Gdański Uniwersytet Medyczny

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Rozprawa doktorska

Analiza farmakoterapii i potencjalnych interakcji lekowych w reprezentatywnej grupie Polaków powyżej 65. roku życia

Analysis of pharmacotherapy and potential drug-drug interactions
in a representative group of Poles over 65 years old

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WYKAZ PRAC WCHODZĄCYCH W SKŁAD ROZPRAWY DOKTORSKIEJ / LIST OF MANUSCRIPTS INCLUDED IN THE DOCTORAL DISSERTATION

Błeszyńska E, Wierucki Ł, Zdrojewski T, Renke M

Pharmacological interactions in the elderly.

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Prevalence and factors predisposing to potential drug-drug interactions in a Polish community-dwelling geriatric population: An observational, cross-sectional study.

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Polypharmacy among elderly patients in Poland: prevalence, predisposing factors, and management strategies.

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Geriatrics, aging, polypharmacy, drug interactions, multimorbidity, predisposing factors, medication errors/prevention and control, deprescribing, pharmaceutical services.

STRESZCZENIE W JĘZYKU POLSKIM

I. WYKAZ STOSOWANYCH SKRÓTÓW

ATC	(*ang. anatomical-therapeutic-chemical*), anatomiczno-terapeutyczno-chemiczna
CCI	(*ang. Charlson Comorbidity Index*), wskaźnik współchorobowości Charlson
CI	(*ang. confidence interval*), przedział ufności
DDIs	(ang. drug-drug interactions), interakcje lekowe
EPP	(ang. excessive polypharmacy), nadmierna polifarmakoterapia
ICD-10	(*ang. International Classification of Diseases, Tenth Revision*), Międzynarodowa Statystyczna Klasyfikacja Chorób, wersja dziesiąta
IQR	(*ang. interquartile range*), przedział międzykwartylowy
NOMED-AF	(*ang. NOninvasive Monitoring for Early Detection of Atrial Fibrillation*), nieinwazyjny monitoring we wczesnym wykrywaniu migotania przedsionków
NORGEP	(ang. The Norwegian General Practice), norweska praktyka ogólna
OTC	(*ang. over-the-counter*), bez recepty
PP	(*ang. polypharmacy*), polifarmakoterapia
SPCs	(*ang. single pill combinations*), preparaty łączone
WHO	(*ang. World Health Organization*), Światowa Organizacja Zdrowia

II. WPROWADZENIE

Znaczący wzrost średniej długości życia jest uważany za jedno z największych osiągnięć społecznych XX wieku. Jednak ta długowieczność wraz ze spadkiem współczynnika dzietności doprowadziły do postępującego starzenia się populacji. Przewiduje się, że liczba osób w wieku powyżej 65 lat wzrośnie z 524 milionów w 2010 roku (8% światowej populacji) do 1,5 miliarda w 2050 roku (16% światowej populacji).[1]

Leczenie farmakologiczne seniorów jest szczególnie skomplikowane ze względu na postępujące, związane ze starzeniem zmiany metabolizmu oraz wielochorobowość, która wymaga stosowania złożonych schematów lekowych.[2] Ponadto wśród osób starszych obserwuje się rosnące zainteresowanie preparatami dostępnymi bez recepty (ang. over-the-counter, OTC), które są powszechne na rynku farmaceutycznym.[3]

W dostępnym piśmiennictwie opisano wyczerpująco negatywne medyczne, ekonomiczne i społeczne konsekwencje polifarmakoterapii (ang. polypharmacy, PP), definiowanej jako przyjmowanie 5 lub więcej leków, oraz nadmiernej polifarmakoterapii (ang. excessive polypharmacy, EPP), która odnosi się do używania co najmniej 10 leków.[4] Jednym z możliwych do uniknięcia błędów medycznych są interakcje farmakologiczne (ang. drug-drug interaction, DDIs), definiowane jako połączenia co najmniej dwóch 2 leków, które mogą prowadzić do ilościowej i/lub jakościowej zmiany działania jednego z nich.[5]

Prawidłowo prowadzona farmakoterapia zwiększa prawdopodobieństwo uzyskania pożądanego efektu terapeutycznego i poprawy jakości życia poprzez uniknięcie skutków ubocznych związanych z niewłaściwymi połączeniami preparatów.[6] Odpowiednia farmakoterapia wiąże się również ze zmniejszeniem ryzyka rehospitalizacji i zgonu, co redukuje obciążenie finansowe systemu opieki zdrowotnej.[7-8] Koszt jatrogennych błędów farmakoterapii w Europie szacuje się na 290–850 milionów euro rocznie. Badania sugerują, że 11–38% tych błędów można uniknąć.[9] Również dane z USA wskazują na wysokie nakłady finansowe (200 miliardów dolarów rocznie) na leczenie skutków ubocznych farmakoterapii u osób powyżej 65 roku życia.[10]

Negatywne implikacje PP, EPP i DDIs stanowią silną motywację do ciągłego monitorowania farmakoterapii osób starszych w wielu krajach świata.[11-14] Powyższe

zagadnienia zostały dotychczas szeroko przeanalizowane w Europie Zachodniej i USA, niestety dane z Europy Środkowej i Wschodniej są nadal ograniczone.

Stopniowo wzrasta znaczenie depreskrypcji, definiowanej jako proces odstawienia lub zmniejszenia dawki leku, w przypadku którego ryzyko stosowania przewyższa korzyści u określonych pacjentów.[15] Istnieje coraz więcej dowodów na bezpieczeństwo i skuteczność różnych metod depreskrypcji.[16] Jednakże długoterminowe korzyści związane z tymi interwencjami często nie są trwałe lub nie mają znaczenia klinicznego. Ponadto brakuje wiarygodnych dowodów na skuteczność odstawiania leków u seniorów z wielochorobowością i zespołem słabości, ponieważ te grupy pacjentów są rutynowo wykluczane z badań klinicznych.[15] W związku z tym istnieje potrzeba oceny możliwości zastosowania depreskrypcji w rutynowej praktyce klinicznej.

III. CELE PRACY

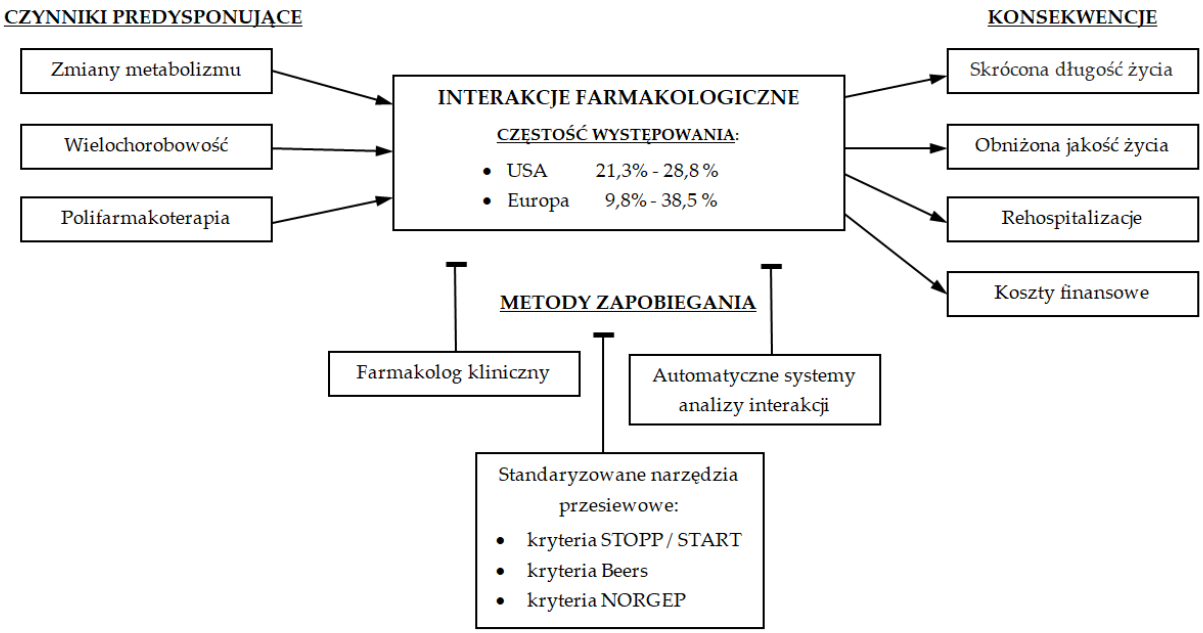
1. Analiza farmakoterapii i potencjalnych interakcji lekowych w reprezentatywnej grupie Polaków powyżej 65. roku życia.
2. Określenie czynników predysponujących do polifarmakoterapii, nadmiernej polifarmakoterapii i interakcji lekowych w polskiej populacji geriatrycznej.
3. Identyfikacja seniorów, którzy z największym prawdopodobieństwem będą wymagać wielodyscyplinarnych interwencji z zakresu farmakoterapii.
4. Przedstawienie dostępnych metod zapobiegania polifarmakoterapii i interakcjom lekowym.
5. Popularyzacja zautomatyzowanych systemów analizy interakcji jako narzędzi pomocniczych do prowadzenia bezpiecznej farmakoterapii osób starszych.

IV. OMÓWIENIE PUBLIKACJI WCHODZĄCYCH W SKŁAD ROZPRAWY DOKTORSKIEJ

i. Publikacja 1.

Pharmacological interactions in the elderly.

Celem pierwszej publikacji było podsumowanie aktualnej wiedzy na temat interakcji lekowych u pacjentów w podeszłym wieku. W pierwszej kolejności przedstawiliśmy główne czynniki predysponujące do interakcji lekowych, takie jak zmiany patofizjologiczne związane z procesem starzenia, które wpływają na farmakokinetykę i farmakodynamikę leków (np. zmiany w składzie ciała, spadek funkcji kluczowych organów), oraz wielochorobowość i polifarmakoterapia. Następnie przeanalizowaliśmy najnowsze badania określające częstość stosowania nieprawidłowych połączeń lekowych w populacjach geriatrycznych na całym świecie. W kolejnej części opisaliśmy konsekwencje interakcji lekowych, m.in. wpływ na długość i jakość życia, częstość rehospitalizacji oraz koszty finansowe. Ostatnie zagadnienie zawarte w publikacji obejmowało przedstawienie zalet i wad różnych metod zapobiegania interakcjom lekowym u osób starszych.



Rycina 1. Podsumowanie czynników predysponujących, częstości występowania, konsekwencji oraz metod zapobiegania interakcjom lekowym wśród osób starszych.

ii. Publikacja 2.

Prevalence and factors predisposing to potential drug-drug interactions in a Polish community-dwelling geriatric population: An observational, cross-sectional study.

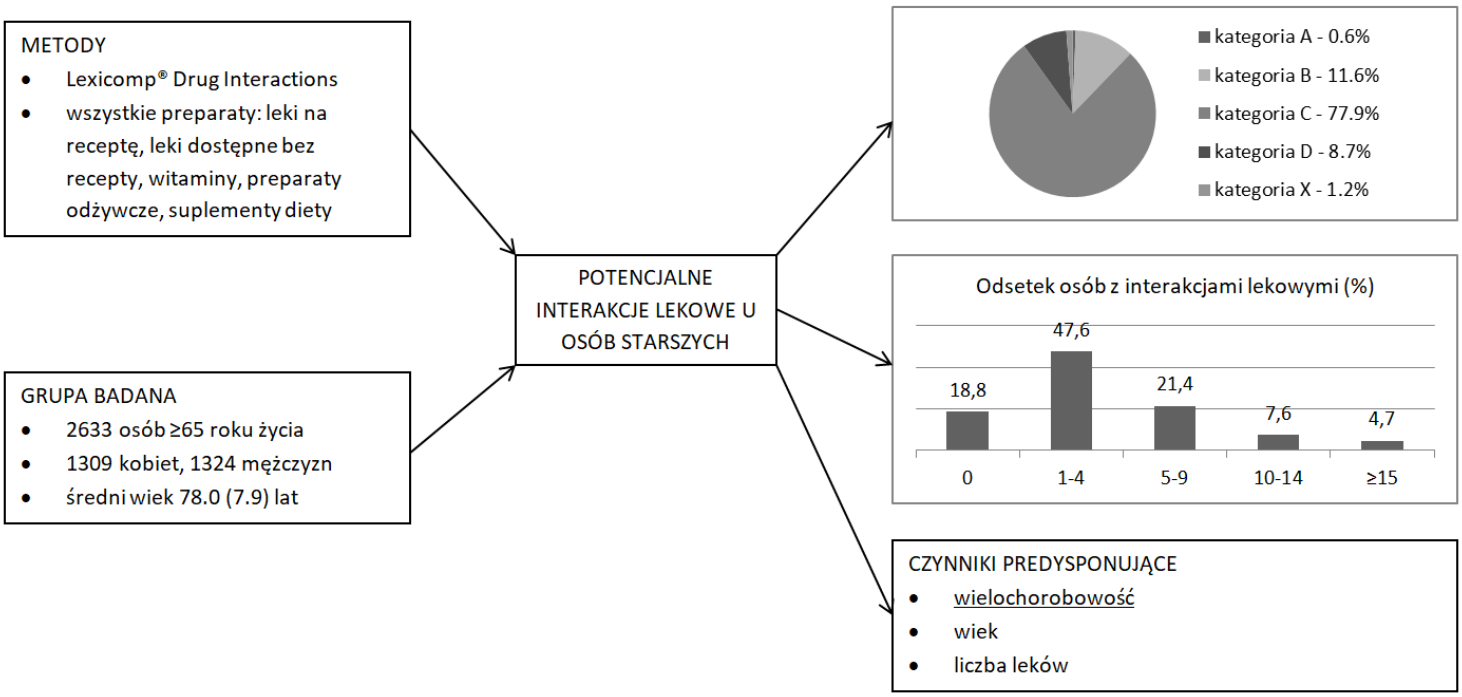
Celem drugiego badania było dostarczenie aktualnych danych na temat rozpowszechnienia i czynników predysponujących do potencjalnych interakcji lekowych w polskiej populacji geriatrycznej. Ponadto naszym celem było spopularyzowanie automatycznych systemów analizy interakcji jako narzędzi pomocniczych do prowadzenia bezpiecznej farmakoterapii.

Do badania włączono 2633 osoby mieszkające w domu w wieku ≥65 lat, uczestniczące w ogólnopolskim, przekrojowym badaniu obserwacyjnym NOMED-AF przeprowadzonym w latach 2017-2018. Respondenci zostali wylosowani przez Ministerstwo Cyfryzacji Rzeczpospolitej Polskiej na podstawie bazy numerów PESEL, stanowili więc reprezentatywną próbę dla Polski pod względem płci, wieku i miejsca zamieszkania. Szczegółowy opis losowania próby został przedstawiony w osobnej publikacji metodologicznej badania NOMED-AF.[16] Specyficznym kryterium włączenia do tego niniejszego badania było stosowanie co najmniej 2 substancji czynnych zawartych w preparatach. Dane pozyskiwane były przez przeszkoloną pielęgniarkę bezpośrednio od respondentów, ich rodzin lub opiekunów na podstawie szczegółowego kwestionariusza oraz prezentacji opakowań wszystkich leków. Badane zmienne obejmowały wiek, płeć, miejsce zamieszkania, poziom wykształcenia oraz wielochorobowość. Ocenę interakcji farmakologicznych pomiędzy substancjami czynnymi wchodzącymi w skład wszystkich rodzajów preparatów (leków na receptę, leków dostępnych bez recepty, witamin, preparatów odżywczych i suplementów diety) stosowanych co najmniej raz w ciągu 2 tygodni poprzedzających badanie przeprowadzono przy użyciu bazy danych Lexicomp® Drug Interactions. Do przeważenia struktury próby względem populacji polskiej w 2017 r. wykorzystano metodę poststratyfikacji, zatem otrzymane wyniki odzwierciedlają populację geriatryczną Polski.

Interakcje lekowe stwierdzono u 81.2% grupy badanej. Średnia liczba wszystkich interakcji lekowych wyniosła 4.24 (95% CI, 4.02–4.46), a wartość mediany wyniosła 3 (IQR, 1–6). Co najmniej jedną interakcję kategorii C („monitoruj terapię”) zaobserwowano u 75.8% uczestników badania, 24.3% osób prezentowało jedną lub więcej interakcji kategorii D („rozważ modyfikację terapii”), a u 4.3% wykryto jedną lub więcej interakcji kategorii X

(„unikaj połączenia"). Zaobserwowano statystycznie istotną korelację między rosnącą liczbą interakcji a zaawansowanym wiekiem, podstawowym poziomem wykształcenia, mieszkaniem na terenach wiejskich, wielochorobowością i rosnącą liczbą przyjmowanych leków.

Na całym świecie przeprowadzono kilka badań oceniających częstości występowania interakcji lekowych u osób starszych przy użyciu narzędzia Lexicomp® Drug Interactions, a uzyskane wyniki były podobne do rezultatów naszej analizy.[17-19] Różnice można tłumaczyć odmiennymi warunkami badania (pacjenci zinstytucjonalizowani vs ambulatoryjni), włączeniem młodszych respondentów poniżej 65. roku życia lub koncentracją na seniorach z nadmierną polifarmakoterapią (≥10 leków). Dane dotyczące częstości interakcji lekowych w polskiej populacji geriatrycznej z wykorzystaniem automatycznych systemów analizy interakcji są ograniczone. Według naszej wiedzy jest to pierwsze badanie w Polsce opisujące występowanie interakcji lekowych przy użyciu narzędzia Lexicomp® Drug Interactions.



Rycina 2. Rozpowszechnienie i czynniki predysponujące do potencjalnych interakcji lekowych w polskiej populacji geriatrycznej.

iii. Publikacja 3.

Polypharmacy among elderly patients in Poland: prevalence, predisposing factors, and management strategies.

Celem trzeciej pracy była analiza farmakoterapii w populacji geriatrycznej Polski, określenie czynników predysponujących tę grupę do PP i EPP oraz zidentyfikowanie seniorów, którzy z największym prawdopodobieństwem mogą wymagać interdyscyplinarnych interwencji z zakresu farmakoterapii. Omówiliśmy również dostępne metody zapobiegania polifarmakoterapii.

Do badania włączono 3014 osób mieszkających w domu w wieku ≥65 lat objętych ogólnopolskim, przekrojowym badaniem obserwacyjnym NOMED-AF. Proces losowania próby badanej i pozyskiwania danych był taki sam jak w pierwszej pracy oryginalnej i został szczegółowo przedstawiony w osobnej pracy metodologicznej.[16] Specyficznym kryterium włączenia do niniejszego badania była zgoda na udzielenie informacji o przyjmowanych lekach. W analizie uwzględniliśmy liczbę tabletek (nie substancji czynnych) skategoryzowanych na podstawie bazy danych Urzędu Rejestracji Produktów Leczniczych, Wyrobów Medycznych i Produktów Biobójczych.[20] Z analizy wyłączono produkty niewymienione w powyższej bazie, w tym większość suplementów diety, które nie posiadają jasnej klasyfikacji i informacji o dokładnym składzie. Jeżeli ta sama substancja była sprzedawana jednocześnie jako lek na receptę i preparat bez recepty, zaliczano ją do pierwszej kategorii. Badane zmienne obejmowały wiek, płeć, miejsce zamieszkania, poziom wykształcenia oraz wielochorobowość. Odnotowaliśmy również częstość preparatów łączonych (SPCs), które definiuje się jako leki zawierające 2 lub więcej składników aktywnych połączonych w postaci pojedynczej dawki. Analizę jakościową farmakoterapii przeprowadzono zgodnie z klasyfikacją ATC.[21] Respondenci udzielili informacji na temat rozpoznanych chorób przewlekłych oraz byli proszeni o przedstawienie kart informacyjnych z dotychczasowych hospitalizacji. Na podstawie tych danych przypisano kody z klasyfikacji ICD-10. Do określenia stopnia wielochorobowości wykorzystano Charlson Comorbidity Index (CCI). Dzięki zastosowaniu poststratyfikacji uzyskane wyniki odzwierciedlają populację geriatryczną Polski.

Stosowanie przynajmniej jednego leku deklarowało 90.7% badanych, a średnia liczba zażywanych leków wyniosła 5.01 (95% CI, 4.87–5.15). Co najmniej jeden lek bez recepty

stosowało 44.2% respondentów, w średniej liczbie 0.52 (95% CI, 0.49–0.55). Więcej niż 5 leków zażywało 53.5% całej populacji, a ponad 10 leków stwierdzono u 8.7% ankietowanych. Preparaty łączone stanowiły 27.2% leków. Średnia wartość CCI wyniosła 4.38 (95% CI, 4.30–4.47) punktów. Najczęstszymi chorobami przewlekłymi były nadciśnienie tętnicze, cukrzyca i przewlekła niewydolność serca. Analiza jakościowa farmakoterapii oparta na klasyfikacji ATC wykazała, że osoby starsze najczęściej stosowały preparaty wpływające na układ sercowo-naczyniowy, krew i układ krwiotwórczy oraz przewód pokarmowy.

Zaobserwowaliśmy wysokie spożycie leków w populacji geriatrycznej Polski. W porównaniu z innymi badaniami dotyczącymi PP wśród polskich seniorów, takimi jak „Polsenior", „Polsenior2" czy badaniem Kardasia i wsp., dane te mogą wskazywać, że PP wśród seniorów w Polsce stanowi rosnący problem.[22-24] Według naszej wiedzy niniejsze badanie jako pierwsze przedstawiło szczegółową analizę preparatów łączonych stosowanych przez polskich seniorów wraz z omówieniem zalet i wad stosowania ich u osób starszych. Wyniki te mogą zmienić rozumienie potencjalnych korzyści SPSc w zakresie wyników zdrowotnych u pacjentów w podeszłym wieku.

W kolejnej części przedstawiliśmy zalety i wady różnych strategii optymalizacji farmakoterapii u pacjentów w podeszłym wieku, znanych jako metody depreskrypcji, takie jak: interwencje kierowane przez lekarzy, systemy wspomagania decyzji klinicznych, programy edukacyjne dla lekarzy przepisujących recepty, przeglądy leków prowadzone przez farmaceutów, edukacja skierowana bezpośrednio do pacjenta i interwencje interdyscyplinarne. Odnieśliśmy się również do nadchodzącej nowości w polskim systemie ochrony zdrowia, jaką jest pilotaż skoordynowanej opieki farmaceutycznej.[25] Wykazaliśmy, że PP i EPP częściej występowała u mężczyzn, w wieku od 85 do 89 lat, u osób z niższym wykształceniem oraz mieszkających w małych i średnich miastach. Głównym czynnikiem predysponującym osoby starsze do PP i EPP była wielochorobowość. Częstość występowania najczęstszych chorób współistniejących zidentyfikowanych w naszym badaniu była porównywalna z danymi z projektu Collaborative Research on Aging in Europe oraz WHO Study on Global Aging and Adult Health.[26]

V. PODSUMOWANIE

Prace wchodzące w skład rozprawy doktorskiej dostarczyły aktualnych danych na temat rozpowszechnienia, czynników predysponujących i strategii postępowania w przypadku polifarmakoterapii i interakcji lekowych w polskiej populacji geriatrycznej. W kontekście wysokiego spożycia leków z powodu wielochorobowości wśród polskich seniorów oraz udokumentowanego wcześniej negatywnego wpływu PP i EPP na jakość i długość życia, uzyskane wyniki wskazują na dużą potrzebę wprowadzenia skoordynowanej opieki medycznej i farmaceutycznej nad osobami starszymi. Zidentyfikowaliśmy grupy wysokiego ryzyka pacjentów w podeszłym wieku, którzy wymagają szczególnej uwagi i mogą odnieść największe korzyści z interdyscyplinarnych interwencji z zakresu farmakoterapii.

SUMMARY IN ENGLISH

I. LIST OF ABBREVIATIONS

ATC	anatomical-therapeutic-chemical
CCI	Charlson Comorbidity Index
CI	confidence interval
DDIs	drug-drug interactions
EPP	excessive polypharmacy
ICD-10	International Classification of Diseases, Tenth Revision
IQR	interquartile range
NOMED-AF	NOninvasive Monitoring for Early Detection of Atrial Fibrillation
NORGEP	The Norwegian General Practice
OTC	over-the-counter
PP	polypharmacy
SPCs	single pill combinations
WHO	World Health Organization

II. INTRODUCTION

A significant increase in life expectancy is considered one of the greatest social achievements of the 20th century. However, this longevity, together with declining fertility rates, have led to a progressive aging of the population. The number of individuals over the age of 65 years is projected to increase from 524 million in 2010 (8% of the world's population) to 1.5 billion (16% of the world's population) by 2050.[1]

Pharmacological therapy in seniors is particularly complicated due to progressive aging-related changes in metabolism and the coexistence of multiple diseases that require complex drug regimens.[2] Additionally, there has been a growing interest among older adults in over-the-counter (OTC) drugs that are widely available on the pharmaceutical market.[3]

The literature provides a broad and thorough description of the negative medical, economic, and social consequences of polypharmacy (PP), defined as taking 5 or more drugs, and excessive polypharmacy (EPP), which refers to using at least 10 drugs.[4] One of the avoidable medical errors is drug-drug interactions (DDIs), described as an interaction of at least 2 drugs that can lead to a quantitative and/or qualitative change in the action of one of them.[5]

Properly conducted pharmacotherapy increases the likelihood of achieving the desired therapeutic effect and improving quality of life by avoiding the side effects associated with improperly combined preparations.[6] Appropriate pharmacotherapy is also associated with a decreased risk of rehospitalization and death, which reduces the financial burden on the healthcare system.[7-8] The cost of iatrogenic pharmacotherapy errors in Europe (11–38% of which are avoidable) has been estimated between €290 and €850 million per year.[9] Data from the USA also indicate high financial expenditure ($200 billion per year) to treat the side effects of pharmacotherapy in people over 65 years of age.[10]

The negative implications of PP, EPP and DDIs are a strong motivation for the continuous monitoring of pharmacotherapy in older adults in many countries around the world.[11-14] These topics were analyzed extensively in Western Europe and the USA, but data from Central and Eastern Europe are still limited.

There has also been a growing recognition of the importance of deprescribing, defined as the process of withdrawal or dose reduction of a drug for which the risk outweighs the

benefit in specific patients.[15] There is accumulating evidence for the safety and clinical effectiveness of various deprescribing methods; unfortunately, the long-term benefits associated with the intervention are often not sustainable or clinically meaningful.[16] Moreover, there is a lack of robust evidence for the effectiveness of deprescribing in seniors with multimorbidity and frailty, as these patients are routinely excluded from clinical trials.[15] Nevertheless, the need to explore the implementation of deprescribing into routine clinical practice is of major importance across health care settings worldwide.

III. AIMS OF THE STUDY

1. Analysis of pharmacotherapy and potential drug-drug interactions in a representative group of Poles over 65 years old.
2. Determination of factors predisposing to polypharmacy, excessive polypharmacy and potential drug-drug interactions in the Polish geriatric population.
3. Identification of seniors who are most likely to require multidisciplinary interventions in the field of pharmacotherapy.
4. Discussing available methods of preventing polypharmacy and drug interactions.
5. Popularization of automated interaction analysis systems as auxiliary tools for conducting safe pharmacotherapy among elderly patients.

IV. DESCRIPTION OF THE PUBLICATIONS INCLUDED IN THE DOCTORAL THESIS

i. Publication 1.

Pharmacological interactions in the elderly.

The aim of the first paper was to summarize current knowledge on drug interactions in elderly patients. First, we presented main factors predisposing to drug interactions, such as pathophysiological changes associated with aging, which affect pharmacokinetics and pharmacodynamics of drugs (e.g. changes in body composition, decline in the function of vital organs), as well as multimorbidity and polypharmacy. Secondly, we reported prevalence of drug interactions in geriatric populations across countries according to the latest research studies. In the next part, we described the consequences of drug interactions, for example the impact on life expectancy, quality of life, frequency of rehospitalizations and financial costs. Finally, we discussed advantages and disadvantages of different measures to prevent drug interactions in the elderly.

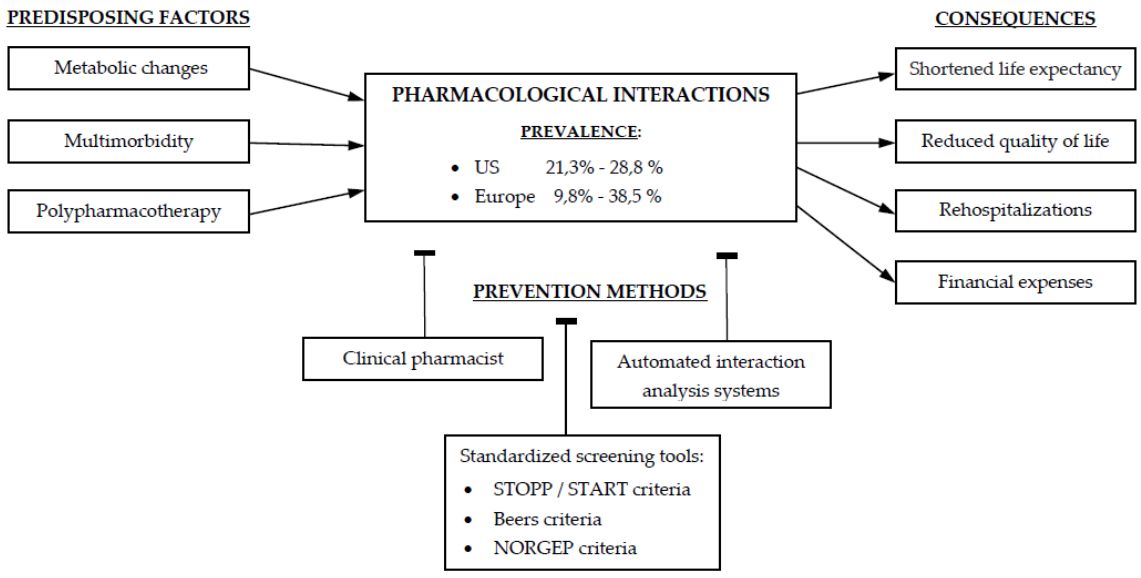


Figure 1. Summary of predisposing factors, prevalence, consequences and preventive methods of drug interactions in the elderly.

ii. Publication 2.

Prevalence and factors predisposing to potential drug-drug interactions in a Polish community-dwelling geriatric population: An observational, cross-sectional study.

The second study was performed to provide up-to-date data on prevalence and predisposing factors of possible drug-drug interactions in the Polish geriatric population. In addition, we aimed to popularize automated interaction analysis systems as auxiliary tools for conducting safe pharmacotherapy.

We used the Lexicomp® Drug Interactions database to assess pharmacological interactions between active substances included in all types of preparations (prescription drugs, over-the-counter drugs, vitamins, nutritional preparations, and dietary supplements) used at least once in the 2 weeks preceding the study, among 2633 home-dwelling people aged ≥65 years included in the nationwide, cross-sectional observational study NOMED-AF conducted from 2017 to 2018. Respondents were randomly selected by the Ministry of Digitization of the Republic of Poland based on a social security number database; therefore, they constituted a representative sample for Poland in terms of sex, age, and place of residence. A detailed description of the methodology of the NOMED-AF study was presented in a separate, methodological publication.[16] The specific inclusion criterion for this study was the use of at least 2 active substances included in the preparations. Based on a detailed questionnaire, the data were obtained by a trained nurse directly from the respondents, their families or their caregivers, followed by a presentation of the packaging of all of their drugs. The variables measured included age, sex, place of residence, level of education, and multimorbidity. Post-stratification was used to outweigh the sample structure against the Polish population in 2017; therefore, the obtained results reflect the geriatric population of Poland.

Drug interactions were identified in 81.2% of all individuals. The mean number of all drug interactions was 4.24 (95% CI, 4.02–4.46), and the median value was 3 (IQR, 1–6). At least 1 category C interaction (“monitor therapy”) was observed in 75.8% of all study participants, 24.3% had 1 or more category D interaction (“consider modifying therapy”), and 4.3% had 1 or more category X interaction (“avoid combination”). There was a statistically significant correlation between the increasing number of interactions and the

high number of drugs taken, advanced age, primary level of education, living in rural areas, and multimorbidity.

Several studies have been conducted worldwide to assess the prevalence of drug interactions in older adults using the Lexicomp® Drug Interactions Tool, and the obtained results were similar to our research.[17-19] The differences may be explained by various settings (inpatient vs outpatient), inclusion of younger respondents <65 years old or concentration on seniors with excessive polypharmacy (≥10 drugs). Data on the frequency of possible drug interactions assessed with an automated analysis programs concerning the Polish geriatric population are lacking. To our knowledge, this is the first study to report the prevalence of drug interactions using the Lexicomp® Drug Interactions Tool.

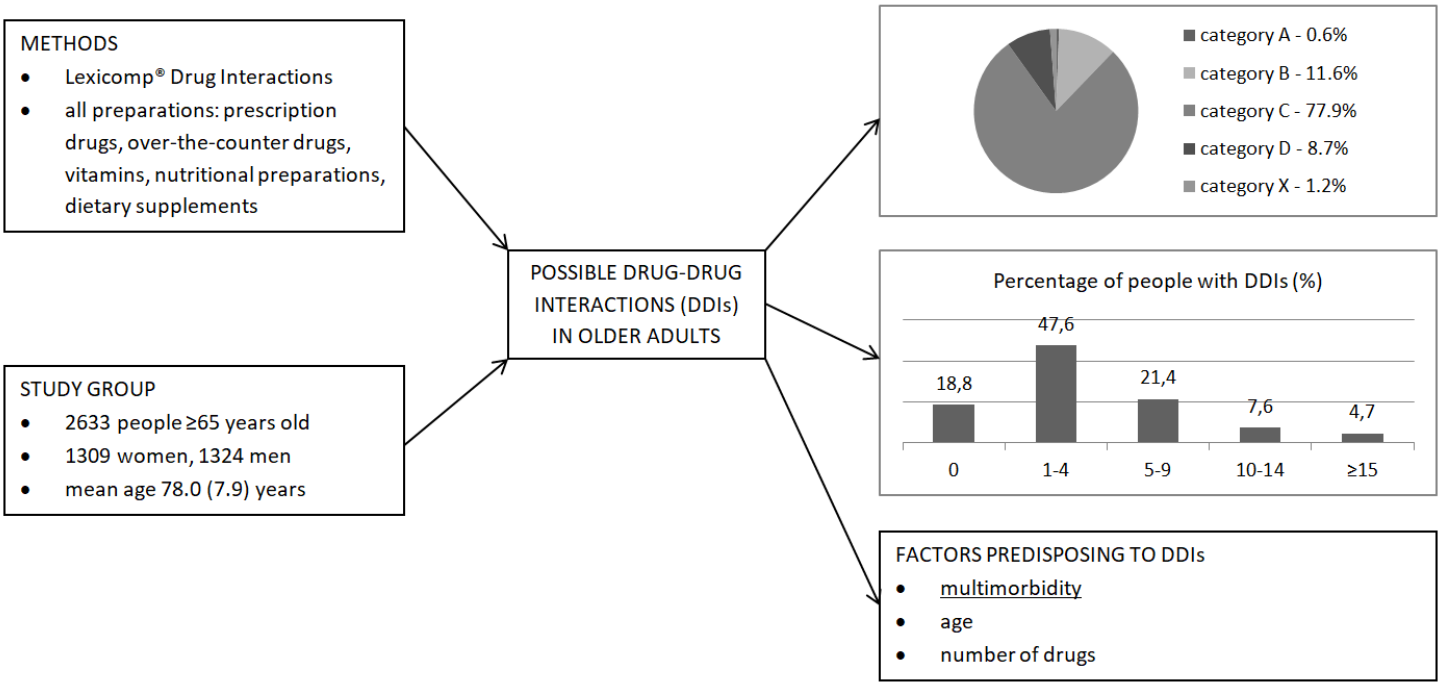


Figure 2. Prevalence and factors predisposing to potential drug-drug interactions in Polish geriatric population.

iii. Publication 3.

Polypharmacy among elderly patients in Poland: prevalence, predisposing factors, and management strategies.

The objective of the third study was to provide an up-to-date assessment of pharmacotherapy in the geriatric population of Poland. Furthermore, we aimed to determine the factors predisposing this population to PP and EPP, and to identify the seniors who are most likely to require multidisciplinary interventions in the field of pharmacotherapy. We also discussed available methods of preventing polypharmacy.

The study group comprised of 3014 home-dwelling people aged ≥65 years included in the nationwide, cross-sectional observational study NOMED-AF. The process of sampling and data acquirement was the same as in the first original paper, and was presented in details in the separate, methodological paper.[16] The specific inclusion criterion for the present study was the consent to provide information on taken drugs. In the analysis, we considered the number of pills (not active substances) categorized according to the database of the Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products.[20] The products not listed in this database, including the majority of dietary supplements, which lack clear classification and information on exact formulations, were excluded from the analysis. If the same substance was sold simultaneously as a prescription drug and an OTC preparation, it was classified as the former category. The variables measured included age, sex, place of residence, level of education, and multimorbidity. We also noted the frequency of single-pill combinations (SPCs), which are defined as drugs that include 2 or more active ingredients combined in a single-dose form. Qualitative analysis of pharmacotherapy was performed according to the ATC classification.[21] The respondents provided information on diagnosed chronic diseases and were asked to present discharge cards from previous hospitalizations. Based on these data, codes from the ICD-10 classification were assigned. The Charlson Comorbidity Index (CCI) was used to determine the degree of multimorbidity. Due to application of postratification, the obtained results reflect the geriatric population of Poland.

Consumption of at least 1 drug was reported by 90.7% of the participants, and the mean number of drugs used was 5.01 (95% CI, 4.87–5.15). At least 1 non-prescription drug was used by 44.2% of the respondents, with a mean number of 0.52 (95% CI, 0.49–0.55).

More than 5 drugs were taken by 53.5% of the entire population, while the use of more than 10 drugs was reported by 8.7% of the respondents. SPCs accounted for 27.2% of medications. The mean value of the CCI was 4.38 (95% CI, 4.30–4.47) points. The most frequent chronic diseases were arterial hypertension, diabetes mellitus, and chronic heart failure. As a result, the qualitative analysis of pharmacotherapy based on the ATC classification showed that older adults most often used preparations affecting the cardiovascular system, blood and the hematopoietic system, and gastrointestinal tract.

We observed a high consumption of drugs among the geriatric population of Poland. In comparison with other studies on PP among Polish seniors, such as “Polsenior”, “Polsenior2” or the survey by Kardaś et al., these data indicate that PP among seniors in Poland is an increasing problem.[22-24] To our knowledge, this study was the first to present detailed analysis of SPCs in seniors, together with discussing pros and cons of those types of preparations in older adults. These results may change the understanding of the potential benefits of SPSc on health outcomes in elderly patients.

In the next part we presented advantages and disadvantages of various management strategies to optimize pharmacotherapy and prevent medication-related problems in geriatric patients, known as methods of deprescribing, such as physician-led interventions, clinical decision support systems, prescriber education programs, pharmacist-led medication reviews, direct-to-patient education, and multidisciplinary interventions. We also referred to upcoming novelty in the Polish healthcare system, which is the pilot program for the new regulation of coordinated pharmaceutical care.[25] We showed that PP and EPP occurred more often in men, in the age group 85 to 89 years, in individuals with lower level of education, and those living in small or medium-sized cities. The main factor predisposing older people to PP and EPP was multimorbidity. The prevalence of the most common comorbidities identified in our study was comparable with data from the Collaborative Research on Ageing in Europe project and the WHO Study on Global Ageing and Adult Health.[26]

V. SUMMARY

The manuscripts included in the doctoral dissertation delivered up-to-date data on prevalence, predisposing factors, and management strategies of PP and DDIs in Polish geriatric population. In the context of the high consumption of drugs due to multimorbidity among the Polish seniors, and the previously documented negative impact of PP and EPP on the quality of life and life expectancy, our findings reveal a great need for the introduction of combined medical and pharmaceutical care of older adults. We identified high-risk groups of elderly patients, who are most likely to require special attention and may receive the greatest benefits from multidisciplinary interventions in the field of pharmacotherapy.

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PUBLIKACJE WCHODZĄCE W SKŁAD ROZPRAWY DOKTORSKIEJ / MANUSCRIPTS INCLUDED IN THE DOCTORAL DISSERTATION

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Review

Pharmacological Interactions in the Elderly

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Abstract: Pharmacological therapy in the elderly is particularly complicated and challenging. Due to coexistence of three main predisposing factors (advanced age, multiple morbidity and polypharmacotherapy), this group of patients is prone to occurrence of drug interactions and adverse effects of incorrect drug combinations. Since many years patient safety during the treatment process has been one of key elements for proper functioning of healthcare systems around the world, thus different preventive measures have been undertaken in order to counteract factors adversely affecting the therapeutic effect. One of the avoidable medical errors is pharmacological interactions. According to estimates, one in six elderly patients may be at risk of a significant drug interaction. Hence the knowledge about mechanisms and causes of drug interactions in the elderly, as well as consequences of their occurrence are crucial for planning the process of pharmacotherapy. For the purpose of pharmacovigilance, a review of available methods and tools gives an insight into possible ways of preventing drug interactions. Additionally, recognizing the actual scale of this phenomenon in geriatric population around the world emphasizes the importance of a joint effort among medical community to improve quality of pharmacotherapy.

Keywords: geriatrics; aging; drug interactions; medication errors/prevention and control; polypharmacy; multimorbidity

1. Introduction

Patient safety during the treatment process is one of key elements for proper functioning of healthcare systems around the world. An increasing emphasis is being placed on preventive measures to counteract the occurrence of events adversely affecting the therapeutic effect. One of the avoidable medical errors is pharmacological interactions, defined as an interaction of two drugs that can lead to a quantitative and/or qualitative change in the action of one of them [1]. Undesirable pharmacological interactions may increase toxicity of a drug or reduce its effectiveness.

Predisposing factors for the occurrence of adverse effects of incorrect drug combinations are primarily advanced age, multiple morbidity and polypharmacotherapy [2]. It is estimated that in developed countries about 30–40% of people over 65 years old take 5 or more drugs, while 12% of patients in this age group use 10 or more different medicines [2]. Patients burdened with the coexistence of several chronic diseases have a greater risk of drug interactions due to complexity of the treatment process and more frequent contacts with various representatives of the healthcare system [3]. Pharmacological therapy in the elderly is particularly complicated due to age-related changes in pharmacokinetic and pharmacodynamic metabolism of drugs that increase or decrease sensitivity of these patients to chemical substances [4].

A significant increase in life expectancy in the 20th century is considered to be one of the greatest social achievements. In combination with a decreasing fertility rate, it leads to a progressive aging

of the population. The population over 65 years old is expected to increase from 524 million in 2010 (8 percent of the world population) to 1.5 billion (16 percent of the world population) in 2050. This increase will be mostly pronounced in developing countries [5].

Understanding the basis of drug interactions in the elderly and the consequences of their occurrence, as well as knowledge of the actual scale of this phenomenon in the population and available methods of side effects prevention, can help optimize the process of pharmacotherapy, and thus increase safety of elderly patients.

2. Metabolism in the Old Age

The aging process is characterized by significant changes in body composition and physiological decline in the function of most organs. With age, total body fat mass increases, water content decreases, which in combination with a reduction in muscle mass can lead to sarcopenia and changes in distribution of drugs [6]. It is estimated that body fat content over the age of 70 is about 25% in men and 40% in women, which is 1.5 times more than in young people aged 20–29 [7]. As a result, distribution volume of lipophilic drugs increases in elderly patients. Aging is also associated with a progressive decrease in body water content, which causes a decrease in distribution volume of hydrophilic compounds [8]. From early adulthood up to the age of 79–80 men present a gradual decline in total body water of 0.3 kg per year, while in women total body water remains relatively constant from youth up to the age of 70, when there is a decrease of 0.7 kg per year [9].

The most important pharmacokinetic changes include decreased renal secretory capacity and impaired hepatic metabolism. Due to the decrease in the secretory capacity of kidneys, removal of hydrophilic substances through kidneys may be significantly impaired and requires adjustment of drug dose to renal parameters [10]. Changes in liver during its aging may affect drug metabolism in many ways. Size of liver decreases with age by 20–40%, while blood flow through this organ decreases by 40–60%. In people over 70 years old, cytochrome P450 (CYP450) oxidase activity may decrease by up to 30% compared to young adults [11].

In addition, plasma protein concentration changes with age, including albumin and alpha-1 acid glycoprotein, the main roles of which are transport and storage of most exogenous and endogenous substances in bloodstream [12]. The level of albumin in the elderly is on average 19% lower than in young population. An increased free drug concentration of substances strongly bound to albumin may be a potential cause of toxicity, even if a total drug concentration is within a therapeutic range [13]. A slight increase in alpha-1 acid glycoprotein, observed in healthy elderly, but less pronounced in the presence of a disease, may cause an increase in the concentration of some substances, e.g., propranolol [14].

Studies have also shown lower levels of p-glycoprotein concentration in brain and intestinal tissue of elderly people, especially in the presence of dementia [15,16]. This membrane protein transports various substrates across the cell membrane including drugs, such as steroids or cardiac glycosides like digoxin.

Another important change observed in elderly is a decrease in cellular metabolism, which can significantly reduce the activity of substances administered in the form of prodrugs [17].

Pharmacodynamic changes are also common and are associated with changes in drug sensitivity, regardless of chemical compounds distribution in tissues [10,11]. This is illustrated by a decrease in cardiovascular sensitivity of the elderly to agonists and antagonists of beta-adrenoreceptors and an increase in frequency of orthostatic hypotension episodes after antihypertensive drugs.

Moreover, central nervous system of elderly patients is becoming more susceptible to agents affecting brain function, e.g., opioids, benzodiazepines and psychotropic drugs [6].

3. Multimorbidity

Multimorbidity is a co-occurrence of at least two chronic diseases that cannot be cured at the current state of knowledge, but it is possible to control them by means of pharmacology or other

therapeutic methods. According to estimates, the incidence of this phenomenon in older people is 65–98% [18–20] and is gradually increasing due to a better quality of healthcare and aging of the population [21,22]. Nearly half of people over 65 years old have at least three chronic diseases, while one in five people is affected by five or more chronic diseases [23,24]. The most common are hypertension, osteoarthritis, ischemic heart disease and diabetes [25].

By 2035, it is prognosed that the number of people living with two or more chronic conditions will increase by 86.4%—with the biggest rises observed for cancer (increase by 179.4%) and diabetes (increase by 118.1%) [26].

Multimorbidity in the elderly can impair drugs handling and administration. This concerns especially chronic conditions like dementia, Parkinson's disease, stroke, esophageal diseases (e.g., gastro-esophageal reflux disease), the presence of visual or cognitive impairments and swallowing difficulties [27].

Compared with people burdened with one chronic disease, patients with multiple diseases have an increased risk of functional impairment [28,29], deterioration in quality of life [30,31] and increased mortality [32,33]. Due to the coexistence of many chronic diseases, the elderly are the main consumers of both prescription and OTC (over-the-counter) drugs, buying 15% more than they did about 10 years ago [24].

4. Polypharmacotherapy

Polypharmacotherapy is traditionally defined as a long-term use of five or more drugs. It is estimated that in developed countries about 30–40% of people over 65 years old take 5 or more drugs, while 12% of patients in this age group use 10 or more different medicines [2]. The report of the World Health Organization in 2019 confirms that polypharmacotherapy is a common problem, but diverse structures of healthcare provision and different information collection systems make it difficult to compare data from individual countries [34].

In addition, in recent years there has been a growing interest among older people in dietary supplements, which are widely available on the pharmaceutical market. It is estimated that over 40% of people over 60 years old declare to consume products from this group, and the value of dietary supplements market in the European Union is estimated at five billion euros. The most commonly used supplements are vitamin and mineral products, fish oils, probiotics and some herbal products [35].

It is worth emphasizing the role of excipients, which are generally considered to be biologically inert or inactive. Recent research has proven they can influence a drug effect by contributing synergistically (e.g., antitumor activity and cardiovascular benefits of gamma-linolenic acid and omega-3 fatty acids) or by reducing drug effectiveness through different mechanism (e.g., degradation of neomycine by sodium carboxymethylcellulose or absorption of nitrazepam in tablet dosage form by colloidal silicon) [36]. Excipients can also alternate (decrease or increase) the permeability of intestinal membrane, and therefore affect bioavailability of the drug [37]. Due to age-related changes in metabolism, accumulation of excipients may occur in older patients, leading to toxicity and adverse effects. A list of such excipients are summarized in a review [38].

The literature provides a broad and accurate description of negative medical, economic and social consequences of polypharmacotherapy. The most dangerous are drug interactions, cognitive impairment [23], weight loss and malnutrition [39], falls and bone fractures [40], rehospitalization [41], reduced quality of life [42] and death [42].

Poor nutritional status and malnutrition in the elderly population are important areas of concern, associated with an increased financial cost burden [43] and reduced quality of life [44]. Drug classes with potentially significant drug–nutrient interactions include: antihypertensives by causing zinc deficiency (thiazide diuretics, angiotensin receptor blockers, angiotensin converting enzyme inhibitors and potassium-sparing diuretics); acetylcholinesterase inhibitors; proton pump inhibitors and metformin by causing vitamin B12 deficiency; HMG-Co reductase inhibitors (statins) by causing reductions in CoQ10, a-tocopherol, b-carotene and lycopene and long-term, high-dose aspirin by causing vitamin C

deficiency [45]. Additionally, polypharmacy may negatively affect the therapeutic success of vitamin D supplementation by reduced compliance and adherence to treatment, and interference with drug adsorption, revealing the need for a higher amount of vitamin D supplements [46].

Drugs frequently consumed by the elderly (including antihypertensives, hypolipemic, hypoglycemics or drugs for acid- or nervous-related disorders) may trigger hypohydration by means of increased water elimination (through diarrhea, urine or sweat); decreased thirst sensation or appetite or alteration of central thermoregulation. On the other hand, excipients induce alterations in hydration status by decreasing gastrointestinal transit time or increasing the gastrointestinal tract rate or intestinal permeability [47].

Studies show that, on average, 1 in 5 commonly used drugs by the elderly should not be recommended [48], while for people in nursing homes and other institutions this problem may affect up to 30–50% of patients [49]. According to estimates, one in six elderly patients may be at risk of a significant pharmacological interaction [24].

5. Prevalence of Drug Interactions

The phenomena of polypharmacotherapy and pharmacological interactions have been intensively analyzed in Western Europe and the United States, while data from Central and Eastern European countries are still limited. Most of the analyses were based on screening tool of older persons' potentially inappropriate prescriptions (STOPP)/screening tool to alert doctors to the right treatment (START) or Beers criteria and concerned outpatient patients.

A research conducted in 2009 on nearly 1300 Northern Ireland citizens over the age of 65 showed that 18.3% of them used dangerous drug combinations [50]. A comprehensive study conducted in the United Kingdom in 2003 included 131 primary care outpatient clinics with approximately 162,000 patients over 65 years old annually—24.8% of them were shown to use abnormal drug combinations, while 20.5% of patients took high-risk drugs [51]. A nationwide survey conducted in Lithuania in 2017 on over 400,000 citizens over the age of 65 years old showed a higher percentage of incorrect drug combinations, of around 25% [52]. A similar result was obtained in 2005 in Portugal, where more than 25% of 213 examined patients over 65 years old used at least one drug not indicated for use in the elderly [53]. In some countries lower values of incorrect drug connections have been reported in the elderly, e.g., 9.8% in Turkey [54] or 12.5% among Finnish citizens [55].

So far, a study was conducted in Poland in 2007 on 1000 seniors from Poznań and Głogów, finding the percentage of incorrect drug combinations of 28.6% [56]. This relatively high rate may be due to consumption of OTC drugs that accounted for 5.5% of incorrect connections. Unfortunately, there is a lack of national data determining the incidence of pharmacological interactions in Polish elderly patients.

The percentage of incorrect drug combinations in European studies ranges between 9.8 and 38.5% and is relatively higher than in the United States (21.3–28.8%) [57–60]. The reasons for the observed discrepancies are unclear and may be due to differences in the availability of drugs in individual countries, different practices of prescribing drugs or verifying prescriptions by pharmacists.

6. Consequences of Pharmacological Interactions

6.1. Impact of Pharmacological Interactions on Life Expectancy

The most serious effect of adverse reactions due to pharmacological interactions is death [61]. Studies in the United States have shown a 1.6-fold increase in mortality in people taking abnormal drug combinations [62]. Importantly, inclusion of another maladjusted drug is associated with a relative increase in mortality by 39%, regardless of the number of medicines [63]. Particularly strong association was observed between an increase in mortality and incorrect combinations with drugs rising the risk of falls in elderly (STOPP criteria version 2, category K), e.g., benzodiazepines, neuroleptics, hypnotics from the Z group [64].

6.2. Impact of Pharmacological Interactions on Quality of Life

Definition of health-related quality of life (HRQoL) includes a subjective perception of the ability to perform activities that are important to a person and are affected by current health [65]. In previous studies, association between a large number of drugs taken, potential pharmacological interactions and reduced quality of life has been observed [66]. These patients had significantly reduced health-related quality of life self-assessment scores on the EQ-VAS scale (mean 63.12 ± 17.37 points) [67]. This effect was intensified by an accompanying deterioration of mobility, functional fitness and cognitive functions [67,68].

6.3. Impact of Pharmacological Interactions on the Frequency of Rehospitalization

Adverse reactions due to pharmacological interactions are among the most common causes of hospitalization in the elderly [69]. In a nationwide observational study in the United States, the incidence of sudden hospitalizations due to adverse drug reactions was 99,628 cases per year [70]. For the same reason, in 2005 the number of visits to various health care institutions was around 4.3 million [71]. It is estimated that in two out of three cases rehospitalization could be avoided [69].

6.4. Impact of Pharmacological Interactions on Financial Costs

In the United States the cost of medical treatment due to medical errors and side effects in the elderly population is estimated at over $200 billion a year [72]. In European countries this phenomenon is also a significant problem [73–75]. Frequent visits to emergency departments and outpatient facilities, rehospitalizations, as well as purchase of many pharmacological products are a financial burden for individual patients and the entire healthcare system [2].

7. Prevention of Drug Interactions

Due to the research carried out by specialists in the field of gerontology and geriatrics, the knowledge about mechanisms of the aging process is growing. Through further analyses, the main factors predisposing to the occurrence of pharmacological interactions have been recognized and it is more probable to identify patients who are particularly at risk of drug side effects. In addition, there is an awareness of the consequences of pharmacological interactions, which not only affect health and quality of life of patients, but also disrupt the therapeutic process and constitute a financial burden on health care systems.

Previous studies show that 80% of serious drug side effects are caused by an incorrect prescription. Moreover, on average 87.9% of these events are potentially predictable and avoidable [61].

A variety of standardized tools are available to assist in the planning of pharmacotherapy according to individual needs and capabilities of older people. Some of them contain concise guidelines for recommended and contraindicated drugs in geriatric patients, e.g., Beers criteria, STOPP criteria (screening tool of older persons' potentially inappropriate prescriptions) and START (screening tool to alert doctors to the right treatment). Their effectiveness has been extensively studied in many countries [76], indicating the predominance of STOPP/START criteria in identifying inadvisable drugs [77]. In addition, unlike Beers' criteria, STOPP/START criteria were created for usage as a checklist, which means that they are often applied in clinical work and as a part of research protocols [2]. Some countries have developed tools adapted to specifics of its geriatric population and availability of drugs on a given market, such as the Norwegian NORGEP criteria (The Norwegian General Practice) [78].

The role of a clinical pharmacist is also emphasized, whose actions can identify and minimize problems associated with incorrect pharmacotherapy. This solution has been successfully implemented many years ago in the United States and Great Britain, as well as in many European countries, leading to improved therapeutic effects and bringing economic benefits [79].

Automated interaction analysis systems are a solution that has a potential to increase recognition of drug interactions. Along with computerization of healthcare systems, various forms of dedicated programs are available around the world: on-line tools, applications for mobile devices, software modules or even as part of a medical information network—the SureScripts network in the United States [80]. Unfortunately, a reported low alert specificity can be a serious obstacle to an effective use of information and actual increase of patient safety during pharmacotherapy [81].

Despite extensive research and many years of experience, data from an overwhelming number of countries around the world still indicate an alarmingly high percentage of incorrect drug combinations in the elderly. What could be the reasons for this phenomenon?

Some researchers emphasize the imperfection of specific criteria for drugs not indicated in geriatric patients, assessing them as inflexible and not taking into account all factors determining a high quality individualized healthcare [59]. Older people are often excluded from randomized clinical trials that provide information on adverse effects associated with specific drugs [59]. Therefore, there is a lack of accurate data on relative risk and benefits of therapeutic measures in this group of patients [57].

Some specialists note a significant heterogeneity of the elderly population, which means that the risk–benefit ratio will vary depending on the patient's clinical condition [57]. Multimorbidity among seniors results in the use of complex treatment regimens. Doctors may be reluctant to change a scheme that works because there is no evidence of a harmful effect of therapy [59]. In addition, drugs identified as not recommended in geriatric patients may be suitable as second-line medicines for a person who has not responded or does not tolerate the preferred agent [57]. Moreover, the cost of therapy is often an important factor in choosing a specific drug [57]. In some circumstances, the use of a medicine may be clinically justified, if the benefits outweigh the risks to the patient [57].

Most experts agree that all available support tools for identifying pharmacological interactions and abnormal drug combinations can best be used as a screening tool to identify elderly people at high risk of suboptimal pharmacotherapy, and to recognize and prioritize problem areas rather than as a final measure of quality or efficiency of healthcare [57].

8. Concluding Remarks

In the face of reported data on the high incidence of abnormal drug combinations and undeniable negative consequences of pharmacological interactions, it is necessary to draw attention of the medical community to the existing problem and to make a joint effort to improve quality of pharmacotherapy, thereby increasing safety of patients. So far, surveys conducted among physicians indicate their limited ability to recognize potential drug interactions, which creates a need to find solutions supporting the work of clinicians [82]. In the face of computerization of medicine, automatic interaction analysis systems are becoming an increasingly common source of information about potential drug interactions, however, they still meet with skepticism of part of the medical community [83]. Therefore, there is a need to improve and disseminate electronic sources of information on drug interactions, in order to create a better auxiliary tool in conducting a safe pharmacotherapy.

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AHEAD OF PRINT

Prevalence and factors predisposing to potential drug–drug interactions in a Polish community-dwelling geriatric population: An observational, cross-sectional study

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Abstract

Background. Due to advanced age, multimorbidity and polypharmacotherapy, older patients are predisposed to drug interactions and the adverse effects of inappropriate drug combinations.

Objectives. To provide up-to-date data on predisposing factors and the prevalence of possible drug interactions in the Polish geriatric population and to promote automated analysis programs as part of safe pharmacotherapy.

Materials and methods. We used the Lexicomp® Drug Interactions database to assess pharmacological interactions between active substances included in all types of preparations (prescription drugs, over-the-counter drugs, vitamins, nutritional preparations, and dietary supplements) used at least once in the 2 weeks preceding the study, among 2633 home-dwelling people aged >65 years. The variables measured included age, sex, place of residence, level of education, and multimorbidity. Post-stratification was used to weigh the sample structure against the Polish population in 2017.

Results. Drug interactions were identified in 81.2% of all individuals. The mean number (with 95% confidence interval (95% CI)) of all drug interactions was 4.24 (4.02–4.46), and the median value (with 1st and 3rd quartiles (Q1–Q3)) was 3 (1–6). At least 1 category C interaction was observed in 75.8% of all study participants, 24.3% had 1 or more category D interaction, and 4.3% had 1 or more category X interaction. The most important predisposing factor to drug interactions was multimorbidity.

Conclusions. This study identified a high prevalence of potential drug interactions in the Polish geriatric population. Automated analysis systems deliver useful information on pharmacological interactions and should be promoted in the Polish healthcare community as tools to support pharmacotherapy.

Key words: polypharmacy, geriatric, drug interactions, multimorbidity, medication errors, medical error prevention, control

Background

A pharmacological interaction is an interaction of 2 drugs that can lead to a quantitative and/or qualitative change in the action of one of them.[1] Older adults are particularly prone to adverse drug interactions due to advanced age, multimorbidity and polypharmacy.[2] Of pertinent concern is the growing interest among older adults in over-the-counter drugs, which are widely advertised on the pharmaceutical market.[3] Properly conducted pharmacotherapy increases the likelihood of achieving the desired therapeutic effect and improving quality of life by avoiding the side effects associated with improperly combined preparations.[4–6] Appropriate pharmacotherapy is also associated with a decreased risk of rehospitalization[7] and death,[8] which reduces the financial burden on the healthcare system.[2] The cost of iatrogenic pharmacotherapy errors in Europe (11–38% of which are avoidable) has been estimated between €290 and €850 million per year.[9–11] Data from the USA also indicate high financial expenditure ($200 billion per year) to treat the side effects of pharmacotherapy in people over 65 years of age.[12] Therefore, knowledge about the prevalence of pharmacological interactions in older patients, as well as the preventive methods available, is very important in terms of clinical practice and the efficient functioning of the healthcare system.

The topics of polypharmacy and pharmacological interactions have been analyzed extensively in Western Europe and the USA, but data from Central and Eastern Europe are limited. Most of the previous studies were conducted in the inpatient setting and were based on the Beers criteria,[13] the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criteria, the Screening Tool to Alert doctors to the Right Treatment (START) criteria,[14] or the Fit OR The Aged (FORTA) list.[15] The percentage of inappropriate drug combinations in European studies ranges from 9.8% to 38.5%, while it is 21.3% to 28.8% in the USA.[16–19]

Automated interaction analysis systems are a solution that could increase the recognition of drug interactions. Along with the computerization of healthcare systems, various forms of dedicated programs are available worldwide, such as online tools, applications for mobile telephone devices and software modules, even as part of a medical information network (e.g., the Surescripts network in the USA).[20–23] However, no such solution has yet been introduced on a national level in the Polish healthcare system.

Objectives

This study was performed to provide up-to-date data on the predisposing factors and prevalence of possible drug interactions in the Polish geriatric population. In addition, we aimed to popularize automated interaction analysis systems as auxiliary tools for conducting safe pharmacotherapy.

Materials and methods

Ethics approval

All participants provided written informed consent prior to participation in the study. The study was approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdańsk (approval No. 13/2020; 2020-04-21) and the Bioethics Commission at the Silesian Medical Chamber in Katowice (approval No. 26/2015; 2015-07-01). The study was conducted in compliance with the Declaration of Helsinki.

Study design

The study group consisted of participants from the nationwide, cross-sectional observational study NOninvasive Monitoring for Early Detection of Atrial Fibrillation (NOMED-AF). The main objective of the NOMED-AF study was to evaluate the prevalence of atrial fibrillation and its associated comorbidities. It included electrocardiographic monitoring, completion of a detailed questionnaire, a follow-up survey, blood pressure measurements, and blood/urine sample collection. A detailed description of the methodology and sampling of the NOMED-AF study was presented in a separate publication.[24]

Setting

The study was conducted from March 2017 to March 2019. Respondents were selected randomly by the Ministry of Digitization of the Republic of Poland based on a social security number database; therefore, they constituted a representative sample for Poland in terms of sex, age and place of residence. Based on a detailed questionnaire, the data were obtained by a trained nurse directly from the respondents, their families or their caregivers, followed by a presentation of the packaging of all of their drugs. The interview covered all preparations (prescription drugs, over-the-counter drugs, vitamins, nutritional preparations, and dietary supplements) taken at least once in the 2 weeks preceding the study (including drug name, form, single dose, and dosing frequency). The respondents provided information on diagnosed chronic diseases and were asked to present discharge cards from previous hospitalizations. Based on these data, individuals were assigned codes from the International Classification of Diseases, 10th Revision (ICD-10).

Participants and sample size

The specific inclusion criteria for this study were the use of at least 2 active substances included in the preparations and an agreement to provide information on the drugs taken. The study group comprised 2633 respondents aged ≥65 years, and consisted of 1309 women and

1324 men. The mean ± standard deviation (M ±SD) age of the entire sample was 78.0 (±7.9) years (78.9 (±7.9) years for women and 78.0 (±7.8) years for men).

Variables

The analysis of drug interactions between active substances was performed using Lexicomp® Drug Interactions by Wolters Kluwer Clinical Drug Information (www.wolterskluwer.com/en/solutions/lexicomp/), which enables a simultaneous analysis of 50 active substances. Detected interactions are classified into one of the 5 categories: A – no known interaction; B – no action required; C – monitor therapy; D – consider modifying therapy; X – avoid combination.

A further analysis of the detected drug interactions was based on the following variables: sex (male, female), age (in cohorts: 65–69, 70–74, 75–79, 80–84, 85–89, ≥90 years old), place of residence (village, small city with less than 50,000 inhabitants, medium-sized city with 50,000–200,000 inhabitants, large city with more than 200,000 inhabitants), level of education (primary, secondary/vocational, higher) and multimorbidity (determined using the Charlson Comorbidity Index (CCI)).

Qualitative analysis of pharmacotherapy was performed according to the Anatomical Therapeutic Chemical (ATC) classification.[25] The 2 most commonly used definitions were applied: taking 5 or more drugs was considered polypharmacy (PP), while excessive polypharmacy (EPP) was defined as taking more than 10 drugs.[26]

Statistical analyses

Post-stratification was used to adjust the sample structure against the Polish population in 2017. Data normality was verified using the Shapiro–Wilk test. The results are presented as percentages and median values with 1st and 3rd quartiles (Q1–Q3). A simple single-factor analysis based on the χ^2 test was performed in order to assess the relationship between one variable in relation to another. Multivariate logistic regression was performed for the whole set of variables, and odds ratios (ORs) were calculated together with 95% confidence intervals (95% CIs). The quality of the overall regression models was measured using Nagelkerke's R^2, and p-values for the models were calculated. A value of $p < 0.05$ was considered statistically significant. The analysis was performed using the statistical package R v. 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria) and SAS v. 9.4 TS Level 1M5 (SAS Institute, Inc., Cary, USA).

Results

The obtained results were stratified according to age structure in order to reflect the distribution of the Polish population over 65 years old in 2017; therefore, they reflect the geriatric population of Poland. A detailed description of the sampling and subsequent weighing can be found in the methodological publication.[24]

Analyses of all drug interactions

Number of drug interactions

At least 1 drug interaction was found in 81.2% of all individuals aged ≥65 years, with a median value of 3 (Q1–Q3: 1–6). Most often, older adults had 1–4 interactions (47.6%). At least 5 interactions were found in 33.7% of all respondents, more than 10 interactions in 12.3% of participants, and 4.7% of seniors had ≥15 interactions. Detailed data are presented in Table 1,2.

Drug interactions and number of drugs

The median value of interactions and the frequency of multiple interactions (5, 10 and 15) increased with the number of medications taken. Detailed data are presented in Table 1,2. A single-factor analysis showed a significant correlation between the number of interactions and the number of drugs taken ($p < 0.001$).

Drug interactions and sex

The median value of interactions was higher in men than in women: 3 (Q1–Q3: 1–7) and 2 (Q1–Q3: 1–6), respectively. Detailed data are presented in Table 1,2. The multivariate logistic regression model also showed that being male predisposed the participants to having ≥10 interactions ($p < 0.05$) (Table 3–5). The Nagelkerke's R^2 values for all 3 multivariate logistic regression models were relatively small.

Drug interactions and age

The median value of all interactions was the highest among seniors aged 85–89 years. The frequency of multiple interactions (5, 10 and 15) increased with age. Detailed data are presented in Table 1,2. A single-factor analysis showed a significant positive correlation between the number of interactions and age ($p < 0.001$); however, this was not confirmed by the multivariate logistic regression model (Table 3–5).

Drug interactions and place of residence

There were no noticeable differences in the median value of all interactions in relation to the place of residence. People living in rural areas had a lower frequency of multiple drug interactions (5, 10 and 15) than those living in urban areas. Detailed data are presented in Table 1,2. A single-factor analysis showed a significant correlation between the number of interactions and place of residence ($p < 0.001$); however, this was not confirmed by the multivariate logistic regression model (Table 3–5).

Table 1. Percentage of older people with drug interactions by gender (%)

Variable	All					Women					Men				
	number of all interactions					number of all interactions					number of all interactions				
	0	1–4	5–9	10–14	≥15	0	1–4	5–9	10–14	≥15	0	1–4	5–9	10–14	≥15
All	18.8	47.6	21.4	7.6	4.7	21.1	47.0	21.5	6.3	4.0	15.1	48.5	21.2	9.6	5.7
Age [years]															
65–69	25.0	48.4	18.0	5.5	3.1	30.8	47.4	17.8	2.9	1.1	17.2	49.5	18.4	9.0	5.8
70–74	22.7	45.7	19.8	6.9	4.9	26.5	44.5	18.7	6.1	4.2	17.2	47.5	21.3	8.0	6.0
75–79	12.9	47.9	25.0	9.1	5.1	14.3	47.7	25.1	7.3	5.6	10.6	48.3	25.0	11.8	4.4
80–84	13.8	48.5	22.7	9.4	5.6	13.2	47.6	25.4	9.5	4.3	15.2	50.2	17.1	9.2	8.4
85–89	8.8	50.4	26.2	9.1	5.5	7.3	50.8	27.3	8.4	6.2	12.4	49.3	23.7	10.7	4.0
90+	19.2	42.2	23.1	8.8	6.7	22.8	44.2	17.7	7.4	7.9	7.1	35.5	41.1	13.4	2.8
Number of drugs															
2–4	46.7	52.7	0.6	0.0	0.0	49.6	50.1	0.3	0.0	0.0	41.4	57.4	1.2	0.0	0.0
5–9	4.7	54.1	32.7	7.4	1.1	5.7	53.9	33.6	5.9	0.8	3.1	54.4	31.3	9.5	1.6
10+	0.0	3.6	31.6	30.6	34.2	0.0	4.7	33.9	28.9	32.5	0.0	2.1	28.5	32.9	36.6
Education															
Primary	15.0	49.0	22.0	9.7	4.4	15.6	48.8	22.4	8.4	4.8	13.6	49.4	21.1	12.5	3.4
Secondary/vocational	21.1	45.5	21.8	6.8	4.9	25.0	43.8	21.7	5.4	4.1	15.4	47.8	21.9	8.9	6.0
Higher	19.3	52.2	18.9	5.1	4.5	22.7	55.4	18.0	3.0	0.9	15.9	49.1	19.7	7.1	8.2
Residence															
Village	15.9	51.2	20.9	8.3	3.6	17.2	50.8	19.8	8.3	4.0	13.9	51.8	22.7	8.5	3.1
City <50 M	21.4	45.2	22.3	7.3	3.8	23.5	47.4	22.6	4.5	2.0	17.8	41.5	21.7	11.9	7.0
City 50–200 M	21.6	42.9	21.9	9.1	4.5	25.4	41.1	22.2	8.0	3.2	15.1	46.0	21.4	10.9	6.7
City >200 M	18.3	48.0	21.0	5.5	7.2	21.2	45.3	22.6	3.9	7.0	14.0	52.1	18.4	7.8	7.7

M – 1000. The results consider the use of a complex scheme of randomizing respondents. The data are presented after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table 2. Number of all drug interactions

Variable	Sample size, n			Median value (Q1–Q3)		
	women	men	all	women	men	all
All	1309	1324	2633	2 (1–6)	3 (1–7)	3 (1–6)
Age [years]						
65–69	226	218	444	1 (0–4)	3 (1–6)	2 (1–5)
70–74	273	257	530	2 (0–5)	3 (1–7)	2 (1–6)
75–79	243	285	528	3 (1–6)	4 (1–7)	3 (1–7)
80–84	255	228	483	4 (1–7)	3 (1–7)	3 (1–7)
85–89	181	225	406	4 (2–6)	4 (1–7)	4 (1–6)
90+	131	111	242	2 (1–7)	5 (2–8)	3 (1–7)
Number of drugs						
2–4	437	401	838	1 (0–1)	1 (0–2)	1 (0–1)
5–9	716	730	1446	4 (2–6)	4 (2–7)	4 (2–6)
10+	156	193	349	11 (8–16)	13 (9–18)	12 (8–17)
Education						
Primary	598	424	1022	3 (1–6)	3 (1–7)	3 (1–6)
Secondary/vocational	590	680	1270	2 (0–6)	3 (1–7)	3 (1–6)
Higher	115	216	331	2 (1–4)	3 (1–7)	2 (1–5)
Residence						
Village	528	461	989	3 (1–6)	3 (1–6)	3 (1–6)
City <50 M	315	327	642	2 (1–5)	3 (1–7)	3 (1–6)
City 50–200 M	246	261	507	2 (0–6)	3 (1–8)	2 (1–7)
City >200 M	220	275	495	3 (1–6)	3 (1–7)	3 (1–6)

M – 1000. The results are presented as medians with the 1st and 3rd quartile (Q1–Q3). The results take into account the use of a complex scheme of randomizing respondents. The data are presented after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table 3. Logistic regression model results for predisposing factors to at least 5 drug interactions

Variable	OR	95% CI	p-value
Sex			
Women (ref)	–	–	–
Men	1.18	0.98–1.43	0.088
Age [years]			
65–69 (ref)	–	–	–
70–74	0.84	0.56–1.27	0.053
75–79	0.68	0.45–1.02	0.792
80–84	0.50	0.32–0.78	0.181
85–89	0.63	0.39–1.01	0.097
90+	0.94	0.55–1.61	0.702
Education			
Primary (ref)	–	–	–
Secondary/occupational	1.17	0.96–1.43	0.120
Higher	1.16	0.86–1.56	0.334
Charlson Comorbidity Index			
2 (ref)	–	–	–
3–6	4.62	2.67–8.01	<0.001
7+	13.21	7.40–23.57	<0.001
Residence			
Village (ref)	–	–	–
City <50 M	1.00	0.80–1.25	0.990
City 50–200 M	1.05	0.82–1.34	0.687
City >200 M	1.00	0.77–1.29	0.976

OR – odds ratio; 95% CI – 95% confidence interval; M – 1000; ref – reference. Nagelkerke's R^2: 0.11; $p < 0.001$. The results take into account the use of a complex scheme of randomizing respondents. The data are presented after weighing the sample in relation to the structure of the Polish population aged 65 in 2017.

Table 4. Logistic regression model results for predisposing factors to at least 10 drug interactions

Variable	OR	95% CI	p-value
Gender			
Women (ref)	–	–	–
Men	1.50	1.14–1.96	0.003
Age [years]			
65–69 (ref)	–	–	–
70–74	0.77	0.50–1.20	0.254
75–79	0.94	0.61–1.44	0.763
80–84	0.84	0.54–1.31	0.442
85–89	0.66	0.41–1.06	0.082
90+	0.66	0.39–1.13	0.133
Education			
Primary (ref)	–	–	–
Secondary/occupational	1.04	0.79–1.38	0.778
Higher	1.06	0.71–1.60	0.764
Charlson Comorbidity Index			
2 (ref)	–	–	–
3–6	11.05	2.63–46.50	0.001
7+	36.08	8.45–154.09	<0.001
Residence			
Village (ref)	–	–	–
City <50 M	1.02	0.74–1.40	0.915
City 50–200 M	1.15	0.82–1.61	0.420
City >200 M	1.06	0.74–1.51	0.758

OR – odds ratio; 95% CI – 95% confidence interval; M – 1000; ref – reference. Nagelkerke's R^2: 0.10; $p < 0.001$. The results take into account the use of a complex scheme of randomizing respondents. The data are presented after weighing the sample in relation to the structure of the Polish population aged 65 in 2017.

Drug interactions and education

There were no noticeable differences in the median value of all interactions in relation to the education level. As education level increased, there was a reduction in the frequency of ≥5 and ≥10 interactions. A different trend was observed in the case of ≥15 interactions: the lowest percentage was found among people with primary education and the highest among people with secondary/vocational education. Detailed data are presented in Table 1,2. A single-factor analysis showed a significant correlation between the number of interactions and education level ($p < 0.001$), but this was not confirmed by the multivariate logistic regression model (Table 3–5).

Analysis of drug interactions by category

The percentage distribution among different categories of detected drug interactions was 0.6% in category A, 11.6% in category B, 77.9% in category C, 8.7% in category D, and 1.2% in category X. Further analysis focused on categories C, D and X due to their clinical importance and the possibility/necessity of intervention.

We found that 75.8% of all study participants had ≥1 interaction from category C, with the highest percentage among respondents aged 85–89 years, living in rural areas, with primary education, who took ≥10 drugs. Detailed percentage data are presented in Supplementary Fig. 1. Factors predisposing to interactions from category C included male sex, a high number of drugs and multimorbidity, whereas living in a small city had a protective effect.

The analysis showed that 24.3% of all study participants had ≥1 interaction from category D, with the highest percentage among respondents aged 85–89 years, living in rural areas, with primary education, who took ≥10 drugs. Detailed percentage data are presented in Supplementary Fig. 2. A high number of drugs taken predisposed respondents to interactions from category D, whereas male sex and living in small and big cities had protective effects.

We found that 4.3% of all study participants had ≥1 interaction from category X, with the highest percentage

Table 5. Logistic regression model results for predisposing factors to at least 15 drug interactions

Variable	OR	95% CI	p-value
Sex			
Women (ref)	–	–	–
Men	1.37	0.89–2.10	0.151
Age [years]			
65–69 (ref)	–	–	–
70–74	1.01	0.51–2.01	0.973
75–79	0.98	0.49–1.95	0.947
80–84	0.92	0.46–1.87	0.825
85–89	0.75	0.35–1.60	0.458
90+	0.44	0.17–1.15	0.093
Education			
Primary (ref)	–	–	–
Secondary/occupational	1.41	0.89–2.22	0.144
Higher	1.42	0.75–2.67	0.282
Charlson Comorbidity Index			
2 (ref)	–	–	–
3–6	4804075.21	0.00–Inf	0.975
7+	14383699.59	0.00–Inf	0.974
Residence			
Village (ref)	–	–	–
City <50 M	1.01	0.60–1.70	0.974
City 50–200 M	1.12	0.65–1.94	0.690
City >200 M	1.53	0.90–2.61	0.116

OR – odds ratio; 95% CI – 95% confidence interval; M – 1000; ref – reference; Inf – infinite. Nagelkerke's R^2: 0.08; $p < 0.001$. The results take into account the use of a complex scheme of randomizing respondents. The data are presented after weighing the sample in relation to the structure of the Polish population aged 65 in 2017

among the oldest individuals (≥90 years), from large cities, with primary education, who took ≥10 drugs. Detailed percentage data are presented in Supplementary Fig. 3. Factors predisposing to interactions from category X included a high number of drugs taken and advanced age (≥90 years).

Analysis of drugs being taken

The median value (Q1–Q3) of all drugs consumed was 5 (4–8); it was slightly higher in men (6 (4–8)) than in women (5 (3–8)). Polypharmacy was reported in 63.4% of all individuals over 65 years of age, whereas EPP was reported in 10.4%. The median value (Q1–Q3) was 5 (3–7) for prescription drugs and 1 (0–1) for nonprescription drugs. Detailed data concerning the consumption of all drugs are presented in Supplemenary Table 1,2.

A qualitative analysis of pharmacotherapy based on the ATC classification showed that older adults most often used preparations affecting the cardiovascular system, with drugs acting on the renin–angiotensin–aldosterone system being used most often, followed by β-blockers, hypolipidemic drugs and diuretics. The 2nd main group of drugs were preparations influencing blood and the hematopoietic system, including anticoagulants and preparations used in the treatment of anemia. The 3rd main group of drugs included preparations affecting the gastrointestinal tract, such as antidiabetic drugs, followed by preparations to reduce gastric juice acidity and supplements for mineral deficiency. Detailed characteristics of the pharmacotherapy in relation to the ATC classification are presented in Supplementary Table 3.

Comorbidities

The median value (Q1–Q3) of the CCI was 4 points (3–6); it was 4 points (3–6) in men and 4 points (3–5) in women. A result of ≥7 points (estimated chance of 10-year survival at level of 0%) was obtained for 16.3% of participants, while 6 points (2% chance of surviving 10 years) was achieved by just over every tenth respondent (11.1%). In comparison, a 90% chance of surviving 10 years (2 points) was estimated for 11.7% of all seniors. The distribution of the CCI is presented in Supplementary Fig. 4. The most common chronic diseases were arterial hypertension, osteoarthritis, ischemic heart disease, and diabetes.

Discussion

In its 2019 report, the World Health Organization (WHO) underlined that PP is a widespread concern in many countries around the world.[27] In this study, the prevalence of PP among people over 65 years was similar to the PP rate reported in the national study assessing health conditions of elderly Poles – "Polsenior2".[28] The data from both studies show that more than half of all seniors were taking at least 5 or more drugs.

Multimorbidity is a well-documented factor predisposing to PP.[6] An average senior in our study group was diagnosed with 4 chronic conditions and was being treated with 5 drugs. The most frequently used drug groups, as well as the most prevalent chronic diseases in our study, were similar to other geriatric populations.[29] The literature provides a broad and accurate description of the negative medical, economic and social consequences of adverse drug reactions emerging from polypharmacy and numerous drug interactions. The most dangerous are cognitive impairment, weight loss and malnutrition, falls and fractures, rehospitalization, reduced quality of life, and death.[30–32]

Several studies have been conducted to assess the prevalence of drug interactions in older adults using the Lexicomp® Drug Interactions Tool. Compared to out study, a study in Croatia, which included 354 people over 65 years of age, showed not only a higher number of clinically important drug interactions but also a higher percentage of participants with ≥1 category C (91.2% compared

to 75.8%), category D (50.8% compared to 24.3%) and category X interactions (9.1% compared to 4.3%). These differences may be explained by the fact that the Croatian respondents were inpatients, and the analysis considered medications upon hospital discharge. In contrast, the participants in our study were home-dwelling adults, presumably with relatively lower morbidity.

In a study conducted in Bulgaria, 248 participants diagnosed with heart failure (New York Heart Association (NYHA) class 2–4) were assessed for drug interactions upon hospital discharge. The number of all detected drug interactions (categories A, B, C, D, and X) was higher than that determined in our study. In both studies, the number of category D interactions was similar; however, our population was characterized by a higher occurrence of category X interactions.[34] These differences may be explained by the inclusion of younger adults (aged <60 years, 15% of the study cohort) in the Bulgarian research.

A study in Slovenia on a group of 243 adults over 65 years old in an ambulatory setting with a diagnosed cardiovascular disease (according to the ICD-10 classification) revealed a higher percentage of the most dangerous drug interactions (category X) than that in our study (16.5% compared to 4.3%).[35] This difference could be explained by the fact that the authors included only older adults with EPP (≥10 drugs) who carried a greater risk of drug interactions than participants who were taking fewer drugs.

Data on the frequency of possible drug interactions assessed with an automated analysis program concerning the Polish geriatric population are lacking. To our knowledge, this is the first study to report the prevalence of drug interactions using the Lexicomp® Drug Interactions Tool.

Our findings indicate that there is a significant correlation between the increasing number of interactions and the high number of drugs taken, advanced age, primary level of education, living in rural areas, and multimorbidity. The influence of age and the number of drugs taken on the frequency of drug interactions has already been documented, and our results are consistent with the current literature.[14,36–38] Studies defining a direct relationship between drug interactions and level of education are lacking. However, the connection between low educational attainment and polypharmacy,[39] noncompliance with treatment[40] and less positive beliefs toward medication[41] has been confirmed, which may explain the more frequent prevalence of drug interactions in our study. An increased risk of drug interactions in older adults from rural areas has been observed in other studies,[42] but the reasons are unclear. Presumably, areas with a larger population have greater access to healthcare and academic medical centers, which may lead to a lower prevalence of drug interactions.[43] Finally, the results of the multivariate logistic regression model showed that the strongest predisposing factor to drug interactions was multimorbidity, which has been observed in other populations.[44,45]

Limitations

There are some limitations that need to be acknowledged and addressed regarding the present study. The use of an automatic interaction analysis system led to low specificity.[46,47] Furthermore, unlike the START/STOPP criteria, the Beers criteria or the FORTA list, we were not able to fully address the clinical context of the detected drug interactions. This is particularly important in older patients with multiple morbidities who require multidrug regimens to treat chronic diseases in accordance with the guidelines of evidence-based medicine. Finally, the clinical picture of drug interactions consists not only of drug–drug interactions but also drug–diet, drug–disease and drug–patient interactions,[48–50] which we did not investigate.

Conclusions

Our study delivers up-to-date data from a representative sample of older, home-dwelling adults in Poland. Despite being based on theoretical knowledge, our results highlight the important problem of possible drug interactions in the Polish geriatric population, which constitutes a major challenge for clinicians and disrupts the therapeutic process. Tools supporting the identification of patients with inappropriate polypharmacy[51] should be further developed and popularized in the healthcare community, along with other preventive measures, such as systematic reviews of pharmacotherapy and support from clinical pharmacologists. Future studies are needed to assess the clinical context of drug interactions detected with automated analysis systems.

Supplementary materials

The supplementary materials are available at https://doi.org/10.5281/zenodo.7027709. The package contains the following files:

Supplementary Fig. 1. Percentage of people with at least 1 drug interaction from category C (monitor therapy) broken down by main variables.

Supplementary Fig. 2. Percentage of people with at least 1 drug interaction from category D (consider modifying therapy) broken down by main variables.

Supplementary Fig. 3. Percentage of people with at least 1 drug interaction from category X (avoid combination) broken down by main variables.

Supplementary Fig. 4. Distribution of the Charlson Comorbidity Index (CCI) values in the entire population by gender.

Supplementary Table 1. Percentage of older people taking drugs.

Supplementary Table 2. Number of all drug interactions.

Supplementary Table 3. Percentage of people taking drugs based on the Anatomical Therapeutic Chemical

(ATC) classification (%). Detailed results in subgroups are presented for values above 5%.

Supplementary Table 4. Results of data normality checked with the Shapiro–Wilk test.

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Figure 1. Percentage of people with at least one drug interaction from category C (monitor therapy) broken down by main variables.

Note: The results presented in the figure take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and in 2017. M – one thousand.

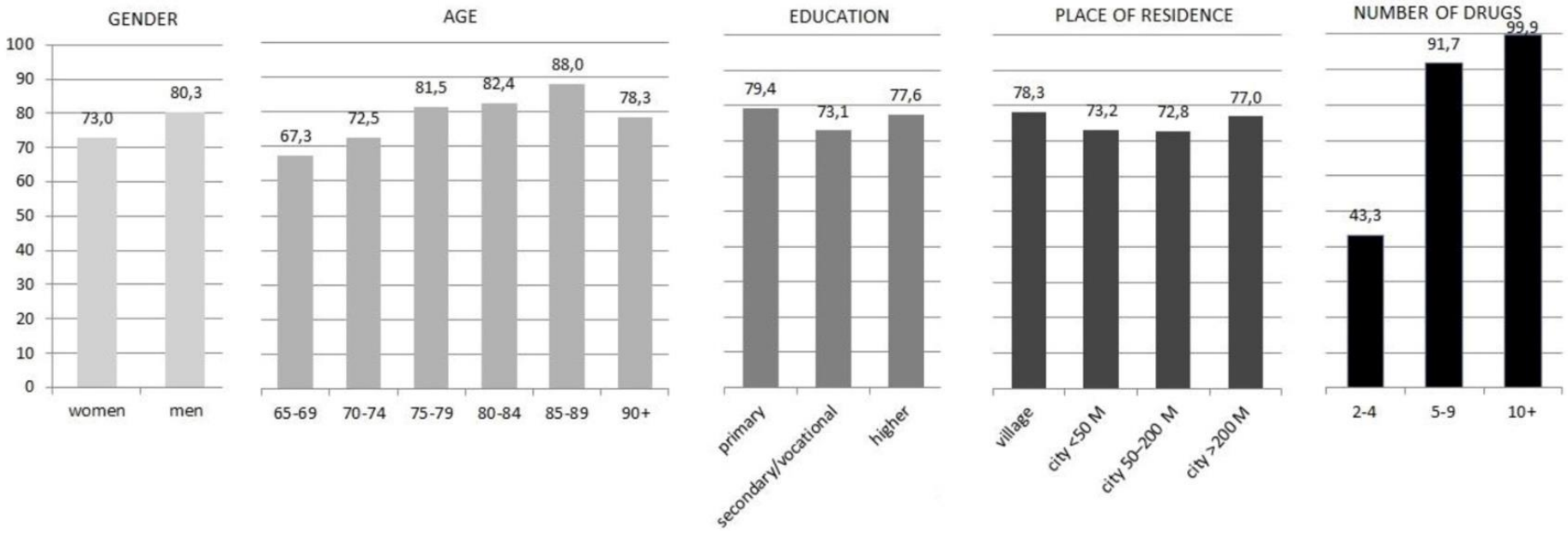

Figure 2. Percentage of people with at least one drug interaction from category D (consider modifying therapy) broken down by main variables.

Note: The results presented in the figure take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and in 2017. M – one thousand.

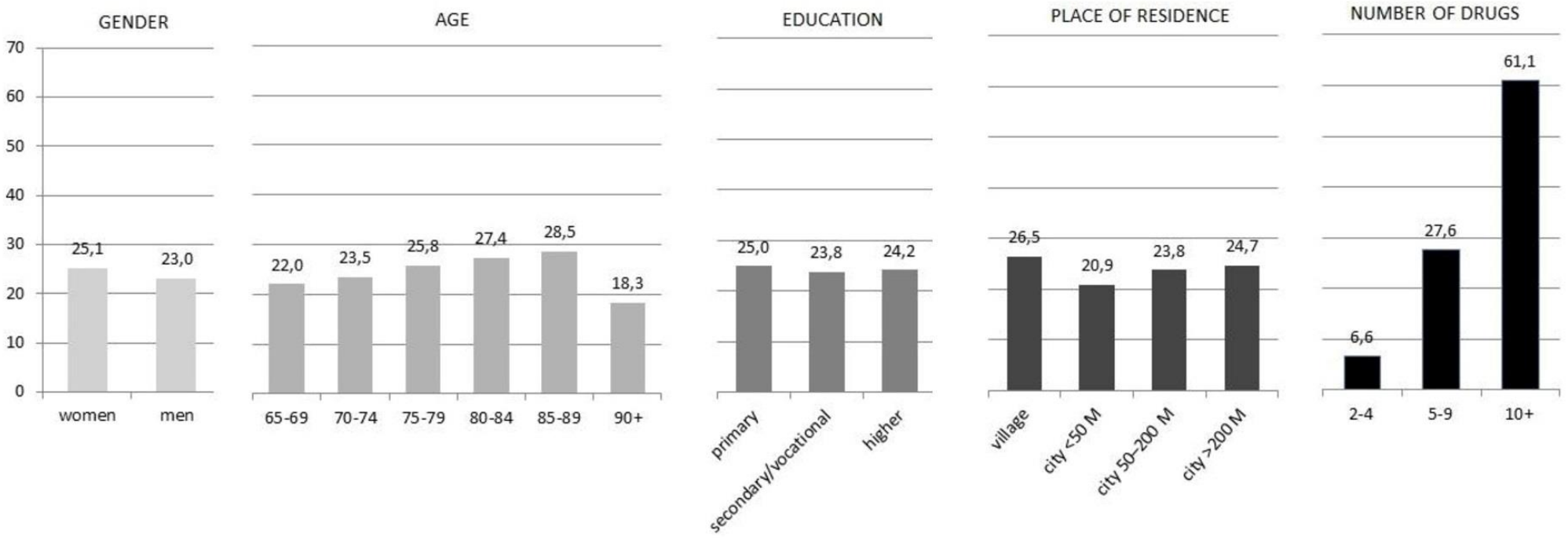

Figure 3. Percentage of people with at least one drug interaction from category X (avoid combination) broken down by main variables.

Note: The results presented in the figure take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and in 2017. M – one thousand.

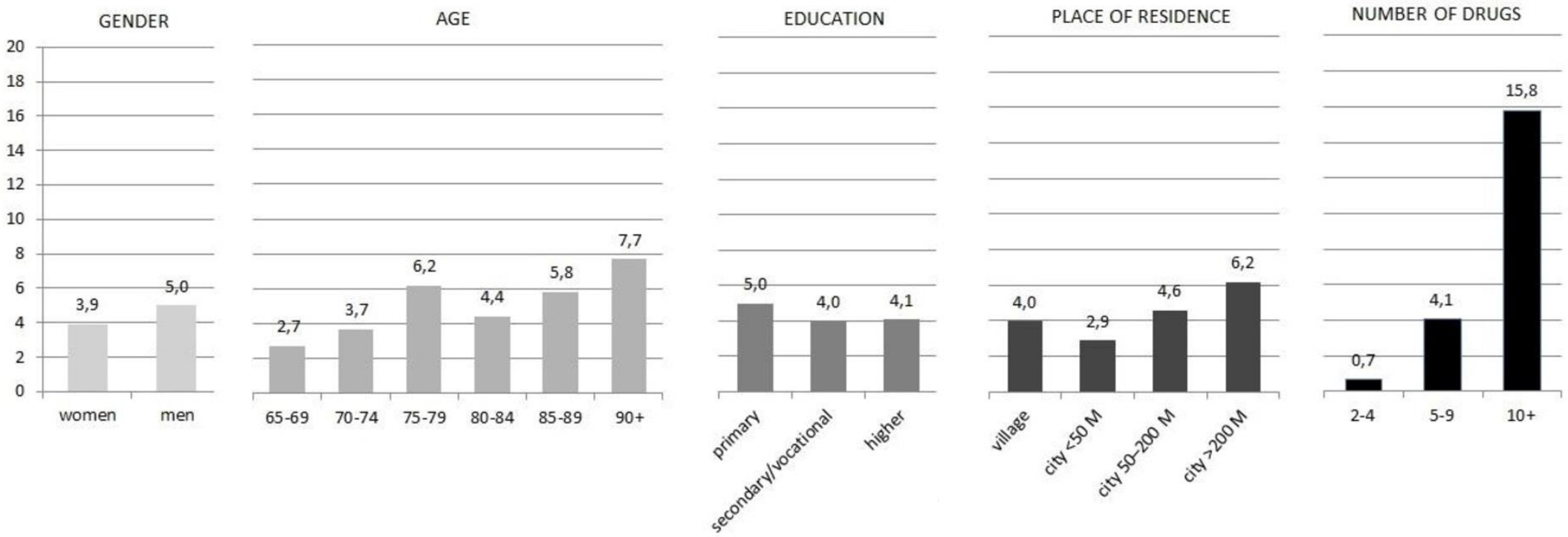

Table 1. Percentage of older people taking drugs (%).

	Number of all drugs			Number of prescription drugs				Number of non–prescription drugs			
	2–4	5–9	≥10	0–1	2–4	5–9	≥10	0–1	2–4	5–9	≥10
Sex											
All	36.6	53.1	10.4	3.8	40.9	48.7	6.6	92.9	6.9	0.2	0
Women	38.3	52.8	8.9	4.6	41.3	48.7	8.7	91.9	7.9	0.2	0
Men	33.9	53.4	12.7	2.5	40.2	48.6	5.3	94.6	5.3	0.1	0
Age (years)											
65–69	48.8	44.4	6.9	5.8	50.6	39.0	4.6	94.0	5.9	0.1	0
70–74	39.7	51.3	9.0	3.4	45.1	45.9	5.6	96.7	3.3	0	0
75–79	29.9	57.7	12.3	3.3	35.3	53.4	8.0	91.1	8.4	0.5	0
80–84	26.4	60.9	12.7	2.4	31.0	58.5	8.1	88.0	11.9	0.1	0
85–89	23.1	61.7	15.2	2.5	28.4	58.9	10.2	91.6	7.9	0.4	0
90+	30.5	55.9	13.6	1.7	37.4	53.0	7.9	92.8	7.2	0	0

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table 2. Number of all drug interactions. The results are presented as medians with the first and third quartiles.

	All drugs			Prescription drugs			Non–prescription drugs		
	Women	Men	All	Women	Men	All	Women	Men	All
Total	5 (3-8)	6 (4-8)	5 (4-8)	5 (3-7)	5 (3-7)	5 (3-7)	0 (0-1)	1 (0-1)	1 (0-1)
Age (years)									
65–69	4 (3-6)	5 (4-7)	5 (3-7)	4 (3-6)	5 (3-7)	4 (3-6)	0 (0-1)	1 (0-1)	0 (0-1)
70–74	5 (3-7)	6 (4-7)	5 (4-7)	5 (3-7)	5 (3-7)	5 (3-7)	0 (0-1)	1 (0-1)	0 (0-1)
75–79	6 (4-8)	6 (4-8)	6 (4-8)	5 (3-7)	5 (4-8)	5 (3-7)	0 (0-1)	1 (0-1)	1 (0-1)
80–84	6 (5-8)	6 (4-9)	6 (4-8)	6 (4-8)	5 (4-8)	6 (4-8)	1 (0-1)	1 (0-1)	1 (0-1)
85–89	6 (5-8)	6 (4-8)	6 (5-8)	6 (4-8)	6 (4-7)	6 (4-8)	1 (0-1)	1 (0-1)	1 (0-1)
90+	6 (4-8)	7 (5-9)	6 (4-8)	5 (3-7)	6 (4-8)	5 (3-7)	1 (0-1)	1 (0-1)	1 (0-1)

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table 3. Percentage of people taking drugs based on the anatomical-therapeutic-chemical classification (ATC) (%). Detailed results in subgroups are presented for values above 5%.

ATC Code		Women	Men	All
A - Alimentary tract and metabolism		44.9	45.7	45.2
	A02	18.3	17.9	18.1
	A10	20.4	24.3	21.9
	A12	13.2	12.7	13.0
B - Blood and hematopoietic system		45.9	55.0	49.5
	B01	44.6	53.9	48.3
C - Cardiovascular system		83.4	80.0	82.1
	C01	14.1	10.7	12.8
	C02	2.0	10.7	5.4
	C03	34.0	30.1	32.4
	C07	51.8	51.9	51.9
	C08	22.6	19.3	21.3
	C09	57.1	57.2	57.2
	C10	41.7	46.8	43.7
D - Medicines used in dermatology		0.1	0.2	0.1
G - Genitourinary system and sex hormones		2.0	25.5	11.3
	G04	1.7	25.3	11.0
H - Hormones. excluding sex hormones and insulin		17.2	6.0	12.8
	H03	15.9	5.0	11.6
J - Systemic anti-infective drugs		1.6	1.3	1.5
L - Antineoplastic and immunomodulating drugs		2.0	1.3	1.7
M - Musculoskeletal system		15.6	15.0	15.4
	M01	6.2	4.3	5.5
	M04	5.8	9.3	7.2
N - Nervous system		33.5	20.2	28.3
	N02	6.8	3.4	5.4
	N05	11.2	4.4	8.5
	N06	20.3	11.2	16.8
P - Antiparasitic drugs. insecticides and repellants		0.2	0	0.1
R - Respiratory system		9.9	10.1	10.0
	R03	7.4	9.2	8.1
S - Sensory organs		1.8	1.4	1.7

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Figure 4. Distribution of the Charlson Comorbidity Index (CCI) values in the entire population and by sex.

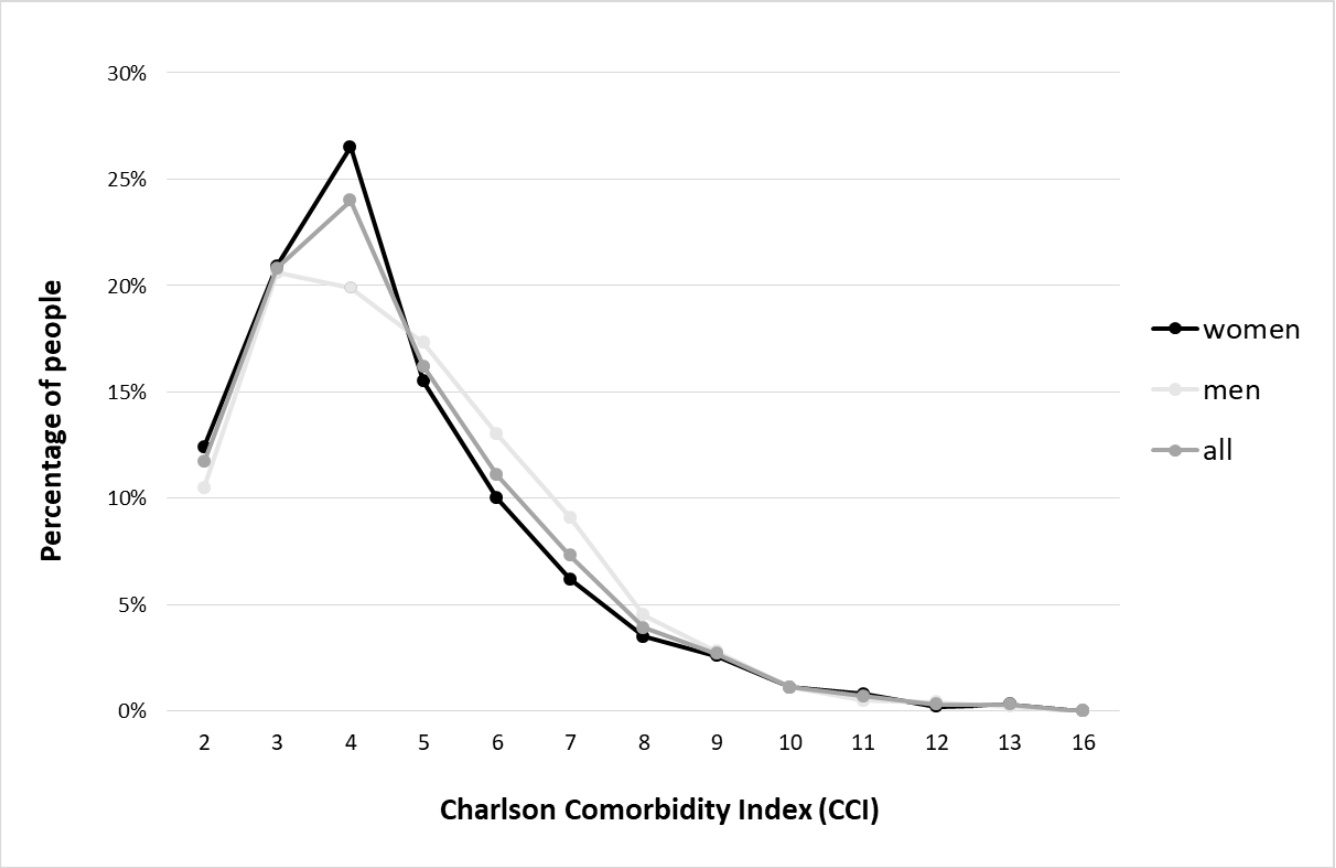

Table 4. Results of data normality checking with Shapiro-Wilk test.

	Variable	W	P-value
Sex			
Women	Number of drugs	0.9552713	<0.001
Men	Number of drugs	0.9560467	<0.001
Sex			
Women	Number of interactions	0.8005437	<0.001
Men	Number of interactions	0.8170585	<0.001
Age (years)			
65–69	Number of interactions	0.7796551	<0.001
70–74	Number of interactions	0.7593731	<0.001
75–79	Number of interactions	0.8154239	<0.001
80–84	Number of interactions	0.8259945	<0.001
85–89	Number of interactions	0.8210102	<0.001
90+	Number of interactions	0.8583622	<0.001
Education			
Primary	Number of interactions	0.8104134	<0.001
Secondary/occupational	Number of interactions	0.8054972	<0.001
Higher	Number of interactions	0.8082684	<0.001

	Variable	W	P-value
Residence			
Village	Number of interactions	0.8102124	<0.001
City <50 M	Number of interactions	0.8288142	<0.001
City 50–200 M	Number of interactions	0.7897155	<0.001
City >200 M	Number of interactions	0.8028310	<0.001
Sex			
Women	Charlson Comorbidity Index	0.9075677	<0.001
Men	Charlson Comorbidity Index	0.9347815	<0.001

M – one thousand.

ORIGINAL ARTICLE

Polypharmacy among elderly patients in Poland: prevalence, predisposing factors, and management strategies

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KEY WORDS

geriatrics, multimorbidity, pharmaceutical services, polypharmacy, predisposing factors

ABSTRACT

INTRODUCTION The world's elderly population is growing dramatically. Pharmacotherapy in seniors is particularly challenging due to changes in metabolism, multimorbidity, and a great interest in nonprescription drugs.

OBJECTIVES We aimed to provide up-to-date data on pharmacotherapy in the geriatric population of Poland, to determine factors predisposing to polypharmacy and excessive polypharmacy, and to identify seniors who are most likely to require multidisciplinary interventions in the field of pharmacotherapy.

PATIENTS AND METHODS We analyzed the use of all prescription and nonprescription drugs taken within 2 weeks preceding the study in a representative national sample of 3014 home-dwelling seniors aged over 65 years. The variables of age, sex, place of residence, level of education, and multimorbidity were considered. Poststratification was used to balance the sample structure to match the Polish population of 2017.

RESULTS Consumption of at least 1 drug was reported by 90.7% of the participants, and the mean number of drugs used was 5.01 (95% CI, 4.87–5.15). At least 1 nonprescription drug was used by 44.2% of the respondents, with a mean number of 0.52 (95% CI, 0.49–0.55). More than 5 drugs were taken by 53.5% of the entire population, while the use of more than 10 drugs was reported by 8.7% of the respondents, with multimorbidity as the most predisposing factor. Single-pill combinations accounted for 27.2% of medications.

CONCLUSIONS The high prevalence of polypharmacy resulting from multimorbidity confirms the need for the implementation of combined medical and pharmaceutical care of the geriatric patients.

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INTRODUCTION A significant increase in life expectancy is considered one of the greatest social achievements of the 20th century. However, this longevity, together with declining fertility rates, have led to a progressive aging of the population. The number of individuals over the age of 65 years is projected to increase from 524 million in 2010 (8% of the world's population) to 1.5 billion (16% of the world's population) by 2050.[1]

Pharmacological therapy in seniors is particularly complicated due to progressive aging-related changes in metabolism and the coexistence of multiple diseases that require complex drug regimens.[2] Additionally, there has been a growing interest among older adults in over-the-counter (OTC) drugs that are widely available on the pharmaceutical market.[3]

The literature provides a broad and thorough description of the negative medical, economic,

WHAT'S NEW?

Our study reveals that Polish home-dwelling seniors consume a high number of prescription and nonprescription drugs. The factors predisposing to polypharmacy and excessive polypharmacy include multimorbidity, male sex, age of 85 to 89 years, low level of education, and living in a small or medium-sized city. Moreover, we provide unique data on the consumption of single-pill combinations in elderly Polish patients. Polypharmacotherapy can have negative health consequences; therefore, actions must be taken in the field of complex medical and pharmaceutical care of the geriatric patients. Various management strategies are available to optimize pharmacotherapy and prevent medication-related problems. Unfortunately, there is still limited clinical evidence for long-term benefits of these interventions in elderly people. Our results provide additional information supporting the introduction of coordinated pharmaceutical care in Poland.

and social consequences of polypharmacy (PP), defined as taking 5 or more drugs, and excessive polypharmacy (EPP), which refers to using at least 10 drugs.[4] The negative implications of PP and EPP are a strong motivation for the continuous monitoring of pharmacotherapy in older adults in many countries around the world.[5-8] There has also been a growing recognition of the importance of deprescribing, defined as the process of withdrawal or dose reduction of a drug for which the risk outweighs the benefit in specific patients.[9] The available methods include physician-led interventions, clinical decision support systems, prescriber education programs, pharmacist-led medication reviews, direct-to-patient education, and multidisciplinary interventions.[10] There is accummulating evidence for the safety and clinical effectiveness of deprescribing; unfortunately, the long-term benefits associated with the intervention are often not sustainable or clinically meaningful.[11] Moreover, there is a lack of robust evidence for the effectiveness of deprescribing in seniors with multimorbidity and frailty, as these patients are routinely excluded from clinical trials.[10]

Nevertheless, the need to explore the implementation of deprescribing into routine clinical practice is of major importance across health care settings worldwide. An example of such an intervention is a new regulation introduced by the Ministry of Health of the Republic of Poland in December 2021, which aims to implement pharmaceutical support in the form of drug interviews as a new service in the Polish health care system.[12]

The objective of this study was to provide an up-to-date assessment of pharmacotherapy in the geriatric population of Poland. Furthermore, we aimed to determine the factors predisposing this population to PP and EPP, and to identify the seniors who are most likely to require multidisciplinary interventions in the field of pharmacotherapy.

PATIENTS AND METHODS The study group consisted of patients who participated in the NOMED-AF (NOninvasive Monitoring for Early Detection of Atrial Fibrillation), a nationwide, cross-sectional, observational study conducted from 2017 to 2019. The participants were randomly selected by the Ministry of Digital Affairs of the Republic of Poland from the social security number database; therefore, they constituted a sample representative of the Polish population in terms of sex, age, and place of residence. A detailed description of the methodology of the NOMED-AF study was presented in a separate publication.[13] All participants provided their written informed consent prior to enrolment. The study was approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdansk (13/2020; 2020-04-21) and by the Bioethics Commission at the Silesian Medical Chamber in Katowice (26/2015; 2015-07-01).

The specific inclusion criterion for the present study was the consent to provide information on taken drugs. We analyzed the pharmacotherapy in 3014 respondents, including 1479 women and 1535 men over 65 years of age. The mean (SD) age of the entire sample was 77.5 (7.9) years, and the mean age for separately men and women was also 77.5 (7.9) years. The data were obtained by trained nurses using a detailed questionnaire, either directly from the respondents or from their family members or caregivers. During the interviews, the respondents or their representatives were asked to present the packaging of all the drugs they had consumed at least once in the 2 weeks preceding the study. The interviewer gathered information on each medication, including drug name, form, single dose, and dosing frequency. In the analysis, we considered the number of pills (not active substances) of prescription or nonprescription / OTC drugs, based on the database of the Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products.[14] The products not listed in this database, including the majority of dietary supplements, which lack clear classification and information on exact formulations, were excluded from the analysis. If the same substance was sold simultaneously as a prescription drug and an OTC preparation, it was classified as the former category.

The analysis of pharmacotherapy was performed for all drugs together and independently for prescription and nonprescription drugs, taking into account the following variables: sex (male, female), age (in cohorts: 65–69, 70–74, 75–79, 80–84, 85–89, >90 years), place of residence (village, small city with <50 000 inhabitants, medium-sized city with 50 000 to 200 000 inhabitants, large city with >200 000 inhabitants), and the level of education (primary, secondary / vocational, higher). We also noted the frequency of single-pill combinations (SPCs), which are defined as drugs that include 2 or more active ingredients combined in a single-dose form. Qualitative analysis of pharmacotherapy was performed according

TABLE 1 Pharmacotherapy in the elderly population of Poland[a]

Parameter		Number of all drugs				Number of prescription drugs				Number of nonprescription drugs			
		0	1–4	5–9	≥10	0	1–4	5–9	≥10	0	1–4	5–9	≥10
Sex	All	9.3	37.1	44.8	8.7	11.2	41.6	41.5	5.7	55.8	44.0	0.1	0
	Women	7.9	39.2	45.2	7.6	10.3	42.8	42.3	4.6	57.5	42.3	0.1	0
	Men	11.4	33.9	44.2	10.5	12.7	39.8	40.3	7.3	53.1	46.7	0.1	0
Age, y	65–69	12.7	47.8	34.2	5.3	15.4	50.6	30.4	3.6	60.9	39.0	0.1	0
	70–74	11.6	38.7	42.3	7.4	12.7	44.3	38.3	4.7	60.0	40.0	0	0
	75–79	7.5	30.0	51.5	11.0	9.5	35.3	48.0	7.2	54.0	45.5	0.4	0
	80–84	5.0	27.6	55.8	11.7	6.9	31.9	53.8	7.5	45.5	54.4	0.1	0
	85–89	5.0	24.6	56.4	13.9	6.6	29.4	54.5	9.4	51.4	48.2	0.2	0.2
	≥90	1.1	32.0	53.8	13.1	1.5	39.9	51.0	7.6	44.0	56.0	0	0
Level of education	Primary	9.2	33.1	49.2	8.5	11.6	38.3	44.6	5.4	53.4	46.6	0	0
	Secondary/vocational	9.8	39.3	41.9	9.1	11.4	42.7	39.9	5.9	58.2	41.6	0.2	0
	Higher	7.8	38.5	45.6	8.1	9.1	45.4	40.1	5.5	52.5	47.2	0.2	0
Place of residence	Village	9.2	36.6	46.9	7.3	11.2	41.8	42.6	4.4	54.5	45.5	0	0.1
	City <50 000 inhabitants	7.8	37.9	48.3	6.1	8.8	42.8	44.2	4.3	55.8	44.0	0.2	0
	City 50 000–200 000 inhabitants	8.9	39.4	39.2	12.5	11.1	42.0	38.6	8.4	59.0	41.0	0.1	0
	City >200 000 inhabitants	11.3	35.5	42.2	10.9	13.9	39.8	39.2	7.1	55.5	44.1	0.3	0

Data are presented as the percentage of patients.

a The results presented in all tables are based on a complex scheme of randomization of respondents. The data were obtained after weighing the sample in relation to the structure of the Polish population aged ≥65 years in 2017.

to the anatomical-therapeutic-chemical (ATC) classification.[15]

The respondents provided information on diagnosed chronic diseases and were asked to present discharge cards from previous hospitalizations. Based on these data, codes from the *International Classification of Diseases, Tenth Revision* (ICD-10) were assigned. The Charlson Comorbidity Index (CCI) was used to determine the degree of multimorbidity. We applied the 2 most commonly used definitions: taking 5 or more drugs was considered PP, while EPP was defined as the use of more than 10 drugs.[16]

Statistical analysis Poststratification was used to adjust the sample structure to match the Polish population of 2017. The results are presented as percentages, medians with interquartile ranges (IQRs), and means with 95% CIs. Normality of the data distribution was verified using the Shapiro–Wilk test—some of the variables were not normally distributed. Stepwise logistic regression was performed, and odds ratios with 95% CIs were calculated. The analysis was performed using the R statistical package, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.4 TS Level 1M5 (SAS Institute, Inc., Cary, North Carolina, United States). A *P* value below 0.05 was considered significant.

RESULTS

The results were stratified according to the age structure to reflect the Polish population aged over 65 years in 2017. Therefore, the results are representative of the general population of Poland. A detailed description of sampling and subsequent weighing can be found in the methodological publication.[13]

Consumption of all drugs Consumption of at least 1 drug was admitted by 90.7% of all respondents, and was more common among women (92.1%) than men (88.6%). The mean number (95% CI) of all drugs consumed was 5.01 (4.87–5.15), and the median value (IQR) was 5 (3–7). Most respondents took 5 to 9 pills per day. Detailed data concerning the consumption of all drugs are presented in TABLES 1 and 2.

PP was identified in 53.5% of all individuals over 65 years old, most frequently in men, in the age group of 85 to 89 years, in the participants with primary education, and those living in small cities. The strongest predisposing factor for PP was multimorbidity. Of note, in the age groups of 70 to 74 years and 80 to 84 years, as well as in the respondents older than 90 years, the risk of PP was lower than in the youngest cohort (65–69 years). Other factors had no influence on the frequency of PP (TABLE 3).

EPP was identified in 8.7% of all respondents, most frequently in men, in the age group of 85 to 89 years, in the participants with secondary/vocational education, and those living in medium-sized cities. The strongest predisposing factor for EPP was multimorbidity. Male sex and living in medium-sized or large cities were also relevant variables, whereas other factors were not significant (TABLE 4).

TABLE 2 Number of all drugs consumed by the geriatric population of Poland

Parameter		Sample size, n			Mean (95% CI)			Median (IQR)		
		Women	Men	All	Women	Men	All	Women	Men	All
Overall		1479	1535	3014	4.97 (4.79–5.16)	5.06 (4.84–5.27)	5.01 (4.87–5.15)	5 (3–7)	5 (2–7)	5 (3–7)
Age, y	65–69	281	291	572	3.83 (3.51–4.14)	4.30 (3.85–4.76)	4.04 (3.77–4.31)	3 (2–6)	4 (1–6)	4 (2–6)
	70–74	325	307	632	4.57 (4.18–4.96)	4.91 (4.51–5.30)	4.71 (4.43–4.99)	4 (2–7)	5 (2–7)	4 (2–7)
	75–79	268	317	585	5.42 (4.94–5.89)	5.83 (5.47–6.20)	5.58 (5.25–5.90)	5 (3–8)	6 (4–8)	5 (3–8)
	80–84	274	255	529	6.14 (5.75–6.53)	5.83 (5.38–6.28)	6.04 (5.73–6.34)	6 (4–8)	6 (3–8)	6 (4–8)
	85–89	195	247	442	6.26 (5.70–6.81)	5.84 (5.41–6.26)	6.13 (5.72–6.53)	6 (4–8)	6 (4–8)	6 (4–8)
	≥90	136	118	254	5.83 (5.16–6.51)	6.66 (6.01–7.32)	6.03 (5.49–6.56)	5 (4–8)	6 (4–9)	6 (4–8)
Level of education	Primary	668	498	1166	5.31 (5.02–5.59)	4.93 (4.55–5.31)	5.19 (4.95–5.41)	5 (3–8)	5 (2–7)	5 (3–8)
	Secondary/vocational	674	788	1462	4.80 (4.53–5.07)	5.02 (4.72–5.33)	4.89 (4.69–5.09)	4 (2–7)	5 (2–7)	5 (2–7)
	Higher	131	245	376	4.59 (4.05–5.12)	5.43 (4.94–5.91)	5.01 (4.63–5.38)	4 (3–6)	6 (3–8)	5 (3–7)
Place of residence	Village	593	536	1129	5.09 (4.83–5.36)	4.75 (4.43–5.06)	4.95 (4.75–5.16)	5 (3–7)	5 (2–7)	5 (3–7)
	City <50 000 inhabitants	351	376	727	4.84 (4.51–5.16)	5.15 (4.73–5.58)	4.96 (4.70–5.22)	5 (3–7)	5 (2–8)	5 (3–7)
	City 50 000–200 000 inhabitants	275	308	583	5.13 (4.72–5.54)	5.20 (4.58–5.81)	5.16 (4.81–5.51)	5 (3–7)	5 (2–8)	5 (3–7)
	City >200 000 inhabitants	260	315	575	4.82 (4.31–5.32)	5.35 (4.89–5.82)	5.03 (4.66–5.39)	5 (2–7)	5 (3–8)	5 (2–7)

Abbreviations: IQR, interquartile range

Consumption of prescription drugs Consumption of at least 1 prescription drug was declared by 88.8% of all respondents; slightly more often by women (89.7%) than by men (87.3%). The mean number (95% CI) of all prescription drugs used was 4.49 (4.35–4.62), and the median value (IQR) was 4 (2–6). Most respondents took 1 to 4 prescription pills per day. Detailed data concerning the consumption of all prescription drugs are presented in Supplementary material, *Table S1*. Qualitative analysis of the prescription drugs according to the ATC classification is presented in Supplementary material, *Table S2*.

Consumption of nonprescription drugs Consumption of at least 1 nonprescription drug was reported by 44.2% of all respondents; more often by men (46.9%) than by women (42.5%). The mean number (95% CI) of all nonprescription drugs was 0.52 (0.49–0.55). Most respondents took 1 to 4 nonprescription pills per day. Detailed data concerning the consumption of all nonprescription drugs are presented in Supplementary material, *Table S3*.

Single-pill combinations The percentage of all individuals taking SPCs was 27.2%, with no significant difference between the sexes. SPCs were most often used by older adults in the age group of 75 to 79 years, those with higher education, and living in medium-sized cities. Detailed data concerning the consumption of SPSs are presented in Supplementary material, *Tables S4* and *S5*.

Comorbidities The mean value (95% CI) of the CCI was 4.38 (4.30–4.47) points, and it was slightly higher in men (4.46 [4.34–4.58] points) than in women (4.34 [4.22–4.45] points). The median value (IQR) of the CCI in the entire cohort was 4 (3–5) points—4 (3–6) points in men and 4 (3–5) points in women. The distribution of the CCI in the study population is presented in Supplementary material, *Figure S1*.

The most frequent chronic diseases were arterial hypertension, diabetes mellitus, and chronic heart failure. Detailed data concerning the prevalence of the most common chronic conditions are presented in Supplementary material, *Table S6*.

DISCUSSION We observed a high consumption of drugs among the geriatric population of Poland. The 2019 World Health Organization (WHO) report[17] confirms that PP is a widespread concern in many countries around the world. In the 2018 Polsenior study,[18] the first national study assessing the health condition of elderly Poles, the prevalence of PP among people aged over 65 years was higher than that reported in

TABLE 3 Logistic regression model identifying factors predisposing to polypharmacy

Parameter		OR	95% CI	*P* value
Sex	Women (ref)	1.00	–	–
	Men	1.04	0.87–1.25	0.64
Age, y	65–69 (ref)	1.00	–	–
	70–74	0.71	0.56–0.89	0.003
	75–79	1.24	0.96–1.60	0.1
	80–84	0.73	0.54–0.99	0.04
	85–89	0.71	0.49–1.03	0.07
	≥90	0.61	0.38–0.98	0.04
Level of education	Primary (ref)	1.00	–	–
	Secondary/vocational	0.98	0.81–1.20	0.87
	Higher	1.30	0.98–1.74	0.07
Charlson Comorbidity Index		1.95	1.82–2.09	<0.001
Place of residence	Village (ref)	1.00	–	–
	City <50 000 inhabitants	0.99	0.79–1.23	0.9
	City 50 000–200 000 inhabitants	0.79	0.61–1.02	0.07
	City >200 000 inhabitants	0.90	0.72–1.14	0.38

Abbreviations: OR, odds ratio; ref, reference

TABLE 4 Logistic regression model identifying factors predisposing to excessive polypharmacy

Parameter		OR	95% CI	*P* value
Sex	Women (ref)	1.00	–	–
	Men	1.45	1.06–1.98	0.02
Age, y	65–69 (ref)	1.00	–	–
	70–74	0.75	0.48–1.16	0.19
	75–79	1.13	0.73–1.75	0.57
	80–84	0.71	0.44–1.15	0.16
	85–89	0.71	0.41–1.22	0.21
	≥90	0.66	0.33–1.33	0.24
Level of education	Primary (ref)	1.00	–	–
	Secondary/vocational	1.14	0.82–1.60	0.44
	Higher	1.01	0.61–1.67	0.97
Charlson Comorbidity Index		1.65	1.54–1.77	<0.001
Place of residence	Village (ref)	1.00	–	–
	City <50 000 inhabitants	0.76	0.50–1.15	0.20
	City 50 000–200 000 inhabitants	1.74	1.16–2.59	0.007
	City >200 000 inhabitants	1.56	1.05–2.30	0.03

Abbreviations: see TABLE 3

our research; however, the results of that study were not weighted according to age structure of the Polish population. The PP rate in our analysis was similar to that observed in the follow-up national study, Polsenior 2[19] from 2018–2019, even though that study also included younger respondents aged 60 to 65 years.[19] Kardas et al[20] reported an even higher prevalence of PP based only on the use of prescription drugs among the geriatric population of Poland in 2019. Overall, these data may indicate that PP among seniors in Poland is an increasing problem.

Under the guidelines of evidence-based medicine, multidrug regimens using prescription drugs are often part of the treatment in elderly people with multiple morbidities. However, the consumption of nonprescription drugs and dietary supplements without medical recommendation may not be medically justified and can be outright harmful.[21] As observed in this study, 44.2% of all people aged over 65 years admitted to using at least 1 nonprescription drug. These results are comparable with those of previous international studies that reported the prevalence of self-medication between 20% and 60%, depending on the methodology of the study.[22] The mean number of nonprescription drugs in our analysis was also similar to that reported in the Polsenior and Polsenior 2 studies.[18,19]

Reduction of inappropriate polypharmacy is a major public health goal identified by the WHO Third Global Patient Safety Challenge: Medication Without Harm.[11] Various management strategies are available to optimize pharmacotherapy and prevent medication-related problems in geriatric patients. Physician-led interventions are based on standardized tools, such as the Beers' criteria,[23] the STOPP criteria (Screening Tool of Older Persons' potentially inappropriate Prescriptions), and the START criteria (Screening Tool to Alert doctors to the Right Treatment),[24] as well as the FORTA (Fit For the Aged) list,[25] the PRISCUS list,[26] the Medication Appropriateness Index,[27] or the Good-Palliative-Geriatric Practice Algorithm.[28] Reduced exposure to potentially inappropriate medication is associated with a lower risk of adverse drug reactions and hospitalization in elderly individuals; however, it has no influence on mortality.[29] Prescriber education programs are another strategy to reduce prescription errors, although there is no robust evidence for health benefits associated with this intervention.[30] Clinical decision support programs are becoming more accessible due to gradual computerization of health care systems. The available literature proves their effectiveness in terms of deprescribing; however, these interventions have little effect on hospital admissions or mortality in general.[31] With the increasing importance of shared decision-making, studies indicate that direct-to-patient education about the benefits and harms of drugs can lead to a significant decrease in the use of potentially inappropriate medications.[32] Pharmacist-led medication reviews vary across countries, and may include services such as medication assessments, care plans, and follow-up evaluations. These interventions are cost-saving due to anticipated reduction in the number of adverse outcomes, and can also improve appropriateness of prescribing and physical functioning of patients.[33] However, they have no significant influence on hospital admissions or mortality.[34] Overall, deprescribing is an established management strategy to minimize polypharmacy and potentially

inappropriate medications. Unfortunately, there is still limited clinical evidence for its efficacy in terms of geriatric outcomes.[35]

The new Polish regulation[12] is an example of a strategy to optimize pharmacotherapy. It aims to establish comprehensive medical and pharmaceutical care of patients based on drug reviews conducted by pharmacists. Currently, a pilot project of the program is being introduced by the Medical University in Poznań, which is responsible for choosing and supervising 75 community pharmacists from all Polish voivodeships (both urban and rural areas) participating in the project. The project involves 3 patient consultations with a pharmacist within 1 month. The pilot testing includes a group of 750 to 1000 Poles chosen by the pharmacists, comprised of individuals aged 18–60 years who take at least 5 drugs and persons over the age of 60 years who consume more than 10 drugs in their normal regimens.

The responsibilities of the pharmacists include identification of the patient's actual or potential drug-related problems and their causes (eg, level of compliance based on an interview), and ranking these problems according to their importance and the level of risk for the patient. Moreover, the pharmacists will educate the patients on appropriate drug administration, preventive health regimens, importance of compliance, and the patient's right to obtain comprehensive information about the pharmacotherapy during each medical or pharmaceutical visit. If any of the identified problems are related to nonprescription drugs, the pharmacist will issue a written recommendation to optimize pharmacotherapy and inform the patient about the dangers of self-treatment. If the problems are related to prescription drugs, the pharmacist will contact the physician directly on behalf of the patient or write a recommendation to establish contact between the patient and the physician. The drug review will result in the development of an individual pharmaceutical care plan (IPCP) for each patient, based on the therapeutic outcome monitoring and sum-of-the-parts analysis methods along with the principles of evidence-based medicine. Paper versions of the IPCP forms will be forwarded to a coordinating center for data collection and further analysis. The main goals of IPCPs include improvement of patients' quality of life and achievement of therapeutic, economic, and financial benefits. The end of the pilot project is planned for December 2022.[12]

Our study results highlight the importance of pharmaceutical care of geriatric patients. We showed that PP and EPP occur more often in men, in the age group 85 to 89 years, in individuals with lower level of education, and those living in small or medium-sized cities. The main factor predisposing older people to PP and EPP was multimorbidity. The prevalence of the most common comorbidities identified in our study is comparable with data from the Collaborative Research on Ageing in Europe project and the WHO Study on Global Ageing and Adult Health.[36] The Polish geriatric population is characterized by the most frequent multimorbidity patterns, namely, cardio-respiratory (angina, asthma, and chronic obstructive pulmonary disease), metabolic (diabetes, obesity, and hypertension), and mental-articular (arthritis and depression).[37,38] The identified high-risk groups of elderly patients are most likely to require special attention and may receive the greatest benefits from multidisciplinary interventions in the field of pharmacotherapy.

Another area of great interest is the use of SPCs, which is associated with a decrease in the risk of adverse drug reactions and, due to reduced pill burden, an increase in patient compliance.[39,40] These effects are more pronounced with increasing age of the patients and the number of drugs taken.[41] However, the literature provides little evidence on the efficacy of SPCs in elderly patients with multimorbidity, where the lack of dosing flexibility for individual SPCs components can limit the effectiveness of reaction in the case of rapid changes in a patient's clinical state.[42] To our knowledge, there are no Polish population studies on the frequency of the use of combined preparations among older adults. In our study, cardiovascular drugs represented 51.1% of all SPCs, while multivitamin / multielectrolyte preparations accounted for 22.3%, and the combination of paracetamol and tramadol made up 11.6% of all SPCs. These results may change our understanding of the potential benefits of SPSc on health outcomes in elderly patients.

The strengths of our study include the use of real-life settings and a representative sample of elderly, home-dwelling Poles. These approaches enabled us to obtain unique, up-to-date data on pharmacotherapy among the Polish geriatric population. A few limitations are present in our study. First, the data were obtained during interviews, risking an inherent possibility that the respondents would not fully reveal their drug consumption information. Second, even though the study was designed in such a way as to reflect the demographic structure of the Polish population, the oldest respondents who consented to participate in the study were probably a selected group with relatively low morbidity. Together with the exclusion of institutionalized patients, this bias might have resulted in an underestimation of the number of drugs reported in our study.

Conclusions In the context of the high consumption of drugs due to multimorbidity among the Polish geriatric population, and the previously documented negative impact of PP and EPP on the quality of life and life expectancy, our findings reveal a great need for the introduction of combined medical and pharmaceutical care of older adults. Coordinated pharmaceutical care may play a significant role in improving the safety and quality of pharmacoterapy in the elderly, and is in accordance with the plans for the development of

such a care in Poland. Follow-up studies will be required to assess the results of this strategy in Polish geriatric patients.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT All authors made substantial contributions to this work. EB-M, ŁW, TZ, MS, ZK, KM, and KR conceived the concept of the study. EB-M, ŁW, and KJ designed the study, acquired the data, and performed the analyses. EB-M, ŁW, TZ, and MS interpreted the data. EBM drafted the manuscript and coordinated the feedback of the coauthors. ŁW, MS, MR, TG, KM, ZK, KR, and TZ substantially revised the manuscript. All authors have read and approved the published version of the manuscript.

CONFLICT OF INTEREST None declared.

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Supplementary material

Błeszyńska-Marunowska E, Jagiełło K, Grodzicki T, et al. Polypharmacy among elderly patients in Poland: prevalence, predisposing factors, and management strategies. Pol Arch Intern Med. 2022; 132: 16247. doi:10.20452/pamw.16247

Table S1. Number of prescription drugs taken. The results are presented as mean values with 95% confidence intervals and medians with the first and third quartiles.

	Sample size, N			Mean value (95% CI)			Median value (Q1–Q3)		
	Women	Men	All	Women	Men	All	Women	Men	All
All	1479	1535	3014	4.46 (4.28-4.63)	4.53 (4.33-4.74)	4,49 (4.35-4.62)	4 (2–6)	4 (2–7)	4 (2–6)
Age, years									
65–69	281	291	572	3.40 (3.10-3.69)	3.84 (3.41-4.26)	3.59 (3.34-3.85)	3 (1–5)	3 (1–6)	3 (1–5)
70–74	325	307	632	4.20 (3.83-4.56)	4.39 (4.02-4.76)	4.28 (4.01-4.54)	4 (2–6)	4 (2–6)	4 (2–6)
75–79	268	317	585	4.81 (4.37-5.25)	5.31 (4.97-5.66)	5.00 (4.70-5.31)	5 (2–7)	5 (3–7)	5 (3–7)
80–84	274	255	529	5.44 (5.07-5.82)	5.18 (4.76-5.60)	5.35 (5.07-5.64)	5 (4–7)	5 (3–7)	5 (3–7)
85–89	195	247	442	5.65 (5.12-6.18)	5.26 (4.85-5.66)	5.53 (5.14-5.92)	5 (4–8)	5 (3–7)	5 (3–7)
90+	136	118	254	5.23 (4.58-5.88)	5.89 (5.25-6.53)	5.39 (4.87-5.90)	5 (3–7)	6 (4–8)	5 (3–7)
Education									
Primary	668	498	1166	4.77 (4.50-5.04)	4.37 (4.02-4.72)	4.64 (4.43-4.85)	5 (3–7)	4 (2–7)	5 (2–7)
Secondary/vocational	674	788	1462	4.30 (4.04-4.56)	4.54 (4.25-4.83)	4.40 (4.21-4.59)	4 (2–6)	4 (2–7)	4 (2–6)
Higher	131	245	376	4.07 (3.59-4.54)	4.81 (4.35-5.27)	4.44 (4.10-4.78)	4 (2–6)	5 (2–7)	4 (2–6)
Residence									
Village	593	536	1129	4.53 (4.28-4.78)	4.23 (3.93-4.51)	4.41 (4.22-4.60)	4 (2–7)	4 (2–6)	4 (2–6)
City <50 M	351	376	727	4.37 (4.07-4.67)	4.59 (4.20-4.98)	4.46 (4.22-4.70)	4 (2–6)	4 (2–7)	4 (2–6)
City 50–200 M	275	308	583	4.62 (4.23-5.01)	4.75 (4.14-5.35)	4.67 (4.33-5.01)	4 (3–6)	4 (2–7)	4 (2–7)
City >200 M	260	315	575	4.32 (3.85-4.79)	4.81 (4.36-5.25)	4.51 (4.17-4.84)	4 (2–6)	5 (2–7)	4 (2–7)

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017. CI–confidence interval, M – one thousand.

Table S2. Percentage of people taking drugs based on the anatomical-therapeutic-chemical classification (ATC) (%). Detailed results in subgroups are presented for values above 5%.

ATC Code		Women	Men	All
A - Alimentary tract and metabolism		44.9	45.7	45.2
	A02	18.3	17.9	18.1
	A10	20.4	24.3	21.9
	A12	13.2	12.7	13.0
B - Blood and hematopoietic system		45.9	55.0	49.5
	B01	44.6	53.9	48.3
C - Cardiovascular system		83.4	80.0	82.1
	C01	14.1	10.7	12.8
	C02	2.0	10.7	5.4
	C03	34.0	30.1	32.4
	C07	51.8	51.9	51.9
	C08	22.6	19.3	21.3
	C09	57.1	57.2	57.2
	C10	41.7	46.8	43.7
D - Medicines used in dermatology		0.1	0.2	0.1
G - Genitourinary system and sex hormones		2.0	25.5	11.3
	G04	1.7	25.3	11.0
H - Hormones. excluding sex hormones and insulin		17.2	6.0	12.8
	H03	15.9	5.0	11.6
J - Systemic anti-infective drugs		1.6	1.3	1.5
L - Antineoplastic and immunomodulating drugs		2.0	1.3	1.7
M - Musculoskeletal system		15.6	15.0	15.4
	M01	6.2	4.3	5.5
	M04	5.8	9.3	7.2
N - Nervous system		33.5	20.2	28.3
	N02	6.8	3.4	5.4
	N05	11.2	4.4	8.5
	N06	20.3	11.2	16.8
P - Antiparasitic drugs. insecticides and repellants		0.2	0	0.1
R - Respiratory system		9.9	10.1	10.0
	R03	7.4	9.2	8.1
S - Sensory organs		1.8	1.4	1.7

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table S3. Number of non-prescription drugs taken. The results are presented as mean values with 95% confidence intervals and medians with the first and third quartiles.

	Sample size, N			Mean value (95% CI)		
	Women	Men	All	Women	Men	All
All	1479	1535	3014	0.52 (0.48-0.56)	0.53 (0.49-0.56)	0.52 (0.49-0.55)
Age, years						
65–69	281	291	572	0.45 (0.35-0.51)	0.46 (0.39-0.54)	0.46 (0.39-0.50)
70–74	325	307	632	0.39 (0.31-0.44)	0.48 (0.44-0.59)	0.43 (0.39-0.48)
75–79	268	317	585	0.62 (0.49-0.72)	0.51 (0.45-0.59)	0.56 (0.50-0.65)
80–84	274	255	529	0.69 (0.60-0.79)	0.64 (0.56-0.75)	0.67 (0.61-0.75)
85–89	195	247	442	0.67 (0.49-0.73)	0.58 (0.49-0.67)	0.62 (0.51-0.69)
90+	136	118	254	0.59 (0.48-0.72)	0.76 (0.63-0.92)	0.67 (0.54-0.74)
Education						
Primary	668	498	1166	0.56 (0.48-0.59)	0.55 (0.49-0.63)	0.56 (0.50-0.59)
Secondary/vocational	674	788	1462	0.54 (0.44-0.56)	0.53 (0.43-0.53)	0.54 (0.45-0.53)
Higher	131	245	376	0.57 (0.37-0.66)	0.60 (0.51-0.72)	0.59 (0.48-0.66)
Residence						
Village	593	536	1129	0.61 (0.51-0.62)	0.54 (0.45-0.59)	0.58 (0.50-0.59)
City <50 M	351	376	727	0.49 (0.39-0.54)	0.57 (0.49-0.64)	0.53 (0.45-0.56)
City 50–200 M	275	308	583	0.52 (0.42-0.60)	0.54 (0.36-0.54)	0.53 (0.42-0.55)
City >200 M	260	315	575	0.53 (0.40-0.60)	0.54 (0.47-0.63)	0.54 (0.45-0.59)

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017. CI–confidence interval, M – one thousand.

Table S4. Percentage of older people using single pill combinations (SPCs), %.

	Number of SPCs			
	0	1	2	3
Sex				
All	72.3	24.6	2.7	0.4
Women	71.8	25.0	2.7	0.5
Men	73.2	23.9	2.7	0.2
Age, years				
65–69	74.9	22.4	2.2	0.4
70–74	72.5	25.8	1.6	0.1
75–79	69.2	26.7	3.8	0.3
80–84	70.5	24.9	3.9	0.6
85–89	71.3	23.1	4.8	0.8
90+	71.9	27.6	0.0	0.5
Education				
Primary	71.4	24.5	3.5	0.6
Secondary/vocational	73.5	24.0	2.2	0.3
Higher	69.8	27.1	2.6	0.4
Residence				
Village	71.3	25.2	3.4	0.1
City <50 M	73.3	24.8	1.3	0.7
City 50–200 M	70.3	26.3	2.4	1.0
City >200 M	74.3	22.1	3.4	0.1

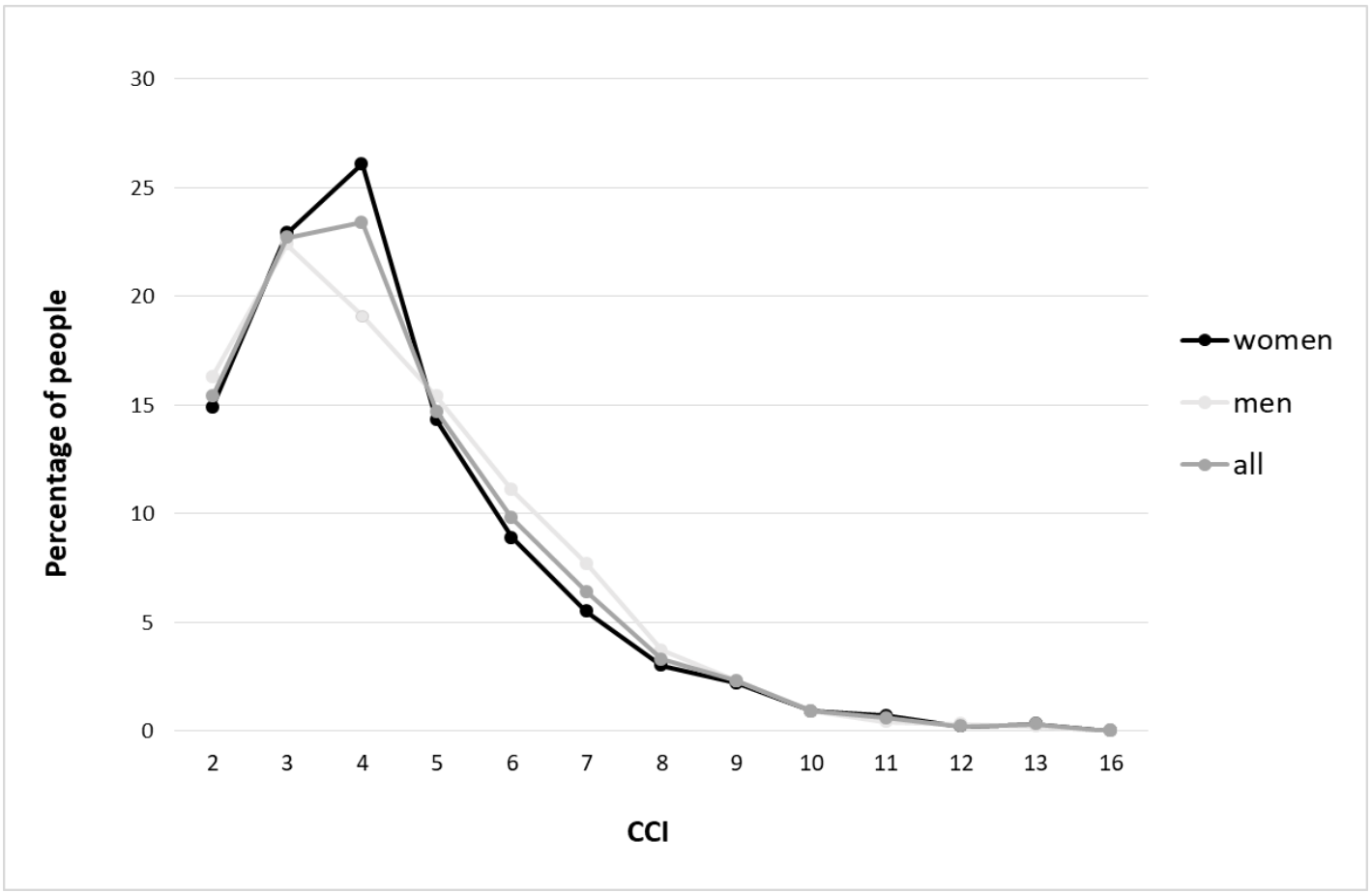
Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data were obtained after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017. M – one thousand.

Table S5. Analysis of single pill combinations (SPCs), %.

SPCs		%
Cardiovascular drugs		**51.1**
	ARB + TTD	22.0
	DHP-CCB +ACEI	10.3
	TLD + ACEI	6.0
	TTD + PSD	5.2
	ACEI + DHP-CCB + TLD	3.2
	ACEI + TTD	2.5
	DHP-CCB + TLD	1.8
	NG + PET	0.9
	ARB + DHP-CCB	0.7
	BB + DHP-CCB	0.6
	BB + TTD	0.5
	BB + ASA	0.5
	ARB + DHP-CCB + TTD	0.4
	ACEI + BB	0.2
	HMGCRI + DHP-CCB	0.2
	TTD + AL	0.1
	ARNI + ARB	0.1
Painkillers and muscle relaxants		**14.9**
	PCM + TRA	11.6
	NSAID + LDC	0.7
	NSAID + CAF	0.7
	NSAID + PPI	0.5
	AVC + SIM	0.5
	PCM + CAF	0.2
	PCM + AA + PM	0.2
	NSAID + TRA	0.2
	NSAID + PSE	0.1
	PCM + DXM + PSE	0.1
Others		**30.0**
	MV/ME	22.3
	DA + DDCI	6.0
	MT + DPP-4I	1.3
	5-ARI + AB	0.2
	MTX + FolA	0.1

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data was given after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017. AA – ascorbic acid; AB – alpha-blocker; ACEI – angiotensin-converting enzyme inhibitor; AL – alkaloid; ARB – angiotensin receptor blocker; ARNI – angiotensin receptor-nephrilysin inhibitor; ASA – acetylsalicylic acid; AVC – alverine citrate; BB – beta-blocker; CAF – caffeine; DA – dopamine agonist; DDCI – dopa-decarboxylase inhibitor; DHP-CCB – dihydropyridine calcium channel blocker; DPP-4I – DPP4 inhibitor; DXM – dextromethorphan; FolA – folic acid; HMGCRI – HMG-CoA Reductase Inhibitor; LDC – lidocaine; MF – metformin; MTX – methotrexate; MV/ME – multivitamin/multi-electrolyte preparation; NG – nitroglycerin; NSAID – Non-steroidal anti-inflammatory drug; PCM – paracetamol; PET – pentaerythritol; PM – pheniramine maleate; PPI – proton pump inhibitor; PSD – potassium-sparring diuretic; PSE – pseudoephedrine; SIM – simethicone; TLD – thiazide-like diuretic; TRA – tramadol; TTD – thiazide-type diuretic; 5-ARI – 5α-Reductase inhibitor

Figure S1. Distribution of the Charlson Comorbidity Index (CCI) values in the study group.



Note: The results presented in the figure take into account the use of a complex scheme of randomizing respondents. The data were obtained after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017.

Table S6. Percentage of older people with chronic diseases, %.

	Chronic disease										
	AH	CKD	CLD	COPD	DE	DM	D/A	HF	ND	OA	TIA/CVA
Sex											
All	71.7	7.8	6.6	7.9	1.0	24.3	12.8	20.2	13.0	11.0	12.5
Women	74.1	7.6	7.1	7.1	1.3	22.5	16.1	17.4	13.4	12.0	13.0
Men	67.9	8.1	5.8	9.0	0.6	27.1	7.7	24.4	12.4	9.4	11.8
Age, years											
65–69	67.8	5.5	7.5	6.1	0.3	20.9	14.6	13.5	10.5	9.8	9.7
70–74	70.2	5.9	8.3	5.6	0.8	28.5	10.2	15.9	12.3	9.3	12.8
75–79	73.3	7.2	3.9	9.8	0.4	28.2	12.7	20.6	18.5	12.9	11.5
80–84	78.2	11.1	6.2	10.8	0.3	23.9	12.3	25.3	14.2	13.4	15.1
85–89	73.1	14.4	5.8	10.8	3.4	23.0	13.7	37.9	13.8	14.2	18.0
90+	78.6	13.1	4.4	10.9	6.3	16.7	12.3	39.4	8.8	6.5	16.0
Education											
Primary	73.5	8.5	4.1	7.2	0.8	25.7	11.8	23.6	10.3	13.0	14.9
Secondary/vocational	70.7	7.4	7.5	7.8	1.2	24.2	12.9	19.2	13.2	9.6	11.6
Higher	70.6	7.5	9.8	10.5	0.3	21.6	15.3	15.1	19.7	11.4	9.8
Residence											
Village	74.4	7.8	4.4	6.9	0.3	23.2	11.5	23.5	8.9	12.3	11.7
City <50 M	70.6	6.8	6.3	9.0	1.3	26.4	12.8	21.3	12.8	11.4	14.3
City 50–200 M	72.2	7.4	7.1	7.4	1.7	26.4	13.3	17.4	15.5	13.6	12.8
City >200 M	68.2	8.9	9.8	8.6	1.1	22.4	14.3	15.9	17.7	6.6	11.7

Note: The results presented in the table take into account the use of a complex scheme of randomizing respondents. The data were obtained after weighing the sample in relation to the structure of the Polish population aged 65 and over in 2017. AH – arterial hypertension; CKD – chronic kidney disease; CLD – chronic liver disease; COPD – chronic obstructive pulmonary disease; D/A – depression/anxiety; DE – dementia; DM – diabetes mellitus; HF – heart failure; M – one thousand; ND – neoplastic disease; OA – osteoarthritis; TIA/CVA –transient ischemic attack/cerebrovascular accident