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Title: Patterns of Cost-related Medication Underuse among Canadian Adults with Cancer

Short title: CRMU and Cancer Patients.

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ABSTRACT

Objective:

To assess the patterns of cost-related medication underuse (CRMU) among Canadian adults with cancer in a contemporary population-based cohort.

Methods:

Datasets from the Canadian Community Health Survey (CCHS) (2015-2016) were accessed and adults (≥ 18 years) with a history of cancer were reviewed. Information about sociodemographic features, health behaviors and CRMU were reviewed. Multivariable logistic regression analysis for factors associated with CRMU was conducted.

Results:

A total of 8581 eligible participants were included in the current study; including 460 participants (5.4%) who reported CRMU and 8121 participants who did not report CRMU (94.6%). The following factors were associated with CRMU in multivariable logistic regression analysis: younger age (OR: 2.937; 95% CI: 2.365-3.646), female sex (OR for male sex versus female sex: 0.694; 95% CI: 0.552-0.872), indigenous racial background (OR for indigenous versus white racial group: 1.552; 95% CI: 1.077-2.236), unmarried status (OR for married versus unmarried: 0.667; 95% CI: 0.525-0.849), poor self-perceived health (OR for excellent versus poor self-perceived health: 0.494; 95% CI: 0.304-0.805), lower income (OR for income <20,000 versus income \geq 80,000: 2.449; 95% CI: 1.878-2.910).

Conclusion:

CRMU is not uncommon among adults with cancer in Canada. The toll of the problem seems to be unequally carried by women, racial minorities and non-elderly (<65 years) uninsured individuals. Discussion about a national pharmacare program for uninsured individuals is needed.

KEYWORDS:

Financial toxicity; pharmacare; cancer; Insurance coverage.

INTRODUCTION

According to the Canadian constitution and Canada Health Act, healthcare is a provincial jurisdiction; but each province needs to provide medically necessary interventions in order to receive federal transfer payments (1). Therefore, and with very few exceptions, provincial healthcare insurance plans cover all procedures/treatments deemed medically necessary for cancer treatment (2).

That being said, additional supportive treatments not deemed medically necessary are not covered by these provincial plans and they have to be paid either privately or through other insurance plans. Moreover, the above-described provincial plans apply only to eligible individuals (including Canadian citizens, permanent residents and some residents on temporary visas). Unfortunately, it is not uncommon for some ineligible temporary workers or other migrants to fall in the cracks of the system and not to be covered for healthcare services (including cancer care). Moreover, and in some provinces, Canadian citizens and permanent residents have to wait for three months before their provincial coverage starts if they are moving from outside of the country (3).

All the above factors contribute to the ongoing problem of cost-related medication underuse (CRMU), where individuals either not fill a prescription or skip doses of a prescribed medicine because of financial hardship and lack of prescription medication coverage (4). While CRMU prevalence and associations in Canada have been evaluated in the non-cancer population in a number of studies before (5-7), prevalence and associations of CRMU among cancer patients and survivors have not been properly studied in a national cohort yet.

The Canadian Community Health Survey (CCHS) is a national annual survey that provides population-level data on social determinants of health, health behaviors and experiences of Canadians with healthcare system (8). It thus provides a good opportunity to examine factors associated with non-adherence/ underuse of prescribed medications which can be linked to different sociodemographic features.

OBJECTIVE:

To assess the patterns of CRMU among Canadian adults with cancer in a contemporary population-based cohort.

METHODS

DATA SOURCES AND COHORT SELECTION

CCHS is a cross-sectional survey that is conducted annually to provide data about various health aspects of the residents of Canada who are older than 12 years (including attitudes, behaviors and conditions). It is estimated that approximately 97% of Canadians are represented within this survey and its sampling strategy follows a combination of area framing, phone list framing in addition to random dialing in some health regions. Underrepresentation/ non-representation have been reported for some individuals in some Quebec health regions, full-time members of the Canadian forces and those living in indigenous settlements. Further information about sampling strategy of the CCHS was provided in its publicly available documents (9). The current study is based on CCHS datasets for 2015-2016 (because detailed information about CRMU as well as insurance coverage were provided in these datasets).

The following criteria were used for cohort selection: 1) participants with history of cancer (defined by answering yes to either of these two questions: do you have cancer?; have you ever been diagnosed with cancer?); 2) complete information about CRMU (defined by the question coded PEX_090 within the survey: During the last 12 months, was there a time when you did not fill or collect a prescription for medicine, or you skipped doses of your medicine because of the cost?). Participants who were not prescribed a medication in the last 12 months were excluded from the current cohort.

DATA COLLECTION

The following data were included from each participant (where available): age at survey completion, sex, racial background (white, indigenous or others), marital status, income, insurance coverage (yes or no), type of insurance, educational level, self-perceived health and self-perceived mental health, food security (defined by whether participant was worried food would run out in the past 12 months or not), working status last week, emergency department visits and overnight hospital admission visits in the past 12 hours.

Based on whether participants reported current diagnosis or past diagnosis of cancer, they were classified into current cancer patients or cancer survivors. Moreover, the presence (self-reporting) of any of the following comorbidities was reviewed: asthma, chronic obstructive pulmonary disease, sleep apnea, fibromyalgia, arthritis, osteoporosis, hypertension, dyslipidemia, heart disease, stroke effects, diabetes mellitus, migraine, mood disorder and anxiety disorder.

STATISTICAL ANALYSES

The main hypothesis of this study is that insurance coverage for prescription medications as well as higher socioeconomic status is associated with less CRMU among adults with history of cancer in Canada. In order to study this hypothesis, the following analysis were conducted:

- Differences between participants who have versus those who have not history of CRMU were determined through Chi-Squared testing (for categorical variables) and independent t-test (for continuous variables). Interactions between age, insurance status, CRMU and other sociodemographic characteristics were further explored through Chi-Square testing.
- 2) Multivariable logistic regression was then conducted to evaluate the factors associated with CMRU among all participants. This model included age at survey completion, sex, racial background, marital status, income, insurance coverage, educational level, self-perceived health and self-perceived mental health. The presence of comorbidities was not included in this model because of the potential of collinearity between the presence of comorbidities and self-perceived health and self-perceived mental health (the presence of comorbidities should correlate significantly with each of these variables).
- 3) In order to further assess the impact of working status (unemployment) on CRMU among non-elderly (<65 years) adults with cancer, another multivariable logistic regression analysis was conducted which included all the variables as detailed above with exclusion of age (as all participants in this cohort were younger than 65 years) and including working status from the last week. The reason for limiting</p>

this analysis to the cohort of non-elderly individuals is because most of elderly individuals (>65 years) should be retired by that age.

All statistical analyses were conducted through SPSS software (version 26.0, IBM, NY).

RESULTS

PARTICIAPNTS' CHARACTERISTICS

A total of 8581 eligible participants were included in the current study; including 460 participants (5.4%) who reported CRMU and 8121 participants who did not report CRMU (94.6%). Comparing both groups together, participants with CRMU were more likely to have younger age (P<0.001), female sex (P<0.001), non-white race (P<0.001), poor self-perceived health (P<0.001) and poor self-perceived mental health (P<0.001), higher burden of comorbidity (P<0.001), lower income (P<0.001), and more likely to be unmarried (P<0.001). Those patients were also more likely to visit the emergency department (P<0.001), be admitted in the hospital (P<0.001) and experience food insecurity (P<0.001) (Table-1).

CRMU rates within different Canadian jurisdictions were described in figure-1a and it seems to be highest in British Columbia at 8% and lowest in Yukon at 0%. When the data were limited to non-elderly adults (<65 years), rates were higher in all jurisdictions (highest in Prince Edwards Island at 13.2% and lowest in Yukon at 0%) (Figure-1b).

Participants with CRMU were also more likely to lack insurance for prescription medications (P<0.001) and when the cohort was stratified by insurance status and age, 19.1% of non-elderly (<65 years) participants with no insurance coverage reported CRMU in the past 12 months prior to survey completion.

Within the cohort of non-elderly participants (<65 years), CRMU was associated with not having a job (CRMU was 12.6% among individuals who did not have a job versus 6.3% among individuals who worked in the last week before survey completion; P<0.001). Distribution of unemployment according to racial background and sex was further explored among non-elderly participants. Non-elderly individuals with indigenous racial background were more likely not to have a job at the time of survey (53.2% versus 42.2%

among individuals with white background; P= 0.038); on the other hand, sex did not appear to associate with unemployment (P=0.527).

FACTORS ASSOCIATED WITH CRMU AMONG ALL PARTICIPANTS

The following factors were associated with CRMU in multivariable logistic regression analysis: younger age (OR: 2.937; 95% CI: 2.365-3.646), female sex (OR for female sex versus male sex: 0.694; 95% CI: 0.552-0.872), indigenous racial background (OR for indigenous versus white racial group: 1.552; 95% CI: 1.077-2.236), unmarried status (OR for married versus unmarried: 0.667; 95% CI: 0.525-0.849), poor self-perceived health (OR for excellent versus poor self-perceived health: 0.494; 95% CI: 0.304-0.805), lower income (OR for income <20,000 versus income \geq 80,000: 2.449; 95% CI: 1.698-3.533) and lack of insurance for prescription medications OR: 2.337; 95% CI: 1.878-2.910) (Table-2).

FACTORS ASSOCIATED WITH CRMU AMONG NON-ELDERLY PARTICIPANTS (< 65 YEARS)

The following factors were associated with CRMU in multivariable logistic regression analysis: female sex (OR for male sex versus female sex: 0.687; 95% CI: 0.506-0.932), indigenous racial background (OR for indigenous versus white racial group: 1.693; 95% CI: 1.116-2.568), unmarried status (OR for married versus unmarried: 0.636; 95% CI: 0.465-0.871), poor self-perceived health (OR for excellent versus poor self-perceived health: 0.442; 95% CI: 0.225-0.866), lower income (OR for income <20,000 versus income \geq 80,000: 1.942; 95% CI: 1.222-3.087) and lack of insurance for prescription medications OR: 2.705; 95% CI: 2.026-3.611) (Supplementary Table-1). Working status did not seem to impact CRMU (OR for not having a job versus work in the past week: 1.320; 95% CI: 0.967-1.801).

DISCUSSION

The current study evaluates the patterns of CRMU among Canadian adults with cancer in a contemporary population-based study. It suggested that CRMU is not uncommon among adults with cancer in Canada. The toll of the problem seems to be unequally carried by women, racial minorities and non-elderly (<65 years) uninsured individuals.

These results should ring the alarm bell with regards to this phenomenon and should lead to a real discussion about the position of a national pharmacare program to cover expenses for prescription medications for those individuals.

Canada prides itself with a publicly funded healthcare system that provides coverage for all interventions deemed medically necessary; and in the context of cancer care, covers the expenses of necessary investigations and most of the approved anticancer treatments. While this is all true, it should be remembered also that many of those individuals with history of cancer have other medical conditions that might require treatment with other medications which are mostly not covered by provincial healthcare insurance plans. Because of the recorded association of cancer diagnosis and treatment with unemployment and long-term disability (10), consequences can be severe for cancer patients suffering from short- or long-term effects of cancer and its treatment and who are unable to provide for the expenses of medications. Equally alarming is the observation in the current study that many of those individuals with CRMU are struggling with food insecurity, with recent data suggesting higher mortality among Canadians struggling with food insecurity (11, 12). It is possible that the lack of financial means to provide for food has been an indirect result for the expenses of medications those patients have to pay for. It is important here also to highlight that linking drug plans to employment would mean that people who are chronically unemployed or underemployed (which include many cancer patients/ survivors) are going to be affected more. This is an important argument in favor of a universal drug coverage plan regardless of employment status.

The toll of these expenses seems to be unequally carried by some vulnerable subgroups of the society (including women and racial minorities). This is probably linked to lower socioeconomic status for these groups and subsequently inability to cover the expenses of medications. This is also consistent with previous studies suggesting worse cancer-specific and non-cancer-specific outcomes of cancer patients with lower socioeconomic status compared to those with higher socioeconomic status (13-16). Moreover, non-elderly (<65 years) individuals with a history of cancer seem to be particularly affected. The reason for this observation seems to be related to the fact that, within most Canadian jurisdictions, old age security plans provide some form of prescription medication

coverage. Looking at figure 2, it is notable that individuals with governmental insurance still have considerable CRMU (5.2%). This type of insurance is usually provided to older individuals (as part of old age security programs), as well as those on disability and income supports. We need to look more as to why governmental coverage is underperforming compare to other forms of coverage. Of note here is that many people with drug plans still have co-pays and if some of the drugs are expensive (like many supportive medications for cancer patients) they may not be able to afford the copay even if they have insurance. Moreover, some drug plans have annual or lifetime caps on how much they reimburse participants (which may also be linked to all members coverage by the plan) leaving some people in a decision that they may not want to use up their coverage for their terminal condition and leave behind a spouse who has no coverage because it was all exhausted or they may have no more coverage because it was all used up.

While this data was collected pre COVID-19 pandemic, in the COVID era there are issues related to dispensing of drugs in only one-month supplies which means more dispensing fees. Initially, many oncologists would prescribe cancer supportive care medications to supply all scheduled cycles at once. This is not doable in the COVID era; so, these ancillary costs also make out of pocket expense go up for many cancer patients/ survivors.

Acknowledging the differences in healthcare organization and delivery between Canada and the United States, it remains valuable to compare the results of the current study with contemporary US studies evaluating CRMU. In a recent study based on the National Health Interview Survey (2011-2017), implementation of patient protection and Affordable Care Act led to a decrease in CRMU among cancer survivors, particularly nonelderly (<65 years) and those with lower income (17). These findings do highlight the positive impact of national programs providing medication coverage for vulnerable groups of the population. In another US study, also based on the National Health Interview Survey (2013-2015), adolescent and young adult cancer survivors were more likely to report CMRU and subsequently nonadherence to prescribed medications (18).

The current study has a few limitations that need to be addressed. First, the self-reporting basis of the CCHS regarding the diagnosis of cancer, insurance coverage and CRMU

might raise some concerns regarding a possible bias in reporting. While this is possible, it should be remembered that many of the studies evaluating the same questions within Canada, US or elsewhere were based on similar self-reporting surveys (e.g. National Health Interview Survey in the US). For practical reasons, it is extremely difficult to answer these questions (with such a sufficiently large size of participants) using some forms of prospective research. Second, and like previously published CCHS studies, information about cancer primary site, treatment or stage are not available. Third, granular details about the medication being underused and possible linkage to overall and cancer-specific mortality are not available. While these are relevant data to look at, we know from previous population-based studies the serious consequences of medication nonadherence among cancer patients as well as the general population (19-21). These limitations need to be counterbalanced with the strengths of this study including the contemporaneous nature of data collection, large sample size as well as broad national view providing information about important inter-jurisdictional differences in Canada.

While it is expected that similar findings will be observed in a national non-cancer-specific cohort of participants in Canada, individuals with history of cancer represent a special subgroup that needs to be evaluated separately. Reasons include both the long-term socioeconomic and medical challenges brought about by cancer diagnosis with many of survivors who are cured from cancer being left with a host of medical problems that need to be treated as well as with possible treatment-related disabilities that would prevent them from working to provide for themselves, their families and their medical expenses (22). Thus, the burden of CRMU would be expected to be higher in this subgroup of the population and a special attention should be paid to them.

The current study also suggested that individuals with CRMU were more likely to visit emergency departments as well as be hospitalized. While this may be related to the observed imbalance in baseline comorbidities as well as to many other possible confounders, this also might suggest that apparent cost savings from lack of universal prescription medication coverage might backfire later on and cost public healthcare systems more through hospital admissions and other sequelae. This question needs to be formally addressed in a cost-effectiveness study. In conclusion, CRMU is not uncommon adults with cancer in Canada. The toll of the problem seems to be unequally carried by women, racial minorities and non-elderly (<65 years) uninsured individuals. Discussion about a national pharmacare program for uninsured individuals is needed.

Acknowledgment

Compliance with ethical standards

Ethical approval statement

Because this study was based on the publicly available, open license, anonymized dataset, ethical approval was not required. The study was performed following the

ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments

Disclosure of potential conflicts of interest

The authors have no conflicts of interest

Patient consent statement

All included CCHS participants have signed informed consent as dictated by Statistics Canada policies.

Figure legends:

Figure-1: Geographic distribution of CRMU among a) all participants; b) non-elderly adults (<65 years).

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Figure-2: Rate of CRMU according to the type of medication insurance coverage.

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Variable	CRMU in the past 12 months (460	No CRMU in the past 12 months	P value
	participants)	(8121 participants)	
Age			
18-64 years	288 (62.6%)	2890 (35.6%)	<0.001
≥65 years	172 (37.4%)	5231 (64.4%)	
Sex			<0.001
Males	122 (26.5%)	3176 (39.1%)	
Females	338 (73.5%)	4945 (60.9%)	
Racial background			<0.001
White	388 (84.3%)	7429 (91.5%)	
Indigenous	43 (9.3%)	333 (4.1%)	
Others	25 (5.4%)	292 (3.6%)	
Unknown	4 (0.9%)	67 (0.8%)	
Marital status			<0.001
Married	125 (27.2%)	3821 (47.1%)	
Unmarried	334 (72.6%)	4281 (52.7%)	
Unknown	1 (0.2%)	19 (0.2%)	
Self-perceived health		1%.	<0.001
Excellent	30 (6.6%)	820 (10.1%)	
Very good	57 (12.4%)	2285 (28.3%)	
Good	147 (32.1%)	2807 (34.7%)	
Fair	139 (30.3%)	1473 (18.2%)	
Poor	85 (18.6%)	698 (8.6%)	
Self-perceived mental health			<0.001
Excellent	85 (18.5%)	2546 (30.3%)	
Very good	125 (27.2%)	2825 (34.9%)	
Good	132 (28.8%)	2105 (26%)	
Fair	93 (20.3%)	559 (6.9%)	
Poor	24 (5.2%)	156 (1.9%)	
Total household income			<0.001
<20,000	118 (25.7%)	1013 (12.5%)	
20,000- <40,000	151 (32.8%)	2097 (25.8%)	

•	
3	40,000- <60
4	60,000- <80
5	>80,000
0	Education
8	Less than se
9	Secondary
10	Post-secon
11	Insurance fo
12	medication
13	Voc
14	No
15	
16	Cancer stati
17	Current dia
18	Survivor
19	Emergency
20	the past 12
21	Overnight h
22	past 12 mor
24	Yes
25	No
26	Worried foo
27	the past 12
28	Often true
29	Sometime
30	Never true
31	Comorbiditi
32	No comort
33	
34 25	More than
36	Unknown
37	
38	*CRIVIU: COSI
39	
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42	
43	
44	
45	
46	
47	

),000- <60,000	84 (18.3%)	1551 (19.1%)	
),000- <80,000	38 (8.3%)	1103 (13.6%)	
30,000	69 (15%)	2349 (29%)	
ucation			0.247
ess than secondary school	92 (20.5%)	1866 (23.3%)	
econdary school	110 (24.5%)	1751 (21.9%)	
ost-secondary education	247 (55%)	4396 (54.9%)	
surance for prescription			<0.001
	306 (66 8%)	6698 (83 1%)	
0	152 (33.2%)	1359 (16.9%)	
ncer status		× 7	0.419
urrent diagnosis	100 (21.7%)	1639 (20.2%)	
urvivor	360 (78.3%)	6482 (79.8%)	
nergency department visits in	1.39; 3.036	0.73; 1.911	<0.001
e past 12 months (mean; SD)			
ernight hospital visits in the			<0.001
st 12 months		\mathbf{O}	
es	100 (21.7%)	1228 (15.1%)	
0	360 (78.3%)	6885 (84.9%)	
orried food would run out in			<0.001
e past 12 months			
Often true	68 (21.8%)	98 (1.8%)	
Sometimes true	72 (23.1%)	258 (4.9%)	
Never true	172 (55.1%)	4880 (93.2%)	
morbidities			<0.001
lo comorbidities	25 (5.4%)	1062 (13.1%)	
ne comorbidity	64 (13.9%)	1666 (20.5%)	
Iore than one comorbidity	353 (76.7%)	5058 (62.3%)	
Inknown	18 (3.9%)	335 (4.1%)	

*CRMU: Cost-related medication underuse.

Factors	OR (95% CI)	P value
Age		<0.001
<u>></u> 65 years	Reference	
18-64 years	2.937 (2.365-3.646)	
Sex		0.002
Females	Reference	
Males	0.694 (0.552-0.872)	
Racial background		
White	Reference	
Indigenous	1.552 (1.077-2.236)	0.018
Others	1.304 (0.829-2.051)	0.251
Marital status		0.001
Unmarried	Reference	
Married	0.667 (0.525-0.849)	
Self-perceived health		
Poor	Reference	
Excellent	0.494 (0.304-0.805)	0.005
Very good	0.329 (0.219-0.493)	<0.001
Good	0.639 (0.463-0.881)	0.006
Fair	0.903 (0.662-1.231)	0.518
Self-perceived mental health		
Poor	Reference	
Excellent	0.642 (0.374-1.102)	0.108
Very good	0.804 (0.478-1.353)	0.412
Good	0.843 (0.508-1.401)	0.511
Fair	1.445 (0.862-2.423)	0.162
Total household income		
<u>≥</u> 80,000	Reference	
<20,000	2.449 (1.698-3.533)	<0.001
20,000- <40,000	2.363 (1.693-3.298)	<0.001
40,000- <60,000	1.797 (1.265-2.553)	0.001
60,000- <80,000	1.118 (0.732-1.708)	0.606

Education		
Post-secondary education	Reference	
Less than secondary school	0.664 (0.506-0.870)	0.003
Secondary school	0.962 (0.753-1.228)	0.756
Insurance for prescription medications		<0.001
Yes	Reference	
No	2.337 (1.878-2.910)	





Figure-1b

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Figure-2

Supplementary table 1: Multivariable logistic regression analysis for factors associated with CRMU among non-elderly participants (<65 years):

Factors	OR (95% CI)	P value
Working status last week		
Worked at a job/business	Reference	
Absent from work	1.065 (0.611-1.855)	0.824
Did not have a job	1.320 (0.967-1.801)	0.080
Sex		0.016
Females	Reference	
Males	0.687 (0.506-0.932)	
Racial background		
White	Reference	
Indigenous	1.693 (1.116-2.568)	0.013
Others	1.460 (0.851-2.503)	0.169
Marital status		0.005
Unmarried	Reference	
Married	0.636 (0.465-0.871)	
Self-perceived health	40	
Poor	Reference	
Excellent	0.442 (0.225-0.866)	0.017
Very good	0.343 (0.199-0.592)	<0.001
Good	0.711 (0.466-1.087)	0.115
Fair	1.121 (0.754-1.667)	0.573
Self-perceived mental health		
Poor	Reference	
Excellent	1.043 (0.515-2.111)	0.907
Very good	1.316 (0.671-2.583)	0.424
Good	1.476 (0.766-2.844)	0.244
Fair	2.250 (1.167-4.338)	0.015
Total household income		
<u>≥</u> 80,000	Reference	
<20,000	1.942 (1.222-3.087)	0.005
20,000- <40,000	2.448 (1.617-3.707)	<0.001
40,000- <60,000	1.500 (0.963-2.337)	0.073

60,000- <80,000	1.030 (0.616-1.720)	0.911	
Education			
Post-secondary education	Reference		
Less than secondary school	0.685 (0.468-1.003)	0.052	
Secondary school	0.827 (0.603-1.134)	0.238	
Insurance for prescription medications		<0.001	
Yes	Reference		
No	2.705 (2.026-3.611)		