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REVIEW

Guidance to manage inappropriate polypharmacy in older people: systematic review and future developments

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ABSTRACT

Introduction: Single disease state led evidence-based guidelines do not provide sufficient coverage of issues of multimorbidities, with the cumulative impact of recommendations often resulting in overwhelming medicines burden. Inappropriate polypharmacy increases the likelihood of adverse drug events, drug interactions and non-adherence.

Areas covered: A detailed description of a pan-European initiative, 'Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly, SIMPATHY', which is a project funded by the European Commission to support innovation across the European Union. This includes a systematic review of the literature aiming to summarize and review critically current policies and guidelines on polypharmacy management in older people. The policy driven, evidence-based approach to managing inappropriate polypharmacy in Scotland is described, with consideration of a change management strategy based on Kotter's eight step process for leading sustainable change.

Expert opinion: The challenges around promoting appropriate polypharmacy are on many levels, primarily clinical, organisational and political, all of which any workable solution will need to address. To be effective, safe and efficient, any programme that attempts to deal with the complexities of prescribing in this population must be patient-centred, clinically robust, multidisciplinary and designed to fit into the healthcare system in which it is delivered.

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Aged; inappropriate prescribing; literature review; organisational change; polypharmacy; SIMPATHY

1. Introduction

1.1. Multimorbidity

Multimorbidity is defined by the World Health Organization as 'the co-occurrence of two or more chronic medical conditions in one person' [1]. Epidemiological data indicate that multimorbidity increases markedly with age, being prevalent in almost two-thirds of individuals aged 80 years and over [2,3]. On average, those with multimorbidities have at least three long-term conditions, with cardiovascular (87.7 % of individuals), metabolic (62.2 %), and rheumatoid (40.2%) being the three most common. There is a significant relationship between multimorbidities and the use of health services; multimorbidity is related positively to interaction with community-based health services (twice as high as non-multimorbid), and hospitalization (three times higher) [4]. Multimorbidities impact quality of life, being associated with multiple symptoms, disabilities such as cognitive impairments, limited activities of daily living, and reduced mobility hence are major public health issues [5]. One consequence is high economic burden due to complex healthcare needs and frequent interaction with healthcare services [6].

1.2. Polypharmacy

While the United Nations (UN) refers to those aged 60 years and over as 'older people,' most developed countries have accepted the chronological age of 65 years as the definition of an 'older person' [7]. Given advances in pharmacotherapy, older people are likely to be prescribed multiple medicines to manage their multimorbidities. Single-disease state-led evidence-based guidelines do not provide sufficient coverage of issues of multimorbidities or the effects of old age, with the cumulative impact of treatment recommendations often resulting in overwhelming medicines burden [4,8]. Furthermore, as life expectancy increases, not only will people take medicines for a longer period of time but may develop more conditions that have the potential to need treatment but for which there is limited evidence of efficacy in extremes of age.

There is a wealth of recent evidence on the prevalence of prescribing of multiple medicines in older people. Data originating in the UK, published in 2014, highlighted that 20.8% of those with two clinical conditions were prescribed four to nine medicines, and 10.1% of patients ten or more medicines; in patients with six or more comorbidities, values were 47.7%

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Article highlights

- Single disease state led evidence-based guidelines do not provide sufficient coverage of issues of multimorbidities
- While traditionally polypharmacy has been classified in terms of the number of medicines, there is now a change in emphasis from 'inappropriate polypharmacy' to 'appropriate' or 'optimal polypharmacy'
- A critical review of current policies and guidelines on polypharmacy management people identified the Scottish Polypharmacy Guidance as scoring high of the AGREE II instrument (The Appraisal of Guidelines for REsearch & Evaluation)
- This guidance describes a 7 step process provides a standardised structure for medicines review
- SIMPATHY (Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly) aims to stimulate and support innovation across the European Union

This box summarizes key points contained in the article.

and 41.7%, respectively, and these figures increase with age [9]. A recent analysis of prescribing trends in the USA found that, between 1999 and 2012, polypharmacy (defined as ≥ 5 prescription medicines) increased from 24% to 39% for those aged 65 and above [10]. While there may be variability across countries, a narrative literature review published in 2005 identified this is a widespread global issue [11].

Polypharmacy, the prescribing of multiple medicines, is considered to be 'one of the greatest prescribing challenges,' increasing the likelihood of adverse drug events, drug interactions, and contributing to non-adherence to medicines regimens [12]. Furthermore, polypharmacy impacts significantly health outcomes and healthcare resources. While traditionally polypharmacy has been classified in terms of the number of medicines (usually defined as the use of five or more medicines) [13], Patterson et al. suggested, as part of a Cochrane review in 2012 (later updated in 2014), that there should be a change in emphasis from 'inappropriate polypharmacy' (prescribing of multiple medicines which are either inappropriate or no longer indicated) to 'appropriate' or 'optimal polypharmacy' (appropriate prescribing of multiple medicines) [14–16].

1.3. Managing inappropriate polypharmacy

It is evident that inappropriate polypharmacy is a major concern, hence promoting appropriate polypharmacy at the point of medicines initiation or during medicines review is, therefore, of the utmost importance and deserves greater attention.

A systematic review reported by Patterson et al. aimed to determine which interventions, alone, or in combination, were effective in improving appropriate polypharmacy and reducing medicines-related problems in older people. The review findings were based upon ten papers, with the authors concluding that, while there is uncertainty about the elements of intervention that impact positively appropriate polypharmacy, pharmaceutical care appears to improve prescribing [15,16].

There are a number of tools which may assist in promoting appropriate prescribing in older people. A systematic review by Kaufmann et al. aimed to create a comprehensive and structured overview of existing tools to assess potentially inappropriate

prescribing [17]. Findings identified 46 different tools, with variation in methodological aspects and a general lack of validation in clinical settings. While many might serve as useful aids to improve prescribing, each tool has its limitations, strengths, and weaknesses, and most were specific to the region and context in which they were developed. These tools were categorized as explicit, implicit, or mixed. While implicit criteria focus on clinician interpretation and are time consuming, explicit criteria are designed to be easily and effectively interpreted. They provide details of categories of medicines and associated prescribing indicators to enhance reliable treatment evaluation. The most widely used include Beers Criteria, STOPP-START, and Laroche Criteria [18–20]. The authors concluded that this review could serve as a summary to assist readers in choosing a tool, either for research purposes or for daily practice [17].

There remains, however, the need to translate the research evidence to policies and guidance for practitioners managing inappropriate polypharmacy and promoting appropriate polypharmacy. Developing, implementing, and sustaining change requires commitment and investment at all levels of healthcare systems. The emphasis of the remainder of this paper is on a detailed description of a pan-European initiative, with emphasis on the policy-driven management of inappropriate polypharmacy in Scotland.

2. Stimulating innovation management of polypharmacy and adherence in the elderly

2.1. SIMPATHY

Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly (SIMPATHY) is a project funded by the European Union's Health Programme (2014–2020, 21), which commenced in June 2015 and will be complete by summer of 2017. Polypharmacy is the primary focus, with a secondary-related focus on patient non-adherence to medicines. The SIMPATHY consortium comprises: healthcare policy-makers; practicing physicians; pharmacists; health economists; professionals responsible for large database evaluation; and leading academic researchers, as shown in Figure 1, representing ten institutions in eight European countries.

The project target stakeholders are those who can provide valuable and complementary contributions in tackling inappropriate polypharmacy in older people, namely: politicians; policymakers; healthcare commissioners; healthcare providers; professional bodies and regulators; educators; and patient representatives.

2.2. SIMPATHY aim and work program

The overarching aim of SIMPATHY is to stimulate and support innovation across the EU in the management of polypharmacy and adherence in the elderly, with specific focus on addressing inappropriate polypharmacy. There is much emphasis on translating evidence to practice impacting healthcare structures, processes, and patient outcomes (clinical, humanistic, and economic). The consortium program of work will provide case studies in a range of different environments, identifying the framework and politicoeconomic basis for an EU-wide



Figure 1. SIMPATHY organisations.

benchmarking exercise. Furthermore, the development of contextualized change management approaches and tools will aid target stakeholders who can influence and implement the necessary changes. Carefully targeted and comprehensive dissemination and engagement activities will be deployed to stimulate and support the innovation necessary to address this major EU healthcare challenge.

Work streams comprise: a systematic review of the published and gray literature of identified policies and guidelines across the EU for promoting appropriate polypharmacy in older people; case studies of the management of polypharmacy in the consortium countries; a benchmarking survey, aiming to collect quantitative and qualitative data from across the EU to provide a picture of progress toward addressing the urgent challenges associated with polypharmacy; a Political, Economic, Sociocultural, Technological, Environmental and Legal (PESTEL) analysis [22] and analysis of the Strengths, Weaknesses, Opportunities and Threats (SWOT) relating to polypharmacy and adherence management in the consortium countries; and, validation of SIMPATHY findings through an EU-wide consensus (modified Delphi) study.

The remainder of this paper focuses on the evidence derived from the literature review, the approach employed around change management, and the case studies.

3. Literature review

3.1. Aim

Several published systematic literature reviews have focused on aspects of polypharmacy management [14–16], but with little emphasis on gray literature, notably policies and guidelines. The aim of this review was to summarize and review critically current policies and guidelines on polypharmacy management in older people (publications dated: 1 January 2010–30 June 2015).

3.2. Methods

A comprehensive, multifaceted search strategy was devised to target publications outlining strategic guidance for addressing inappropriate polypharmacy (but not implementation of guidance) in clinical practice, healthcare systems, or research.

To be included, at least one major-stated purpose had to be the development of policies or guidelines to improve at least one component of polypharmacy management in older people and had to specify explicitly the guidance. Publications that only made recommendations as a part of the conclusions were excluded.

There were several methods employed for the search, including a targeted database search, online gray literature search, desk review, and contact with key stakeholders.

A database search was conducted on Medline (via PubMed), Embase, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and The Cochrane Library, according to PRISMA-P 2015 guidelines [23]. Comprehensive search strings were developed, for example for Medline: (multimed^a* [ti] OR 'multiple medication' [ti] OR polifarma* [ti] OR polyfarma* [ti] OR polimed^a* [ti] OR polymed^a* [ti] OR poli-pharma* [ti] OR polypharma* [ti] OR polipragma* [ti] OR polypragma* [ti] OR politerap* [ti] OR polyterap* [ti]) AND (elder* [ti] OR old* [ti] OR age* [ti] OR geriatric* [ti])

An online search of the gray literature of policies and guidelines was performed in ten European countries (Germany, Greece, Italy, Northern Ireland, Poland, Portugal, Spain, Sweden, the Netherlands, and Scotland). The search strategy included all 24 combinations of keywords from the following two groups,

Group 1: multimедication, multiple medication, polymedicine, polypharmacy, polypragmasy, polytherapy

Group 2: aged, elder, geriatric, old

After translating for each country, and cross-checking that these translated keywords were applicable to the management of polypharmacy, a search was performed using the Google search engine. The country-specific search was restricted to the relevant country domain (i.e. .de for Germany, .gr for Greece, etc.). In order to allow for comparable results to be obtained, and avoid the effect of cookie files, the previous search history was disabled, and the 'private' or 'incognito' mode of the search enabled (wherever applicable). For each combination of keywords, the first ten results generated by the Google search (giving a total of 240) was registered in a dedicated spreadsheet, and analyzed for each of the search-based countries.

The search was complemented with any guidance documents known to the SIMPATHY consortium, as well as those identified through targeted contact with local stakeholders (two physicians, two pharmacists, and one politician) in each country. Guidance documents were entered into a dedicated spreadsheet and screened to remove duplicate. Titles and

abstracts of each item were reviewed independently by two reviewers in each country who were fluent in the relevant language. Final eligibility to be included in the review was determined by screening of full texts.

Data extracted from relevant guidance documents were entered into a dedicated spreadsheet and quality rated using the AGREE II instrument (The Appraisal of Guidelines for REsearch & Evaluation) which has 23 items organized into domains of: scope and purpose; stakeholder involvement; rigor of development; clarity of presentation; applicability; and editorial independence [24]. Each item was scored independently on a seven-point scale by two individuals educated to doctoral level and with expertise in the field of polypharmacy. A score of one indicated an absence of information or that the concept was reported very poorly. A score of seven indicated that the quality of reporting was exceptional and all criteria were met. A score between two and six indicated that the reporting of the AGREE II item did not fully meet the criteria. The overall score is the median of the 23-item scores.

To broaden the search beyond the consortium countries, the search was also conducted in the US Agency for Healthcare Research and Quality National Guidelines Clearinghouse and also the Guidelines International Network [25,26].

3.3. Results

There were 444 hits, of which 214 duplicates were removed, 136 were excluded for not dealing with polypharmacy management in older people, and 11 for other reasons (e.g. type of publication such as opinion, case report). The full-text review of 83 papers revealed only one which fulfilled the eligibility criteria.

The number of keyword combinations varied between countries, with a range of 3–24 due to issues in translation of keywords and applicability to the local literature on polypharmacy management. Furthermore, the Google search did not always retrieve the target number of ten. The total number of Google search results assessed against the eligibility criteria was 1705. Of these, 807 were excluded for not focusing on polypharmacy management in older people and 810 for other reasons, usually not providing guidance. The full text of 88 items was reviewed, with ten fulfilling all criteria to be retained in the review. Full details are provided in Table 1.

Table 1. Summary of the gray literature search.

Country	No. of keyword combinations used for the search (No. of individual keywords from Group 1 & 2)	No. of search results	Excluded after screening:		No. of full-text items assessed	No. of identified guidance documents fulfilling all criteria
			For not dealing with polypharmacy management in older people	For other reasons		
Germany	24 (6 * 4)	240	89	102	49	1
Greece	24 (6 * 4)	179 ^b	166	13	0	0
Italy	12 ^a (4 * 3)	100 ^b	46	47	7	0
The Netherlands	4 ^a (2 * 2)	40	19	20	1	1
Poland	24 (6 * 4)	233 ^b	165	55	13	0
Portugal	24 (6 * 4)	150 ^b	113	29	8	0
Sweden	3 ^a (3 * 1)	30	0	26	4	4
Spain	8 ^a (2 * 4)	66 ^b	2	63	1	0
Scotland	24 (6 * 4)	240	156	80	4	4
Northern Ireland	24 (6 * 4)	187 ^b	21	165	1	0
Non-country-specific search	24 (6 * 4)	240	30	210	0	0
Total		1705	807	810	88	10

^a Number of the keywords has been adjusted to the local language

^b Number of search results lower than the target due to some combination of keywords retrieving <10 results.

Table 2. Guidance documents identified through other methods.

Country	No. of identified guidance documents
Germany	1
Greece	0
Italy	0
The Netherlands	4
Poland	0
Portugal	0
Sweden	4
Spain	1
United Kingdom	4
Total	14

An additional 14 guidance documents were identified, as shown in Table 2.

Combining the guidance documents derived from all sources and removing duplicates gave a final total of 19 documents from five countries, as listed in Table 3, which also highlights quality according to the AGREE II-GRS criteria. The median overall score was 5, with a range of 3–7; three documents scored the maximum of seven, originating from Scotland, Germany, and the Netherlands.

The comprehensive and quality-assured approaches employed in this literature review identified that only five EU countries had produced guidance documents which focus specifically on polypharmacy management in older people. In addition, only three of these were found to be fully satisfactory in terms of the AGREE II criteria. Most of the identified guidance documents targeted both polypharmacy in older people and also other groups of vulnerable people. All but one was generic (not specific to any single medical condition). Most paid attention to medicines selection at the point of prescribing (e.g.

avoiding certain high-risk medicines, dose adjustment, and a ‘start low and go slow’ approach), and the need for regular review of medicines. Physicians and pharmacists were identified as key players, with a focus on multidisciplinary care and team working. Only seven guidance documents had any coverage of issues of non-adherence to medicines in older people.

The wider search identified further guidance documents from Australia [46–48], the US [49,50], and New Zealand [51].

Despite the comprehensive search and quality assurance approaches, there are several limitations to this review hence the findings should be interpreted with some caution. Gray literature searches are always limited in terms of retrieving all relevant literature. The search was restricted to Google and while this is the most widely used search engine, it is possible that not all guidance and policies were captured. In addition, it is highly likely that less widely used or disseminated policies and guidelines, such as those operating at local levels, were not retrieved. It is therefore important that those developing and implementing strategic approaches to the management of polypharmacy in older people disseminate widely.

The Scottish polypharmacy guidance was identified as one of the documents that scored the highest score of the AGREE II criteria [28], hence is described in greater detail, with emphasis on the evidence used to derive the guidance.

3.4. Policy-driven approach to management of inappropriate polypharmacy in Scotland

Like many areas in the developed world, Scotland has had to face the challenge of providing healthcare to an aging population. From 2006 to 2031, there is a 62% projected rise in

Table 3. Guidance documents identified with AGREE II scores.

Guidance document details	Country of origin	Overall score according to AGREE II
Regionala läkemedelsrådet i Uppsala-Örebroregionen. Behandlingsrekommendationer 2015. Läkemedelsbehandling av de mest sjuka äldre. Version 1.2: Updated March 2015 [27]	Sweden	6
Scottish Government Model of Care Polypharmacy Working Group. Polypharmacy Guidance (2nd edition). March 2015 [28]	Scotland	7
Västerbottens läns landsting. Terapirekommendationer, 2015 [29]	Sweden	5
Västra Götalandsregion. Äldre och läkemedel, 2015 [30]	Sweden	4
Bergert FW, Braun M, Ehrental K, et al. Recommendations for treating adult and geriatric patients on multimедication, 2014 [31]	Germany	7
Corrine Zara. Rational drug use. Medication management in the complex chronic patient: reconciliation, revision, deprescription and adherence, 2014 [32]	Spain	5
Ingrid Schubert, Hausärztlicher Leitliniengruppe Hessen und DEGAM. Hausärztliche Leitlinie „Multimedikation“, 2014 [33]	Germany	5
Midlöv P, Kragh A. Chapter: Läkemedelsbehandling hos äldre. In: Läkemedelsboken. Uppsala: Läkemedelsverket. 2014 [34]	Sweden	3
Verenso. Handreiking Geriatrisch assessment door de specialist ouderengeneeskunde. Utrecht: Verenso. 2014 [35]	The Netherlands	3
Duerden M, Avery T, Payne R. Polypharmacy and medicines optimisation: Making it safe and sound. The King's Fund. November 2013 [36]	England	6
Jones E. Polypharmacy: Guidance for Prescribing in Frail Adults. NHS Wales. May 2013 [37]	Wales	5
Nederlandse Vereniging voor Klinische Geriatrie. Richtlijn comprehensive geriatric assessment. Utrecht: Nederlandse Vereniging voor Klinische Geriatrie. 2013 [38]	The Netherlands	5
Socialstyrelsen. Läkemedelsgenomgångar för äldre ordinerade fem eller fler läkemedel. Stockholm: Socialstyrelsen. 2013 [39]	Sweden	5
Stockholms läns landsting. Äldre och läkemedel, 2013 [40]	Sweden	5
Nederlands Huisartsen Genootschap. Multidisciplinaire richtlijn Polyfarmacie bij ouderen 2012. Utrecht: Nederlands Huisartsen Genootschap. 2012 [41]	The Netherlands	6
NHS Greater Glasgow & Clyde. Mindful Prescribing Strategy – Polypharmacy. NHS. December 2012 [42]	Scotland	6
Melander A, Nilsson LG. Olämpliga listan – Koll på läkemedel, 2011 [43]	Sweden	5
Verenso. Multidisciplinaire richtlijn diabetes bij kwetsbare ouderen. Utrecht: Verenso. 2011 [44]	The Netherlands	7
Socialstyrelsen. Indikatorer för god läkemedelsterapi hos äldre. Stockholm: Socialstyrelsen. 2010 [45]	Sweden	5

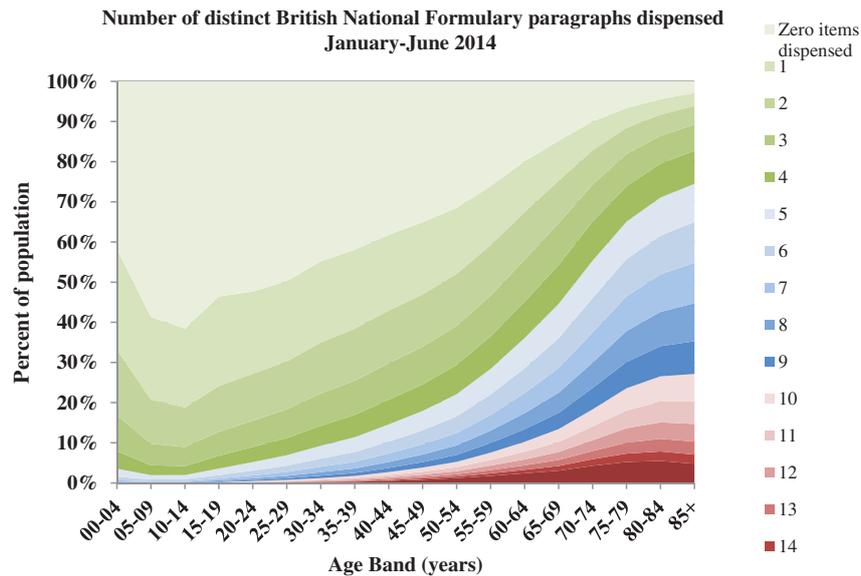


Figure 2. Medicines dispensed per age banding, January – June 2014. Source, Prescribing Information System, NHS Scotland.

those aged 65 years and older, a 144% projected rise in those aged 85 years and older, and a projected increased prevalence of long-term conditions, notably chronic obstructive pulmonary disease and diabetes mellitus [52]. Figure 2 provides analysis of Scottish data relating to number of medicines dispensed in the community by age band, highlighting the increasing trend of positive relationship between age and number of prescribed medicines. Around 35% of those aged 85 years and above are receiving more than ten medicines.

Two key Scottish Government policy documents led to scrutiny of medicines-related issues in older people. The Reshaping Care for Older People: A Programme for Change 2011–2021 (2020 vision) aims to improve the quality and outcomes of current models of care for older people [53]. The 2010 Healthcare Quality Strategy recommends more team working and that optimal use of skills of different healthcare professionals should be considered in order to address future workforce challenges and to enable delivery of clinical care in a sustainable way [54].

With publication of these strategic documents, and a significant drive from clinicians, local guidelines to promote appropriate polypharmacy started to develop from 2010 onwards. This culminated in the publication in 2012 of national guidance on managing inappropriate polypharmacy [55] which was updated in 2015 and upgraded to be available across a variety of digital platforms [28]. These were developed by a multidisciplinary group of professionals from across primary and secondary care, led by pharmacy and medical specialists serving as policy-makers, with input from other members of the multidisciplinary team and patients. Evidence-based approaches are key hallmarks of these guidelines.

The definitions of appropriate and inappropriate polypharmacy were expanded from those of Patterson et al. [14–16]. Appropriate polypharmacy is present when: all medicines are prescribed for the purpose of achieving specific therapeutic objectives that have been agreed with the patient; therapeutic

objectives are actually being achieved or there is a reasonable chance they will be achieved in the future; medicines have been optimized to minimize the risk of ADRs; and the patient is motivated and able to take all medicines as intended. Inappropriate polypharmacy is present when: one or more medicines are prescribed that are not (or no longer) needed, either because there is no evidence-based indication, the indication has expired or the dose is unnecessarily high; one or more medicines fail to achieve the therapeutic objectives they are intended to achieve; one, or the combination of several medicines, cause unacceptable ADRs, or put the patient at an unacceptably high risk of such ADRs; and the patient is not willing or able to take one or more medicines as intended.

In the absence of definitive evidence on which patients are most likely to benefit from a holistic review of their medicines, the guidelines suggest prioritizing two groups of patients. The first group includes those in care homes aged 50 years and over, regardless of the number of medicines prescribed. The second is all those aged 75 years (progressing to 65–74 years as resources allow) prescribed ten or more medicines, one of which is considered a high-risk medicine (e.g. benzodiazepines, anticholinergics) and with a Scottish Patients at Risk of Readmission and Admission (SPARRA) score in the range of 40–60%. SPARRA estimates the risk of emergency admission in the next 12 months for approximately 3.6 million individuals aged 16 years and over [56]. These patients can be identified from primary care medical practice databases.

While not intending to be exhaustive, the guidelines highlight high-risk medicines in older people, providing an amalgamation of existing collections of explicit medication assessment tools [17]. Emphasis is also placed on identifying high-impact medicines which ideally should be continued or started. Furthermore, practitioners are encouraged to consider the likely impact of medicines on the individual patient. Being aware of the number needed to treat (NNT) of different therapies for the same disorder can help to inform rational and

patient-centered therapy [57]. Drug efficacy information (clinical trial data on intervention, comparator, study population, duration, NNT and annual NNT) is presented for the management of hypertension, heart failure, cerebrovascular disease, diabetes mellitus, and osteoporosis.

The 2015 guidance builds on and refines the medicines review process described in the 2012 guidance. The seven step process provides a standardized structure for the medicines review, with greater focus on patient-centeredness and a holistic approach, which considers ‘no therapy’ solutions. There is acknowledgment that decision-making is complex and should take into account multimorbidities, safety, efficacy and acceptability of medicines, the patient’s wellbeing, social circumstances, and desires. Each of the seven steps focus on a different aspect which, in conjunction, are designed to lead to a patient specific and holistic review of medicines. Importantly, the seven-step process commences and ends with focus on patient-specific clinical outcomes related to health and wellbeing, as defined by the patient. Evidence-based recommendations focus on which medicines to consider stopping and starting [19,58], and high-risk medicines such as anticholinergics [59,60]. The seven steps are summarized in Table 4.

An Australian group addressing polypharmacy through a program of ‘deprescribing’ present a five-step process which considers similar aspects [61].

The polypharmacy guidance has been disseminated widely to policy-makers, health professionals, and patient groups in Scotland. Given that general practitioners are responsible for the majority of prescribing in Scotland, the delivery of the strategy was designed initially around primary care. It was therefore a major milestone when, in 2013, polypharmacy medicines review, as part of anticipatory care reviews, was added to the general practitioners’ contract. This requires a quota of reviews to take place, where possible with the support of a pharmacist [62]. It is, however, recognized that other health professionals (predominantly nurses) with patient contact and medicines-related training have responsibilities around promoting appropriate

polypharmacy in older people. Notably, nurse- and pharmacist-independent prescribers may, within their competence, prescribe the same range of medicines as physicians [63]. In 2013, the Scottish Government published its strategy for pharmaceutical care, ‘Prescription for Excellence,’ which describes an integrated, multidisciplinary approach to optimizing pharmaceutical care [64]. This strategy articulates the role of pharmacist-independent prescribers in patient management and that by 2023, all patient facing pharmacists will be independent prescribers managing caseloads of patients, which will provide greater opportunity for promoting appropriate polypharmacy.

The polypharmacy guidance is also being integrated within undergraduate and postgraduate education and training programs in Scotland, to embed and normalize the seven-step process. Recently, a mobile phone app has been developed to enable easy access to the guidance. The processes of medicines prescribing and review will continue to evolve and adapt over time as the health service in Scotland adapts to care for a changing population.

4. Other SIMPATHY work packages

4.1. Case studies

SIMPATHY involves several interrelated work packages. One of the foundational work packages is a series of nine case studies conducted in eight EU countries (Germany, Greece, Italy, Poland, Portugal, Spain (Catalonia), Sweden, and the UK (Scotland and Northern Ireland)). A case study investigation is described as a ‘wrapper for different methods’ [65], or a means with which ‘to explain present circumstances... [through]...in-depth description of social phenomenon’ [66]. The aim of conducting the case studies is to understand what types of polypharmacy programs have been developed, mapping out the structures, processes, and outcomes of policies and practices at the institutional, local, regional, and national levels. These case studies inform for the development of

Table 4. An overview of the seven steps process (adapted from 29).

Domain	Steps	Process
Aims	1. Identify objectives of drug therapy	Review diagnoses and identify therapeutic objectives with respect to management of existing health problems and prevention of future health problems
Need	2. Identify essential drug therapy	Identify essential drugs (not to be stopped without specialist advice). These include drugs that have essential replacement functions (e.g. levothyroxine) and drugs to prevent rapid symptomatic decline (e.g. for Parkinson’s disease)
	3. Does the patient take unnecessary drug therapy?	Identify and review the (continued) need for drugs such as those with: temporary indications; higher than usual maintenance doses; limited benefit in general or the indication they are used for; limited benefit in the patient under review
Effectiveness	4. Are therapeutic objectives being achieved?	Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives of: symptom control; biochemical/clinical targets; preventing disease progression/exacerbation
Safety	5. Does the patient have ADR or is at risk of ADRs?	Identify patient safety risks by checking for: drug–disease interactions; drug–drug interactions; robustness of monitoring mechanisms for high-risk drugs; risk of accidental overdosing Identify adverse drug effects by checking for: specific symptoms/laboratory markers; cumulative adverse drug effects; drugs that may be used to treat ADRs caused by other drugs
Cost effectiveness	6. Is drug therapy cost effective?	Identify unnecessarily costly drug therapy by considering more cost-effective alternatives (but balance against effectiveness, safety, convenience)
Adherence/ Patient centeredness	7. Is the patient willing and able to take drug therapy as intended?	Identify risks to patient non-adherence by considering if: the medicine is in a form that the patient can take; the dosing schedule is convenient; the patient is able to take medicines as intended Ensure drug therapy changes are tailored to patient preferences by: discussing with the patient/carer/welfare proxy therapeutic objectives and treatment priorities; deciding with the patient/carer/welfare proxies what medicines have an effect of sufficient magnitude to consider continuation or discontinuation

change management tools that will be developed by SIMPATHY. The case studies in each country consist of three phases of: a desk review of published and gray literature describing the legislation, policies, and procedures that support the program; one-to-one key informant interviews with policy makers, managers, and clinicians to assess the change management and leadership strategies involved in implementing the program; and focus group discussions with healthcare providers, and policy-makers.

4.2. Change management

Securing change in large healthcare systems is a major challenge. There is a natural inertia which must be overcome by conceiving, implementing, and coordinating an accessible, achievable change management program. The first test for any would be implementer is to ask, 'do compelling reasons for change exist?' In several countries, there is evidence that the necessary impetus is present to drive ongoing transition toward substantial health reforms focusing on appropriate polypharmacy. The catalytic trigger is the burden imposed by the epidemics of noncommunicable diseases (NCDs) including cardiovascular, respiratory, metabolic, rheumatologic and neurologic disorders, and cancers, and inevitable multimorbidities [67]. Two additional key factors are accelerating changes in healthcare: the need for generating efficiencies which allow further investment in innovation without increasing overall health costs; and, the paradigm change in the understanding of the underlying mechanisms of these NCDs and the focus on strategic partnerships involving all stakeholders associated with patient-centered care [68].

Managing inappropriate polypharmacy and promoting appropriate polypharmacy is complex with multiple aspects of healthcare practice and delivery of care. To understand fully the current situation in the EU, mixed-methods approach is being used in SIMPATHY, drawing on methodologies, methods, and theories from multiple disciplines applied by a multi-disciplinary research team.

Kotter's eight-step process for leading change [69] involves the following steps: create a sense of urgency; build guiding coalitions; form strategic vision and initiatives; enlist volunteers; enable action by removing barriers; generate short-term wins; sustain acceleration; and, thereby institute sustainable change. There are several key organizational features which are more likely to lead to adaptive change. These include organizations which are open to exploring different methods of achieving a task making iterative changes where and when necessary [70], adaptive leadership where strategic behaviors are encouraged or if individuals feel safe to take risks or not [71], leading cross-functional teams [72]. An outline change management program, based upon these principles, is set out in Table 5.

This mixed-method, multi-pronged approach will provide a rich assessment of current polypharmacy management in Europe. It will be the foundation for future change management tools which enable other countries to address the growing concern of inappropriate polypharmacy. These tools will be adaptable and applicable to a range of healthcare settings, enabling local policy makers and clinicians to create programs

Table 5. Polypharmacy change management program.

1. Establish a sense of urgency	Communicating to stakeholders the need to change current ways of reviewing medicines to benefit patient care. Examining other projects that are developing and whether they pose a threat to the development of the framework
2. Form a powerful guiding coalition	Facilitate the assembly of a project group including in each country comprising both primary and secondary care and collaborative leads locally and nationally for long-term health conditions. These groups should then engage with the work of those responsible for the delivery of healthcare and public health both locally and nationally
3. Create a vision	The vision describes 'how we want the story of polypharmacy in each country to turn out.' It should be compelling in the way it addresses the concerns and issues of different stakeholders
4. Communicating the vision	This is the heart of the change management process and involves hard work on the part of the teams in each country to show tenacity and persistence in winning hearts and minds to the need for change and how it can be realized in practical steps
5. Empowering others to act on the vision	Visions succeed when the means of achieving them cascades from the top level to the lowest level of delivery. Understand the obstacles to change at each level so that they take ownership of problems and solutions. Provide feedback and facilitate adaptation of the protocol e.g. link with anticipatory care plans

that reflect their specific patient populations, cultures, and healthcare systems.

Innovations in the management of polypharmacy are key themes within the European Union Framework Programme for Research and Innovation. In addition to SIMPATHY, there are several high profile projects. PRIMA-EDS (Polypharmacy in chronic diseases: Reduction of Inappropriate Medication and Adverse drug events in elderly populations by electronic Decision Support) aims to first gather current best evidence regarding drug treatment of multimorbid elderly patients then develop an electronic decision support tool (eDS-tool) to aid physicians and patients to make use of current best evidence when coming to a shared decision regarding multiple drug treatment of the most common chronic diseases. The final stage is a randomized controlled trial with hospital admission rate and mortality as primary clinical outcomes [73]. OPERAM (OPTimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly) aims to test the effect of a software-based intervention in 1,900 comorbid elderly patients [74]. SENATOR (Development and clinical trials of a new Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older peRsons) aims to develop a highly powered and efficient software engine (SENATOR). It is hoped that SENATOR will be capable of individually screening the clinical status and pharmacological and non-pharmacological therapy of older people with multi-morbidity in order to define optimal drug therapy [75].

5. Expert opinion

Each succeeding generation of healthcare providers faces new challenges. While there have been remarkable developments in pharmacotherapy, coupled with the plethora of evidence-based clinical guidelines to support the management of single conditions, we now need the clinical and management courage to recognize that these approaches address poorly the

needs of older people who constitute an ever increasing proportion of the population [8].

The challenges are on many levels, primarily clinical, organizational, and political, and any workable, sustainable solution will need to address each and all of these. To be effective, safe, and efficient, any program that attempts to deal with the complexities of prescribing and promoting appropriate polypharmacy in this population must be patient-centered, clinically robust, multidisciplinary, and designed to fit into the healthcare system in which it is delivered.

Within the clinical domain, it is essential to ensure that guidance is evidence based but also pragmatic. This requires consideration of where strong evidence exists for a specific treatment strategy but also highlighting where evidence is lacking or where, due to a lack of applicability and generalizability, it would be ineffective or potentially harmful to extrapolate recommendations to multimorbid older people. Guidelines for this population need to be based on a holistic approach to prescribing, with subsequent, regular medicines review. This must be based on the individual needs, goals, and desires of the individual patient, considered alongside the efficacy or otherwise of the medicines regimen.

Clinical consensus and workable guidance are not, however, the only criteria for success. To be considered truly successful, any program needs to be judged by those commissioning healthcare as a cost-effective, as well as clinically effective, approach to increasing quality of care. It is relatively simple to outline the complexities, issues and gaps in knowledge around prescribing for frail older people and the consequences of ever increasing burden of medicines. For commissioners, however, these messages may be lost amidst the clamor of many competing and equally worthy demands. The managers of these polypharmacy programs need to be able to communicate the clinical sense of urgency at the highest levels to demand and drive sustainable change. This requires a very clear strategy which outlines a workable, deliverable, and cost-effective solution acceptable to clinicians and patients.

SIMPATY, with its focus on existing guidance documents promoting appropriate polypharmacy aims to identify best practice and collaborative learning from EU countries to stimulate further workable innovation, with lessons which could be implemented globally [21]. Work completed to date suggests that to succeed and importantly be sustained, any program would be best developed and implemented within a framework of a clear change management strategy. Without this comprehensive, coordinated strategy it is unlikely that any program can be delivered consistently, equitably and be sustained across a population, irrespective of clarity and robustness of the clinical aspects of any guidance.

The Scottish experience is perhaps the furthest developed in the sense of having robust and evidence-driven guidance, coupled with a clear delivery strategy [28]. There was early recognition of a need for promoting appropriate polypharmacy in older, multimorbid people to be part of standard practice. The change management strategy aligned to Kotter's eight-step process [69] encourages engagement of senior management at the government level, as well as practising members of the multidisciplinary team and

patients, at a very early stage. Initial pilot work and implementation on the national scale involved monitoring and providing feedback of estimations of clinical and economic impact. Creating a sense of urgency and vision for such a strategy to help address the political and economic factors has been an iterative process that is reviewed continually over time. Acceptance of the program by patients is powerful in political terms. These are essential elements in successful delivery and sustainability.

Considerable work was undertaken to ensure the polypharmacy guideline was approved and hosted by the Scottish Intercollegiate Guidelines Network (SIGN), the main center for national disease-specific guidelines [76]. The polypharmacy guidance is now the most downloaded guidance on the SIGN website. It is now imperative that robust and rigorous evaluative research data are gathered demonstrate the impact of the guidance in terms of clinical, humanistic, and economic outcomes. In conclusion, there is a need to manage inappropriate polypharmacy and promote appropriate polypharmacy in an increasingly complex, multimorbid aging population. In clinical terms, this will require clinicians across multiple healthcare disciplines in each country to agree on guidance that will begin to take account of adults whose prescribing needs require a much more holistic approach. The evidence demonstrates clearly that the time has come to reject the reliance on single-disease state focused guidelines when treating multimorbid patients. In future, plans must be developed and implemented within a framework of a clear change management strategy and be coupled with rigorous and robust evaluation.

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Declaration of interest

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