

Patterns of borrowing to finance out-of-pocket prescription drug costs in Canada: results from a  
national cross-sectional survey

Running Head: Borrowing for prescription drug costs

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## CONFLICTS OF INTEREST

Michael Law has consulted for Health Canada and acted as an expert witness for the Attorney General of Canada. Anne Holbrook is a therapeutics expert and drug policy consultant for the Ontario Public Drug Program. All other authors report no potential conflicts of interest.

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ABSTRACT

*Introduction*

Out of pocket drug costs leads many Canadians to engage in cost-related non-adherence, but our understanding of other consequences such as borrowing money remains incomplete. Therefore, we quantified the frequency and characteristics of Canadians who borrowed money to pay for prescription drugs.

*Methods*

In partnership with Statistics Canada, we designed and administered a module in the Canadian Community Health Survey between January and June 2016. We used logistic regression to identify characteristics associated with borrowing.

*Results*

We found 2.5% of study respondents, representing an estimated 731,000 Canadians, reported borrowing money to pay for prescription drugs. The odds of borrowing were higher among younger adults. People in poor health had almost 8-fold higher odds of borrowing compared to people in excellent health. Individuals lacking drug insurance and those with public drug insurance were twice as likely as individuals with employer sponsored drug insurance to borrow money. Other factors associated with increased adjusted odds of borrowing were having two or more chronic conditions, having a household income less than \$40,000, and higher out-of-pocket prescription drug costs.

### *Interpretation*

Many Canadians borrow money to pay for out-of-pocket prescription drug costs. Borrowing is more prevalent among already vulnerable groups that also report other compensatory behaviours to address challenges in paying for prescription drugs. Future research should investigate policy responses intended to increase equity in access to prescription drugs.

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3 **INTRODUCTION**  
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5 All Canadian residents are insured for medically necessary hospital care and physician services,  
6 without out-of-pocket charges at the point of care. However, this federally-mandated insurance  
7 does not include prescription drugs used outside of hospitals. Many Canadians have some form  
8 of prescription drug insurance through work-related benefits or public programs (such as those  
9 for the elderly or those on social assistance); however, others do not have prescription drug  
10 coverage.<sup>1</sup> Additionally, Canadians with prescription drug insurance still often have to bear  
11 some or all of the costs of their drugs due to insurance plan deductibles, co-payments, and gaps  
12 in insurance where some drugs are not covered.<sup>1,2</sup> The out-of-pocket pharmaceutical costs  
13 borne by uninsured or under-insured Canadians can be substantial and tend to  
14 disproportionately affect potentially vulnerable populations,<sup>3-6</sup> including those who are  
15 socioeconomically disadvantaged, are in poor health, are children or elderly, or are ethnic  
16 minorities.<sup>7,8</sup>  
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37 Patients experience a range of consequences when facing high out-of-pocket costs. For  
38 example, patients have reported engaging in a variety of compensatory behaviours including  
39 cost-related non-adherence where patients reduce medication doses to stretch out  
40 prescriptions, delay filling or not fill prescriptions at all, or take less costly and clinically sub-  
41 optimal substitute medicines.<sup>6,11,12</sup> Prior survey studies have found that cost-related non-  
42 adherence affects approximately 8 percent of Canadians with a prescription.<sup>10,13-15</sup> Patients also  
43 make trade-offs against spending in other areas of household budgets to be able to afford  
44 prescription drugs.<sup>6,11,16-18</sup> For example, our recent research found that 4.7% of Canadians  
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(representing an estimated 1.5 million individuals) reported prioritizing spending on prescription drugs instead of other needs including food, heat, housing, and transportation.<sup>10</sup>

Another compensatory behaviour patients facing high drug costs have reported is borrowing money. Studies have found patients report increasing credit card debt, or borrowing money from family and friends as a way to cope with high healthcare costs.<sup>12,19–22</sup> However, almost all of this evidence is from the United States, which has a markedly different health insurance system and different levels of out-of-pocket drug costs than Canada. Further, many of these studies do not make a distinction between medication costs specifically and healthcare costs in general. Further, existing studies have tended to focus on patients with illnesses such as cancer which require costly medicines, and chronic conditions like COPD and arthritis, rather than the general population.<sup>19,21–23</sup>

In sum, little is known about borrowing to finance prescription medicine in Canada. Therefore, we sought to quantify the frequency of borrowing to pay for prescription drugs in Canada, predictors of such activity and its relationship with cost-related non-adherence.

## METHODS

### *Data Sources*

The data for this study came from a cross-sectional rapid response module in the Canadian Community Health Survey (CCHS) administered by telephone to Canadians aged 12 and older between January and June, 2016. The design and content of this survey are described

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3 elsewhere.<sup>10</sup> In brief, the survey asked respondents a range of socio-demographic and health  
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5 questions, including whether they borrowed money to pay for prescription medicines using the  
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7 following question: *“In the last 12 months, have you or anyone else in the household ever had to*  
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9 *borrow money to pay for your prescriptions?”* The specific phrasing of this question was  
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11 developed through rigorous pilot testing conducted by Statistics Canada and intentionally did  
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13 not mention specific examples of kinds of borrowing (e.g. from friends or family, on a credit  
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15 card) in order to minimize confusion for the respondent. We restricted our analyses to those  
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17 respondents who provided an answer to this question.  
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25 **Statistical Analysis**

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27 We calculated the total number of respondents and nationally representative estimates of the  
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29 weighted proportions of the population reporting having to borrow money to pay for  
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31 prescription drugs. We used multivariate logistic regression to investigate the factors associated  
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33 with a patient reporting they had borrowed money to pay for prescription drugs. We included  
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35 variables previously shown to be associated with difficulty paying for medications: sex, age,  
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37 self-reported health status, number of chronic conditions (including arthritis, chronic  
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39 obstructive pulmonary disease, diabetes, cancer, heart disease, high blood pressure and mood  
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41 disorders), ethnicity, household income, education, and prescription drug insurance status.<sup>5,6</sup>  
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49 We used step-wise multiple imputation methods to fill in missing data: we first imputed values  
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51 for the variable missing the most amount of data, and then used the imputed values to the next  
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53 highest, and so on until all missing variables had been imputed.<sup>24,25</sup> Once the imputation for  
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each variable was complete, we recombined the datasets to incorporate the adjustments to variance. To incorporate the complex sampling design of the CCHS into our population estimates, we used survey weights provided by Statistics Canada and bootstrapping to calculate confidence intervals.<sup>26</sup>

## RESULTS

### *Descriptive Characteristics*

Of the 28,091 respondents to the entire module, 572 (2.0% of the total sample) were excluded because they responded, “Don’t know” or refused to answer the question on borrowing. In this study, data on one or more variables were missing for 1,390 respondents (5.1% of the total sample) across 4 variables (self-reported health status, out of pocket drug costs, education, and prescription drug insurance), with a maximum of 2.4% of the total sample for any single variable (out of pocket drug costs). Table 1 presents weighted proportions of the total population: 51% of the respondents to our survey were female, and 49% were under the age of 45, 11% reported having fair or poor health, 20.3% had an annual household income of less than \$40,000, and 20.3% reported having no prescription drug insurance.

Overall, we found that 2.5% (95%CI: 2.2% to 2.8%) of respondents borrowed money to pay for prescription medications in the previous year (Table 1). At the population level, this is equivalent to an estimated 731,000 Canadians (95%CI: 639,000 to 824,000). Those reporting having borrowed money to pay for prescription medications tended to be younger, in poorer

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3 health, have more chronic conditions, and report government or no prescription drug insurance  
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6 than those not reporting borrowing.  
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9 Figure 1 (A-D) provides an illustration of some of the differences in rates of borrowing money to  
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11 pay for prescription drugs across different groups in our sample. Adults aged 19-34 had the  
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13 highest rates of borrowing (3.7%, 95% CI 2.9 to 4.4) compared to other age groups (Fig 1A).  
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16 Canadians with a household income of less than \$20,000 a year have more than twice the rate  
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18 of borrowing (6.6%, 95% CI 5.0 to 8.3) than Canadians earning \$40,000 a year or more (Fig 1B).  
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21 Canadians lacking any kind of prescription drug insurance had the highest rates of borrowing  
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23 (4.6%, 95% CI 3.5 to 5.7), while those with employer-based drug insurance had the lowest rates  
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25 of borrowing (1.3, 95% CI 1.0 to 1.6; Fig 1C). As Canadians' annual out of pocket costs on  
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27 prescription drugs increase, they were more likely to report borrowing money to pay for  
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29 prescription drugs (\$501-1000: 9.5, 95% CI 6.9 to 12.0; ≥\$1000: 11.5, 95% CI 8.6 to 14.3; Fig 1D).  
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36 *Borrowing to finance out-of-pocket prescription drug costs*  
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39 Our multivariate logistic regression model found that younger age was associated with higher  
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41 odds of borrowing to pay for prescription medications. Controlling for other factors (including  
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43 insurance status and size of out-of-pocket costs), adults aged 19-34 had over three and a half  
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45 times the odds of borrowing (adjusted odds ratio [AOR] 3.7, 95% CI 2.3 to 5.7) compared to  
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47 adults aged 45-54 (Table 2). Adults aged older than 54 had less than half the odds of borrowing  
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49 compared to adults aged 45-54. Having poor self-reported health status was associated with  
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51 substantially higher odds of borrowing (AOR 7.7, 95% CI 3.7 to 15.9) compared to having  
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53 excellent health. Insurance coverage was also important; respondents who reported having  
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either government drug insurance or no drug insurance had twice the odds of borrowing to pay out-of-pocket costs for prescriptions compared to individuals with employer sponsored drug insurance (AOR 2.0, 95% CI 1.4 to 2.9). Other factors associated with increased adjusted odds of borrowing were having two or more chronic conditions, having a household income less than \$40,000, and spending more money out-of-pocket on prescription drugs compared to those who had lower out-of-pocket drug costs. Residents of Quebec had lower adjusted odds of borrowing compared to other provinces.

#### *Extent of Out-of-pocket Costs Among Borrowers*

Among those who reported borrowing money to pay for prescription drugs (n = 6,798), the largest group borrowed money to pay for comparatively low drug costs, between \$1-200 over the year (33.8%, 95% CI 28.1 to 39.5). Another 26.8% (95% CI 21.2 to 32.4) borrowed money to pay for out-of-pocket drug costs in the range of \$201-500. 19.6% (95% CI 14.7 to 24.6) and 15.5% (95% CI 11.8 to 19.2) of those who reported borrowing money did so for out-of-pocket drug costs in the range of \$501-1,000 and more than \$1,000, respectively.

#### **INTERPRETATION**

The out-of-pocket costs associated with having to pay for prescription drugs have important implications for Canadians. We found that 2.5% of Canadians, or an estimated 731,000 people, borrowed money to pay for the out-of-pocket costs of their prescription drugs in the previous year. This represents another form of compensatory behaviour to deal with drug charges on top of the significant rates of cost-related non-adherence and trade-offs with other

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expenditures in Canada.<sup>10</sup> Further, we found that borrowing was most common among groups who also display these other compensatory behaviours, including younger age, lower self-reported health, government or no drug insurance, and lower household income.<sup>10</sup> Notably, we found that borrowing to pay for prescription drugs occurred at all levels of out-of-pocket costs for patients and over 60% of borrowing reported by patients in our study occurred for out-of-pocket costs of \$500 or less per year.

Our findings are consistent with other research on cost-related non-adherence and associated compensatory behaviours.<sup>10,11,27</sup> Other studies from the US have found cost-related non-adherence to be associated with food insecurity and cutting back on necessities.<sup>12,17</sup> This is sobering, in light of the fact that the majority drugs for which patients need to make these trade-offs are relatively inexpensive.<sup>10,11</sup> Our findings suggest the consequences of high drug costs are more extensive than just reducing adherence to medicines; there are likely impacts other aspects of patient quality of life.

There is an opportunity for healthcare providers and prescribers to intervene and initiate conversations with patients to help support those who are at greatest risk of cost-related non-adherence and the attendant compensatory behaviours, keeping in mind that it is not just costly medications that put patients at risk. Multiple policy interventions can be used to address the negative impacts on patients from struggling to pay for prescription drugs.<sup>28</sup> For example, some provinces have recently implemented policy changes to help address cost-related non-adherence: Ontario implemented a universal pharmacare program for youth under the age of

25 and British Columbia has reduced or eliminated public drug insurance deductibles for families earning less than \$45,000 per year.<sup>29,30</sup> Future studies should investigate the impact of such changes on both cost-related nonadherence and borrowing behaviours.

### *Limitations*

Like other survey-based study designs, our results are based on patient self-report that is potentially susceptible to recall bias and social desirability bias. If it had an effect on our findings, recall bias likely would have resulted in conservative estimates.<sup>31</sup> We were unable to ask more specific questions about the kinds of borrowing patients engaged in (e.g. from family and friends, a financial institution, a pay day loan or cash advance lender, against a mortgage or home, on a credit card) and are unable to assess how patients interpreted the question or to gauge the amount of money that might have been borrowed.

### *Conclusion*

Our findings show that many Canadians are borrowing money to pay for out-of-pocket prescription drug costs. Borrowing occurs for relatively inexpensive drugs as well as more costly ones, and disproportionately affects vulnerable groups such as those who have low income, poor self-reported health status, and lack prescription drug insurance. In Canada, provinces are already taking steps to implement policy changes to help these more vulnerable groups address cost-related non-adherence and other associated behaviours. Future research should investigate the impacts of such changes that could increase equity in access to prescription drugs.

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**Table 1: Characteristics and prevalence of patients reporting having to borrow money to pay for prescription drugs among respondents to the Canadian Community Health Survey between January and June 2016**

Variable	No. of Respondents	Weighted proportion of total population (95% CI)	Weighted proportion (%) who report borrowing=1 (95% CI)
Total	27,519	100.0 (100.0 to 100.0)	2.5 (2.2 to 2.8)
Female	13,949	50.7 (50.5 to 50.9)	3.2 (2.7 to 3.7)
Male	13,570	49.3 (49.1 to 49.5)	1.74 (1.4 to 2.1)
<b>Age</b>			
12-18	2,372	8.6 (8.3 to 8.9)	1.8 (1.1 to 2.5)
19-34	6,954	25.3 (25.0 to 25.6)	3.7 (2.9 to 4.4)
35-44	4,045	14.7 (14.2 to 15.2)	2.4 (1.5 to 3.3)
45-54	4,667	17.0 (16.2 to 17.7)	2.3 (1.5 to 3.1)
55-64	4,447	16.2 (15.6 to 16.7)	2.2 (1.4 to 3.0)
65-74	3,156	11.5 (11.1 to 11.8)	1.9 (1.2 to 2.7)
≥75	1,877	6.8 (6.5 to 7.1)	1.1 (0.6 to 1.6)
<b>Self-reported Health Status</b>			
Excellent	6,591	24.0 (23.1 to 24.9)	0.6 (0.3 to 0.8)
Very good	10,350	37.6 (36.7 to 38.5)	1.3 (0.9 to 1.8)
Good	7,510	27.3 (26.4 to 28.2)	3.2 (2.5 to 4.0)
Fair	2,213	8.0 (7.5 to 8.6)	6.4 (5.0 to 7.8)
Poor	856	3.1 (2.8 to 3.4)	13.8 (10.1 to 17.4)
<b>Chronic Conditions, no.</b>			
0	13,927	50.6 (49.7 to 51.6)	0.9 (0.7 to 1.2)
1	7,147	26.0 (25.1 to 26.8)	2.7 (2.0 to 3.4)
2	3,514	12.8 (12.2 to 13.4)	3.6 (2.6 to 4.6)
3	1,723	6.3 (5.9 to 6.7)	5.9 (4.3 to 7.5)
≥4	1,208	4.4 (4.0 to 4.8)	11.1 (8.6 to 13.5)
<b>Cultural Background</b>			
White	20,416	74.2 (73.2 to 75.2)	2.3 (2.0 to 2.6)
South Asian / East Asian	2,466	9.0 (8.3 to 9.7)	0.8 (0.2 to 1.4)
Aboriginal	1,018	3.7 (3.4 to 4.1)	5.2 (3.3 to 7.2)
Other	3,619	13.2 (12.4 to 13.9)	3.7 (2.3 to 5.1)
<b>Total Household Income, \$</b>			
<20,000	1,885	6.9 (6.4 to 7.3)	6.6 (5.0 to 8.3)
20,000-39,999	3,690	13.4 (12.8 to 14.0)	5.1 (4.0 to 6.1)
40,000-59,999	3,833	13.9 (13.3 to 14.6)	2.9 (1.9 to 3.8)
60,000-79,999	3,577	13.0 (12.3 to 13.7)	2.1 (1.3 to 2.9)
80,000-99,999	3,214	11.7 (11.0 to 12.3)	1.8 (1.2 to 2.5)
100,000-149,999	5,501	20.0 (19.2 to 20.8)	1.2 (0.6 to 1.7)
≥150,000	5,818	21.1 (20.3 to 22.0)	1.0 (0.5 to 1.5)
<b>Education</b>			
Less than secondary	3,321	18.9 (18.3 to 19.6)	3.0 (2.3 to 3.6)

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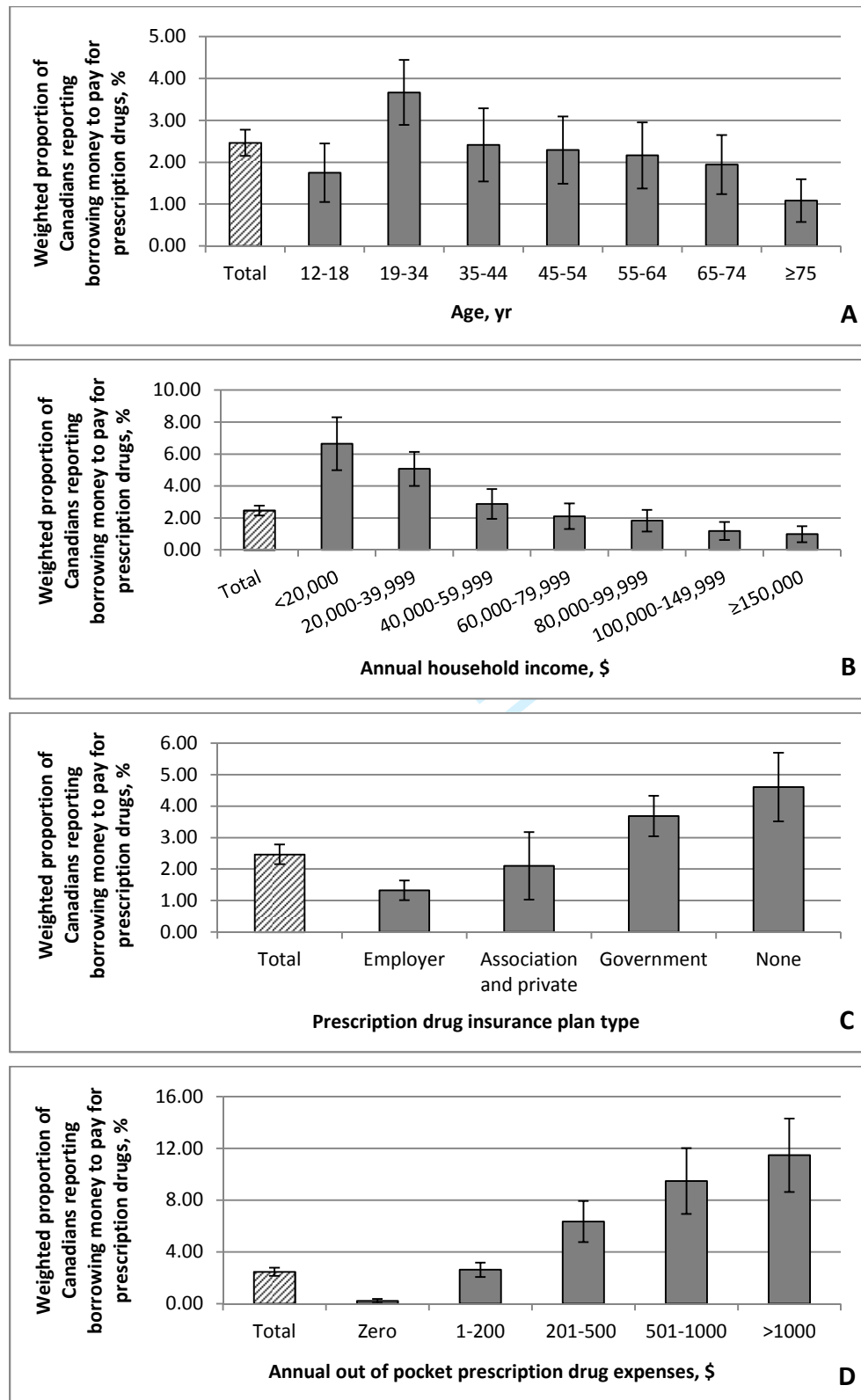
school			
Secondary school	3,527	23.4 (22.6 to 24.3)	2.7 (2.0 to 3.4)
Post-secondary school	8,547	57.7 (56.7 to 58.6)	2.2 (1.8 to 2.6)
Prescription Drug Insurance			
Employer plan	14,855	54.0 (53.0 to 55.0)	1.3 (1.0 to 1.6)
Association plan	2,284	8.3 (7.8 to 8.8)	2.1 (1.0 to 3.2)
Government plan	4,802	17.5 (16.8 to 18.1)	3.7 (3.0 to 4.3)
None	5,578	20.3 (19.5 to 21.1)	4.6 (3.5 to 5.7)
Out of Pocket Prescription Drug Spending (prior 12 months), \$			
0	13,575	49.3 (48.4 to 50.3)	0.2 (0.1 to 0.4)
1-200	8,759	31.8 (31.0 to 32.7)	2.6 (2.1 to 3.2)
201-500	2,862	10.4 (9.9 to 10.9)	6.4 (4.8 to 7.9)
501-1000	1,406	5.1 (4.8 to 5.5)	9.5 (6.9 to 12.0)
>1000	916	3.3 (3.0 to 3.7)	11.5 (8.6 to 14.3)
Province			
Newfoundland and Labrador	418	1.5 (1.5 to 1.54)	3.1 (1.5 to 4.6)
Prince Edward Island	116	0.4 (0.4 to 0.4)	3.2 (1.4 to 4.9)
Nova Scotia	749	2.7 (2.7 to 2.7)	4.1 (2.6 to 5.6)
New Brunswick	575	2.1 (2.1 to 2.1)	2.9 (1.7 to 4.2)
Quebec	6,340	23.0 (22.9 to 23.2)	1.6 (1.1 to 2.0)
Ontario	10,628	38.6 (38.4 to 38.9)	3.0 (2.3 to 3.7)
Manitoba	947	3.4 (3.4 to 3.5)	2.8 (1.4 to 4.2)
Saskatchewan	826	3.0 (3.0 to 3.0)	2.0 (1.0 to 2.9)
Alberta	3,231	11.7 (11.7 to 11.8)	2.2 (1.5 to 2.8)
British Columbia	3,690	13.4 (13.3 to 13.5)	2.3 (1.6 to 3.0)

Table 2: Logistic Regression on Borrowing Money to Pay for Prescription Drugs

	OR (with 95% CI)	p value
<b>Sex</b>		
Female	1.3 (1.0 to 1.8)	0.10
Male	Reference Group	
<b>Age, yr</b>		
12 to 18	2.7 (1.2 to 6.5)	0.02
19-34	3.7 (2.3 to 5.7)	<0.01
35-44	2.1 (1.2 to 3.9)	0.01
45-54	0.5 (0.3 to 0.9)	0.02
55-64	0.2 (0.1 to 0.4)	<0.01
65-74	0.1 (0.1 to 0.2)	<0.01
≥75	Reference Group	
<b>Self-reported Health Status</b>		
Very good	1.5 (0.8 to 2.7)	0.3
Good	3.0 (1.7 to 5.3)	<0.01
Fair	4.5 (2.4 to 8.4)	<0.01
Poor	7.7 (3.7 to 15.9)	<0.01
Excellent	Reference Group	
<b>Chronic Conditions, no.</b>		
1	1.8 (1.1 to 3.1)	0.02
2	2.2 (1.4 to 3.5)	<0.01
3	2.4 (1.4 to 4.2)	<0.01
≥4	4.5 (2.5 to 8.1)	<0.01
0	Reference Group	
<b>Cultural Background</b>		
Aboriginal	6.7 (2.2 to 20.6)	<0.01
Other	7.6 (2.6 to 21.9)	<0.01
White	4.6 (1.7 to 12.6)	<0.01
East Asian / South Asian	Reference Group	
<b>Total Household Income, \$</b>		
<20,000	3.9 (1.9 to 8.2)	0.001
20,000-39,999	2.7 (1.3 to 5.4)	0.01
40,000-59,999	1.9 (0.9 to 3.9)	0.07
60,000-79,999	1.5 (0.7 to 3.2)	0.26
80,000-99,999	1.3 (0.6 to 2.6)	0.53
100,000-149,999	0.9 (0.4 to 1.9)	0.71
≥150,000	Reference Group	
<b>Education</b>		
Secondary school	0.8 (0.5 to 1.3)	0.35
Post-secondary school	0.8 (0.5 to 1.2)	0.34
Less than secondary school	Reference Group	

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Prescription Drug Insurance		
Association plan and private plan	1.7 (1.0 to 3.0)	0.06
Government plan	2.0 (1.4 to 2.9)	<0.01
None	2.3 (1.5 to 3.5)	<0.01
Employer plan	Reference Group	
Out of Pocket Prescription Drug Spending, \$		
0	0.1 (0.0 to 0.2)	<0.01
201-500	2.5 (1.7 to 3.7)	<0.01
501-1000	3.6 (2.3 to 5.7)	<0.01
>1000	3.8 (2.2 to 6.6)	<0.01
1-200	Reference Group	
Province		
Newfoundland and Labrador	2.5 (1.1 to 5.7)	0.03
Prince Edward Island	2.1 (0.9 to 4.9)	0.11
Nova Scotia	3.5 (1.7 to 7.2)	<0.01
New Brunswick	2.5 (1.3 to 4.8)	0.01
Ontario	3.0 (1.8 to 4.8)	<0.01
Manitoba	2.7 (1.3 to 5.8)	0.01
Saskatchewan	1.3 (0.6 to 2.7)	0.51
Alberta	2.2 (1.3 to 3.7)	<0.01
British Columbia	2.6 (1.4 to 4.7)	<0.01
Quebec	Reference Group	



**Figure 1: Weighted proportion of borrowing Canadians borrowing money to pay for prescription drugs by age (Fig 1A), annual household income (Fig 1B), prescription drug insurance plan (Fig 1C), and annual out of pocket expenses on prescription drugs (Fig 1D). Error bars indicate 95% confidence intervals. Hatched bar indicates the estimated national rate of borrowing.**

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Location in study
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	Title
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction
Objectives	3	State specific objectives, including any pre-specified hypotheses	Page 7, para 3
Methods			
Study design	4	Present key elements of study design early in the paper	Page 8, para 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Page 8, para 1
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 8, para 2
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods
Bias	9	Describe any efforts to address potential sources of bias	Page 8, para 2
Study size	10	Explain how the study size was arrived at	Page 8, para 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 8
		(b) Describe any methods used to examine subgroups and interactions	

(c) Explain how missing data were addressed

(d) *Cohort study*—If applicable, explain how loss to follow-up was addressed

*Case-control study*—If applicable, explain how matching of cases and controls was addressed

*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy Page 8, para 2

(e) Describe any sensitivity analyses

## Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	Page 9, para 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Page 9, para 1; Table 1 Page 9, para 2
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Results
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 10, para 2 Table 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 11, para 2

## Discussion

Key results	18	Summarise key results with reference to study objectives	Page 11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 13, para 2
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13, para 3

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Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13, para 3
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<b>Other information</b>			
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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Acknowledgements

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

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