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Real-life dosing conditions in older adults and geriatric patients in Poland – An international questionnaire study to investigate the regional differences in drug intake behaviour in the older population

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ABSTRACT

Older people represent approximately 20% of the Polish population and are the primary population using medications. Behaviours connected with drug intake (such as dosage form modifications, type and amount of fluid and/or food accompanying administration) are crucial for drug efficacy and avoidance of adverse effects. The presented study had three research aims; firstly, to investigate the real-life drug administration process among older adults and geriatric patients in Poland. Secondly, to compare data from Poland with data from a previous study performed in Germany, based on the same questionnaire. Thirdly, to discuss the potential influence of dosing conditions on the behaviour of orally administered medications (especially drug absorption) and identify potential problems with drug intake itself. This questionnaire-based study was conducted in the form of in-person interviews led by research team members. In this study, 174 participants, aged 65–94 years old were recruited from three settings in the Pomeranian region of Poland: home setting, nursing home and hospital. In Poland, the preferred method of medication intake was administration of all medications simultaneously. Patients were taking their medications most often directly after food ingestion, which commonly consisted of bread with butter, ham or cheese and black tea. The most common fluid for drug administration was either a few sips or 100 mL of non-carbonated water (mineral or tap water) as well as black tea. Dividing tablets (defined as splitting tablets in parts) was the most common modification. There were many similarities in the way of administering medications between the Polish and German older populations, specifically the use of non-carbonated water as the most common fluid for medication intake as well as bread as the main ingredient of breakfast and dinner. The biggest difference between populations was the choice of black tea as a medium for medication intake much more frequently in the Polish population than the German (who also preferred mint, herbal and fruit teas), and using a smaller volume of fluid. The presented study gives insight into the medication intake process in the older Polish population from the Pomeranian region in North Poland in comparison to the German population from the Pomeranian region in North East Germany. The results may help to identify factors that could decrease medication efficacy and safety, which is crucial, especially for the older population. Furthermore, the collected data may be useful for in vitro or *in silico* simulations to enhance drug development based on real-life data.

1. Introduction

The absorption of orally administered drugs is affected not only by their solubility, permeability of the mucosa, and gastrointestinal stability but also by the conditions under which medication is administered (Alqahtani et al., 2021). Proper dosing conditions ensure that a medication will be effective and safe for its users. The literature demonstrates data about the influence of dosing conditions on medication after oral administration with a well-known example being alendronate, which needs several conditions to be fulfilled in order to be absorbed: a fasted

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state (at least 30 min before food ingestion), intake with at least 200 mL of water (not even mineral, no other fluid allowed) and upright position at least 30 minutes after administration (Organon Pharma (UK) Limited). Another example presented by Baekdal et al. is semaglutide; their results demonstrated that clinically relevant semaglutide exposure was assured when the semaglutide tablets were administered in the fasted state with up to 120 mL of water and a minimum of 30 min of fasting after administration (Bækdal et al., 2021). Both drugs are commonly used among the older population since osteoporosis and diabetes are typical diseases in the advanced-age population. Correct administration of pharmaceuticals is essential, particularly for medications aimed at reducing morbidity or prolonging life, which is often one of the main objectives in treating older adults (Tyson et al., 2020). Although patients get recommendations about drug administration from their health care professionals or information leaflets, they often may be noncompliant and take their medications in their own way. Therefore, it is important to collect data about drug intake of real patients to assess the influence of dosing conditions on drug absorption and potential risks for patients, particularly older ones. In the previous study *Investigation of real-life drug intake behaviour in older adults and geriatric patients in Northern Germany – a biopharmaceutical perspective,* data about dosing conditions among the older German population was collected and discussed considering the influence of different factors on the absorption of orally administered medications (Sarwinska et al., 2024). The study concluded that older adults mostly co-administered their medications with 100 or 200 mL of non-carbonated water, herbal and fruit tea, or carbonated water. Additionally, the typical meal eaten before drug intake consisted of a bread roll or bread with jam and coffee for breakfast and bread with ham, cheese, and tea for dinner. The most prevalent dosage form modification was dividing tablets, performed mainly due to medical advice. Furthermore, the most common time for drug intake was directly after breakfast, directly after dinner, and 30 min before breakfast. After finalizing the study in Germany, we decided to expand the study and investigate drug intake behaviours in older populations in a different European country to see if there are regional differences in the drug intake process. In the interest of being able to relate the findings of the German study to another European country, Poland was chosen for the next study for several reasons.

Poland is located in central Europe. It shares a direct border with Germany and acts as a bridge between Western and Eastern European countries, absorbing influences from both regions. Based on this geographical and historical context, it was hypothesized that the drug intake behaviours of older adults in (North) Poland and (North East) Germany may show similarities. This is particularly relevant for individuals born in 1959 and earlier, as they experienced the immediate aftermath of World War II. During this period, both Poland and East Germany were under significant socio-political transformations, which might have influenced the behaviours and lifestyles of their populations. Despite these similarities, currently both countries seem to differ with regards to the economy, healthcare system, politics, and culture. Moreover, the attitudes and beliefs of the populations living in these countries also differ, shaped by their unique historical and social contexts

According to the latest available Eurostat data, in Germany, approximately 22.1% of the population is aged 65 and older, compared to 19.9% in Poland (European Commission Eurostat, 2024). Fig. 1 depicts the life expectancy in Poland and Germany as a whole population, as well as regarding sex. There are notable differences in life expectancies between sexes and general populations between countries as well as within a country with the shortest life span among Polish men, and the longest among German women. The total life expectancy of Germans is higher than that of Poles. Several factors may contribute to the notable differences in life expectancies between sexes and general populations, including variations in the burden of disease, socioeconomic conditions, availability of medical services, dietary and lifestyle choices, and medication management. In comparing the availability of

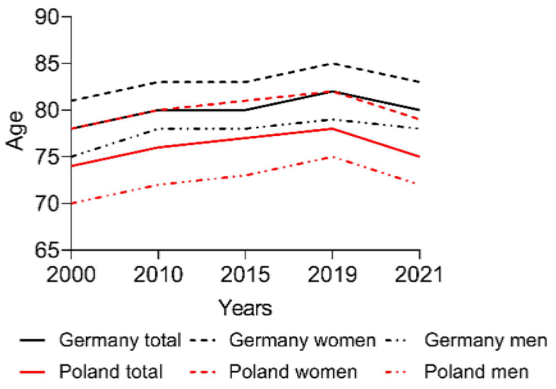

Fig. 1. Life expectancy in Poland and Germany according to WHO (WHO, 2021).

healthcare services between Poland and Germany, it is evident that both countries demonstrate distinct approaches shaped by their economic capacities and healthcare expenditure priorities. As of 2022, Poland, with a Gross Domestic Product (GDP) per capita of 28,044 € purchasing power parity (ppp), allocated 4.4% of its GDP to healthcare spending, while Germany, with a higher GDP per capita of 41,246 € ppp, dedicated 8.0% of its GDP to healthcare (European Commission Economic and Financial Affairs, 2024; OECD/European Observatory on Health Systems And Policies, 2023b, 2023a). Long-term care spending as a percentage of GDP also shows a contrasting approach - Poland allocated 0.5%, whereas Germany allocated 1.9% (European Commission Economic and Financial Affairs, 2024). The Polish population encounters several challenges related to medication management. Self-medication is widely observed among the older population across Europe and is particularly pronounced among those with chronic diseases and physical discomfort - common in the senior population (Brandão et al., 2020). According to data from the Brandão et al. study, self-medication in Europe occurs at an average prevalence of 26.3% among people aged 65 and older living in private households, however, of all the 14 countries studied, it is highest in Poland at a rate of 49.4%. As assessed in a Polish study, this demographic group often exhibits suboptimal practices regarding the use of over-the-counter medications (Cybulski et al., 2018). Moreover, another study conducted by a team of Polish researchers showed that intentional non-adherence to prescribed treatment regimens is common among older adults, and their reported adherence rates tend to underestimate the actual incidence of self-administration (Dworakowska et al., 2021).

The main aim of the presented study was to learn how older adults and geriatric patients from Poland take their medications in real life. The second aim was to compare the obtained data from the international study in Poland with the data from a previous study performed in Germany to see where are the similarities and differences between the two populations. The third aim was to further discuss the potential influence of dosing conditions on orally administered medications that were not discussed in the German edition of the study.

2. Materials and methods

The primary tool of this study was a questionnaire about drug intake. The questionnaire was developed, validated, and used for the previous study in this project performed among the German population (Sarwinska et al., 2024). In this study, the questionnaire translated into Polish language was used. No changes were made to the content of the questionnaire. Questions in the questionnaire referred to drug intake in older adults and geriatric patients. The questionnaire was divided into six sections: General Information (demographic data: age, BMI, place of living, level of independence in drug management); Medication Intake (amount of medications); Medication Intake with Food; Fluids, Vehicles,

and Way of Taking Medications; Modifications of Drug Forms and Final Questions. The study was performed digitally via the web tool SoSci Survey (https://www.soscisurvey.de/), Version 3.5.00, SoSci Survey GmbH, Germany). Participants did not fill out the questionnaire independently, the study was conducted in the form of in-person interviews where study participants were asked direct questions by a member of the research team. No medical intervention was performed.

2.1. Study population

Study participants from Poland were recruited between February and April 2024 from three settings: home, nursing home, and hospital. The places for recruitment included several hospital wards of the University Clinical Center in Gdańsk ($n = 57$): two Clinics of Cardiology, a Clinic of Hypertension and Diabetology, a Clinic of Rheumatology, and a Clinic of Immunology, Geriatrics and Internal Medicine. Participants were recruited also in five nursing homes ($n = 41$) in two cities in the Pomeranian region (with large and medium city populations) and among the family members of the research team and the students of Scientific Circle of Public Health from the Medical University of Gdańsk ($n = 76$), who resided in various cities in the Pomeranian region. Informed consent was obtained from all subjects involved in the study. The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the ethical review board at the University Medicine of Greifswald, Germany as a multicenter study (ethical protocol no. BB 095/22a, 15.01.2024). A positive vote was also obtained from the local ethical review board at the Medical University of Gdańsk (KB/763/2023–2024, 19.01.2024). The participants were selected according to the following criteria: age 65 years or older, male or female gender, use of at least one oral medication, and the ability to provide informed consent (no cognitive impairment, no dementia or delirium). The mental and cognitive state of the study subjects in the hospital setting was assessed by hospital personnel (physicians, nurses). In the home setting, the cognitive condition of patients was assessed based on the knowledge of students and family about patients, the course of the interview, and the consistency of given answers. No special examination was performed to keep time expenditure as short as possible for the aged volunteers.

2.2. Sample size considerations

In order to choose the sample size for the study in Poland, the same approach as in Germany was undertaken. Assessing the population of people aged at least 65 years old in Pomeranian Voivodeship (Voivodeship - similar to county/region) (2021) as 415 300, a confidence level of 80 % and a margin of error of 5%, the sample size was assessed also as 164 participants (SurveyMonkey https://www.surveymonkey.com/mp/sample-size-calculator/, Version: November 20, 2023, SurveyMonkey Europe UC, Shelbourne Road, Dublin, Ireland, (Urzad Statystyczny w Gdansku, 2023). Finally, the number of participants interviewed was similar to the previous study in Germany ($n = 167$).

2.3. Data evaluation and statistical analysis

The data was evaluated via descriptive analysis. The presented results, collected from older Poles, were compared with the results from the German edition of the survey, as a whole population, without comparing individual subgroups between countries. Comparison of data from different subgroups is not presented here due to general similarities and the fact that small differences are not relevant from a biopharmaceutical point of view. The data from different countries were also not compared between subgroups, due to limited sample sizes in some cases and differences (age, number of taken medications, health condition) that could bias the results. Due to the differences in age distribution between Polish and German study populations, an age group analysis was additionally performed to assess if the differences in these groups affected the results from the whole population.

The majority of acquired data were qualitative; therefore, no statistical tests were conducted. A statistical comparison was conducted between general populations regarding the fluid volume co-administered with medications. The data was tested for normality using the Kolmogorov–Smirnov and Shapiro–Wilk tests. According to the non-gaussian distribution, the Mann-Whitney test was performed to compare subgroups. Data were regarded as significant if the p-value was below 0.05. A statistical analysis was conducted to determine the odds ratio (OR) for the proportion of water and other fluids co-administered with medications. The odds ratio > 1 means that water is more often chosen within a population. Tap water, mineral water, and carbonated water were considered as "water". The odds ratio was calculated only for the type of fluid since this factor was considered to be the most critical for the absorption of orally administered medications and was possible to qualitatively assess it.

Equation 1

$$OR_{within\ a\ population} = \frac{number\ of\ answer\ "water"}{number\ of\ answers\ "fluids\ other\ than\ water"}$$

Equation 2

$$OR_{between\ countries} = \frac{\frac{number\ of\ answer\ "water"}{number\ of\ answers\ "fluids\ other\ than\ water"}}{\frac{number\ ofthe\ study\ participants\ in\ Germany}{number\ ofthe\ study\ participants\ in\ Poland}}$$

The BMI values were adjusted to the older adult population according to literature advice (Winter et al., 2014). The normal weight was defined as a BMI value between 23 and 30, underweight < 23, and overweight > 31.

Based on the caloric calculator (www.myfitnesspal.com/, last accessed on 26.06.2024) the caloric value of breakfast and dinner variants was estimated.

For the data analysis and representation, MS Excel (Version 2019, Microsoft Corporation, USA) and GraphPad Prism 9 (Version 9.5.1 (733)) were used.

3. Results

3.1. Demographics – Study population

The final study population was 174 participants from three settings: home (43.68%), nursing home

(32.76%), and hospital (23.56%). The characteristics of the participants are presented in Table 1. The overall gender distribution in the study population was almost equal for men and women.

All interviewed participants were from the Pomeranian Voivodeship recruited in Pomeranian hospitals, nursing homes, or private residences. The age range of the respondents was 65 - 94 years, with the most numerous age group of study participants being 75 - 79 years old (29%). The age range of respondents roughly mirrored the age group distribution of the older population in Poland, as detailed in Fig. 2.

In contrast, when comparing the current Polish study population with the German population from the previous study referenced in this article, notable differences in age distribution were observed. The Polish

Table 1
Demographic characteristics of Polish and German study population (Sarwinska et al., 2024).

	Polish study population, $n = 174$	German study population $n = 167$
Gender balance	m: 47%, f: 53%	m: 44%, f: 56%
Age in years	65 – 93	65 – 96
(range, median, mean	75	80
± SD)	75.7 ± 6.5	78.4 ± 7.0
BMI in kg/m²	18 – 43	17 – 42
(range, mean ± SD)	27.8 ± 4.5	27.0 ± 4.7 $n = 165$

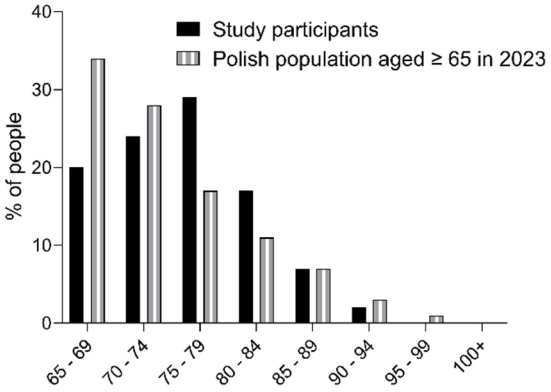

Fig. 2. Age groups - comparison between the study population and the Polish older population in 2023. The age groups are presented as a percentage of the Polish population being 65 years and older (Populationpyramid.Net Poland, 2023).

study group had a notably higher proportion of younger age groups (65–69, 70–74 and 75-79) and less from the older age groups (80–84 and 85–89) than the German study population. A detailed comparison of these populations is presented in Fig. 3. Although the range of age and mean age of study participants were similar, the median age was quite different (75 years in Poland vs. 80 years in Germany) (Table 1). Therefore, to assess if the differences in age distribution affected the general results, age analysis was performed for age groups 70 – 79 years old and 80 – 89 years old, since in these ranges the differences were the biggest. In the group 70 – 79 years there were 93 participants in Poland and 49 in Germany, in the group 80 - 89 there were 42 participants in Poland and 87 in Germany. The analyzed aspects included: the amount of medications taken, the amount of fluid used for medication intake and % of participants, who used water for drug intake. The results of the age group analysis are available in supplementary data.

3.2. Medications

47% of the interviewed Polish participants reported a chronic use of 5 to 9 medications. The second most frequently reported category was the intake of more than 10 medications, declared by 28% of respondents (Fig. 4). Similarly, in Germany 5 to 9 medications were also the most common answer (46%), however the second answer was 2 to 4 medications (29%). The age group analysis confirmed the results from the general population.

In both, the current Polish population and the German population from the previous survey, the predominant method of medication intake

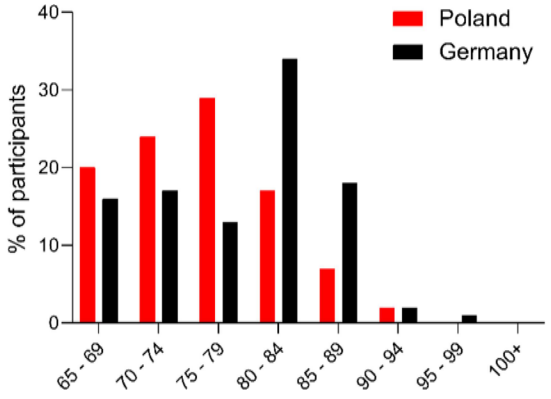

Fig. 3. Comparison between the study population in Poland (n = 174) and Germany
(n = 167) (Sarwinska et al., 2024).

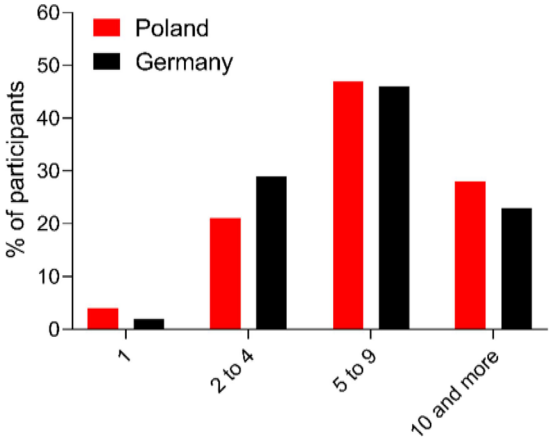

Fig. 4. Amount of chronically taken medications among all study participants in Poland (n = 174) and in Germany (n = 167) (Sarwinska et al., 2024).

at a given time of day was to take all medications simultaneously (45% and 54%, respectively). Within the Polish population intake of medications separately was chosen to a similar extent (40%) as intake of drugs altogether. In comparison, in Germany, intake of medications separately was chosen less often (24%) (Fig. 5).

3.3. Dosage form modifications

Dosage form modifications were performed by 21% of Polish study participants, which is less than reported in Germany (29%) (Sarwinska et al., 2024). The most common dosage form modifications are presented in Fig. 6. By far the predominant type of drug modification was dividing tablets (83% of answers), similar to the German population (84% of answers). Individuals in Poland declared also other modifications like crushing, chewing and dissolving tablets and opening capsules. No one declared adding tablets to a meal or holding the medicine in the mouth until it dissolved. No data about modifications of specific products were collected.

In the study, participants were asked for the reasons for performed dosage form modifications. Nearly 40% of the participants who admitted to altering their medications did it because of their problems with swallowing (14 out of 36 participants who modified their medications). Participants who answered that they crushed tablets all were performing this modification due to problems with swallowing and did

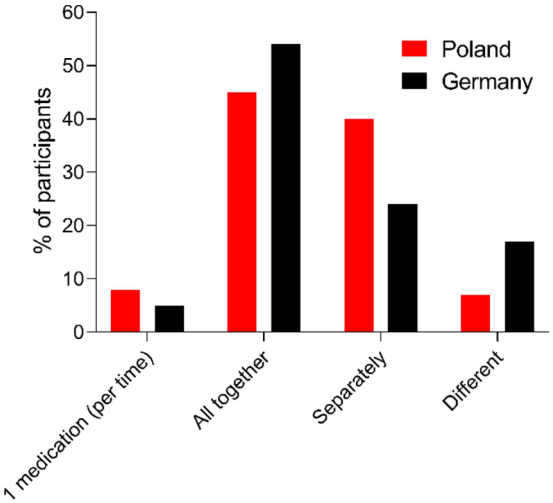

Fig. 5. Way of taking medications by the whole study population in Poland (n = 174) and Germany (n = 167) (Sarwinska et al., 2024).

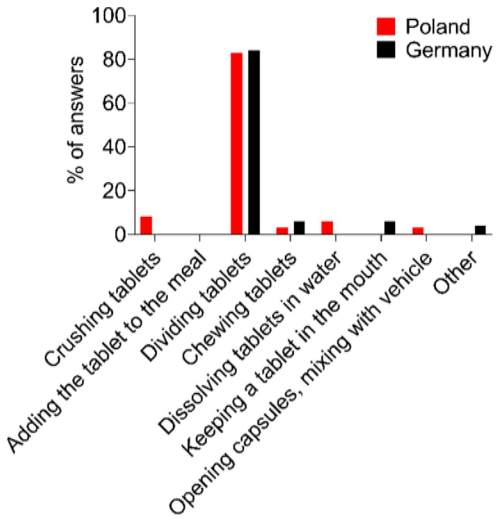

Fig. 6. The most common dosage form modifications performed by Polish (n = 36) and German (n = 48) study participants. Multiple choice question, n = 37 answers in total from the Polish population and n = 51 answers in total from the German population, n = 174 participants in total in Poland and n = 167 participants in total in Germany (Sarwinska et al., 2024).

not report using food vehicles for drug administration. Moreover, the single study participant who reported chewing medications was doing so when tablets were big. Around 28% of participants who altered their medications, did it with a doctor's approval and due to medical indications, and 22% did it to adjust the dose correctly. The least number of changes in the dosage forms were performed without any reason whatsoever or just due to patients' habits (11%).

3.4. Body position

The body position at which study participants took their medications is presented in Fig. 7. Most of the study participants in the Polish survey declared taking medications in a sitting position (64% of answers), similarly to in Germany (69% of answers). The second most common answer was standing position, which was slightly more common in Poland (29% of answers vs. 25%).

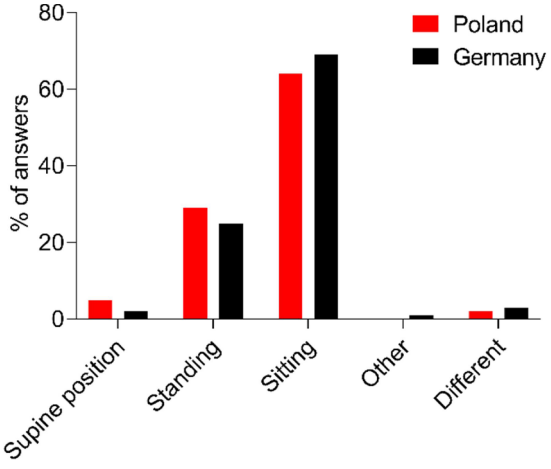

Fig. 7. Body position while drug administration among the Polish study population, n = 174, multiple choice question, n = 204 answers in total in Poland and n = 189 answers in total in Germany (Sarwinska et al., 2024).

3.5. Drug intake regarding meals

Study participants were asked to describe their typical meal in case they were taking medications around that meal. The choice of the meal constituents was inclusive. Study participants could choose as many options as they wanted. The most common food categories chosen by Polish study participants for breakfast and dinner are presented in Figs. 8A and B.

3.5.1. Breakfast

For breakfast, 654 answers in total were collected. The most commonly chosen options for breakfast were bakery products (22% of answers), dairy products (17%), meat products (17%), and a drink (21%). Generally, the results were similar to German results, particularly about the bakery products (25% of answers), and drink (25 % of answers). The biggest difference was in using a bread spread, which was much more common in Germany than in Poland (21% vs. 7% of answers). In contrast, in Poland, dairy products (17% vs. 12%), meat products (17% vs. 9%) and eggs (8% vs. 2%) were more prevalent.

Specifically, the most commonly described options in every category were: 2 slices (n = 43) or 1 slice (n = 22) of bread, ham (n = 72) or sausage (n = 19), cheese (n = 47) and cottage cheese/twaróg (n = 33), tomato (n = 15), boiled egg (n = 35), butter (n = 19). As a drink, black tea was chosen over coffee (n = 78 and n = 47, respectively).

A typical breakfast variant was 2 slices of bread with butter and ham with black tea. The second variant of a typical breakfast was 2 slices of bread with butter, one with cheese and one with ham, together with a black tea.

3.5.2. Lunch

For lunch, 161 answers in total were collected. It was impossible to assess the typical lunch specifically. In general, the lunch consisted of soup (24% of answers), potatoes/rice/pasta/buckwheat (24%), meat products (23%), some vegetables (10%), and a drink (17%). The usual drink for lunch was water or fruit compote.

3.5.3. Dinner

For dinner, 435 answers in total were collected. The most commonly chosen options for dinner were bakery products (24% of answers), dairy products (15%), meat products (14%) and a drink (22%). Typical dinner variants were two slices of bread with butter, ham, and tea or two slices of bread with butter and cheese or cottage cheese (pol. twaróg) and tea. The Polish dinner is highly comparable with the results from Germany (bakery products 22%, dairy products 16%, meat products 18% and drink 23%).

3.5.4. Time of dosing regarding meal intake

Figs. 9A and B depict the time of the drug intake regarding meal ingestion. Similarly to the German study population, most of the Polish study participants took their medications directly after their meal (breakfast 32% of answers in Poland vs. 39% of answers in Germany as well as dinner 33% of answers in Poland and 52% of answers in Germany). Conversely, in Poland drug intake 30 min before breakfast was not prevalent (8% of answers vs. 20%).

Since the typical breakfast and dinner in Poland were in fact the same, the caloric value for the typical meal variants (without distinction) were assessed. The typical variants are available in the supplementary materials - caloric tables. The caloric value of 121 - 380 kcal was used to calculate the potential gastric emptying time. It was reported that generally the gastric content is being emptied from the stomach with a velocity of 2 – 4 kcal/min (Kong et al., 2008). Considering these values, the gastric emptying of a typical meal as assessed in the study should be between 30 min and 3 h

3.5.5. Food vehicles

In the presented study, a food vehicle was considered as a food item

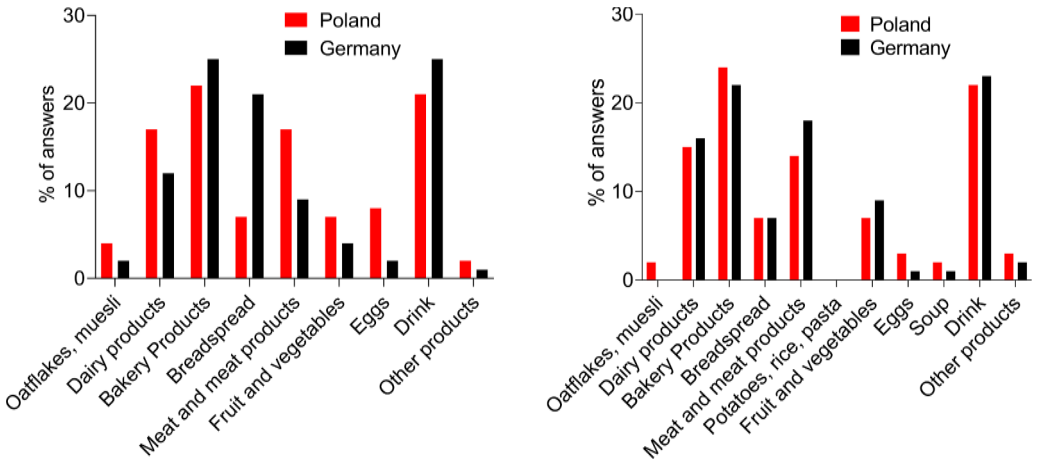

Fig. 8. A) Typical breakfast of the Polish and German study participants, who take their medications at breakfast time ($n = 163$ and $n = 164$, respectively), multiple choice question ($n = 628$ and $n = 635$ answers in total, respectively). B) Typical dinner for Polish and German study participants, who take their medications at dinner time ($n = 130$ for both study populations), multiple choice question, ($n = 435$ and $n = 541$ answers in total, respectively) (Sarwinska et al., 2024).

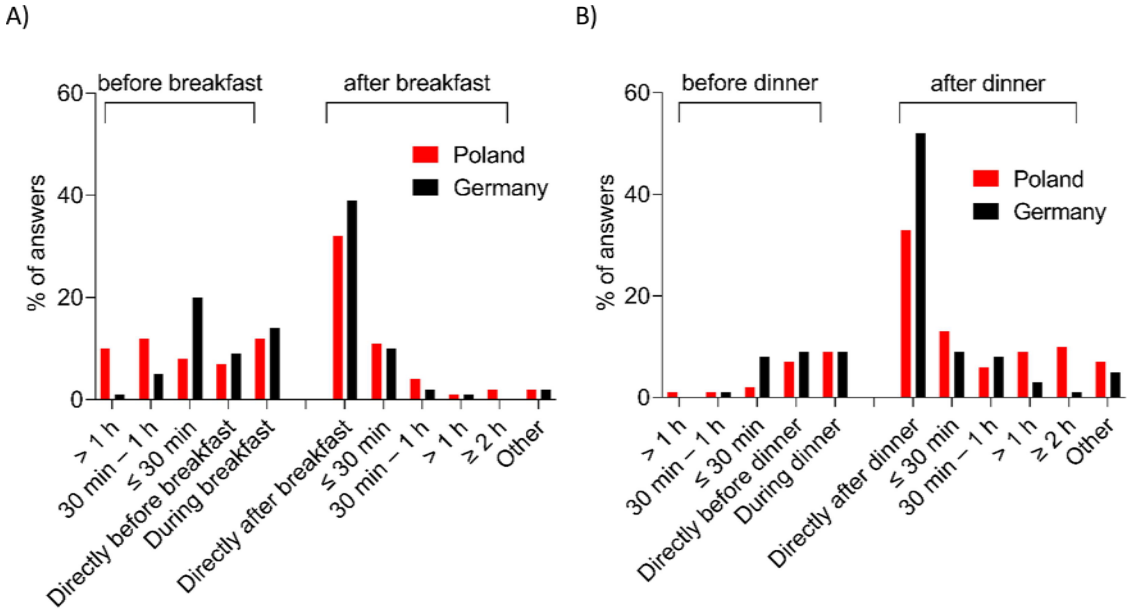

Fig. 9. Time of medication intake regarding the food intake among Polish and German study participants. On the left side (A) answers about breakfast are presented ($n = 163$ participants and $n = 222$ answers in total for Poland and $n = 164$ participants and 198 answers in total) and on the right side (B) about dinner ($n = 130$ participants and $n = 137$ answers in total for Poland and $n = 130$ participant and $n = 133$ answers in total) (Sarwinska et al., 2024).

used to aid in medication intake, mostly in swallowing difficulties. Some participants in the study reported using a variety of food products. Six respondents mentioned bakery products such as bread, while two mentioned cereals or muesli. Two others noted fruit products, and one respondent each mentioned using milk products or soup for this purpose. The most common reason for mixing medications with a food vehicle was to ease the swallowing process (6). Only one person reported doing so to mask the bitter taste of the medication and one to avoid taking medications on an empty stomach. Two people had other reasons, that were not specified.

3.6. Fluids co-administered with medications

3.6.1. Type of fluid

Fluids used for drug administration by the Polish and the German population are presented in Fig. 10. The most prevalent fluids chosen by Polish participants were non-carbonated water, mineral (28% of answers) as well as tap water (23%), and tea (black tea) (24%). Less often chosen options include coffee (5%), sparkling water (5%), and juices other than grapefruit juice (tomato, carrot, orange, raspberry, strawberry, black currant, apple) (5%). One person from the Polish study population mentioned drug intake with strong alcohol. Interestingly, 15% of answers about tap water in Poland also included information about using tap water that was boiled and cooled before drinking. In general, non-carbonated water (mineral 29% and tap 30%) was also the most prevalent in Germany. Tea, however, was not so prevalent among Germans (14%).

Odds ratio analysis was performed in order to assess how often study participants chose water (tap, mineral, carbonated) over fluids other than water. Polish study participants chose water 1.5 times more often than other fluids, and German 2.3 times more often (Eq. 1). Comparing Poland and Germany, study participants from Germany chose water 1.5 times more often than study participants from Poland (Eq. 2).

The age groups analysis was performed to assess how often study

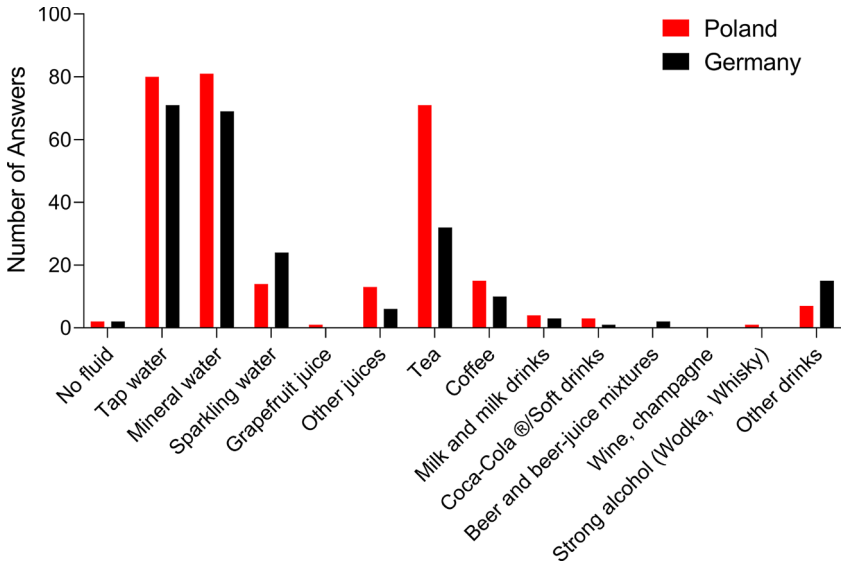

Fig. 10. Type of fluid co-administered with medications by Polish ($n = 174$) and German ($n = 167$) study participants, multiple choice question ($n = 292$ answers in total from Polish participants and n = 235 answers in total from German participants) (Sarwinska et al., 2024).

participants from age groups 70 – 79 and 80 – 89 years old used water for drug administration. Similarly to the mentioned odds ratios for general populations Polish participants used water less often than Germans, however in the group 80 – 89 years, this difference was smaller.

3.6.2. *Amount of fluid*

The most frequent answers about the amount of fluid co-administered with medications in Poland were a few sips and a small cup of 100 mL (35% and 32% of answers, respectively). The answer 200 mL was chosen in 20% of cases (Fig. 11). In Germany, generally higher volumes were used by study participants: 100 mL (32% of answers), 200 mL (30% of answers), and a few sips (21%).

To assess the significance of differences in volumes used by participants to administer medications, the Mann-Whitney test was performed. The general comparison of Polish and German populations demonstrated a significant difference in mean volumes of fluid used to administer medications. The mean volume used by the whole Polish study population was 102 ± 76 mL. In Germany, it was 135 ± 150 mL. The difference was significant ($p = 0.007$), even though high variability was present. The median value was 100 mL for both study populations. Scatter plots of answers can be found in supplementary data.

The results of the age group analysis demonstrated that the median value for both age groups and populations was also 100 mL. For the age group 70 - 79 years, the difference in mean volumes was significant with p value = 0.0276 (similar to the results from the general populations). However, the difference was only approximately 30 mL. In the age group 80 - 89 the difference was not significant.

4. Discussion

The presented study gives a general overview of the drug intake behaviour of the older population in Poland. The study was a follow-up

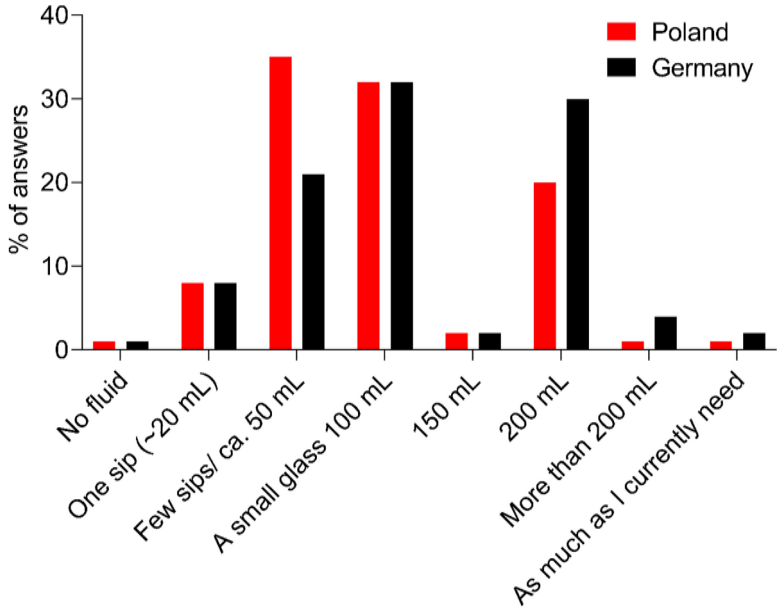

Fig. 11. Amount of fluid co-administered with medications by study population in Poland ($n = 174$, multiple choice question, $n = 181$ answers in total) and in Germany ($n = 167$, $n = 169$ answers in total), (Sarwinska et al., 2024).

of the previously performed study with the German older population (Sarwinska et al., 2024). The method of medication intake was similar in both Polish and German study populations. The primary and most important similarity between Polish and German older adults was using water as the most common fluid for medication intake. The second was using bread as a main ingredient of the typical breakfast and dinner. The third was that drug intake was performed most often directly after food ingestion. Moreover, in both countries dividing tablets was the most common dosage form modification and participants tended to take all medications together. Conversely, Polish study participants reported the use of smaller volumes of fluid for medication intake than German. The second notable difference was that in the Polish population, fluids other than water (specifically black tea) were frequently co-administered with medications, which was not found in the German population. In the following section, we broaden the discussion about the influence of the mentioned dosing conditions (way of taking medications, dosage form modifications, type and amount of fluid co-administered with a dosage form, food ingested while drug intake) on biopharmaceutics, especially on drug absorption. Based on the potential effect of dosing conditions on dosage forms, collected data may be further used for in vitro or *in silico* simulations. A similar approach was already presented in the literature, where the data from questionnaires, mostly about the typical fluids used for drug administration by real-life patients, was used as either a dissolution medium for *in vitro* studies or as a drink for dosage form administration for in vivo studies (Hens et al., 2017, 2020; Huang et al., 2024).

4.1. Demographic data

A comparison of the current Polish study with the previous German study revealed notable differences in the age distribution of participants. This discrepancy can be attributed to the notable divergence in life expectancies between Poland and Germany, as previously discussed in the introduction. Life expectancy in Germany is 78.1 years for men, 82.9 years for women and 80.7 years for the whole population (World Health Organization, 2022a). On the contrary, life expectancy in Poland is lower, with men living 71.6 years, women living 79.4 years and the general population 77.4 years (World Health Organization, 2022b). It is worth noting that while in Germany 7.2% of the total population is aged 80 years and over, in Poland the aged population represents 4.3% of the total population (European Commission Eurostat, 2024). Interestingly, the median age of both study populations corresponds with the general life expectancies in certain countries. This demonstrates that although the participants interviewed from both populations had different age distributions, they represented rather accurately the same characteristics within the population. Shorter life expectancy and thus, a smaller percentage of older adults aged at least 80 years may be caused by lower healthcare expenditure and spending on long-term care mentioned in the introduction, which contribute to a generally worse health condition of Polish older adults and higher morbidity. Furthermore, the differences in life expectancy are also the reason for the differences in gender balance in the older population, where women prevail. However, in our study, this prevalence was not notable.

Additionally, the participants for the study were chosen randomly (if they met inclusion criteria), however, the recruitment site could affect these differences. In the German study population, there were more participants from the hospital setting than in the Polish study population (44 % vs. 33 %) (Sarwinska et al., 2024). Moreover, in both countries, geriatric patients were recruited from different units (two geriatric wards in Germany and a Clinic of Rheumatology, Clinical Immunology, Geriatrics and Internal Medicine, a Clinic of Hypertension and Diabetology and two Clinics of Cardiology), therefore, their health conditions were not the same, and it could affect drug intake process. Geriatric patients (patients from geriatric wards) are generally more affected by multimorbidity and conditions typical for this group (such as frailty) than patients from the specific clinics. Furthermore, in the Polish study, some participants (24%) were recruited in nursing homes, however, this setting combines features of both other settings (home and hospital).

4.2. Medications

The results of our study demonstrated that the phenomenon of polypharmacy is also pervasive among the Polish population. The majority of the surveyed Polish participants reported taking between 5 and 9 medications daily. The high prevalence of polypharmacy is further evidenced by the fact that the second most numerous group of respondents were taking more than 10 medications daily. These findings were the same for the age groups 70 – 79 years and 80 – 89 years, which demonstrates that the results for the whole population were representative. By defining polypharmacy as the dispensation of a minimum of five prescription medications, this issue affected 75% of participants from our Polish study in comparison to the German study population, where it was 69% (Sarwinska et al., 2024). However, it has to be noted that in our studies only participants who take medications were included, not healthy older adults, who may take no medications. The study by Brandão et al. mentioned in the introduction, demonstrated that in Poland self-medication was the highest among investigated European countries (Brandão et al., 2020). This also might contribute to the high number of medications taken by older Polish adults.

The number of medications taken by study participants can also be a factor that influences the way medications are taken. In the Polish population, both answers, intake of all medications at once and taking medications separately were frequently selected. In the German study, however, participants reported taking all their medications together much more often than separately. Although participants were not asked about the reason for taking all medications at once, a possible reason for it could be the fact that multiple medications are easier to take all at once than separately due to time or comfort. Since most of the study participants took at least 5 medications, more people may take them all at once. Intake of several medications at once may also result in different final volumes of fluid available for dosage forms. The influence of the amount of fluid co-administered with a medication will be discussed further in the publication. Moreover, the intake of many medications together may change the conditions for drug release in GIT that influence dosage forms, especially the absorption process, due to certain drug-drug interactions. The best known is the pH-dependent drug-drug interactions of several medications with antacids which are commonly used by older populations (Mitra et al., 2020; Welling, 1984).

Conversely, the intake of several medications separately may be also a sign of swallowing difficulties. The study by Schiele et al. reported that only 21.1% of participants with swallowing difficulties (mean age 61.8 $\pm$ 15.6) were swallowing more than one solid dosage form simultaneously (Schiele et al., 2013). Another reason for swallowing medications separately may be the idea that taking medications separately allows avoiding interactions between them, or just the habit of the person.

4.3. Dosage form modifications

About 20% of participants made some kind of modifications to their medications. In almost all of the cases, modifications were made to tablets. Similarly to the German study, the most prevalent modification was dividing tablets. In the Polish study, people also reported crushing tablets, dissolving them in water, and chewing them. It is possible that such modifications were performed without supervision, and it could affect the behaviour of medications. Older patients are often compelled to alter their tablets, risking mistakes in dosage which may result in numerous complications. For instance, crushing or splitting extended-release tablets can cause the release of the entire active ingredient at once, leading to toxicity (Taylor, 2018). Inappropriate and unnecessary alteration of medications is undesirable and could cause some adverse effects such as gastric problems or insufficient activity of the drug

(Jaspersen et al., 2000). Moreover, crushing tablets leads to the loss of the powder and thus, active pharmaceutical ingredient (API). Prior data in Casiraghi et al. demonstrated a mean loss of 6.27% of powder and 8.53% of API in the case of dividing riluzole 50 mg tablets by 15 healthy volunteers (Casiraghi et al., 2023). In this study, received values could have been even higher when used by the older population due to their common dexterity issues. Crushing tablets is a practice that may be particularly hazardous in the case of medications with a narrow therapeutic window e.g. some antibiotics, warfarin, digoxin, and theophylline (Kang et al., 2009). Many of these medications are commonly used among the older population. Furthermore, dosage form modification destroys the drug formulation. Drug formulation gives a drug substance a special form and thus, properties, which are tested and ensure the safest and most effective pharmacotherapy.

Literature data has reported that older people are statistically more likely to have swallowing difficulties (Perrie et al., 2012; Stegemann et al., 2012). Similarly, our results reported that several older adults had problems with swallowing their medications or modifying their medications due to the drug's large size, which was expressed as the reason for dosage form modifications. This demonstrated that problems with drug intake may be due to the size or shape of a dosage form. Thus, often a change in the sizes and shapes of the tablets, while formulation development, could be a good strategy to ease medication intake for patients, and to minimize the occurrence of dosage form modifications (Perrie et al., 2012; Stegemann et al., 2012). Conversely, literature reported also strategies that patients can use by themselves (instead of dosage form modifications) to ease swallowing difficulties in the case of the big size of a dosage form. One strategy is called systematic desensitization, where patients swallow several small objects (e.g. jellies) whose sizes increase until they reach the medication size (Lau et al., 2018). As mentioned in the result section, some study participants performed dosage form modifications due to habit, which may indicate unsupervised drug modifications. Although this group was small (4 out of 36 participants who reported dosage form modifications), it cannot be said that 14 participants who modified their medications because of problems with swallowing and too large size of the tablet were doing it with medical advice. That indicates that the problem of unsupervised drug modifications may be bigger than assessed and affect 50% of participants who performed modifications.

Our findings highlight the necessity for enhanced awareness and education regarding the potential hazards of modifying solid dosage forms. Ensuring accurate and proper medication administration can prevent the deterioration of drug efficacy and the emergence of adverse side effects.

4.4. Body position

A comparison of the results from the German study with the current data from the Polish survey demonstrated similarities in body position, where the majority of Polish and German participants reported taking their medications while sitting, with an additional high proportion preferring to stand. In general, it means that almost all of the participants from both populations took their medications in the upright position. These parallels suggest consistent drug intake behaviours across both populations. Often, the body position during medication intake is a person's habit or is spontaneously chosen depending on their current situation.

From a biopharmaceutical point of view, body position may be important due to the potential effect on drug absorption, oesophagal transit and adhesion of a dosage form to the oesophagus. The study by Channer et al. demonstrated that the upright body position was relevant to ensure the normal transit of tablets. For example, paracetamol absorption from the tablets administered in the supine position was affected due to a delay in oesophagal motility (Channer et al, 1985). Literature reports that dosage forms that have a high potential to adhere to the oesophagus are gelatin capsules and cellulose films. Conversely, coated forms (aqueous dispersion or sugar) appear to have low adherence (Marvola et al., 1983). Similarly, the results from a recent study by Hummler et al. demonstrated that gelatine capsules had prolonged oesophagal transit, whereas uncoated and particularly coated tablets demonstrated reduced adhesion to the oesophagus (Hummler et al., 2024). Moreover, the results obtained in another study for zopiclone tablets administered in supine and upright positions demonstrated that the fast and full hypnotic effect of a drug was achieved when the tablet was administered while standing. Drug administration in the supine position caused an increase in the lag time ($>$ 20 min) before the beginning of the absorption process and reduced the rate constant of absorption. Body position, however, did not change the drug exposure (Channer et al., 1984).

Even with several old and hospitalized patients, findings in both of our studies showed that drug intake in the supine position was not prevalent, which is a good outcome that does not put patients at risk of adverse effects and ineffective pharmacotherapy. Nevertheless, the number of bedridden patients could have been underrepresented in our study for this aged population. Due to comorbidities and statistically more prevalent cognitive impairments in this group of patients, they were not screened for study participation and therefore, the answers were not collected.

4.5. Drug intake regarding meal intake

4.5.1. Time of dosing regarding meal intake

Among the Polish respondents, the most frequently selected times for medication intake in relation to mealtimes were immediately after breakfast and immediately after dinner. This coincides with data from the German population from the previous study (Sarwinska et al., 2024). In the German edition of the study, drug intake 30 min before breakfast (mostly in the case of L-thyroxine or Proton Pump Inhibitors) was also notable, contrary to the Polish population. However, the recommendation is to take the mentioned medications not shorter than 30 min before breakfast, so this time can be longer than 30 min e.g. 1 hour. Considering all answers up to 30 min before breakfast, the data for Polish and German populations are comparable (29 % vs. 26%), which indicates adherence to this recommendation. Furthermore, a similar situation can be observed when drugs are taken after dinner. German study participants mostly took their medications directly after dinner and the number was notably higher than in Poland. However, comparing the total number of answers after dinner is similar (75% of answers in Poland and 72 % of answers in Germany). Polish study participants were taking their medications not directly after the food intake but rather within a longer time period. This approach may reduce the influence of food on the administered medication, or after the ingestion of a light meal and no food intake between main meals, results in fasted-state conditions again.

Data from both the Polish and German studies suggested that participants tended to organize their drug intake around mealtime. Drug intake with a meal ensures adherence and may decrease the possibility of forgetting about drug intake (Sanders et al. 2013).

Our study is not linked to any concrete medication plan of any individual participant, therefore we cannot directly assume if medication intake in correlation to the patients' meals was correct. Nevertheless, it is worth mentioning that the literature suggests that in the case of some drugs commonly used also in the older population, it could be beneficial for patients to take their medications at mealtimes. It could be observed e.g. in the case of certain drugs that cause gastrointestinal irritation e.g. non-steroidal anti-inflammatory drugs (NSAIDs). In these instances, consumption with food may reduce the irritation, when compared to ingestion with water alone (Fleisher, D., et al., 2009).

Furthermore, in the case of chronically taken medications, it can be beneficial to take medications always in the same manner, also with regards to food, because it allows obtaining a steady state in terms of concentration of a drug or avoiding possible interactions with a specific

food (University Hospitals Coventry and Warwickshire NHS Trust, 2023). The importance of a consistent diet is particularly visible in the example of the common medication used in the older population - warfarin, which interacts with vitamin K from green leafy vegetables (Bushra et al., 2011). This interaction may occur when patients change their meal routine suddenly e.g. start a new diet (e.g. vegan), or during summer, when they tend to eat more vegetables since they are easily available.

It is of concern that a lack of awareness of the potential for significant drug–food interactions may result in suboptimal clinical outcomes (Wenzler et al., 2018).

4.5.2. Standardised clinical study meal versus real-life breakfast

Similarly to the study in Germany, the basis of breakfast as well as dinner of the Polish population was bread. The typical meal consisted of two slices of bread with butter, ham or cheese or twaróg and tea (usually black). The choice of these food products strengthened the idea of a typical light breakfast eaten by the older population (at least in the Pomeranian Region of North East Germany and North Poland) to be sweet or savoury variants of sandwiches. Similarly, like in the German study, the estimated caloric value of the typical meal was quite low and varied between 121 and 380 kcal (in Germany: 107 – 286 kcal for breakfast and 137 – 366 kcal for dinner). Assuming that people do not eat anything between main meals, after such a small meal they will not be in a postprandial state for a long time. The calculated approximate gastric emptying time of a typical Polish meal was between 30 min and 3 h, which is almost the same as in the case of the German meal. Generally, the values 2 – 4 kcal/min regard the general adult population. Considering gastric emptying in the older population, several studies demonstrated contradictive results, however, the general findings reported that healthy ageing causes moderate slowing of gastric emptying, still in the norms for the younger population (Kuo et al., 2007). Therefore, it may be assumed that the higher end of the mentioned gastric emptying time range would be more appropriate for the older population. Additionally, the rate of gastric emptying is also reduced by fat, since fat has higher caloric density in comparison to proteins and carbohydrates (9 kcal/g vs. 4 kcal/g) (Kong and Singh, 2008). In our studies, fat came mostly from butter and cheese. Reported Polish meal depending on the variant contained between 5 and 19 g of fat (on average 4.8 g). The German breakfast was mostly low-fat with 2 to 10 g of fat (on average 6.2 g) and finally German dinner with higher fat content between 6 and 23 g (13 g on average). Dinner variants from the German population were the most caloric meal with the highest fat content and therefore, it may be assumed that it will be emptied slower than other meals.

In the presented study we also compared our real-life scenario with a worst-case scenario from the FDA. Once more, a typical meal eaten by the study population in Poland differed considerably in the composition and the caloric value from the FDA breakfast, which is calorically much higher (800 – 1000 kcal) (FDA, 2014). That is a favourable situation because the worst-case scenario will not be fulfilled in real-life. The real-life meal may not extend the transit time of monolithic forms in GIT, will not cause such a strong physiological response of the organism as the FDA breakfast and the food effects that were detected during studies with a high-fat, high-caloric meal will not appear, what also hinders the risk for patients.

Conversely, there are several examples of medications that should be taken with meals e.g. already mentioned NSDAIs which should be taken with food to avoid the irritation of GIT (Fleisher et al., 2009). Another example could be posaconazole, an antifungal drug, whose absorption from the small intestine was increased by high-fat meal (Kersemaekers et al., 2015). The third example connects both aspects. The antibiotic Augmentin® should be taken at the beginning of meal intake in order to reduce the potential gastrointestinal intolerance (e.g. nausea) as well as to optimize the absorption (GlaxoSmithKline). The real-life meals reported by participants from both studies were not high-fat meals, like FDA breakfast. Therefore, in the case of drugs that need high-fat content to be better absorbed it may not be sufficient. However, in the case of drugs, which need the protection of the stomach, due to irritation of GIT, a real-life meal may be sufficient. However, further studies are needed to compare the effect of real-life meals with the suggested FDA breakfast on drug absorption and behaviour.

4.5.3. Food vehicles

Results of our study demonstrated that only a few people used food vehicles, such as bread, cereals, fruit and milk products with their medications. The bread was administered with a tablet in one bite and after administration, forming a kind of coating for a tablet in the mouth. Therefore, patients felt like they were eating a bite of the food, not swallowing a tablet. This is one of the strategies used to ease swallowing difficulties and, in the literature, it is called disguise as a smooth bolus (Lau et al., 2018). The most common reason for using food vehicles by study participants was to ease problems with swallowing. This again indicates that difficulties in swallowing are common in the group of older adults, and some medications may not be suitable enough for intake in this special population. Patients with swallowing difficulties may want to avoid taking drugs or try to modify their formulation to make it easier to swallow because of the discomfort that occurs during this activity. Furthermore, one person declared that the reason to mix medications with food was to mask the bad taste of the tablet. Even though it was only one person, it is still worth mentioning as the flavour of tablets could further be optimized and masked during formulation development in specific cases and it could at least a bit minimize the risk of older people mixing their medications with food vehicles resulting in suboptimal activity of the drug. Even though mixing medications with food could help with some problems, it may impact the drug's effectiveness and therefore, it should be consulted with a health care provider.

4.6. Fluids co-administered with medications

4.6.1. Type of fluid

In our study, the most common fluid used for medication intake, which was non-carbonated water, was the same in the German edition of the study. This finding demonstrated that people are generally aware of taking their medications with neutral fluid. Mineral water was considered as still water from the bottle, therefore, it was included together with tap water in the category of non-carbonated water. As mentioned in the results section, some percentage of older participants in Poland used also boiled and cooled tap water, which is a matter of habit of older adults, who were living in the after-war time, when tap water did not have a proper quality. However, currently, tap water is safe to drink without boiling.

In the general population, as well as in the age groups 70 – 79 and 80 – 89 years, German study participants tended to use any type of water more often than Polish participants, which also demonstrates that this is a representative result.

Interestingly, among Polish study participants, tea (black tea) was the second most used fluid. The usage of tea was notably higher than in Germany. A similar trend was observed in the usage of coffee. Poles consume an average of 0.44 kg of tea per person per year, mostly black, brewed at home (Food and Agriculture Organization, 2021; Czarnieck-a-Skubina et al., 2022). Coffee is popular in Poland - more than 80% of adults drink it daily, although annual consumption is around 2.23 kg per person (Food and Agriculture Organization, 2021). The German population exhibits lower tea consumption per capita as compared to Poland (0.31 kg annually). Although in Germany per capita coffee consumption is higher (approximately 6.09 kg per year), using coffee as fluid for medication intake was less common than in Poland (Food and Agriculture Organization, 2021).

Black tea combines several biologically active ingredients and may interfere with drug release. In their study, Akshay and colleagues observed a pronounced reduction in the release of paracetamol from

tablets in the black tea (with Simulated Gastric Fluid) (Akshay et al., 2021). These results demonstrated that using tea for drug administration may have some implications, however, this influence has to be investigated more, especially in vivo. Similarly to tea, the paracetamol release was also reduced in coffee (50 °C), however, the influence was less prominent than in the tea (Akshay et al., 2021). Literature data indicates that coffee may also affect the absorption of many orally administered drugs by different mechanisms among others alteration of the pH values in the gastrointestinal tract (GIT) (midazolam, levodopa), influence on gastric emptying time (aspirin, felodipine), insoluble complex formation (escitalopram oxalate, iron), or inhibition of the glucose-6-phosphatase (Belayneh et al., 2020). Moreover, the absorption of L-thyroxin and alendronate was reduced when administered with coffee (Benvenga et al., 2008; Gertz et al., 1995).

Furthermore, in Poland, the usage of fruit juices (other than grapefruit juice) was more common than in Germany. Fruit juices could cause interactions due to their carbohydrate content and their respective effect on small intestinal fluids. The delay in gastric emptying and increase of the water content in the small intestine was observed in the study by Grimm et al. for grapefruit juice, however, this effect is also possible for other fruit juices (Grimm et al., 2018). Similarly, the literature data also demonstrated that the effect of fructose and glucose (which are ingredients of fruit juices) on small intestinal water content. The small intestinal water content was increased in the case of fructose and decreased in the case of glucose (Murray et al., 2014). Alterations in GIT conditions after administration of fruit juices may also alter the drug pharmacokinetics, especially absorption.

Fruit juice components were also reported to inhibit the OATPs (organic anion transporting polypeptide) and therefore, reduce drug bioavailability after oral administration (Dresser et al., 2002). The absorption of alendronate was reduced by 60% not only when administered with coffee but also with apple juice (Gertz et al., 1995). The study of celiprolol with orange juice also revealed a decrease in bioavailability (Lilja et al., 2004). Interestingly, apple juice presented a dose-dependent interaction with atenolol and fexofenadine. In both cases, the systemic exposure was reduced when administered with a higher volume of the juice (Luo et al., 2016; Jeon et al., 2013). Older adults frequently take medications such as alendronate, celiprolol, or atenolol, and this population is more susceptible to adverse effects, therefore, interactions with fruit juices can be potentially hazardous.

Although there was only one case of taking medications with strong alcohol, this situation is potentially dangerous. In the case of the intake of modified release forms with alcohol, alcohol-induced dose dumping (AIDD) can occur (European Medicines Agency, 2013). Dose dumping occurs when the whole dose (intended to be released within a few hours, much higher than a single dose) is immediately and unintentionally released from the modified release dosage form. AIDD leads to side effects, overdosing, and can be fatal. AIDD is especially dangerous in the case of medications with a narrow therapeutic index or opioids (D'Souza et al., 2017). Although luminal ethanol concentrations at the site of dissolution and absorption are shown to be rather low even after intake of stronger alcoholic beverages, the effect is probably not so prominent, however further risks need to be considered (Rubbens et al., 2016). For example, alcohol ingestion together with NSAIDs increases the risk of haemorrhage in the gastrointestinal tract (Fraser, 1997). NSAIDs are common medications in the older population, due to common occurrence of pain in this population. Moreover, alcohol is metabolized by the same enzymes as many commonly taken medications (cytochrome P450 CYP2E1), which may also lead to ineffective pharmacotherapy and adverse effects (Fraser, 1997). Drug intake with alcohol should be considered individually for a certain patient and medication and in case of interactions patients should be warned about the interaction in the information leaflet.

A study by Hens et al. reported the drug intake process in another European country - Belgium. The study investigated the fluids used for medication administration, and although the results did not come from the older population but from the general population of adults (aged at least 16 years old), water was also the most frequently chosen fluid (92% of respondents). Interestingly, the second fluid was soda (13%) which was uncommon in both Poland and Germany. Moreover, tea was chosen only by 3% of the respondents, which is notably lower than in Poland and Germany (Hens et al., 2017). The positive aspect of these findings is that water seems to be the first choice for medication intake for most of the patients, also in the general population. Other fluids are generally the same, however, they are chosen with varied frequency, which may depend on the location, age, or habits of people. Therefore, further investigations are needed to assess regional and age-related differences in fluids used for drug intake.

4.6.2. Amount of fluid

The calculated average difference in the amount of fluid used to administer medications by the Polish and the German population (and also in the age group 70 – 79 years) was significant, however, it might not be clinically relevant. Although in both populations people used on average 100 mL of fluid, the bigger difference can be observed in the distribution of answers between both study populations. German study population tended to use more fluid (200 mL) and the Polish less (few sips).

Our results again confirmed that in real life, people do not use 240 mL of water, which is a standard from FDA studies (FDA, 2014). Additionally, the recommendation from EMA of at least 150 mL of water is not met in real life (EMA, 2010). In comparison to the mentioned study by Hens et al. from the general adult population in Belgium, around 120 mL of fluid (half of a glass) was the most common volume for drug administration (46.7%). Although the study by Hens et al. investigated the drug intake in the general adult population (from 16 years old) not older adults, it seems to be the general finding to use about 100 – 120 mL of fluid, since that was also the average volume reported in our studies from both populations (Hens et al., 2017).

The volume of co-administered fluid is important for orally administered medications and may change the pharmacokinetics. The gastric emptying of non-caloric fluids depends on the volume of fluid administered and it is described with the first-order kinetics. More fluid is emptied faster, and as time passes by the velocity decreases (Leiper, 2015).

As mentioned in the previous section, the volume of co-administered apple juice altered the systemic exposure when administered with fexofenadine and atenolol. The systemic exposure was reduced when administered with a higher volume of fluid (150, 300, and 600 mL for fexofenadine, and 600 and 1200 mL for atenolol) (Luo et al., 2016; Jeon et al., 2013). Although 600 and 1200 mL of apple juice seems to be much to drink at once, in the study, these volumes were not administered at once. Study participants drank 300 mL with a drug and the rest was consumed in 0.5 h intervals. Therefore, this study design can resemble a real-life situation.

Administration of large volumes of juices matters not only because of the volume itself but also due to its pH values which change the pH in the GIT. Moreover, fruit juices also have a certain caloric value. It is assumed that caloric content is emptied from the stomach at a velocity of 2 to 4 kcal per minute, therefore the more juice is administered the more calories it contains, which extends the gastric emptying process (Kong and Singh, 2008). Moreover, the increase in juice volumes also enhances the inhibitory effect on enzymes, which has further effects on the absorption and metabolism of administered drugs (Veronese et al., 2003).

Conversely, the amount of co-administered fluid also influences the oesophagal transit of tablets. The study by Channer et al. mentioned before demonstrated that to obtain the optimal and fast absorption of paracetamol, the tablets should be swallowed with at least 60 mL of water (vs. 15 mL) and in the upright position (Channer et al. 1985). Another study confirmed these findings and suggested the intake of at least 50 mL of fluid in the upright position to avoid the oesophagal retention of solid dosage forms (Osmanoglou et al., 2004). Presented

examples demonstrated the risk of drug intake with small volumes of fluid, which was common among the Polish population from our study, who mostly took their medications with few sips of fluid.

4.7. Limitations

The presented study had some limitations. By performing a questionnaire study, the answers of participants could be affected by their personal bias and emotions, however, it cannot be determined whether that is the case. Moreover, the participation in the study was voluntary, so we could not get opinions from people who declined to participate, which is unfortunate as it could provide information from a whole different spectrum of patients and it might bias the outcome for the aged population. Despite only interviewing people who had been assessed by doctors or nurses as having no cognitive impairment, it cannot be certain if all of them were actually in an acceptable level of the cognitive state as they were all over 65 years old and their state was not assessed by a professional such as psychiatrists or neuropsychologists. Finally, the study was performed only in one location (Pomeranian Voivodeship), therefore it is considered to be performed locally. Conversely, the study was not conducted only in one city, as the participants were recruited from both countryside and cities. Therefore, even though we believe that the collected data can be applied to the Pomeranian population, we cannot generalize the results for the population of the whole country.

5. Conclusion

To conclude, drug intake behaviour among the older population in Poland and Germany was highly similar. There were small differences that, in fact, are mostly irrelevant from a biopharmaceutical point of view. Moreover, age groups analysis performed for the two age groups with the biggest differences in the number of participants demonstrated that the results are representative of the whole study population. These findings demonstrated consistency in drug intake in the older population and no regional differences in the Pomeranian region of two countries, Poland and Germany. The data from other European countries or even other countries worldwide would be interesting, particularly from countries that are culturally different from Poland and Germany. The presented results are important to understand the drug intake process in the older population, identify potential problems and try to find individualized solutions to specific issues to make pharmacotherapy safe and effective. Furthermore, the data from the study may be used as input data for several in vitro or *in silico* studies to better understand the drug behaviour after oral administration and allow patient-centric drug development.

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CRediT authorship contribution statement

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejps.2024.107001.

Data availability

Data will be made available on request.

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