resulting numbers are noticeably conservative, given the cascade of attributable fractions applied to the original sample as per the worked example above.

The estimated maximum number of avoidable admissions ranged from 3,700 in ROI; 1,500 in NI; and 4,600 in Scotland if the full population of those aged 65 and over (75+ in NI) taking five or more medicines received a comprehensive medicines review.

The associated maximum avoidable inpatient cost ranged from £24.7 million (€28.9 million) for the Republic of Ireland; £11.0 million (€12.9 million) for Northern Ireland; and £36.0 million (€42.1 million) for Scotland.

Assuming cases are drawn from the stratified population, 100 reviewed cases would be associated with between 0.8 and 1.1 avoided admissions (weighted average 0.9), 7 to 10 avoided inpatient days (weighted average 8 days), and an avoided inpatient cost of between £5,900 (€6,904) and £8,100 (€9,478) (average £6,600 (€7,723)).

These estimates are conservative and are based on a number of strong assumptions. Varying assumptions such as the relationship between stratified populations and admission rates significantly impacts the results.

4.2.1 Sensitivity analysis: Increasing the target population to 50+

Including a bigger cohort of all aged 50+ in the group for consideration for medicines review significantly increases the population size (from 1.86m to 4.38m, or 135% increase for the three regions), but doesn't proportionately increase the stratified population (increase from 1.15m to 1.93m or 68% increase) and the associated admissions (increase from 470,000 to 710,000, or 52% increase). That is because the majority of admissions fall into the higher age-bands. The estimated number of avoidable ADR-related admissions therefore also rises less than proportionately, from 9,800 to 12,300, or 26%.

As a result, the extrapolated estimate of average number of ADR-related admissions avoidable for 100 reviews decreases from 0.9 admissions, if carried out in the 65+ (75+ in NI) group, to 0.7 admissions, if they were to be carried out in the larger, less focused, group of 50+.

Table 23: ADR-related admissions avoidable from medication reviews, associated inpatient days and cost

Potentially avoided admissions	ROI		NI		Scotland		Comments
	Age band		Age band		Age band		
Population	65+	637,600	75+*	151,500	65+	1,073,900	*note different age bands, due to data availability
Stratified population: on 5+ meds	65+	417,000	75+	136,400	65+	594,800	
Stratified population: on 5+ meds (%)	65+	65.4%	75+	90.0%	65+	55.4%	
Admissions	65+	167,600	75+	50,100	65+	249,700	NI: Admissions by age band from data request, DoH NI
Admissions in people with 5+ meds	65+	109,600	75+	45,100	65+	138,300	assumption that % 5+ meds in population also applies to % admissions
Maximum ADR admissions avoidable by med review	65+	3,700	75+	1,500	65+	4,600	16.5% of admissions linked to ADR, 40.4% of ADRs avoidable/ possibly avoidable, 50% avoidable ADR admissions avoided by medicines review. Factor = 3.33%
Average length of stay (LOS), inpatient bed days per admission	65+	8.2	75+	8.7	65+	10.7	NI: LOS by age band from data request, DoH NI
Maximum inpatient bed days avoidable by med review	65+	29,800	75+	13,100	65+	49,500	
Average cost per inpatient bed day	All spec, all ages	£829 (€970)	All spec, all ages	£843 (€987)	All spec, all ages	£728 (€852)	NI: inpatient cost per day from data request, DoH NI
Maximum inpatient cost avoidable	65+	£24,687,400 (€28,893,595)	75+	£11,027,100 (€12,905,878)	65+	£36,028,800 (€42,172,110)	

Sources: Scotland: PHS | NI: Hospital statistics: inpatient and day case activity 2021/22, HRG cost 2019/20 (data request), **https://www.health-ni.gov.uk/sites/default/files/publications/health/Transforming-medication-safety-in-Northern-Ireland_1.pdf** | ROI: Department of Health (health-ni.gov.uk)

Table 24: ADR-admissions avoided for 4,933 cases and for 100 cases in each region.

iSIMPATHY associated avoidable admissions, inpatient cost	Region			Total
	ROI	NI	Scotland	
Total 65+/75+ stratified population	417,000	136,400	594,800	1,148,200
ADR admissions avoidable by med review	3,700	1,500	4,600	9,766
Inpatient bed days avoidable by med review	29,800	13,100	49,500	92,400
Inpatient cost avoidable	£24,687,400 (€28,893,595)	£11,027,100 (€12,905,878)	£36,028,800 (€42,172,110)	£71,743,300 (€83,961,166)
For 4,933 iSIMPATHY cases	2,336	1,485	1,112	4,933
ADR admissions avoidable by med review	20	16	9	42
Inpatient bed days avoidable by med review	167	142	92	402
Inpatient cost avoidable	£138,300 (€161,847)	£120,100 (€140,54)	£67,400 (€78,876)	£325,700 (€381,169)
For 100 cases in each region	100	100	100	100
ADR admissions avoidable by med review	0.9	1.1	0.8	0.9
Inpatient bed days avoidable by med review	7	10	8	8
Inpatient cost avoidable	£5,900 (€6,905)	£8,100 (€9,479)	£6,100 (€7,139)	£6,600 (€7,725)

5. Literature

Campbell et al (2014) A systematic review of the effectiveness and cost-effectiveness of interventions aimed at preventing medication error (medicines reconciliation) at hospital admission, The University of Sheffield, School of Health and Related Research (ScHARR) **http://www.eprescribingtoolkit.com/wp-content/uploads/2013/11/PatientSafetyMedsSystematicReview.pdf**

Osanlou, R., Walker, L., Hughes, D., Burnside, G., & Pirmohamed, M. (2022). Adverse drug reactions, multimorbidity and polypharmacy: A prospective analysis of one month of medical admissions. BMJ Open, 12(7), [e055551]. **https://doi.org/10.1136/bmjopen-2021-055551**

Eadon, E. (1992) Assessing the quality of ward pharmacists' interventions, The International Journal of Pharmacy Practice 1992, 1,145-7

6. Descriptive statistics, assumptions and background data

Table 25: Three country population profile

Persons	ROI	NI	Scotland
All	4,761,865	1,904,563	5,479,900
0-15	1,068,195	388,176	911,522
16-18	183,601	69,401	168,533
19-24	331,208	131,205	389,283
25-34	659,410	241,372	754,051
35-44	746,881	250,170	692,525
45-54	612,844	251,551	728,089
55-64	508,958	243,463	762,036
65-74	373,508	177,682	595,578
75+	264,059	151,543	478,283

Sources: ROI – 2016 Census; NI: NISRA mid-2021 population profile; SCO: NRS mid-2021 population estimates

Table 26: Staff / review cost assumptions

General practitioner		Scientific and professional staff: Band 8a		ROI: Senior Pharmacist mid-point[2]
Net remuneration	£125,323 (€146,730)	wages/salary	£50,570 (€59,207)	£69,892 (€81,829)
On-cost[1] %	25%	On-cost %	31%	11%
On-cost	£31,331 (€36,681)	On-cost	£15,727(€18,413)	£8,683 (€10,166)
Total	£156,653 (€156,653)		£66,297(€66,297)	£78,575 (€91,989)
weeks per year	42	weeks per year	42.6	44
hours per week	41.4	hours per week	37.5	35
minutes per year	104,328	minutes per year	95,850	92,400
£ per GP minute	£1.50 (€1.76)	£ per pharmacist minute	£0.69 (€0.80)	£0.85 (€1.0)

excl. practice expenses excl. overheads

Uplifted to 2022/23 prices

[1]SG / PHS WF assumption

[2]Pharmacy salaries calculated at the mid-point of the Senior Pharmacist scale including PRSI and 10% non-pay costs

Table 27: Medication differences

Number of occurrences of medication difference	Region			Total	Total medication increase/ decrease
Medication difference before/ after review	1 ROI	2 NI	3 Scotland		
-18	1			1	-18
-16	1			1	-16
-13	3			3	-13
-12	2			2	-12
-10	4			4	-10
-9	3	2		5	-9
-8	9			9	-8
-7	16		1	17	-7
-6	36	1	3	40	-6
-5	43	3	5	51	-5
-4	83	8	16	107	-4
-3	158	11	50	219	-3
-2	301	31	115	447	-2
-1	438	117	199	754	-1
0	633	261	237	1,131	0
1	133	114	46	293	1
2	39	40	7	86	2
3	4	19	1	24	3
4	3	3		6	4
5	2	2	1	5	5
6	1	2		3	6
7	1			1	7
10	1			1	10
Grand Total	1,915	614	681	3,210	Grand Total

Note: includes 18 non-validated cases across the three regions

Table 28: Cost per item assumptions

Cost per item assumptions	ROI	NI	Scotland
Average Cost per item (inflated to 2022 prices)	£15.32 (€17.94)	£12.04 (€14.10)	£12.04 (€14.10)
Number of repeats per item stopped (chronic)	1+12	1+12	1+12

Table 29: Summary of QALY loss and healthcare costs associated with Eadon scores

Eadon score description	ScHARR QALY			ScHARR Cost[3]		
	min	max	average	min	max	average
1. Detrimental to patient[1]						
2. No significance to patient[2]	0	0	0	£0	£7 (€8)	£4 (€5)
3. Significant: does not improve patient care[2]	0	0	0	£0	£7 (€8)	£4 (€5)
4. Significant: improves patient care	0.001	0.008	0.0045	£80 (€94)	£184 (€213)	£132 (€155)
5. Very significant: prevents a major organ failure or adverse reaction of similar importance	0.061	0.09	0.0755	£877 (€1,027)	£1,824 (€2,135)	£1,350 (€1580)
6. Potentially lifesaving	1	4.41	2.705	£1,334 (€ 1,562)	£2,606 (€3,051)	£1,970 (€2,306)

[1]Eadon 1 not costed and no QALY loss level given in ScHARR (2014)

[2]no QALY loss estimates estimated for Eadon 2 and Eadon 3 – set to 0 here

[3]ScHARR (2014) cost estimates inflated to 2022 prices using ONS CPI Health Deflators

Annex B Output of multivariate analysis

1. What elements contribute most to the number of medicines a patient takes?

Number of long-term conditions is the single biggest predictor of the number of medicines a patient will be taking, explaining 26% of the variance in number of medicines pre-review. Gender, region, and socio-economic status improved the predictive power of the model, but only explained an additional 2% bringing the model to 28%. Age was found to not have any predictive power when the other variables were included in the model.

Table 30: Model summary table for a multiple linear regression with 'Number of medicines pre-review' as the dependent variable

Model Summary[c]

					Change Statistics					
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	R Square Change	F Change	df1	df2	Sig. F Change	Durbin-Watson
1	.511[a]	.261	.260	4.249	.261	1140.607	1	3236	.000	
2	.530[b]	.281	.280	4.191	.020	30.629	3	3233	.000	1.723

a. Predictors: (Constant), Number of long-term conditions

b. Predictors: (Constant), Number of long-term conditions, socio-economic status, region, gender

c. Dependent Variable: Number of medicines pre-review

Table 31: Coefficients table for a multiple linear regression with 'Number of medicines pre-review' as the dependent variable.

		Unstandardised Coefficients		Standardised Coefficients			Collinearity Statistics	
Model		B	Std. Error	Beta	t	Sig.	Tolerance	VIF
1	(Constant)	6.370	.179		35.522	.000		
	Multiple long-term conditions	.942	.028	.511	33.773	.000	1.000	1.000
2	(Constant)	7.433	.402		18.471	.000		
	Multiple long-term conditions	.947	.028	.514	34.334	.000	.994	1.006
	Gender	.511	.148	.052	3.455	.001	.995	1.005
	Socio-economic status	-.342	.128	-.040	-2.662	.008	.999	1.001
	Region	-.751	.089	-.126	-8.400	.000	.995	1.005

Note: R2= .26 for step 1 (p<0.001), R2=0.28 for step 2 (p<0.001)

2. What contributes most to the number of interventions made by the pharmacists?

Number of medicines pre-review was the best predictor of the number of interventions a pharmacist was likely to make, explaining 17% of the variance in number of interventions. When multimorbidity, age, socio-economic status and region were included in the model, the variance explained rose to 20%. Gender wasn't a significant predictor when other variables were included within the model.

Table 32: Model summary table for a multiple linear regression with 'Number of interventions' as the dependent variable (excluding pre-review PC-MAI scores).

Model Summary[d]

					Change Statistics					
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	R Square Change	F Change	df1	df2	Sig. F Change	Durbin-Watson
1	.415[a]	.172	.172	3.370	.172	672.253	1	3233	.000	
2	.420[b]	.177	.176	3.362	.004	17.632	1	3232	.000	
3	.451[c]	.203	.202	3.308	.027	36.249	3	3229	.000	1.557

a. Predictors: (Constant), Number of medicines pre-review

b. Predictors: (Constant), Number of medicines pre-review, Number of long-term conditions

c. Predictors: (Constant), Number of medicines pre-review, Number of long-term conditions, socio-economic status, region, age

d. Dependent Variable: Number of interventions

Table 33: Coefficients table for a multiple linear regression with 'Number of interventions' as the dependent variable (excluding pre-review PC-MAI scores).

		Unstandardised Coefficients		Standardised Coefficients			Collinearity Statistics	
Model		**B**	**Std. Error**	**Beta**	**t**	**Sig.**	**Tolerance**	**VIF**
1	(Constant)	5.151	.154		33.389	.000		
	Number of medicines pre-review	.311	.012	.415	25.928	.000	1.000	1.000
2	(Constant)	4.876	.167		29.139	.000		
	Number of medicines pre-review	.281	.014	.375	20.201	.000	.739	1.353
	Number of long-term conditions	.108	.026	.078	4.199	.000	.739	1.353
3	(Constant)	8.735	.443		19.727	.000		
	Number of medicines pre-review	.266	.014	.355	19.201	.000	.720	1.388
	Number of long-term conditions	.167	.026	.121	6.405	.000	.690	1.450
	Region	-.617	.073	-.138	-8.402	.000	.918	1.089
	Age	-.030	.005	-.103	-6.096	.000	.869	1.150
	Socio-economic status	-.437	.102	-.068	-4.304	.000	.994	1.006

Note: R2= .17 for step 1 (p<0.001), R2= .18 for step 2 (p<0.001), R2= .20 for step 3 (p<0.001).

When pre-review PC-MAI scores were included in the analysis, only number of medicines pre-review contributed to the model. Pre-review PC-MAI scores accounted for 39% of the variance in number of interventions, when number of medicines pre-review was also included in the analysis this rose to 43% of the variance explained. Including PC-MAI scores reduces the sample size.

Table 34: Model summary table for a multiple linear regression with 'Number of interventions' as the dependent variable (including pre-review PC-MAI scores).

Model Summary[d]

					Change Statistics					
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**	**R Square Change**	**F Change**	**df1**	**df2**	**Sig. F Change**	**Durbin-Watson**
1	.625[a]	.391	.389	3.281	.391	240.237	1	374	.000	
2	.654[b]	.428	.425	3.184	.037	24.049	1	373	.000	
3	.658[c]	.432	.428	3.176	.004	2.843	1	372	.093	1.508

a. Predictors: (Constant), Pre-review PC-MAI

b. Predictors: (Constant), Pre-review PC-MAI, number of medicines pre-review

c. Predictors: (Constant), Pre-review PC-MAI, number of medicines pre-review, number of long-term conditions

d. Dependent Variable: interventions

Table 35: Coefficients table for a multiple linear regression with 'Number of interventions' as the dependent variable (including pre-review PC-MAI scores).

		Unstandardised Coefficients		Standardised Coefficients			Collinearity Statistics	
Model		**B**	**Std. Error**	**Beta**	**t**	**Sig.**	**Tolerance**	**VIF**
1	(Constant)	6.722	.288		23.373	.000		
	Pre-review PC-MAI	.177	.011	.625	15.500	.000	1.000	1.000
2	(Constant)	5.030	.444		11.332	.000		
	Pre-review PC-MAI	.137	.014	.484	9.951	.000	.648	1.542
	Number of medicines pre-review	.204	.042	.239	4.904	.000	.648	1.542
3	(Constant)	4.717	.480		9.829	.000		
	Pre-review PC-MAI	.138	.014	.488	10.051	.000	.647	1.547
	Number of medicines pre-review	.174	.045	.204	3.864	.000	.549	1.821
	Multiple long-term conditions	.106	.063	.073	1.686	.093	.805	1.242

Note: R2= .39 for step 1 (p<0.001), R2= .43 for step 2 (p<0.001), R2= .43 for step 3 (p=.093).

3. What contributed most to inappropriate prescribing pre-review?

Number of medicines pre-review was the best predictor of the patients' pre-review PC-MAI score, explaining 35% of the variance. When number of medicines was controlled for, no other variable significantly explained the remaining variance apart from region. When region was included in the model, the two variables accounted for 44% of the variance in a patient's pre-review PC-MAI score.

Table 36: Model summary table for a multiple linear regression with 'Pre-review PC-MAI scores' as the dependent variable.

Model Summary[c]

					Change Statistics					
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**	**R Square Change**	**F Change**	**df1**	**df2**	**Sig. F Change**	**Durbin-Watson**
1	.593[a]	.352	.350	11.955	.352	202.847	1	374	.000	
2	.660[b]	.436	.433	11.163	.085	55.968	1	373	.000	1.555

a. Predictors: (Constant), Number of medicines pre-review
b. Predictors: (Constant), Number of medicines pre-review, region
c. Dependent Variable: Pre-review PC-MAI

Table 37: Coefficients table for a multiple linear regression with 'Pre-review PC-MAI scores' as the dependent variable.

		Unstandardised Coefficients		Standardised Coefficients				
Model		**B**	**Std. Error**	**Beta**	**t**	**Sig.**	**Tolerance**	**VIF**
1	(Constant)	-1.661	1.664		-.998	.319		
	Number of medicines pre-review	1.790	.126	.593	14.242	.000	1.000	1.000
2	(Constant)	8.462	2.061		4.107	.000		
	Number of medicines pre-review	1.649	.119	.546	13.875	.000	.975	1.026
	Region	-5.311	.710	-.295	-7.481	.000	.975	1.026

Note: R2= .35 for step 1 (p<0.001), R2= .44 for step 2 (p<0.001).

4. What contributed most to number of medicines post-review?

The number of medicines pre-review is closely correlated with the number of medicines post-review (accounting for 86% of the variance in medicines post). All other factors examined accounted for only an additional 1% of the remaining variance.

Table 38: Model summary table for a multiple linear regression with 'number of medicines post review' as the dependent variable (including number of medicines pre review).

Model Summary[e]

					Change Statistics					
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**	**R Square Change**	**F Change**	**df1**	**df2**	**Sig. F Change**	**Durbin-Watson**
1	.929[a]	.863	.862	1.670	.863	20272.781	1	3231	.000	
2	.932[b]	.869	.869	1.628	.007	171.170	1	3230	.000	
3	.933[c]	.870	.870	1.622	.001	24.621	1	3229	.000	
4	.933[d]	.871	.871	1.617	.001	11.507	2	3227	.000	1.757

a. Predictors: (Constant), Number of medicines pre-review
b. Predictors: (Constant), Number of drugs before, number of interventions
c. Predictors: (Constant), Number of drugs before, number of interventions, number of multiple long-term conditions
d. Predictors: (Constant), Number of drugs before, number of interventions, number of multiple long-term conditions, socio-economic status, age
e. Dependent Variable: Number of medicines post-review

Table 39: Coefficients table for a multiple linear regression with 'Number of medicines post-review' as the dependent variable (including number of medicines pre-review).

Coefficients[a]

Model		Unstandardised Coefficients		Standardised Coefficients			95.0% Confidence Interval for B		Correlations			Collinearity Statistics	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound	Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	.887	.076		11.603	.000	.737	1.037					
	Number of medicines pre-review	.846	.006	.929	142.383	.000	.835	.858	.929	.929	.929	1.000	1.000
2	(Constant)	1.461	.086		16.896	.000	1.292	1.631					
	Number of medicines pre-review	.881	.006	.967	138.351	.000	.868	.893	.929	.925	.880	.828	1.208
	Number of interventions	-.111	.009	-.091	-13.083	.000	-.128	-.095	.310	-.224	-.083	.828	1.208
3	(Constant)	1.319	.091		14.532	.000	1.141	1.497					
	Number of medicines pre-review	.865	.007	.949	121.354	.000	.851	.879	.929	.906	.769	.656	1.524
	Number of interventions	-.114	.009	-.094	-13.458	.000	-.131	-.098	.310	-.230	-.085	.824	1.214
	Number of long-term conditions	.062	.012	.037	4.962	.000	.037	.086	.496	.087	.031	.735	1.360
4	(Constant)	1.794	.201		8.925	.000	1.400	2.188					
	Number of medicines pre-review	.868	.007	.952	121.675	.000	.854	.882	.929	.906	.768	.651	1.537
	Number of interventions	-.116	.009	-.095	-13.605	.000	-.133	-.099	.310	-.233	-.086	.814	1.228
	Number of long-term conditions	.073	.013	.043	5.741	.000	.048	.097	.496	.101	.036	.705	1.418
	Age	-.010	.002	-.029	-4.425	.000	-.015	-.006	.160	-.078	-.028	.919	1.089
	Socio-economic status	.104	.050	.013	2.096	.036	.007	.202	-.025	.037	.013	.989	1.011

a. Dependent Variable: Number of medicines post-review

If number of medicines pre-review was removed from the model, then number of interventions became the best predictor, accounting for 10% of the variance, when multimorbidity was also included this increased to 28%.

Table 40: Model summary table for a multiple linear regression with 'number of medicines post-review' as the dependent variable (excluding number of medicines pre-review).

Model Summary[d]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					
					R Square Change	F Change	df1	df2	Sig. F Change	Durbin-Watson
1	.310[a]	.096	.096	4.284	.096	342.380	1	3231	.000	
2	.529[b]	.280	.279	3.825	.184	823.691	1	3230	.000	
3	.530[c]	.281	.280	3.822	.002	3.658	2	3228	.026	1.731

a. Predictors: (Constant), Number of interventions

b. Predictors: (Constant), Number of interventions, number of long-term conditions

c. Predictors: (Constant), Number of interventions, number of long-term conditions, socio-economic status, age

d. Dependent Variable: Number of medicines post-review

Table 41: Coefficients table for a multiple linear regression with 'Number of medicines post-review' as the dependent variable (excluding number of medicines pre-review).

Model		Unstandardised Coefficients		Standardised Coefficients				
		B	Std. Error	Beta	t	Sig.	Tolerance	VIF
1	(Constant)	7.606	.195		38.950	.000		
	Number of interventions	.377	.020	.310	18.504	.000	1.000	1.000
2	(Constant)	4.519	.205		22.061	.000		
	Number of interventions	.231	.019	.190	12.247	.000	.928	1.078
	Multiple long-term conditions	.748	.026	.445	28.700	.000	.928	1.078
3	(Constant)	3.572	.474		7.540	.000		
	Number of interventions	.234	.019	.192	12.314	.000	.919	1.089
	Multiple long-term conditions	.729	.027	.433	26.967	.000	.862	1.160
	Age	.015	.006	.042	2.704	.007	.926	1.080
	Socio-economic status	-.026	.118	-.003	-.219	.827	.989	1.011

Note: R2= .31 for step 1 (p<0.001), R2= .53 for step 2 (p<0.001). R2= .53 for step 3 (p<0.05).

5. What contributed most to post-review PC-MAI?

Pre-review PC-MAI scores were the best predictor of post-review PC-MAI scores explaining 48% of the variance in post-review MAI scores. When number of medicines pre- and post-review; number of interventions; region and deprivation were added to the model (no other variable was found to significantly explain the remaining variance), the model's predictive power increased to 59% of the variance.

Table 42: Model summary table for a multiple linear regression with 'Post-review PC-MAI scores' as the dependent variable.

Model Summary[e]

					Change Statistics					
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**	**R Square Change**	**F Change**	**df1**	**df2**	**Sig. F Change**	**Durbin-Watson**
1	.690[a]	.476	.474	6.347	.476	326.510	1	360	.000	
2	.703[b]	.495	.492	6.239	.019	13.526	1	359	.000	
3	.760[c]	.578	.573	5.718	.083	35.228	2	357	.000	
4	.768[d]	.590	.583	5.651	.012	5.241	2	355	.006	1.552

a. Predictors: (Constant), Pre-review PC-MAI

b. Predictors: (Constant), Pre-review PC-MAI, number of interventions

c. Predictors: (Constant), Pre-review PC-MAI, number of interventions, number of medicines post-review, number of medicines pre-review

d. Predictors: (Constant), Pre-review PC-MAI, number of interventions, number of medicines post-review, number of medicines pre-review, socio-economic status, region

e. Dependent Variable: Post-review PC-MAI scores

Table 43: Coefficients table for a multiple linear regression with 'Post-review PC-MAI scores' as the dependent variable.

		Unstandardised Coefficients		Standardised Coefficients			Collinearity Statistics	
Model		**B**	**Std. Error**	**Beta**	**t**	**Sig.**	**Tolerance**	**VIF**
1	(Constant)	-1.473	.567		-2.597	.010		
	Pre-review PC-MAI	.402	.022	.690	18.070	.000	1.000	1.000
2	(Constant)	.972	.868		1.120	.263		
	Pre-review PC-MAI	.467	.028	.800	16.639	.000	.608	1.643
	Number of Interventions	-.365	.099	-.177	-3.678	.000	.608	1.643
3	(Constant)	-.507	.950		-.534	.593		
	Pre-review PC-MAI	.558	.030	.956	18.419	.000	.439	2.280
	Number of Interventions	-.419	.094	-.203	-4.444	.000	.567	1.764
	Number of medicines pre-review	-1.440	.194	-.810	-7.427	.000	.099	10.073
	Number of medicines post-review	1.614	.193	.811	8.375	.000	.126	7.926
4	(Constant)	3.549	1.568		2.263	.024		
	Pre-review PC-MAI	.536	.031	.918	17.116	.000	.401	2.492
	Number of Interventions	-.440	.093	-.213	-4.714	.000	.563	1.776
	Number of medicines pre-review	-1.407	.192	-.792	-7.332	.000	.099	10.105
	Number of medicines post-review	1.594	.191	.801	8.357	.000	.126	7.949
	Socio-economic status	-1.148	.473	-.083	-2.427	.016	.982	1.018
	Region	-.910	.392	-.086	-2.321	.021	.839	1.191

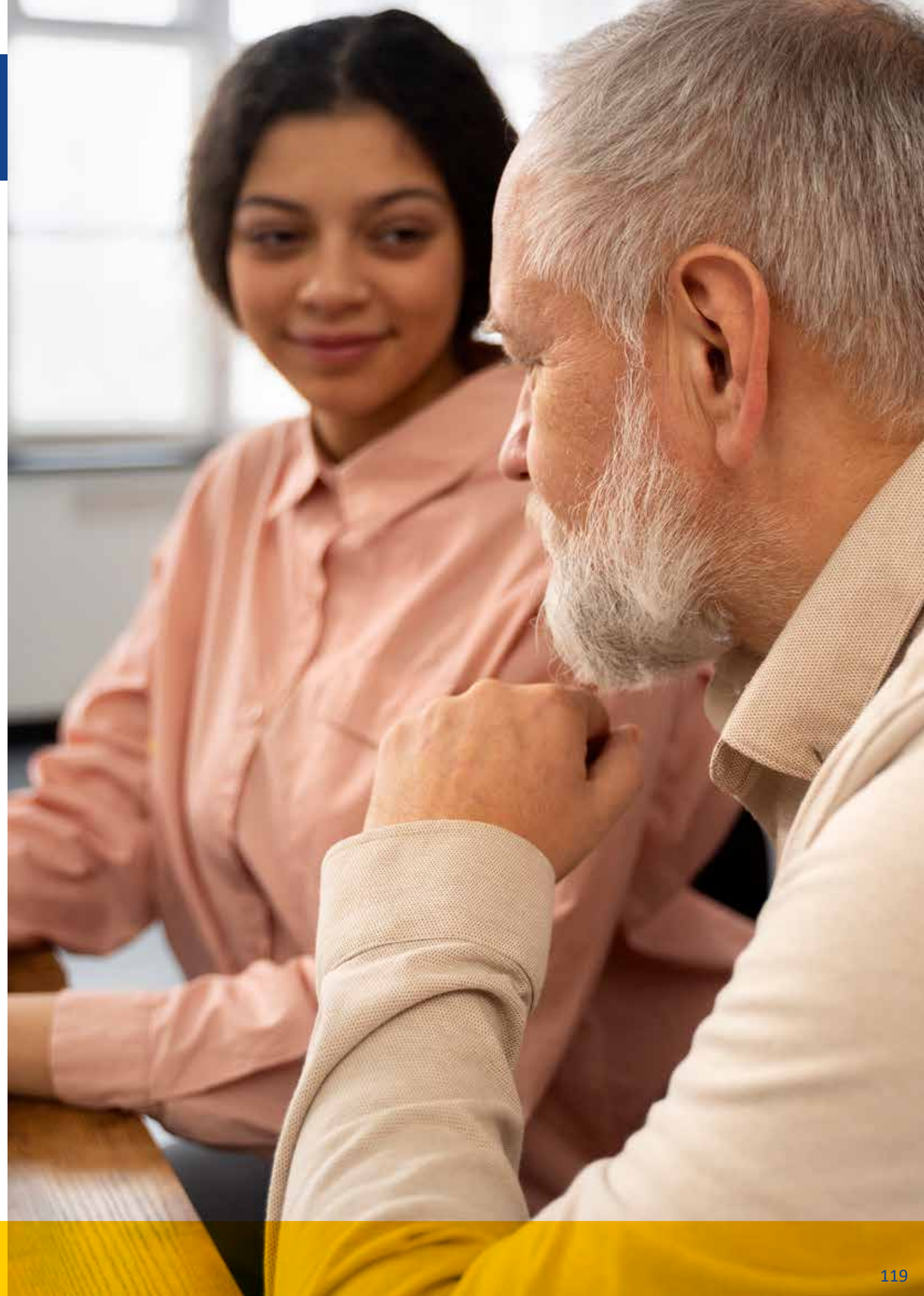
Note: R2= .48 for step 1 ($p<0.001$), R2= .50 for step 2 ($p<0.001$). R2= .58 for step 3 ($p<0.001$). R2= .59 ($p<0.01$)

Annex C Data Collection Dataset Values

Table 44: Data collection dataset

Value	Core/Additional
Region	Core
Unique ID	Core
Age at Review	Core
Gender	Core
Deprivation Index	Core
Project cohort indicators (5 or more medicines, high risk drugs, care home, end of life care)	Core
Co-morbidities	Core
Number of drugs (pre-review)	Core
Number of drugs (post-review)	Core
Time Taken for review (pre/during/post)	Core
Number of changes/interventions	Core
Changes/Interventions	Core
EADON scale	Core
Drugs list PRE-review	Additional
Drugs list POST-review	Additional
Polypharmacy indicator	Additional
MAI (pre-review)	Additional
MAI (post-review)	Additional

Values listed as “core” were required to be collected for all reviews, those listed as “Additional” collected in addition to core values for a 10% sample.



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