Research in Social and Administrative Pharmacy 17 (2021) 701–706

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

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

Evolution of potentially inappropriate medication use in nursing homes: Retrospective analysis of drug consumption data

Damien Cateau [a,b,c,*], Olivier Bugnon [a,b,c], Anne Niquille [a,c]

[a] Community Pharmacy, Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland
[b] School of Pharmaceutical Sciences, University of Geneva, Geneva, Switzerland
[c] Institute of Pharmaceutical Sciences of Western Switzerland, University of Geneva, University of Lausanne, Geneva, Switzerland

ARTICLE INFO

Keywords:
Potentially inappropriate medication list
Nursing homes
Defined daily dose
Deprescribing
Beers' list
NORGEP-NH

ABSTRACT

Background: The use of potentially inappropriate medication (PIMs) is frequent in nursing homes (NHs), and leads to worsened health outcomes for their residents. Numerous initiatives to curb their use have been launched. Most studies of PIMs use in NHs, however, focused on their prevalence, and provide few insights on the evolution of their use.
Objective: The objective of this analysis is to measure the evolution of PIMs use in the nursing NHs of western Switzerland taking part in an integrated pharmacy service (IPS).
Methods: Drug consumption data from 166 NHs were collected for 2014 to 2018, through the monitoring of the IPS. These data were cross-referenced with validated PIMs lists (Beers' list and Norwegian General Practice-Nursing Home, NORGEP-NH) to compute the number of potentially inappropriate defined daily doses per average resident (DDD/res) in each NH. Linear mixed-effects models were used to assess the evolution of PIMs use over time, following the NORGEP-NH classification of PIMs and the drug classes involved.
Results: In 2018, the number of DDD/res was 7.3 (SD 1.9); of those, 2.2 (SD 0.8) were potentially inappropriate. Psycholeptics, psychoanaleptics and antihypertenseives were the most-used PIMs. Between 2014 and 2018, the number of potentially inappropriate DDD/res decreased by 0.03 per year (CI_{95} [−0.05; −0.01]).
Conclusions: This study complements others that focused on the prevalence of PIMs use in NHs. The statistically significant reduction in the use of PIMs is an encouraging sign, but is probably not clinically meaningful for NH residents. With the growing concerns of the potential harms of these drugs, more specific interventions and implementation strategies need to be developed to help clinicians further reduce their use in NHs.

Introduction

Context

Elderly persons living in nursing homes (NH) are among the frailest members of our societies: their health status is among the lowest, their life expectancy among the shortest, and they are often prescribed some of the heaviest load of medicine.[1,2] Physiological changes due to aging makes them more susceptible and more sensitive than younger adults to adverse drug reactions.[3]

A significant proportion of these NH residents receive potentially inappropriate medications (PIMs), drugs whose associated risks outweigh the potential benefits for the elderly patients[4]: a 2016 meta-analysis found that around half of NH residents worldwide are prescribed PIMs, with slight regional differences.[5] Recent European studies estimate the prevalence of PIMs among NH residents at between 43% and 88%,[6,7] depending on the setting and methodology. Similarly, a 2019 study found that between 59% and 79% of Swiss NH residents received at least one PIM every quarter, depending on the criteria used to define PIMs.[8] The use of PIMs by NH residents is associated with negative health outcomes such as falls,[9] fractures,[10] greater risks of hospitalization and higher hospitalization costs,[9–11] and a lower quality of life.[12]

In an effort to curtail the use of these potentially harmful drugs, various PIMs lists[13,14] have been published since the seminal Beers' list,[4] including its multiple updates by the American Geriatrics Society.[15,16] Some of the most recent ones include a new concern: the need for a specific attention to reevaluating, or deprescribing, long-term use

* Corresponding author. Community Pharmacy, Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland.
E-mail address: damien.cateau@unisante.ch (D. Cateau).

https://doi.org/10.1016/j.sapharm.2020.05.032
Received 2 March 2020; Received in revised form 28 April 2020; Accepted 29 May 2020
Available online 12 August 2020
1551-7411/© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

medicine.[17,18] One such list, the Norwegian General Practice – Nursing Home criteria (NORGEP-NH),[17] includes "Deprescribing criterias", emphasizing the need to reassess long-term treatment of NH residents with drugs such as bisphosphonates, urinary spasmolytics, and antidepressants.

Most epidemiologic analysis of the use of PIMs in NHs are cross-sectional studies of their prevalence.[5–9,19–21] While these evidences are extremely valuable, both for clinicians and policy-makers, they capture only part of the picture, as they do not take into account the amount of drug received over time, nor the doses used, which are both important parameters. Indeed, receiving one inappropriate drug at a low dose for a short time is less likely to cause harm than the same drug taken at a higher dose or for a longer time. In addition, these studies provide few insights into the evolution of PIMs use over time. Thus, we aimed to provide a more nuanced picture on the use of PIMs in NHs of western Switzerland, by using a longitudinal data set and taking into account the amount and dose of PIMs used.

Objectives

Using drug consumption data collected for the monitoring of an Integrated Pharmacy Service (IPS), the goals of this study are to quantify the use of PIMs in NHs of the cantons of Vaud and Fribourg, and analyse its evolution over five years. Analysis of the evolution of subgroups of PIMs, as categorized by NORGEP-NH, and according to the Anatomical Therapeutic Chemical (ATC) classification, will also be performed.

Methods

Local context and data sources

In Switzerland, about 15.7% of the population aged 80 and over resided permanently in a NH in 2018 (average age of residents: 84); 71.4% of residents are women, and 32–45% of the residents were admitted to NHs from hospital.[22] The NHs provide long-term care including nursing care services. Medical care is usually provided by local primary care physicians, supported by a network of specialists, particularly in psychogeriatrics and palliative care. Entry prescriptions, including from hospital discharge, are not systematically reviewed with the goal of reducing PIMs use.

An innovative interprofessional pharmaceutical service (IPS) was implemented in 2002–2018 in the canton of Fribourg (42 NHs, both French- and German-speaking), resp. since 2010 in the canton of Vaud (about 140 NHs, French-speaking), two of the 26 Swiss cantons. This service is based on interprofessional collaboration between pharmacists, physicians, and nurses, with the goal of optimizing the efficiency and safety of drugs use in the NH.[23,24] The volume and price of drugs used in the NH are evaluated each year by the pharmacist, then discussed with the other involved clinicians in light of the relevant scientific literature and clinical guidelines, using quality circles methodology. These quality circles result in local prescribing consensus, internal to the NH; although they are not publicly available, some may address PIMs use.

A centralized monitoring system assesses the effects of the IPS and suggests improvements, with NH pharmacists required to provide complete drug consumption data every year. Drug consumption data in NHs were provided for this analysis by the monitoring of the IPS; data, aggregated at the NH level, consist of the designation of the product, Swiss therapeutic product code, and number of packages used. The number of days spent by residents in each NH every year was also provided. No data on the indication of treatment were available, nor health-related information on the NH residents; no data on individual residents were collected for this analysis.

Linkage to the ATC/DDD system

Using the 2019 ATC classification,[25] these data were linked to the Defined Daily Dose (DDD) of their active ingredient. The DDDs, defined by the WHO Collaborating Centre for Drug Statistics Methodology (WHOCC), represents "the assumed average maintenance dose per day for a drug used for its main indication in adults". DDDs are not recommended or target doses, especially not for elderly patients in which typical doses are lower than for younger adults, but rather a means to enable and standardize research and monitoring by allowing the use of different drugs to be compared.[25]

ATC codes or specific administration routes for which no DDD was defined were assigned one by the investigators. Most of these refer to drug combinations; in that case, a main active substance was selected by the investigators, and its DDD was assigned to the association (e.g. ATC code A10BD02 (metformin and sulfonylureas) was assigned the DDD of metformin). For non-association ATC codes lacking a DDD, it was defined as the minimum daily dose recommended by the manufacturer for adults. The list of investigator-assigned DDDs is available in Table A1.

ATC codes and products exclusion

Some ATC codes were excluded from analysis, as a DDD proved impossible to compute (e.g. Emollients and protectives, ATC code D02) or was not applicable (e.g. Vaccines, J07). Specific products used in NHs were excluded because they could not be assigned an ATC code (e.g. alternative medicine products), or because no dosing information were available (e.g. some pharmacy-compounded products). Complete lists of excluded ATC codes and products, including exclusion reason, are available in Table A2 and Table A3.

PIMs classification

Two validated PIMs lists were combined for the classification of drugs: the American Geriatric Society 2015 Updated Beers Criteria (Beers list),[15] and NORGEP-NH.[17] The Beers list was chosen for its large use in research and clinical practice (the updated AGS 2019 Beers list was not available at the time of analysis),[16] and NORGEP-NH because it is, to our knowledge, the only one specifically designed for use with NH residents in Europe.

Following NORGEP-NH's classification, drugs present in either list, as single drug or in combination, were classified as *Avoid* or *Reevaluate*. Drugs present in the NORGEP-NH "Regular use should be avoided" category or in the Beers list with an "Avoid" recommendation were classified as *Avoid*. Drugs in the NORGEP-NH "Deprescribing criteria" or present in the AGS 2015 Beers list with a recommendation to avoid use in specific circumstances (e.g. nitrofurantoine, "Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression of bacteria") were classified as *Reevaluate*.

The NORGEP-NH criteria "Drug lowering blood pressure" is open to interpretation; we applied it to all antihypertensive drugs (ATC C02), low-ceiling diuretics (C03A & C03B), calcium-channel blockers (C08), renin-angiotensin system blockers (C09), and their combinations, but not to beta-blockers (C07) or peripheral vasodilatators (C04), as these are not frequently used to lower blood pressure, but rather for congestive heart failure or angina pectoris. The Beers list criterion "Insulin, sliding scale" was not included in the analysis, as it could not be assessed given the data at our disposal. For the same reason, the following NORGEP-NH criteria were excluded from analysis: "Combinations to avoid", "Any preventive medication", and "Regular use of hypnotics". Hypnotics (benzodiazepine) use is, however, addressed by the relevant Beers' list criteria.

The ATC codes assigned to each category and corresponding criteria from the Beers' and NORGEP-NH lists are found in Table A4.

Data analysis

All drugs were assigned an ATC code, a number of galenic units, a

dose per unit, and a route of administration. For transdermal patches, as the amount of active ingredient in each patch is greater than the dose delivered, the dose per galenic unit was set as the dose delivered during the recommended application time.

Each line with an ATC code meeting a criterion in the combined PIMs list was classified according to this criterion's category (either "Avoid" or "Reevaluate").

The number of DDD per average resident (*DDD/res*) for each line was computed using the following formula:

$$\frac{(number\ of\ boxes\ used)\cdot(number\ of\ units\ per\ box)\cdot(dose\ per\ unit)}{(DDD\ according\ to\ ATC\ code\ and\ administration\ route)\cdot(days\ spent\ in\ the\ NH\ during\ the\ year)}$$

Dividing the toal amount of drug used in the NH by the DDD gives the total number of DDD for a year; further division by the number of days spent by all residents in the NH gives the daily amount per average resident.

The evolution of the number of DDD/res was analyzed using linear mixed models with the year as independent variable and the NH as clustering variable, with random effects on the slope and intercept. Adherence of the data to the underlying hypothesis of the model (homoscedasticity, normal distribution of residuals) were verified by visual inspection of the relevant plots. The 5% significance level was considered.

Data were stored in MariaDB v10.1.36 (MariaDB Corporation Ab, Espoo, Finland), and computation of the number of DDD/res were done using Microsoft Excel PowerPivot (Microsoft Corporation, Redmond WA, USA). All statistical analyses were performed in Stata v16 (StataCorp LLC, College Station, TX, USA).

Ethical considerations and reporting

As no individual resident data were used in this analysis, no ethical approval was necessary under the applicable Swiss laws. This article was prepared following the RECORD-PE statement.[26]

Results

Data concerning 166 NHs caring for geriatric patients with or without cognitive problems were provided by the IPS monitoring. NH characteristics and data availability are presented in Table 1. Not all NH had data available for each year, either because of their creation, closure or merger of NHs, or their entry in their respective IPS during the study period. Data from 37 NHs were excluded in 2018, because they participated in a clinical trial of deprescribing interventions specifically targeting PIMs (see clinicaltrials.gov/ct2/show/NCT03688542, 19 NHs), or because data were not available for the whole year (18 NHs).

In 2018, the median number of DDD/res (without regard for appropriateness) was 7.3 (SD 1.9) (see Table 2). Linear mixed modeling shows a yearly increase of 0.09 DDD/res between 2014 and 2018 (CI_{95} [0.03; 0.14]) (see Table 3).

Table 1
Nursing homes for which data were available in a given year, by mission.

	2014	2015	2016	2017	2018
Total	105	148	156	159	128‡
Geriatrics	75 (71.4%)	97 (65.5%)	101 (64.7%)	104 (65.4%)	79 (61.7%)
Psycho-ger. *	12 (11.4%)	26 (17.6%)	27 (17.3%)	28 (17.6%)	24 (18.8%)
Mixed†	18 (17.1%)	25 (16.9%)	28 (17.9%)	27 (17.0%)	25 (19.5%)

All data are n (% of column); NH: nursing home; *: psycho-geriatrics, care for geriatric patients suffering from cognitive disorders; † both Geriatrics and Psycho-geriatrics mission; ‡ 19 NHs excluded for taking part in a clinical trial of deprescribing interventions targeting potentially inappropriate medications, 18 because data were not available for the whole year.

Use of potentially inappropriate DDDs and evolution since 2014

In 2018, the median number of potentially inappropriate DDD/res was 0.3 (SD 0.3) for the Avoid category, and 1.9 (SD 0.6) for the Reevaluate category (see Table 2). There were important variations between NHs, with the values for the Avoid and Reevaluate categories ranging from 0.0 to 3.2, respectively 0.6 to 5.8, DDD/res.

Linear mixed modelling shows a reduction in the use of PIMs between 2014 and 2018, with 0.03 fewer potentially inappropriate DDD/res for each passing year (CI_{95} [−0.05; −0.01]). Models for the individual Avoid and Reevaluate categories show a similar evolution, with 0.01 (CI_{95} [−0.02; −0.00]), respectively 0.02 (CI_{95} [−0.04; −0.01]), fewer DDD/res per year (see Table 3).

Table 1 shows that the proportion of NHs with a psycho-geriatric mission changed between 2014 and 2015–2018; this could have an influence on the results. Linear mixed modelling excluding the year 2014 shows a similar reduction in the number of potentially inappropriate DDD/res, both overall (−0.03, CI_{95} [−0.06; −0.01]) and for the individual Avoid category (−0.01, CI_{95} [−0.02; −0.00]), and a similar trend towards reduction for the Reevaluate category, although without reaching statistical significance (−0.02, CI_{95} [−0.04; 0.00]).

ATC classes involved and evolution

ATC classes contributing the most to the Avoid category in 2018 are the Psycholeptics (ATC N05, consisting of Antipsychotics, Anxiolytics, and Hypnotics and sedatives), with a median of 0.25 potentially inappropriate DDD/res, and Anti-inflammatory (ATC M01), with 0.04 DDD/res. Psychoanaleptics (ATC N06, mostly Antidepressants), Agents acting on the renin-angiotensin system (ATC C09) and Drugs for acid-related disorders (ATC A02) are the classes contributing the most to the Reevaluate category, with respective medians of 0.47, 0.41 and 0.29 potentially inappropriate DDD/res (see Table 4).

Evolution of the use of the ten most used PIM-containing second-level ATC classes was estimated between 2014 and 2018 (see Table 4). Five of the ten classes see a statistically significant diminution, and four other show no evolution. Only the ATC C10 category (Lipid modifying agents, which includes statins) show a statistically significant increase.

Discussion

The high number of DDD/res found in this analysis, both for PIMs and non-PIMs, are consistent with the other data on drug use by NH residents found in the literature: the analysis by Schneider at al. found high prevalence of both polypharmacy (85%) and PIMs use (79%) among Swiss NH residents.[8] While not directly comparable with these, our results show a similar high use of drugs by NH residents, with a median number of 7.3 DDD/res, well above the common cutoff of 5 drugs per day for polypharmacy.

Table 2
Defined daily doses per average resident.

Year	All DDDs	DDDs to avoid	DDDs to reevaluate	DDDs to avoid or reevaluate
2014	7.1 ([3.6–12.5], 1.8)	0.4 ([0.1–1.7], 0.2)	2.0 ([0.7–3.6], 0.5)	2.4 ([1.0–5.4], 0.6)
2015	7.2 ([3.4–12.0], 1.7)	0.4 ([0.1–1.9], 0.2)	2.0 ([0.9–3.6], 0.4)	2.3 ([1.1–5.6], 0.6)
2016	7.3 ([3.4–11.5], 1.6)	0.4 ([0.0–2.0], 0.2)	2.0 ([0.9–4.2], 0.5)	2.4 ([1.2–6.2], 0.6)
2017	7.4 ([3.0–13.4], 1.8)	0.4 ([0.0–1.9], 0.2)	1.9 ([0.3–4.0], 0.5)	2.4 ([0.6–5.9], 0.6)
2018	7.3 ([2.7–12.1], 1.9)	0.3 ([0.0–3.2], 0.3)	1.9 ([0.6–5.8], 0.6)	2.2 ([0.7–8.9], 0.8)

All data are median ([range], SD); DDD: defined daily dose.

While a statistically significant diminution in potentially inappropriate DDD/res was observed, PIM use remains high in the NHs studied, with 2.2 potentially inappropriate DDD dispensed to the average NH resident every day in 2018. The reduction observed, 0.03 fewer DDD/res for each passing year, while a positive trend, can hardly be considered clinically relevant. Variations between NHs were important, indicating that their populations may have different characteristics, that their clinicians have different practices, or both. Specifically, the NH mission may have an impact on the use of PIMs, as the results were slightly different when excluding the year 2014, in which the proportion of psycho-geriatric NHs was lower than for the 2015–2018 period. These hypotheses should be the subject of future investigations, aiming to better understand the clinical context in which PIMs are or are not prescribed. Practices around admissions from hospitals, or return after an hospitalization, could be of particular interest, as it has been shown that patients discharged from hospital to long-term care have a higher chance of PIM prescription than patients discharged to the community.[27]

The reduction in DDD/res observed could be caused by a change in the population of studied NHs between 2014 and 2018; however, data from Swiss Federal Office of Statistics suggest that it is not the case: the population living in these NHs did not significantly change between these years regarding the age and sex of residents, or the time required for daily care, reflecting the gravity of cases.[22,28]

In the years covered by this study, numerous initiatives have been launched to curtail the use of inappropriate procedures and medications. For example, through the Choosing Wisely initiative, multiple professional associations in the United States have published guidelines aimed at nurses, pharmacists and physicians[29–32]; they include recommendations to avoid the use of antipsychotics for the treatment of behavioral and psychological symptoms of dementia,[31] limit the use of lipid-lowering drugs for people with limited life-expectancy,[29] and use non-pharmacological approaches to prevent or treat delirium,[30] which could all contribute to reduce the use of PIMs in NHs. Similar recommendations have been issued in Switzerland,[33] discouraging prolonged use of high-dose proton-pump inhibitors (PPIs) or the use of drugs with a high risk of hypoglycemia for the treatment of diabetes.[34,35] Other local guidelines, jointly developed by physicians and NH pharmacists of the canton of Fribourg, promote the use of non-pharmacological approaches for the treatment of behavioral and psychological symptoms of dementia.[36] These campaigns seem, however, to have had a very limited impact on the practice of clinicians in the NHs studied, as no clinically relevant change in the use of PIMs has occurred in the five years studied here.

In the past years, the idea of deprescribing, withdrawing or reducing the dose of drugs with a negative risk-benefit balance (adapted from Reeve et al.),[37] has gained traction in the field of geriatrics. The ATC classes containing the most PIMs in this study align with the deprescribing guidelines published by groups like Primary Health Tasmania (e.g. anti-hypertensive agents or NSAIDS)[38] or the Bruyère Deprescribing Guidelines in the Elderly Project (e.g. PPIs and antipsychotics),[39] and also with clinican's perception of deprescribing priorities.[40] The low level of change in the four years leading to 2018 found in this analysis indicates that specific interventions aiming to implement such guidelines would probably be beneficial to the NH residents. Deprescribing interventions have indeed been shown to reduce the number of drugs received by NH residents,[41,42] including potentially inappropriate ones, and mortality and falls.[43] In the NHs of Vaud, the combination of cantonal prescribing guidelines and IPS improved the appropriate prescribing of antibiotics.[24] This approach could be leveraged to reduce the use of PIMs in nursing homes where IPS exists.

Table 3
Evolution of the number of DDD per average resident between 2014 and 2018.

	Yearly change	CI_{95}	p-value
All DDDs	+0.087	[+0.033; +0.140]	0.001
DDDs to avoid	−0.010	[−0.017; −0.004]	0.001
DDDs to reevaluate	−0.022	[−0.039; −0.005]	0.011
DDDs to avoid or reevaluate	−0.033	[−0.052; −0.013]	0.001

DDD: defined daily dose; CI_{95}: 95% confidence interval.

Strength and limitations

The main strength of this analysis is its comprehensive inclusion of all drugs used in the studied NHs over five years, enabling us to detect small differences in drug utilization trends. Another strength of the methodology used is its high degree of automation, necessitating only a minimal clinical input, for the construction of missing DDDs. This makes

Table 4
Number of potentially inappropriate DDD per average resident for the 10 largest PIM-containing ATC classes in 2018 and evolution since 2014.

	DDD per average resident in 2018 *		Evolution since 2014†		
	Avoid	Reevaluate	Yearly change	CI_{95}	p-value
A02 (Drugs for acid related disorders)	–	0.293 (0.214)	−0.010	[−0.017; −0.003]	0.003
C01 (Cardiac therapy)	–	0.017 (0.024)	−0.002	[−0.003; −0.001]	<0.001
C03 (Diuretics)	–	0.032 (0.036)	−0.004	[−0.006; −0.002]	<0.001
C08 (Calcium channel blockers)	–	0.177 (0.107)	0.003	[−0.002; 0.007]	0.26
C09 (Agents acting on the renin-angiotensin system)	–	0.405 (0.184)	−0.012	[−0.018; −0.006]	<0.001
C10 (Lipid modifying agents)	–	0.153 (0.153)	0.009	[0.005; 0.014]	<0.001
G04 (Urologicals)	–	0.048 (0.039)	−0.001	[−0.003; 0.001]	0.27
M01 (Antiinflammatory and antirheumatic products)	0.036 (0.061)	–	−0.002	[−0.005; −0.000]	0.026
N05 (Psycholeptics)	0.251 (0.262)	0.110 (0.262)	−0.006	[−0.014; 0.003]	0.18
N06 (Psychoanaleptics)	0.003 (0.050)	0.472 (0.203)	−0.004	[−0.010; 0.002]	0.23

DDD: Defined Daily Dose; CI_{95}: 95% confidence interval; ATC: Anatomical Therapeutic Chemical classification; *: median (SD); †: evolution of the combination of Avoid and Reevaluate categories, estimated using linear mixed models with nursing home as clustering factor.

it a useful and easy to deploy tool for supporting programs aiming to reduce the use of potentially harmful drugs: at program onset, such an analysis could focus efforts on the most-used PIMs, or on NHs using the most, and then be used to monitor the effects of the program on a regular basis. It could also be easily adapted for the monitoring of other kind of problematic drugs, in NHs or elsewhere, such as substances with anticholinergic properties.

The main limitation of this analysis is the limited scope of the data at our disposal, rendering us unable to connect the evolution of PIMs use with clinical, humanistic, or health-service utilization outcomes, such as falls, hospitalizations, or quality of life. It is thus unknown if the small reduction in the use of PIMs that we observed translated in real-life benefits for the NH residents. This limitation also prevented the use of PIMs identification tools making use of clinical information, such as the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy.[44]

In addition, the lack of information on the indication of treatment could lead to misclassification in some cases. For example, midazolam can be used both as an anxiolytic and for palliative sedation, in which case it should not be considered inappropriate. These misclassifications could artificially increase the number of DDDs classified as PIMs. On the other hand, our strict adherence to the published Beers and NORGEP-NH lists implies that problematic drugs not marketed in the United States or Norway will be misclassified as "non-PIM". In the same way, our interpretation of the NORGEP-NH "Drugs lowering blood pressure" criteria is conservative; a broader inclusion of all drugs with the effect to reduce blood pressure, such as beta-blockers, could increase the number of DDDs to Reevaluate. These uncertainties could be resolved by using data extracted from the NH medical records, which include indication. However, the use of such data would also introduce problems, such as the uncertainty over whether reserve drugs were given or not, which is not routinely documented. In addition, obtaining such data for research purpose would necessitate the consent of all individual NH residents in the Swiss legal framework; such consent would be unlikely to be given uniformly, which would introduce new bias in the data.

Our construction of DDDs for combination products underestimates the doses received by NH residents, as only one of the active substances is considered. This underestimation could lead to an artificial lowering of the DDDs computed if NH residents were switching away from separate drugs and to fixed-dose combinations, as the new fixed-dose combination would only count as one drug. However, as the practice to treat patients with fixed-dose combinations was well-established before 2014, it is doubtful that such an effect would be significant.

The metric we used, DDD/res, cannot distinguish between the use of a large number of drugs (either potentially inappropriate or not) at a low dose, or a few drugs at a high dose. However, both patterns of use should warrant attention from clinicians: using a large number of drugs increases the risk of drug-drug interactions, and using drugs at high doses in elderly patients, while sometimes necessary, is frequently inappropriate, given the heightened sensibility of this population to adverse drug reactions.[3]

Finally, our approach cannot detect other problematic prescribing practices, such as drugs combinations and missing prescriptions. Thus, it only addresses part of the inappropriate prescribing problems that can be found in NHs.

Conclusion

PIMs remain a significant part of NH residents' drug regimen in Switzerland, with one in three drug dose dispensed to these residents potentially inappropriate. With the growing concerns over the potential harms of these drugs, interventions and implementation strategies need to be developed to help clinicians reduce their use in NHs. These interventions will require rigorous evaluation on outcomes relevant for both the residents and the healthcare system.

The tool developed for this analysis could help clinicians focus their deprescribing efforts on the most problematic drug classes, steer efforts to promote the responsible use of specific drug classes, and allow for the monitoring of their impact. It will indeed be used to evaluate the effect of two deprescribing interventions actually under clinical trials in Swiss NHs.[45]

Funding

This work was supported by the Swiss National Science Foundation, through the National Research Program 74 "Smarter Health Care" (grant 167509), and by the State of Vaud, through a block grant to Prof. Olivier Bugnon.

The Swiss National Science Foundation and the State of Vaud played no role in the design or conduct of the study, and the preparation of this article.

CRediT authorship contribution statement

Damien Cateau: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft, Writing - review & editing. **Olivier Bugnon:** Conceptualization, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Anne Niquille:** Conceptualization, Methodology, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interests

The authors declare no conflicts of interests relative to this study.

Acknowledgements

The authors thank Stephanie Mena, Gordana Simic, Florent Aeby and Frédéric Klee, of Unisanté, for their help in data collection, and Pierluigi Ballabeni for his advice regarding statistical analysis. They also thank all pharmacists and nursing homes who provided data to the monitoring of the IPS.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.sapharm.2020.05.032.

References

1. Lau H, Lam S, Ho C, et al. Comparison of frailty of elders living in community and residential care homes. *J Am Geriatr Soc*. 2018;66:S32. https://doi.org/10.1111/jgs.15376.
2. Donovan MO, Sezgin D, Galluzzo L, et al. Frailty at population level in Europe: a systematic review and meta-analysis. *Age Ageing*. 2018;47. https://doi.org/10.1093/ageing/afy141.53.
3. McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. *Pharm Rev*. 2004;56:163–184. https://doi.org/10.1124/pr.56.2.4.
4. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med*. 1991;151:1825–1832. https://doi.org/10.1001/archinte.1991.00400090107019.
5. Morin L, Laroche M-L, Texier G, Johnell K. Prevalence of potentially inappropriate medication use in older adults living in nursing homes: a systematic review. *J Am Med Dir Assoc*. 2016;17. https://doi.org/10.1016/j.jamda.2016.06.011, 862.e861-862.e869.
6. Nyborg G, Brekke M, Straand J, Gjelstad S, Romøren M. Potentially inappropriate medication use in nursing homes: an observational study using the NORGEP-NH criteria. *BMC Geriatr*. 2017;17:220. https://doi.org/10.1186/s12877-017-0608-z.
7. Anrys PMS, Strauven GC, Foulon V, Degryse JM, Henrard S, Spinewine A. Potentially inappropriate prescribing in Belgian nursing homes: prevalence and associated factors. *J Am Med Dir Assoc*. 2018;19:884–890. https://doi.org/10.1016/j.jamda.2018.06.010.
8. Schneider RR, Blozik E, Früh M, Signorell A, Meier C, Schwenkglenks M. Drug prescription patterns, polypharmacy and potentially inappropriate medication in Swiss nursing homes: a descriptive analysis based on claims data. *Swiss Med Wkly*. 2019;149. https://doi.org/10.4414/smw.2019.20126.

9. Renom-Guiteras A, Thürmann PA, Miralles R, et al. Potentially inappropriate medication among people with dementia in eight European countries. *Age Ageing*. 2018;47:68–74. https://doi.org/10.1093/ageing/afx147.
10. Hyttinen V, Jyrkkä J, Saastamoinen LK, Vartiainen A-K, Valtonen H. The association of potentially inappropriate medication use on health outcomes and hospital costs in community-dwelling older persons: a longitudinal 12-year study. *Eur J Health Econ*. 2019;20:233–243. https://doi.org/10.1007/s10198-018-0992-0.
11. Wang KN, Bell JS, Chen EYH, Gilmartin-Thomas JFM, Ilomäki J. Medications and prescribing patterns as factors associated with hospitalizations from long-term care facilities: a systematic review. *Drugs Aging*. 2018;35:423–457. https://doi.org/10.1007/s40266-018-0537-3.
12. Mongkhon P, Tanasombat T, Jeenapongsa R, Kongkaew C. The association between inappropriate medication use and health-related outcomes among nursing home residents: a systematic review and meta-analysis. *Drug Saf*. 2018;41:1171–1172. https://doi.org/10.1007/s40264-018-0719-2.
13. Niehoff KM, Mecca MC, Fried TR. Medication appropriateness criteria for older adults: a narrative review of criteria and supporting studies. *Ther Adv Drug Saf*. 2019;10. https://doi.org/10.1177/2042098618815431.
14. Motter FR, Fritzen JS, Hilmer SN, Paniz EV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. *Eur J Clin Pharmacol*. 2018. https://doi.org/10.1007/s00228-018-2446-0.
15. American Geriatrics Society Beers Criteria Update Expert Panel. American geriatrics society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015;63:2227–2246. https://doi.org/10.1111/jgs.13702.
16. American Geriatrics Society Beers Criteria Update Expert Panel. American geriatrics society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2019;67:674–694. https://doi.org/10.1111/jgs.15767.
17. Nyborg G, Straand J, Klovning A, Brekke M. The Norwegian General Practice–Nursing Home criteria (NORGEP-NH) for potentially inappropriate medication use: a web-based Delphi study. *Scand J Prim Health Care*. 2015;33:134–141. https://doi.org/10.3109/02813432.2015.1041833.
18. Tommelein E, Petrovic M, Somers A, Mehuys E, van der Cammen T, Boussery K. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP^{3}S) tool. *J Public Health*. 2015;38:e158–e170. https://doi.org/10.1093/pubmed/fdv090.
19. Chen LL, Tangiisuran B, Shafie AA, Hassali MA. Evaluation of potentially inappropriate medications among older residents of Malaysian nursing homes. *Int J Clin Pharm*. 2012;34:596–603. https://doi.org/10.1007/s11096-012-9651-1.
20. Peskircioglu DH, Torun B, Ozkan O, Okuyan B. Utilization of potentially inappropriate medication in nursing home residents. *J Am Coll Clin Pharm*. 2018;1:191. https://doi.org/10.1002/jac5.1059.
21. Reich O, Rosemann T, Rapold R, Blozik E, Senn O. Potentially inappropriate medication use in older patients in Swiss managed care plans: prevalence, determinants and association with hospitalization. *PloS One*. 2014;9, e105425. https://doi.org/10.1371/journal.pone.0105425.
22. Swiss Federal Statistical Office (OFS). *Statistique des institutions médico-sociales 2018 – Tableaux standard*. OFS; 2019. available from https://www.bfs.admin.ch/bfs/fr/home/statistiques/catalogues-banques-donnees/tableaux.assetdetail.10627269.html.
23. Locca JF, Ruggli M, Buchmann M, Huguenin J, Bugnon O. Development of pharmaceutical care services in nursing homes: practice and research in a Swiss canton. *Pharm World Sci : PWS*. 2009;31:165–173. https://doi.org/10.1007/s11096-008-9273-9.
24. Pluss-Suard C, Niquille A, Hequet D, et al. Decrease in antibacterial use and facility-level variability after the introduction of guidelines and implementation of physician-pharmacist-nurse quality circles in Swiss long-term care facilities. *J Am Med Dir Assoc*. 2020;21:78–83. https://doi.org/10.1016/j.jamda.2019.05.016.
25. WHO Collaborating Center for Drug Statistics Methodology. *Guidelines for ATC classification and DDD assignment 2019*. 2018. Oslo, Noway.
26. Langan SM, Schmidt SA, Wing K, et al. The reporting of studies conducted using observational routinely collected health data statement for pharmacoepidemiology (RECORD-PE). *BMJ*. 2018;363:k3532. https://doi.org/10.1136/bmj.k3532.%JBMJ.
27. Bo M, Quaranta V, Fonte G, Falcone Y, Carignano G, Cappa G. Prevalence, predictors and clinical impact of potentially inappropriate prescriptions in hospital-discharged older patients: a prospective study. *Geriatr Gerontol Int*. 2018;18:561–568. https://doi.org/10.1111/ggi.13216.
28. Swiss Federal Statistical Office (OFS). *Statistique des institutions médico-sociales 2014 – Tableaux standard*. OFS; 2016. available from https://www.bfs.admin.ch/bfs/fr/home/statistiques/sante/systeme-sante/etablissements-medico-sociaux.assetdetail.276031.html.
29. *AMDA – the Society for Post-Acute and Long-Term Care Medicine, Ten Things Physicians and Patients Should Question*; 2017. accessed on http://www.choosingwisely.org/societies/amda-the-society-for-post-acute-and-long-term-care-medicine/. Accessed February 3, 2020.
30. American Academy of Nursing. *Twenty-Five Things Nurses and Patients Should Question*; 2018. accessed on http://www.choosingwisely.org/societies/american-academy-of-nursing/. Accessed February 3, 2020.
31. American Geriatrics Society. *Ten Things Clinicians and Patients Should Question*; 2015. accessed on http://www.choosingwisely.org/societies/american-geriatrics-society/. Accessed February 3, 2020.
32. American Society of Health-System Pharmacists. *Five Things Physicians and Patients Should Question*; 2017. accessed on http://www.choosingwisely.org/societies/american-society-of-health-system-pharmacists/. Accessed February 10, 2020.
33. Smarter Medicine - Choosing Wisely Switzerland. www.smartermedicine.ch. Accessed February 3, 2020.
34. Swiss Society of General Internal Medicine. *Top Five List for « Choosing Wisely » in the Inpatient Sector*; 2016. accessed on https://www.smartermedicine.ch/fr/liste-top-5/medecine-interne-generale-ambulatoire.html. Accessed February 3, 2020.
35. Professionelle Suisse de Gériatrie Société. Comment smarter medicine peut s'appliquer en gériatrie?. accessed on https://www.smartermedicine.ch/fr/liste-top-5/geriatrie.html; 2017. Accessed February 3, 2020.
36. Anguish I, Locca JF, Bula C, Zumbach S, Bugnon O. Pharmacologic treatment of behavioral and psychological symptoms of dementia in nursing homes: update of the 2008 JAMDA recommendations. *J Am Med Dir Assoc*. 2015;16:527–532. https://doi.org/10.1016/j.jamda.2015.03.014.
37. Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice. *Br J Clin Pharmacol*. 2015;80:1254–1268. https://doi.org/10.1111/bcp.12732.
38. Primary health Tasmania, deprescribing guides. https://www.primaryhealthtas.com.au/resources/deprescribing-guides/. Accessed April 18, 2019.
39. Bruyère Deprescribing Guidelines in the Elderly Project, Deprescribing Guidelines and Algorithms, https://deprescribing.org [Accessed 18 April 2019].
40. Farrell B, Tsang C, Raman-Wilms L, Irving H, Conklin J, Pottie K. What are priorities for deprescribing for elderly patients? Capturing the voice of practitioners: a modified delphi process. *PloS One*. 2015;10, e0122246. https://doi.org/10.1371/journal.pone.0122246.
41. Wouters H, Scheper J, Koning H, et al. Discontinuing inappropriate medication use in nursing home residents: a cluster randomized controlled trial. *Ann Intern Med*. 2017;167:609–617. https://doi.org/10.7326/m16-2729.
42. Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The feasibility and the effect of deprescribing in older adults on mortality and health: a systematic review. *Br J Clin Pharmacol*. 2016;82:583–623. https://doi.org/10.1111/bcp.12975.
43. Kua CH, Mak VSL, Huey Lee SW. Health outcomes of deprescribing interventions among older residents in nursing homes: a systematic review and meta-analysis. *J Am Med Dir Assoc*. 2018;20:362–372. https://doi.org/10.1016/j.jamda.2018.10.026.
44. Lavan AH, Gallagher P, Parsons C, O'Mahony D. STOPPFrail (screening tool of older persons prescriptions in Frail adults with limited life expectancy): consensus validation. *Age Ageing*. 2017;46:600–607. https://doi.org/10.1093/ageing/afx005.
45. Optimising the medication of elderly persons living in nursing homes. http://www.nfp74.ch/en/projects/in-patient-care/project-bugnon. Accessed February 3, 2020.