Research in Social and Administrative Pharmacy 19 (2023) 1372–1379

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

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

Regional variation of potentially inappropriate medication use and associated factors among older adults: A nationwide register study

Jasmin Paulamäki [a,b,*], Johanna Jyrkkä [b], Virva Hyttinen [c], Heini Huhtala [d], Esa Jämsen [e,f]

[a] Faculty of Medicine and Health Technology, Clinical Medicine, Tampere University, FI-33014, Tampere University, Finland
[b] Development and Information Services, Finnish Medicines Agency Fimea, P.O. Box 55, FI-00034, FIMEA, Finland
[c] Department of Health and Social Management, University of Eastern Finland, P.O. Box 1627, FI-70211, Kuopio, Finland
[d] Faculty of Social Sciences, Health Sciences, Tampere University, FI-33014, Tampere University, Finland
[e] Faculty of Medicine (Clinicum), University of Helsinki, P.O. Box 63, FI-00014, University of Helsinki, Finland
[f] Department of Geriatrics, Helsinki University Hospital, P.O. Box 340, FI-00029, Helsinki, HUS, Finland

ARTICLE INFO

Keywords:
Aged
Potentially inappropriate medication
Health service accessibility
Regional variation
Medicine use

ABSTRACT

Background: Certain medications should be used with caution in older persons, which challenges rational prescribing. Potentially inappropriate medications (PIMs) are defined as medicines whose potential risk of harm typically outweighs the clinical benefits in geriatric population. Earlier studies have found regional differences in PIM use, but the factors underlying this phenomenon are unclear.

Objective: To compare prescription PIM prevalence among Finnish hospital districts and determine which population characteristics and factors related to social and health care are associated with regional variation.

Methods: This nationwide register study was based on the Prescription Centre data on all people aged ≥75 years in 2017–2019. Hospital district (n = 20) characteristics were drawn from the Finnish Institute for Health and Welfare's, Finnish Medical Association's, and Finnish Medicines Agency's publicly open data. PIMs were defined according to the Finnish Meds75+ database. A linear mixed-effect model was used to analyze potential associations of regional characteristics with PIM prevalence.

Results: Prevalence of PIMs varied between 16.4% and 24.8% across regions. The highest prevalence was observed in the southern regions, while the lowest prevalence was on the west coast. Hospital district characteristics associated with higher PIM prevalence were higher share of population living alone, with excessive polypharmacy, or assessed using the Resident Assessment Instrument, shortage of general practitioners in municipal health centers, and low share of home care personnel. Waiting time in health care or share of population with morbidities were not associated with PIM use. Of the total variance in PIM prevalence, 86% was explained by group-level factors related to hospital districts. The regional variables explained 75% of this hospital-district-level variation.

Conclusions: PIM prevalence varied significantly across hospital districts. Findings suggest that higher PIM prevalence may be related to challenges in the continuity of care rather than differences in health care accessibility or share of the population with morbidities.

1. Introduction

Older persons are typically treated with a high number of medications. Although polypharmacy may be well indicated, the more medicines a person takes, the higher the risk for interactions and adverse drug events.[1] Old age is also associated with age-related changes in pharmacokinetics and pharmacodynamics, which result in drug sensitivity. Given these features, optimal prescribing of medications in older

Abbreviations: PIM, potentially inappropriate medication; SII, the Social Insurance Institution of Finland; THL, the Finnish Institute for Health and Welfare; FMA, Finnish Medical Association; GPs, general practitioners; LMM, linear mixed-effect model; CI, confidence interval; AIC, Akaike information criterion; ICC, intraclass correlation coefficient; RAI, Resident Assessment Instrument; OTC, over the counter.

* Corresponding author. Faculty of Medicine and Health Technology, Clinical Medicine, Tampere University, FI-33014, Tampere University, Finland.
E-mail addresses: jasmin.paulamaki@tuni.fi (J. Paulamäki), johanna.jyrkka@fimea.fi (J. Jyrkkä), virva.hyttinen@uef.fi (V. Hyttinen), heini.huhtala@tuni.fi (H. Huhtala), esa.jamsen@helsinki.fi (E. Jämsen).

https://doi.org/10.1016/j.sapharm.2023.06.005
Received 3 April 2023; Received in revised form 6 June 2023; Accepted 17 June 2023
Available online 17 June 2023

persons challenges health care professionals, and certain medications should be prescribed with caution.

Potentially inappropriate medications (PIMs) are often defined as medicines whose potential risk of harm outweighs the clinical benefits in geriatric population.[2] Earlier studies have found that PIM use is associated with negative outcomes, such as risk for falls, poor health-related quality of life, and risk of emergency hospital attendance in older persons.[3,4] Several criteria for PIMs have been published to guide clinicians to avoid prescribing such medications for older persons.[5,6] In Finland, the Meds75+ database is developed to improve the safety of pharmacotherapy in older persons aged 75 and over and is intended to define PIMs.[7]

Despite the known risks, PIM use is common among the older population with a prevalence of 22.6% in Europe.[8] Several studies have also determined the inappropriate prescribing nationally and found regional variations.[9–14] These studies raise a question of which factors explain the non-uniform distribution of PIMs.

Various studies have reported patient-related factors associated with PIM use, such as weak physical performance, depression,[8] cognitive impairment,[15,16] emergency department visits,[17] hospitalization,[18] living alone,[19] and polypharmacy and multimorbidity.[8,20–22] However, studies determining the association between factors related to social and health care, such as waiting times, and PIM use are scarce. However, previous studies have identified a lack of geriatric knowledge, busy working environment, and polypharmacy as perceived barriers to follow published PIM criteria.[23,24] These findings underline the importance of studying the association of differences related to social and health care service provision with PIM prevalence.

The hypothesis of this study was that significant regional variation in PIM use exists. The aim was to recognize which differences in population characteristics and factors related to social and health care are associated with higher PIM use among Finnish hospital districts. Data from nationwide registers was applied to assess the regional variation in PIM use and possible underlying factors.

2. Methods

2.1. Context

The Finnish health care system is based on public services divided into primary and specialized health care.[25] Public primary health care services are provided at municipal health centers, and municipalities form hospital districts (n = 21) that are responsible for specialized medical care. The Social Insurance Institution (SII) of Finland provides National Health Insurance (i.e., tax-supported public social security coverage) for Finnish residents, including coverage for sickness-related expenses (e.g., reimbursements for medicine expenses).[26] The reimbursability of a medicine (reimbursement rate 40%–100% of the price) is confirmed for prescription medicines and treating of an illness or clinical condition stated in the summary of product characteristics.[27] Unless the reimbursability is confirmed, customers must pay the full price. Approximately 90% of the Finnish prescription medicines available in the pharmacies are reimbursable.[28]

In Finland, the mean population aged ≥75 years increased from 500,821 to 518,276 between the years 2017–2019, and the proportion of this age group of the total population varied between 6.8% and 14.3% across hospital districts (n = 21).[29]

2.2. Definition of the prevalence of PIM use

The data to calculate the prevalence of PIM use were obtained from the Prescription Centre, which is a national database of human prescription data maintained by the SII.[30] The database includes all prescriptions (including information on the physician's specialty) and their purchasing events made by pharmacies in electronic form. The data are nationally comprehensive since 2017. The study data considered all dispensed prescription PIM purchases by Finnish persons aged ≥75 years in 2017–2019. PIMs were defined according to the Finnish Meds75+ database.[7] The database includes prescription medicines used mainly in primary health care that have at least 500 users aged ≥75 years annually. The database places drug substances in one of the four categories: suitable for older persons (category A), current evidence or experience on the use in older persons is vague, or efficacy of the medicine is insufficient (B), suitable for older persons with specific cautions (C), and avoid use in older persons (D). The category D medicines are considered PIMs. The database is continuously updated, and, for the purpose of this study, the list of PIMs was formed on July 2, 2020, and it consists of 91 active substances (see Additional file 1).

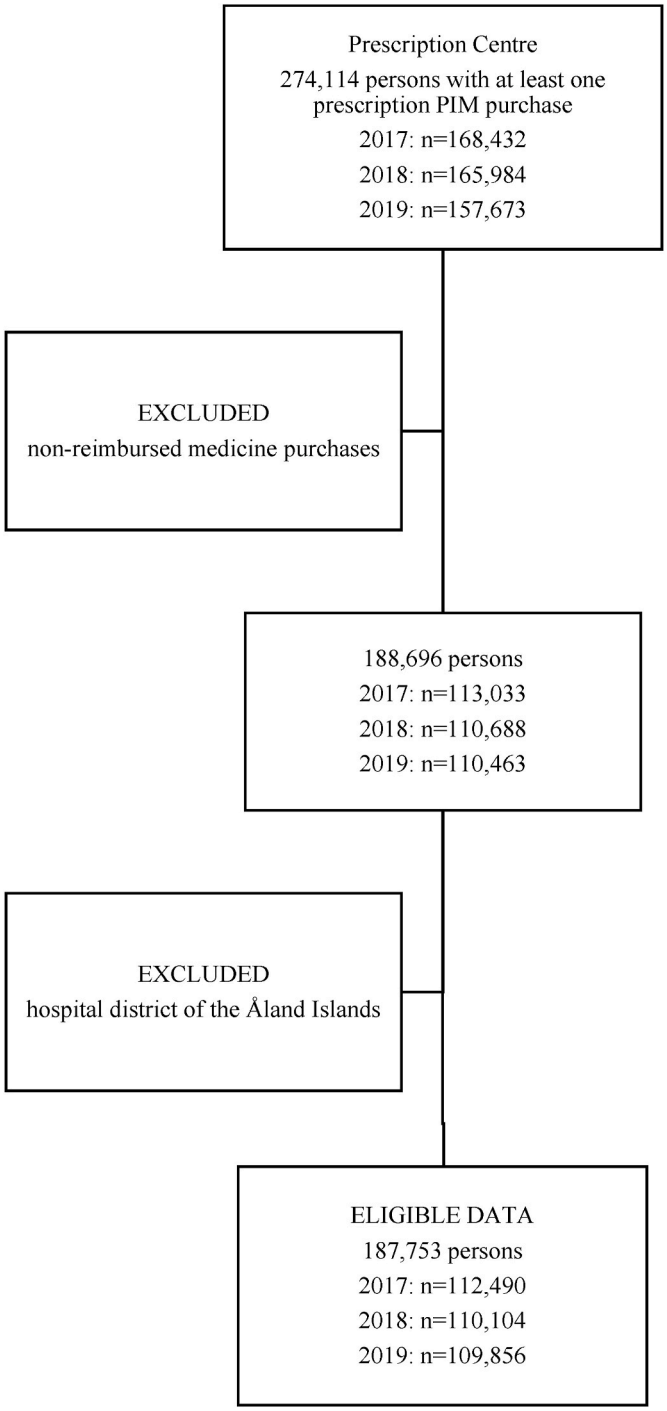

Fig. 1. Flowchart of the data to calculate the prevalence of PIM use.

Altogether, there were 274,114 persons aged ≥75 who had at least one prescription PIM purchase during the observation period (Fig. 1). Since the information of the hospital district was only available for reimbursed PIM purchases, the non-reimbursed purchases were excluded from the data, leaving 188,696 older persons. In addition, certain regional explanatory statistics for the hospital district of the self-governing province of the Åland Islands (mean population aged ≥75 years in 2017–2019: N = 2652–2,874[29]) were missing or invalid and, therefore, excluded. Finally, to calculate the prevalence of PIM use and to assess regional variation in 20 hospital districts, the data consisted of 187,753 older persons. The prevalence of PIM use was calculated based on the census data obtained from Statistics Finland (mean population aged ≥75 years in 2017 (N = 500,821), 2018 (N = 506,885) and 2019 (N = 518,276)).[29]

2.3. Regional variables

Population characteristics and factors related to social and health care (later referred to as "regional variables") were drawn from public data sources of the Finnish Institute for Health and Welfare (THL), the Finnish Medical Association (FMA), Finnish Medicines Agency Fimea,[31] and Official Statistics of Finland.[29] THL is a state-owned expert and development institute that gathers and produces information based on research and register data as publicly open data.[32] The data on social and health care and population characteristics are provided in the Sotkanet Indicator Bank.[33] The Sotkanet provides both nationwide data and descriptions on interpretations and data sources, and it is utilized by many entities, including authorities, social- and health-care organizations, and citizens. For example, adequate staffing levels in older people services have been monitored by THL since 2014. Personnel vacancy data are collected from municipalities (response rate 71–95% in year 2018) and reported as share of home care personnel of the total number of personnel in units of home care and 24-h care for older people. The FMA is a professional organization that annually publishes register- and survey-based data on the number of general practitioners (GPs) and physicians' employment, such as shortage of GPs (i.e., share of unfilled positions of all GP vacancies, the positions have been open for application but have not been occupied).[34]

Potential regional variables were searched from Sotkanet, FMA, and Fimea data. Identified variables were grouped into the following five categories: 1) sociodemographic factors, 2) morbidity and medication use, 3) functional ability and quality of life (such as physical, mental, cognitive, and social), 4) social and health care service provision, and 5) economic factors (see Additional file 2). Earlier studies[8,15–21,23,24] were utilized to select appropriate explanatory variables from the identified potential options. The variables were reviewed for missing data and to avoid duplication and excess multicollinearity. Descriptive analyses were conducted to provide a summary of the 15 selected explanatory variables (Table 1).

2.4. Statistical analyses

The regional prevalence was calculated by dividing the number of older persons with at least one PIM purchase by annual mean population aged ≥75 years. PIM prevalence was presented as annual percentages per hospital district. In addition, the change in the number of PIM users from 2017 to 2019 was presented as percentages per hospital district.

A linear mixed-effect model (LMM) with PIM prevalence as the dependent outcome measure was conducted to determine the association of regional variables with PIM prevalence (see Additional file 3). LMM was used because it accounts for the expectation that the repeated measures from the same hospital district are more similar to each other than to those from other hospital districts. Therefore, the assumption of independence of observations and equal variance across hospital districts may be violated. In addition, the correlation between observations within three years is not constant, as observations closer to each other in

Table 1
Characteristics of explanatory variables of Finnish hospital districts (n = 20) in 2017–2019.

Category	Explanatory variable	Median	Min	Max	Level[a]
Sociodemographic factors	Proportion of persons aged ≥85 years, % of total population aged ≥75[29]	29.4	26.4	31.9	Year
	Living alone, population aged ≥75 years, % of total home-dwelling population of same age[33]	47.2	40.8	50.2	Year
Morbidity and medication use	Reimbursement for antidepressants in those aged ≥65 years, % of total population of same age[33]	11.8	8.8	14.4	Year
	Reimbursement for medicines for the treatment of Alzheimer's disease in those aged ≥65 years, % of total population of same age[33]	3.3	1.1	6.0	Year
	Ten or more reimbursed medications purchased in those aged ≥75 years, % of total population of same age[b], [31]	13.1	9.0	17.2	Year
Functional ability and quality of life	Regular home care clients aged≥75 years, % of total population of same age[33]	17.6	9.1	23.8	Year
Social and health care service provision	Proportion of persons aged ≥75 hospitalized during the year per 1000 persons of same age[33]	342.2	238.5	424.8	Year
	Emergency department visits in specialized health care of those aged ≥75 years per 1000 persons of the same age[33]	457.8	243.4	1011.4	Year
	Emergency visits in primary health care of those aged ≥75 years (incl. joint emergency department) per 1000 per persons of the same age[33]	679.0	11.2	1692.5	Year
	PIM prescribed by a geriatrician, % of total number of PIM users[30]	2.6	0.3	7.5	Year
	Assessed using the RAI[c], persons aged ≥75, as % of total population of same age[33]	11.0	0.1	22.1	Year
	Waiting time for elective outpatient visit (physician) in primary health care exceeds 7 days from assessment of need for treatment, % of all appointments[d], [33]	49.3	11.6	71.8	Year
	Waiting time for elective outpatient visit (physician) in primary health care exceeds 3 months from assessment of need for treatment, % of all appointments[d], [33]	2.6	0.0	17.3	Year
	Physician shortage in municipal health centers, %[e], [34]	8.5	1.4	31.4	Hospital district
	Share of home care personnel of the total personnel in services for older people, %[f], [33]	37.0	28.0	50.0	Hospital district

PIM potentially inappropriate medication; RAI Resident Assessment Instrument.
[a] Year = 1-level, data available for three years 2017–2019; hospital district = 2-level, contextual variables, data available for one year only.
[b] During August to November.
[c] a comprehensive, person-centered, standardized and internationally widely used tool for assessing health status, needs and planning care services for older people in home care and long-term care.
[d] In October.
[e] Data available only for 2020, proportion of unfilled positions of all GP vacancies.
[f] Data available only for 2018, proportion of home care personnel of the total number of personnel in home care and 24-h care.

time are more similar than observations more distant in time.

Given the dependence between observations (i.e., repeated measures within a hospital district), the data were considered 2-level data (Fig. 2).[35] The explanatory observations at set time points (i.e., year) and the dependent variable (i.e., annual PIM prevalence) were on the first level, whereas the individual hospital districts under study were on the second level. The covariance structure for the random errors associated with observed values of the dependent variable was estimated as first-order autoregressive structure with heterogeneous variances. The continuous regional explanatory variables were considered as fixed effects and the model was fitted by maximum likelihood estimation.

In the LMM, *p*-values are provided for each estimate of fixed effects and 95% confidence interval (CI) was provided for each fixed coefficient. Akaike information criterion (AIC) was used for assessing model fit, and *p*-values <0.05 were considered to indicate statistical significance. The observations within each hospital district are correlated and, therefore, random intercepts and random slopes were modelled for each hospital district. These accounted for the clustering of the data and provided estimates of hospital-district-level variation. The statistical analyses were performed using the IBM© SPSS© Statistics software, version 27.

The appropriateness of the LMM modelling approach was evaluated by testing a "Null model" (no explanatory variables) including only the dependent variable (i.e., PIM prevalence) and the grouping variable (i.e., hospital district). The intraclass correlation coefficient (ICC) of the Null model describes to what extent the overall variance in PIM prevalence is explained by differences between hospital districts during the three-year observation period. The Null model revealed significant ($p < 0.05$) variation between hospital districts, supporting the multilevel modelling. Since the use of the multilevel model was appropriate, the model included the explanatory variables and time as fixed effects. In this study design, explanatory variables were analyzed as within-subject covariates (1-level). However, GP shortage and share of home care personnel were available only for 2020 and 2018, respectively, and were considered as contextual variables (2-level). The coefficient of determination of the final model describes the proportion of the variation in PIM prevalence that was explained by the regional variables in the model.

3. Results

Altogether, 187,753 older persons (mean age 81.6 [SD 5.0] years, 65% female) had purchased at least one PIM during the observation period, resulting in annual prevalence of 21.3%–22.6% across the country. The annual prevalence of PIM use varied from 16.4% to 24.8% across hospital districts (Table 2). The highest prevalence was in the southern regions, whereas the lowest was on the west coast (Fig. 3). The PIM use was higher in the southern regions, such as Helsinki and Uusimaa, where the share of population aged ≥75 years was the lowest. The annual PIM prevalence constantly decreased during the three-year period across the regions. Moreover, the number of PIM users decreased in all regions except for Helsinki and Uusimaa (Table 2).

Table 2
The annual prevalence of PIM use across Finnish hospital districts in 2017–2019.

Hospital districts	Year			Percentage change in the number of PIM users from 2017 to 2019
	2017%	2018%	2019%	
Overall prevalence in Finland	22.6	21.9	21.3	−2.3
Kymenlaakso	24.8	24.1	24.1	−1.2
Helsinki and Uusimaa	24.2	23.6	22.9	1.3
Central Ostrobothnia	23.9	22.8	22.8	−1.9
North Savo	23.7	22.7	22.3	−5.2
Kainuu	23.7	23.0	22.7	−4.0
Päijät-Häme	23.1	22.3	21.7	−1.7
Southwest Finland	23.0	22.6	22.1	−0.7
Central Finland	22.8	21.8	21.3	−4.1
North Karelia	22.5	21.5	21.5	−3.5
South Karelia	22.4	22.7	21.6	−2.4
South Savo	22.4	20.9	21.1	−4.6
Pirkanmaa	22.3	21.5	20.6	−4.1
Kanta-Häme	22.3	21.4	21.0	−3.0
Satakunta	21.1	20.2	20.0	−3.8
Lapland	20.7	20.2	19.0	−7.3
South Ostrobothnia	20.6	20.1	20.0	−2.3
Northern Ostrobothnia	20.3	19.5	18.9	−3.7
East Savo	20.3	18.7	18.1	−10.0
Länsi-Pohja	18.7	18.4	16.4	−11.7
Vaasa	18.3	17.2	16.6	−6.8

PIM potentially inappropriate medication.

3.1. Factors associated with higher PIM use

The results of the LMM model showed that a higher share of the population living alone, with excessive polypharmacy (i.e., concomitant use of ten or more medicines), and assessed using the Resident Assessment Instrument (RAI), higher physician shortage in health centers and lower share of home care personnel of the total personnel in services for older persons were associated with higher PIM prevalence (Table 3). However, factors such as waiting time and share of population with Alzheimer's disease or depression, were not associated with PIM use. The AIC for Null model (197.8) decreased (i.e., improved) as the explanatory variables were included in the final model (131.5). According to the ICC of the Null model, 86% of the total variance in PIM prevalence was explained by group-level factors related to hospital districts. Furthermore, the regional variables explained 75% of the hospital-district-level variation in PIM prevalence.

4. Discussion

In line with the study hypothesis, PIM prevalence varied markedly across the Finnish hospital districts in years 2017–2019. Every sixth or even as many as every fourth older person had at least one prescription

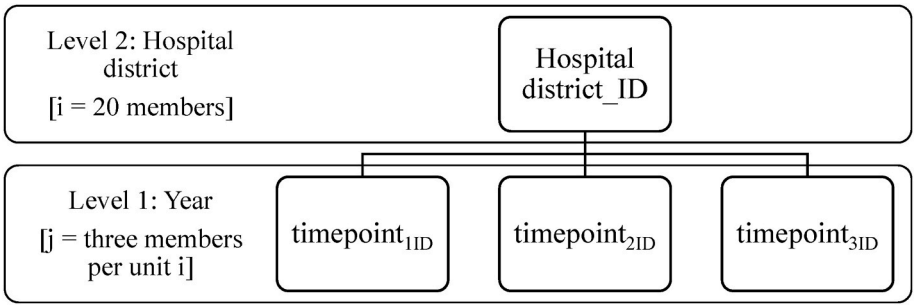

Fig. 2. Format of the mixed model diagram for 2-level hierarchical study of hospital districts and repeated measurements over time.

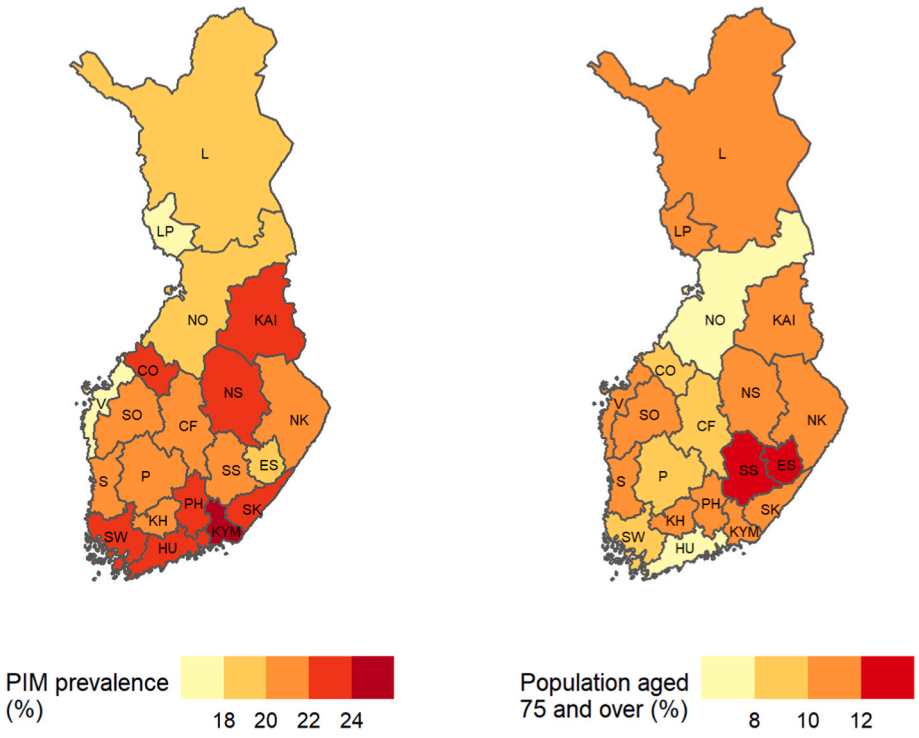

Fig. 3. Regional variation of the mean PIM prevalence and mean proportion of population aged ≥75 years across the hospital districts in years 2017–2019. Mean population aged ≥75 years in Finland in 2017: N = 500,820.5; 2018: N = 506,884.5; and 2019: N = 518,276.0).[29] CF Central Finland; CO Central Ostrobothnia; SO South Ostrobothnia; ES East Savo; HU Helsinki and Uusimaa; KAI Kainuu; KH Kanta-Häme; KYM Kymenlaakso; L Lapland; LP Länsi-Pohja; NK North Karelia; NO Northern Ostrobothnia; NS North Savo; P Pirkanmaa; PH Päijät-Häme; S Satakunta; SK South Karelia; SS South Savo; SW Southwest Finland; V Vaasa.

PIM purchase annually. Earlier studies in the United States have found higher variation in PIM prevalence, from 5% to 55% among persons aged ≥65 years with a similar regional pattern.[9–12] This study also reports lower variation compared to the study conducted in the municipalities of Northern France, which found higher variation from 24% to 54% among older people aged ≥75 years.[13] Compared to an earlier Finnish population-based register study reporting a PIM prevalence from 27% to 39% across Finnish hospital districts, the present study found a lower prevalence.[14] Although PIM use has decreased from the earlier study, the prevalence between hospital districts in the present study varies approximately ten percentage points, indicating that regional variation is still large.

The present study also found that regional differences in social and health care service provision are associated with variation in PIM use, whereas, contrary to expectations and earlier studies,[8,15,16] share of the population with morbidities (e.g., reimbursements for Alzheimer's disease and antidepressants) or factors related to weakened functional performance (e.g., share of home care clients) were not. These findings are similar to an earlier Finnish study, which found no association between morbidity index and PIM use.[14] Furthermore, PIM use was not pronounced in the regions with the highest share of older population.

This study concluded that a shortage of GPs in municipal health centers, a higher share of older persons with excessive polypharmacy, and a lower share of home care personnel are associated with higher PIM prevalence. These associations may be a result of insufficient resourcing and poor continuity of social and health care. In most areas the attempt is that the patient visits the same GP but because of inadequate recourses and increasing workload in primary health care, personal doctor schemes can rarely be applied.[36] Physicians may repeat the prescriptions without face-to-face contact, which is problematic especially in the case of medicines, such as hypnotics, that are intended for short-term use only.[37] GPs also perceive renewing electronic prescriptions as more of a technical task[38] and feel they do not have time to convince the patient of a more appropriate medication while having a busy schedule.[39] This fallen patient-doctor relationship is especially problematic in the case of frail older people if changes in their chronic diseases and treatment needs are not recognized. In addition, the share of posts filled by substitutes in Finnish primary health care has increased, meaning that the increasing number of GPs does not bring continuity of care.[40] However, continuity of care as such could not be analyzed in this study. On the other hand, the present study found that factors related to service accessibility, such as visits to the emergency department, need for hospital care, or waiting time in primary health care, were not associated with PIM prevalence. This finding supports previous conclusions, according to which the mere monitoring of waiting time for the initiation of care does not describe the quality of care or development of continuity.[41]

The association between excessive polypharmacy and higher PIM prevalence existed, as expected, as older persons often have an increasing number of comorbid conditions whose treatment may require controlled use of PIMs. With such patients, continuity of care is especially important, and monitoring of chronic illnesses should take place in primary health care. However, due to the shortage of GPs, multiple physicians may be involved in a patient's pharmacotherapy. This is problematic since an earlier review has identified physicians' unwillingness to discontinue medications started by a colleague as a barrier to effective and appropriate prescribing in older persons.[42]

The present study also found that the higher the share of persons aged ≥75 years living alone, the higher the PIM prevalence. The association is not unexpected since older people living alone can be considered more vulnerable, as they are at risk for negative physical and mental health outcomes and loneliness.[43,44] These outcomes may be further treated with PIMs. Two previous studies have further demonstrated that social networks and support are related to better self-management.[45,46] The present finding is also supported by an earlier study based on the Beers and French criteria concluding that the risk for PIM consumption was higher with older persons living alone.[19]

The association between less personnel assigned to home care and higher PIM use may indicate under-resourcing. Home care nurses have identified challenges in managing polypharmacy, and a lack of communication with GPs leads to a lack of proper follow-up and inappropriate medication use.[47] In addition, the low share of personnel may lead to busy or missed home care visits.[48] According to an annual national report, 25% of Finnish home care units experience personnel

Table 3
Linear mixed-effect model for PIM use and association of factors related to social and health care and population characteristics in hospital districts in 2017–2019.

	Estimate	95% Confidence Interval		p-value
		Lower Bound	Upper Bound	
Intercept	6.438	−9.686	22.563	0.426
Year 2017	Reference			
Year 2018	−0.972	−1.626	−0.318	0.004
Year 2019	−1.761	−2.700	−0.822	<0.001
1-level variables				
Proportion of persons aged ≥85, % of total population aged 75 and older	−0.267	−0.560	0.027	0.073
Living alone, population aged ≥75, % of total home-dwelling population of the same age	0.498	0.264	0.732	<0.001
Reimbursement for antidepressants in those aged ≥65, % of total population of the same age	0.180	−0.195	0.554	0.331
Reimbursement for medicines for the treatment of Alzheimer's disease in those aged ≥65, % of total population of the same age	−0.017	−0.437	0.402	0.933
Ten or more medications purchased in those aged ≥75, % of total population of the same age[a]	0.270	0.038	0.502	0.024
Proportion of persons aged ≥75 hospitalized during the year per 1000 persons of the same age	−0.001	−0.010	0.008	0.809
Emergency department visits in specialized health care in those aged ≥75 per 1000 persons of the same age	−0.001	−0.004	0.001	0.269
Emergency visits in primary health care in those aged ≥75 (incl. joint emergency department) per 1000 persons of the same age	<0.001	−0.001	0.000	0.088
PIM prescribed by a geriatrician, % of total number of PIM users	0.088	−0.049	0.224	0.203
Regular home care clients aged ≥75, % of total population of the same age	−0.024	−0.137	0.090	0.674
Assessed using the RAI, persons aged ≥75, as % of total population of the same age	0.072	0.019	0.124	0.009
Waiting time for elective outpatient medical visit (physician) in primary health care exceeds 7 days from assessment of need for treatment, % of all appointments[b]	<0.001	−0.014	0.013	0.986
Waiting time for elective outpatient medical visit (physician) in primary health care exceeds 3 months from assessment of need for treatment, % of all appointments[b]	−0.005	−0.042	0.032	0.786
2-level variables				
Physician shortages in municipal health centers, %[c]	0.105	0.034	0.175	0.007
Share of home care personnel of the total personnel in services for older people, %[d]	−0.143	−0.233	−0.052	0.005

PIM potentially inappropriate medication.
RAI Resident Assessment Instrument.
[a] During August to November.
[b] In October.
[c] Proportion of unfilled positions of all GP vacancies.
[d] Proportion of home care personnel of the total number of personnel in home care and 24-h care.

shortage.[49] Working overtime in home care units is common, causing strain for the personnel. This should be taken into consideration when planning services for older people, as studies from nursing homes show that staff distress is associated with the prescribing of antipsychotics and anxiolytics.[50,51]

Interestingly, higher coverage of RAI was associated with higher PIM prevalence. This finding is contrary to assumptions, since RAI is a person-centered standardized tool to provide comprehensive information on the health status and needs of the older person and is intended for making a treatment and service plan,[52,53] and high utilization of RAI demonstrates that services are targeted more efficiently and equal access to health services is ensured.[54] The reasons underlying this finding remain unclear, but it is possible that RAI assessments point out health concerns and needs of medical therapy that might otherwise be left unnoticed and are further treated with PIMs.

4.1. Strengths and limitations

The present study has several strengths. First, this study is based on nationwide prescription register data covering most medication use in Finland. In addition, the Sotkanet Indicator Bank, utilized also by authorities and policy makers, provided comprehensive data on social and health services and population characteristics. These data are based on mandatory national reporting, ensuring high coverage.[55] Second, the present study includes several factors on the level of social and health care, whose association with PIM use have not been studied before. While the present study found an association between social and health care service provision and higher PIM use, the results also pointed out important factors not associated with PIM use, such as waiting time in primary health care.

There are also limitations that should be noted. First, the data were restricted to reimbursed prescription purchases delivered from pharmacies, meaning that non-reimbursed purchases as well as institutional, hospital, and over-the-counter (OTC) medicines were not included. Therefore, the prevalence of PIM use may be underestimated, but the deficit is expected to be small since 90% of the prescription medicines available from Finnish pharmacies are reimbursable and only approximately 1% of persons aged ≥75 years live in institutions. In addition, only nine out of 91 substances defined as PIMs in Meds75+ database are available also without prescription, and as OTCs are intended for short term use only. Moreover, these limitations are unlikely to negate the observed associations with PIM use. Second, the regional factors explained only partially the variation in PIM prevalence across the hospital districts. Although the coefficient of determination was high and the CIs of fixed coefficients were narrow, indicating there was no considerable variation between the districts, it must be noted that the effect of individual variables is weak. Thus, there are also other factors explaining PIM use. It would have been interesting to study, for example, age-specific economic factors, such as expenditures in specialized health care, but necessary data were not available. Also, the search of regional explanatory variables identified many potential variables, such as morbidity index, that had to be excluded to avoid overlap and excess correlation of factors in the model. Finally, regional variation in PIM use between municipalities within hospital districts has been shown to be large.[14] Therefore, municipality-level data might have provided a more accurate picture of the association between factors related to social and health care and PIM prevalence.

5. Conclusions

PIM prevalence varied across the Finnish hospital districts. The findings suggest that higher PIM prevalence may be related to the challenges in the continuity of care rather than to differences in health care accessibility, share of the older population, or share of the population with morbidities such as Alzheimer's disease or depression. The previously identified challenges (e.g., insufficient resources) and risks

(e.g., excessive polypharmacy) in social and primary health care seem to challenge the implementation of rational pharmacotherapy for older persons. This should motivate policy makers and future studies to examine whether targeting these factors have an impact on reducing PIM use and improving rational pharmacotherapy in older persons.

Funding

This work was supported by the Competitive State Research Financing of the Expert Responsibility area of Tampere University Hospital (project 9AB016).

Statements and declarations

Conflicts of interest Authors Paulamäki, Jyrkkä, Hyttinen and Huhtala declare that they have no conflict of interest. **Author Jämsen** has received lecture fees (from lectures partly related to the present study) from medical companies (Chiesi, Lundbeck, Novartis, Nutricia, Orion Pharma) and professional organizations (Finnish Medical Society Duodecim, Pihlajalinna Ltd, Finnish Medical Association, Fioca Ltd, the Young Doctors Association). **Authors Paulamäki, Jyrkkä, and Jämsen** are also members of the advisory board of the Meds75+ database.

Ethics approval

According to the Finnish Medical Research Act 488/1999, retrospective register-based studies in which the subjects are not in contact/are not subject to intervention are not considered medical research and, therefore, ethical committee approval is not required. According to Finnish legislation (including European Union General Data Protection Regulation 679/2016; Data Protection Act 1050/2018; Act on Electronic Prescriptions 61/2007; Act on the Secondary Use of Health and Social Data 552/2019) retrospectively collected health register data can be used for research with permission from the register owner. This administrative permission and institutional approval were obtained from the register owner Social Insurance Institution of Finland (Kela) (Dnro 96/522/2020). Data obtained from the Prescription Centre were pseudonymized (i.e., authors cannot convert the data into identifiable form) before submission to the authors. This study was performed in accordance with relevant guidelines and regulations.

Availability of data and material

The data that support the findings of this study are available from the Social Insurance Institution of Finland, the Finnish Institute for Health and Welfare, and Finnish Medical Association. Restrictions apply to the availability of these data, which were used under permission for this study. Prescription data are available from the Social Insurance Institution of Finland with the permission of the Finnish Social and Health Data Permit Authority Findata. Regional health care and population characteristics data are available in Sotkanet Indicator Bank at https://sotkanet.fi/sotkanet/en/index, and the General Practitioner shortage report is available in The Finnish Medical Association at https://www.laakariliitto.fi/en.

Author contributions

Jasmin Paulamäki: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review and editing, Visualization **Johanna Jyrkkä**: Conceptualization, Investigation, Resources, Writing – review and editing, Supervision **Virva Hyttinen**: Writing – review and editing, Supervision **Heini Huhtala**: Methodology, Formal analysis, Writing – original draft, Writing – review and editing, Visualization, Supervision **Esa Jämsen**: Conceptualization, Writing – review and editing, Supervision, Funding acquisition.

Multiple publication

Abstracts concerning this research were published as part of three academic meetings: Multidisciplinary Primary Health Care Research Days September 8–9, 2022 (word count 253) available (in Finnish and only during the congress): https://www.helsinki.fi/fi/konferenssit/monitieteiset-perusterveydenhuollon-tutkimuksen-paivat-2022/ohjelma Accessed 12 September 2022, Nordic PharmacoEpidemiological Network meeting November 16–18, 2022 (word count 298) (not available online), and Gerontology congress February 8–10, 2023 (word count 238) (in Finnish): https://events.tuni.fi/gerontologia2023/posterisessio-2/ Accessed 27 January 2023.

Acknowledgements

The authors wish to thank D.Sc. & M.Sc. (Econ.) Antti Hyvärinen from Finnish Medicines Agency for his help with the figures and associate professor Tuomas H. Koskela from Tampere University for his expertise on reviewing the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2023.06.005.

References

1. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol*. 2004;57:6–14. https://doi.org/10.1046/j.1365-2125.2003.02007.x.
2. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med*. 1991;151:1825–1832. https://doi.org/10.1001/archinte.1991.00400090107019.
3. Wallace E, McDowell R, Bennett K, Fahey T, Smith SM. Impact of potentially inappropriate prescribing on adverse drug events, health related quality of life and emergency hospital attendance in older people attending general practice: a prospective cohort study. *J Gerontol A Biol Sci Med Sci*. 2017;72:271–277. https://doi.org/10.1093/gerona/glw140.
4. Early NK, Fairman KA, Hagarty JM, Sclar DA. Joint effects of advancing age and number of potentially inappropriate medication classes on risk of falls in Medicare enrollees. *BMC Geriatr*. 2019;19:194. https://doi.org/10.1186/s12877-019-1202-3.
5. Kaufmann CP, Tremp R, Hersberger KE, Lampert ML. Inappropriate prescribing: a systematic overview of published assessment tools. *Eur J Clin Pharmacol*. 2014;70:1–11. https://doi.org/10.1007/s00228-013-1575-8.
6. Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. *Eur J Clin Pharmacol*. 2015;71:861–875. https://doi.org/10.1007/s00228-015-1860-9.
7. Finnish Medicines Agency. *Meds75+*; 2021. https://www.fimea.fi/web/en/databases_and_registeries/medicines_information/database_of_medication_for_older_persons. Accessed September 14, 2021.
8. Tommelein E, Mehuys E, Petrovic M, Somers A, Colin P, Boussery K. Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. *Eur J Clin Pharmacol*. 2015;71:1415–1427. https://doi.org/10.1007/s00228-015-1954-4.
9. Rothberg MB, Pekow PS, Liu F, et al. Potentially inappropriate medication use in hospitalized elders. *J Hosp Med*. 2008;3:91–102. https://doi.org/10.1002/jhm.290.
10. Finlayson E, Maselli J, Steinman MA, Rothberg MB, Lindenauer PK, Auerbach AD. Inappropriate medication use in older adults undergoing surgery: a national study. *J Am Geriatr Soc*. 2011;59:2139–2144. https://doi.org/10.1111/j.1532-5415.2011.03567.x.
11. Lund BC, Charlton ME, Steinman MA, Kaboli PJ. Regional differences in prescribing quality among elder veterans and the impact of rural residence. *J Rural Health*. 2013;29:172–179. https://doi.org/10.1111/j.1748-0361.2012.00428.x.
12. Lund BC, Schroeder MC, Middendorff G, Brooks JM. Effect of hospitalization on inappropriate prescribing in elderly Medicare beneficiaries. *J Am Geriatr Soc*. 2015;63:699–707. https://doi.org/10.1111/jgs.13318.
13. Beuscart JB, Genin M, Dupont C, et al. Potentially inappropriate medication prescribing is associated with socioeconomic factors: a spatial analysis in the French Nord-Pas-de-Calais Region. *Age Ageing*. 2017;46:607–613. https://doi.org/10.1093/ageing/afw245.
14. Saastamoinen L, Verho J. Regional variation in potentially inappropriate medicine use in older adults. - a national register-based cross-sectional study on economic, health system-related and patient-related characteristics. *Res Soc Adm Pharm*. 2021;17:1223–1227. https://doi.org/10.1016/j.sapharm.2020.08.018.
15. Montastruc F, Gardette V, Cantet C, et al. Potentially inappropriate medication use among patients with Alzheimer disease in the REAL.FR cohort: be aware of atropinic

and benzodiazepine drugs. *Eur J Clin Pharmacol*. 2013;69:1589–1597. https://doi.org/10.1007/s00228-013-1506-8.
16. Johnell K. Inappropriate drug use in people with cognitive impairment and dementia: a systematic review. *Curr Clin Pharmacol*. 2015;10:178–184. https://doi.org/10.2174/1574884710666150609154741.
17. Jirón M, Pate V, Hanson LC, Lund JL, Jonsson Funk M, Stürmer T. Trends in prevalence and determinants of potentially inappropriate prescribing in the United States: 2007 to 2012. *J Am Geriatr Soc*. 2016;64:788–797. https://doi.org/10.1111/jgs.14077.
18. Di Giorgio C, Provenzani A, Polidori P. Potentially inappropriate drug prescribing in elderly hospitalized patients: an analysis and comparison of explicit criteria. *Int J Clin Pharm*. 2016;38:462–468. https://doi.org/10.1007/s11096-016-0284-7.
19. Bongue B, Naudin FN, Laroche ML, et al. Trends of the potentially inappropriate medication consumption over 10 years in older adults in the East of France. *Pharmacoepidemiol Drug Saf*. 2009;18:112–133. https://doi.org/10.1002/pds.1762.
20. Bradley MC, Motterlini N, Padmanabhan S, et al. Potentially inappropriate prescribing among older people in the United Kingdom. *BMC Geriatr*. 2014;14:72. https://doi.org/10.1186/1471-2318-14-72.
21. Price SD, Holman CD, Sanfilippo FM, Emery JD. Are older Western Australians exposed to potentially inappropriate medications according to the Beers Criteria? A 13-year prevalence study. *Australas J Ageing*. 2014;33:E39–E48. https://doi.org/10.1111/ajag.12136.
22. Hsu K-C, Lu H-L, Kuan C-M, et al. Potentially inappropriate medication among older patients who are frequent users of outpatient services. *Int J Environ Res Publ Health*. 2021;18:985. https://doi.org/10.3390/ijerph18030985.
23. Ramaswamy R, Maio V, Diamond JJ, et al. Potentially inappropriate prescribing in elderly: assessing doctor knowledge, confidence and barriers. *J Eval Clin Pract*. 2011;17:1153–1159. https://doi.org/10.1111/j.1365-2753.2010.01494.x.
24. Cullinan S, Fleming A, O'Mahony D, et al. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: a qualitative study. *Br J Clin Pharmacol*. 2014;79:860–869. https://doi.org/10.1111/bcp.12555.
25. Ministry of Social Affairs and Health. Social welfare and health care system in Finland, responsibilities. https://www.stm.fi/en/social-and-health-services/responsible-agencies; 2022. Accessed March 21, 2022.
26. Social Insurance Institution of Finland. With you throughout life – supporting you through times of change. https://www.kela.fi/web/en/operations-kela-in-brief1; 2022. Accessed March 21, 2022.
27. Social Insurance Institution of Finland. Inclusion of medicines in the reimbursement scheme. https://www.kela.fi/web/en/inclusion-of-medicines; 2020. Accessed August 18, 2022.
28. Pharma Industry Finland. Reimbursability of medicines. https://www.pif.fi/medicines/reimbursability-of-medicines.html; 2022. Accessed September 13, 2022.
29. Official Statistics of Finland. Population structure [e-publication]. ISSN=1797-5395. Helsinki: Statistics Finland; 2021. https://www.stat.fi/til/vaerak/index_en.html. Accessed October 13, 2021.
30. Kanta. Prescription. www.kanta.fi/en/web/guest/professionals/prescription; 2022. Accessed March 21, 2022.
31. Jauhonen HM, Jyrkkä J. Moniläkitys ja lääkekustannukset kasvussa iäkkäillä [Polypharmacy and medical expenses are increasing among older persons]. https://sic.fimea.fi/arkisto/2020/3_2020/palstat-/monilaakitys-ja-laakekustannukset-kasvussa-iakkailla; 2020. Accessed November 11, 2021.
32. Finnish Institute for Health and Welfare. Open data. https://thl.fi/en/web/thlfi-en/statistics-and-data/data-and-services/open-data; 2022. Accessed February 5, 2022.
33. Finnish Institute for Health and Welfare. *Sotkanet.fi. Statistical Information on Welfare and Health in Finland*; 2021. https://sotkanet.fi/sotkanet/en/index. Accessed November 11, 2021.
34. Finnish Medical Association. Lääkärityövoima [Physicians' employment] https://www.laakariliitto.fi/laakariliitto/tutkimus/laakarityovoima/; 2022. Accessed February 5, 2022.
35. Monsalves MJ, Bangdiwala AS, Thabane A, Bangdiwala SI. LEVEL (Logical Explanations & Visualizations of Estimates in Linear mixed models): recommendations for reporting multilevel data and analyses. *BMC Med Res Methodol*. 2020;20:3. https://doi.org/10.1186/s12874-019-0876-8.
36. Eskola P, Tuompo W, Riekki M, Timonen M, Auvinen J. Reports and memos by the ministry of social affairs and health 2022:17: Omalääkäri 2.0-selvityksen loppuraportti [final report of the personal doctors 2.0 survey]. https://julkaisut.valtioneuvosto.fi/handle/10024/164291. Accessed May 24, 2023.
37. Sundseth AC, Gjelstad S, Straand J, Rosvold EO. General practitioners' prescriptions of benzodiazepines, Z-hypnotics and opioid analgesics for elderly patients during direct and indirect contacts. A cross-sectional, observational study. *Scand J Prim Health Care*. 2018;36:115–122. https://doi.org/10.1080/02813432.2018.1459164.
38. Oravainen T, Airaksinen M, Hannula K, Kvarnström K. How physicians renew electronic prescriptions in primary care: therapeutic decision or technical task? *Int J Environ Res Publ Health*. 2021;18, 10937. https://doi.org/10.3390/ijerph182010937.
39. Voigt K, Gottschall M, Köberlein-Neu J, Schübel J, Quint N, Bergmann A. Why do family doctors prescribe potentially inappropriate medication to elderly patients? *BMC Fam Pract*. 2016;17:93. https://doi.org/10.1186/s12875-016-0482-3.
40. Finnish Medical Association. Lääkäriliiton linjaus: Perusterveydenhuollon pelastaminen [Saving primary health care]. https://www.laakariliitto.fi/uutiset/linjauksia/perusterveydenhuollon-pelastaminen/; 2019. Accessed October 30, 2019.
41. Pelttari H, Kaila M. "Kiireettömään hoitoon pääsyn selvitys." Nykytila ja toimenpide-ehdotuksia [Investigation into access to non-urgent care: current situation and proposed measures. https://julkaisut.valtioneuvosto.fi/handle/10024/70295; 2014. Accessed November 15, 2022.
42. Lau S, Lun P, Ang W, Tan KT, Ding YY. Barriers to effective prescribing in older adults: applying the theoretical domains framework in the ambulatory setting – a scoping review. *BMC Geriatr*. 2020;20:459. https://doi.org/10.1186/s12877-020-01766-7.
43. Ng N, Santosa A, Weinehall L, Malmberg G. Living alone and mortality among older people in Västerbotten County in Sweden: a survey and register-based longitudinal study. *BMC Geriatr*. 2020;20:1–7. https://doi.org/10.1186/s12877-019-1330-9.
44. Vo MTH, Nakamura K, Seino K, Vo TV. Greater risk of negative health outcomes of older adults living alone in Vietnam: a community survey. *Int J Environ Res Publ Health*. 2021;18, 11115. https://doi.org/10.3390/ijerph182111115.
45. Gallant MP. The influence of social support on chronic illness self-management: a review and directions for research. *Health Educ Behav*. 2003;30:170–195. https://doi.org/10.1177/1090198102251030.
46. Maulik PK, Eaton WW, Bradshaw CP. The effect of social networks and social support on mental health services use, following a life event, among the Baltimore Epidemiologic Catchment Area cohort. *J Behav Health Serv Res*. 2011;38:29–50. https://doi.org/10.1007/s11414-009-9205-z.
47. Sun W, Tahsin F, Barakat-Haddad C, Turner JP, Haughian CR, Abbass-Dick J. Exploration of home care nurse's experiences in deprescribing of medications: a qualitative descriptive study. *BMJ Open*. 2019;9, e025606. https://doi.org/10.1136/bmjopen-2018-025606.
48. Härkänen M, Vehviläinen-Julkunen K, Murrells T, Paananen J, Franklin BD, Rafferty AM. The contribution of staffing to medication administration errors: a text mining analysis of incident report data. *J Nurs Scholarsh*. 2020;52:113–123. https://doi.org/10.1111/jnu.12531.
49. Kehusmaa S, Alastalo H. Vanhuspalvelujen työvoimapula kärjistyy kotihoidossa – neljännes yksiköistä tekee joka viikko töitä riittämättömällä henkilöstöllä ja ylityöt ovat yleisiä [Personnel shortages culminating in home care of older people – a quarter of the units are under-staffed every week and overtime is common]. https://www.julkari.fi/handle/10024/143733; 2022. Accessed November 15, 2022.
50. Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RT. Psychotropic drug prescription in nursing home patients with dementia: influence of environmental correlates and staff distress on physicians' prescription behavior. *Int Psychogeriatr*. 2011;23:1632–1639.
51. Walsh KA, Sinnott C, Fleming A, et al. Exploring antipsychotic prescribing behaviors for nursing home residents with dementia: a qualitative study. *J Am Med Dir Assoc*. 2018;19:948–958. https://doi.org/10.1016/j.jamda.2018.07.004.
52. Hawes C, Morris JN, Phillips C, Fries BE, Murphy K, Mor V. Development of the nursing home resident assessment instrument in the USA. *Age Ageing*. 1997;26:19–25. https://doi.org/10.1093/ageing/26.suppl_2.19.
53. Landi F, Tua E, Onder G, et al. Minimum data set for home care: a valid instrument to assess frail older people living in the community. *Med Care*. 2000;38:1184–1190. https://doi.org/10.1097/00005650-200012000-00005.
54. Finnish Institute for Health and Welfare. *Information on the RAI assessment system*; 2022. https://thl.fi/en/web/ageing/assessment-of-service-needs-with-the-rai-system/information-on-the-rai-assessment-system. Accessed April 14, 2022.
55. Laugesen K, Ludvigsson JF, Schmidt M, et al. Nordic health registry-based research: a review of health care systems and key registries. *Clin Epidemiol*. 2021;13:533–554. https://doi.org/10.2147/CLEP.S314959.