- 8. Sulmasy DP, Astrow AB, He MK, et al. The culture of faith and hope: patients' justifications for their high estimations of expected therapeutic benefit when enrolling in early phase oncology trials. *Cancer*. 2010;116:3702-3711.
- Zier LS, Sottile PD, Hong SY, Weissfield LA, White DB. Surrogate decision makers' interpretation of prognostic information: a mixed-methods study. *Ann Intern Med.* 2012;156: 360-366.

DOI: 10.1111/jgs.17124

# The effect of mail order pharmacy outreach on older patients with diabetes

#### BACKGROUND

Diabetes is one of many chronic conditions that affect the geriatric population in which medication adherence plays an important role in preventing its complications.<sup>1</sup> Observational studies investigating the effect of pharmacy options on medication adherence for chronic diseases, including diabetes, show that mail order pharmacy (MOP) use is associated with higher adherence for diabetes medications,<sup>2</sup> better glycemic control, lower emergency department use, and fewer hospitalizations.<sup>3</sup> We also have seen that financial incentives to use MOP resulted in a greater uptake of this delivery model.<sup>4</sup> Studies which specifically investigate interventions used to optimize the health of the geriatric population are of significant interest, and their importance will increase in the coming years as the older patient population continues to grow.<sup>5</sup> This study uniquely contributes to the literature by examining whether the effects of direct-topatient outreach on MOP use differ by age and improve medication adherence in the older population.

#### **METHODS**

The Encouraging Mail Order Pharmacy Use to Improve Outcomes and Reduce Disparities (EMPOWER) Study conducted through Kaiser Permanente Northern California (KPNC) was a randomized pragmatic trial to encourage the use of MOP with the aim of improving adherence of oral cardiovascular drugs (such as antihypertensives, lipid lowering drugs, and other oral diabetic medications) in patients with diabetes. Participants included adults with diabetes, poor medication adherence (proportion of days covered <80%), and no MOP use in the prior 12 months, who were randomized to receive no intervention (control) or MOP outreach (intervention). This outreach consisted of a mailed letter, secure email message, and automated phone call outlining benefits of MOP. Outcomes examined **TABLE 1**Initiation of mail order pharmacy (MOP) use andadherent to metformin by age group

	Initiation of MOP use	Adherent to metformin
Age <60, odds ratio (95% confidence interval [CI])	1.08 (0.99, 1.17)	1.05 (0.95, 1.16)
Age ≥60, odds ratio (95% CI)	1.23 (1.14, 1.34)	1.15 (1.03, 1.29)
Interaction term between study arm and age <i>p</i> -value	0.025	0.235

were initiation of MOP use and medication adherence during 12 months of follow-up.<sup>6</sup> We further examined if the effect of direct-to-patient outreach on MOP use and medication adherence differed by age group by adding an interaction term between study arm and age, where age was a categorical variable with two levels (age <60 and  $\geq$ 60 years). This study was approved by the Kaiser Permanente Northern California Institutional Review Board.

#### RESULTS

Among 43,012 KPNC patients included in this study, 23,447 (54.5%) were aged  $\geq 60$  years. The prevalence of secure messaging was lower in the older age group. Benefits for the older aged group more frequently included a MOP incentive (defined as a discount in which the patient received three refills for the price of 2). The older age group had a significantly higher number of classes of oral cardiovascular drugs with p < 0.0001 for all comparisons.

A total of 10.7% of patients  $\geq$ 60 years and 11.9% of patients <60 years initiated MOP use, and 54.9% of patients  $\geq$ 60 years and 49.0% of patients <60 years became adherent to metformin. There was a positive effect of MOP outreach on MOP initiation in both age

groups with a larger positive effect (p = 0.025) in the age group  $\geq 60$  years as shown in Table 1 (age  $\geq 60$ : odds ratio [OR] 1.23 [confidence interval (CI) 1.14–1.34], age <60: OR 1.08 [CI 0.99–1.17]).

### CONCLUSION

Geriatric patients are particularly susceptible to medication non-adherence and may benefit from the use of MOP. Factors which can influence medication adherence in the older adult population are numerous, including both patient and medication factors such as logistics obtaining medications (transportation to pharmacy, cost), complexity of medication regimens, the patient-prescriber relationship, and social support.<sup>7</sup> This study examined whether the effects of direct-to-patient outreach on MOP use and subsequent impact on medication adherence are larger in the older population. Our study showed that reaching out to patients directly to encourage MOP use can be an effective way to increase MOP enrollment in the older population as we saw increased use of MOP in the intervention group, with a significantly larger effect observed in the older age group ( $\geq 60$  years). Although the benefit observed seems small, it is statistically and, we believe, clinically significant because it demonstrates increased MOP use at a population level. It is important to keep in mind that this is a low-cost pragmatic intervention that can easily be implemented and may be more beneficial for older adults based on this analysis. Our study is one of the first to examine whether the effect of an MOP encouragement intervention differed by age. During the pandemic, when older patients with diabetes are particularly vulnerable, MOP use is encouraged by the Centers for Disease Control to combine convenience with safety; this study shows that older patients are responsive to outreach efforts to increase MOP use.<sup>6</sup>

Further studies could examine the effect of human contact reminders versus recordings for encouragement,<sup>8</sup> MOP enrollment opportunities in routine clinic visits, or preference for technology in older adults (mail vs. email vs. phone).

#### ACKNOWLEDGMENTS

#### **CONFLICT OF INTEREST**

Chelsea Gong, Wendy Dyer, Maher Yassin, Romain Neugebauer, Andrew J. Karter, and Julie A. Schmittdiel have no conflicts of interest to disclose.

#### **AUTHOR CONTRIBUTIONS**

Chelsea Gong, Wendy Dyer, Romain Neugebauer, Andrew J. Karter, and Julie A. Schmittdiel conceived the study and developed the study plan; Wendy Dyer and Maher Yassin

conducted the data analyses; all authors contributed to the interpretation of results; Chelsea Gong wrote the first draft of the paper; and all authors critically reviewed and revised the manuscript for important intellectual content and approved the final manuscript for publication.

#### **SPONSOR'S ROLE**

This work represents the findings and opinions of the study authors and not those of the study sponsor.

#### FINANCIAL DISCLOSURE

This project was supported by a grant from National Institutes of Health, NIH/NIDDK 1R18DK104249-01A1. Julie A. Schmittdiel and Andrew J. Karter also received support from the Health Delivery Systems Center for Diabetes Translational Research (P30 DK092924).

Chelsea Gong MD<sup>1</sup> Wendy Dyer MS<sup>2</sup> Maher Yassin MPH<sup>2</sup> Romain Neugebauer PhD<sup>2</sup> Andrew J. Karter PhD<sup>2</sup> Julie A. Schmittdiel PhD<sup>2</sup>

<sup>1</sup>Department of Medicine, Kaiser Permanente Oakland Medical Center, Oakland, California, USA <sup>2</sup>Division of Research, Kaiser Permanente Northern California, Oakland, California, USA

#### **Funding information**

Health Delivery Systems Center for Diabetes Translation Research, Grant/Award Number: P30 DK092924; National Institute of Diabetes and Digestive and Kidney Diseases, Grant/Award Number: 1R18DK104249-01A1

#### REFERENCES

- Pladevall M, Williams LK, Potts LA, Divine G, Xi H, Lafata JE. Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. *Diabetes Care*. 2004;27(12): 2800-2805. https://doi.org/10.2337/diacare.27.12.2800.
- Fernandez EV, McDaniel JA, Carroll NV. Examination of the link between medication adherence and use of mail-order pharmacies in chronic disease states. *J Manag Care Spec Pharm.* 2016;22(11): 1247-1259. https://doi.org/10.18553/jmcp.2016.22.11.1247.
- Neil WP, Shiokari CE, Burchette RJ, Stapleton D, Ovbiagele B. Mail order pharmacy use and adherence to secondary prevention drugs among stroke patients. *J Neurol Sci.* 2018;390:117-120. https://doi.org/10.1016/j.jns.2018.04.001.
- Karter AJ, Parker MM, Schmittdiel JA, et al. Impact of a pharmacy benefit change on new use of mail order pharmacy among diabetes patients: the Diabetes Study of Northern California (DISTANCE). *Health Serv Res.* 2015;50(2):537-559. https://doi. org/10.1111/1475-6773.12223.
- Alzheimer's Association. 2019 Alzheimer's disease facts and figures. *Alzheimer's Dement*. 2019;15(3):21-87.

2030 I

- Ramachandran B, Trinacty CM, Schmittdiel JA, et al. A randomized encouragement trial to increase mail order pharmacy use and medication adherence in patients with diabetes. *J Gen Intern Med.* 2020;36:154-161. https://doi.org/10.1007/s11606-020-06237-8.
- 7. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking

beyond cost and regimen complexity. *Am J Geriatr Pharmacother*. 2011;9(1):11-23. https://doi.org/10.1016/j. amjopharm.2011.02.004.

 Marcum ZA, Hanlon JT, Murray MD. Improving medication adherence and health outcomes in older adults: an evidencebased review of randomized control trials. *Drugs Aging*. 2017; 34(3):191-201. https://doi.org/10.1007/s40266-016-0433-7.

#### DOI: 10.1111/jgs.17165

## Recent Medicare Part D beneficiary claims for desmopressin medications

## INTRODUCTION

Nocturia (waking at night to pass urine<sup>1</sup>) is common in older adults. The US Food and Drug Administration (FDA) recently approved two desmopressin formulations (Noctiva<sup>®2</sup> and Nocdurna<sup>®3</sup>) for the indication of frequent urination at night due to overproduction of urine. Desmopressin, a synthetic analog of the pituitary hormone 8-arginine vasopressin, is an antidiuretic that increases renal water reabsorption.<sup>2,3</sup> Older formulations of desmopressin, developed decades ago for bed-wetting in children, central diabetes insipidus, and platelet-related bleeding dysfunction, are still available and used offlabel<sup>4</sup> for nocturia in adults. Desmopressin is regarded as a potentially inappropriate medication<sup>5</sup> for older adults because of the increased risk of potentially severe hyponatremia that may be life-threatening.<sup>2,3</sup> There are marketing efforts<sup>6</sup> and consensus panels<sup>7</sup> advocating use of new desmopressin formulations in seniors even despite the black-box warning. We therefore sought to better understand recent usage trends of desmopressin formulations in older adults.

#### **METHODS**

We used the most recent, de-identified, publicly available data<sup>8</sup> on US Medicare Part D beneficiaries reimbursement claims for 2018 and 2019. We categorized desmopressin formulations as *any generic* or a specific *branded* formulation; we sub-categorized branded desmopressin as *indicated for nocturia due to nocturnal*  polyuria (Noctiva<sup>®</sup> and Nocdurna<sup>®</sup>), often used off-label for nocturia (DDAVP<sup>®</sup>),<sup>7</sup> or as being indicated for nonurological conditions (Stimate<sup>®</sup>).<sup>9</sup> Those receiving any generic formulation or one branded formulation would be counted as a unique beneficiary each calendar year; individuals using a generic and a branded desmopressin, or multiple branded desmopressin, would be counted as a unique beneficiary for each different formulation used. We calculated the percentage of generic claims over the total desmopressin claims for both 2018 and 2019.

#### RESULTS

Our main results are presented in Table 1. There were 39,576 and 43,051 Medicare Part D beneficiary claims for desmopressin in 2018 and 2019. Noctiva<sup>®</sup> (864) and Nocdurna<sup>®</sup> (897) claims were highest in 2018 and 2019, respectively. Over 90% of all desmopressin claims were for generic formulations. Considering Stimate<sup>®</sup> (a branded medication for bleeding disorders)<sup>9</sup> as unlikely to be used off-label for nocturia made generics 97.2% (2018) and 95.7% (2019) of total desmopressin claims.

#### DISCUSSION

Use of a potentially inappropriate medication such as desmopressin in an older population is concerning.<sup>5</sup> Medicare Part D claims for both branded and generic desmopressin increased slightly from 2018 to 2019.

An International Continence Society consensus panel offered that new FDA-approved medications<sup>2,3</sup> for