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Epidemiology

Multimorbidity, polypharmacy and primary prevention in community-dwelling adults in Quebec: a cross-sectional study

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Abstract

Background. Polypharmacy carries the risk of adverse events, especially in people with multimorbidity.
Objective. To investigate the prevalence of polypharmacy in community-dwelling adults, the association of multimorbidity with polypharmacy and the use of medications for primary prevention.
Methods. Cross-sectional analysis of the follow-up data from the Program of Research on the Evolution of a Cohort Investigating Health System Effects (PRECISE) in Quebec, Canada. Multimorbidity was defined as the presence of three or more chronic diseases and polypharmacy as self-reported concurrent use of five or more medications. Primary prevention was conceptualized as the use of statin or low-dose antiplatelets without a reported diagnostic of cardiovascular disease.
Results. Mean age 56.7 ± 11.6, 62.5% female, 30.3% had multimorbidity, 31.9% had polypharmacy (n = 971). The most common drugs used were statins, renin–angiotensin system inhibitors and psychotropics. Compared to participants without any chronic disease, the adjusted odds ratios (ORs) for having polypharmacy were 2.78 [95% confidence interval (CI): 1.23–6.28] in those with one chronic disease, 8.88 (95% CI: 4.06–19.20) in those with two chronic diseases and 25.31 (95% CI: 11.77–54.41) in those with three or more chronic diseases, $P < 0.001$. In participants without history of cardiovascular diseases, 16.2% were using antiplatelets and 28.5% were using statins. Multimorbidity was associated with increased likelihood of using antiplatelets (adjusted OR: 2.98, 95% CI: 1.98–4.48, $P < 0.001$) and statins (adjusted OR: 3.76, 95% CI: 2.63–5.37, $P < 0.001$) for primary prevention.
Conclusion. There was a high prevalence of polypharmacy in community-dwelling adults in Quebec and a strong association with multimorbidity. The use of medications for primary prevention may contribute to polypharmacy and raise questions about safety.

Key words: Antiplatelets, multimorbidity, polypharmacy, primary health care, primary prevention, statins.

Key Messages

- The prevalence of polypharmacy in community-dwelling adults in Quebec was high.
- Treatment burden should be assessed in patients with multimorbidity.
- The risk–benefit of medications for primary prevention should be considered.

Introduction

Multimorbidity has become a major issue in primary care. The prevalence of multimorbidity is around 20–30% in the general population and up to 66% in people aged 65 or older (1). In a report in 2016, the estimated prevalence of multimorbidity in Canada ranged from 16.9% to 59.4% in the general population and 29.5% to 69.5% in primary care settings (2). As the current clinical practice follows guidelines that focus on individual conditions (3), patients with multimorbidity frequently receive multiple medications. Managing patients with multimorbidity is challenging and there has been evidence that optimal treatment of each of their chronic diseases is not always equal to an ideal management of these patients (4). In addition, the use of medications for primary prevention alongside the treatment of existing chronic diseases also increases the risk of polypharmacy. In the past years, polypharmacy has become a public health concern. Polypharmacy is usually defined as the concurrent use of five or more medications (5). Polypharmacy carries the risk of drug–drug and drug–disease interactions and increases health care cost (6). In primary care, the frequency of medication errors has been shown to be higher in patients with polypharmacy (7). There is evidence that polypharmacy also increases the risk of mortality, functional decline, falls and hospitalization (8–10). The risks associated with polypharmacy are even higher in people with multimorbidity (11). However, there have been limited studies on polypharmacy and the use of medications for primary prevention in patients with multimorbidity (4).

Therefore, this study aims to investigate the prevalence of polypharmacy in community-dwelling adults in Quebec, Canada, the association of multimorbidity with polypharmacy and the use of medications for primary prevention in this population.

Methods

Study design and settings

The present study is a cross-sectional analysis from the data of the second follow-up (24 months after recruiting) of the Program of Research on the Evolution of a Cohort Investigating Health System Effects (PRECISE) study (12). The PRECISE is a cohort study that was designed to investigate patients' experience with primary health care over time and how it impacts on their health care use and chronic diseases burden. The cohort was selected in 2010 in urban, rural and remote areas of Quebec, Canada. One part of the cohort was recruited by random digit dialling (community cohort, n = 2406) and the other from the waiting rooms of primary care clinics (clinic cohort, n = 1029). The present study only used data from the community sample, of which 1718 (71.4%) responded to the baseline questionnaire and constituted the cohort for follow-up. At the second follow-up, 1407 (81.9%) participants remained in the community cohort. Of these, 971 participants provided answers about medication utilization and 436 participants did not provide answers (Supplementary Fig. S1). General characteristics of these two groups are presented in Supplementary Table S1. Compared to participants with medication information, those without medication information were significantly younger and had fewer chronic health conditions and lower prevalence of overweight and obesity. The PRECISE study received ethics approval from the local ethics committees. Informed consent was obtained in all participants.

Measures

Multimorbidity was defined as the presence of three or more chronic conditions, measured by a simple count of the number of conditions from a list of 14 self-reported and enduring health conditions (hypertension, hypercholesterolaemia, asthma, chronic obstructive pulmonary disease, diabetes, thyroid disorder, osteoarthritis, rheumatoid arthritis, osteoporosis, colon problem, angina/coronary artery disease, stroke, congestive heart failure and cancer) (13).

Medication assessment

Participants were asked to report the names of all the medications they were using. Polypharmacy was defined as the concurrent use of five or more medications (5). The drug names of medications used were recoded into major classes of renin–angiotensin system inhibitors, beta blockers, statins, calcium channel blockers, diuretics, antiplatelets, oral anticoagulants, psychotropics (include antidepressants, antipsychotics and hypnotics), hypoglycaemic drugs, bronchodilators, drugs for acid-related disorders, thyroid analogue, drugs for pain relief, bisphosphonates, hormone drugs, vitamins and supplements. Participants on statins or low-dose antiplatelets (aspirin 80–81 mg per day or clopidogrel 75 mg per day) were considered as receiving primary prevention of cardiovascular disease if there was no report of coronary disease, stroke or heart failure.

Covariates

We selected variables based on the expectation that they may have impacts on medication use and polypharmacy, including age, gender and socio-economic status (5,14). Socio-economic status was classified into four categories as applied in our previous study (13):

(i) Elite group: College or university education and perceived financial situation as 'comfortable' or 'very comfortable'.
(ii) Middle-high: College or university education or perceived financial situation as 'comfortable' or 'very comfortable'.
(iii) Middle-low: High school education and perceived financial situation as 'modestly comfortable' or less than high school education and perceived financial situation less than 'tight' but possess a retirement plan and complimentary medical insurance.
(iv) Low: Less than high school education and perceived financial situation less than 'tight' but does not possess a retirement plan or complimentary medical insurance.

Statistical analysis

Analysis of the data was performed using SPSS for Windows 24.0. Continuous variables are presented as mean ± standard deviation or median (range) and categorical variables as frequency and percentage. Comparisons between groups were assessed using chi-square tests for categorical variables and Student's t-tests for

continuous variables. Results with two-tailed *P*-values <0.05 were considered statistically significant.

Logistic regression was applied to investigate the impact of number of chronic diseases on polypharmacy (outcome variable), adjusted for potential covariates that can have influence on medication use and chronic illness burden, such as age, gender and socio-economic status. Results are presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Chi-square tests were performed to compare the prevalence of use of statins or antiplatelets medications in patients with and without multimorbidity. Logistic regression was applied to investigate the impact of multimorbidity on the use of statins or antiplatelets for primary prevention, adjusted for potential covariates that can have influence on the use of these medications, such as age, gender and socio-economic status. Results are presented as ORs and 95% CIs.

In this study significant missing data only occurred with age (12 cases), socio-economic status (36 cases) and body mass index (BMI; 56 cases). The missing data were random; therefore, we analysed only the available data (i.e. the missing data were ignored by SPSS).

Results

Of the 971 participants with reported use of medications, mean age 56.7 ± 11.6, 62.5% female, 30.3% had multimorbidity. The prevalence of polypharmacy was 31.9% in all participants [63.8% in participants with multimorbidity, 17.8% in those without multimorbidity, χ^2 (1, n = 971) = 200.47, P < 0.001].

Table 1 shows the general characteristics of the participants. Compared to participants without polypharmacy, participants with polypharmacy were older, had higher prevalence of low socio-economic status, higher prevalence of obesity and significant higher prevalence of multimorbidity (having three or more chronic health conditions).

In general, the three most common drugs were statins (34.2), renin–angiotensin system inhibitors (30.3%), psychotropics (26.6%), followed by vitamins/supplements (24.1%), antiplatelets (22.2%) and drugs for acid-related disorders (20.8%). Compared to participants without multimorbidity, participants with multimorbidity had significantly higher prevalence of use in almost all types of medications, except for psychotropics, oral anticoagulants and hormone drugs (Table 2).

Table 1. Characteristics of the study participants

Variables	All (n = 971)	With polypharmacy (n = 310)	Without polypharmacy (n = 661)	P
Age, years (missing: 12)	56.7 ± 11.6	62.2 ± 8.9	54.1 ± 11.8	<0.001
Female (missing: 0)	607 (62.5)	200 (64.5)	407 (61.6)	0.38
Socio-economic class (missing: 36)				
Elite	193 (20.6)	44 (15.0)	149 (23.2)	0.001
Middle-high	419 (44.8)	137 (46.8)	282 (43.9)	
Middle-low	199 (21.3)	58 (19.8)	141 (22.0)	
Low	124 (13.3)	54 (18.4)	70 (10.9)	
BMI classification (missing: 56)				
<18.5	13 (1.4)	4 (1.4)	9 (1.4)	0.05
18.5 to <25.0	295 (32.2)	82 (28.0)	213 (34.2)	
25.0 to 29.9	351 (38.4)	108 (36.9)	243 (39.1)	
≥30.0	256 (28.0)	99 (33.8)	157 (25.2)	
Number of chronic diseases (missing: 0)				
0	195 (20.1)	8 (2.6)	187 (28.3)	<0.001
1	245 (25.2)	31 (10.0)	214 (32.4)	
2	233 (24.0)	81 (26.1)	152 (23.0)	
≥3 (multimorbidity)	298 (30.7)	190 (61.3)	108 (16.3)	
Prevalence of individual chronic conditions (missing: 0)				
Hypertension	357 (36.8)	183 (59.0)	174 (26.3)	<0.001
Hypercholesterolemia	329 (33.9)	173 (55.8)	156 (23.6)	<0.001
Osteoarthritis	270 (27.8)	138 (44.5)	132 (20.0)	<0.001
Thyroid disorder	154 (15.9)	72 (23.2)	82 (12.4)	<0.001
Asthma	118 (12.2)	52 (16.8)	66 (10.0)	0.003
Diabetes	105 (10.8)	76 (24.5)	29 (4.4)	<0.001
Colon problem	89 (9.2)	29 (9.4)	60 (9.1)	0.89
Osteoporosis	74 (7.6)	43 (13.9)	31 (4.7)	<0.001
Angina/coronary artery disease	93 (9.6)	67 (21.6)	26 (3.9)	<0.001
COPD	53 (5.5)	36 (11.6)	17 (2.6)	<0.001
Cancer	43 (4.4)	19 (6.1)	24 (3.6)	0.08
Rheumatoid arthritis	36 (3.7)	20 (6.5)	16 (2.4)	0.002
Stroke	17 (1.8)	8 (2.6)	9 (1.4)	0.18
Heart failure	23 (2.4)	17 (5.5)	6 (0.9)	<0.001

Continuous data are presented as mean ± standard deviation; categorical data are shown as n (%); P-values obtained with chi-square tests for categorical variables and Student's t-tests for continuous variables. Source of subjects: the Program of Research on the Evolution of a Cohort Investigating Health System Effects (PRECISE), year of data collection: 2012.

COPD, chronic obstructive pulmonary disease.

Table 2. Patterns of drug use by multimorbidity status

Medications	All (n = 971)	With multimorbidity (n = 298)	Without multimorbidity (n = 672)	P
Total number of medications (missing: 1)	3.6 ± 2.4	5.5 ± 2.5	2.8 ± 1.9	<0.001
Polypharmacy (≥5 medications) (missing: 0)	310 (31.9)	190 (63.8)	120 (17.8)	<0.001
Statins (missing: 0)	332 (34.2)	181 (60.7)	151 (22.4)	<0.001
Renin–angiotensin system inhibitors (missing: 1)	294 (30.3)	149 (50.0)	145 (21.6)	<0.001
Psychotropics (missing: 1)	258 (26.6)	91 (30.5)	167 (24.9)	0.06
Vitamins and supplements (missing: 1)	234 (24.1)	98 (32.9)	136 (20.2)	<0.001
Antiplatelets (missing: 0)	216 (22.2)	123 (41.3)	93 (13.8)	<0.001
Drugs for acid-related disorders (missing: 1)	202 (20.8)	84 (28.2)	118 (17.6)	<0.001
Drugs for pain relief (missing: 1)	157 (16.2)	62 (20.8)	95 (14.1)	0.009
Thyroid analogue (missing: 1)	154 (15.9)	73 (24.5)	81 (12.1)	<0.001
Diuretics (missing: 1)	149 (15.4)	76 (25.5)	73 (10.9)	<0.001
Beta blockers (missing: 1)	125 (12.9)	78 (26.2)	47 (7.0)	<0.001
Hormone drugs (missing: 1)	122 (12.6)	30 (10.1)	92 (13.7)	0.12
Calcium channel blockers (missing: 1)	118 (12.2)	73 (24.5)	45 (6.7)	<0.001
Hypoglycaemic drugs (missing: 1)	108 (11.1)	79 (26.5)	29 (4.3)	<0.001
Bronchodilators (missing: 1)	79 (8.1)	38 (12.8)	41 (6.1)	<0.001
Bisphosphonates (missing: 1)	58 (6.0)	30 (10.1)	28 (4.2)	<0.001
Oral anticoagulants (missing: 0)	21 (2.2)	10 (3.4)	11 (1.6)	0.09

Continuous data are presented as mean ± standard deviation; categorical data are shown as n (%); P-values obtained with chi-square tests for categorical variables and Student's t-tests for continuous variables. Source of subjects: the Program of Research on the Evolution of a Cohort Investigating Health System Effects (PRECISE), year of data collection: 2012.

On the multivariable logistic regression model, the adjusted OR for having polypharmacy is 2.78 (95% CI: 1.23–6.28) in those with one chronic disease, 8.88 (95% CI: 4.11–19.20) in those with two chronic diseases and 25.31 (95% CI: 11.77–54.41) in those with three or more chronic diseases compared to participants without any chronic disease (Table 3).

The relation between multimorbidity and the use of antiplatelets or statins for primary prevention

Analysis in 857 participants without cardiovascular diseases showed that 29.8% were using statins for primary prevention [54.0% in participants with multimorbidity versus 21.7% in participants without multimorbidity, χ^2 (1, n = 857) = 80.41, P < 0.001] and 16.2% were using antiplatelets for primary prevention [31.6% in participants with multimorbidity versus 11.1% in participants without multimorbidity, χ^2 (1, n = 850) = 49.05, P < 0.001). Compared to non-users, the users of statins or antiplatelets for primary prevention had significant higher total number of chronic conditions and total number of medications (Supplementary Table S2).

On univariate analysis, multimorbidity was associated with increased likelihood of using antiplatelet for primary prevention (unadjusted OR: 3.69, 95% CI: 2.52–5.40, P < 0.001). This association was still significant after being adjusted for age and gender (adjusted OR: 2.98, 95% CI: 1.98–4.48, P < 0.001). Similarly, multimorbidity was associated with increased likelihood of using statins for primary prevention (unadjusted OR: 3.69, 95% CI: 2.52–5.40, P < 0.001) on univariate analysis, and this association was still significant after being adjusted for age and gender (adjusted OR: 3.76, 95% CI: 2.63–5.37, P < 0.001; the univariate analysis of the potential factors that can influence on the use of antiplatelet and statins are presented in Table 4.)

Discussion

In this study, the prevalence of polypharmacy in community-dwelling adults was high (around one-third), and the likelihood of having polypharmacy increased significantly with the increased number of chronic diseases. Among the reported medications, the most common drugs used among participants of this study were statins, renin–angiotensin inhibitors, psychotropics, vitamins/supplements, antiplatelets and drugs for acid-related disorders. Participants with multimorbidity had significantly higher prevalence of use in all types of medications compared to participants without multimorbidity (except psychotropic medications and hormone drugs). This study also found that there was a significant prevalence of using statin or antiplatelets for primary prevention: 29.8% with statins and 16.2% with antiplatelets. This figure was even higher in participants with multimorbidity (54.0% with statins and 32.6% with antiplatelets), and multimorbidity was associated with increased likelihood of using antiplatelets or statins for primary prevention.

Our findings are in accordance with previous reports in Canada. According to the Canadian Health Measures Survey (from 2007 to 2011), in 11 386 participants who provided medication information, approximately 11% of community-dwelling Canadians aged 45–64 years and 30% of those aged ≥65 years took at least five prescription medications concurrently, and the leading medication classes were lipid-lowering agents, angiotensin-converting enzyme inhibitors and acid-related disorders in adults aged 25–79 years (15). This study also found that prescribed drug use was higher among females and among people in poorer health and increased with age (15). In another study based on the data of the Canadian Survey of Experiences with Primary Health Care (in 3132 participants aged ≥65), the prevalence of polypharmacy was 27%, and there was a positive correlation between polypharmacy prevalence and the number of chronic illness (13% in participants with one chronic

Table 3. Results of logistic regression models of the associated factors for polypharmacy

	Univariate analysis[a]		Multivariate analysis[b]	
	Unadjusted OR (95% CI)	*P*	Adjusted OR	*P*
Age (per year)	1.07 (1.06–1.09)	<0.001	1.04 (1.03 – 1.06)	<0.001
Female	1.14 (0.86–1.50)	0.377	–	–
Low socio-economic status	1.85 (1.26–2.72)	0.002	1.63 (1.03–2.57)	0.038
Number of chronic diseases				
0	1 (Reference)	<0.001	1 (Reference)	<0.001
1	3.39 (1.52–7.55)		2.78 (1.23–6.28)	
2	12.46 (5.84–26.56)		8.88 (4.11–19.20)	
≥3	41.12 (19.50–86.71)		25.31 (11.77–54.41)	

[a]Separate regression models for each covariate; OR show likelihood of having polypharmacy.

[b]All covariates were included in regression analysis (age, female, low socio-economic status, categories of number of chronic diseases). The final model only contains those variables with a *P*-value <0.05.

Table 4. Univariate logistic regression analysis of associated factors with the use of antiplatelets and statins for primary prevention

	Antiplatelets		Statins	
	Unadjusted OR (95% CI)	*P*	Unadjusted OR (95% CI)	*P*
Multimorbidity (≥3 chronic conditions)	3.69 (2.52–5.40)	<0.001	4.24 (3.06–5.88)	<0.001
Age (per year)	1.06 (1.04–1.08)	<0.001	1.06 (1.04–1.07)	<0.001
Female gender	0.47 (0.32–0.68)	<0.001	0.44 (0.33–0.60)	<0.001
Low socio-economic status	0.93 (0.52–1.67)	0.807	1.49 (0.96–2.30)	0.074

condition, 33% in those with two conditions and 62% in those with three or more conditions) (14).

The prevalence of statin use for primary prevention in this studied population was higher compared to other studies. According to a study published in 2017 in 149 262 participants in Manitoba, Canada, the prevalence of statin use in participants without a history of cardiovascular disease was 4% (9% in participants aged ≥75) (16). In a study in primary care settings in the UK, among 341 099 patients aged 30–74 years without cardiovascular diseases or diabetes, 22 393 (6.6%) were prescribed statins (17). In another study in 5618 community-dwelling participants aged 50 years or older in Ireland, around 20% were taking statins for primary prevention (18). The prevalence of aspirin use for primary prevention in this study was lower compared to other studies in the USA. In a study in 252 789 patients attending primary care in the USA, the average prevalence of aspirin use for primary prevention from 2007 to 2015 was 43% (19). In a study in 1564 men in North Carolina, USA, in 2013, the prevalence of using aspirin for primary prevention was 41.2% (20).

Implications for research and practice

This study found that the most common drugs used among participants in primary care were statins, renin–angiotensin inhibitors, psychotropics, vitamins/supplements, antiplatelets and drugs for acid-related disorders. Those types of drugs have been shown to be highly involved in cytochrome P450 (CYP450) mediated drug–drug interaction, especially with cardiovascular drugs, proton pump inhibitors and psychotropics (21–23). It is evident that one of the primary causes of drug interactions is the CYP450 enzyme system and most drugs are metabolized *via* these enzymes (24). Although most of these interaction observations are often based on *in vivo* testing, caution should be taken when prescribing a drug that is a CYP450 inhibitor or inducer (25).

The use of medicines for primary prevention in patients with multimorbidity has recently been addressed by a key recommendation in the National Institute for Health and Care Excellence (NICE) Guidelines in 2016 as 'Be aware that the management of risk factors for future disease can be a major treatment burden for people with multimorbidity and should be carefully considered when optimising care' [1; recommendation 1.1.2] (26). The use of antiplatelets and statins in primary prevention may contribute to the risk of having polypharmacy and adverse health events. The role of statins in secondary prevention for patients with a history of cardiovascular disease is substantial, but its role in primary prevention is controversial (27). Statin use is usually associated with adverse effects on muscle such as myopathy and muscle pain (28). In addition, statin use may contribute to reduced muscle strength and alter energy metabolism during physical exercise and increase the risk of drug interactions, especially with CYP450 drugs (29,30). The use of antiplatelets for primary prevention also needs to be taken into consideration carefully. Studies have shown that the beneficial effect of aspirin for the primary prevention of cardiovascular disease is modest compared to the increased risk of major bleeding (31,32). In people with multimorbidity, the interaction between drugs and drugs and drugs and diseases may leave them particularly vulnerable to adverse events, especially in the senior and frail. A recent systematic study showed that around 6% of the general adult population have both of multimorbidity and frailty, a common geriatric syndrome (33). In old and frail patients, there was evidence of reduced activity of plasma aspirin esterase (an enzyme that helps convert aspirin to salicylic and acetic acid), which in turn can lead to increased plasma level of aspirin (34). These findings suggest further research of the effect of aspirin and statins in primary prevention to better balance the risk versus benefit of this treatment option. In some countries, general practitioners are urged to calculate absolute cardiovascular risk and manage patients based on this evaluation (35). As the number of

people living with multimorbidity is increasing and polypharmacy can bring additional risks to patients with multimorbidity, this study also suggests more research on the impact of polypharmacy on adverse health outcomes in this population. Treatment burden should be assessed and discussed with the patients (36). Addressing treatment burden is a part of good patient-centred care (37).

Strengths and limitations

This is the first study to investigate the impact of multimorbidity on polypharmacy and patterns of drug use in community-dwelling people in a French-speaking population in Canada with a large sample size. Second, this study adds to the limited literature on epidemiology of the use of medications for primary prevention in general practice. The major limitation is that the record of medication use and chronic health conditions was based on participants' self-report. However, previous study in Quebec showed that the use of self-reported chronic conditions in the study of multimorbidity may reduce biased estimates of multimorbidity (38). Secondly, the rate of missing medication data was also high. As the non-participants were younger and had fewer chronic diseases and lower prevalence of overweight/obesity, this might well have an impact on the prevalence of multimorbidity, polypharmacy and the use of preventive medicines (Supplementary Table S1). We were also unable to judge on the appropriateness of the medications from the data. In addition to polypharmacy, the use of potentially inappropriate medication such as proton pump inhibitors and psychotropic medications has become a public health concern (39,40).

Supplementary material

Supplementary material is available at *Family Practice* online.

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Declaration

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Ethical approval: the PRECISE study received ethics approval from the ethics committees of the Centre de santé et de services sociaux de Chicoutimi and Hôpital Charles-LeMoyne, Longueuil, Quebec. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained in all participants.

Conflict of interest: none.

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