

# Sex and gender differences in polypharmacy in persons with dementia: A scoping review

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## Abstract

**Purpose:** To date, research studies in most disciplines have not made sex-based analysis a priority despite increasing evidence of its importance. We now understand that both sex and gender impact medication prescribing, use, and effect. This is particularly true for older adults with dementia who have alterations in drug metabolism, drug response, and the permeability of the blood–brain barrier. To better understand the influence of sex and gender on drug use in older adults with dementia, we conducted a scoping review.

**Methods:** This scoping review systematically searched the Medline, Embase, Web of Science, CINAHL, and ProQuest databases to find published reports on polypharmacy in populations of older adults with dementia that included a sex- or gender-based analysis.

**Results:** A total of 12 published reports were identified. Findings were cohort studies and case-control trials that commented on sex-related differences in medication use as a secondary analysis to the studies' primary objective. These studies showed that community-dwelling women received more potentially inappropriate medications and more psychotropic medications, while nursing home dwelling men received more potentially inappropriate medications, cholinesterase inhibitors, and antipsychotics. None of the identified studies explicitly examined gender-related differences in medication use.

**Conclusion:** This scoping review supports that there is inadequate understanding of both sex and gender differences in drug use in older men and women with dementia. To tailor medication-specific interventions to improve drug therapy for older adults with dementia, it is important that future work includes sex- or gender-based analysis of drug use.

## Keywords

Polypharmacy, sex, gender, dementia

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## Knowledge into practice

### *What was known about this topic?*

People with dementia are often excluded from clinical study and very little attention has been given to sex- or gender-based differences in medication use. It is recognized that men and women have differences in pharmacokinetics and likely seek treatment for different medical conditions. These sex-related differences likely affect medication doses or profiles, but these differences are not well understood and no studies to date tackle the differences in drug use in older adults with dementia.

### *What does this study add?*

By examining secondary findings of the studies included in the scoping review, we found that in the community, women are more likely to receive potentially inappropriate medication

(PIM). Men in the community used more cholinesterase inhibitors. In nursing homes, men receive more PIM and more antipsychotics. Men with dementia in nursing homes take more medications overall. Women with dementia use more psychotropic medications than men. The drug–drug interaction of a cholinesterase inhibitor combined with an anticholinergic medication occurs similarly in men and women.

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## What are the implications for pharmacy practice?

This study confirms that when rationalizing drug therapy for older men and women with dementia, there are sex-specific challenges to consider.

### Introduction

Polypharmacy is a well-recognized concern for older adults.<sup>1,2</sup> Worldwide estimates of polypharmacy vary by country, sex, age, and accepted definition.<sup>1–6</sup> At present, there is not a universally accepted definition of polypharmacy. Polypharmacy was investigated in a recent systematic review<sup>6</sup> where authors identified 138 different definitions. Polypharmacy definitions included numerical definitions determined by the number of drugs used, descriptive definitions which considered co-prescribing of multiple medications, and appropriate or inappropriate polypharmacy which examined drugs used even though they are recommended to be avoided, according to consensus-based tools such as Beers criteria<sup>7</sup> or the medication inappropriateness index.<sup>8</sup> Regardless of definition, polypharmacy is a problem for older adults. In the United States, 30% of adults aged 65 years and older are taking six or more drugs daily,<sup>3</sup> and in Canada, estimates suggest 63% of seniors are taking more than 5 medications and 30% of those older than 85 years are taking more than 10 medications.<sup>9</sup> Dementia increases the risk for polypharmacy<sup>5</sup> with pharmacotherapy being an exceedingly common treatment for the behavioral and psychological symptoms of dementia (BPSD).<sup>10–12</sup> This is despite the knowledge that drug therapy has limited beneficial effect on BPSD.<sup>11,13</sup>

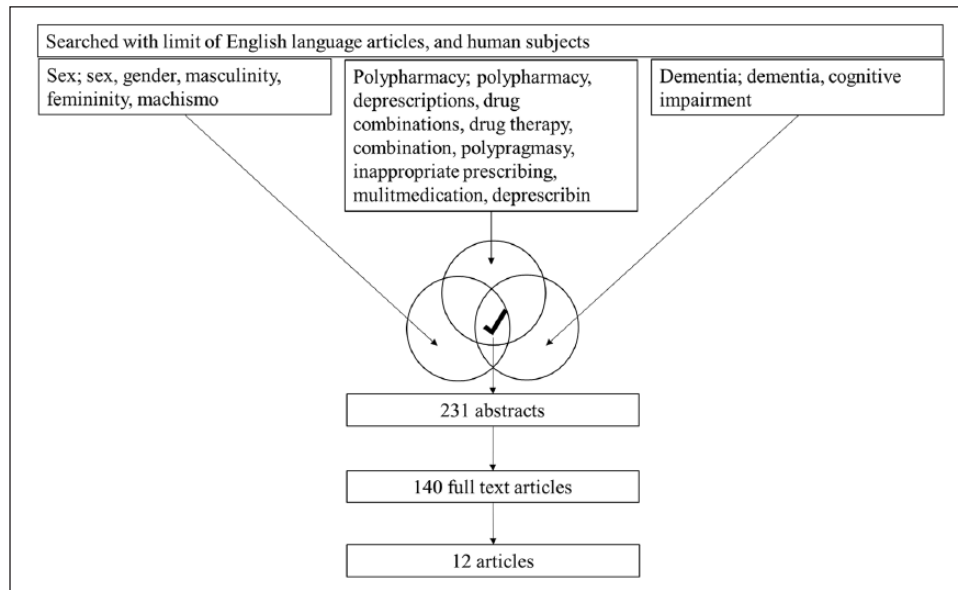
In general, studies enroll younger populations<sup>14</sup> and rarely include those with frailty or complex comorbidities with the resulting complex medication regimen.<sup>15–17</sup> Extrapolating from younger populations to older individuals or those with dementia is not ideal given pharmacokinetic and pharmacodynamic differences in medication response between older adults and their younger and healthier counterparts.<sup>18–30</sup> Pharmacokinetic changes that need to be considered include the following: drug elimination slowing with age due to decreasing kidney function,<sup>31,32</sup> changes in body composition with age which may significantly influence drug distribution and effect,<sup>33</sup> and decreasing cytochrome P450 enzyme content,<sup>21</sup> which alters drug metabolism. In addition, characteristics of the blood–brain barrier change<sup>34</sup> which alters drug introduction to the central nervous system. This is especially true for those with dementia.<sup>35</sup> These changes associated with aging may unpredictably influence serum drug concentrations, drug effect, and toxicity. Even so, age-related changes in drug effect are recognized by clinicians in many guidelines and tools to help guide clinical decision-making for drug use for older adults.<sup>7,36</sup>

Differences in drug pharmacokinetics and pharmacodynamics are not limited to the effect of aging; there are also differences in drug metabolism between males and females. These poorly understood sex-related differences are compounded by the age-related changes and include differences in hepatic metabolism,<sup>21,37–44</sup> intestinal metabolism,<sup>40</sup> drug distribution,<sup>42</sup> and renal clearance.<sup>43</sup> These sex differences have been identified but have not been well delineated and their clinical significance is thus not well understood.

The lived experience of dementia also differs between men and women. Older women are more likely to develop dementia, with 38% greater risk than older men.<sup>45</sup> In North American populations, women with dementia live on average 6 months longer than men with dementia, and women with Alzheimer's Disease (AD) are more likely to live in a nursing home than men with AD. In addition, North American women with dementia spend 94% of their time with dementia in a nursing home, whereas men spend closer to 60% of their time with the disease in nursing homes.<sup>45</sup> Some of these differences likely relate to sex (biological differences, e.g. metabolism), while others relate to gender (social roles, e.g. caregiving roles and longevity in relation to a caregiving spouse).<sup>46</sup> Gender roles may also lead to men and women seeking treatment for different conditions and may influence prescribing practices, with drug selection being influenced by physician gender biases.<sup>47,48</sup> While investigations into gender differences in prescribing have not specifically focused on older adults with dementia, there is no reason to believe that these principles do not apply. Indeed, these differences may be even more important to understand in older adults with dementia due to their susceptibility to adverse drug reactions.<sup>49</sup>

To date, randomized controlled trials designed to evaluate drug use for older adults with dementia have not investigated sex differences sufficiently to help guide practice. We can likely assume that drugs that are temporally associated with improvements in BPSD or improvements in monitoring parameters of optimal health (such as blood pressure, heart rate, or cognition) are continued, whereas therapies that do not seem to be working are discontinued. This leads to the hypothesis that due to gender and sex differences in medication prescription, use, and response, women and men with dementia will end up on different drug profiles. This is expected to be exacerbated by the differences in comorbidity expression in men and women. Comorbidity, frailty, and cognitive impairment will mean that most of older adults with dementia will be taking more than five medications daily and this polypharmacy profile may differ between men and women based on the many sex and gender differences discussed.

This objective of this scoping review was to understand differences in polypharmacy as determined by medication use including the number of medications or concomitant medications used by older men and women with dementia,



**Figure 1.** Search strategy and study selection.

with the aim of informing recommendations for research and guiding initiatives to improve drug use.

## Methods

A systematic review was not possible as there were no studies designed with a primary objective to explore sex or gender differences in drug use in older adults with dementia. The scoping review methodology was selected for this investigation due to the ability of this approach to present a general overview of a topic area while identifying gaps in the literature base.<sup>50,51</sup> Arksey and O'Malley<sup>50</sup> have a five-stage framework and this approach guided the present review.

### Stage 1: identify the research question

What is the relationship between sex or gender and polypharmacy in older adults with dementia?

### Stage 2: identify relevant studies

A search of each of the databases Medline, Embase, Web of Science, CINAHL, and ProQuest was conducted in January 2016 to identify all published research that commented on drug use in people with dementia. Each database was searched from inception to 1 January 2016. The only limit applied to the search was that the article had to be available in English.

Searches were completed for each of three concepts independently, and then the three searches were combined. The search terms included (1) Sex, gender, masculinity,

femininity, machismo; (2) Polypharmacy, deprescriptions, drug combinations, drug therapy combination, polypragmasy, inappropriate prescribing, multimedication, deprescribing; (3) Dementia, cognitive impairment. The search strategy is shown in Figure 1.

### Stage 3: study selection

All identified abstracts were reviewed by two reviewers with the aid of Distiller SR software<sup>®</sup>. Abstracts were selected for full-text review if they (1) were in English, (2) reported on an original study with human subjects among whom at least a subset had cognitive impairment, and (3) reported on older adults 65 years of age or older. Articles identified from the abstract review were reviewed by two reviewers. Articles were included in the final scoping review if they (1) were in English, (2) reported on original research, (3) if the subjects (or an identifiable subset) were 65 years of age or older, (4) if there was a clear population with dementia, (5) if those with dementia were subdivided into males and females, and (6) if some medication-specific information was provided by sex or gender. Conflicts at either stage of review were resolved via consensus reached after discussion focused on the relevant selection criteria.

While study quality is not typically a component of a scoping review, quality was assessed using the National Institutes of Health (NIH) sponsored National Heart, Lung, and Blood Institute's Quality Assessment for Case-Control Studies or Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies as appropriate<sup>52</sup> (and rated as good, fair, or poor) or the Cochrane Collaboration's tool for assessing risk of bias for randomized controlled trials<sup>53</sup> (and

rated as low or high risk). The quality of studies was subjectively rated by the two reviewers and based on the criteria in the tools. This was done to explore the merits of the included studies in an effort to identify the level of attention to sex- or gender-specific findings regarding polypharmacy but did not impact decisions regarding inclusion/exclusion of articles in the scoping review process.

#### *Stage 4: charting the data*

Data are charted in a summary table. Details of the studies that were of interest for the review included study design, study purpose/objective, subject population, analytic model, key findings, and an appraisal of evidence quality.

#### *Stage 5: collating, summarizing, and reporting the results*

Study findings and characteristics were considered with respect to what they revealed about the role of sex or gender on polypharmacy in older adults with dementia by each of the study authors. This led to the summary of findings and a description of the gaps in the existing literature.

### **Results**

In total, 231 unique abstracts were identified for review. In addition to the search strategy, Figure 1 shows the process followed for article selection. Only 140 abstracts met inclusion criteria and went on to full-text review. Of the 140 full-text articles reviewed, 12 were appropriate for inclusion in the final review. A summary of the 12 included papers is provided in Table 1.

#### *Findings for men*

In general, the included studies reported increased use of antipsychotics and cholinesterase inhibitors among men. In a Finnish cohort of community-dwelling seniors with dementia, using more than one antipsychotic medication at a time was associated with male sex.<sup>54</sup> Men with dementia and no diagnosis of schizophrenia who were inpatients in acute care hospitals in England had a 10% increased use of antipsychotics.<sup>55</sup> Nursing home dwelling men near end of life were taking 1.36 times as many medications per day as women, and these men were more likely to be using a medication considered to be potentially inappropriate by the study authors at end of life.<sup>57</sup> In a longitudinal cohort comprising people with cognitive impairment across 59 sites in the United States and Canada, cholinesterase inhibitor use was more common in men (93.8%) compared to women (78.4%) ( $p=0.002$ ).<sup>60</sup> Logistic

regression showed that male sex (odds ratio (OR) = 3.61; 95% confidence interval (CI) = 1.35–9.66) was associated with increased use of cholinesterase inhibitor treatment.<sup>60</sup> Men received more lipid-lowering therapy than women.<sup>63</sup> None of the studies reported on gender-specific findings for men.

#### *Findings for women*

The review showed that women were generally exposed to more psychotropic medication. In a German study of community-dwelling people with dementia, female sex was associated with an increased risk of inappropriate medication use (OR = 10.36, 95% CI = 1.28–83.87) according to the PRISCUS list.<sup>56</sup> In community-dwelling seniors with dementia in France, female sex was associated with increased odds of PIM use according to the LaRoche list (OR = 1.5; 95% CI = 1.1–2.2).<sup>59</sup> The second study from France analyzing the cohort of the first 5000 subjects initiated on tacrine, the first drug available for dementia treatment and a centrally acting anticholinesterase and indirect cholinergic agonist, considered their medication use 3 months prior to enrollment in the cohort showed that benzodiazepine users were more likely to be female ( $p < 0.001$ ).<sup>61</sup> Female residents of Dutch nursing homes had increased use of antidepressant medications in both models explored (OR = 1.44 and 1.49). The first model adjusted for Neuropsychiatric Inventory Nursing Home symptoms, and the second model adjusted for the Cohen Mansfield Agitation Inventory symptoms.<sup>62</sup> In a group of subjects with confirmed dementia from Stockholm's Kungsholmen district born in or before 1912, there was a statistically significant ( $p < 0.05$ ) association between female sex and use of a number of medication classes: hypnotics and sedatives (OR = 1.70), anxiolytics (1.90), potassium (1.43), minor analgesics and antipyretics (1.42), thiazides (1.82), non-steroidal anti-inflammatory drugs (NSAIDs, 2.32), thyroid preparations (5.12), centrally acting muscle relaxants (2.02), multivitamins (4.95), and psychotropic drugs (1.87).<sup>65</sup> None of the studies reported on gender-specific findings for women.

#### *General sex-specific findings*

In community-dwelling seniors in the United States with dementia, use of a drug with anticholinergic activity was not significantly related to sex ( $\chi^2=1.07$ ;  $p=0.300$ ).<sup>58</sup> In older community-dwelling adults living alone who were followed in the Swedish Alzheimer's Treatment Study, no significant sex differences were observed in drug therapy at the initiation of cholinesterase inhibitor therapy.<sup>63</sup> Patients receiving cholinesterase inhibitors in the preceding year were more

**Table 1.** Results of scoping review search to determine what the literature can tell us about the role of sex or gender on polypharmacy in persons with dementia.

Number	Author	Study design	Study purpose/objective	Subject population	Analytic model	Key findings	Appraisal of evidence quality
1	Taipale et al. <sup>54</sup>	Observational cohort study	To describe prevalence and risk factors associated with antipsychotic polypharmacy among antipsychotic users with AD	9803 community-dwelling persons with clinically verified AD residing in Finland who used antipsychotics between 2006 and 2009	Cox proportional hazards model	Antipsychotic polypharmacy was associated with male sex (unadjusted HR 1.2 (1.03–1.39), adjusted HR 1.18 (1.02–1.38)). Among antipsychotic users, no sex difference for number of antipsychotic polypharmacy episodes.	Good
2	Stephens et al. <sup>55</sup>	Retrospective longitudinal cohort study	To describe the change in prescribing of antipsychotics in people with dementia treated as inpatients in England and to understand the impact of clinical and sociodemographic factors on use	63,079 adult patients above 58 years of age with a dementia diagnosis recorded in their clinical record between January 2010 and October 2012	Chi square test at univariate level for trends and backward stepwise logistic regression in a multivariate analysis	Male sex was associated with a 10% increase in the likelihood of antipsychotic prescribing OR 1.1 (1.06–1.15)	Fair
3	Fiss et al. <sup>56</sup>	Prospective cohort study	To analyze the occurrences of PIM in older adults and the determinants for PIM use in patients with suspicion of dementia	342 patients in primary care in Germany who screened positive for cognitive impairment	Multiple binary logistic regression analyses	Female sex (OR 10.36 (1.28–83.87)) was a positive determinant for PIM use per the PRISCUS list	Poor
4	Tjia et al. <sup>57</sup>	Prospective cohort study	To examine daily medication use in advanced dementia with attention to end of life	323 nursing home residents with advanced demented living in 22 Boston area facilities recruited from 1 February 2003 to 30 September 2006	Negative binomial regression using generalized estimating equations	Men were taking 1.36 times as many medications per day as women. Male sex was associated with a higher number of daily medications and never appropriate drug use.	Good
5	Roe et al. <sup>58</sup>	Retrospective cohort study	To compare prevalence of anticholinergic drug use in a sample of patients with probable dementia to a sample of older adults without dementia	418 individuals using donepezil and 418 comparators identified from a pharmacy benefit management company in the United States	McNemar's test and chi-square analysis to compare anticholinergic use between groups and a discontinuation analysis to see if anticholinergics were stopped once donepezil was started	Use of an anticholinergic agent was not related to sex in those taking donepezil	Good
6	Montastruc et al. <sup>59</sup>	Prospective cohort study	To assess the prevalence of potential PIM use in community-dwelling patients with mild-to-moderate dementia and to identify factors associated with PIM	684 subjects with mild-to-moderate dementia cared for by an informal caregiver in France	Binary analysis with Fisher's exact test, Pearson's $\chi^2$ , student's t-test or Mann-Whitney's parametric test, then a backward multivariate logistic regression analysis to find factors associated with PIM use	Female sex was associated with PIM use OR 1.5 (1.1–2.2) per the LaRoche list	Good
7	Epstein et al. <sup>60</sup>	Prospective cohort study	To characterize medication use in older adults in the ADNI study	818 participants in the ADNI cohort	ANOVA and logistic regression	In those with AD, more men were using a cholinesterase inhibitor (93.8% vs 78.4%, $p = 0.002$ ). Male sex was associated with cholinesterase inhibitor treatment in AD (OR 3.61 (1.35–9.66)).	Fair

(Continued)

Table 1. (Continued)

Number	Author	Study design	Study purpose/objective	Subject population	Analytic model	Key findings	Appraisal of evidence quality
8	Lagnaoui et al. <sup>61</sup>	Cross-sectional study	To assess prevalence of benzodiazepine use in AD patients and to examine patient and drug characteristics and associated use	5000 patients treated with tacrine for mild-to-moderate AD	Chi-square analysis and multivariate regression	Benzodiazepine users were more likely to be female	Good
9	Nijk et al. <sup>62</sup>	Cohort study	To investigate psychotropic drug use in Dutch nursing home patients with dementia and the association between age, sex, severity of dementia, and type of neuropsychiatric symptoms	1322 patients with dementia who had resided in a nursing home for more than 4 weeks	Binomial logistic regression	Women had an increased risk for the use of antidepressant medication (OR 1.44 and 1.49 using different methods of measuring neuropsychiatric symptoms)	Fair
10	Wattmo et al. <sup>63</sup>	Prospective open nonrandomized multicenter cohort study	To describe the long-term cognitive and functional abilities of solitary living individuals with AD, to compare these outcomes with those living with a family member and to identify the potential predictors of usage of community-based home-help services and nursing home placement for these two living status groups	1258 patients recruited from memory clinics in Sweden	ANOVA, independent samples t-tests, chi-square test, binary logistic regression	Females used more antidepressant medication, more antipsychotic medication, and less lipid-lowering agents. No significant sex-based differences were noted per the number of medications used at the time a cholinesterase inhibitor was initiated.	Good
11	Huisman et al. <sup>64</sup>	Case control	To determine whether anticholinergic agents are prescribed to people on cholinesterase inhibitors	10,989 patients treated with anticholinergic bladder antispasmodics and 32,967 controls	Regression analysis	There was no sex difference in patients receiving both cholinesterase inhibitors and anticholinergic bladder antispasmodics	Fair
12	Wills et al. <sup>65</sup>	Case control	To describe the use of drugs in an older population with respect to dementia status while considering age, sex, and housing type	1810 people from Stockholm who were born in or before 1912	Logistic regression	For many drug classes (hypnotics and sedatives, anxiolytics, potassium, minor analgesics and antipyretics, thiazides, NSAIDs, thyroid preparations, centrally acting muscle relaxants, multivitamins, and psychotropic drugs), the proportion of users was larger in women. The number of medications used was similar in men and women with dementia.	Good

AD: Alzheimer's Disease; OR: odds ratio; PIM: potentially inappropriate medications; CI: confidence interval; ADNI: Alzheimer's Disease Neuroimaging Initiative; ANOVA: analysis of variance; NSAIDs: nonsteroidal anti-inflammatory drugs.

likely to receive anticholinergic spasmolytics (OR = 5.6; 95% CI = 3.7–8.5), and this drug–drug combination did not differ between sexes.<sup>64</sup>

### General gender-specific findings

Surprisingly, none of the studies reported on gender-specific findings.

## Discussion

This scoping review identified 12 papers that provided insight into sex-related differences in polypharmacy in those with dementia; however, none of the papers made any comment on gender-related differences. The identified papers highlight several findings. Most notably, among community-dwellers, women were more likely to receive PIMs,<sup>56,59</sup> whereas among residents of nursing homes, men received more PIMs.<sup>57</sup> Men with dementia in nursing homes were taking more medications overall<sup>57</sup> and in particular, more antipsychotics.<sup>54,55</sup> Men in the community used more cholinesterase inhibitors than women.<sup>60</sup> Women with dementia used more psychotropic medications than men.<sup>61–63,65</sup> The existence of the drug–drug interaction of a cholinesterase inhibitor combined with an anticholinergic medication did not differ by sex.<sup>58,64</sup>

Antipsychotic use was higher among hospitalized and institutionalized men. Taipale et al.<sup>54</sup> showed that using more than one antipsychotic was more common in men with dementia, and Stephens et al.<sup>55</sup> found that male sex was associated with a 10% increase in the likelihood of antipsychotic use in hospitalized individuals with dementia. This is not surprising, given concerns that men may be more prone to experiencing violent responsive behaviors and using antipsychotics is a culturally acceptable method to attempt to reduce BPSD despite a lack of scientific data supporting their use.<sup>66</sup> It follows then that in nursing home patients with advanced dementia, men are more likely to take a PIM,<sup>57</sup> this is likely driven by the increased use of the antipsychotics<sup>55</sup> in this population. This is contrasted with the findings of Wattmo et al.,<sup>63</sup> who suggest that community-dwelling women with dementia use more antipsychotics. It is conceivable that increased antipsychotic use by community-dwelling women with dementia is simply reflective of the increased use of psychotropic medications by women with dementia in general.<sup>65</sup>

Women with dementia's increased use of psychotropic medication is driven by an increased use of antidepressants,<sup>62,63</sup> hypnotics, sedatives, and anxiolytics.<sup>61,63</sup> Antidepressants reach higher serum concentrations in women<sup>67</sup> which may be mediated by gastric pH, which is higher in females, and may increase absorption of medications whose active ingredients possess basic functional groups such as many antidepressants.<sup>67</sup> It is worth questioning whether the reduced use of antidepressants in men with

dementia is due to their reduced effect driven by lower serum concentrations being achieved.

In one study of community-dwelling seniors with AD, men were more likely to be taking a cholinesterase inhibitor.<sup>60</sup> This is a surprising finding as women with AD in the community are otherwise more likely to use psychoactive medication. The lower use of cholinesterase inhibitors among women might be related to their lower body weight and a reluctance by clinicians to initiate this therapy with its attendant risk of gastrointestinal upset and weight loss. It is also a consideration that women likely achieve higher serum concentrations of cholinesterase inhibitors due to their higher gastric pH,<sup>67</sup> that they experience the adverse effects at a greater rate, and thus are unable to tolerate and continue treatment. However, the finding that men with dementia use more lipid-lowering therapies suggests that cardiac comorbidities are more common in community-dwelling men with dementia<sup>63</sup> but may also reflect known differences in cardiovascular comorbidity identification and treatment between men and women in the general population.<sup>68</sup>

Urinary incontinence is a well-known side-effect of cholinesterase inhibitors. Despite the antagonistic nature of using an anticholinergic medication to control urinary incontinence in an individual on a cholinesterase inhibitor, this strategy is attempted by some clinicians. This drug combination is generally not considered to be appropriate due to the side-effect profile of bladder antispasmodic agents and because of the counter-productive drug interaction whereby they offset the activity of the cholinesterase inhibitor. No sex differences have been identified in the use of this combination of drugs.<sup>58,64</sup>

Our most startling finding was the lack of research on the topic of sex differences in drug use in older adults with dementia. None of the studies we identified were designed to focus on sex-related differences in drug use in older adults with dementia. Reported sex differences are not the primary objective of any of the studies but instead represent secondary findings. When sex differences were presented, the majority of studies commented only on the use of central nervous system active agents, but we know from prior work that frailty and many other social, economic, and health-related factors influence outcomes in dementia and should influence overall medication use. The quality of the studies was variable, though the majority of the included trials were agreed to be of good quality according to the National Heart, Lung, and Blood Institute's criteria for observational cohort and cross-sectional studies and case-control studies.<sup>52</sup> Also, no studies made any comment about participant gender or gender-related factors, which prevents any gender-based analysis of findings. Even so, our search strategy was designed to be as broad as possible, inclusive of many definitions of polypharmacy, and the scoping review methodology (as opposed to a systematic review) allowed for more detailed investigation of the existing literature. None of the studies identified were randomized controlled trials. The

studies identified were only observational. Certainly, this limits the ability to draw firm conclusions based on this scoping review in isolation, but it does permit us to identify areas that require further study. It is also important to point out that none of the identified studies discussed polypharmacy from the perspective of effect on quality of life such as impact on BPSD, time to admission to nursing home or the lived experience of dementia.

## Conclusion

In closing, there are many findings in this scoping review that can help characterize polypharmacy in men and women with dementia. Clinicians should be aware of the tendency toward increased psychotropic medication use and inappropriate medication use in women with dementia; ideally, the goal should be to reduce or eliminate the use of PIM. Clinicians should carefully review men and women's medication lists for anticholinergic drug and cholinesterase inhibitor, drug–drug interaction, and seek to discontinue the anticholinergic agents. This potentially inappropriate drug combination should be kept in mind for both men and women.<sup>58,64</sup> Antipsychotics continue to be used in populations with dementia. Men and women seem to use antipsychotics to greater extents dependent on their living environment (women in the community and men in long-term care facilities). Antipsychotics are also potentially inappropriate and thus clinicians still need to be vigilant for opportunities to reduce their use. Even though the literature is sparse regarding sex and gender differences in medication use in men and women with dementia, further research and knowledge translation efforts are required to understand how we can build upon and use the knowledge of these differences to improve medication use for individuals with dementia.

## Author contributions

S.C.T. is the corresponding author; S.C.T. developed the study methods and completed the initial searches of all databases; S.C.T. was one of the two reviewers; S.C.T. made decisions about study inclusion and drafted the paper; S.C.T. made corrections and approved the final paper. M.R. was the second reviewer; M.R. reviewed all abstracts and all full-text articles; M.R. made decisions about study inclusion, made comments on the draft, and helped prepare the final manuscript; M.R. approved the final paper. M.K.A. was the supervisor of the entire project; M.K.A. provided substantial contributions to conception and design of the study and guidance on development of the study methods; M.K.A. reviewed the draft manuscript and revised it critically for important intellectual content; M.K.A. made corrections, and edited and approved the final paper.

## Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declaration of conflicting interests

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