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Stakeholders' perspectives about challenges, strategies and outcomes of importance associated with adherence to appropriate polypharmacy in older patients – A qualitative study

Hanadi A. Al Shaker [a,b], Heather E. Barry [a], Carmel M. Hughes [a,*]

[a] *School of Pharmacy, Queen's University Belfast, Belfast, United Kingdom*
[b] *Faculty of Pharmacy and Medical Sciences, University of Petra, Amman, Jordan*

ABSTRACT

Background: Older patients experience challenges when taking polypharmacy. Studies have applied different interventions to improve adherence to polypharmacy. However, inconsistencies in outcomes have impeded the synthesis of evidence. To generate high-quality studies and selectively report outcomes, a Core Outcome Set (COS) is advocated.

Objective(s): This study explored stakeholders' perspectives about the challenges older patients face when taking polypharmacy, strategies to overcome each challenge, and outcomes of importance that may contribute to COS development.

Methods: Semi-structured interviews were undertaken with academics, healthcare professionals, and public participants. A series of open-ended questions investigated challenges with adherence to polypharmacy in older patients and strategies to overcome these challenges. A list of outcomes ($n = 7$) compiled from previous studies associated with adherence to polypharmacy was presented to participants for their views. Content analysis was conducted to identify key themes and outcomes proposed by participants.

Results: Participants suggested 11 multidimensional healthcare system-related, medication-related, patient-related, and socioeconomic-related challenges and 16 educational and behavioural strategies associated with adherence to polypharmacy in older patients. Participants agreed with the importance of the seven outcomes presented and suggested a further six outcomes they deemed to be important for use in trials aimed at improving adherence to appropriate polypharmacy in older patients.

Conclusions: Adherence to polypharmacy was deemed challenging, requiring supportive interventions. A list of 13 outcomes in the context of adherence to appropriate polypharmacy in older patients was identified to inform a future study that will develop a COS for clinical trials targeting interventions to improve adherence to appropriate polypharmacy in older patients.

1. Introduction

Globally, the older population (aged ≥65 years) is growing faster compared to other age groups. Over 54% of older adults suffer from two or more chronic conditions known as multimorbidity.[1] As a result, polypharmacy (≥4 medications) has become increasingly prevalent in treating multimorbid older patients.[2] Appropriate polypharmacy refers to prescribing evidence-based multiple medications to ensure patients receive the best beneficial treatment plan by focusing on safety,

therapeutic objectives and clinical appropriateness.[2–4] Conversely, inappropriate polypharmacy caused by inappropriate prescribing has been linked to adverse medication reactions and increased hospitalisation.[3,5,6] Inappropriate prescribing, encompassing overprescribing, underprescribing and misprescribing, has imposed additional financial costs and burdens on patients and the healthcare sector.[3,7] Additionally, drug-drug interactions associated with complex medication regimens have increased the difficulty of taking medications as advised.[8,9]

Medication non-adherence occurs when patients deviate from the

instructions and recommendations for a prescribed therapeutic plan.[10–12] This could be attributed to patients' beliefs about medications, costs, or side effects, whereby patients deliberately decide not to follow the treatment regimen.[13,14] On the other hand, some non-adherent older patients cannot recall treatment and medication information or suffer from cognitive and/or physical disabilities.[15] Consequently, fewer benefits are obtained from treatment, leading to increased medication wastage and healthcare costs.[16,17] Therefore, it is crucial to understand the challenges contributing to medication non-adherence to appropriate polypharmacy in older adults to develop effective interventions.[18] These interventions should focus on identifying and addressing the reasons for medication-taking errors and non-adherence to appropriate polypharmacy.[19,20]

A recent Cochrane review which focused on interventions to improve older patients' adherence to multiple medicines, concluded high-quality evidence is scarce, owing to the variety of intervention types, outcomes selected and outcome measurement instruments used, which precluded synthesising reliably informed conclusions.[20] Consequently, well-designed intervention studies involving defined outcomes and outcome measurement tools are needed to provide reliable evidence.[20,21]

The Core Outcome Measures for Effectiveness Trials (COMET) initiative encourages researchers, healthcare professionals (HCPs), healthcare service users/public members policymakers, carers, and patients to develop core outcome sets (COS) for clinical trials in a particular field of health.[21] A COS is a standardised list of outcomes that should be reported and measured in all clinical trials in a specific area.[21] The COMET initiative recommends a stepwise method to develop COSs in a particular field of health. This involves: (1) determining the scope of the COS; (2) specifying the need for the COS; (3) developing a protocol regarding 'what' outcomes to measure; (4) determining '*what*' outcomes should be measured by (i) identifying existing knowledge, (ii) gathering perspectives and information about important outcomes in qualitative studies (e.g. focus groups and interviews) and (iii) conducting consensus meetings to finalise the recommended COS (e.g. Delphi consensus exercise, Nominal Group Technique); (v) Reporting the work using the COS-STAR guidance. Step 5 outlines '*how*' to measure the included outcomes in the COS (Fig. 1).[21]

Accordingly, the objectives of this study aimed to explore the perspectives of academics, HCPs and members of the public about the
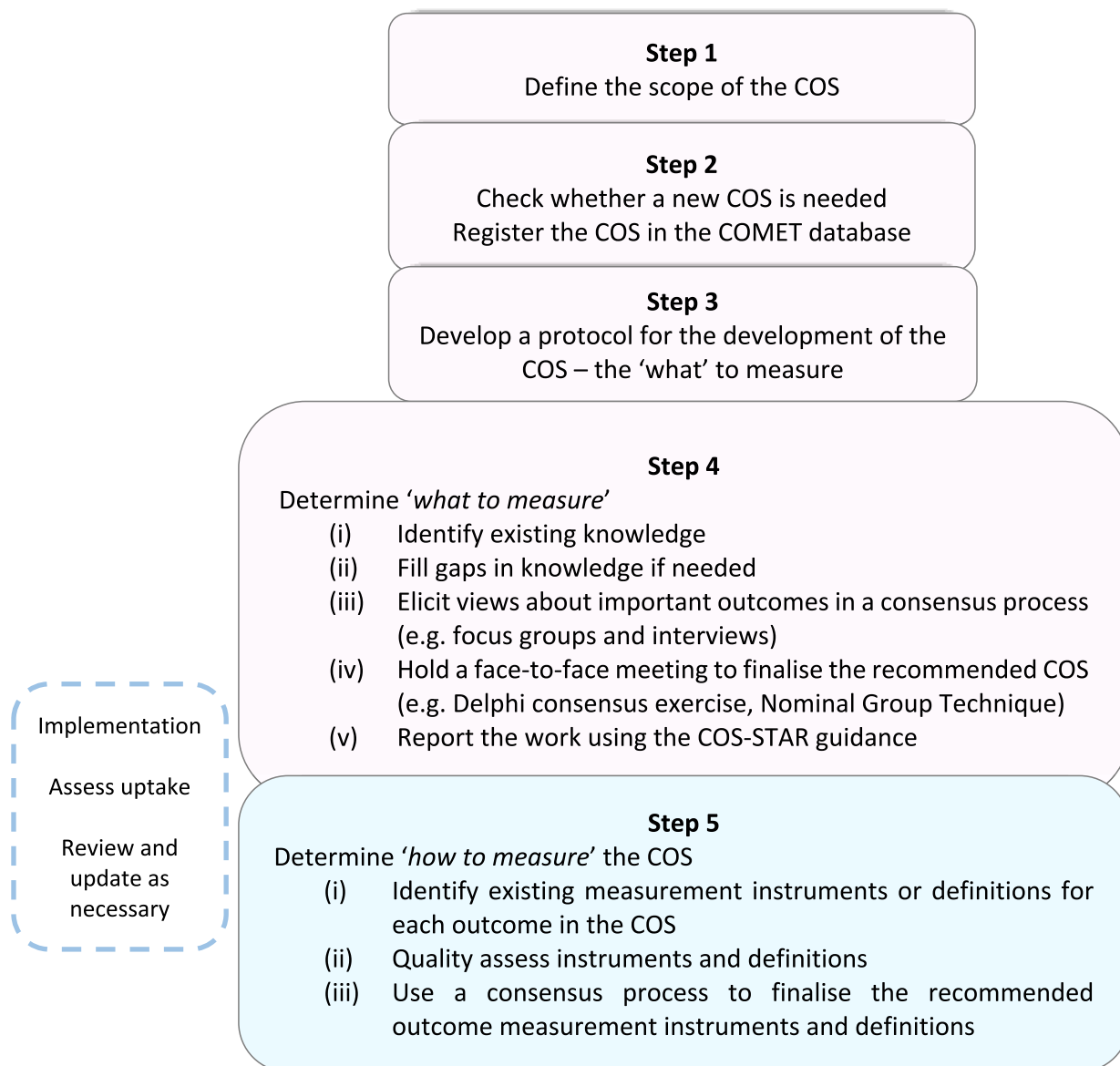
Fig. 1. The core outcome set (COS) development process. Adapted from: Williamson et al. (2017, p. 6).
COMET: Core Outcome Measures in Effectiveness Trials, COS: Core Outcome Set, COS-STAR: Core Outcome Set–STAndards for Reporting.

challenges older people face with adherence when prescribed appropriate polypharmacy, identify potential strategies/solutions to overcome these challenges and compile a list of outcomes related to adherence to appropriate polypharmacy to inform the development of a COS for trials assessing adherence to appropriate polypharmacy.

2. Methods

2.1. Study context and design

The context for the development of this COS focused on older patients (aged ≥65 years) taking multiple medications (≥4 regular medications), living in their own homes (e.g. discharged from hospital or community-dwelling patients), and who could manage their medications. Virtual semi-structured interviews were conducted with academics, HCPs and public participants globally. Ethical approval was granted by the Queen's University Belfast Faculty of Medicine, Health and Life Sciences Research Ethics Committee (MHLS 22_80).

2.2. Extraction and compilation of a list of relevant outcomes

A list of outcomes was compiled from a recent Cochrane review focusing on interventions to improve adherence to multiple medicines in older people[20] and two other relevant studies.[22,23] The list of outcomes was included in the topic guides used in the interviews (Supplementary Material Table 1).

2.3. Participant sampling and recruitment

The COMET initiative recommends that a COS be applicable across different disciplines worldwide.[21] Therefore, we sought to recruit stakeholders from across the world to participate in interviews, namely: academics with experience and knowledge about adherence research, polypharmacy and older people; HCPs [community pharmacists and general practitioners (GPs) in primary care settings]; and members of the public (public participants) who were advocates for patients in healthcare.[24] Academics and HCPs were identified by searching academic publication profiles. Similarly, patient advocacy group employees were also identified and approached using publicly available contact details. We contacted 13 public charities and organisations (focusing on supporting healthcare delivery, the well-being of older people and their needs) within the United Kingdom and internationally to help recruit public members and enhance public participation.

In order to enhance recruitment and ensure no important challenges, strategies or outcomes were overlooked, purposive (using maximum variation) and snowball sampling approaches were used.[25,26]

2.4. Data collection

Informed consent was obtained electronically or by post before each interview. Two piloted topic guides containing open-ended questions were developed; the first was for academics and HCPs, and the second was for public participants (Supplementary Material Table 1). Both topic guides were prepared by referring to the literature and through discussion within the research team.[19,20,22,23,27,28] Prompts were provided when necessary to probe further. To facilitate participation, interviewees were offered the opportunity to opt for face-to-face interviews, via telephone or Microsoft Teams®. This allowed the compilation of detailed information related to the topic under investigation.[29]

The key issues discussed were challenges related to adherence to appropriate polypharmacy in older patients, strategies to overcome these challenges and improve adherence, and meaningful outcomes for use in interventions to improve adherence to appropriate polypharmacy in older people. Interviews were conducted until data saturation was achieved.[30]

All interviews were audio-recorded via a digital recorder with participants' permission, and transcribed verbatim. All participants were assigned a unique identification number based on their category and interviewing sequence. For example, A1, HCP1, and PP1 were assigned for the first academic, HCP and public member interviewed, respectively.

2.5. Data analysis

One researcher conducted data collection and analysis to monitor saturation. Another double-checked the transcripts against the recordings and data analysis to ensure accuracy. Transcripts and recordings were read and listened to repeatedly to facilitate contextual understanding. After familiarisation, content analysis was performed to identify themes representing challenges, strategies/solutions, and outcomes of interest. Transcripts were organised and managed using NVivo Pro® software, version 12 (QSR International Pty Ltd.). Potential challenges and strategies were summarised, reviewed and agreed upon by the research team. Similarly, outcomes suggested by participants were revised and screened to produce a refined list of outcomes important to stakeholders.

The study was reported following the COnsolidated criteria for REporting Qualitative research (COREQ) checklist (Supplementary Material Table 2).[31]

3. Results

3.1. Compilation of an inventory list of outcomes of adherence to appropriate polypharmacy

A total of seven outcomes were compiled from a recent Cochrane review[20] and two other studies related to adherence to multiple medicines.[22,23] The list of outcomes was refined, screened and included in the topic guides for academics, HCPs and public participants, using concise and straightforward language (Supplementary Material Table 1).

3.2. Participant characteristics

A total of 107 individuals comprising academics, HCPs ($n = 80$) and public participants ($n = 27$) were identified and approached via purposive and snowball sampling. Three academics/HCPs and two members of the public declined to take part, while 54 academics/HCPs and 16 members of the public did not respond. Of the 13 public organisations and charities approached to help recruit public members, two declined to assist, and none of the remaining organisations responded. Fifteen academics, eight HCPs, and six public members agreed to participate ($n = 29$; 20 females and nine males), from across a number of geographical locations. Regarding the six public members, three were identified by snowball sampling, whereby participants who had completed interviews were asked to suggest other potential participants who might be interested in taking part in this study. The public members consisted of older patients, caregivers, and advocates for patients' interests in healthcare.

Three interviews were conducted over the telephone, and the remaining 26 were via Microsoft Teams®. Interview duration ranged from 11 to 41 min (Table 1).

3.3. Issues around adherence to appropriate polypharmacy

The first two questions of the interview discussed challenges older people faced when taking appropriate polypharmacy, as well as strategies to overcome these challenges. Accordingly, four factors affecting adherence to appropriate polypharmacy were identified and classified into four general categories: patient-related, medication-related, healthcare system-related and socioeconomic-related factors. These categories were further subdivided into more detailed sub-categories, comprising 11 distinct challenges and 16 corresponding strategies to

Table 1
Characteristics of participants (*n* = 29).

Job title		Female	Male	Location of participants		
				Europe (*n* = 15)	Australia (*n* = 9)	USA (*n* = 5)
HCPs (n = 8)	Pharmacists (*n* = 6)	4	2	NA	5	1
	GPs (n = 2)	0	2	2	NA	NA
Academics (n = 15)		11	4	8	4	3
Public participants (n = 6)		5	1	5	NA	1

HCP: healthcare professionals, GP: general practitioners, NA: not applicable.

address each challenge. Table 2 presents these challenges and strategies/solutions to overcome these challenges.

3.3.1. Challenges with adherence to appropriate polypharmacy

Participants listed several challenges associated with adherence to appropriate polypharmacy and described these challenges as multifaceted and myriad (Supplementary Material Table 3):

"The challenges are multifactorial; there are so many different challenges."

Table 2
Summary of challenges associated with adherence to appropriate polypharmacy, along with strategies to overcome each challenge.

Factors affecting medication adherence	Challenges with adherence to appropriate polypharmacy		Strategies to overcome challenges with adherence to appropriate polypharmacy
Patient-related factors	1) Physical functioning and cognitive impairment.	Physical functioning Cognitive impairment	1) Large print labels and packaging change.
	2) Memory		2) Reminders
	3) Low health literacy		3) Enhance patients' health literacy
	4) Medication beliefs		4) Modify/address various patients' beliefs.
	5) Inability to manage multiple medications.		5) Improve patients' medication-taking behaviour.
			6) Use packaging interventions.
			7) Apply personalised/tailored interventions.
Medication-related factors	6) Inappropriate treatment regimens		8) Ensure comprehensive and recent evidence-based prescribing (e.g. medication review).
	7) Complex medication regimens		9) Reduce medication regimen complexity.
			10) Polypills.
	8) Medication side effects		11) Discuss side effects with patients.
Healthcare system-related factors	9) Issues related to the healthcare system and services.		12) Enhance the healthcare professional-patient relationship.
			13) Improve patients' accessibility to healthcare services.
			14) Continuity of care.
Socioeconomic factors	10) Costs of medications		15) Minimise treatment costs and apply cost-cutting strategies.
	11) Lack of family and/or community support		16) Engage family and/or community members in the healthcare process.

[A_08]

Additionally, participants believed these challenges were mainly ascribed to the characteristics of the ageing process, such as cognitive or physical disabilities, forgetfulness and poor understanding:

"…older age are potentially forgetting; understanding the instructions of the medications prescribed. If a person doesn't have the ability, whether it's cognitive or physical…"

[A_13]

Participants noted other challenges older patients face when taking appropriate polypharmacy, including medication beliefs, inability to manage multiple medications, complex medication regimens, medication side effects, and problems related to the healthcare system and services:

"I'm taking like four tablets around lunchtime, and then the evening's other seven different ones. So, like that's 11, 11 tablets I have to sort out on a daily basis, you know? Yeah, it's basically, you know, you know, morning things that I would take…"

[PP_03]

Public members also expressed concerns about treatment regimens not being updated according to the best and most recent available evidence:

"…the patient could be assured of the latest [medication]*, not remaining on an older medication."*

[PP_02]

Others referred to socioeconomic factors, including costs of medications and lack of family and/or community support:

"…when it's cost or, you know, sort of socioeconomic factors. I think the public health system plays a role; the pharmaceutical industry plays a role."

[HCP_07_Pharm]

"If you live alone is not possible if you're dependent on carers who may change every day. Umm, if you don't have family to remind you or administer to you."

[PP_01]

3.3.2. Strategies to overcome challenges with adherence to appropriate polypharmacy

Analysis resulted in 16 strategies being identified to improve adherence to appropriate polypharmacy, including behavioural and educational approaches to overcome adherence challenges:

"You could go perhaps to use maybe some, some more maybe behavioural way…"

[A_10]

"I think the main solution is education, so you have to, like educate them…"

[HCP_05_Pharm]

Participants believed that multi-compartment compliance aids and reminders were helpful interventions. Public members expressed their reassurance with the use of pillboxes, as they proved to be helpful facilitators in monitoring medication intake:

"…from my own experience of my father, who had, he had to take lots of medications, and he had to take them at different times, and I think the bubble pack obviously helps!"

[PP_02]

Better HCP-patient relationships, shared decision-making and applying a personalised intervention were considered important in improving adherence and treatment plans:

"…clinical interview or the discussion with the, with the person, and for that, you have all the communication techniques, and you know, motivational interviewing, active listening, and so on problem-solving."

[A_10]

"Adherence can also be improved by having a good relationship with their [older patients'] *healthcare providers."*

[HCP_06_Pharm]

Involving older patients could help patients feel that their preferences, fears, beliefs and opinions were heard and respected, leading to better health outcomes:

"…the healthcare professionals that deal with these people [older patients] *have to recognise, identify the problem and manage their uncertainty, and manage their fears, and their fears of side effects and their beliefs about medication."*

[A_06]

Supplementary Material Tables 3 and 4 display the complete set of challenges related to adherence to appropriate polypharmacy, and associated strategies to tackle each challenge, along with supporting explanations and illustrative quotes.

3.4. Outcomes deemed important to participants

A list of 13 outcomes, including the seven outcomes presented during the interviews and six additional outcomes suggested by participants, were considered important to be measured in studies aimed at improving adherence to appropriate polypharmacy in older people. All participants ($n = 29$) agreed with the inclusion of most outcomes presented in the topic guides, including medication adherence across multiple medications, patient/carer satisfaction, and healthcare utilisation. Twenty-six participants supported condition-specific outcomes, 27 interviewees agreed with the inclusion of health-related quality of life and cost-effectiveness ($n = 27$), and 28 agreed with including adverse events and side effects.

3.5. Outcomes presented during the interviews

3.5.1. Medication adherence across multiple medications

All participants acknowledged that medication adherence was the pivotal and fundamental outcome to measure in interventions aiming to improve adherence to appropriate polypharmacy in older patients:

"Medication adherence makes sense because that's your primary."

[HCP_01_Pharm]

Academics and HCPs discussed measuring adherence and the inconsistencies between various measurement tools in the literature. Others pointed out that no accurate method had been developed to estimate adherence across multiple medications:

"…how you actually measure adherence, particularly in the context of polypharmacy, so whether you can measure adherence to one medication versus multiple medications and the huge variety everything from…."

[A_03]

Participants also wondered whether adherence could be measured for multiple medications:

"One of the challenges with doing this [measuring medication adherence across multiple medications] *is how do you ensure you're capturing lots of different medicines because many of the adherence screeners were designed and developed just, you know, kind of in either specific conditions, or focusing on a particular medicine."*

[A_07]

"I do like to make sure that medication adherence is across multiple medications is measured across different ways, whether it's like a survey,

or using like an electronic monitor or like through the electronic medical record."

[HCP_01_Pharm]

3.5.2. Condition-specific outcomes

Condition-specific outcomes were considered important to measure in studies aiming at improving adherence to appropriate polypharmacy:

"…Of course, if you can measure something that's directly related to, to a specific medication or a specific disease, that's the most powerful, of course."

[A_01]

"Condition-specific outcomes, yes, absolutely; I think that's important."

[PP_02]

However, considering the high number of chronic conditions and the accompanying clinical outcomes available (e.g. laboratory measures and indicators), some participants expressed concern regarding the feasibility of condition-specific outcomes in practice. Additionally, it was believed that evaluating the effectiveness of a general intervention covering a broad range of medications used to treat chronic conditions would be challenging and arduous to apply:

"…how on earth you measure effectiveness in a generic intervention, which can cover all medicines because you'd have to have a list of, you know, who knows how many different outcomes for each individual condition. We've done a study suggesting we have 40 different conditions covering about 50% of all illnesses. Then, you've got hundreds and hundreds of other conditions covering the other half of all illnesses."

[A_13]

3.5.3. All adverse events and side effects

A number of participants deemed adverse events and side effects a crucial outcome to ensure the intervention was effective. Participants also emphasised the importance of being aware of side effects in order to prevent the initiation of new medicines that could be added to treat the unwanted side effects of another (i.e. prescribing cascade):

"…They may have side effects and be unaware if those are due to ageing, or due to the medication or due their [older patients'] *disease. So, they may experience a symptom and not understand if it's a problem from their medicines; they* [older patients] *may have to have additional medications to treat a side effect. So, they might just add more medicines for them."*

[A_02]

Furthermore, some academics believed severe medication side effects and adverse events would negatively affect patients' health-related quality of life and healthcare utilisation:

"If they had an adverse event or a side effect, then healthcare utilisation wouldn't improve; it would get worse…"

[A_05]

"Some of these medications may have serious side effects for them. So, they may experience side effects that affect their quality of life."

[A_06]

Public members underscored the importance of prescribing the safest and most appropriate choice of medications for older patients to avoid drug-drug interactions when medications were taken concurrently:

"I think older people, perhaps if a GP prescribed something, they don't really understand the effects of one medication [referring to medication A]*, and how the medication B* [another medication] *must be taken in order to prevent very serious side effects."*

[PP_02]

3.5.4. Health-related quality of life

Health-related quality of life was deemed a comprehensive measure and a core outcome for evaluating the overall healthcare process of a patient:

> *"If you look at pharmaceutical care, health-related quality of life should be sort of the centre."*
>
> [A_01]

Further, participants believed an effective adherence intervention would positively impact health-related quality of life:

> *"If you're measuring quality of life, so you're thinking that the intervention to improve adherence is gonna also improve quality of life…"*
>
> [A_04]

> *"I would say definitely health-related quality of life…."*
>
> [PP_04]

However, a few participants noted that the association between health-related quality of life and appropriate polypharmacy was poor and resistant to change:

> *"I think you've probably should measure it* [health-related quality of life] *because it's a generic thing, but it's very unresponsive to change. If it did change, it's probably nothing to do with polypharmacy, or it might be but often won't be."*
>
> [HCP_08_GP]

Academics argued that health-related quality of life overlapped with treatment burden or patient satisfaction:

> *"Health-related quality of life, um… I think that's; I think that's a very good one to do. Treatment burden, for example, which is a bit more generic."*
>
> [A_13]

> *"I guess the satisfaction of patients and carers has some crossover with quality of life."*
>
> [A_15]

3.5.5. Patient/carer satisfaction

Patient and carer satisfaction was considered a beneficial and important outcome to measure in the context of adherence to appropriate polypharmacy. Academics emphasised the importance of clearly conceptualising and articulating satisfaction aspects, whether directly related to adherence or the overall healthcare process:

> *"Patient/carer satisfaction, I think that's a really important one. I think you have to think again about, you know, what aspect of satisfaction are we thinking about here? Are we talking about satisfaction with their overall care, or with satisfaction with their medicines specifically?"*
>
> [A_13]

Public members described the 'patient and carer satisfaction' outcome using the term 'trust'. They believed that establishing trust between older patients and the healthcare team was crucial to encouraging adherence to prescribed treatments:

> *"The patient will be happy and satisfied with the quality; I can say he will trust the healthcare system and the medical staff; this is outcome number four* [patient/carer satisfaction].*"*
>
> [PP_02]

3.5.6. Healthcare utilisation

Participants considered healthcare utilisation a relevant and important outcome for managers, policymakers and researchers:

> *"…some of the outcomes that service, providers, managers, policymakers would be wanting to look at, you know, the healthcare utilisation."*
>
> [A_07]

Some participants believed that healthcare utilisation was closely related to cost-effectiveness and was often considered in conjunction with cost-effectiveness:

> *"I guess healthcare utilisation kind of goes hand in hand with that, in terms of looking at those kinds of outcomes and cost-effectiveness."*
>
> [A_03]

Nevertheless, determining the aspect of healthcare utilisation that needed to be measured was considered an essential step towards an accurate assessment:

> *"healthcare utilisation, yeah, I think that's, that's a tricky one because it depends on what aspect of healthcare utilisation you're interested in."*
>
> [A_13]

3.5.7. Cost-effectiveness

Cost-effectiveness of a healthcare intervention was considered a good measure to determine whether an intervention was equally effective and value for money when compared to usual care to convince decision-makers to support a new intervention:

> *"…We've got to measure the cost-effectiveness when you're measuring interventions because it's the only way you will persuade policymakers to pay for things if they know it's cost-effective, and a… So, we do need to incorporate that, so cost-effectiveness definitely should be included as an outcome."*
>
> [A_13]

Cost-effectiveness, however, was thought to be challenging to measure, with inconsistencies in how it was measured and reported in studies:

> *"…the one that gives me hesitation is cost because it's really hard to measure, and it's hard to measure well, and people measure it differently."*
>
> [HCP_01_Pharm]

> *"…cost-effectiveness, one, I think that's, that seems pretty tricky to me. I'm not… I think it's an important part of the equation, but I'm not sure how you actually evaluate that."*
>
> [PP_05]

In addition, it was noted that cost-effectiveness and all adverse events and side effects were inadequately reported in trials aimed at improving adherence to appropriate polypharmacy in older patients.

> *"Cost-effectiveness and adverse events were things that were fairly poorly reported."*
>
> [HCP_02_Pharm]

3.6. Additional outcomes suggested

A small number of participants suggested six additional outcomes, including treatment burden, mortality, falls, frailty, medication wastage, and health-related quality of life for caregivers. Treatment burden was supported by a number of academics who believed that if a healthcare intervention was designed to improve medication adherence, it would implicitly reduce the treatment burden on patients:

> *"The intervention to improve adherence should also reduce treatment burden. So that's why I'm thinking it could be something worth measuring."*
>
> [A_04]

All outcomes suggested were compiled and summarised in Table 3.

4. Discussion

This study met its objectives in relation to the perspectives of key

Table 3

Additional outcomes, along with the number of participants who suggested each outcome, explanation and excerpt/s.

Additional outcomes suggested by participants	Number of participants who suggested each outcome	Explanation and interview excerpt/s
Treatment burden	4	One participant pointed out the practical aspects of managing multiple medications. This includes taking many medications, which can create difficulties in organising and keeping track of doses, medication timing schedules, and refilling prescriptions, increasing the overall workload on patients: *"Managing the burden of polypharmacy, and with regards to burden, not just the number of medicines, but the logistics that come with being on so many medicines."* [A_07] Some participants highlighted that 'treatment burden' was an all-encompassing outcome. They emphasised that treatment burden and health-related quality of life were separate concepts: *"Treatment burden, for example, is a bit more generic and isn't, I guess, captured so readily by any of these other indicators, these other outcomes looking at it. So, treatment burdens, obviously, a little bit different to quality of life."* [A_13]
Mortality	2	Mortality was also considered significant due to the correlation between higher mortality rates and poor medication adherence: *"Mortality is of common one that I would've expected to see. A lot of medicines that we are giving medicines intended to prolong life."* [A_08] *"We might be able to get all-cause mortality as a, as a measure as well. It's obviously not going to lend itself well to a lot of things."* [HCP_07_Pharm]
Falls	2	Academics considered falls as a way of ensuring that the patient had received effective and evidence-based treatment. Higher falling risks were likely to be associated with poor medication adherence: *"Because that's [falls] also a way of making sure that the person is getting appropriate treatment, whether that's not getting too many or not getting that as a side effect and the medications are appropriate."* [A_08]
Frailty	1	Frailty was considered an important outcome to determine the potential impact of an adherence intervention on the incidence of frailty: *"…might be interesting to consider, would be something like frailty, which you're looking to see how an adherence intervention whether it can impact upon frailty or not."* [A_07]
Medication wastage	1	Medication wastage was deemed important to measure, as non-

Table 3 (*continued*)

Additional outcomes suggested by participants	Number of participants who suggested each outcome	Explanation and interview excerpt/s
Health-related quality of life for caregivers	1	adherent patients returned medications that were no longer used due to side effects, medication ineffectiveness, or other reasons: *"…something is not on here; medication wastage, so this is something pharmacists mentioned a lot in a study I was involved in, in terms of medications coming back to the pharmacy from patients."* [A_15] Health-related quality of life for caregivers was another important outcome to be reported and measured since carers play a central role in supporting older patients, which would affect caregivers' mental and physical health: *"It's [health-related quality of life for caregivers], it's simply the fact of life that you take care of people, which is great and nice, but then who's taking care of you, and what happens when something happens to you because you're burned out emotionally or physically? And then what happens to, to the person you're taking care of? So, that's why I think that it's important to measure that…"* [PP_04]

stakeholders on challenges associated with medication adherence to appropriate polypharmacy and strategies to overcome these challenges. Seven outcomes were considered important for studies aimed at improving adherence to appropriate polypharmacy in older patients. A further six outcomes were suggested by participants.

Many participants believed that age-related cognitive and physical disabilities contributed to medication non-adherence in older patients. They also reported that medication beliefs, poor health knowledge, education and medication information and forgetfulness were important causes of medication non-adherence. These patient-related barriers reiterate previous findings in the literature.[32–35] Additionally, other participants argued that the complexity of the medication regimens led to difficulties in managing medications, resulting in dose skipping and irregular medication intake. The link between complex medication regimens and medication non-adherence[9] and the inability to manage medications[36] has been well-documented in previous reviews.

Public members emphasised the importance of ensuring appropriate evidence-based prescribing instead of remaining on outdated medications. Previous studies reported that this stemmed from communication breakdown and the involvement of multiple specialists from different healthcare settings, each seeking to maintain his/her prescribing authority.[37] Another socioeconomic challenge was the inability of low-income or uninsured older patients to afford medications due to higher medication costs. However, Baird et al.[38] showed this depended on the cost-sharing regulations implemented across different countries.[38] As the number of medications increases, healthcare expenses and medication costs rise, adding additional burdens on patients and healthcare services.[39]

A range of strategies was suggested to overcome obstacles to adherence. The majority of participants believed multi-compartment compliance aids and reminders were problem-solving, pragmatic and convenient solutions. Furthermore, many participants acknowledged that shared decision-making should be the starting point to improve

adherence rather than adopting the paternalistic doctor-patient relationship. Previous studies reported that a good HCP-patient relationship would promote trust for open conversations about treatment regimens, patients' perceived benefits or risks, needs, beliefs, fears and concerns regarding their medicines, conditions, and side effects.[34,35,40,41] In addition, comprehensive medication review, motivational interviews and patient education ensured the prescribed medicines were appropriate, current, and effective. Other socioeconomic solutions were reducing medication costs and involving caregivers, as they played an important role in monitoring and supporting the treatment journey of older patients.

It is worth noting that medication non-adherence in adults is not confined to patients taking multiple medicines; instead, it may affect individuals taking fewer medications (e.g. <4 regular medications).[42,43] Indeed, non-adherence is a consequence of complex, interrelated factors, including patient-related, medication-related, healthcare system-related, disease-specific, financial and logistical factors. Therefore, there is a pressing need to apply comprehensive, tailored and complex interventions targeting adherence-related factors and patients' needs. The development of theory-informed interventions to address adherence behaviours and prescribing appropriate medications should be advocated as a way to tackle non-adherence, in addition to rigorous evaluation.[44]

The seven outcomes extracted from a recent Cochrane review[20] and two other adherence studies[22,23] received almost unanimous support for inclusion in future trials. Medication adherence across multiple medications was considered the key outcome. Nevertheless, participants argued that measuring adherence was challenging, and no universally accepted approach has been identified to assess medication adherence.[11,45] Therefore, researchers have employed a combination of subjective and objective techniques to measure adherence to single medications.[46] More importantly, no accurate method has been designed to measure adherence to appropriate polypharmacy, and previous methods have measured adherence to a single medication rather than appropriate polypharmacy.[47] This emphasises the need to develop a reliable and valid technique to measure adherence to appropriate polypharmacy.[47] Additionally, academics deemed 'condition-specific outcomes' important and straightforward, as they may directly detect patients' medication consumption, whether overutilisation or underutilisation.[20] However, given the high number of long-term conditions and the associated clinical outcomes,[28] further consideration would need to be given as to how measurement could be achieved, as there is no single outcome measurement tool for assessing multiple long-term conditions.

Participants also emphasised the importance of 'adverse events and side effects', particularly for older patients taking appropriate polypharmacy, as they could be more susceptible to a prescribing cascade. This could be attributed to age-related pharmacokinetic and pharmacodynamic characteristics.[48] Academics highlighted that adverse events and side effects were negatively associated with health-related quality of life and healthcare utilisation. Indeed, medication-related harm and side effects have been recognised as the root cause of hospital admissions and utilisation of healthcare services in older adults.[49] Additionally, some academics indicated that the negative impact of multiple medicines was not only linked to adverse events and side effects, but also affected patients' health-related quality of life. Previous studies have shown that the higher the number of medications prescribed, the worse the health-related quality of life.[50,51] A few participants emphasised that intervention studies designed to address the negative effect of appropriate polypharmacy had no significant influence on health-related quality of life. Additionally, it was noted that health-related quality of life overlapped with patient satisfaction. This was supported by a previous study, whereby both outcomes were affected by multidimensional factors like socioeconomic and clinical factors (e.g. education and HbA1c levels).[52] Therefore, reduced patient satisfaction levels could be a reliable predictor of poor health-related quality of life.[53]

Academics and HCPs noted that the outcome 'patient and carer satisfaction' was important as it reflects the quality of the healthcare services provided.[54] However, they emphasised the need to standardise this concept and specify what it would measure in relation to adherence. Indeed, the terminology used to define satisfaction has been vague and varies greatly in the academic literature due to its complex nature.[55] For example, in previous studies, adherence of patients receiving multiple medicines was measured by gauging their satisfaction with the quality of pharmaceutical care and the overall services provided in the healthcare sector.[56] Another study measured patients' satisfaction with respect to the most recent pharmacy visit[57] or satisfaction with pharmacy-related services.[58] It is, therefore, essential to specify how satisfaction would be measured in studies aimed at improving adherence to appropriate polypharmacy.

Similarly, healthcare utilisation was another important outcome measured differently in studies, highlighting the need to harmonise this outcome to ensure consistency in measuring and reporting it across studies. Previous studies which evaluated adherence in patients receiving multiple medicines measured hospital admissions and emergency department visits, whereas others measured unscheduled GP visits.[20] Academics reported that healthcare utilisation and cost-effectiveness were closely related. Indeed, the information derived from healthcare utilisation has been used as input data to calculate cost-effectiveness.[56,57] However, some participants reported that measuring cost-effectiveness was challenging due to inconsistencies in the methods used in previous adherence studies. This is due to differences in the clinical indicators (e.g. short-term disability costs, outpatient and inpatient costs or total costs) used for analysis in adherence studies, methodological approaches, and study designs used.[59]

Participants suggested a further six outcomes, but in a number of cases, the outcome was proposed by only one participant. These outcomes were mortality, treatment burden, falls, frailty, medication wastage and health-related quality of life for caregivers. According to previous reviews, some of these outcomes were reported in very few studies, such as mortality[20] and medication wastage.[60] West et al.[60] identified inconsistencies in the terminologies used to define medication wastage, and only a small number aimed to reduce this outcome. Additionally, medication wastage and healthcare utilisation are linked, with medication wastage being identified as one of the major contributors to healthcare utilisation.[61]

'Treatment burden' was another indicator of non-adherence and was considered similar to health-related quality of life. However, earlier studies that evaluated adherence to appropriate polypharmacy in older patients did not measure the treatment burden outcome.[20] Instead, the pill burden index was used to measure if medication prescribing and the overall medication burden imposed on older patients improved due to a polypill intervention.[62] Treatment burden and pill burden are linked as the latter can significantly impact the former, thereby representing one aspect of the broader concept of treatment burden.[62,63]

Only a small number of participants recommended considering frailty and falls as additional outcomes to measure adherence to appropriate polypharmacy in older people. However, previous studies reported frailty as a risk factor or a determinant of suboptimal adherence rather than an adherence-related outcome.[20] In addition, earlier studies that aimed to reduce the risk of falling by improving adherence to appropriate polypharmacy in older patients revealed conflicting results, with either no significant change[64] or showed a decrease in falls.[65] Finally, previous studies have found a negative association between caregiving and health-related quality of life for caregivers. However, this finding mostly relied on the extent to which caregivers were actively involved in providing care.[66]

4.1. Strengths and limitations

To our knowledge, no previous studies have explored outcomes of importance related to adherence to appropriate polypharmacy in older

patients. This study has addressed this gap, and supports previous literature in identifying obstacles older patients encounter when taking appropriate polypharmacy, as well as potential strategies to tackle these challenges. A major strength is data triangulation by gathering perspectives from various stakeholders with diverse backgrounds and locations. This minimised selection bias and enhanced the applicability, transferability, and future uptake of the COS.

However, this study has two major limitations. A small number of public participants were recruited. This stakeholder group was challenging to engage with despite using different sampling techniques and contacting 13 public organisations across a number of countries. This may potentially affect the relevance of our findings for a number of international settings. This issue is also reflected in the second limitation in that most participants were based mainly in Europe, with no participants from low- and middle-income countries.

5. Conclusion

This study has highlighted the challenges associated with adherence to appropriate polypharmacy. To overcome these challenges and ensure effective medication management and better adherence, strategies should be personalised and based on collaborative teamwork among HCPs across all healthcare sectors and with patients. In addition, seven outcomes related to adherence to appropriate polypharmacy, compiled from previous studies on adherence to multiple medicines in older patients, were presented. These seven outcomes included medication adherence across multiple medications, health-related quality of life, all adverse events and side effects, healthcare utilisation, cost-effectiveness, patient/carers satisfaction and condition-specific outcomes. A small number of participants also suggested an additional six outcomes, namely treatment burden, falls, frailty, medication wastage, mortality and health-related quality of life for caregivers. This list of 13 outcomes will be used in a future consensus study to identify the final list of outcomes (COS) for trials to improve adherence to appropriate polypharmacy in older patients. Thereafter, outcome measurement instruments will be selected for each outcome in the COS to assess the impact of adherence to appropriate polypharmacy in older patients.

Consent for publication

All participants provided their consent before participating in the interviews and were aware that quotations from the interviews may be used; however, all information has been completely anonymised.

CRediT authorship contribution statement

Hanadi A. Al Shaker: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Heather E. Barry:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization. **Carmel M. Hughes:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2024.100479.

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