ARTICLE IN PRESS

Research in Social and Administrative Pharmacy xxx (xxxx) xxx

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

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

Prescribing quality indicators applicable to register data: A scoping review

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ABSTRACT

Background: Cross-linkable register data enable reuse of healthcare data to assess and improve prescribing quality. A first step in the developing of quality indicators is summarising existing evidence.

Objectives: To identify prescribing quality indicators (PQIs) suitable for population-level assessment of outpatient prescribing across and within countries and regions, and applicable using the Nordic (Denmark, Iceland, Finland, Norway, Sweden) registers.

Design: Bibliographic databases were searched for original research articles published 2000–2023 in English or Nordic languages from high-income European, North American, East Asian and Pacific countries. Eligible studies included at least one explicit PQI for assessing outpatient prescribing or pharmacotherapy quality, calculable using aggregate- or individual-level structured data on sales, consumption, prescriptions or dispensings. Exploratory and snowballing strategies were used to complement searches.

Results: We identified 173 articles, of which 90% focused solely on pharmacotherapy and 10% had a broader service scope. Fifty-one percent focused on a specific disease or medication class (e.g., asthma, diabetes, opioids, antibiotics), 35% on a specific population subgroup (e.g. older adults, children), and 14% had a more general scope (e.g. general practitioner prescribing). We extracted 11 lists of potentially inappropriate medicines (PIM) for older adults validated for Nordic/European settings, and 915 PQIs. All PQIs adressed process dimension and 96% the effectiveness/safety aspects of quality; 50% required individual-level data on dispensings and diagnoses, 35% individual-level data on dispensings, and 16% were calculable using aggregate data.

Conclusion: Numerous register-applicable PQIs were identified, providing a basis for further quality framework development and validation across purposes and contexts.

1. Introduction

The quality of prescribing and medication use remains a critical concern for clinicians, policymakers and patients. The quality of prescribing is typically anchored to the concept of the rational use of medicines.[1–3] Recommendations regarding good prescribing[4] and frameworks for the development, validation, and classification of prescribing quality indicators (PQIs)[2,5–8] have further contributed to efforts to improve quality. Nevertheless, quality can encompass various elements depending on the definition, perspective and context.[9,10]

PQI has been defined as 'a measurable element of prescribing performance for which there is evidence or consensus that it can be used to assess quality and, hence, be used in changing the quality of care provided'.[2,11] The previous literature in this area is extensive. Important sub-areas include the quality of pharmacotherapy in old age, as part of which lists of potentially inappropriate medications (PIMs or PIM lists) or prescribing and deprescribing tools have been developed.[12–17] To a lesser degree, PIM lists have been developed for other population and disease groups.[18–20] Numerous previous reviews have focused on PQIs exclusively or on quality indicators more broadly but including at least

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https://doi.org/10.1016/j.sapharm.2026.06.003
Received 28 January 2026; Received in revised form 27 April 2026; Accepted 9 June 2026
Available online 12 June 2026

some PQIs for medicines or disease groups, such as antimicrobials,[21–24] diabetes,[25,26] cardiovascular diseases,[27] dementia,[28] and osteoarthritis.[29] One previous review focused on PQIs that were developed using consensus methods.[3] Synthesising evidence, nevertheless, remains challenging due to the heterogeneous and inconsistent key words and MeSH (Medical Subject Headings) terms widely used for measurement without any inference about quality.[15,30,31]

Thus, reviews on PQIs with different scopes and purposes are needed. This review is driven by the goal of reusing existing data (secondary use of data) to enhance healthcare delivery and policymaking, as exemplified by initiatives like the European Health Data Space.[32] The focus is on explicit PQIs calculable using *register data* (sometimes referred to as *administrative data*, *routine healthcare data* or *Real World Data, RWD*[9,32]), by which we mean data that accumulates through healthcare processes for administrative, accountability, payment or managerial purposes, or that is collected for national statistics (births, deaths, hospital discharges). Register data has the advantage of being readily available for large, or even entire populations. Such data are typically of high quality and reliability, as they are professionally maintained, including quality control procedures and comprehensive metadata. However, as these data are not primarily collected for research purposes, they may lack relevant information. For example, detailed clinical data, such as laboratory results or adverse effects of medications, may not be available at all, or in structured format. Furthermore, the completeness/comprehensiveness is also dependent on the quality of the clinical coding, at system and individual health personnel level.

The Nordic countries (Denmark, Finland, Iceland, Norway, Sweden) have for long paved the way to register-based pharmacoepidemiologic and drug utilisation research, by virtue of their rich cross-linkable longitudinal registries covering the life-cycles of entire populations.[11,33,34] These countries also have extensive experience in data standardizations and harmonisations.[35–38] Increasing efforts have been made to enrich register data with detailed health records and to develop regional and/or national healthcare quality registries.[32,39–41] European and Nordic research networks on drug utilisation and pharmacoepidemiology have produced a large body of comparative literature.[2,34,42] Nevertheless, cross-national assessments of prescribing quality beyond individual disease, medicine class or indicator are still scarce even in the Nordic context.

With reference to the PCC (population, concept, context) framework,[43] the aim of this scoping review is to systematically map prescribing PQIs (concept) applicable for population-level quality assessment across and within countries (population), using the Nordic, relatively comparable register data settings (context). This review formed part of a broader project in which the identified PQIs subsequently underwent consensus validation and feasibility testing (to be reported separately). The systematic synthesis of existing indicators is a standard step in the development of new indicator sets; however, the data collected here can also be utilised more broadly in comparable projects. The review differs from previous reviews by focusing specifically on register-based measures, the identification of which has been hampered by their dispersion across an extensive and conceptually heterogeneous literature. The applied classification systems facilitate conceptual links between subfields of the literature.

A scoping review was selected because register-applicable QIs were envisaged to exist in various literature subfields and were referred to using heterogeneous terminology.

2. Methods

2.1. Protocol and registration

A protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) guideline,[44] to the extent it is applicable to scoping reviews. The reporting of the review follows the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews PRISMA-ScR.[43] The study, including the protocol, was registered prospectively with the Open Science Framework on 22 September 2023.[45] The protocol was amended once, on 19 December 2023, regarding the selection process (instead of duplicate selection and charting, the work of one reviewer was checked by the other).

2.2. Eligibility criteria

2.2.1. Article types and years

Peer-reviewed original research articles written in English or in a Nordic language and published between January 2000 and August 2023 were included. The planned search strategy (protocol) also included grey literature; however, due to the wealth of literature, only the results from peer-reviewed articles are reported in this article.

2.2.2. Concept

To be included in the review, articles needed to include at least one PQI, defined as explicit medication-related indicator, measure or criterion (assessment against prespecified rules) applicable for evaluating the quality or performance of prescribing or pharmacotherapy, in the context of responsible use of medicines, in outpatient settings, including primary care. Explicitness meant that PQIs were calculable based on predefined criteria without (implicit) subjective judgements or opinions.[17] To be included, PQIs did not need to be referred to as PQIs; instead, a variety of search terms were used.

If publications concerned the same project or PQI, only the most recent publication was included. Regarding studies applying consensus methods, only PQIs that the study assessed to be acceptable/valid were included.

2.2.3. Population

To be included, identified PQIs needed to be applicable at different levels of the health-care system in high-income country settings relatable to Nordic contexts (European Union, United Kingdom, European Free Trade Association (EFTA), United States, Canada, Australia, New Zealand, Japan, South Korea, Singapore).

2.2.4. Context

PQIs were considered register-based if they were assessed as calculable using the Nordic register data, which is extensively described elsewhere.[11,33,34,46] To summarise the key criteria applied, PQIs were included if they were calculable using cross-sectional or longitudinal, aggregate- or individual-level data on the sales, consumption, prescriptions or dispensings of medications, with or without structured individual-level patient register data (diagnoses and procedures in specialised care including hospitalisations) and/or socio-demographic characteristics.[11,33] PQIs did not have to be technically operationalised to (Nordic) register data.

2.2.5. Exclusion criteria

Articles were excluded if they did not fit the conceptual framework of the study (responsible use of medications); they measured quality of interventions that did not include pharmacotherapy; they assessed complementary or alternative medicine; they were limited to in-hospital or self-prescribed (over-the-counter) pharmacotherapy; they focused solely on assessing performance of other prescribers (nurses, pharmacists) besides doctors; they applied a previously published criterion without a purpose of development, variation, update, implementation, or validation; or, they proposed licensed indicators useable by purchase only.

PQIs were excluded if they required data that is not comprehensively available in the Nordic registers, including primary care diagnoses, information given to or discussed with the patient, patient-specific contraindications, or detailed medical records (e.g. electronic health records EHR) about, for instance, disease severity, monitoring, diagnostics, imaging, laboratory tests; or their results. The focus was on outpatient prescribing; thus, PQIs related to pharmacotherapy administered by healthcare personnel (e.g. vaccines) or predominantly in inpatient settings (e.g. cancer care) were also excluded. Full criteria are included as online material (Supplemental material 1).

2.3. Information sources

The bibliographic databases searched were PubMed, Scopus, CINAHL (including Embase), Web of Science, and Cochrane Library. The search strategy was built adapting a strategy by Fujita et al.,[3] in consultation with an experienced librarian [Information Specialist Leeni Lehtiö at Turku University Library], and it was further refined through research team feedback. The reference management software Zotero was used to identify duplicates for a manual check. The final search strategy for PubMed is as follows (latest search conducted: 26.10.2023):

((Inappropriate Prescribing[MeSH Terms] OR Quality Indicators, Health Care[MeSH Terms] OR Potentially Inappropriate Medication List [MeSH Terms] OR "Inappropriate Prescribing" OR "Quality Indicators, Health Care" OR "Potentially Inappropriate Medication List") OR (((quality[Title] OR clinical[Title] OR performance[Title] OR safety [Title] OR process[Title] OR outcome[Title]) AND indicator*[Title]) OR ((quality[Title] OR performance[Title] OR process[Title] OR outcome [Title]) AND assess*[Title]) OR (performance[Title] AND (evaluat* [Title] OR measur*[Title])) OR (quality[Title] AND (assurance[Title] OR improv*[Title] OR measur*[Title] OR criteri*[Title])) OR benchmarking[Title])) AND (develop*[Title] OR creat*[Title] OR achiev* [Title] OR formulat*[Title] OR deriv*[Title] OR devis*[Title] OR construct*[Title] OR valid*[Title] OR reliab*[Title] OR guideline*[Title] OR RAND[Title] OR UCLA[Title] OR RAM[Title] OR Delphi[Title] OR consensus[Title] OR "nominal group techni*"[Title] OR "focus group-*"[Title]) AND (prescri*[Title] OR "use of medicine*"[Title] OR "medicine use"[Title] OR drug*[Title] OR medication*[Title] OR medicines [Title]) AND (English[Language] OR Danish[Language] OR Finnish [Language] OR Norwegian[Language] OR Swedish[Language]) AND ("2000/01/01"[Date - Publication]: "2023/08/31"[Date - Publication])

The search was supplemented with exploratory and 'snowballing' strategies. These included hand-searching the reference lists of the identified relevant reviews, searching for more recent versions of the identified indicator sets and exploratory and AI-powered searches (PubMed 'similar articles', Google Scholar 'related articles', Semantic Scholar), using identified key articles and reviews.

2.4. Selection of sources of evidence and data charting process

A list of screening questions (Supplemental material 1) and a data charting form were developed in a pilot, as described by Fujita et al.[3]

Managing records during screening was done using the bibliographic management package Rayyan, which was also used to identify remaining duplicates for a manual check. One reviewer (KA) assessed the titles of articles for relevance. For all titles that appeared to meet the inclusion criteria or where there was any uncertainty, two reviewers (KA and FF) screened the abstracts independently and in duplicate. All articles that were considered relevant by one or both reviewers, or for which there was uncertainty, were read in full text. Both reviewers read the articles in full text, with one reviewer charting data with verification by another. Disagreements were resolved via discussion. Initially extracted data included the publication year, settings (target country or area), target population, main study method, name of the indicator or set (if applicable), definitions (e.g. numerator, denominator), possible references to prior literature and validity assessment (if applicable). Exploratory and hand searches, related data charting and data extraction and checking beyond initial data charting were conducted by one reviewer (KA). Further rounds of data extraction (additional details of articles and PQIs) after the initial data charting were needed because the scope of the literature was not fully known beforehand, thus an inductive approach in structuring the evidence was applied.

2.5. Synthesis of results

Evidence was synthesised at two levels: sources of evidence (articles) and individual PQIs. The synthesis was guided by previous taxonomies of PQIs described in detail below.

The articles were inductively classified with reference to previous conceptualisations of quality[47] and methodological characteristics[5,8,9,47] and were examined in terms of PQI quality assessments; for example, validity, reliability, sensitivity, specificity and discriminative power (ability of an indicator to meaningfully distinguish between high- and low-quality or high- and low-performing entities or units[8,9]) were assessed. Validity assessments could encompass face/content validity (underpinned by evidence and/or consensus[48]), concurrent validity (assessed in terms of sensitivity and positive predictive value in relation to other measures, preferably a 'gold standard'[8]), construct validity (corresponding to the applied theoretical concept of quality[8]), and predictive validity (capacity to predict outcomes[48]).

The individual PQIs assessed as applicable with Nordic data were extracted and classified using multiple taxonomies, as recommended in the previous literature.[2,3,5,9,26,49,50] The applied taxonomies were the WHO Collaborating Centre for Drug Statistics Methodology Anatomical Therapeutic Chemical (ATC) classification[37]; and the Donabedian model of quality dimensions of medical care.[47,49,51] Within the Donabedian taxonomy, *structure* (i.e. input) refers to the care settings, including resources, regulation and contracting. *Process* refers to the actual care delivered (e.g. prescribing patterns). The *outcome* refers to the final effects (e.g. mortality, morbidity, quality of life) and intermediate effects (e.g. hospitalisation) of the structures and processes on the individuals and populations. Furthermore, PQIs were classified based on the main OECD (Organisation for Economic Co-operation and Development) Health Care Quality Indicator (HCQI) project quality dimension(s) assessed (effectiveness/safety, patient-centeredness, efficiency, equity).[50,52]

Based on data requirements,[2] the PQIs were further classified into *medicine-oriented* (only information about the prescribing/dispensing of medications), *disease-oriented* (medications linked with diagnoses or healthcare utilisation) and *patient-oriented* (requiring information about the clinical characteristics of a patients, e.g. disease severity). Based on data granularity, PQIs were classified into *aggregate* (e.g. total sales, total consumption), or *patient-level* (individual-level data, cross-sectional or longitudinal/sequential).[51]

3. Results

3.1. Selection and characteristics of sources of evidence

The total number of included articles was 173 (Fig. 1). Moreover, 23 reviews were scanned for references 3, 12–14, 16–29, 53–57.

3.2. Synthesis of results: Article level

Of the 173 included articles, 18 assessed prescribing/medicine use as a part of the broader set of QIs that focused on service or care quality *(service-oriented*), and 155 were primarily focused on prescribing or medicine use *(prescribing-oriented*) (Table 1). Furthermore, 89 articles were *disease-specific* (focused on specific disease(s) or medication class (es), e.g. asthma or antibiotics), 60 did not focus on any specific disease/ medication but were limited to a specific population subgroup (*population group specific*; e.g., older adults or paediatric patients), and 24 were not limited to any disease/medication or population subgroup (i.e. they were *generic*; e.g. general practitioner prescribing).

The scope, design and main results of the included articles are presented in Supplemental material 2, as well as the purpose and level of quality measurement and PQI evidence base, PQI quality assessment and

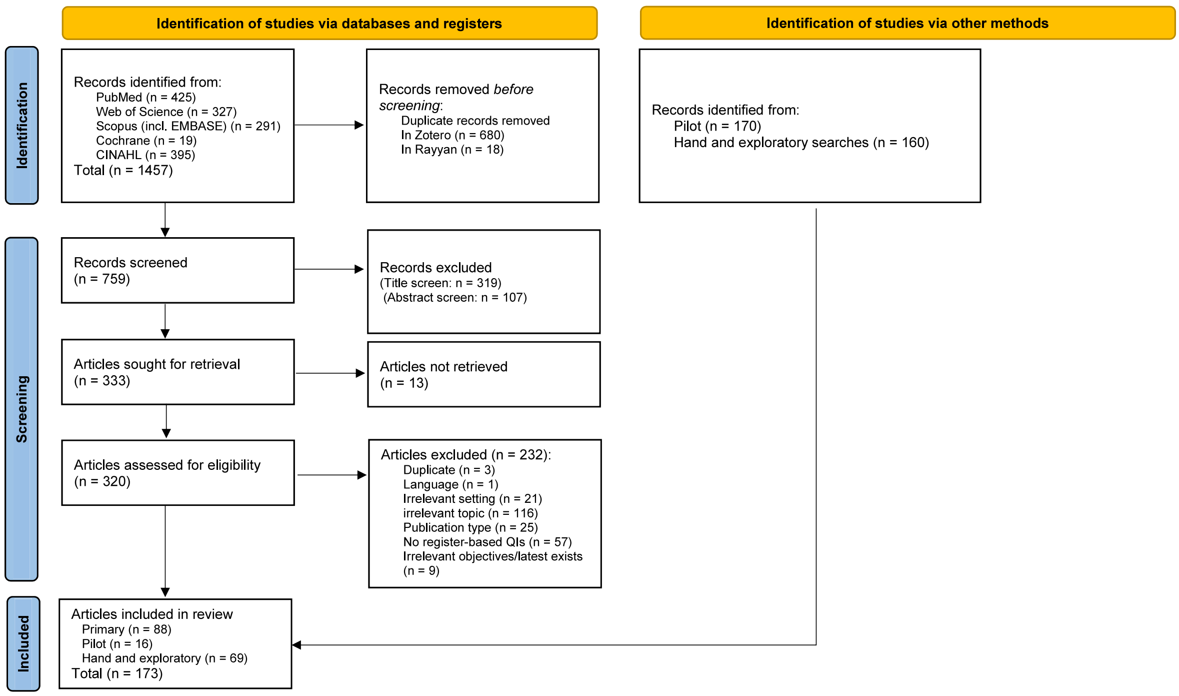

Fig. 1. PRISMA flow diagram of study selection.

intended PQI data source.[9] These information were not always explicitly stated in the article. We distinguished *quality improvement* studies as those that proposed clinical tools for the screening or medication review at the level of individual (patient) and tools for quality audit or academic detailing or those that assessed the effects of a quality intervention (N = 66, not mutually exclusive). *Quality assurance* studies aimed for standards setting, accountability (pay-for-performance), monitoring or benchmarks at various levels of the health system (N = 85). Finally, studies were classified as *methodological* if they contributed to PQI quality assessment (validity, reliability), proposed operationalisations or examined the associations between PQIs and structures (e.g., individual/patient, provider, institutional characteristics) or outcomes (e.g., hospitalisations, mortality, costs) (N = 42).

The *level of quality assessment* (excluding methodological studies) ranged from the level of the individual (patient, N = 36, not mutually exclusive) or health professional (N = 25) to the facility (N = 42), organisation (N = 4), region (province, state, region N = 33), national (national, population-level N = 41) and international levels (N = 7). Including methodological studies, 36 articles concerned more than one country, most commonly countries within the United Kingdom with or without Ireland (14 articles). Five studies concerned two to three European countries of which at least one was other than UK/Ireland. Broader areas such as Europe or the OECD-countries were in focus in 17 studies.

Consensus methods were widely used to select, prioritise and content/face validate indicators (*consensus-based PQIs*, N = 74 articles, not mutually exclusive). Observational studies typically constructed indicators with reflections of national or international guidelines or standards (*guideline-based PQIs*, N = 50 articles). *Data-based PQIs* (N = 8 articles) were either conditioned by constraints related to data availability (e.g. only aggregate data available) or constructed using statistical methods (e.g. factor or cluster analyses). The remaining PQIs, such as polypharmacy and 'Drug Utilisation 90%' (DU90%) were mainly justified by theoretical plausibility (*theory-based PQIs*, N = 9 articles). Iterative application of previously proposed indicators was common (N = 54 articles).

In terms of the quality of PQIs, face/content validity was commonly sought; however, re-validations over time or across settings were rare. Guideline-based studies seldom explicitly discussed PQI validity, however, references to the evidence base of the applied guidelines can be considered content validity.[2] Studies that examined associations between PQIs and outcomes were typically not designed to or able to rule out confounding by indication or reverse causality. Methods used to address confounding by indication included propensity score matching[162] and entropy balancing.[160] Several studies examined concurrent validity aspects, some of which concerned register-based use.[79,88,142,144,190] For example, in one study, none of the examined register-based asthma PQIs were deemed valid in assessing prescriber performance,[88] and in another study, only a weak association was found between register-based proxy (the high use of short-acting beta-agonists, SABAs) and clinically verified uncontrolled asthma.[79]

3.3. Synthesis of results: Indicator (meso and micro) level

During synthesis, we identified a subfield of the literature for which it was more meaningful to summarise and report findings as PQI sets rather than individual PQIs. Specifically, this included *PIM lists for older adults*. In this review, we refer to the analysis of these lists as *meso-level*, to distinguish it from the primary levels of synthesis described in the Methods section: the article-level and PQI-level, the latter of which is referred to as the *micro-level*.

We opted to treat *PIM lists for older adults* as sets, without breaking them down into individual indicators because these had already been thoroughly reviewed[12–14,17] and shown to have substantial overlap due to their iterative development.[17] We further analysed the PIM lists that were content validated for at least one Nordic country or for a pan-European setting. Other identified PIM lists for older adults[109,128,153,156,165–167,169,170,178,179] were not analysed further, since the iterative development of Nordic/European lists already included the synthesis of previous literature into Nordic/European settings.

From the other articles, including those with PIM lists for other age groups, we extracted all register data applicable PQIs (micro-level). Notably, a clear distinction between PIM lists and other types of PQIs cannot be made, since a large portion of PQIs were variants of indicators typical within PIM lists: drug-drug-interations (DDIs), drug-disease-interactions or clinical interactions (DDSIs), potential prescribing

Table 1
Included articles.

Scope	Articles, country or countries
Service-oriented disease-specific studies (SD)	
• Schizophrenia, mental healthcare	Addington et al., 2012,[58] Canada; Hermann et al., 2006,[59] International (OECD)
• Chronic kidney disease	Fukuma et al., 2017,[60] Japan
• Gastrointestinal	Calvet et al., 2014,[61] Spain; Kanwal et al., 2010a,[62] International
• Cardiac, hypertension	Asch et al., 2001,[63] US; Idänpään-Heikkilä et al., 2006,[64] International (OECD); Tu et al., 2008,[65] Canada
• Osteoarthritis and rheumatoid arthritis	Barber et al., 2015,[66] Canada
• End-of-life care Alzheimer's, COPD, (or cancer)	De Schreye et al., 2017,[67] Belgium
• Asthma	To et al., 2010,[68] Canada
• Cirrhosis	Kanwal et al., 2010b,[69] US
• Type 2 diabetes	Mackinnon et al., 2008,[70] Canada
Service-oriented population group-specific studies (SP)	
• Paediatric	Braithwaite et al., 2018,[71] Australia; Gill et al., 2014,[72] UK
• Older adults	Tropea et al., 2011,[73] Australia; Xu et al., 2019,[74] US
Service-oriented generic studies (SG)	
• Primary care	Blozik et al., 2018,[75] Switzerland
Prescribing-oriented disease-specific studies (PD)	
• Asthma	Arnlind et al., 2010,[76] Sweden; Arnlind et al., 2013,[77] Sweden; Breton et al., 2007,[78] Canada; Davidsen et al., 2011,[79] Denmark; FitzGerald et al., 2017,[80] Canada; Frischer et al., 2000,[81] UK; Ingemansson et al., 2012,[82] Sweden; Karlstad et al., 2010,[83] Norway; Laforest et al., 2015,[84] France, UK; Lehtimäki et al., 2022,[85] Denmark, Finland, Sweden; Navaratnam et al., 2008,[86] US; Piecoro et al., 2001,[87] US; Pont et al., 2004,[88] Netherlands; Sadatsafavi et al., 2017,[89] Canada; Sweeney et al., 2014,[90] UK; Tavakoli et al., 2018,[91] Canada; Von Bülow et al., 2014,[92] Denmark
• Opioids	Acebedo et al., 2020,[93] US; Chambers et al., 2022,[94] US; Khalid et al., 2015,[95] US; Koo et al., 2020,[96] US; Krauss et al., 2021,[97] US; Langnas et al., 2022,[98] US; Lee et al., 2019,[99] US; Meyer et al., 2021,[100] US; Milner et al., 2021,[101] US; Navis et al., 2020,[102] US; Phillips et al., 2019,[103] US; Pullman et al., 2020,[104] US; Reiter et al., 2023,[105] US; Shoemaker-Hunt et al., 2021,[106] US; Sutherland et al., 2021,[107] US; Zgierska et al., 2020,[108] US
• Heart failure	Bermingham et al., 2014,[109] Ireland; Bitar et al., 2020,[110] France
• Antibiotics/antimicrobial consumption	Coenen et al., 2007,[111] Europe; De Bie et al., 2016,[112] Italy, Netherlands, UK; Minalu et al., 2011,[113] Europe; Pont et al., 2017,[114] Australia; Pulcini et al., 2013,[115] France; Robertson et al., 2021,[116] International; Simon et al., 2021a,[117] France; Simon et al., 2021b,[118] France; Thilly et al., 2020a,[119] France; Thilly et al., 2020b,[120] France
• NSAIDs	Fernandez Urrusuno et al., 2008,[121] Spain; Pham et al., 2013,[122] US; Rasmussen et al., 2005,[123] Denmark; Skyggedal Rasmussen et al., 2006,[124] Denmark
• Diabetes, cardiovascular	DeSchutter et al., 2022,[125] Europe; Fleetcroft et al., 2012,[126] UK; Frisk et al., 2008,[127] Sweden; Gauci et al., 2017,[128] Malta; Ivanova et al., 2019,[129] Sweden; Manteuffel et al., 2014,[130] US; Martirosyan et al., 2012,[131] Netherlands; Martirosyan et al., 2010,[132] Netherlands; Norman et al., 2009,[133] Sweden; Rashidian et al., 2011,[134] England; Sipilä et al., 2011,[135] Finland; Smits et al., 2017,[136] Netherlands; Wallach-Kildemoes et al., 2016,[137] Denmark
• Mental health problems, schizophrenia	Ichihashi et al., 2020,[138] Japan; Isomura et al., 2016,[139] Sweden; Khawagi et al., 2020,[140] UK; Kyou et al., 2022,[141] Japan; Rickles et al., 2003,[142] US
• Psychotropics, fall risk medicines	Brett et al., 2018,[143] Australia; Lesén et al., 2009,[144] Sweden; Murphy et al., 2015,[145] UK; O'Connor et al., 2018,[146] Australia; Seppälä et al., 2021,[147] Europe; Sidorchuck et al., 2013,[148] Sweden
• Chronic kidney disease	Desrochers et al., 2011,[149] Canada
• Lower urinary tract symptoms	Oelke et al., 2015,[150] International
• Hormone replacement therapy (menopause)	Cordasco et al., 2019,[151] US
Prescribing-oriented population group specific studies (PP)	
• Older adults, PIM-lists	Anrys et al., 2021,[152] Europe; Basger et al., 2012,[153] Australia; Bergman et al., 2007,[154] Sweden; Brown et al., 2016,[155] US; Clyne et al., 2013,[156] Ireland; DeGroot et al., 2014,[157] Netherlands; Foubert et al., 2021,[158] Europe; Fujie et al., 2020,[159] Japan; Heider et al., 2018,[160] Germany; Heinrich et al., 2021,[161] Germany, Netherlands; Hyttinen et al., 2019,[162] Finland; Hyttinen et al., 2023,[163] Finland; Jensen et al., 2014,[164] Denmark; Kim et al., 2018,[165] Korea; Kojima et al., 2016,[166] Japan; Lavan et al., 2017,[167] Ireland; Lavan et al., 2018,[168] Ireland; Lee et al., 2023,[169] Korea; Mann et al., 2023,[170] Austria, Germany; Morin et al., 2018,[171] Europe; Nyborg et al., 2015,[172] Norway; O'Mahony et al., 2023,[173] Europe; Papaioannou et al., 2002,[174] Canada; Parodi Lopez et al., 2023,[175] Sweden; Parodi Lopez et al., 2022,[176] Sweden; Paulamäki et al., 2023,[177] Finland; Pazan et al., 2020a,[178] US; Pazan et al., 2020b,[179] Japan; Pazan et al., 2023,[180] Europe; Renom-Guiteras et al., 2015,[181] Europe; Rognstad et al., 2009,[182] Norway; San Jose et al., 2014,[183] Spain; Schmidt-Mende et al., 2020,[184] Sweden; Tachi et al., 2019,[185] Japan; Van der Linden et al., 2014,[186] Belgium; Wallerstedt et al., 2015,[187] Sweden; Wallerstedt et al., 2022,[188] Sweden

(*continued on next page*)

Table 1 (*continued*)

Scope	Articles, country or countries
• Older adults, other	Belfrage et al., 2015,[189] Sweden; Flanagan et al., 2004,[190] Canada; Gnjidic et al., 2012,[191] Australia; Jyrkkä et al., 2009,[192] Finland; Jyrkkä et al., 2011,[193] Finland; Mackinnon et al., 2002,[194] Canada; Radomski et al., 2022,[195] US; Robertson et al., 2002,[196] Canada; Selim et al., 2013,[197] US
• Paediatric, PIM-lists	Barry et al., 2016,[198] Ireland, UK; Berthe-Aucejo et al., 2019,[199] France; Corrick et al., 2019,[200] UK; Meyers et al., 2020,[201] US; Prot-Labarthe et al., 2014,[202] France; Sadozai et al., 2020,[203] International
• Paediatric, other	Fernandez Urrusuno et al., 2010,[204] Spain
• Middle-age, PIM lists	Cooper et al., 2014,[205] Ireland, UK; Jayesinghe et al., 2022,[206] England
• Indigenous people	Spinks et al., 2019,[207] Australia
Prescribing-oriented generic studies (PG)	
• General practitioner/practice, primary care	Avery et al., 2011,[208] UK; De Bakker et al., 2007,[209] Netherlands; Campbell et al., 2000,[210] UK; Caughey et al., 2014,[211] Australia; Dang et al., 2019,[212] Australia; Dreischulte et al., 2012,[213] UK; Fernandez Urrusuno et al., 2013,[214] Spain; Guthrie et al., 2011,[215] Scotland; Morris et al., 2002,[216] UK; Morris et al., 2003,[217] UK; Morris et al., 2004,[218] UK; Muijrers et al., 2004,[219] Netherlands; Okechukwu et al., 2006,[220] Ireland; Robertson et al., 2002,[221] Australia; Teichert et al., 2007,[222] Netherlands; Wettermark et al., 2003,[223] Sweden
• Specialised care/hospital	Huang et al., 2008,[224] Canada; Desnoyer et al., 2017,[225] Canada, Belgium, France, Switzerland; Thomas et al., 2013,[226] England
• Other	Hovstadius et al., 2010,[227] Sweden; Mull et al., 2011,[228] US; Spackman et al., 2019,[229] Canada; Ziere et al., 2006,[230] Netherlands

COPD = chronic obstructive pulmonary disease; NSAID = Nonsteroidal anti-inflammatory drugs; OECD = The Organisation for Economic Co-operation and Development; PIM = Potentially inappropriate medicines; UK = United Kingdom; US = United States.

omissions (PPOs, i.e., the potential failure to prescribe a medication despite clear and valid indications), and other potentially inappropriate medications/prescribing (PIMs/PIPs, i.e. medications for which risks in most cases outweight benefits for all or for a specific age group, or otherwise inappropriate, risky or hazardous dosing or medication regimen).

3.3.1. *Meso level: PIM lists for older adults*

We identified 11 Nordic/European PIM-lists for older adults (Table 2), of which only one (the EU(7)-PIM list) was primarily developed for population-level assessment within and across countries. The remaining 10 were primarily intended and validated for screening or for guidance at the level of individuals (patients). A population-level assessment was mentioned as a possible application for four lists.[152,171,172,182] Only two lists were directly applicable to register data[150,171]; others would require further operationalisation, as shown in studies focusing on the operationalisation of criteria for health databases.[157,184]

Several articles applied PIM lists developed for national quality assessment purposes in the Nordic countries: The Swedish National Board of Health and Welfare list,[144,154,176,177,187,188] the Finnish Medicines Agency's Meds75+ database,[162,163,177] and the Danish (discontinued) red-yellow-green-list.[164,177] Since these lists were described and published only as national reports or web pages, they were beyond the scope of this review. Nevertheless, studies applying these lists shed light on the applicability of PIM lists in population-level assessments. Validity studies suggest low discriminative power[176,187–189] and mixed results regarding agreement between lists.[153,175]

3.3.2. *Micro-level: prescribing quality indicators (PQIs)*

Table 3 presents the distribution of the 915 PQIs extracted from the literature by quality dimension and ATC-class. Table 4 presents data-oriented classification of the identified PQIs. The full list of extracted PQIs is in Supplementary material 3.

Within OECD HCQI dimensions, the majority (96%) of PQIs addressed effectiveness/safety aspects of quality (Table 3). Placed on the Donabedian taxonomy, all PQIs addressed the process-dimension, and additionally, 3% addressed structure and 18% outcome aspects. The most common anatomic level ATC-classes were the nervous system, anti-infectives for systemic use, cardiovascular system and alimentary tract and metabolism. The high overlap of similar or same PQIs being iteratively used and re-used throughout the sets partly explains the large number of PQIs in these classes.

Regarding data requirements, PQIs that required a higher level of data granularity were the most common (Table 4). Of all the PQIs, 146 required aggregate medicine-oriented data, 316 required individual-level medicine-oriented data and 462 required disease-oriented data (individual-level medicine and clinical data such as diagnoses or hospitalisations).

4. Discussion

The current review scoped the international scientific literature for explicit PQIs with a data-oriented scope. We identified 173 articles that included at least one PQI that deemed calculable using information available in the Nordic registers. The identified articles provide a view to the heterogeneous literature on improving and assessing prescribing quality with different types of PQIs, or contributing to their operationalisation or quality.[2,11] The main contribution of this evidence base is to facilitate further projects aiming to develop and validate register-based PQIs for different purposes. The identification of indicators from heterogeneous literature without systematically applied search terms is labour-intensive, and therefore the work undertaken here is reported comprehensively in the appendices to support reuse in subsequent projects. Although this study was primarily conducted to support further development of indicators in the Nordic country context, the collected

Table 2
Nordic or pan-European content-validated PIM lists for older adults.

Reference	Contents	Scope of validity assessment	Technical applicability with Nordic register data
Anrys et al. 2021[152]	A list of 66 potentially clinically significant DDIs in older people (65+ years) to screen for DDIs at the individual patient level or to assess the prevalence of DDIs at population level.	Delphi survey of 29 experts (incl. geriatricians and clinical pharmacists) from eight European countries (Belgium, Iceland, Ireland, Italy, the Netherlands, Spain, Switzerland, UK).	Explicit combinations are detectable from register data after operationalisation (i.e. defining concurrent use). Broader groups need further defining (e.g. anticholinergic medications).
DeSchutter et al. 2022[125]	RASP_CARDIO (Rationalization of Home Medication by an Adjusted STOPP list in Older Patients - cardiovascular segment) = 95 item explicit screening tool of PIPs of cardiovascular medications at the individual patient level (75+ years, frail, polypharmacy)	Modified Delphi of 29 experts (hospital pharmacists, cardiologists, internal medicine, geriatricians) from seven European countries (Belgium, France, Northern Ireland, Scotland, Sweden, Netherlands and UK).	A limited number of items are potentially applicable to register data after operationalisation; however, the majority of items require clinical judgement and/or detailed medical records or patient interview data.
Foubert et al. 2021[158]	GheOP3S V2 (Ghent Older People's Prescriptions community Pharmacy Screening) tool = screening tool with 64 items (PIMs, DDIs, DDSIs, PPOs) to screen for medication problems at individual level and help in performing medication reviews in older people (65+ years).	Update and revision of the previous version. Modified Dephi of 15 experts (incl. geriatricians, general practitioners, pharmacists) from 7 countries (Belgium, Finland, Australia, Italy, Spain, Netherlands, UK).	Explicit and Implicit items. PIMs, DDIs, DDSIs partly detectable from register data after operationalisation.
Morin et al. 2018[171]	A list of 108 items of adequate, questionable, and inadequate prescribing for older adults (75+ years) at the end of life (estimated life expectancy of ≤3 months) to guide prescribing at the individual patient level and assess quality at the population level.	Delphi panel of 40 experts (incl. palliative medicine, geriatrics, general practitioners, pharmacist/ pharmacologist) from 10 countries (Belgium, France, Germany, Italy, Norway, Portugal, Spain, Sweden, Switzerland, UK).	Explicit list of items (medications or classes) defined with ATC codes applicable to register data.
Nyborg et al. 2015[172]	The Norwegian General Practice – Nursing Home criteria (NORGEP-NH) = List of PIMs (34 items) in patients (70+ years) intended to guide prescribing at the individual patient level, and quality assessment or research at population level.	Delphi survey of 62 experts (incl. geriatrics, clinical pharmacology, pharmacists, nursing home physicians) from Norway.	Explicit PIMs and DDIs mostly detectable from register data after operationalisation. Part of items require explicit definitions to be applied to register data (e.g., 'general use of preventive medication', 'regular use of hypnotics').
Oelke et al. 2015[150]	LUTS-FORTA (Lower urinary tract symptoms - Fit fOR The Aged) = List of 16 medications classified according to FORTA-levels[a] in older people (≥65 years) intended to guide prescribing at the individual patient level	Delphi of five experts (incl. geriatricians, urologists) from five countries (Germany, Spain, France, UK, Canada).	Explicit list of active ingredients (or formulations) directly detectable from register data.
O'Mahony et al. 2023[173]	Screening tool of older people's prescriptions (STOPP) and screening tool to alert to right treatment (START) Version 3. A list of 190 items (133 PIMs and 57 PPOs) intended for use at the individual patient level as part of routine medication review (multimorbid older people with polypharmacy).	Update and revision of the previous version. Delphi of 11 experts (physicians with recognised academic profile in geriatric pharmacotherapy) from eight countries (Italy, Spain, Germany, France, Iceland, Netherlands, Turkey, Belgium).	A limited number of items are potentially applicable to register data after operationalisation, however, the majority of items require information that is not (comprehensively) available in registers without detailed medical records (e.g. 'any drug prescribed without a clinical indication').
Pazan et al. 2023[180]	EURO-FORTA (Fit fOR The Aged) V2 = 267 medications (concerning 27 indications) classified according to FORTA-levels[a] to guide prescribing at the individual patient level. Includes European and country specific lists for Poland, UK/Ireland, Italy, Spain, the Nordic countries, Netherlands and France (238–300 items).	Country/cluster specific Delphi panels with a total of 32 experts (incl. geriatricians, geriatric psychiatrists, geriatric neurologists, pharmacists, clinical pharmacologists) from Poland, UK/Ireland, Italy, Spain, the Nordic countries (four from Sweden, Finland and Iceland), Netherlands and France.	Limited direct applicability to register data because of detailed individual-level data requirements (dosage and indication) and disease-specific ratings of agents. Items related to diseases that can be reliably detected may be detectable from registers after operationalisation.
Renom-Guiteras et al. 2015[181]	The European Union (EU)(7)-PIM list: A screening tool with PIMs for older people (282 chemical substances or medicine classes) intended for the population-level assessment of prescribing patterns within and across countries, and also as a tool to screen patients at individual level.	Delphi survey of 27 experts and final survey of 12 experts from seven countries (Estonia, Finland, France, Germany, the Netherlands, Spain, Sweden)	Explicit list of items (medications or classes) mostly detectable from register data after operationalisation. Part of the definitions require information on dosing or product formulation.
Rognstad et al. 2009[182]	The Norwegian General Practice (NORGEP) criteria: A 36 item list PIMs and DDIs for older people (70+ years) intended to guide prescribing at the individual patient level, and quality assessment or research at the population level.	Delphi survey of 47 experts (clinical pharmacology, geriatrics, general practitioners) from Norway.	Explicit PIMs and DDIs mostly detectable from register data after operationalisation. Part of the definitions require information about dosing.
Seppälä et al. 2021[147]	STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk) = A tool with 14 items (medication classes) of fall-risk-increasing medications intended as deprescribing and clinical tool.	Modified Delphi of 24 experts (incl. geriatricians, pharmacists, general practitioners) from 13 European countries (not specified, European Geriatric Medicine Society group members).	Listed explicit fall-risk medication classes detectable from register data after the further definition of individual active ingredients and operationalisation.

ATC = anatomical therapeutic chemical; DDI = drug-drug-interation; DDSI = drug-disease-interaction; PIM = potentially inappropriate medications; PIP = potentially inappropriate prescribing; PPO = potential prescribing omissions; UK = United Kingdom.

[a] FORTA-levels: A = indispensable or 'absolutely', B = beneficial, C = questionable or 'careful', D = avoid or 'don't'.

body of evidence is not limited to this setting, and can be harnessed to support similar initiatives in other contexts with administrative healthcare databases.

Overall, evidence was skewed towards few subareas, particulary PIM lists for older adults, and studies focusing on asthma, opioid, antimicrobial and cardiovascular medicines. This is likely due to the importance of these areas for population health, and because of the feasibility of developing register-based PQIs in these areas. The reuse of the same PQIs across new contexts also implies that empirical evidence tends to accumulate in areas for which indicators have already been developed. Consequently, further research is needed to identify domains where indicators are currently lacking, and to develop entirely new indicators for them.

Heterogeneity of applied quality concepts challenged synthesising

Table 3
Classification of prescribing quality indicators (PQIs) by different taxonomies with examples. The classifications are not mutually exclusive (i.e. the same indicator may address several quality dimensions and include medicines from more than one ATC class).

Taxonomy	N	%	Examples (Directly cited or slightly modified for consistency)
All indicators	915	100%	
OECD quality dimension(s)			
Effectiveness/safety	875	96%	• Prevalence of antipsychotics without a diagnosis of psychosis amongst nursing home residents.[74] • Citalopram prescribed concomitantly with other QT-prolonging medicines.[226]
Efficiency/costs	82	9%	• Generic prescribing rate (%).[210]
Equity	6	1%	• The proportion of people with asthma (age <45) prescribed a LABA who are not using an ICS (Subgroup analysis would inform equity consideration),[229]
Donabedian quality dimension(s)			
Structure	30	3%	• Use of opioids from multiple prescribers and multiple pharmacies.[101] • The proportion of people taking a brand name medication where a therapeutically equivalent lowest cost generic is available in class.[229]
Process	915	100%	• % of patients in the practice who were prescribed a benzodiazepine more than six times per year.[219]
Outcome	163	18%	• Outcome to avoid: Hospitalisation due to ischaemic event, with preceding pattern of care: history of diabetes; history of ischaemic event; no antiplatelet or lipid-lowering therapy.[207]
ATC class(es) and level ATC3 subclasses with ≥20 PQIs (N)			
A - Alimentary tract and metabolism A02 drugs for acid related disorders (42) A10 drugs used in diabetes (22)	116	13%	• Outcome to avoid: ER visit/hospitalisation due to GI ulcer/bleeding, with preceding pattern of care: 1. Concurrent use of corticosteroids/warfarin or diagnosis of multiple comorbid diseases or history of ulcers; 2. Use of an NSAID; 3. No use of cytoprotection (misoprostol or PPI).[196] • Prescribe metformin as a first-line treatment for pharmacological treatment for type 2 diabetes.[225]
B - Blood and blood forming organs B01 antithrombotic agents (67)	70	8%	• Aspirin on discharge after acute myocardial infarction.[64] • NSAID/antiplatelet/high-risk antibiotic/oral azole antifungal prescribed to current warfarin user.[215]
C - Cardiovascular system C03 diuretics (28) C07 beta-blocking agents (60) C08 calcium channel blockers (25) C09 agents acting on the renin-angiotensin system (56) C10 lipid-modifying agents (45)	116	13%	• Outcome to avoid: GP or hospital contact due to an exacerbation of asthma or COPD, with predecing pattern of care: Use of BB in an individual with asthma or COPD.[218] • Acute myocardial infarction: Adherence to statin therapy 1 year after discharge.[65]
D – Dermatologicals	16	2%	• Topically applied 0.1% tacrolimus before 16 years of age.[200,202,203]
G - Genito urinary system and sex hormones	20	2%	• Oral or transdermal estrogens to a woman with a history of breast cancer.[208]
H – Systemic hormonal preparations, excl. sex hormones and insulins H02 corticosteroids for systemic use (27)	36	4%	• Algorithm developed to identify people with asthma and categorise the intensity of inhaled asthma medication and oral corticosteroid use based on prescription claims data.[85] • A concomitant bisphosphonate should be prescribed if oral corticosteroids are used long-term (greater than three months).[205]
J – Anti-infectives for systemic use J01 antibacterials for systemic use (117)	123	13%	• Seasonal variation of antibiotic prescriptions: (Number of prescriptions during the cold-weather season (January–March, October–December)/Number of prescriptions during the hot-weather season (April–September) – 1) x 100.[120]
L - Antineoplastic and immunomodulating agents	10	1%	• Individual is prescribed more than one strength of methotrexate tablets.[213]
M – Musculo-skeletal system M01 antiinflammatory and antirheumatic products (93)	110	12%	• % of 70+ year-olds treated with NSAIDs, using coxibs[124] • DDSI: NSAID prescribed to an individual with a history of heart failure.[226]
N – Nervous system N02 analgesics (82) N03 antiepileptics (20) N05 psycholeptics (95) N06 psychoanaleptics (57)	224	24%	• Four or more psychotropics prescribed to an individual for more than three months.[140] • The discharge opioid in MED after orthopaedic trauma surgery.[94]
P- Antiparasitic products, insecticides and repellents	8	1%	• PIM, Paediatric: Ivermectin (oral) to be avoided in children aged under one year.[201]
R – Respiratory system R03 drugs for obstructive airway diseases (74) R06 antihistamines for systemic use (20)	102	11%	• % of people with asthma treated with LABA who are not using ICS.[214] • Sedating antihistamines should not be prescribed to children aged under two years.[198]
S – Sensory organs	9	1%	• Outcome to avoid: Hospitalisation due to asthma or COPD with preceding pattern of care: 1. History of asthma or COPD; 2. Use of BB eye drops for glaucoma.[211]
V - Various	1	<1%	• Prescription of naloxone to individuals using opioids for chronic pain.[102]
N/A - ATC not applicable (broad groups that extend across ATC classes, or classes cannot or need to be further defined, e.g., anticholinergic)	76	8%	• Potentially unsafe use: Concomitant use of 2 or more highly anticholinergic drugs or medication classes.[195] • The proportion of people taking a brand name medication where a therapeutically equivalent lowest cost generic is available in class.[229]

ASA = acetylsalicylic acid, aspirin; ATC = anatomical therapeutic chemical; BB = beta-blocker; COPD = chronic obstructive pulmonary disease; DDSI = drug-disease-interaction; ER = emergency room; GI = Gastrointestinal; GP = General practitioner; ICS = inhaled corticosteroids; LABA = long-acting beta-agonist; MED = morphine equivalent dose; NSAID = non-steroidal anti-inflammatory drug; OECD = The Organisation for Economic Co-operation and Development; PIM = potentially inappropriate medications; PPI = proton pump inhibitor.

Table 4
A data-oriented classification of the identified prescribing quality indicators (PQIs), with examples.

Data requirements	Indicator type (N)	Examples (directly cited or slightly edited for consistency or conciseness)
A Aggregate medicine-oriented (146)		
Aggregate pharmaceutical consumption or dispensing data	A1: Consumption (30) A2: Range (15) A3: Rate, ratio (82)	• Overall opioid prescriptions per 100 patients/primary care unit.[101] • Drug utilisation DU90%-method.[223] • The proportion of total consumption that comprised 'Access' (vs. 'Watch' and 'Reserve') agents based on the WHO AWaRe groups of antibiotics.[116]
+ Longitudinal aggregate data	A4: Trends (9)	• Application of mixed-effects models to examine longitudinal antibiotic use patterns.[113]
+ Cost data	A5: Cost indicators (11)	• Costs per daily dose in specific ATC groups relevant in primary care.[75]
B Individual-level medicine-oriented (316)		
Individual dispensings or prescriptions + patients' demographic characteristics	B1: Frequencies, prevalences (13)	• Number of nursing home residents receiving at least 1 antibiotic (J01) per year/total number of residents per year[118]
	B2: PIMs, PPOs based on dose and/or demographics alone (92)	• Number of patients <8 years old who were prescribed loperamide divided by the total number of patients <8 years old x 100%.[219] • Benzodiazepine or Z-drug prescribed to a patient aged ≥65 years (increased risk of falling and fracture).[140]
+ Cross-linkage of individual patient's dispensings	B3: DDIs and PPOs based on cross-linked medicine data (112) B4: Polypharmacy (11)	• Diuretic and NSAID and ACEI or ARB ('triple whammy' = an interaction between three groups of medicines, which can result in acute renal failure.)[212] • The prevalence of each number of dispensed medications weighted by the number of possible one-to-one drug interactions; and the sum of the regional weighted prevalence is divided by the sum of the national weighted prevalence.[227]
+ Longitudinal individual-level data	B5: Medication sequences (washout period, initiation, duration, sequence, follow-up) (56)	• Children with ADHD requiring medication were first prescribed a stimulant medication.[71] • Prescriptions of SABA, ICS, oral corticosteroid, leukotriene receptor antagonist and antibiotic use during 6 to 12 months before initiating ICS/LABA.[90]
+ Estimating diagnoses based on medications	B6: Diagnoses by proxy (34)	• Diabetes: Use of statin. Diabetes patients identified based on the use of oral or non-oral diabetes medicines during the analysis year.[130]
C Disease-oriented (462)		
+ Diagnoses (current or history of)	C1: Disease-specific (DDSI, PPOs) (167)	• Omitted bone protection (bisphosphonate, calcitriol or hormone replacement therapy) in long term (≥12 weeks) oral corticosteroid users aged ≥65 years or with low trauma fracture.[213]
+ Individual-level longitudinal data	C2: Treatment sequences (follow-up after a hospitalisation, adherence, refill patterns, treatment sequences) (133)	• The number of opioid refills on patients after an urologic surgery.[93] • The proportion of individuals (aged ≥18 years) with both an ischemic stroke and atrial fibrillation or flutter who are prescribed and dispensed anticoagulation therapy (warfarin or any DOAC) upon hospital discharge and the proportion receiving anticoagulation who receive a DOAC.[229]
	C3: Outcomes linked with preceding pattern of care (152)	• Outcome to avoid: ER visit/hospitalisation due to fall secondary to the use of a long-acting benzodiazepine.[196]
+ Causes of death	C4: End-of-life treatment (11)	• Inappropriate: Number of people who died with Alzheimer's disease who received statins and did not have declining statin use in the last [12, 6, 1] months prior to death/Number of people who died with Alzheimer's disease and received statins[67]

ACEI = angiotensin-converting-enzyme inhibitor; ADHD = Attention Deficit Hyperactivity Disorder; ARB = angiotensin 2 receptor blocker; ATC = anatomical therapeutic chemical; DDI = Drug-Drug-interation; DDSI = Drug-Disease-interaction; DOAC = direct oral anti-coagulant; ER = emergency room; ICS = inhaled corticosteroids; LABA = long-acting beta-agonist; NSAID = non-steroidal anti-inflammatory drug; PIM = Potentially inappropriate medications; PIP = Potentially inappropriate prescribing; PPO = Potential prescribing omissions; SABA = short-acting beta-agonist; WHO = World Health Organisation.

evidence in terms of purpose and level of assessment. The overarching majority of PQIs addressed *effectiveness and safety* quality dimensions which represent the technical quality in the OECD HCQI framework.[50,52] Notably, patient-centeredness is also part of technical quality; however, given that register data does not include patient-reported outcomes, none of the included PQIs addressed this dimension. Dimensions bridging quality with expenditures (efficiency) and distributional (equity) considerations were less common or rarely addressed. Placed on the Donabedian taxonomy, all PQIs addressed the *process*-dimension, which was expected since prescribing is a process by definition.[47,51] Thus, the lack of variation limited the usability of these taxonomies in synthesising evidence. In relation to data requirements, PQIs were skewed towards a higher level of data granularity.

In 2004, a European expert meeting (DURQUIM) outlined the state of the art of the development and application of PQIs.[2] The literature scoped in this review was predominantly published after their recommendations, making it meaningful to discuss the results in relation to their recommendations. As they anticipated, major improvements have occurred in the development of new indicators and exploiting existing data, in particular enriching medication dispensing registers with clinical data. These advances are likely driven by the computerisation of healthcare. Face and content validity were commonly pursued; however, evidence about concurrent and/or predictive validity is still rare.

Some DURQUIM recommendations remain unadressed. Envisaged international structures, frameworks, and taxonomies appear to not be sufficiently comprehensive and well-known to aid in targeting searches based on the quality measurement purpose, level, or scope. International catalogues of data sources and PQIs were not referred to in the literature. International comparative studies using PQIs at different levels of the health system remain scarce, even in settings with fairly comparable data such as the Nordic countries.

Overall, regarding the scope of the current review, PQI initiatives targeted for international comparison were few, whereas a wealth of national and/or subnational initiatives and research projects exist. Content validated PQIs focus heavily on the lower levels of the system – screening individual patients and assessing the performance of individual doctors or units. Even higher-level studies tend to be limited to one country. Nevertheless, the development of PQIs is international by its iterative nature,[17] meaning that later studies have adapted previously introduced PQIs to new settings and purposes. In our results, this was reflected in the fact that similar PQIs were commonly reused across studies.

Aside from the OECD HCQI framework that includes few PQIs, the European initiatives for monitoring antimicrobial consumption provide examples of harmonised, international, population-level indicators: the European Antimicrobial Resistance Surveillance System (EARSS) since 1999 and the European Surveillance of Antimicrobial Consumption (ESAC, later ESAC-Net) network established in 2001 and coordinated since 2011 by the European Centre for Disease Prevention and Control (ECDC). The aggregate-level antimicrobial consumption indicators were initially published in 2007,[111] and many studies have since applied and further adapted these indicators.

In terms of the number of articles, the largest identified literature subfield focused on the quality of pharmacotherapy in old age, with harmonised methodology and terminology.[15] This literature includes national and international PIM lists, of which several are regularly updated. PIM lists were also used in several register-based studies; however, they seem to be predominantly validated for use in screening individual patients. Methodological studies raised questions about their discriminative power in population-level assessments.[176,187,188]

The search for evidence was undermined by a lack of harmonised terminology. Previous reviews using traditional search strategies have screened over 10,000 to 20,000 titles.[3,17] We combined an initial narrow search strategy with snowballing and exploratory searches. This approach yielded a broad scope of relevant articles without screening an extremely large amount of mostly irrelevant titles. It is thus a useful approach in terms of supplementing traditional searches when specific search terms are lacking.

Furthermore, determining whether the article contained register-applicable PQIs typically required reading the full text, including supplemental materials, as this information was not necessarily discernible from the title and abstract alone. An article could include between less than five to several hundreds of PQIs, of which only part were considered register-applicable. With the exception of PQIs used in register studies conducted in the Nordic countries, the identified PQIs require further technical operationalisation and detailed definitions to be applied to register data. Notably, applicability to register data was only screened based on technical data requirements, while other factors (such as product range and changes in clinical guidelines) may still limit the usability and relevance of PQIs.

A few caveats need to be noted. Given the large volume of the literature and lacking search terms, it is likely that we did not capture every article that would have potentially fit our inclusion criteria. Nevertheless, we conducted several rounds of snowballing and exploratory searches. During the later rounds, new types of indicators were no longer identified. Thus, the variety of indicators is likely to be relatively well captured, although all versions of each PQI might not be included. Furthermore, the search was limited to original research articles. PQIs are routinely used in many countries (including the Nordics) for national purposes. Further searches of grey literature and databases are needed to complement the evidence base.

Overall, few studies were identified with PQIs specifically validated for population-level quality assessment using (Nordic) register data. Nonetheless, ample evidence about prescribing quality measurement and assessment already exists, based on which PQIs are iteratively developed for new settings and purposes. A key challenge in synthesising evidence is the fragmentation of literature across several subfields without common conceptualisations or specific search terms. Harmonising search terms across a large an heterogeneous literature can be challenging, since different disciplines and traditions employ their own concepts and terminologies, and the literature is already extensive. Greater efficiency may instead be achieved through the development and use of more advanced techniques and tools for filtering relevant literature. An example in this review is the use of exploratory and AI-powered searches to complement traditional search strategies. Furthermore, the present review provided a more detailed classification of existing evidence than before, both at the level of articles and PQIs. It is envisaged to provide steps towards organising the literature under a common theoretical framework. The structuring and harmonisation of the evidence base contributes to the reuse of available healthcare data for better healthcare delivery and policymaking, as envisioned in the DURQUIM meeting in 2004 and currently pursued through the European Health Data Space.

CRediT authorship contribution statement

Katri Aaltonen: Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Fatimah Fathy:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Marja-Lisa Laukkonen:** Writing – review & editing, Conceptualization. **Piia Rannanheimo:** Writing – review & editing, Methodology, Conceptualization. **Lotte Rasmussen:** Writing – review & editing, Methodology, Conceptualization. **Hanna Rättö:** Writing – review & editing, Methodology, Conceptualization. **Leena Saastamoinen:** Writing – review & editing, Methodology, Conceptualization. **Per-Jostein Samuelsen:** Writing – review & editing, Methodology, Conceptualization. **Björn Wettermark:** Writing – review & editing, Methodology, Conceptualization. **Sofia Kälvemark Sporrong:** Writing – review & editing, Supervision, Methodology, Conceptualization.

AI statement

Search strategy was supplemented with AI-powered searches using PubMed "similar articles", Google Scholar "related articles", and Semantic Scholar. All inclusion and exclusion decisions were made by the authors. Microsoft Copilot, an AI-based language editing tool was used to enhance the clarity of few sentences in the text. All final edits and content decisions were made by the authors.

Funding

This work is supported by the Academy of Finland Flagship Programme (Decision Number: 345546) and Academy of Finland (Decision Number: 354657).

Competing interests

KA: Part-time employment at the Wellbeing Service County of Southern Finland (Varha). Consulting fees from the Finnish Ministry of Social Affairs and Health. Lecture fees from the University of Tampere. PR: Vice Chairman of the Council for Choices in Health Care in Finland (COHERE Finland). LS: Research grants from the Social Insurance Institution. Lecture fees from the Universities of Eastern Finland and Helsinki. Payments for opponent of a dissertation from Universities of Oslo and Southern Denmark. Chair of the executive committee: Nordic Pharmacoepidemiology Network NorPEN. BW: Scientific advisor to the Swedish Medical Products Agency. Board member of European Drug Utilisation Research group. PJS: Research grants from Northern Norway Regional Health Authority (Helse Nord), Travel support from Uppsala University and Norwegian Association of Researchers (NAR; Forskerforbundet).

Acknowledgements

We would like to thank Information Specialist Leeni Lehtiö from the University of Turku Library for assisting with the searches. We thank Scribendi (www.scribendi.com) for editing the manuscript for English language.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

org/10.1016/j.sapharm.2026.06.003.

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