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Associations between polypharmacy and treatment intensity for hypertension and diabetes: a cross-sectional study of nursing home patients in British Columbia, Canada

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ABSTRACT

Objectives Describe nursing home polypharmacy prevalence in the context of prescribing for diabetes and hypertension and determine possible associations between lower surrogate markers for treated hypertension and diabetes (overtreatment) and polypharmacy.

Design Cross-sectional study.

Setting 6 nursing homes in British Columbia, Canada.

Participants 214 patients residing in one of the selected facilities during data collection period.

Primary and secondary outcome measures Polypharmacy was defined as ≥9 regular medications. Overtreatment of diabetes was defined as being prescribed at least one hypoglycaemic medication and a glycosylated haemoglobin (HbA1c) ≤7.5%. Overtreatment of hypertension required being prescribed at least one hypertension medication and having a systolic blood pressure ≤128 mm Hg. Polypharmacy prescribing, independent of overtreatment, was calculated by subtracting condition-specific medications from total medications prescribed.

Results Data gathering was completed for 214 patients, 104 (48%) of whom were prescribed ≥9 medications. All patients were very frail. Patients with polypharmacy were more likely to have a diagnosis of hypertension (p=0.04) or congestive heart failure (p=0.003) and less likely to have a diagnosis of dementia (p=0.03). Patients with overtreated hypertension were more likely to also experience polypharmacy (Relative Risk (RR))1.77 (1.07 to 2.96), p=0.027). Patients with overtreated diabetes were prescribed more non-diabetic medications than those with a higher HbA1c (11.0±3.7vs 7.2±3.1, p=0.01).

Conclusion Overtreated diabetes and hypertension appear to be prevalent in nursing home patients, and the presence of polypharmacy is associated with more aggressive treatment of these risk factors. The present study was limited by its small sample size and cross-sectional design. Further study of interventions designed to reduce overtreatment of hypertension and diabetes is needed to fully understand the potential links between polypharmacy and potential of harms of condition-specific overtreatment.

Strengths and limitations of this study

- Diabetes and hypertension are highly prevalent risk factors for frail elders, this study provides specific detail about treatment intensity and surrogate outcomes.
- Identification of lower thresholds by which to define overtreatment is a novel addition to polypharmacy research that could have widespread impact.
- Description of a possible link between overtreatment of diabetes and hypertension and more general excessive prescribing could help improve efficacy and reproducibility of polypharmacy interventions.
- This study only used single readings for blood pressure and glycosylated haemoglobin, having multiple measures over time would improve accuracy.
- There are no consensus definitions of what constitutes overtreatment for hypertension and diabetes, and this study relied on an arbitrary starting point that may be inaccurate or contentious.

INTRODUCTION

The right amount of treatment for frail elders living in nursing homes is a complicated formula that includes awareness of a patient's experience of quality of life, personal values and thorough knowledge of the capability of our modern medical interventions. Concern regarding possible harms of excessive prescribed medication has evolved into a field of study captured by the umbrella term 'polypharmacy'. Observational studies have shown associations between polypharmacy and adverse events such as hospitalisations and falls.[1]

Thus far, studies designed to reduce polypharmacy have typically used interventions to reduce overall numbers of drugs or avoid certain categories of drugs thought to be inappropriate.[2] To date, we lack both a

consensus definition of polypharmacy[3] and reliably reproducible tools to decrease polypharmacy and improve patient outcomes.[4 5] To our knowledge, no previous studies examine the potential role of greater treatment intensity (ie, attempts to achieve lower blood pressure (BP) in hypertensives or lower glycosylated haemoglobin (HbA1c) in diabetics) as a potential reason for polypharmacy. Diabetes and hypertension are prevalent and lend themselves well to an exploration of treatment intensity as those conditions have routinely collected surrogate markers (eg, systolic blood pressure (SBP) and HbA1c) that give an objective measure of treatment intensity. Existing research regarding hypertension[6] and diabetes[7] treatments in frail elders has largely been condition-specific observations on proportions of patients being not being treated to specific surrogate measure targets.

The objective of the present study was to examine, within a typical sample of nursing home patients, whether polypharmacy associates with lower surrogates—and in particular, whether it associates with BP and HbA1c below a threshold which might be considered overtreatment of diabetes and hypertension in such a frail population. This exploration may suggest a relationship, between treatment intensity and more general polypharmacy tendencies, which could serve as an adjunct to current approaches that identify overtreatment issues in this population.

METHODS

Setting and participants

This is a cross-sectional study of a sample of 220 nursing home patients in Vancouver, Canada. The patients resided at one of the six not-for-profit nursing homes (total population of 954 patients) that share a similar clinical staffing and pharmacy model. The random sample was selected using an automated program to provide proportional representation from all six facilities. Participants were eligible to participate based on admission to facility on date of initial data gathering. The University of British Columbia-Providence Health Care clinical research ethics board approved the procedures of this minimal risk study and waived the requirement of patient consent.

Data sources

Previous studies have established typical measures related to prevalence of polypharmacy and were used here as a framework for data collection.[8] Prescribing data from the hospital pharmacy on a single date (24 June 2014) was augmented with patient demographics, medical history and additional medical diagnoses (including hypertension and diabetes) from the patient's paper chart (collected July–November 2014). Acute care system use (emergency department visits and hospital admissions) for the subset of patients admitted prior to the date of pharmacy data collection (n=147) was obtained from a local health authority database (October 2014). These three data sources were linked using a unique identifier.

Variables of interest: hypertension and diabetes diagnosis, frailty and hospital transfer status

The included facilities do not use an electronic medical record, and the available paper chart diagnosis summary sheet was variable in its completeness. However, the diagnoses of interest for treatment intensity, namely hypertension and diabetes, have a locally available incentive fee code that requires regular documentation.[9] Dementia diagnosis was anticipated to be reliably noted as it is often the condition that necessitates nursing home placement. Congestive heart failure was identified using: (a) mention on the diagnosis summary sheet and/or (b) prescription of furosemide[10] and was included to identify alternative reasons for observations of low blood pressure.

SBP and HbA1c were single readings recorded from the paper chart within 30 and 90 days, respectively, prior to the pharmacy data collection date. Given the anticipated issues with completeness of the paper chart medical history documentation, additional description of morbidity for the sample is provided with: a calculation of frailty and hospital transfer status. The Canada Health Study of Aging-Clinical Frailty Scale (CHSA-CFS)[11] was calculated using standard functional assessments made by facility therapists. Possible scores are from 1 to 9, ≥7 is severely frail. Frailty score calculation was not possible for those who died during data collection (n=35). 'Do not hospitalise' status was included to provide information about shared patient/family and provider expectations of medical intervention and was identified by recoding of a standard health authority 'do not attempt resuscitation' form.[12]

Polypharmacy definition and medication counting

The number of medications at which polypharmacy is 'diagnosed' varies widely in the published literature. For the present study, ≥9 medications were chosen as the definition as one of the most robust studies done in Canada[13] did the same, and our results will likely be most comparable to data also collected in this country. In Jokanovic *et al*'s systematic review of prevalence, 24 studies used nine medications or greater as the cut-off versus 11 studies using five medications.[8 13] Regular medications, the sum of which equals the polypharmacy measure, are defined as all regularly prescribed items requiring a physician's order, regardless of route and including vitamins and supplements. This definition was selected for the main analysis to describe both regimen complexity and resources required by facilities to dispense and monitor medications.[14]

Treatment intensity and overtreatment definitions

For the purpose of the present study we wished to identify patients whose surrogate measures were lower than the ideal for such a frail, end of life population. Excessive treatment of diabetes was defined as taking at least one hypoglycaemic medication and having an HbA1c of ≤7.5. This HbA1c threshold was chosen as evidence suggests that lower HbA1c is associated with a higher

risk of serious harm due to hypoglycaemia than potential treatment benefit.[15] Overtreatment of hypertension was defined using a study of frail elders by Mossello *et al*[16] who found that an older (mean age: 79) cohort of cognitively impaired (mean Mini Mental Status Exam (MMSE): 22.1) people had increased harm for an accelerated cognitive decline if SBP was ≤128 mm Hg (MMSE reduction: −2.8 points versus −0.7 with higher SBP (p=0.003)). A measure of polypharmacy, independent of condition-specific treatment, was created by subtracting the number of condition-specific medications from the total number of prescribed medications. This allowed exploration of a potential causal relationship between condition-specific overtreatment and more general polypharmacy prescribing tendencies.

Analysis

Previous reported estimates of population prevalence of polypharmacy have had wide variation (2%–91%).[8] Therefore, we used an estimate of prevalence of 50%, based on previous unpublished quality work done in the region, to calculate a sample size of 220 that would provide a precision level of 5%–6% with a 95% CI.[17] Descriptive statistics were used to describe the study population according to polypharmacy status, and the prevalence of polypharmacy and diabetes and hypertension. Tests of association used analysis of variance (ANOVA), unpaired t-tests, χ^2 and Mann-Whitney U test, where appropriate. Values of p<0.05 were considered statistically significant. All statistical analyses were performed with IBM Statistical Package for the Social Sciences software (V.24.0; IBM).

RESULTS

Data gathering was completed for 214 patients (6 died between date of randomization and accessing paper charts). Demographic and medical history characteristics of the study participants are presented in table 1. The mean number of regular medications prescribed was 8.7 (SD ±3.9, 95% CI 8.2 to 9.2) (a frequency table of types of medications prescribed is available in online supplementary table 1). Possible associations between facilities or prescribing doctors and the mean number of medications were assessed using an ANOVA calculation and were not statistically different (online supplementary table 2).

Acute care health services use (hospital admissions and emergency department (ED) visit) were analysed for those patients who were admitted to the nursing homes during the 365-day acute care use data collection period, n=147. There was no difference in acute care service use between those with polypharmacy versus not. Of the 147 included patients, 117 (80%) had no transfers to the ED, and 128 (87%) had no hospital admissions.

Blood pressure measurements were available for all patients in this sample. A total of 92% had a SBP of ≤150 mm Hg and 60% ≤130 mm Hg. There was no significant difference in mean SBP between those patients with or without a diagnosis of congestive heart failure (CHF). At least one hypertension medication was prescribed to 120 people, 16 of those did not have a diagnosis of hypertension in their chart. A total of 85% of the patients with diabetes had an HbA1c ≤8.5%, 74% had an HbA1c ≤7.5% and 26% had an HbA1c ≤6%.

Table 1 Patient characteristics by polypharmacy status

Characteristic	≤8 medications (n=110)	≥9 medications (n=104)	p Value
Age in years, mean±SD	86±9	84±10	p=0.72
Male, n (%)	33 (30)	34 (32)	p=0.67
Length of stay in nursing home in days, median (IQR)	861 (276–1905)	741 (274–1721)	p=0.50
Frailty score (CHSA-CFS),* median (IQR)	n=93 7 (7,7)	n=86 7 (7,7)	p=0.73
Dementia, n (%)	78 (71)	59 (57)	p=0.03
Hypertension, n (%)	72 (66)	81 (78)	p=0.04
Congestive heart failure, n (%)	10 (9)	25 (24)	p=0.003
Diabetes, n (%)	24 (22)	33 (33)	p=0.07
Systolic blood pressure, mm Hg, mean±SD	126±18	127±18	p=0.54
Diastolic blood pressure, mm Hg, mean±SD	66±12	66±10	p=0.94
HbA1c,† % median (IQR)	n=28 6.2 (5.9, 7.0)	n=46 6.2 (5.6,6.7)	p=0.43
Do not hospitalise designation (stay at facility for all care, even in case of acute illness), n (%)	35 (32)	27 (26)	p=0.35

*Calculation of Canada Health Study of Aging-Clinical Frailty Scale (CHSA-CFS)[11] was done October–November 2014, data are missing for 35 participants due to their deaths and subsequent loss of chart access. A higher score=increasing frailty; ≥7 is severely frail.
†Glycosylated haemoglobin (HbA1c) measured on 74 patients, but only 57 have a diagnosis of diabetes.

Table 2 Diabetes and hypertension overtreatment and associations with polypharmacy

Patients with presence of condition noted in chart	Regular meds ≤8	Regular meds ≥9	Relative risk (RR) (95% CI)	p Value (z statistic)
(A) Diagnosis of condition and polypharmacy				
Overtreated diabetes*	2/24 (8.3%)	11/33 (33%)	4.00 (0.97 to 16.41)	0.054
Overtreated hypertension†	16/72 (22%)	32/81 (40%)	1.77 (1.07 to 2.96)	0.027

Patients receiving at least one drug for condition treatment	Total medications prescribed MINUS hypoglycaemic drugs‡, mean±SD	p Value (t-test)
(B) Intensity of condition-specific treatment and general polypharmacy		
Overtreated diabetes, n=13	11.0±3.7	0.01
Treated diabetes, n=12	7.2±3.1	–
	Total medications prescribed MINUS hypotensive drugs§, mean±SD	
Overtreated hypertension, n=50	8.4±3.8	0.285
Treated hypertension, n=60	7.7±2.9	–

*Overtreated diabetes=having a diagnosis of diabetes, taking at least one hypoglycaemic medication and having a glycosylated haemoglobin ≤7.5%.[23]
†Overtreated hypertension=having a diagnosis of hypertension, a systolic blood pressure ≤128 and hypertension medications ≥1.[16]
‡Where hypoglycaemic drugs=biguanides (metformin), sulfonylureas, alpha-glucosidase inhibitors, any insulin and/or dipeptidyl peptidase-4.
§Where hypotensive drugs=angiotensin converting enzyme inhibitors, calcium channel blockers, diuretics, β-blockers, angiotensin II type 1 receptor antagonists and α-adrenergic blocking agents, older agents including: methyldopa, reserpine and hydralazine were not found to be used in this cohort.

Prevalence of overtreatment and association with polypharmacy

Twenty-five of the 57 patients with a diagnosis of diabetes were prescribed at least one regularly dosed hypoglycaemic medication, and 13 of these 25 (52%) patients met our definition of overtreatment (HbA1c≤7.5%).[15] The mean number of hypoglycaemic drugs did not differ between the treated and overtreated groups (1.5±1.2 vs 2.1±0.6). Of the 153 patients with a listed diagnosis of hypertension, 110 were prescribed at least one hypertension treatment medication, and 48 (44%) met the study-defined criteria[16] for overtreatment (SBP ≤128 and ≥1 hypertension medication). The mean number of hypotensive drugs did not differ between those treated and overtreated (1.9±0.9 vs 1.9±0.8). Table 2 presents two measures of association between overtreatment and polypharmacy. In patients with diabetes, those overtreated received 3.8 more medications (excluding hypoglycaemic medications) compared with those not overtreated. For hypertension, the overtreated patients received 0.7 more medications, but this difference was not statistically significant. A detailed description of what was prescribed, to those overtreated or not, can be seen in supplementary tables 3 and 4.

DISCUSSION

The present study demonstrates that polypharmacy is associated with greater (potentially excessive) lowering of surrogates (SBP, HbA1c). Not surprisingly, and consistent with previous polypharmacy studies,[8 18] we found that patients prescribed ≥9 medications were more likely to have diagnoses of hypertension (p=0.04) and CHF (p=0.003).

Severe frailty and risk factor condition treatment

The majority of the present study's participants were severely frail (7/9 score on CHSA-CFS[11]) and had a diagnosis of dementia, which was expected given the strict requirements for nursing home admission in British Columbia. The general patient demographics and medication use patterns of this sample were found to be consistent with previously published observational studies from multiple jurisdictions.[8] Clinical practice guidelines for older adults with hypertension and diabetes have begun to include discussion of frailty-informed treatment decisions with relaxed surrogate marker targets[19 20] but lack specific thresholds for overtreatment or guidance on 'de-intensifying'. Our results show that 54% of treated diabetics have an HbA1c ≤7.5% and 44% of treated hypertensives have an SBP ≤128. There are limited published studies that describe treatment intensity, with which to compare these results. However, there are some reports of condition-specific observations that appear to support the idea that 'lower' surrogates are common. Welsh *et al*'s[6] review of observational studies estimated that 70% of hypertensive patients in nursing homes had blood pressures 'within target range', which they defined as <140/90. Newton *et al* observed a mean HbA1c of 6.7%±1.1% at time of nursing home admission for 1409 nursing home patients. In our view, frailty-specific guidelines that suggest both a lower threshold defining overtreatment,and specifics of deprescribing of blood pressure and glucose lowering drugs could be indicated in such patients.

Overtreatment as an indicator of inappropriate polypharmacy

We have demonstrated a statistically significant association between overtreatment of blood pressure and polypharmacy. We have similarly found an association between polypharmacy and overtreatment of blood sugar (4.0 RR) that borders on statistical significance (p=0.054). Conceivably, these associations may be causal, with lower BP and lower HbA1c being indicators of a more aggressive overall treatment mindset on the part of the prescriber. To our knowledge, no previous research has examined the possible connection between treatment intensity and more general polypharmacy.

Harm reduction in the setting of polypharmacy has often focused on categories of 'inappropriate' medications. However, recent research suggests that 'appropriate' medications, such as those used to treat diabetes and hypertension, are more frequently the cause of adverse drug reactions that result in emergency room visits and hospitalisations.[21] For patients ≥80 years old presenting to the emergency room with an adverse drug event, 15.2% (95% CI 11.4 to 19.0) were due to diabetic agents, whereas only 3.4% were due to Beers criteria medications.[22] Focusing harm reduction on the intensity with which common medications are employed in the elderly might have as much (or more) utility than searching for drugs that are deemed inappropriate.

Limitations

Mortality rate is high in this population, and loss of access to charts on death affected some data collection. Inclusion of surrogate markers, HbA1c and SBP, is unique in the present study; however, a limitation was having only a single measure for each. Measure-to-measure variability is common in this frail population, and a mean of at least three readings could have provided a more robust measure of treatment intensity.

The definitions of overtreatment used in the present study are arbitrary. Given the lack of current evidence on which to create such definitions, the specific thresholds used are debatable and will likely evolve for research purposes as new evidence emerges. They are proposed here, with rationale, as a starting point from which to reconsider the approach to polypharmacy. Finally, our sample size was not large enough to conduct more sophisticated statistical testing (eg, regression modelling), therefore, there are unmeasured variables that could also account for treatment intensity. We suggest more work needs to be done using a larger sample, over a longer observation period and inclusive of a diversity of nursing homes and community dwelling residents.

CONCLUSIONS

Additional research that provides concrete quantifications of benefits and harms for ranges of treatment intensity with a larger sample and more accurate measures of surrogates is needed. In the meantime, the present study is useful in two ways: (1) it suggests that overtreatment in this population may be quite prevalent and (2) the presence of polypharmacy is to some degree associated with more intensive treatment of surrogate markers. Reduction in treatment-specific medications could both reduce potential of harms of overtreatment and reduce the overall number of prescriptions. Future studies to reduce polypharmacy and improve pharmacological appropriateness may benefit from consideration of treatment intensity for hypertension and diabetes.

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Contributors We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. RM conceived the need for the study, provided the initial drafts of its design, supervised all aspects of data collection and performed the data analysis. She also wrote the first drafts of the manuscript. This work is part of her PhD studies at the University of British Columbia. SG supervised and approved all aspects of this study, provided guidance regarding statistical analysis and edited all drafts of the manuscript. MJM, JM and STW provided specific advice regarding the study design and presentation of results and they participated in editing all drafts of the manuscript.

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