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Patient Polypharmacy use Following a Multi-Disciplinary Dementia Care Program in a Memory Clinic: A Retrospective Cohort Study

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ABSTRACT

Introduction. Dementia increases the risk of polypharmacy. Timely detection and optimal care can stabilize or delay the progression of dementia symptoms, which may in turn reduce polypharmacy. We aimed to evaluate the change in polypharmacy use among memory clinic patients living with dementia who participated in a dementia care program compared to those who did not. We hypothesized that patients in the dementia care program would reduce their use of polypharmacy compared to those who were not in standard care.

Methods. We retrospectively analyzed data extracted from electronic medical records from a university memory clinic. Data from a total of 381 patients were included in the study: 107 in the program and 274 matched patients in standard care. We used adjusted odds ratios to assess the association between enrollment in the program and polypharmacy use at follow-up (five or more concurrent medications), controlling for baseline polypharmacy use and stratified polypharmacy use by prescription and over-the-counter (OTC).

Results. The two groups did not differ in the use of five or more overall and prescription medications at follow-up, controlling for the use of five or more of the respective medications at baseline and covariates. Being in the program was associated with a threefold lower odds of using five or more OTC medications at follow-up (adjusted odds ratio = 0.30; p <0.001; 95% Confidence interval = 0.15-0.58) after controlling for using five or more OTC medications at baseline and covariates.

Conclusions. Dementia care may reduce polypharmacy of OTC medications, potentially reducing risky drug-drug interactions. More research is needed to infer causality and understand how to reduce prescription medication polypharmacy. ***Kans J Med 2023;16:237-241***

INTRODUCTION

Alzheimer's disease and related disorders (ADRD) have a serious public health impact in the United States. ADRD refers to complicated neurodegenerative disorders that impair memory and thought processes, which in turn generate disability in instrumental and basic activities of daily living (e.g., cooking, managing finances, bathing or eating).[1] This term includes conditions such as Alzheimer's disease, as well as Vascular, Lewy Body or Frontotemporal dementia.[1] The share of American older adults is increasing, and the risk of ADRD increases with age, affecting approximately one tenth of people 65 and older and four tenths of people 90 and older.[2,3] ADRD is the fifth leading cause of mortality, and its associated disability has increased substantially in the past two decades.[1,4,5]

Younger people living with ADRD have more chronic conditions and use more medications than older adults without ADRD.[1] Treatment of several chronic conditions can lead to polypharmacy, which can increase the risk of drug-drug interactions and drug-disease interactions among individuals with ADRD.[6,7] Furthermore, polypharmacy can lead to increased mortality, adverse medication reactions, falls, and hospital admissions.[7-10]

Optimal ADRD care has the potential to reduce polypharmacy among people with ADRD. Pharmacologic and behavioral interventions can stabilize and delay the progression of cognitive, functional, and behavioral outcomes, which can improve the lives of individuals with ADRD and their families.[11,12] Antipsychotic and antidepressant medications are often used to treat agitation, depression, and other behavioral symptoms of ADRD.[12] The stabilization of behavioral outcomes via non-pharmacological interventions may help reduce the need for psychotropic medications.

Early diagnosis of ADRD can allow both the patient and family to participate in their care plan and begin more efficacious interventions. Timely detection and optimal care can improve the prognosis for patients with ADRD and is a priority for the National Alzheimer's Project Act (NAPA).[13] However, to our knowledge, there is a paucity of published studies that have explored the effect of ADRD care interventions in reducing the use of polypharmacy.

The current project aimed to evaluate the change in polypharmacy use among memory clinic patients living with ADRD who participated in an ADRD care program, the Cognitive Care Network (CCN), compared to those who did not participate in the standard care. We hypothesized that patients in the CCN would reduce their use of polypharmacy compared to standard care.

METHODS

We retrospectively obtained electronic medical record (EMR) data through The University of Kansas Health System informatics data warehouse Healthcare Enterprise Repository for Ontological Narration (HERON aka I2B2).[14] Eligibility criteria included 1) being a memory clinic patient at the University of Kansas Health System, 2) being diagnosed with ADRD during the period comprised by the inception of the CCN and the data extraction from the EMR, 3) having at least two visits during the study period, and 4) being enrolled in the CCN or a patient matched to a CCN patient using the optimal propensity matching score technique, based on their Charlson Comorbidity Index (CCI),[15] race, sex, and marital status. The study population included 5,629 patients who were diagnosed with ADRD at the memory clinic within the University of Kansas Health System from January 1, 2018 (inception of the CCN) to June 30, 2020 (data extraction). Out of the 5,629 patients, 459 had enrolled in the CCN and 5,170 had not. ADRD diagnoses were identified via patients' International Classification of Diseases, 10th Revision (ICD-10) codes. We extracted and matched information such as medical history and comorbidities with patients' medical record number (MRN). We also used patients' MRN to

determine enrollment into the CCN. The Institutional Review Board at The University of Kansas Medical Center has approved the conduct of this study (STUDY00146180).

The CCN was established in 2018 by the University of Kansas (KU) Alzheimer's Disease Research Center to improve the quality of life of families with ADRD in the state of Kansas and the Kansas City region. The CCN provides a range of services to families, including early detection, health navigation, and behavioral interventions. CCN applies standards of care from the Alzheimer's Consensus Toolkit (ACT), a set of evidence-based recommendations for ADRD detection and care.[16] ACT recommends early detection via yearly memory screenings with validated tools and appropriate cognitive impairment work-up when detected. It also prioritizes behavioral interventions over psychotropic medications as first-line interventions.[17]

The CCN also proposes to shift the model of care, by implementing the Client Empowerment Model. This model aligns with strength-based social work philosophy and incorporates components of knowledge/health literacy, shared decision-making, personal control, and positive patient-professional interaction based on the stage of ADRD.[18] The CCN centers navigation services on the patient and their family's needs. Services include coping with a new ADRD diagnosis, behavioral and cognitive techniques to address behavioral symptoms, promoting safety in the home and driving, or referring to community resources. The preventative focus of the CCN program may prevent and reduce behavioral and psychological symptoms of dementia (BPSD). This timeliness and improvement in BPSD may also reduce the use of unnecessary psychotropic medications.

We ascertained the change in the use of polypharmacy from baseline to follow-up. These data were ascertained by extracting the information by the date patients enrolled in the CCN (baseline) and two years later (follow-up). We defined polypharmacy as the overall concurrent use of five or more medications.[7] The primary outcome was overall polypharmacy use. We also explored polypharmacy separately for prescription and OTC medications as the concurrent use of five or more of these types of medications as secondary outcomes. Last, we explored the average change in the number of prescription and OTC medications used as a secondary outcome. For those not in CCN, we extracted the data by matching the dates of baseline and follow-up with CCN patients. A team member with expertise in pharmacology classified all medications as prescription and/or OTC (Supplementary is only available online at journals.ku.edu/kjm).

Statistical Analysis. We used frequencies and percentages, means and standard deviations, and medians and interquartile ranges to describe the patient population (e.g., age, gender, race). We used adjusted odds ratios (aOR) of polypharmacy at follow-up, controlled for polypharmacy at baseline to assess the change in polypharmacy. We used linear regression to calculate adjusted betas of the change from baseline to follow-up in the number of medications in the CCN group compared to standard care. The CCI and sex of the patient were included as covariates in the models. The level of statistical significance for all analyses was set at 0.05. Statistical analyses were performed using R (v4.2.1).[19]

RESULTS

Descriptive statistics of the study population are shown in Table 1. We included a total of 381 patients in the study: 107 in the CCN and 274 in standard care. The average age of patients was 77.09 (SD = 10.62), 48% of patients identified as women, 90% as White ethnicity, 1.9% as Latino ethnicity, and 72% as married. The average baseline CCI score was 3.21 (SD = 1.95), which indicates a mild severity.

Tables 2 and 3 show the change in polypharmacy and number of medications used among patients enrolled in CCN compared to standard care. The CCN and standard care groups did not differ in the overall and prescription polypharmacy use. The CCN and standard care groups did not differ in the average change in these medications from baseline to follow-up. The CCN group was associated with a three-fold lower odds of OTC polypharmacy use (aOR = 0.30; p <0.001; 95% Confidence Interval [95% CI] = 0.15; 0.58). The CCN group also was associated with a reduction in the number of OTC medications compared to standard care, after controlling for covariates (adjusted beta = -0.90; p = 0.004; 95% CI = -1.5; -0.3).

DISCUSSION

This study is one of the first to compare polypharmacy among patients living with ADRD who participate in an ADRD care program. Our study used real-world data from the EMR of patients with ADRD receiving care at a university hospital's memory clinic and results from our study are generalizable to clinics with similar characteristics. We hypothesized that patients in the CCN would reduce their use of polypharmacy among people with ADRD compared to standard care. The hypothesis was developed with the concept that timely detection and optimal care can stabilize or delay ADRD symptoms. The data partially supported this hypothesis. Overall, polypharmacy did not change between patients in the CCN vs. standard care. However, polypharmacy of OTC medications significantly decreased in the CCN group compared to standard care.

Our findings show that OTC polypharmacy use change differed by group. OTC medications account for 56% of the cases of major drug-drug interaction in the U.S., 42% (23.3 million) of older adults use at least one OTC medication, and 12% (23.3 million people) use five or more OTC medications concurrently.[20] Therefore, our data suggest a potential benefit of the CCN in reducing these risky interactions. To our knowledge, studies that implement ADRD care interventions rarely assess and aim to reduce polypharmacy, and even less frequently include intervention targeting OTC polypharmacy, despite these having the potential to reduce drug-drug interaction risk.[21-24]

Contrary to our hypothesis, the change in overall and prescription polypharmacy did not differ between patients in the CCN and standard care. While prescription polypharmacy may have been reduced for some in the CCN, it is possible that patients at higher risk for polypharmacy, with more severe symptoms and more challenging ADRD etiologies, were enrolled in this group to seek support. If patients with higher needs were more likely to enroll in the CCN, they might have required a higher use of medications, obscuring therefore the actual

Table 1. Characteristics of the patient population at baseline.

Characteristic	Cognitive Care Network, N = 107[1]	Standard Care, N = 274[1]	Overall, N = 381[1]
Age			
Mean (SD)	76.35 (8.91)	77.39 (11.22)	77.09 (10.62)
Median (IQR)	78.00 (71.50, 82.00)	79.00 (72.25, 84.00)	79.00 (72.00, 84.00)
Range	52.00, 95.00	21.00, 100.00	21.00, 100.00
Women; n (%)	46 (43%)	137 (50%)	183 (48%)
Race; n (%)			
White	95 (93%)	240 (89%)	335 (90%)
Black	7 (6.9%)	24 (8.9%)	31 (8.4%)
Asian/Pacific Islander	0 (0%)	3 (1.1%)	3 (0.8%)
American Indian	0 (0%)	2 (0.7%)	2 (0.5%)
Unknown	5	5	10
Hispanic, Latino, or Spanish Origin; n (%)	2 (2.3%)	3 (1.7%)	5 (1.9%)
Marital status; n (%)			
Married	78 (73%)	196 (72%)	274 (72%)
Widowed	14 (13%)	39 (14%)	53 (14%)
Single	5 (4.7%)	23 (8.4%)	28 (7.3%)
Divorced	10 (9.3%)	16 (5.8%)	26 (6.8%)
CCI			
Mean (SD)	3.21 (1.84)	3.21 (2.00)	3.21 (1.95)
Median (IQR)	4.00 (1.00, 4.00)	4.00 (1.00, 4.00)	4.00 (1.00, 4.00)
Range	1.00, 7.00	1.00, 8.00	1.00, 8.00
Unknown	18	34	52
5 or more overall medications; n (%)	100 (93%)	253 (92%)	353 (93%)
5 or more prescription medications; n (%)	82 (77%)	218 (80%)	300 (79%)
5 or more over-the-counter medications; n (%)	35 (33%)	122 (45%)	157 (41%)
Number of prescription medications			
Mean (SD)	6.90 (3.47)	8.96 (6.14)	8.38 (5.60)
Median (IQR)	7.00 (5.00, 9.00)	8.00 (5.00, 11.00)	7.00 (5.00, 11.00)
Range	1.00, 20.00	0.00, 49.00	0.00, 49.00
Number of over-the-counter medications			
Mean (SD)	3.88 (3.15)	4.49 (3.28)	4.32 (3.25)
Median (IQR)	3.00 (2.00, 5.50)	4.00 (2.00, 7.00)	4.00 (2.00, 6.00)
Range	0.00, 15.00	0.00, 17.00	0.00, 17.00

Table 2. Adjusted Odds Ratio (OR) of polypharmacy* among patients enrolled in CCN compared to standard care.

	Adjusted OR	95% CI	P value
5 or more overall medications at follow-up**±	0.55	0.14; 2.44	0.410
5 or more prescription medications at follow-up**||	1.02	0.42; 2.69	0.970
5 or more over-the-counter medications at follow-up**#	0.30	0.15; 0.58	<0.001

*Polypharmacy is operationalized as the concurrent use of 5 or more medications at follow-up, controlled for the concurrent use of 5 or more medications at baseline; **Controlled for sex and CCI score; ±Controlled for the concurrent use of 5 or more overall medications at baseline; ||Controlled for the concurrent use of 5 or more prescription medications at baseline; #Controlled for the concurrent use of 5 or more over-the-counter medications at baseline

Table 3. Adjusted change in the number of prescription and over-the-counter medications among patients enrolled in CCN compared to standard care.

	Adjusted Beta	95% CI	P value
Mean change in number of prescription medications from baseline to follow-up*	0.16	-0.68; 1.0	0.700
Mean change in number of over-the-counter medications from baseline to follow-up*	-0.90	-1.5; -0.3	0.004

*Controlled for sex and CCI score

effects of the CCN on polypharmacy. Unfortunately, symptom severity and ADRD etiology were not evaluated. Additionally, with expertise of ADRD-trained specialists identifying BPSD and having experience with medications that can lessen these symptoms may increase the usage rate, rather than if those symptoms are not identified.

Limitations. This study has several limitations. Causality cannot be inferred due to its observational design. Patients may have enrolled in the CCN for specific reasons, including more severe ADRD symptoms or specific ADRD diagnoses with more BPSD, such as dementia with Lewy bodies or frontotemporal dementia. This differential selection might have artificially impacted the associations between participating in the CCN and polypharmacy. The current analysis only includes patients from a university memory clinic. Therefore, findings might be more generalizable to patients in specialized rather than primary care settings. Primary care settings serve a more diverse population with respect to rural, ethnic, and racial backgrounds.[25] While the CCN also is being implemented in primary care clinics, we did not include patients from these clinics in the current study because they do not collect data using HERON. Additionally, HERON may not capture all medications the patients have been prescribed outside of the participating hospital. HERON contains information about medications providers prescribe or patients report to the providers. Many OTC medications may go unreported and adherence to prescription medications is not available. We defined polypharmacy as using five or more medications. Using five or more medications is the most common definition, but it does not account for specific comorbidities present and can make it difficult to assess safety and appropriateness.[7] We do not have information about the adherence of patients to the CCN, their medications, or enrollment into any other ADRD interventions.

Our study has positive implications for practice and research. The ADRD care interventions may help reduce OTC polypharmacy, but they should include deprescribing modules to reduce prescription polypharmacy among people with ADRD. While generalized pharmaceutical care interventions to reduce overall polypharmacy among older adults are rarely successful, emerging models focused on systematically deprescribing these medications are under investigation.[26-29] Future studies of CCN could include a randomized controlled trial to assess its effectiveness in modifying polypharmacy. These studies would benefit from integrating EMRs with partnering clinics to gain further insight into CCN's effectiveness. Further studies should also control for different ADRD diagnoses, different disease stages, and evaluate the mediating role of BPSD to elucidate potential causes and sources of bias.

CONCLUSIONS

Our study found that patients with ADRD who enrolled in the CCN experienced a significant reduction in OTC, but not prescription medication polypharmacy. Reducing OTC polypharmacy use has the potential to reduce drug-drug interactions and drug-disease interactions.[6,7] Further research is indicated to help interpret these findings.

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