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FOOD AND NUTRITION

AWARENESS AND KNOWLEDGE OF DRUG-FOOD INTERACTIONS AMONG POLISH THIRD-AGE UNIVERSITY LISTENERS BEFORE AND AFTER TRAINING – A QUESTIONNAIRE STUDY

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Abstract: The problem of drug-food interactions is of particular concern to the elderly, as polypharmacy is most prevalent in this population. The study assessed the awareness and knowledge of drug-food interactions among Polish third-age university listeners before and after training on that topic. A total of 143 participants, with a mean age of 71.5 ± 5.5 years, took part in the study. 123 participants (86%) completed the pre- and post-training questionnaires. 91% of respondents had heard that food can affect the effectiveness of drugs and a similar number stated that they are aware of what time to take their medications. Information about drug-food interactions was most frequently obtained from the physician (34%), the drug leaflet (30%), or the internet article (23%). The mean percentage of correct answers to questions testing knowledge of drug-food interactions before and after training was 32% and 57%, respectively (Chi^2 test, $p < 0.05$). To determine the structure of relationships between parameters (or categories of parameters), the results were examined using correspondence analysis (CA). The categories of parameters with the highest quality of representation in the CA model were indicated and the parameters characterized by the highest strength of coexistence were determined. The majority of study participants were aware of drug-food interactions, but their knowledge of the topic was poor, and often incorrect. The training significantly increased the knowledge of drug-food interactions. The study indicates the need to educate geriatric patients on the correct use of drugs with food and on the importance of drug-food interactions.

Keywords: Drug, food, interaction, knowledge, geriatric, polypharmacy.

We live in an aging society. In 2021, 20.8% of the European Union population was aged 65 years or above (1). In Poland, the percentage of elderly people is systematically increasing: at the end of 2020 it reached 25.6% which was 1.0% more than in the previous year (2). According to the prognosis of the Central Statistical Office, the number of people aged 60 and over in Poland will continue to rise, and in 2050 they will constitute approximately 40% of the total population (2).

With age, the risk of polypharmacy increases (3). The World Health Organization defines polypharmacy as the simultaneous intake of multiple drugs (4). By convention, „multiple" is 5 or more medications - including both prescription and over-the-counter drugs (5). A cross-sectional analysis based on data collected in the SHARE (Survey of Health, Ageing, and Retirement in Europe) study showed that in Europe, polypharmacy affects (on average) 32.1% of people aged 65 and over, and in Poland is even higher (33.8%) (6).

Not all medications should be routinely prescribed to older adults. Certain drugs are classified as Potentially Inappropriate Medications (PIM) for the elderly because their use may lead to adverse events, such as the increased risk of falling, cognitive impairment, or bleeding (7). Among PIMs are e.g. cholinolytics, opioids, benzodiazepines, H1-receptor antagonists, tricyclic antidepressants, non-steroid anti-inflammatory drugs (NSAIDs), etc. Several continuously updated lists of PIMs are widely available, such as EU(7)-PIM (8), the PRISCUS (9), or Beers list (10), where, in addition to listing inappropriate drugs, safer alternatives are often proposed.

Another challenge is age-related physiological changes in the gastrointestinal tract, liver, and kidneys that may have a significant influence on each step of drug action in the older organism (pharmacokinetics) (7, 11). The most important pharmacokinetic changes in the elderly are summarized in Table 1. Additionally, age-related pharmacodynamic changes

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may occur, such as increased or decreased receptor sensitivity, leading to higher or lower efficacy of certain drugs. For example, older adults show a greater response to opioids, benzodiazepines, and anticoagulants, whereas are less sensitive to beta-antagonists, loop diuretics, or calcium channel blockers (7).

Polypharmacy (often including PIMs), self-medication with dietary and nutritional supplements, and pharmacokinetic or pharmacodynamic changes in the elderly may all contribute to the high risk of drug-food interactions in this population (7).

Drug-food interactions can be defined as interactions between drugs and food ingredients, beverages (including alcohol), or dietary supplements (12). The way of taking drugs with food may have either a negative or positive impact on the patient's safety, quality of life, and effectiveness of therapy (12, 13). Drug-food interactions can, for example, reduce or potentiate the effect of pharmacotherapy, contribute to an increase or decrease in the frequency and severity of adverse drug reactions, cause nutrient malabsorption or improve their bioavailability (12, 13).

Clinically significant drug-food interactions have been proven for many drugs/drug groups that are frequently used by the elderly, e.g. bisphosphonates (14), proton pump inhibitors (15), drugs employed in treating benign prostatic hyperplasia (16), drugs used in the treatment of Parkinson disease (17), levothyroxine (18), etc. Moreover, it was suggested that undetected drug-food interactions in the elderly can be misdiagnosed as the progression of chronic disease, and may lead to serious morbidity and mortality (19).

While general awareness of drug-drug interactions exists, data on patients' awareness and knowledge of drug-food interactions are limited to several survey studies, of which two involved Polish patients (20, 21), and the remaining were performed in the middle eastern countries (22, 23). Only one of these studies focused exclusively on geriatric patients (21).

This study aimed to verify the state of awareness and knowledge of drug-food interactions among Polish third-age university listeners and to investigate whether this knowledge can be improved by providing training on the topic of drug-food interactions.

EXPERIMENTAL

General study characteristics

The study was questionnaire-based. Volunteers were third-age university listeners recruited from three Ptowns in southern Poland, namely Nowy Targ, Szczawnica, and Krosno. No restrictions were made regarding the characteristics of participants (i.e. gender, race, and health status). The exclusion criteria were as follows: the person recruited or already participating in the study refuses to participate further or is unable to answer the questions asked.

Participants completed an anonymous, validated questionnaire on awareness and knowledge of drug-food interactions. This was followed by on-site training on the topic, after which the same

Table 1. Age-related changes in pharmacokinetics.

Pharmacokinetic phase	Physiological changes	Consequences
Absorption	↓ gastrointestinal motility ↓ small intestine surface area ↓ gastric emptying ↓ gastrointestinal blood flow ↓ intestinal cytochrome P450 activity ↓ intestinal P-glycoprotein activity ↑ gastric pH	altered drug absorption (↑ or ↓ depending on the medication) ↓ absorption rate constant
Distribution	↓ albumin level ↓ P-glycoprotein expression and activity ↓ total body water content ↓ lean body mass ↑ total body fat ↑ permeability of the blood-brain barrier	For fat-soluble (lipophilic) drugs: ↑ volume of distribution, ↑ half-life For water-soluble (hydrophilic) drugs: ↓ volume of distribution, ↓ half-life, ↑ serum concentrations
Metabolism	↓ liver weight ↓ hepatic blood flow ↓ cytochrome P450 activity	↓ first-pass metabolism and hepatic clearance
Elimination	↓ kidney weight ↓ renal blood flow ↓ glomerular filtration rate	↓ renal clearance

questionnaire was completed again. The questionnaire consisted of closed questions, in which respondents gave single- or multiple-choice answers.

The study was performed between November 2021 and March 2022. The study protocol was reviewed and approved by the local bioethics committee (consent number: 1072.6120.109.2021).

Questionnaire characteristics

The questionnaire consisted of a short personal survey (date of birth, gender), 3 questions (asked only once) testing awareness of the existence of drug-food interactions, as well as the sources of knowledge on this topic, and 22 single- or multiple-choice questions (asked twice, before and after training) assessing the general and detailed knowledge of drug-food interactions. The questionnaire form is presented in Figure 1. A Microsoft Office Excel spreadsheet was used to arrange the database of survey results in a tabular form.

Questionnaire validation

The questionnaire validation took place in two stages. The first stage was to present the form to two specialists in the study area or non-medical scientists. Each specialist provided their comments, which were incorporated into the questionnaire. In the second stage, 15 individuals completed the form twice, at least seven days apart. All data obtained from the questionnaire were strictly categorized by assigning them logical values. The percentage of repetitive responses to all responses was assessed. 70% was considered the acceptance threshold for repeatability. In addition to the percentages of agreement, the gamma correlations were calculated. As a result of the reliability tests performed, the full applicability of the questionnaire for the study was confirmed (24, 25).

Statistical analysis

The statistical significance of the relationships between the number of correct answers before and after the training was tested using Pearson's Chi^2 test. It was assumed that if $p < 0.05$ then the co-occurrence does exist. The strength of the relationship between the number of correct answers before and after the training was measured using Yule's Q coefficient, which determines the correlation between the variables. It was assumed that the correlation between the features is determined by a value of this test above 0.2 (the closer to 1, the stronger the relationship between the features considered). In addition, OR = odds ratio (the proportion of correct answers to wrong answers after the training compared to the situation before the training) was determined. If OR = 1, the chance of a correct answer occurring before and after the training was the same; if OR < 1, there was a lower chance of a correct answer occurring after the training than before it; if OR > 1, there was a higher chance of a correct answer after the training than before it.

Appropriate correspondence analysis (CA) models were constructed to investigate the structure of the relationship between parameters (categories of parameters). The strength of associations between the parameters was calculated as the algebraic product of their coordinates on the graph of the first two dimensions of the CA model, multiplied by the cosine of the angle between the lines connecting the coordinates of the parameters with the center of the coordinate system. The coefficients obtained in this way are called the association weights. More details of this approach were given in our previous paper (25).

Statistical analysis was carried out using STATISTICA v. 13.3. package (TIBCO Software Inc., Palo Alto, CA, USA). The software delivered by MP System Co. (Chrzanów, Poland) was used to calculate correlation weights for the pairs of parameters in the CA model.

RESULTS

Participants characteristics

A total of 143 participants took part in the study (48% from Nowy Targ, 35% from Szczawnica, and 17% from Krosno). 127 participants specified their age (mean 71.5 ± 5.5 years, range 58-86 years), and 97 stated their gender (95% – women). 137 participants returned the pre-training questionnaire and data from these surveys were used to assess the awareness of the existence of drug-food interactions, as well as the sources of knowledge on this topic. 123 participants completed both surveys (pre- and post-training) and data from these surveys were included in the analysis of general and detailed knowledge of drug-food interactions.

Awareness of the existence of drug-food interactions

91% of respondents had heard that food may influence drug effectiveness. The majority of participants (92%) stated that they are aware of what time to take their medications.

Sources of knowledge of drug-food interactions

Among the sources of knowledge of drug-food interactions, participants most frequently indicated: the doctor (38%), the drug leaflet (30%), and internet

Pre-training questions

1. **Did you hear that food may have an influence on drug effectiveness?** Yes / No

2. **How did you learn that food can interact with the medicines you take? Please tick all matching sources of information:**
   - ☐ the doctor
   - ☐ the pharmacist
   - ☐ the nurse
   - ☐ the dietician
   - ☐ the drug leaflet
   - ☐ the article in the internet
   - ☐ the other source, please specify: .....

3. **Do you know at what time to take your medications?** Yes / No / I don't take any medications.

Pre- and post-training questions

1. **Drug-food interactions refer to interactions between a drug and:**
   - food Yes / No
   - beverages Yes / No
   - alcohol Yes / No
   - dietary supplements Yes / No

2. **Drug-food interactions may result in:**
   - a worsening of the drug's effects following ingestion with food Yes / No
   - enhancement of the drug's effects following ingestion with food Yes / No
   - exacerbation of adverse drug reactions following ingestion with food Yes / No
   - a reduction of adverse drug reactions following ingestion with food Yes / No

3. **Which of these drinks can be safely used to take a medicine (e.g. to sip a tablet)?**
   - coffee Yes / No
   - tea Yes / No
   - water Yes / No
   - fruit or vegetable juice Yes / No

4. **Which of the juices mentioned below is most likely to interact with drugs:**
   A) orange juice
   B) apple juice
   C) grapefruit juice
   D) tomato juice
   E) I don't know

5. **When should levothyroxine be taken (a medication for hypothyroidism, trade name is e.g. *Euthyrox, Letrox*)?**
   A) in the morning
   B) in the evening
   C) in the morning or in the evening
   D) I don't know

6. **How should levothyroxine tablets be taken?**
   A) on an empty stomach
   B) with food
   C) with or without food
   D) I don't know

7. **With what can a levothyroxine tablet be safely taken?**
   A) coffee
   B) milk
   C) water
   D) grapefruit juice
   E) I don't know

8. **How should bisphosphonates be taken (drugs used to treat osteoporosis, trade names are e.g. *Ossica, Bonviva*)?**
   A) on an empty stomach
   B) with food
   C) with or without food
   D) I don't know

9. **How should proton pump inhibitors be taken (drugs used for peptic ulcer and reflux disease, e.g. *Pantoprazol, Nolpaza, Polprazol*)?**
   A) on an empty stomach
   B) with food
   C) with or without food
   D) I don't know

10. **How should furasidine be taken (medicine used in bladder inflammation, trade name *UroFuraginum, NeoFuragina*)?**
    A) on an empty stomach
    B) with food
    C) with or without food
    D) I don't know

11. **Taking furasidine together with vitamin C improves its effect.** Yes / No / I don't know

12. **Most antibiotics can be taken with food to prevent gastric irritation.** Yes / No / I don't know

13. **Taking some antibiotics (e.g. tetracyclines) with yoghurt or dairy products may impair their effectiveness.** Yes / No / I don't know

14. **Drinking alcohol (e.g. beer, wine, vodka) is strictly contraindicated during treatment with all antibiotics.** Yes / No / I don't know

15. **The intake of paracetamol (painkiller, trade name e.g. *Apap, Panadol*) after drinking alcohol is strictly contraindicated - it can lead to serious liver damage.** Yes / No / I don't know

16. **If the patient does not have gastric problems, analgesics of the non-steroidal anti-inflammatory group (i.e. ibuprofen, naproxen, ketoprofen) can be taken before meals - they will act faster.** Yes / No / I don't know

17. **Taking iron preparations (trade name is e.g. *Ascofer*) together with vitamin C improves their effect.** Yes / No / I don't know

18. **People who suffer from hypertension should avoid over-salting their meals.** Yes / No / I don't know

19. **People who are taking diuretics for hypertension should take potassium supplements as well.**
    A) Yes, always.
    B) Sometimes yes, but the doctor should decide.
    C) No, there's no need.
    D) I don't know.

20. **Diuretics should be taken in the morning or by noon.** Yes / No / I don't know

21. **While taking anticoagulants (e.g. warfarin, acenocoumarol), sudden changes in diet should not be undertaken, e.g. dieting or changing the amount of vegetables consumed, especially those containing high levels of vitamin K.** Yes / No / I don't know

22. **All statins (cholesterol-lowering drugs, e.g. atorvastatin, rosuvastatin) must be taken in the evening, before bedtime.** Yes / No / I don't know

Correct answers:

1a-1d:Yes, 2a-2d:Yes, 3a-3b:No, 3c:Yes, 3d:No, 4C, 5C, 6A, 7C, 8A, 9A, 10B, 11:No, 12:Yes, 13:Yes, 14:No, 15:No, 16:Yes, 17:Yes, 18:Yes, 19B, 20:Yes, 21:Yes, 22:No.

Figure 1. The questionnaire form.

articles (23%). Information on drug-food interactions was less often obtained from other healthcare professionals, such as a pharmacist (9%), dietician (5%), or nurse (3%). Among other sources, participants mentioned, i.e. newspapers (5%), television (3%), books (3.5%), and family and friends (2%). 27% of respondents indicated more than one source of information.

General and detailed knowledge of drug-food interactions

The mean percentage of correct answers to questions testing the general and detailed knowledge of drug-food interactions before and after training was 32% and 57%, respectively (Pearson's Chi^2 test = 12.653, df = 1, $p < 0.001$, Yule's Q = 0.476 (95% CI: 0.206–0.679), OR = 2.817 (95% CI: 1.581–5.017). The percentage of correct answers for each of the 22 questions before and after the training is presented in Figure 2, whereas the changes of correct answers in percentage points are presented in Figure 3.

Correspondence analysis

The questionnaire data regarding pre- and post-training answers were tabulated in the corresponding contingency tables, according to the scheme: "question number: correct answer – 1 or incorrect answer – 0". After eliminating some of the parameters (or categories of parameters) most poorly represented by the models, the first two dimensions explained 52.1% of the total variance (inertia) in the correspondence model for data before training, and 52,4% for data after training. Correlation weights for the pairs of parameters before and after training, based on correspondence models, are given in Tables 2 and 3. Coordinate values of the investigated parameters before and after training, in the first two dimensions of the correspondence analysis model, are presented in Figures 4 and 5.

DISCUSSION

Awareness and knowledge of drug-food interactions

The majority of study participants (91%) were aware that food may change the effectiveness of a drug. Interestingly, this is a much higher percentage than in the Saran et al. study, in which almost half of the elderly respondents had never come across information about drug-food interactions (21). Patients' awareness was lower also in a study by Czech et al., in which only 28% of participants

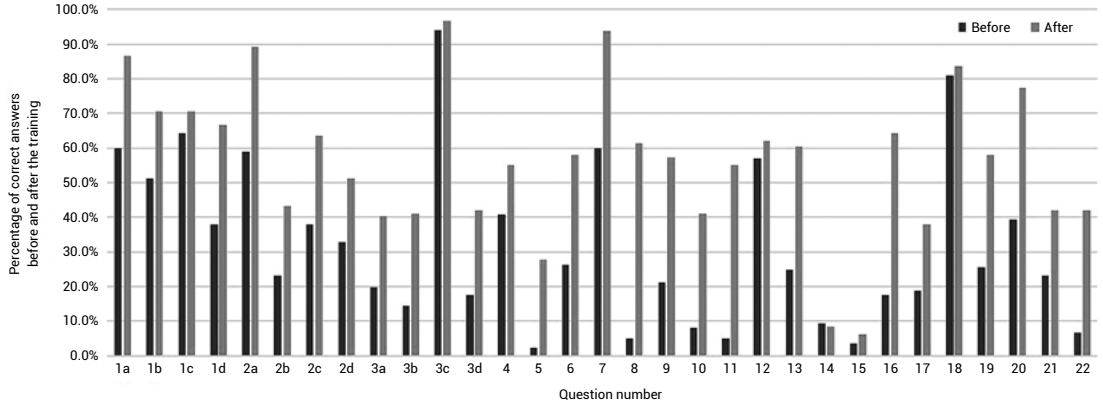

Figure 2. Percentage of correct answers for each question before and after the training.

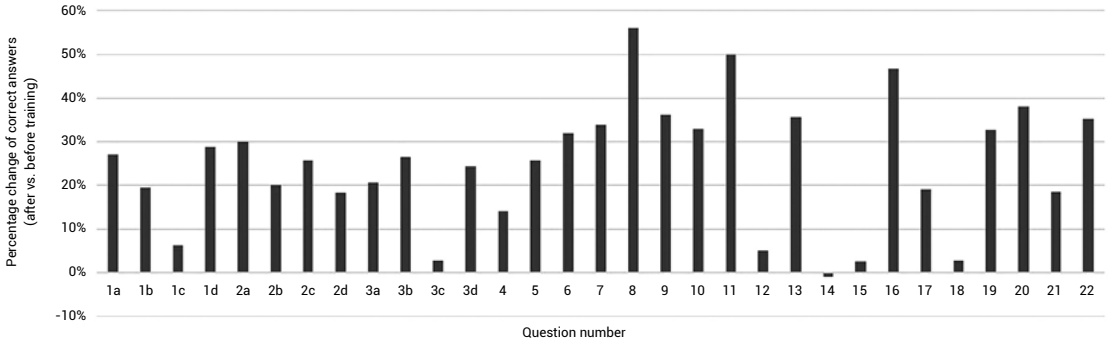

Figure 3. Changes of correct answers after vs. before the training (in percentage points).

declared they had sought information on interactions between drugs and food (20).

In this study, similarly to the Saran et al. survey, two main sources of knowledge of drug-food interactions among the elderly were the doctor and drug leaflet (21). However, Saran et al. reported that a substantial number of patients had gained their knowledge of food-drug interactions from television and newspapers (30% in total), while in this study, the more frequently used source of information was internet articles (21). These differences can be explained by the fact that each year, the proportion of older people using the Internet is increasing (2). As a consequence, its importance as a source of health-related information increase as well.

121 of 132 study participants (92%) stated that they know how to administer their medications correctly. Similar results were obtained by Czech et al. – 97% of respondents declared the knowledge of the dosing regimen of the chronically taken drugs (20). Saran et al. asked a more specific question: are patients aware of what food products they should not take along with their medicines? More than half of the respondents admitted a lack of knowledge in this matter (21).

In this study, like in previous ones, most patients were aware that medicines should be sipped primarily with water. Nevertheless, some respondents declared that tea, coffee, or juice would also be appropriate (20-22). 41% of participants knew that grapefruit juice can interact with drugs. Almost

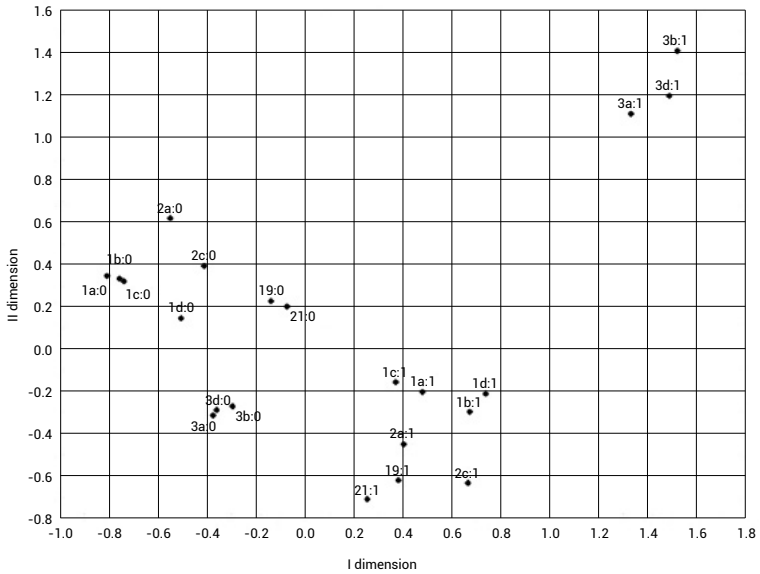

Figure 4. The investigated parameters before training, in the first two dimensions of the correspondence analysis model.

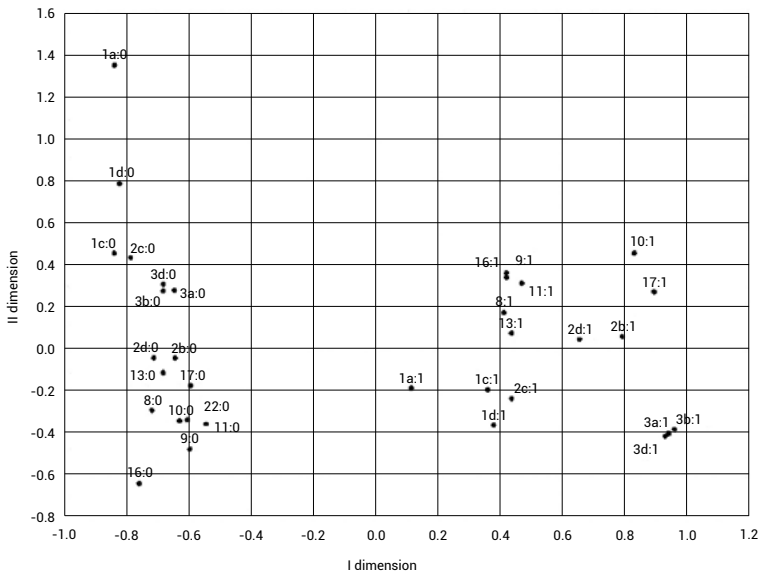

Figure 5. The investigated parameters after training, in the first two dimensions of the correspondence analysis model.

the same result was obtained in Saran et al. study (42%), whereas in the study of Thiab et al., only 28% of respondents correctly chose grapefruit juice as a potential agent interfering with drug action (21, 22).

Knowledge of the possible consequences of interactions between drugs and food was variable. Participants more frequently indicated negative effects of drug-food interactions, such as lower drug effectiveness (59%) or higher incidence of side effects (38%) than positive ones. In studies by Thiab et al. and Zaidi et al., a similar level of patient knowledge in this matter was revealed (22, 23).

Detailed patients' knowledge of drug-food interactions was found to be low. For example, in previous surveys, 27-37% of patients knew that some antibiotics (e.g. tetracyclines) should not be taken with dairy products, whereas in this study the percentage was even lower (25%) (21-23). Regarding other drugs/groups of drugs frequently used by the elderly, the percentage of patients knowing the proper regimen of administration with food was insufficient as well: bisphosphonates – 5%, furasidine – 8%, non-steroidal anti-inflammatory drugs – 17%, proton pump inhibitors – 21%, levothyroxine – 26%, etc.

It was the first study to investigate the change in patients' knowledge of drug-food interactions after training on this topic. Although the mean increase of correct answers by 25 percentage points after the training was statistically significant, it may seem relatively small. However, for some questions, the percentage of correct answers after the training has increased substantially (see Figure 3), e.g. for question 8 (regarding the proper administration of bisphosphonates) – from 5% to 61%, question 11 (regarding the non-indication of furasidine intake with vitamin C) – from 5% to 55%, and question 16 (regarding the possibility to use NSAIDs on an empty stomach in patients without gastrointestinal problems) – from 17% to 64%. The knowledge of the drug-food interaction definition (questions 1a-1d) and possible effects of drug-food interaction (questions 2a-2d) were considerably improved as well.

Table 2. Association weights for the pairs of parameters before training, based on the correspondence model (only the first thirteen association weights with the highest absolute values were shown).

Pairs of parameters		Association weight
3b : 1	3d : 1	2.252
3a : 1	3b : 1	2.021
3a : 1	3d : 1	1.98
3b : 1	3d : 1	1.683
3a : 1	3b : 1	1.565
3a : 1	3d : 1	1.329
1a : 0	3d : 1	-1.153
1a : 0	3b : 1	-1.153
1b : 0	3b : 1	-1.085
1b : 0	3d : 1	-1.084
1c : 0	3d : 1	-1.058
1c : 0	3b : 1	-1.058
1a : 0	3a : 1	-1.029

Table 3. Association weights for the pairs of parameters after training, based on the correspondence model (only the first fourteen association weights with the highest absolute values were shown).

Pairs of parameters		Association weight
1a : 0	1d : 0	1.027
3a : 1	3b : 1	0.903
3b : 1	3d : 1	0.891
3a : 1	3d : 1	0.875
1c : 0	17 : 1	-0.732
10 : 1	17 : 1	0.726
1c : 0	10 : 1	-0.694
2b : 1	17 : 1	0.692
3b : 1	16 : 0	-0.688
3b : 1	8 : 0	-0.686
2c : 0	17 : 1	-0.685
2b : 1	3b : 1	0.684
3a : 1	16 : 0	-0.681
3d : 1	16 : 0	-0.676

Correspondence analysis

Before the training, correct answers to question 3 (i.e. answers to all subquestions within question 3) showed the greatest cooccurrence in the first dimension of the correspondence model (Table 2 and Figure 4). Additionally, those who answered question 1 incorrectly were less likely to answer question 3 correctly. Question 1 tested patients' knowledge of the definition of drug-food interactions. Patients who were unaware that those interactions occur between drugs and not only food but also beverages and alcohol were less likely to answer correctly question 3 regarding beverages that can be safely used to administer the drug. Patients who were aware that drugs should not be taken with coffee knew that other drinks, such as tea, fruit, or vegetable juice, were not suitable for this as well.

After the training, as with the pre-training questionnaire, patients who were aware that drugs should not be taken with coffee understood that other drinks, such as tea or fruit/vegetable juice, were not appropriate for this purpose as well (Table 3, Figure 5). Respondents who knew that drug-food interactions may improve drug effectiveness (question 2b) were also more likely to respond that taking iron preparations together with vitamin C improves their effect (question 17) and were also more likely to know that drug-food interactions can involve drug interactions with beverages. Participants who were unaware that interactions between drugs and alcohol fall within the definition of drug-food interactions were less likely to correctly answer question 10 (how furasidine should be administered) as well as question 17 (benefits of taking iron together with vitamin C). Those who knew how furasidine should be administered (question 10) were also more likely to be aware that taking iron preparations together with vitamin C improves iron effectiveness. Patients who knew that drugs should not be taken with tea (question 3b) were less likely to give the wrong answer to question 8 - on how bisphosphonates should be taken and were also less likely to mark as false the statement that in patients without stomach problems, NSAIDs can be taken before meals (question 16). The correct answer to questions 3a and 3d (that medicines should not be taken with coffee or fruit juice) rarely co-occurred with considering as false the statement that NSAIDs can be taken before meals in patients without gastric problems (question 16).

Limitations of the study

The apparent limitation of the study is the loss of participants and missing data. 123 of 143 (86%) recruited volunteers returned both pre- and post-training surveys. In the included questionnaires, data on participants' age or gender were often not provided. Another significant limitation is the representativeness of the sample to the population of Polish geriatric patients. Given that the study participants were recruited among third-age university listeners, it can be assumed that they are more aware, educated, and potentially have better cognitive functions than the average elderly person. Moreover, due to recruiting volunteers, the majority of respondents were women.

CONCLUSION

Study participants were aware of drug-food interactions and sought information on this topic. However, their general and detailed knowledge of interactions between drugs and food was poor, and often incorrect. The training significantly increased the patient's knowledge. Although research on a more representative sample is required, the study indicates the need to educate geriatric patients on the correct use of drugs with food and on the importance of drug-food interactions. Some educational activities can be undertaken by physicians and pharmacists in their everyday practice, e.g. a thoughtful conversation with the patient when prescribing or dispensing a medicine, or during the medication review service as a part of pharmaceutical care. It could also be beneficial for the older patient to receive an information leaflet introducing the topic of drug-food interactions in an easy-to-understand and accessible way. The creation of a publicly accessible database of such leaflets would be an important step towards broadening the patient's knowledge of drug-food interactions.

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Conflicts of interest

The authors declare no conflict of interest.

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