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Data-Driven Assessment of Potentially Inappropriate Medication in the Elderly

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Abstract. Multimorbid patients taking polypharmacy represent a growing population at high risk for inappropriate prescribing. Various lists for identifying potentially inappropriate medication are spread across scientific journals and difficult to access. To address this ongoing need, a new database named PIMBase is developed which integrates these well-known lists and unifies their rating scales. The analysis of the pharmacovigilance data reveals the benefits of combining the lists. PIMBase is meant to be a web-based system and starting point for the data-driven assessment of polypharmacy to identify inappropriate medication and to improve the quality of prescribing. PIMBase is available at https://pimbase.kalis-amts.de.

Keywords. Drug-Related side effects and adverse reactions, potentially inappropriate medication list, polypharmacy, inappropriate prescribing, medication errors, information systems, decision support systems, computer-assisted decision making

1. Introduction

In aging populations, multimorbidity is increasing with a corresponding increase in polypharmacy, which in turn is the prime risk factor for inappropriate prescribing. The evidence is well-known by several studies that the use of certain groups of medications in elderly and vulnerable patients is associated with falls [1] and an increase in mortality [2]. Furthermore, inappropriate medications can impair cognitive properties [3], reduce the quality of life and cause additional costs for the healthcare system [4].

The major challenges in gerontopharmacology are both over-treatment and under-treatment associated with polypharmacy. In recent years, lists, criteria and classification systems for assessing "potentially inappropriate medication" (PIM) for geriatric patients were developed and published. Besides these PIM lists of medication with a negative risk-benefit balance (i.e. PRISCUS [5], AUSTRIAN PIM [6]), lists with a positive balance (i.e. FORTA [7], EU(7)-PIM [8]) are also becoming the focus of interest. However, those PIM lists are spread across scientific journals and difficult to access for patients or health professionals in the context of treatment. The integration of the various lists into a uniform database and subsequent merging as well as an implementation of a unique rating scale are essential for the qualitative improvement of the drug therapy in elderly and offer opportunities for practical application to identify and reduce inappropriate prescribing.

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2. Methods

The four mentioned PIM lists are published online in different file formats and structures. Thus, all source structures have to be analyzed and transformed into a common schema in order to build up a uniform database of PIMs. Especially the machine processing unfriendly PDF format poses a difficult issue. Additionally, both English and German languages need to be supported. Whereas the FORTA list is available in both languages, the PRISCUS list is provided in German only. The AUSTRIAN PIM and EU(7)-PIM lists are only available in English.

All lists provide the drug name, the expert consensus and selected comments or reasons for each PIM entry. In addition, possible therapy or drug alternatives and dose adjustments are listed in varying detail. Only the EU(7)-PIM list annotates each entry with the respective Anatomical Therapeutic Chemical (ATC) code. The FORTA list groups the entries by indications and the PRISCUS list provides possible contra-indications where applicable.

2.1. Development of the Database "PIMBase"

First, all sources are converted into machine-readable CSV files because all PIM lists can be represented as tables. A simple python script parses the docx file of EU(7)-PIM list and saves only the relevant table as a CSV file. The other lists as PDF files were transferred manually. The ATC classification system is used to annotate all drug names with their respective ATC codes to further unify the different PIM entries for all lists. Additionally, the indications of the FORTA list are annotated with the International Classification of Diseases version 10 (ICD-10) where applicable. The transfer and annotation were validated by several additional people in order to ensure the consistency of the information extracted.

Finally, a python script parses the four generated lists and outputs the uniform MySQL database. Common fields like the drug name and ratings are combined into uniform fields. Additional information such as source references in the EU(7)-PIM list or the drug class in the PRISCUS list is stored in a generic data structure of key-value-pairs where needed.

All PIM entries were rated by expert consensus panels of different research projects. A uniform rating scale was created and all PIM scores transformed into this scale in order to compare all scores efficiently. All lists except the FORTA scale use a 5 points Likert scale for rating. The FORTA list uses four categories for the PIM scores. The missing fifth category in comparison to the other lists is the undecided option. This option is introduced in order to map the FORTA list into the 5 points Likert scale. Since the order of score severities in the FORTA list is descending compared to the ascending severity in the other lists, a simple reversal of the scores results in a uniform rating scale (Table 1).

In future, new or updated PIM lists will be integrated semi-automatically, depending on the form of publication.

Table 1. The uniform 5 points Likert scale for rating potentially inappropriate medication in PIMBase.

1	2	3	4	5
Drug is certainly potentially inadequate for older patients	Drug is potentially inadequate for elderly patients	Undecided	Drug is not potentially inadequate for older patients	Drug is certainly not potentially inadequate for older patients

2.2. Implementation of the Web-based Information System

In order to provide the contents of the PIMBase database in an easy and informative manner to patients and health professionals, a web-based information system was implemented (https://pimbase.kalis-amts.de). The main component is the search tool making it possible to check specific drugs by their name or ATC code for occurrence in the PIM lists. The integrated information outlined above is shown in a user-friendly detail screen and cross-linked to third-party websites (e.g. DrugBank) with further information. Filter parameters allow the selection of all or a subset of PIM lists to be used and the results can be sorted by several criteria. Finally, the results can be printed in a complete overview with all detail information. This print, for example, empowers patients to discuss the results and treatment with their general practitioners. The website uses a REST-API to access the database. This standalone API provides endpoints and an access control management for future developments and interoperability with other systems.

3. Results

A total of 758 different PIM entries were integrated into the PIMBase database. To evaluate the advantage of integrating multiple lists instead of using just a single one, the overlap of ATC codes present in the lists is calculated (Figure 1).

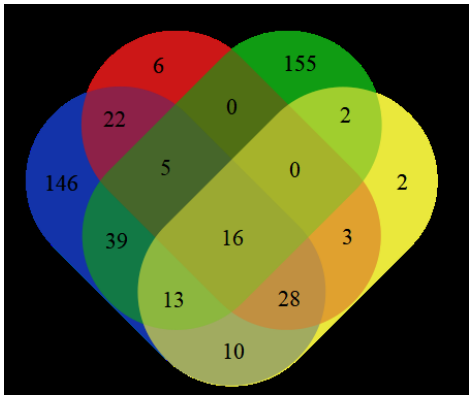

Figure 1. Overlap of different ATC codes covered by the PIM lists.

All lists only overlap in a small fraction of 16 entries. Pairs and triplets of lists show that an overlap is found in all combinations. However, most PIM entries can only be found in a single list, especially EU(7)-PIM and FORTA. This is of course biased by the size

and specificity of the lists. Therefore, using only a subset of the four integrated lists results in a loss of decision-critical information content. Because the lists differ in their focus on different criteria, the combination of information in the PIMBase system allows patients and general practitioners to evaluate different perspectives on the drugs in the context of treatment and improves decision-making.

Evaluation of PIMBase

The systematic analysis of the drug-related problems, i.e. adverse drug reactions (ADRs), is also an important aspect when evaluating the benefits of PIM lists. Therefore, cases of ADRs are analyzed to show the association of polypharmacy and ADRs and the benefits of using the lists integrated in PIMBase.

The data is obtained from the pharmacovigilance databases of the United States (FAERS) [10] and Canada (CVARD) [11]. The databases contain 996,404 cases of patients aged 65 and older with suspected ADRs in the target population.

The analysis of the sample population identifies a high number of cases with patients taking drugs referenced in PIMBase (Table 2). 47.1% of the patient cases in the population take at least one drug that is categorized as certainly or potentially inadequate for the elderly (category 1 or 2), 32.7 % take two or more inadequate drugs.

Table 2. Number of patients taking at least one drug referenced in PIMBase (N (% all cases in population) per category).

1	2	3	4	5	Total	PIMBase lists
Drug is certainly potentially inadequate for older patients	Drug is potentially inadequate for elderly patients	Undecided	Drug is not potentially inadequate for older patients	Drug is certainly not potentially inadequate for older patients		
232,963 (23.4%)	449,861 (45.1%)	20,496 (2.1%)	263,256 (26.4%)	312,345 (31.3%)	604,961 (60.7%)	**All**
41,253 (4.1%)	195,107 (19.6%)	0 (0%)	0 (0%)	0 (0%)	217,439 (21.8%)	**AUSTRIAN**
47,005 (4.7%)	345,035 (34.6%)	17,604 (1.8%)	0 (0%)	0 (0%)	360,418 (36.2%)	**EU(7)-PIM**
216,347 (21.7%)	269,256 (27%)	0 (0%)	263,256 (26.4%)	312,345 (31.3%)	548,129 (55.0 %)	**FORTA**
5,053 (0.5%)	125,152 (12.6%)	2,989 (0.3%)	0 (0%)	0 (0%)	130,941 (13.1%)	**PRISCUS**

The overlap between the ADRs of the PIM lists demonstrates once again the benefit of combining the different lists. The FORTA list seems to be the most comprehensive list in this case. The FORTA list gives a more detailed classification which also takes into account the indication of the drug prescribed. As the EU(7)-PIM list is developed on the PRISCUS list, the majority of identified cases overlap in both lists.

4. Discussion

Pharmacoepidemiologic research has shown that structured interventions like the use of PIM lists help to identify PIMs in elderly patients [9]. The implication for research and daily practice should be the evaluation of interventions like decision support systems that incorporate knowledge sources as PIMBase to improve the assessment of polypharmacy and avoid inappropriate drug usage in multimorbid patients.

5. Conclusion

Based on the standalone PIMBase-API, the database is planned to be integrated as a decision support module in the KALIS system [12] for patient-specific risk assessment of drugs. In future, further third-party integrations of PIMBase into healthcare systems are possible and desirable.

6. Availability and Requirements

PIMBase is available at https://pimbase.kalis-amts.de via a common web-browser.

7. Conflict of Interest

The authors disclose no conflict of interest.

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