Research in Social and Administrative Pharmacy 20 (2024) 92–101

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Original Research

Developing indicators for medication-related readmissions based on a Delphi consensus study

Nicole Schönenberger [a,b,*], Anne-Laure Blanc [c,d], Balthasar L. Hug [e,f], Manuel Haschke [a], Aljoscha N. Goetschi [a,b], Ursina Wernli [a,b], Carla Meyer-Massetti [a,g]

[a] Clinical Pharmacology and Toxicology, Department of General Internal Medicine, Inselspital, Bern University Hospital, 3010, Bern, Switzerland
[b] Graduate School for Health Sciences, University of Bern, 3012, Bern, Switzerland
[c] Pharmacy of the Eastern Vaud Hospitals, 1847, Rennaz, Switzerland
[d] Institute of Pharmaceutical Sciences of Western Switzerland, University of Geneva, 1205, Geneva, Switzerland
[e] Department of Internal Medicine, Lucerne Cantonal Hospital, 6000, Lucerne, Switzerland
[f] University of Lucerne, Faculty of Health Sciences and Medicine, 6005, Lucerne, Switzerland
[g] Institute of Primary Healthcare (BIHAM), University of Bern, 3012, Bern, Switzerland

ARTICLE INFO

Keywords:
Drug-related readmission
Risk factor
Clinical pharmacy
Medication safety
Transition of care
Hospital discharge

ABSTRACT

Background: Medication-related readmissions challenge healthcare systems by burdening patients, increasing costs and straining resources. However, to date, there has been no consensus study on indicators for medication-related readmissions.

Objectives: This Delphi study aimed to develop a consensus-based set of indicators for detecting patients at risk of medication-related readmission.

Methods: An expert panel of clinical pharmacists, physicians and nursing experts participated in a two-round Delphi study. In round 1, 31 indicators taken from the literature were rated for relevance on a scale from 1 to 9, with a median rating of 7 or higher suggesting relevance. The RAND/UCLA method was used to determine consensus. In round 2, indicators lacking consensus were re-rated together with a series of new indicators generated by the experts. Additional details were sought for some indicators. The main outcomes were the relevance of, consensus on, and completeness of the proposed indicators for identifying risks of 30-day medication-related readmission.

Results: Thirty-eight experts participated in round 1. Consensus was found for all the indicators, with 25 included and 6 excluded. Thirty-four experts participated in round 2. Consensus was found for all 5 newly suggested indicators, and 4 were included. The expert panel prioritized the following indicators: (1) insufficient communication between different healthcare providers, (2) polypharmacy (≥7 medications), (3) low rates of medication adherence (twice-weekly mistakes or missing administration), (4) complex medication regimens (≥3 doses, ≥2 dosage forms and ≥2 administration routes per day), and (5) multimorbidity (≥3 chronic conditions). The final set comprised 29 indicators.

Conclusions: The indicator set developed for flagging potential medication-related readmissions could guide priorities for clinical pharmacy services at hospital discharge, improving patient outcomes and resource use. A validation study of these indicators is planned.

1. Introduction

Medication-related readmissions (MRRs) occur when patients are rehospitalized due to issues directly linked to their medications. These include medication errors, inappropriate use of medications like under- or overuse and adverse drug reactions. As medication therapy becomes increasingly complex and is one of the most significant interventions in healthcare,[1–3] it is not surprising that a considerable proportion of readmissions, estimated at 21% (range 3–64%), have been deemed to be potentially medication-related.[4] Furthermore, 69% (range 5–87%) of

* Corresponding author. Inselspital - Bern University Hospital, Department of General Internal Medicine, Clinical Pharmacology, Anna-von-Krauchthal-Weg 7, CH-3010, Bern, Switzerland.
E-mail address: nicole.schoenenberger@insel.ch (N. Schönenberger).

https://doi.org/10.1016/j.sapharm.2024.02.012
Received 11 December 2023; Received in revised form 14 February 2024; Accepted 18 February 2024
Available online 27 February 2024

MRRs are thought to be preventable.[4] Research indicates that readmitted patients face higher mortality and reduced quality of life compared to those who are not readmitted.[5–9] Additionally, readmissions impose economic burdens on healthcare systems and strain their resources.[10,11] Considering the challenges posed by hospital readmissions and the high preventability rate of MRRs, particular attention should be given to mitigate the risk of MRRs.

Clinical pharmacists can play an important role in improving medication safety, especially when they identify and address medication-related issues through medication reconciliation and reviews, counseling and collaborative interventions within healthcare teams.[12–14] Clinical pharmacist interventions have been shown to help optimize medication regimens, ensure adherence and prevent adverse drug events.[15–19] Efforts have also been made to reduce readmissions through clinical pharmacist interventions.[20–25] However, evidence that these interventions significantly reduce readmissions has been inconclusive in many studies.[20–24] This may be because MRRs are not yet fully understood and, therefore, limited clinical pharmacy resources and interventions could not be allocated to the patients who would have benefitted from them most.

Enhancing our understanding of indicators for MRRs to better target and prioritize the patients most likely to benefit from clinical pharmacist interventions thus seems essential. Studies to identify indicators for MRRs have been conducted, and the indicators were summarized in a scoping review by Schönenberger et al.[26] Indicators significantly associated with MRRs included polypharmacy and prescribing issues. Specifically, suboptimal medication selection and under-prescribing were identified as key factors leading to MRRs. Non-adherence and certain medication groups have also shown significant associations with MRRs, including antithrombotic agents, insulin, opioids and diuretics.[26]

However, it is essential to recognize the complexity of MRRs and the diverse characteristics of the factors influencing them.[26] Most research has relied on retrospective study designs, leading to a higher prevalence of such routinely collected data as the number of medications and comorbidities. Sociodemographic factors, such as living arrangements, the scope of support in medication management and educational level, have been under-represented. Aspects requiring thorough assessment during hospitalization, such as medication literacy levels, may also have been insufficiently captured and reported. Consequently, there is currently no consensus on a definitive set of indicators deemed most important for MRRs and it is unclear if these indicators are indeed less important for MRRs or if they are underrepresented due to less frequent collection and analysis. This highlights the need for a more comprehensive, inclusive approach.

Given this lack of consensus, this study aimed to develop a set of indicators encompassing the clinical and sociodemographic factors for MRRs using the Delphi method. This method enables the inclusion of diverse perspectives from experts in the field, which is essential to reaching a consensus on a comprehensive set of indicators for MRRs.

2. Methods

2.1. Design

To develop a set of indicators for MRRs, a two-round Delphi study in Switzerland following the guidance on Conducting and REporting DElphi Studies (CREDES) was conducted.[27] The Delphi study research method uses a panel of experts who provide input through multiple rounds of anonymous surveys to reach a final consensus on a specific topic or problem.[28] The selection of indicators for round 1 was based on a scoping literature review published in 2023.[26] Most of the studies that have been conducted on this topic used either a descriptive or modeling approach. Therefore, certain indicators may be underrepresented in these studies, as they are not routinely collected and cannot be analyzed in such a framework. This consideration was the basis for the decision to conduct a Delphi study. A flow diagram of the Delphi process is shown in Fig. 1.

2.2. Selection of the experts

The selection of experts adhered to the Delphi study guidelines criteria.[29,30] Potential experts were required to have expert knowledge in either MRRs or medication safety, hold Swiss qualifications as a physician, pharmacist or nurse, and have clinical experience in inpatient, outpatient or long-term care settings. Care was taken to ensure that the settings and professional groups were approximately evenly distributed. Moreover, these criteria were intended to ensure homogeneity and multidisciplinary experts to broaden perspectives and improve the generalizability of the results. A panel size of 30–50 experts was targeted, as recommended in the guidelines.[30] Potential experts were selected from the authors' professional networks. Initial invitations were sent to 48 experts by email, with reminders sent to non-responders after 7 days. Experts who failed to respond within another 7 days were not included.

2.3. Indicator development

Initial potential indicators for MRRs were collected from a scoping literature review that found 37 relevant articles.[26] An indicator was included for the consensus analysis if it was mentioned in at least 3 articles. The research team then integrated other potentially relevant indicators that were either not addressed in the literature or addressed less than 3 times. An initial set of 20 indicators was identified in the scoping review, and 11 indicators were developed by the research team. All 31 indicators were reviewed for understandability and completeness, and some were accompanied by an explanation of their intended meaning. The 31 indicators were categorized into 6 topics: (1) patients' sociodemographic factors (n = 19), prescription-related factors (n = 6), adherence issues (n = 1), insufficient ambulatory monitoring (n = 1), transition of care factors (n = 3) and adverse drug reactions (n = 1). Indicators were intentionally defined broadly, i.e. without cut-off values or further specifications. Whether older age was a relevant risk for MRRs was presented without an age cut-off in round 1. Experts were asked to give cut-off values or specifications for indicators found to be relevant in round 1 and made it through to round 2. For example, they were asked to give a cut-off for when older age became a relevant risk for MRRs. Similarly, for prescription-related factors, round 1 asked whether under-prescribing medications in general was relevant to MRRs, and because this item reached round 2, the experts were asked which under-prescribed medications were most likely to cause MRRs.

2.4. Delphi round 1

Experts who had accepted our invitation received the round 1 questionnaire of 31 indicators in an Excel spreadsheet (2016, Microsoft, Redmond, USA) by email. They were asked to rate each indicator for relevance on a scale from 1 to 9 (with 1 indicating "extremely irrelevant", 5 being "uncertain" and 9 being "extremely relevant"). They were also asked to list their top 5 priority indicators, suggest any missing indicators and provide their personal sociodemographic information (e.g. profession, years of work experience, setting). The experts were free to give their written opinions on any of the indicators and to make general comments at the end of the questionnaire. The experts were asked to return the completed questionnaire within 2 weeks. If they failed to respond, a reminder was sent 1 day after the deadline, and they were asked to return the questionnaire within another week.

The median relevance rating and the disagreement proposed by the RAND/UCLA appropriateness method[31] were calculated for each indicator. RAND is a non-profit organization (stands for research and development), while UCLA stands for the University of California, Los Angeles. This method calculates the Interpercentile Range Adjusted for Symmetry (IPRAS), which accounts for rating asymmetry by considering

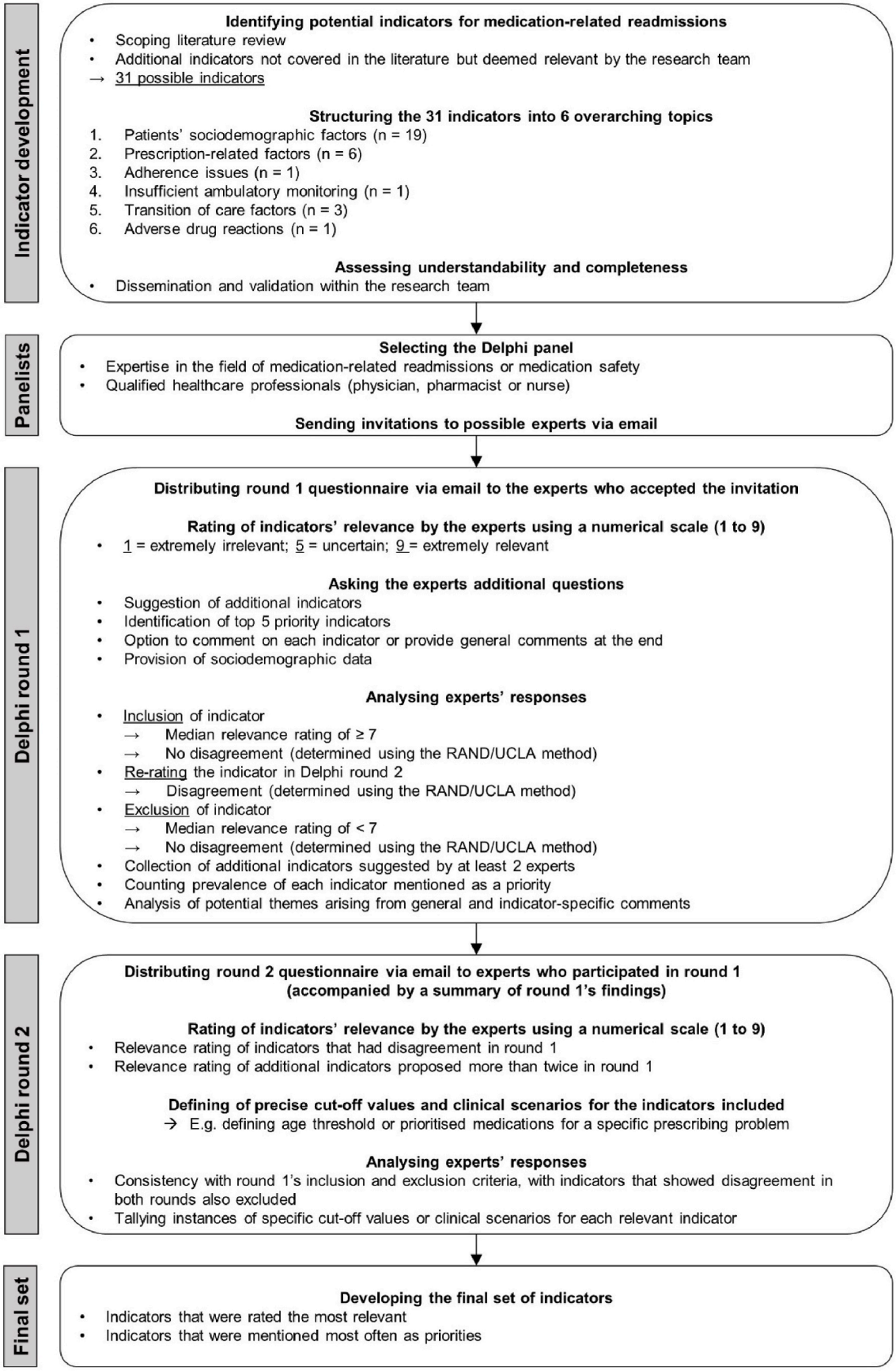

Fig. 1. Delphi process flow diagram.

the distance between the central point on the Interpercentile Range (IPR) and the middle point (5) on the scale from 1 to 9. The Asymmetry Index (AI) is calculated as 5 – IPRCP, where IPRCP is the central point of the IPR. The IPR is a measure of the rating dispersion, and the IPRCP is calculated as (30% quantile + 70% quantile)/2. The formula for calculating the IPRAS is IPRAS = IPRr + (AI * CFA), where IPRr is the IPR required for disagreement when perfect symmetry exists (found to be 2.35), AI is the Asymmetry Index and CFA is the Correction Factor for Asymmetry (found to be 1.5). If a particular indicator's IPR is larger than its IPRAS, then it is classified as a disagreement.

Indicators were included if their median rating was ≥7 without disagreement; they were excluded if their median rating was <7 without disagreement. Whenever disagreement was present, the indicator was rated again during Delphi round 2, irrespective of its initial rating.

If an additional indicators was suggested by at least 2 experts, it was incorporated into Delphi round 2 for an evaluation of its relevance. The frequency with which specific indicators were mentioned was assessed to determine the top 5 indicators. Lastly, experts' indicator-specific or general comments were examined to see whether they contained any potential new themes. The free-text comments were analyzed using a similar approach as for the additional indicators. If a new theme was mentioned or changes were suggested by at least 2 experts, it was considered relevant and included in the summary sent to the experts after round 1, or the change was included as re-rating option for round 2.

2.5. Delphi round 2

Two weeks after the end of Delphi round 1, a summary of its findings was emailed to all the experts who had returned the first questionnaire along with the round 2 questionnaire. The summary included the median relevance rating for all 31 indicators and signaled instances of disagreement. The median ratings given by each professional group (physicians, pharmacists and nurses) were also presented, and each expert received a reminder of their own initial relevance ratings. Thus, each expert could compare each indicator's overall rating, its professional group rating and their own. The summary also identified the newly suggested indicators and the 5 indicators most frequently identified as top priorities, also providing a compilation of the experts' comments.

The round 2 questionnaire was designed so that the experts would assess the relevance of newly suggested indicators and re-rate the indicators with prior disagreements using the same rating methods as in round 1. Indicators that required some clarification requested specific suggested cut-off values or clinical scenarios. Experts could choose predefined cut-off values (e.g. laboratory values) and clinical situations (e.g. specific medication groups) or propose different ones. This evaluation process was used for the newly suggested indicators and those that showed disagreement in round 1. The experts were again able to add written general and indicator-specific comments, and they were asked to return the completed questionnaires within 2 weeks. Failure to respond triggered a reminder sent 1 day after the deadline, and they were given another week to return the questionnaire.

The analysis of relevance ratings followed the methodology used in round 1, with identical inclusion and exclusion criteria. Indicators that caused disagreement across both rounds were excluded. If a newly suggested indicator had shown disagreement, it would have prompted a third round for its re-rating. If re-rating had again resulted in disagreement, the newly suggested indicator would have been excluded. The frequency with which cut-off values and specific clinical scenarios were mentioned was also analyzed. The cut-off value that was most frequently mentioned was subsequently incorporated as the final cut-off value in the indicator set. The experts were informed about round 2's results after these analyses.

2.6. Development of the final indicator set

The definitive set of indicators for MRRs was developed by arranging all the included indicators according to their relevance rating and the frequency with which they were identified as priority indicators.

3. Results

Of 48 experts invited to participate, 39 agreed (81% acceptance rate), 3 declined and 6 did not respond. Of the 39 experts who received the Delphi round 1 questionnaire, 38 returned it (97% response rate), and of the 38 who received the Delphi round 2 questionnaire, 34 participated (89% response rate). Table 1 shows the sociodemographic characteristics of the experts who participated.

Round 1's questionnaire is provided in Appendix 1. Of the 31 round 1 indicators, 25 (81%) were included (median relevance rating ≥7 and no disagreement) and 6 (19%) were excluded (median relevance rating <7 and no disagreement). No indicators showed disagreement. Table 2 summarizes the individual indicators and their respective medians and specifies whether the indicator was developed by the research team or derived from the literature. Median ratings are presented for the entire panel and or each professional group. None of the indicators showed disagreement, either when rated by the entire panel or when rated within a professional group. Table 2 also displays how many times an indicator was chosen as a priority indicator. A single expert missed 1 relevance rating for indicator number 5 (high medication regimen complexity index). For all the other indicators, all 38 experts provided a rating. However, not all the experts prioritized 5 individual indicators, nor did they stick to those provided in round 1's questionnaire. In cases where alternative indicators were mentioned as a priority, they were treated as missing indicators and excluded from the priority list. Overall, 23 of 190 potential priority ratings were missing because experts did not provide an answer. The bold indicator numbers in Table 2 show those that needed further specification in round 2 of the Delphi process.

In round 1, 5 additional indicators for MRRs were suggested for inclusion by at least 2 experts. These were.

1. Suboptimal access to caregivers: suggested 4 times
2. Having multiple prescribers: suggested 3 times
3. Having cognitive impairment: suggested 3 times
4. Being frail: suggested twice
5. Being female versus being male: suggested twice

Some new topics were identified during the analysis of the indicators and the general comments in the completed round 1 questionnaires.

Table 1
Sociodemographic characteristics of the experts who participated in the Delphi study.

Characteristic	Round 1	Round 2
Experts, n (%)	38 (100%)	34 (100%)
Sex		
Female, n (%)	18 (47%)	17 (50%)
Male, n (%)	20 (53%)	17 (50%)
Profession		
Physician, n (%)	15 (39%)	14 (41%)
Pharmacist, n (%)	16 (42%)	14 (41%)
Nurse, n (%)	7 (18%)	6 (18%)
Setting (multiple answers possible)		
Research, n (%)	20 (53%)	18 (53%)
Inpatient, n (%)	19 (50%)	17 (50%)
Outpatient, n (%)	15 (39%)	15 (44%)
Long-term care, n (%)	8 (21%)	7 (21%)
Years of experience		
> 20 years, n (%)	15 (39%)	13 (38%)
16–20 years, n (%)	7 (18%)	7 (21%)
11–15 years, n (%)	11 (29%)	9 (26%)
6–10 years, n (%)	5 (13%)	5 (15%)

Table 2
Results from Delphi round 1 on indicators for medication-related readmissions.

Indicator number	Indicator description	$\tilde{x}$ All experts (n = 38)	$\tilde{x}$ Physicians (n = 15)	$\tilde{x}$ Nurses (n = 7)	$\tilde{x}$ Pharmacists (n = 16)	Mentioned as a priority indicator	Disagreement
Patients' sociodemographic factors							
1	Older age (≥65 years)	7	7	7	6	2	No
2	Polypharmacy (number of drugs in the discharge prescription, ≥5 drugs)	8	8	8	8	15	No
3	Number of drug changes during the last hospital stay (including newly prescribed medications)	7	7	8	7	6	No
4	*Number of unplanned hospitalizations during the year before readmission*	*6.5*	*6*	*5*	*7*	3	*No*
5	High medication regimen complexity index (MRCI)	8	7	8	8	9	No
6	Prescription of potentially inappropriate medications (PIMs) to older adult patients (e.g. according to Beers criteria®[32] or the PRISCUS® list[33])	7	7	7	7	6	No
7 (team)	Patients impaired in the activities of daily living (ADL) (e.g. difficulties in performing self-care tasks like bathing, dressing, using the toilet or eating)	7	7	5	7	2	No
8 (team)	*Patients impaired in the instrumental activities of daily living (IADL) (e.g. managing finances, performing housework, using public transportation)*	*6*	*7*	*6*	*6*	4	*No*
9	*Dependent on help from outpatient, professional caregivers (e.g. home healthcare, living in a nursing home)*	*6*	*6*	*5*	*5*	1	*No*
10	*Dependent on help from informal caregivers (e.g. family members, neighbors)*	*6*	*7*	*5*	*6*	0	*No*
11 (team)	Patient's failure to attend and/or arrange a follow-up appointment with their primary care physician within the recommended timeframe, as stated in the discharge letter	7	7	7	7	7	No
12 (team)	*Limited educational level*	*6*	*6*	*7*	*6*	1	*No*
13 (team)	Low proficiency in the language spoken in the region of the hospital	7	7	7	6	2	No
14 (team)	Patients with little knowledge about their medications (i.e. low medication literacy)	7	7	7	7	5	No
15 (team)	Patients with renal impairment	7	8	6	7	6	No
16 (team)	*Patients with liver impairment/cirrhosis*	*6.5*	*7*	*6*	*6*	1	*No*
17	Number of comorbidities (≥3 chronic conditions)	8	8	7	8	8	No
18 (team)	Not benefitting from a medication reconciliation at hospital admission	7	6	7	7	4	No
19 (team)	Not benefitting from a medication reconciliation at hospital discharge	7.5	7	8	8	11	No
Prescription-related factors							
20	Under-prescribing ("indication, but no drug")	7	6	7	7	3	No
21	Over-prescribing ("drug, but no indication")	7	8	7	7	2	No
22	Overdose	8	8	8	8	7	No
23	Underdose	7	7	7	7	3	No
24	Drug–drug interactions	7	7	7	6.5	3	No
25	Prescription of medication, although at least one absolute contraindication is present	8	8	7	8	3	No
Adherence issues							
26	Low rate of medication adherence	8	8	7	8	12	No
Insufficient ambulatory monitoring							
27	Insufficient monitoring in the outpatient setting before readmission (by the patient or by a professional)	8	8	8	8	5	No
Transition of care factors							
28	Insufficient communication between healthcare providers (e.g. incomplete medication discharge information)	8	8	8	8	20	No
29 (team)	Inadequate medication counseling (at hospital discharge or in the ambulatory setting prior to readmission)	7	7	8	7.5	5	No
30	Insufficient medication supply, e.g. because the new medications are not procured after hospital discharge	7	6	8	7.5	4	No
Adverse drug reactions							
31	Adverse drug reactions (ADRs)	8	8	8	7.5	7	No

$\tilde{x}$: median.
An indicator was included if its overall median rating was ≥7 and it showed no disagreement. Indicators with an overall median rating of <7 and no disagreement were excluded and are printed in *italics*. Disagreement was calculated based on the RAND/UCLA appropriateness method.[31] Indicators developed by the research team have 'team' noted behind the indicator number. All other indicators were derived from a scoping review. Indicator numbers are presented in **bold** font if the indicator was included but required further specification in round 2.

Some participants mentioned age, polypharmacy and the number of comorbidities as being interrelated and that polypharmacy can be an indicator for lower medication adherence or for an increase in the likelihood of taking high-risk medications. Some experts also mentioned that indicators concerning the (instrumental) activities of daily living ((I)ADL) and being dependent on help from outpatient caregivers were not strong risk factors for experiencing an MRR. Instead, relevance depends on whether the patient receives adequate support in taking their medications and on how impaired they are in the (I)ADL; thus, the risk depends on living situations and the level of support received. Being

dependent on help was not seen as a strong enough risk factor for an MRR as long as communication between outpatient and inpatient caregivers was adequate. Some experts noted that certain risks are highly dependent on the patient's clinical situation or the medications involved in a prescribing problem. The corresponding medication groups were evaluated in round 2 of the Delphi study.

The questionnaire for round 2 can be found in Appendix 2. None of the 5 new indicators proposed in Delphi round 1 generated disagreements in round 2, resulting in the completion of the Delphi process. Of these 5 indicators, 4 were incorporated, and 1 was excluded due to its low relevance. Table 3 provides an overview of the relevance ratings assigned to the new indicators suggested in Delphi round 1. All the experts assigned relevance ratings to these new indicators, and there were no disagreements in the subgroup analyses made by the different professional groups.

The experts were also encouraged to select or define cut-off values for relevant indicators from round 1, where appropriate. Out of 578 possible cut-off ratings, 14 ratings by 8 different experts were missing. Table 4 presents the most frequently mentioned cut-off values for the applicable indicators.

Concerning the prescribing problems included in round 1, the experts were requested to determine the top 3 priorities regarding prescribed medication or medication groups. Diuretics were the most frequently mentioned (56 times) prescribed medications, followed by anticoagulants (51 times), insulin (38 times), opioids (36 times), and benzodiazepines and Z-drugs (28 times). Out of 612 possible ratings (34 experts x 18 priority medication ratings x 6 prescribing problems), 6 different experts missed out a total of 42 ratings. Table 5 provides a summary of the prescribed medications or medication groups that were most commonly mentioned as priorities for each individual prescribing problem, along with the corresponding number of experts who selected those medications or medication groups.

During Delphi round 2, several experts provided feedback that completing it was difficult, particularly the section related to prioritizing medication groups for the prescribing problems.

Table 6 shows the final set of indicators for MRRs selected. They are listed first by median relevance rating and then their number of mentions as a top 5 priority indicator. This list of indicators could be used to prioritize patients who require clinical pharmacy services at hospital discharge to mitigate their risk of an MRR.

4. Discussion

In an effort to establish a comprehensive set of indicators for MRRs, the present iterative 2-round Delphi study involved experts from diverse healthcare professions and settings and culminated in the selection of a final set of 29 indicators. The indicators span a wide range of domains, including patients' sociodemographic characteristics and factors relating to prescriptions, adherence and transitions of care. The experts ranked the 5 top priority indicators as follows: inadequate communication among the patient's different healthcare providers, polypharmacy, low medication adherence, high medication complexity and multimorbidity. These findings were consistent with earlier research, underscoring the importance of factors such as polypharmacy, adherence and transitions of care in contributing to MRRs.[34–41]

The literature mentions multimorbidity and medication complexity less frequently in connection with MRRs. This could be attributed to their interconnection with polypharmacy and, thus, why they are not being analyzed independently.[42] The study also identified specific medication groups linked to prescribing issues that deserve heightened attention and comprehensive medication reviews. Diuretics, anticoagulants, insulins, opioids, and benzodiazepines and Z-drugs were the medication groups most frequently mentioned among the prescribing problems included in the indicator set. The first 4 medication groups were also those found most frequently in the literature.[26] As such, this Delphi study confirmed the relevance of numerous indicators identified in previous research.

This Delphi study also highlighted such indicators as inadequate medication counseling or reconciliation as important. Although the literature does not explicitly mention them as increasing the risk of MRRs, some studies have shown that medication counseling and reconciliation interventions can reduce all-cause readmission rates.[43–45] Insufficient medication literacy or limited language skills were also considered relevant indicators but were not described in the literature as factors contributing to MRRs. However, the broader concept of lower health literacy has been shown to be associated with higher all-cause readmission rates.[46,47]

Previous studies mostly employed descriptive statistics or modeling approaches, which primarily capture indicators already routinely collected. The methodology of this study ensured that the same attention was given to the indicators regardless of whether they are already collected in usual care. This approach provides a rationale for intensifying systematic, structured data collection about such indicators and implementing interventions aimed at mitigating their risks.

Certain well-established indicators in the literature may have an inherently higher level of relevance, as observed in the present study. Alternatively, the fact that the indicators developed by the research team received lower relevance ratings than those taken from the existing literature might be because participants were inclined to view established indicators as more relevant, due to their familiarity rooted in their connections to the literature. Although the experts were not asked to consider whether indicators were measurable, the limited measurability of some of the team-developed indicators might also have influenced experts' relevance ratings. Furthermore, the exclusion of 3 indicators derived from the literature and the inclusion of 8 research-team-developed and 4 newly proposed indicators underscores the valuable

Table 3
Results for the new indicators suggested for medication-related readmissions proposed in Delphi round 1.

Indicator number	Indicator description	$\tilde{x}$ All experts (n = 34)	$\tilde{x}$ Physicians (n = 14)	$\tilde{x}$ Nurses (n = 6)	$\tilde{x}$ Pharmacists (n = 14)	Disagreement
Newly suggested indicators						
32 (new)	Access to caregivers (i.e. not having a family doctor, or difficult-to-reach caregivers due to impaired mobility, long distance or difficulties arranging appointments, etc.)	7	8	8	8	No
33 (new)	*Being female versus being male*	*5*	*4*	*5*	*5*	*No*
34 (new)	Having several prescribers simultaneously or changing prescribers (hospital, rehabilitation facility, family doctor, specialist)	8	7	8	7.5	No
35 (new)	Being cognitively impaired and having no support from family or professional caregivers	8	8	9	8	No
36 (new)	Being frail, according to the Clinical Frailty Scale	7	7	7	7	No

$\tilde{x}$: median.

Table 4
Cut-off values of the indicators included for medication-related readmissions most frequently chosen by the experts.

Indicator number	Indicator description	Cut-off	Number of experts (n)
1	Older age	- ≥ 75 years old	20
2	Polypharmacy	- ≥ 7 medications	17
3	Number of drug changes during the last hospital stay	- ≥ 2 changes	13
5	Medication complexity	- ≥ 3 doses per day and ≥2 different dosage forms per day and ≥2 administration routes	19
6	Prescription of potentially inappropriate medications	- PRISCUS® list[33] as the most suitable list for medication-related readmissions	12
7 (team)	Impaired activities of daily living	- Moderate impairment: patient requires assistance or supervision to complete some self-care tasks, e.g. needing help with bathing, using the toilet or managing medications	27
13 (team)	Low proficiency in the language spoken	- Patient's ability to communicate in the region's language is significantly limited, requiring language support services. They may struggle to understand complex medical instructions or explanations and may have difficulty expressing their own symptoms or concerns	25
14 (team)	Low medication literacy	- Limited understanding of medication purpose, instructions and potential side effects, leading to difficulty adhering to medication regimen and identifying problems	25
15 (team)	Patients with renal dysfunction	- Estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2	9
17	Number of comorbidities	- ≥ 3 chronic conditions	17
24	Drug–drug interactions	- One or more interactions with a severity level of 'not recommended'	10
26	Medication non-adherence	- Medium non-adherence: 2–4 times per week: forgets to take medication or wrong administration	27
29 (team)	Insufficient medication counseling	- Counseling is inadequate and leaves the patient with significant knowledge gaps, e.g. the patient may not be told anything about their medication or may only be given a brief explanation with no follow-up instructions. A written medication plan is provided	16
30	Insufficient medication supply	- 4–7 days	17
34 (new)	Number of prescribers	- ≥ 2 prescribers - ≥ 3 prescribers	Each: 15
35 (new)	Cognitive impairment	- Medium cognitive impairment without any form of support	21
36 (new)	Frailty	- Clinical Frailty Scale scores ≥6	14

Table 5
Most frequently mentioned medication groups in reference to each prescribing problem included in Delphi round 1.

Indicator number	Prescribing problem	Medication groups	Number of experts (n)
21	Over-prescribing	Benzodiazepines and Z-drugs	20
		Opioids	11
		Antipsychotics/neuroleptics	11
22	Overdose	Anticoagulants	15
		Insulins	12
		Opioids	10
		Cardiac glycosides	10
20	Under-prescribing	Diuretics	13
		Inhaled therapies for asthma and/or chronic obstructive pulmonary disease (COPD)	12
		Insulins	9
		ACE inhibitors or AT-II antagonists	9
23	Underdose	Diuretics	11
		ACE inhibitors or AT-II antagonists	10
		Anticoagulants	9
27	Insufficient ambulatory monitoring	Diuretics	15
		Anticoagulants	13
		Opioids	8
		Insulins	8
		Cardiac glycosides	8
24	Drug–drug interactions	Sedative burden	25
		Burden of drugs increasing the likelihood of falls	24
		Interactions of antithrombotic agents	18

contribution that qualitative research methods can have in the domain of indicator development when performed alongside quantitative studies.

Although the set was not specifically developed for prioritizing patients for interventions by clinical pharmacists at hospital discharge, it could be applied in this context. Some indicators, such as polypharmacy, can be used directly at discharge for prioritization, while others require information from previous hospitalizations or observations during the current hospital stay. For example, the indicator "insufficient communication" can be applied if communication was inadequate in previous hospitalizations, at admission or during the current hospitalization (e.g., delayed or incomplete transfer of medication information). These indicators have the added advantage of providing insights into potential interventions, such as improving communication about medication information.

This study recruited a diverse panel of experts representing various healthcare professions and settings involved in medication use processes. Physicians and pharmacists were equally well represented, however, fewer nurses participated. This may have resulted in different outcomes compared to a scenario with equal numbers of all 3 professional groups. The lower number of nurses did not stem from a lower willingness to participate but from problems identifying nurses who met the predefined selection criteria. Nevertheless, we are confident that our multidisciplinary approach ensured a comprehensive evaluation of MRR indicators.

The comprehensiveness of our approach resulted in the inclusion of a relatively high number of indicators and the exclusion of but a few. Although this suggests that our set of indicators is relatively complete, it may make its practical application challenging. Depending on a hospital's electronic patient record, not all of the indicators may be available for analysis, and implementing its use at scale could be too time-consuming. Although the immediate applicability of this set of indicators is not inconceivable, the aim is to develop a shorter version or a scoring system after a validation study's results become available. This validation study will identify MRRs and assess whether the identified indicators were present in patients who experienced MRRs compared to

Table 6
Final set of indicators for medication-related readmissions with their corresponding cut-off values or medication groups (where applicable). The indicators are sorted by median relevance rating and their ranking as priority indicators.

Indicator number	Indicator description	Median relevance	Mentioned as priority indicator
28	There are signs that the different healthcare providers communicate insufficiently with each other (e.g. incomplete discharge or admission medication plans)	8	20
2	The patient takes ≥7 medications	8	15
26	The patient forgets to take their medications or administers them wrongly at least twice per week	8	12
5	The patient follows a medication regimen that involves taking ≥3 doses per day, using ≥2 different dosage forms and administering them via ≥2 different routes each day	8	9
17	The patient has ≥3 chronic conditions	8	8
22	If the patient is treated with anticoagulants, insulin, opioids or cardiac glycosides: verify that the dosage is accurate and not too high	8	7
31	If the patient is treated with diuretics, anticoagulants or insulins: assess for any signs of adverse drug reactions	8	7
27	If the patient is treated with diuretics, anticoagulants, opioids, insulin or cardiac glycosides: ensure that the medications are accurately monitored in the outpatient setting	8	5
25	The patient receives at least 1 medication for which an absolute contraindication exists	8	3
34 (new)	The patient has >2 prescribers	8	-[a]
35 (new)	The patient has at least a medium degree of cognitive impairment and no support from family or professional caregivers	8	-[a]
19 (team)	The patient did not benefit from a medication reconciliation at hospital discharge	7.5	11
11 (team)	The patient lacks the ability to attend and/or schedule a follow-up appointment with their primary care physician within the recommended timeframe, as specified in the discharge letter	7	7
3	The patient had ≥3 medication changes during the last hospital stay; medication changes include newly prescribed medications	7	6
6	The patient is treated with potentially inappropriate medications (PIMs) as defined in the PRISCUS® lis[33] t	7	6
15 (team)	The patient has an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2	7	6
14 (team)	The patient has a limited understanding of their medications' purposes, instructions and potential side effects, which leads to challenges in adhering to the medication regimen and identifying problems	7	5
29 (team)	The medication counseling at hospital discharge is inadequate and leaves the patient with significant knowledge gaps, e.g. the patient may receive a written medication plan but be told nothing about their medication or may only have received a brief explanation without any follow-up instructions	7	5
18 (team)	The patient did not benefit from a medication reconciliation at hospital admission	7	4
30	Insufficient medication supply, e.g. because the new medication prescriptions are not collected after hospital discharge	7	4
20	If the patient has a condition that requires the prescription of a diuretic, an inhalation therapy for asthma and/or chronic obstructive pulmonary disease (COPD), an insulin therapy, or an ACE inhibitor or AT-II antagonist: verify whether the respective medications are prescribed	7	3
23	If the patient is treated with diuretics, ACE inhibitors or AT-II antagonists, or anticoagulants: verify that the dosage is accurate and not too low	7	3
24	If the patient is treated with medications known for causing sedation, increasing the risk of falls, or with antithrombotics: assess the sedative or fall-inducing drug burden, or examine whether adjustments to the antithrombotics regimen are necessary due to potential interactions	7	3
1	The patient is ≥ 75 years old	7	2
7 (team)	The patient experiences moderate impairment in the activities of daily living, necessitating assistance or supervision to accomplish certain self-care tasks, e.g. requiring aid with bathing, using the toilet or managing medications	7	2
13 (team)	The patient possesses a significantly limited capacity to communicate in the language commonly used in their hospital region, necessitating the provision of language support services. This limitation could result in challenges understanding complex medical instructions or explanations and articulating their personal symptoms or concerns	7	2
21	If the patient is treated with benzodiazepines or Z-drugs, opioids or antipsychotics/neuroleptics: ensure the presence of an indication for the respective medications	7	2
32 (new)	The patient has limited access to caregivers, i.e. no family doctor, hard-to-reach caregivers (either due to impaired mobility, long distance or reasons like difficulties arranging appointments)	7	-[a]
36 (new)	The patient is frail and scores at least 6 on the Clinical Frailty Scale	7	-[a]

[a] The newly suggested indicators do not have priority ratings because the priority rating was done during Delphi round 1. 'New' means that the indicator was proposed in Delphi round 1, 'team' means that the indicator was developed by the study team. If there is only a number, the indicator was derived from the literature.

those who did not.

The present study has some limitations that should be considered when interpreting the results. The indicators' feasibility and measurability were not assessed and, therefore, some of them (e.g. low medication adherence or patients not being able to organize follow-up appointments), may be a challenge in terms of data collection, standardization and clinical implementation. The experts did not assess feasibility and measurability because accessibility to structured healthcare data varies widely across regions and countries.[48,49] Thus, an argument could be made for conducting feasibility and measurability assessments at the relevant level (e.g. specific hospitals). The indicator set could then be adapted to the type and quality of data available. Because this study only involved healthcare professionals working in Switzerland, some indicators may reflect issues unique to the country's healthcare system, potentially limiting the generalizability of some indicators (e.g. in other countries than Switzerland patients might always receive medication reconciliation by a pharmacist). Nonetheless, since this Delphi study was performed rigorously and preceded by an extensive literature review, the results would probably not have differed significantly, even if an international panel had been involved. An additional weakness lies in the study's recruitment strategy, which primarily drew on experts from the authors' professional networks, potentially limiting the panel's diversity and representativeness. Another aspect to consider is that the indicator set may be incomplete. While the anonymity ensured by the Delphi process is advantageous for fostering open communication, free from the influence of dominant personalities, it is conceivable that this anonymity could have inadvertently lowered expert engagement with the process. Consequently, participants might not have been actively thinking about potential missing indicators and might have given this more thought had their contributions not been anonymous. Lastly, the Delphi approach has inherent limitations; in particular, a certain subjectivity during the evaluation of free-text responses cannot be ruled out.

5. Conclusions

This study used a Delphi process involving a diverse panel of healthcare experts to create a comprehensive set of 29 indicators for MRRs. These indicators spanned several domains, including patient sociodemographics, prescribing factors, adherence variables and elements of care transitions. The findings underscored the importance of addressing multifaceted medication-related issues to reduce readmissions. Poor communication between healthcare providers emerged as the top priority, emphasizing the need for seamless information exchange during care transitions. In addition, certain medication groups, such as diuretics, anticoagulants, insulins, opioids, and benzodiazepines or Z-drugs were identified as high-risk. The final set of indicators provides a starting point from which to prioritize the patients who should be the focus of clinical pharmacy services before and during hospital discharge. Future research should validate and adapt these indicators. Ultimately, this study contributes to ongoing efforts to better understand MRRs and to provide targeted support to patients at a high risk for MRRs.

Funding

This research received no dedicated grants from funding agencies in the public, commercial or not-for-profit sectors.

CRediT authorship contribution statement

Nicole Schönenberger: Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Anne-Laure Blanc:** Writing – review & editing, Methodology, Conceptualization. **Balthasar L. Hug:** Writing – review & editing, Methodology, Conceptualization. **Manuel Haschke:** Writing – review & editing, Methodology, Conceptualization. **Aljoscha N. Goetschi:** Writing – review & editing, Methodology, Conceptualization. **Ursina Wernli:** Writing – review & editing, Methodology, Conceptualization. **Carla Meyer-Massetti:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

None.

Acknowledgements

The authors are very grateful to the panel of experts who provided their experience and knowledge throughout the Delphi process and made this study possible.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2024.02.012.

References

1. Bryant BM, Libby AM, Metz KR, et al. Evaluating patient-level medication regimen complexity over time in heart transplant recipients. *Ann Pharmacother*. 2016;50:926–934.
2. Franchi C, Tettamanti M, Pasina L, et al. Changes in drug prescribing to Italian community-dwelling elderly people: the EPIFARM–Elderly Project 2000–2010. *Eur J Clin Pharmacol*. 2014;70:437–443.
3. Hovstadius B, Hovstadius K, Åstrand B, Petersson G. Increasing polypharmacy - an individual-based study of the Swedish population 2005-2008. *BMC Clin Pharmacol*. 2010;10:16.
4. El Morabet N, Uitvlugt EB, van den Bemt BJF, van den Bemt PMLA, Janssen MJA, Karapinar-Carkit F. Prevalence and preventability of drug-related hospital readmissions: a systematic review. *J Am Geriatr Soc*. 2018;66:602–608.
5. Aljishi M, Parekh K. Risk factors for general medicine readmissions and association with mortality. *N Z Med J*. 2014;127:42–50.
6. Hutchinson AF, Graco M, Rasekaba TM, Parikh S, Berlowitz DJ, Lim WK. Relationship between health-related quality of life, comorbidities and acute health care utilisation, in adults with chronic conditions. *Health Qual Life Outcome*. 2015;13:69.
7. Kareliusson F, De Geer L, Tibblin AO. Risk prediction of ICU readmission in a mixed surgical and medical population. *Journal of Intensive Care*. 2015;3:30.
8. Robinson T, Kerse N. Medical readmissions amongst older New Zealanders: a descriptive analysis. *N Z Med J*. 2012;125:24–34.
9. Rodríguez-Artalejo F, Guallar-Castillón P, Pascual CR, et al. Health-related quality of life as a predictor of hospital readmission and death among patients with heart failure. *Arch Intern Med*. 2005;165:1274–1279.
10. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the medicare fee-for-service program. *N Engl J Med*. 2009;360:1418–1428.
11. Smeraglio A, Heidenreich PA, Krishnan G, Hopkins J, Chen J, Shieh L. Patient vs provider perspectives of 30-day hospital readmissions. *BMJ Open Qual*. 2019;8,e000264.
12. Schepel L, Aronpuro K, Kvarnström K, et al. Strategies for improving medication safety in hospitals: evolution of clinical pharmacy services. *Res Soc Adm Pharm*. 2019;15:873–882.
13. Leguelinel-Blache G, Arnaud F, Bouvet S, et al. Impact of admission medication reconciliation performed by clinical pharmacists on medication safety. *Eur J Intern Med*. 2014;25:808–814.
14. Wilson AJ, Palmer L, Levett-Jones T, Gilligan C, Outram S. Interprofessional collaborative practice for medication safety: nursing, pharmacy, and medical graduates' experiences and perspectives. *J Interprof Care*. 2016;30:649–654.
15. Al-Hashar A, Al-Zakwani I, Eriksson T, et al. Impact of medication reconciliation and review and counselling, on adverse drug events and healthcare resource use. *Int J Clin Pharm*. 2018;40:1154–1164.
16. Marinović I, Bačić Vrca V, Samardžić I, et al. Impact of an integrated medication reconciliation model led by a hospital clinical pharmacist on the reduction of post-discharge unintentional discrepancies. *J Clin Pharm Therapeut*. 2021;46:1326–1333.

17. Buckley MS, Harinstein LM, Clark KB, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. *Ann Pharmacother*. 2013;47:1599–1610.
18. Cani CG, Lopes LdSG, Queiroz M, Nery M. Improvement in medication adherence and self-management of diabetes with a clinical pharmacy program: a randomized controlled trial in patients with type 2 diabetes undergoing insulin therapy at a teaching hospital. *Clinics*. 2015;70.
19. Choudhry NK, Isaac T, Lauffenburger JC, et al. Effect of a remotely delivered tailored multicomponent approach to enhance medication taking for patients with hyperlipidemia, hypertension, and diabetes: the STIC2IT cluster randomized clinical trial. *JAMA Intern Med*. 2018;178:1182–1189.
20. Aniemeke E, Crowther B, Younts S, Hughes D, Franco-Martinez C. Clinical pharmacy discharge counseling service and the impact on readmission rates in high-risk patients. *Hosp Pharm*. 2017;52:348–352.
21. Gustafsson M, Sjölander M, Pfister B, Jonsson J, Schneede J, Lövheim H. Pharmacist participation in hospital ward teams and hospital readmission rates among people with dementia: a randomized controlled trial. *Eur J Clin Pharmacol*. 2017;73:827–835.
22. Montross M, Douthit S, Learn L, Dombrowski SK, Hanna C, Gruver B. Impact of interdisciplinary case management and pharmacist transitions of care interventions on 30-day readmissions. *Res Soc Adm Pharm*. 2023;19:1214–1217.
23. Ravn-Nielsen LV, Duckert M-L, Lund ML, et al. Effect of an in-hospital multifaceted clinical pharmacist intervention on the risk of readmission: a randomized clinical trial. *JAMA Intern Med*. 2018;178:375–382.
24. Fennelly JE, Coe AB, Kippes KA, Remington TL, Choe HM. Evaluation of clinical pharmacist services in a transitions of care program provided to patients at highest risk for readmission. *J Pharm Pract*. 2020;33:314–320.
25. Park B, Baek A, Kim Y, et al. Clinical and economic impact of medication reconciliation by designated ward pharmacists in a hospitalist-managed acute medical unit. *Res Soc Adm Pharm*. 2022;18:2683–2690.
26. Schönenberger N, Meyer-Massetti C. Risk factors for medication-related short-term readmissions in adults – a scoping review. *BMC Health Serv Res*. 2023;23:1037.
27. Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: recommendations based on a methodological systematic review. *Palliat Med*. 2017;31:684–706.
28. Cantrill JA, Sibbald B, Buetow S. The Delphi and nominal group techniques in health services research. *Int J Pharm Pract*. 2011;4:67–74.
29. Jaam M, Awaisu A, El-Awaisi A, Stewart D, El Hajj MS. Use of the Delphi technique in pharmacy practice research. *Res Soc Adm Pharm*. 2022;18:2237–2248.
30. Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: how to decide its appropriateness. *World J Methodol*. 2021;11:116–129.
31. Fitch K, Bernstein SJ, Aguilar MD, et al. *The RAND/UCLA Appropriateness Method User's Manual*. Santa Monica, CA: RAND Corporation; 2001.
32. By the American geriatrics society beers Criteria® update expert panel American geriatrics society 2023 updated AGS beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71:2052–2081.
33. Holt S, Schmiedl S, Thürmann PA. Potentially inappropriate medications in the elderly: the PRISCUS list. *Deutsches Ärzteblatt international*. 2010;107:543–551.
34. Dalleur O, Beeler PE, Schnipper JL, Donze J. 30-Day potentially avoidable readmissions due to adverse drug events. *J Patient Saf*. 2021;17:e379–e386.
35. Glans M, Kragh Ekstam A, Jakobsson U, Bondesson A, Midlov P. Medication-related hospital readmissions within 30 days of discharge-A retrospective study of risk factors in older adults. *PLoS One*. 2021;16, e0253024.
36. Rothwell M, Jukka C, Lum E, Mitchell C, Kyriakides P. Retrospective analysis of emergency readmissions to rural and regional hospitals. *J Pharm Pract Res*. 2011;41:290–294.
37. Toh MR, Teo V, Kwan YH, Raaj S, Tan SY, Tan JZ. Association between number of doses per day, number of medications and patient's non-compliance, and frequency of readmissions in a multi-ethnic Asian population. *Prev Med Rep*. 2014;1:43–47.
38. Uitvlugt EB, Janssen MJA, Siegert CEH, et al. Medication-related hospital readmissions within 30 Days of discharge: prevalence, preventability, type of medication errors and risk factors. *Front Pharmacol*. 2021;12, 567424.
39. Whitaker AS, Cottrell WN. What proportion of unplanned re-presentations to an emergency department are medication related and preventable? *J Pharm Pract Res*. 2019;49:546–556.
40. Willson MN, Greer CL, Weeks DL. Medication regimen complexity and hospital readmission for an adverse drug event. *Ann Pharmacother*. 2014;48:26–32.
41. Witherington EM, Pirzada OM, Avery AJ. Communication gaps and readmissions to hospital for patients aged 75 years and older: observational study. *Qual Saf Health Care*. 2008;17:71–75.
42. Mannucci PM, Nobili A, Investigators R. Multimorbidity and polypharmacy in the elderly: lessons from REPOSI. *Internal and Emergency Medicine*. 2014;9:723–734.
43. Zemaitis CT, Morris G, Cabie M, Abdelghany O, Lee L. Reducing readmission at an academic medical center: results of a pharmacy-facilitated discharge counseling and medication reconciliation program. *Hosp Pharm*. 2016;51:468–473.
44. Bellone JM, Barner JC, Lopez DA. Postdischarge interventions by pharmacists and impact on hospital readmission rates. *J Am Pharmaceut Assoc*. 2012;52:358–362.
45. Liu VC, Mohammad I, Deol BB, Balarezo A, Deng L, Garwood CL. Post-discharge medication reconciliation: reduction in readmissions in a geriatric primary care clinic. *J Aging Health*. 2018;31:1790–1805.
46. Bailey SC, Fang G, Annis IE, O'Conor R, Paasche-Orlow MK, Wolf MS. Health literacy and 30-day hospital readmission after acute myocardial infarction. *BMJ Open*. 2015;5, e006975.
47. Mitchell SE, Sadikova E, Jack BW, Paasche-Orlow MK. Health literacy and 30-day postdischarge hospital utilization. *J Health Commun*. 2012;17:325–338.
48. Milea D, Azmi S, Reginald P, Verpillat P, Francois C. A review of accessibility of administrative healthcare databases in the Asia-Pacific region. *J Mark Access Health Policy*. 2015;3.
49. Unim B, Mattei E, Carle F, et al. Health data collection methods and procedures across EU member states: findings from the InfAct Joint Action on health information. *Arch Publ Health*. 2022;80:17.