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Positive impact of clinical pharmacist interventions on antipsychotic use in patients on excessive polypharmacy evidenced in a retrospective cohort study

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Abstract

Objectives: Although antipsychotic prescribing in elderly patients using polypharmacy has not been studied in well-designed clinical trials and meta-analyses, there is an urgent need to monitor prescribing practice in this population. One of the possible approaches to optimize pharmacotherapy may be the involvement of clinical pharmacists (CPs). The aim of this research was to examine whether the involvement of a CP can improve treatment guidelines adherence and change the total number of medications per patient in older patients who are treated with excessive polypharmacy that includes antipsychotics.

Methods: This cohort retrospective study included older patients (65 years or older) treated with at least one antipsychotic and excessive polypharmacy (10 or more medications concurrently) between 2012 and 2014 in primary care. The main outcome measures were antipsychotic treatment guidelines' adherence and the total number of medications per patient after the CP's interventions. Only interventions including antipsychotics were studied in detail (i.e., discontinuation, switching, initiation, dose adjustment, change of another medication because of a drug-related problem). Data on diagnoses, patient pharmacotherapy and the CP's interventions were obtained from clinical records and medical reviews. Age and acceptance of the CP's interventions were used as predictive factors for antipsychotic treatment guidelines' adherence.

Results: Forty-nine patients were included. The CP suggested 21 different interventions of which nine (42.8%) were accepted by the general practitioners. The number of medications that patients received decreased after the CP's interventions (N of medications before: 15.4; N of medications after: 12.0, $p < 0.05$). The acceptance of the CP's recommendations, but not age, improved antipsychotic treatment guidelines' adherence ($p = 0.041$).

Conclusions: These results show that a collaborative care approach including a CP in primary care significantly improved the adherence to treatment guidelines. The results also support the implementation of this service in the Slovenian healthcare system, although more studies are needed.

Keywords

Polypharmacy, clinical pharmacy, psychopharmacology, antipsychotics, aging, primary care

INTRODUCTION

The population in developed countries is aging, and consequently, more psychotropics are being used in clinical practice, which can lead to medically unnecessary polypharmacy (i.e., irrational polypharmacy). The term *excessive polypharmacy* is also often used to refer to patients taking 10 or more substances daily (Stuhec M & Gorenc K, 2019; Rieckert A et al., 2018). Four out of five people aged 75 or more are taking medications, and 36% receive four or more medications at the same time (Quality and Outwork framework, 2012). Although well-designed network meta-analyses and

randomized controlled trials (RCTs) are often presented as a gold standard in evidence-based pharmacotherapy, they often exclude older patients with polypharmacy, which is why there is a need for trials with high ecological validity, such as large cross-sectional trials (Quality and Outwork framework, 2012; Cipriani A et al., 2009; Stuhec M & Serra-Mestres, J 2018).

In addition, irrational polypharmacy is prevalent in elderly patients with mental disorders, because they are often treated with psychotropics to manage insomnia, depression and behavioural symptoms of dementia treatment, although such use is not always evidence-based (Meesters PD et al., 2012).

Antipsychotics are often present in irrational polypharmacy combinations in elderly patients and antipsychotic polypharmacy (APP) is often used before clozapine, which is not supported by existing treatment guidelines (Hasan A et al., 2012; Goodwin G et al., 2009; Stahl SM, 2013; Taylor DM et al., 2003; Howes OD et al., 2012). Irrational polypharmacy can lead to potentially inappropriate medications in the elderly (PIMs), which increase morbidity, hospitalization rate, adverse events and health care costs (Mann E et al., 2013; Centorrino F et al., 2004; Schumacher JE et al., 2003). An Austrian cross-sectional retrospective study also suggests that among irrational polypharmacy recipients, psychotropics are often PIMs. The study included 48 out of 50 nursing homes and 1,844 out of 2,005 residents in Austria and found a high prevalence of PIMs related to psychotropics, with antipsychotics being especially problematic. The number of residents with at least one psychotropic PIM in this study was 1.014 (55%). The most commonly prescribed PIM was the antipsychotic prothipendyl (25.9% residents), which is a low-potency antipsychotic (Mann E et al., 2013). These results suggest that effective interventions are needed to improve adherence to the existing treatment guidelines and to reduce PIMs and excessive polypharmacy with a particular focus on elderly patients with mental disorders and dementia and on antipsychotics prescribing (O'Dwyer M et al., 2016).

Some possible approaches to manage antipsychotic use in elderly patients with excessive polypharmacy are active prescription monitoring with educational interventions and collaborating with a clinical pharmacist (CP) (Hashimoto Y & Tensho M, 2016; Hazra M et al., 2011; Stuhec M & Gorenc, K 2019). One Japanese study on CPs' interventions compared pre- and post-intervention results and found a significant reduction of the dose (982.6 mg pre vs. 857.6 mg post; $p < 0.01$) and the number of antipsychotics ($p < 0.05$) at 1 year (Hashimoto Y & Tensho M, 2016; Hazra M et al., 2011).

These results suggest that the CP's interventions may optimize medication prescribing in these patients. Although the results are interesting, there is no evidence on a similar collaborative care approach in most European countries, including those in Central Europe. The aim of this study was to determine whether the involvement of a CP directly into the patients' treatment process can improve the antipsychotic treatment guidelines' adherence and minimize the number of medications in older primary care patients receiving excessive polypharmacy that includes antipsychotics. We hypothesize that the CP's interventions will improve treatment guidelines' adherence and lower the number of medications per patient.

METHODS

General description of community services in Slovenia in primary care

In Slovenia, patients with mental disorders and dementia in primary care are treated by their general practitioners (GPs), who can refer the patients to psychiatrists in cases of mental disorders and to neurologists or psychiatrists in cases of dementia. Patients in nursing homes are treated by GPs and also by psychiatrists in cases of mental disorders or dementia.

After 2016, CPs have also been included in Slovenian health services for patients referred by their GPs, which is a new clinical practice in Slovenia. CPs prepare a medical review and advise GPs (but have no prescribing rights). CPs communicate with GPs through the medical review and by phone, if necessary. On average, a CP produces 4–6 medical reviews in 6–8 hours, and after a successful trial, this service has been adopted in the Slovenian healthcare system in 2016, which has been described in a previous publication (Stuhec M et al., 2019). This service was initiated by the Institute for Health Insurance of Slovenia, because of many patients who were treated with excessive polypharmacy (Stuhec M et al., 2019).

Study design and Inclusion and exclusion criteria

Our retrospective cohort study examines patients from the Ljutomer Health Centre in the northeast of Slovenia. A control group was not used in this study. We included patients aged 65 or more, who were receiving excessive polypharmacy (10 or more medications), who were treated with at least one antipsychotic between 2012 and 2014 (no indication selection), and who used the CP's service. Only patients with no missing data were included. Patients treated with antipsychotic monotherapy as well as polypharmacy were included. There was also no randomization process within this study. All patients who fulfilled the inclusion criteria were included. Patients without the CP's report were excluded from this study. Each patient participated in the study only once (first visit). After the CP's interventions, patients were followed up until the first visit to their GP (study duration), when the acceptance or rejection of the changes suggested by the CP was recorded. Changes were checked both manually (paper chart) and electronically (dispensed medication). After the first post-intervention visit to the GP, patients were not followed up and clinical outcomes were not measured. Patients were selected according to the GPs' referral papers (no impact on selection criteria). The STROBE Statement checklist was used in this study to insure the inclusion of all items that should be included in reports of observational

studies (von Elm E et al., 2008). Excessive polypharmacy was defined in accordance with previous papers on this topic, that is, as patients taking 10 or more medications daily (Stuhec M & Gorenc K, 2019; Rieckert A et al., 2018).

Outcomes

The main outcome measures were antipsychotic treatment guidelines adherence and the total number of medications per patient after the CP's interventions. Only the CP's interventions related to antipsychotics were studied in detail (e.g., discontinuation, switching, initiation, dose adjustment, change of another medication because of drug-related problem). All patients were diagnosed according to the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (details in Results). Antipsychotics were mainly prescribed by psychiatrists and other medications by GPs.

Clinical pharmacist's interventions

The CP (Pharm.D.) had a specialization in clinical pharmacy (3 years) and over five years of experience working in a psychiatric hospital and in ambulatory work in primary care (e.g., daily team rounding, inpatients and outpatients consultations, medical reviews). The referred patients had a discussion with the CP that included the identification of drug-related problems. Afterwards, the CP prepared a medical review that was sent to the general practitioner. The CP's medical review included potential type X drug-drug interactions (pXDDIs), as identified by the Lexicomp Online™ software, possible adverse events, existing drug indications, PIMs, an evaluation of drug adherence and final recommendations depending on the patient's outcomes. The GP then also sent the medical review to a psychiatrist who made a final decision about the acceptance or rejection of the CP's recommendations. The CP mostly recommended drug discontinuation, drug initiation, and dose adjustment.

Data collection

The data was compiled in 2016 and 2017 by a MPharm student (KG) under the supervision of a clinical pharmacist specialist (MS) directly from the patients' paper medical charts and paper medical reviews. KG collected pXDDIs from paper medical reviews because each medical review included pXDDIs and their categorization according to the Lexicomp Online™ software. The clinical relevance of pXDDIs was assessed by KG and MS directly from medical reviews (using the Lexicomp® drug-drug interaction checker 2017). Pharmacotherapy details

(e.g. medications, doses, potential drug-drug interactions) were obtained from the medical review. Information on the acceptance of the recommendations was obtained from the patients' charts after their first post-intervention visit to the GP. The PRISCUS list was used to identify PIMs (Holt S et al., 2010).

In addition, several antipsychotic treatment guidelines were followed by the authors of this article to evaluate the CP's recommendations (Hasan A et al., 2012; Goodwin G et al., 2009; Stahl SM., 2013). For this purpose, all patients with all various diagnoses (e.g., schizophrenia, insomnia, dementia, etc.) were included. Treatment guidelines adherence was assessed on a case by case basis (Hasan A et al., 2012; Goodwin G et al., 2009; Stahl SM, 2013). In cases where there was no data in the treatment guidelines, various studies and summaries of product characteristics were used to determine the appropriateness of antipsychotic use. The researchers did not have any contact with the study participants during the study. A hypothesis-based approach was used in this paper for manuscript writing (Heun R, 2018).

Patients for this study were extracted from a large study *Pharmacist Consultant (non-prescriber)* that included all patients (with all diagnoses), but did not examine antipsychotic treatment guidelines adherence. In the mentioned study, a CP was included into each medical primary community healthcare team. Each team consisted of all GPs at a community health centre and one CP. This collaboration was funded by the Health Insurance Institute of Slovenia (Slovene: *Zavod za zdravstveno zavarovanje Slovenije*, a funding body in Slovenia) and has already been described in the literature (Marušič Premuš A 2014). This study was approved by the National Medical Ethics Committee of the Republic of Slovenia in 2016.

Analysis

The baseline characteristics of patients were described as the mean \pm standard deviation (SD). A statistical model was created using multivariable logistic regression to evaluate the impact of the independent variables (age and acceptance of the proposed CP's interventions) on the dependent variable (guidelines adherence) to verify whether the connection is random or significant. In addition, the difference in the number of medications after the interventions for each patient was checked using the Wilcoxon signed-rank test. The statistical significance threshold was set at $p < 0.05$. Analyses were carried out with the Statistical Package for Social Science 22.0 for Windows® (SPSS). The study size was not calculated, because we included all available patients. Because of the

small predicted sample size we only included two independent variables in the multivariable logistic regression.

RESULTS

General data

Forty-nine patients were included. The basic demographic data of these patients is shown in *Table 1*. Antipsychotics were used in 21 men and 28 women (49 in total). Patients using antipsychotics were aged from 68 to 95 years. Prior to the medical review process, patients using antipsychotics received 755 different medications, which is an average of 15.4 medications per patient. After the CP's interventions, the total number of medications that patients using antipsychotics received decreased to 586 medications, which is an average of 12.0 medications per patient ($p < 0.05$). Antipsychotics represented 5.33% of all discontinuations. There were no missing variables in this study, so all enrolled patients were included in the final analysis (49 patients).

For patients treated with antipsychotics, the CP suggested 359 different interventions of which 179 (49.9%) were accepted. In 15 patients, the CP did not recommend any treatment changes and proposed optimization of antipsychotic pharmacotherapy in 34 patients. Quetiapine was the most frequently used antipsychotic in this study and was used by 30 of 49 patients included in the study (61.2%), of which 21 patients were receiving small doses of quetiapine (25–100 mg per day) and nine patients over 100 mg per day. *Table 2* shows all the recommendations by the CP in detail.

Clinical pharmacist's recommendations and adherence to treatment guidelines

The GPs and psychiatrists accepted the following recommendations by the CP: 1) switching from a clozapine and risperidone combination to clozapine monotherapy in a patient with chronic schizophrenia without history of clozapine monotherapy treatment, 2) switching from a fluphenazine and quetiapine combination to fluphenazine monotherapy in a patient with chronic schizophrenia and diabetes, 3) discontinuation of a clozapine and aripiprazole combination in a patient with a history of seizures, 4) switching from olanzapine treatment to quetiapine treatment in a patient with severe Alzheimer's disease with behavioural disturbances, 5) switching from a quetiapine and domperidone combination to quetiapine and ondansetron in a patient with a severely prolonged QTc and a history of tachycardia, 6) switching from a sulpiride and haloperidol combination to quetiapine monotherapy, 7 & 8)

Table 1. Demographic data of included patients

GENDER	NUMBER OF PATIENTS
Male	21
Female	28
AGE	
65–70 years	8
71–80 years	17
81–90 years	15
90 years and more	9

discontinuation of quetiapine in small doses for insomnia and zolpidem initiation, 9) quetiapine discontinuation immediately after a stroke. The rejected recommendations are also described in the *Table 2*. In 21 patients receiving antipsychotics, non-compliance with the existing treatment guidelines, summaries of product characteristics, and studies was found (discrepancies are presented in the *Table 2*) (Hasan A et al., 2012; Goodwin G et al., 2009; Stahl SM, 2013). The acceptance of the CP's recommendations had an influence on improved adherence to antipsychotic treatment guidelines ($p = 0.041$, $\beta = 1.477$, $R^2 = 0.123$), whereas age was not significantly related to better adherence ($p = 0.318$, $\beta = 0.039$).

DISCUSSION

Key results and interpretation

The main finding of this study is that the CP's service improved the adherence to antipsychotic treatment guidelines in the study population, which is in line with our hypothesis. The results also show a reduction in polypharmacy, which was also observed in a previous study (Stuhec et al., 2019). Although the clinical outcomes of reduced polypharmacy were not recorded, the data is still useful as shown in bipolar disorders (Holzapfel E & Szabo C, 2018). In addition, these results show the important role of CPs in the selection of antipsychotics and in disseminating pharmacological knowledge, which is a novel approach in psychiatric practice in Central Europe. Although it is the first of this type in Central Europe and brought encouraging results, our study should be replicated because of its small sample size and many study limitations (e.g., no randomization, no RCT design, no control group, no long-term monitoring).

The results also show that instances of particularly problematic combinations of antipsychotics (e.g., APP) were reduced after the CP's interventions. There are no similar results so far in the literature on primary care, although Gören et al. published

Table 2. Examples of identified discrepancies with the treatment guidelines and clinical pharmacist recommendations in the treatment with antipsychotics (D = daily, M = monthly)

Patient number	Treatment guidelines issue	Age	Diagnoses and details	Clinical pharmacist recommendations	Final acceptance (YES/NO)
1.	4 different antipsychotics concomitantly: sulpiride, haloperidol, risperidone in quetiapine	69	Psychosis Sulpiride: 3 x 200 mg D Haloperidol: 3 x 100 mg D Risperidone: 1 x 25 mg (depot) twice M, Quetiapine: 1 x 400 mg and 1 x 100 mg D	Sulpiride and haloperidol discontinuation	NO
2.	Sulpiride and paliperidone treatment concomitantly	68	Psychosis Sulpiride: 2 x 50 mg D Paliperidone: 1 x 6 mg D	Paliperidone and sulpiride discontinuation and aripiprazole initiation	NO
3.	Clozapine and risperidone treatment concomitantly	66	Personality disorder and moderate mental retardation with behavioural disorder Clozapine: 1 x 25 mg D Risperidone: 2 x 0.25 ml D	Clozapine discontinuation	YES
4.	Quetiapine and fluphenazine treatment concomitantly in patients with diabetes	66	Moderate mental retardation with behavioural disorder Fluphenazine decanoate injection: 25 mg/mL/4 weeks Quetiapine: 3 x 200 mg D	Quetiapine discontinuation	YES
5.	Clozapine and aripiprazole treatment concomitantly in patients with seizures	65	Schizophrenia Clozapine: 2 x 200 mg D Aripiprazole: 1 x 15 mg D	Monitoring	YES
6.	Olanzapine treatment in patient with Alzheimer's dementia	71	Undetermined organic personality and behavioural disorder due to brain disease and moderate mental retardation Olanzapine: 1 x 5 mg D	Quetiapine initiation and olanzapine discontinuation	YES
7, 8.	Domperidone and quetiapine treatment concomitantly (X potential DDI)	85 (7) 90 (8)	Undefined dementia (7) Alzheimer's dementia (8) Quetiapine: 1 x 25 mg D (7, 8) Domperidone: 2 x 10 mg D (7, 8)	Domperidone discontinuation and ondansetron initiation	YES
9.	Haloperidol and quetiapine treatment concomitantly (X potential DDI)	90	Alzheimer's dementia Haloperidol (2 mg/ml): 2 x 15 drops D Quetiapine: 1 x 25 mg D	Quetiapine discontinuation	NO
10.	Haloperidol and quetiapine treatment concomitantly (X potential DDI)	82	Undefined dementia Haloperidol (5 mg/ml) as needed D Quetiapine: 1 x 100 mg D	Haloperidol discontinuation	NO
11, 12.	Haloperidol and sulpiride treatment concomitantly (X potential DDI)	81 (11) 82 (12)	Dementia (11) Undefined dementia (12) Sulpiride: 3 x 50 mg D (11, 12) Haloperidol (5 mg/ml): 2 x 1 D (11) Haloperidol: 2 x 5 mg D (12)	Sulpiride and haloperidol discontinuation and quetiapine initiation	YES
13.	Promazine treatment	83	Organic mood disorders Promazine: 1 x 12.5 mg D	Promazine discontinuation and quetiapine initiation	NO
14.	Amisulpride and sulpiride treatment concomitantly (X potential DDI)	72	Organic blurred disorder and Alzheimer's dementia Amisulpride: 2 x 50 mg D Sulpiride: 3 x 50 mg D	Amisulpride discontinuation	NO
15, 16, 17.	Quetiapine for insomnia treatment	86 (15) 76 (16) 73 (17)	Insomnia (15, 16, 17) Quetiapine: 1 x 50 mg D (15, 16) 1 x 25 mg D (17)	Quetiapine discontinuation and zolpidem initiation	YES, YES, NO
18.	Risperidone and quetiapine treatment concomitantly (X potential DDI)	85	Dementia Risperidone: 1 x 0.5 mg D Quetiapine: 1 x 50 mg D	Risperidone discontinuation	NO
19.	No clear indication for quetiapine	84	Quetiapine: 2 x 25 mg D	Quetiapine discontinuation	NO
20.	Quetiapine treatment immediately after stroke	72	After stroke condition Quetiapine: 1 x 50 mg D	Quetiapine discontinuation	YES
21.	Clozapine treatment in patient with seizures and heart rhythm disorders	84	Undefined dementia and moderate mental disorder Clozapine: 3 x 50 mg D	Clozapine discontinuation	NO

the results of a study of US psychiatric hospitals, which are in line with our results (Gören JL et al., 2010). These findings are very important in the field of evidence-based medicine, because the patients in our study population are not included in the existing treatment guidelines despite representing a sizable part of the patients in clinical practice (Goodwin G et al., 2009; Stahl SM, 2013). The results also illustrate the importance of a clinical pharmacy service in complex cases of patients with excessive polypharmacy. Some studies showed that interventions in this field are meaningful for the optimization of antipsychotic therapy, although older adults with polypharmacy were not the main focus group (Gören JL et al. 2010; Stuhec M 2014).

The next important finding is the frequent use of quetiapine in small doses for behavioural symptoms of dementia and insomnia. The CP suggested discontinuation in most of such cases and the intervention was accepted by the GPs and psychiatrists in 50% of the cases (three out of six patients). Such use is not in line with the clinical guidelines for antipsychotic use and insomnia treatment, according to which, quetiapine is not a first line treatment, especially for insomnia, because of weak evidence (Taylor DM et al., 2003; Wilson SJ, 2010). Furthermore, the CP suggested quetiapine initiation in two patients and an APP discontinuation in one. A 2009 study reports a significantly increased long-term risk of mortality in patients with dementia, who are prescribed antipsychotic medication (Ballard C et al., 2009). Therefore, the CP's suggestions about quetiapine discontinuation were evidence based interventions.

The next important finding is that the CP's service influenced APP treatment, which should be considered only after clozapine treatment when possible. (Taylor DM et al., 2003; Howes OD et al., 2012). The results show that the CP reduced the use of APP and often suggested antipsychotic discontinuation in cases of excessive APP. One patient in the study was treated with four different antipsychotics concomitantly, which is not supported by evidence. Furthermore, Suzuki et al. showed that APP could, in most cases, be replaced with antipsychotic monotherapy. The medical charts of patients with at least minimal improvement of symptoms were reviewed retrospectively and the results from a 12-week follow-up after completely switching showed that the Global Assessment of Functioning score improved from 32 to 47, while the number of antipsychotic medications and total psychotropic medications were significantly reduced from 3.5 to 1.1 and 6.8 to 2.6, respectively (Suzuki T et al., 2004). Thus, the CP service in our study improved the quality of antipsychotic prescribing in patients treated with APP.

The CP's service also affected the treatment of patients with schizophrenia. In a comprehensive Finnish nationwide cohort study, the risk of psychiatric rehospitalization was used as a marker for relapse among 62,250 patients with schizophrenia. Twenty-nine different antipsychotic monotherapy and polypharmacy types were used between January 1, 1996, and December 31, 2015. Combining aripiprazole with clozapine was associated with the lowest risk of rehospitalization, indicating that certain types of polypharmacy may be feasible in the treatment of schizophrenia (Tiihonen J et al., 2019). In our results, the CP's interventions led to a lower number of patients treated with APP that included two strong D2 antagonists (e.g., sulpiride-haloperidol, paliperidone-sulpiride). In these cases, clozapine monotherapy or even a combination with aripiprazole would be a more appropriate pharmacological option (Tiihonen J et al., 2019). The use of two similar D2 antagonists could cause treatment failure (e.g., due to competitive binding) and increase extrapyramidal symptoms. In addition, many of the CP's interventions were related to sulpiride use. Sulpiride use is contraindicated in patients with a prolonged QT or/and concomitant use of medications with known QT prolongation (Summary of Product Characteristics of Sulpiride, 2017). These interventions mean that the CP recognized contraindicated combinations and suggested important treatment alternatives (e.g., quetiapine monotherapy instead of APP including sulpiride and haloperidol). Additionally, the CP suggested risperidone discontinuation in schizophrenia patients treated with a combination of risperidone and clozapine, which is in line with the evidence (Honer WG et al., 2006).

Many patients treated with antipsychotics experience various adverse events associated with their use (Cipriani A et al., 2009; Krause M et al., 2018). Adverse events are even more important in elderly patients, since they often suffer from multiple diseases, including cardiovascular diseases. The results of our study show that the CP suggested many different interventions including aripiprazole initiation and quetiapine initiation instead of olanzapine, which can reduce the risk of important cardiovascular adverse events (Cipriani A et al., 2009). These important interventions show that long-term monitoring in terms of avoidance of adverse events is important to minimize antipsychotic-induced adverse events.

Antipsychotic use in patients with excessive polypharmacy can lead to potentially and clinically important drug-drug interactions, which could lead to important adverse events. Antipsychotics are often part of important drug-drug interactions as shown by Stuhec et al. (2019), which found that antipsychotics were commonly part of pXDDIs. Although the potential reduction of pXDDIs as a result of involving CPs has

been described in many papers (Stuhec et al., 2019; Beovic B et al., 2016), the results of our study showed that the CP's interventions reduced the number of important pXDDIs in patients using antipsychotics.

It is also worth noting that not all interventions were accepted by the GPs and that we did not monitor the reasons for rejecting interventions, which could be improved in further research through a questionnaire study. Despite that, our results are similar to those in previous studies (Stuhec et al., 2019).

Study limitations

This study also has many important limitations which should be addressed. Patients were not monitored over a longer period of time (e.g., six months), limiting the scope of our results. There was no special protocol for patient selection, because the GPs referred patients to the CP, which might have introduced selection bias. The patients were also not monitored directly with different scales and tests (e.g., measuring outcomes with a questionnaire), although that would require a complex approach in patients with a large variety of indications and medications. Another very important limitation is the small sample size and the heterogeneity of the study population. Although study population homogeneity is generally considered helpful in evidence-based medicine, such an approach would not allow us to study the clinical practice related to patients with polypharmacy. Many of these limitations are due to the design of the pilot trial of the Health Insurance Institute of Slovenia, which was a practice-oriented project within one primary care community system and has been discussed in detail elsewhere (Marušič Premuš A, 2014). These limitations could be overcome with prospective studies in real clinical settings. Despite the limitations, our study is (to the best of our knowledge) the first in Central Europe to examine the impact of a collaborative care approach with a CP on clinical practice related to antipsychotic treatment in older adults with excessive polypharmacy.

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CONCLUSION

Our results show that a CP's consultative role can contribute to increased antipsychotic treatment guidelines' adherence and has a potential to optimize medication prescribing in older patients treated with antipsychotics. This study is the first of its kind in Central Europe and can inform antipsychotic treatment of patients on excessive polypharmacy, despite its important limitations (heterogeneous population, no RCT design, no randomization, no long-term outcomes, small sample size).

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ETHICAL APPROVAL

This study was approved by the National Medical Ethics Committee of the Republic of Slovenia in 2016 (Number 0120–528/2016–2; approved 10.11.2016).

INFORMED CONSENT

No informed consent was required because it was a retrospective chart study.

CONFLICTS OF INTEREST

The authors declare no conflict of interest in conducting this review.

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