The impact of prescription medication cost coverage on optimal adherence to Hypertension and Diabetes Mellitus oral medications

by
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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Background: It can be difficult for patients who do not have prescription medication cost coverage to adhere to their medications. No previous study has examined the time-trend and impact of absence of coverage on adherence to oral diabetes and hypertension medications in Canada.

Methods: Using data from the Canadian Community Health Survey cycles 2007, 2008, 2013, and 2014, I included individuals from participating provinces that opted to include questions about coverage (Ontario and New Brunswick). Included adults had either hypertension or diabetes and answered questions on both coverage and adherence to medications. A multivariate-adjusted logistic regression model was fitted to estimate the odds of non-adherence depending on coverage. I adjusted for confounding variables including demographic factors (socioeconomic status; age, education, sex, province of residence), and health system and behaviour variables (such as smoking, having a regular doctor, not receiving a flu shot, as well as having additional comorbidities).

Results: The pseudo-cohort included 23,215 individuals. The weighted average age was 60 years. 20% of participants reported absence of coverage. This percentage increased slightly over the study period. Patients with no prescription medication coverage were at 23% higher odds of not adhering to their medication (adjusted odds ratio (OR) 0.77; 95% CI (Confidence Interval) 0.657 - 0.911). Subgroup analysis revealed that patients aged less than 65 years, lived in Ontario, and had a middle-income were also at a statistically significant lower odd for adherence with absence of insurance.

Conclusion: Absence of prescription medication coverage is associated with a reduced adherence to diabetes and hypertension oral medications. Providing medication coverage may help in increasing the probability for adherence. As such, there is a need for further studies to quantify the effect of recent changes of provincial insurance coverage.

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Author's Disclosure

Mandatory, as stated in the Microdata Research Contract: "Although the research and analysis are based on data from Statistics Canada, the opinions expressed do not represent the views of Statistics Canada."

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List of Abbreviations

CCHS	Canadian Community Health Surveys
CI	Confidence Interval
CSs	Cross-sectional study
DM	Diabetes Mellitus
DM II	Diabetes Mellitus type II
FCS	Fully Conditional Specification
HTN	Hypertension
OR/ ORs	Odds Ratio/ Odds Ratios
PMCC	Prescription medication cost coverage
RCTs	Randomized Controlled Trials
WHO	World Health Organization

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1.1. Chapter 1: Introduction The epidemiology and cost of Hypertension and Diabetes

Hypertension (HTN) and Diabetes Mellitus (DM) are among the most widespread chronic diseases (CDs) in Canada; and they have profound effects on the Canadian population.[1] In general, CDs are noncontagious diseases with multiple risk factors.[2] They are known to progress slowly and their symptoms arise after they have progressed. Thus, they are considered to have a long latency period; and they eventually cause functional impairment or disability.[2] CDs can also be referred to as chronic illnesses, non-communicable diseases, and degenerative diseases.[1] HTN is defined as having an ambulatory blood pressure measurement of systolic and/or diastolic blood pressure equal to or above 135/85 mm Hg.[3,4] DM, on the other hand, is defined as having a fasting blood glucose ≥ 7.0 mmol/L, 2-hour plasma glucose of ≥ 11.1 (using mmol/L (using in a 75 g oral glucose tolerance test), a glycated Hemoglobin ≥ 6.5% , or Random Plasma Glucose≥ 11.1 mmol/L.[5]

In Canada, the current estimated prevalence of HT among adults aged 18 years and over is 17.3%, while that of DM is 7.1%.[1] In 2011, it was estimated that 1 in 4 Canadians is either diabetic or pre-diabetic and the projection is that this will increase to 1 in 3 by 2020.[6] By then, HTN and DM are projected to rise to 23% and 10.8% respectively.[6,7] One in five Canadians with HTN also has DM.[8] Financially, HTN and DM are placing a burden on the Canadian health care system with a significant cost on its economy. In 2010, the cost attributed to HTN was estimated to be $13.9 billion; whereas DM's cost was estimated to be $11.7 billion.[6,7]

Extrapolation of these costs to the year 2020 is expected to result in a significant rise to $20.5 billion for HTN and $16 billion for DM.[6,7]

1.2. Management of Hypertension and Diabetes

As with other CDs, HTN and DM do not occur from one cause, but originate from complex and multilevel risk factors over an extended period of time.[9] Additionally, health care system related factors are important in the management and clinical outcome improvement of HTN and DM.[10] These factors include the inadequate delivery of proper healthcare services by healthcare providers, either due to lack of knowledge and training, work-overload, or insufficient or absence of reimbursement by health insurance plans.[9] These elements play an important role in the management and development of disease complications in patients with chronic diseases such as HTN or DM.[11,12]

Upon diagnosis of HTN and DM, an optimal management plan is usually pursued in order to control and prevent adverse health outcomes from progression. Norris *et al.* propose a definition for chronic disease management based on a systematic review and Wagner's model for chronic disease management.[13,14] This definition entails centralizing the patient in healthcare delivery and providing healthcare through an organised, proactive, and multi-component approach. In this regard, evidence-based medications are the cornerstone of HTN and DM management.[3,5] These include oral medications that can not only slow the progression of HTN and DM, but also reduce clinical adverse outcomes. In spite of the availability of such medications, several impediments still prevent the achievement of optimal results from the organized management plan.[15,16] As a result, it is estimated-for example in HTN-that less than

25% of patients achieve optimal outcomes.[17] Sub-optimal adherence is considered to be the main cause for non-ideal HTN and DM management.[5,17]

1.3. Medication adherence

In 2003, the World Health Organization (WHO) defined adherence to be: "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider".[9] Other terms that are closely related to adherence are: compliance, concordance, persistence, and obedience. Although compliance and adherence were interchangeably used in the past, adherence is currently preferred because it suggests the involvement of patients in the decision-making process of their chronic disease management plan.[18,19] This involvement does not necessarily mean that the patient will be choosing their therapy regimen. Rather, it signifies the patient as an important key for the success of their therapy plan by understanding the importance of treatment and contributing to the decision-making process.

In reality, involvement of patients with their management plan can improve adherence to their medication regimen as prescribed.[20-22] On the other hand, a lack of involvement may create doubts among patients that can impact following their regimen as prescribed. Thus, unlike compliance, the term "adherence" recognizes the importance of patients' involvement in their prescribed medication regimen.[16,23] In fact, optimizing pharmacological therapy before considering patient's medication adherence is inaccurate and can be costly.[24]

Adherence to medications in CDs has been found to be associated with improved clinical outcomes.[25] In a meta-analysis that looked back at three decades of research, sixty-three

related studies were assessed for the existence and magnitude of the correlation between adherence and clinical outcomes.[25] In total, most studies (51 out of 63) had found optimal adherence to be related to positive outcomes, whereas 8 showed no effects on outcome, and 4 had negative outcomes. Overall, adherent patients were at a 26% increase in the likelihood of experiencing positive outcomes in comparison to their non-adherent counterparts.[25] However, some researchers have argued that adherence could not be significantly proven to mediate positive clinical outcomes.[26,27] For example, in a prospective cohort study, 319 elderly patients (≥ 65 years old) were recruited, had their medication adherence assessed (using the Morisky *et al.*'s 4 question self-report scale), and were followed-up starting one year from their time of assessment.[26] Although 123 participants were classified as non-adherent, statistically significant differences were not found between the adherent and the non-adherent patients for risk of selected adverse clinical outcome of hospitalisation, including emergency department visits, or death.[28] Similarly, a systematic review looking at studies published from 1985 to 2003, investigated whether a relationship between adherence and blood pressure control existed.[27] Studies were included if they had used electronic records as their data source. The study concluded that there was no significant relationship between adherence and blood pressure control.[27] The findings of this study and similar studies may be due to a small sample size, variation between definitions of adherence, absence of a cut-off point between adherence and non-adherence, and inconsistencies in measuring adherence.[26,27,29] In fact, the choice for valid and suitable measurement of adherence is critical in order to evaluate the impact of adherence on clinical outcomes.[18]

1.4. Methods of assessing adherence

It is necessary to have an accurate measurement method to assess adherence in order for treatment planning to occur effectively. Robust assessment is also necessary to examine the impact of treatment plan on health outcomes accurately. Hence, if outcomes are suboptimal, no alterations are made in the management plan until adherence has been validated by a reliable adherence measurement method.[9]

The literature provides a wide range of options concerning adherence assessment, but a "gold standard" for the measurement of adherence in patients does not exist.[18] Adherence assessment methods are categorized by the WHO as objective and subjective methods.[9,20,30] Objective adherence measures include pill counts, pharmacy dispensing records databases, and electronic Medication Event Monitoring System (MEMS) devices.[31-33] Other more intrusive methods in assessing adherence behaviour are biochemical tests and blood level monitoring of the medication of interest.[34] Subjective measures include: patient-kept diaries,[18] physician reports,[32] report by others such as health care providers or family members,[18] standardized patient administered questionnaires (such as Morisky's structured questionnaire),[28] and patient directed surveys (self-reporting)[35,36]such as the Canadian Community Health Survey that is carried out every year by Statistics Canada.[37] Surveys are well known for their relative simplicity, effectiveness, and practicality, especially when assessment is needed to be carried out on a population level.[35,36]

1.5. Precision and practicality of different adherence measures in population-based epidemiological studies

The effectiveness of self-reported surveys in estimating CD prevalence has been validated by previous research. For example, a study from Brazil, which included 907 participants, interviewed patients and then measured their blood pressure. The specificity and sensitivity of self-reported HTN were 86.4% (95% CI: 84.3-88.6%) and 72.1% (95% CI: 69.3-75.0%), respectively. HTN prevalence was estimated in this study to be 27.2% (95% CI: 24.4-30.1%), which was similar to the accepted prevalence of this CD at the time (23.3%; 95% CI: 20.7-26.1%).[38] In terms of medication use, self-reported surveys also showed clear effectiveness. For example, in one study, which was carried out on 223 women (50 years and above), from the Women's Health Initiative Study, the researchers compared the agreement between length of medication use in self-reported surveys with that of pharmacy records. The sensitivity and specificity for the medication assessed was greater than 95%.[39] Similarly, using the self-report surveys method, a study assessed the validity of medication use among 170 patients with type II diabetes and assessed blood sample levels of Glycated hemoglobin (HbA_{1c}).[40] The study also validated self-reported adherence in a subsample by using MEMS- measured adherence as a comparison. Self-reported adherence had significant association with optimal levels of HbA_{1c}.[40] Also, within the subsample of 88 participants, self-reported adherence was found significantly associated with the MEMS-measured adherence. Self-report measures, when compared as a measurement tool for adherence to pill-counts, had better correlation with serum levels. Fletcher *et al.* tested and compared the correlation of digoxin serum levels in patients with a cardiovascular disease, with pill counts and self-reported

interviews.[41]During the interview, patients were provided with a range of adherence levels (percentages) on visible cards and were asked to quantify their adherence. Meanwhile, in a different room, patients' pills were counted. Following the interview, blood samples were taken to assess serum levels of digoxin. The participant's responses received during the interview correlated with digoxin serum levels more than the pill count method.[41]

Self-reporting through patients' surveys are the most practical and sound approach in assessing medication adherence determinants - especially for patient populations with chronic diseases including HTN and DM.[42,43] The self-reporting method is evidently simple and valid compared with other measures.[35,36] Although self-report subjective methods have been found to overestimate adherence more than objective measures. This overestimation may have been due to patient recall bias and social desirability and studies' characteristics can impact this phenomenon .[31,44-47] For example, in a systematic review of predictors of adherence, overestimation of self-report measures was evident if studies had smaller sample size.[31] However, when all studies were combined, self-reports measures had lower adherence estimates.[31] Variability among self-reported studies is most likely due to the low power of some studies. Accordingly, self-reports tend to be robust in large populations.[31]

The pill count measurement method is simply carried out by counting the present number of dosage units (pills, capsules, tablets, puffs, etc.) returned by patient on the date of follow up. The dosage units are compared with the initial number of units that were provided and were expected to have been consumed by the specified scheduled date of follow up.[18] The percentage of adherence is calculated by subtracting those two numbers (number present on the day of follow up from number initially provided) and dividing by the number of units that

should have been consumed. Multiplying the result obtained by a 100 gives us the adherence percentage. Pill counting can vary in accuracy in estimating the percentage of medication adherence. In fact, studies have shown that the pill count method tends to overestimate adherence levels.[33,48] One example can be shown for this when patients discard their medication rather than consume it.[49] Pill count, through comparing the number of pills with the original number dispensed, cannot convey the reasons behind non-adherence.[18] Furthermore, counting can impose a sense of lack of trust in the patient that can further harm the relationship with health care professionals. Most importantly, this method is not practical in population-based studies due to the reasons discussed above.[50] For these reasons, pill counts should not be chosen as an optimal measure of adherence, especially on a wide level involving many participants.[51,52]

Prescription refill records are centralized database systems that record patients' medication prescription dispensing.[46] Assessing adherence by these records relies on an assumption that upon dispensing the medications, patients are solely relying on one system for receiving and taking their medication.[18] However, this method cannot verify if the patient did in fact consume the medication; and it also ignores the possibility that a patient may be receiving his/her medication elsewhere - such as from free samples from their health practitioner.[46] Finally and most notably, on a population level, electronic databases cannot provide the wealth of information that self-reports can, especially when financial, insurance, and or socioeconomic status are needed to be measured and accounted for.[32]

MEMS are devices comprising of programmed unit bottles that record the time and day when the medication container is opened, a pill is removed from a blister pack, or an inhalation

device is actuated.[18,33] MEMS cannot, however, monitor if the patient in fact ingested the medication. This leads to overestimating adherence, which occurs when patients open their monitored bottle without ingesting any pill.[53] Alternatively, adherence may be underestimated in the MEMS method. This can occur in "pocket-dosing", which is the act of removing more than one dose, ingesting one dose and placing the rest in their pocket to be taken later.[53,54] Above all, MEMS are inconvenient, expensive and cannot be practically representative in the real-world of adherence in the population.[18]

Biochemical tests and blood level monitoring sometimes use nontoxic biological markers combined to the medication and can measure patients' blood or urine medication levels. These levels can indicate adherence of patient to the particular medication.[34] In some simplistic scenario cases, biochemical test monitoring serves in screening patients for adherence.[55] Not all medications can be assessed following this method since some factors may affect blood levels besides adherence, such as diet and drug-drug interactions.[46] Furthermore, serum medication levels can reflect only short-term adherence, hence patients who are aware of their monitoring may take their medication specifically for the test.[56] Additionally, this objective measuring method has limited feasibility because it is expensive, invasive and impractical in large population studies.[19]

1.6. Current adherence levels among populations with chronic diseases

One quantitative review of 50 years of research looking at studies from 1948 to 1998 concluded that the average rate of non-adherence to chronic disease medications is currently at 25%.[31] Other studies report that, depending on patients' conditions and how complex their treatment regimens were, 40% of patients or fewer generally do not take their medications as

prescribed.[20] The World Health Organization (WHO) also reported that, in developed countries, on average, 50% of those with CDs are non-adherent to their medications.[9,57,58]

Studies that have specifically measured HTN's or DM's medication non-adherence levels were alarming. A retrospective cohort study in the US included 21,723 participants who had started a single anti-hypertensive prescription-medication for their first time.[59] Participants were considered adherent if they had dispensed their medication up to three months after their one-year prescription anniversary of the medication. The non-adherence percentage rate was 36% for angiotensin-II receptors antagonist (ARBs), 42%for angiotensin converting enzyme inhibitors (ACEIs), 50% for calcium channel blockers (CCBs), 57% for beta-blockers, and 62% for thiazide diuretics.

Non-adherence levels tend to increase over time. A Canadian retrospective cohort study recruited 1220 subjects that had experienced their first cardiovascular event and then received statins for the first time. After one year of follow up, the linked prescription databases revealed that 39.7% of the study participants had stopped refilling their statin medication.[60] This percentage increased to 71.8% by the 5th year of follow up.

Similarly, primary non-adherence (also known as never taking the medication prescribed) is suboptimal in Canada.[61] In a recent study in Quebec, patients - selected from linked electronic medical databases - were chosen if they have recently been prescribed a drug that they have never received before. Patients were considered non-adherent if they received a prescription and did not have it dispensed within a 9-month period.[62] Almost one-third (31.3%) of 37,506 prescriptions were never filled by the 15,961 participants. Of the patients' prescribed

anti-diabetic or anti-hypertensive medication, 29% (972 patients) and 42.3% (2,246 patients) never filled their medication prescriptions respectively.

1.7. Importance and impact of non-adherence

Medications are the cornerstone of effective chronic disease management plans. Thus, it is important for patients to adhere to their medications to prevent further complications of their disease.[63] Adherence indirectly saves further avoidable costs. These costs can be related to occurrence or the acceleration of onset of complications, increasing risks of hospitalization and healthcare costs.[63,64] Non-adherent patients face adverse events and poor health outcomes that are avoided by adherent patients.[19] For example, non-adherence to anti-hypertensive medications can increase the risk of stroke by two folds.[65] Similarly, non-adherence to anti-diabetic medications can significantly increase the risk of cardiovascular and cerebrovascular complications.[63,66]

1.8. Determinants of non-adherence/ adherence barriers

When identifying adherence barriers, studies have shown that these barriers are interlinked. Accordingly, the reasons behind non-adherence are considered to be multifactorial.[31,67] In the 2003 report on adherence for chronic diseases, the WHO illustrated adherence as a multi-dimensional factorial model.[9] This model comprised of the five following constructs: 1) social and economic factors (which includes: poverty, low level of education, unemployment, and culture and lay beliefs about treatment and illness); 2) health-care team and system-related factors (which includes: poor health services, absence or poor financial support by health insurance plans, short duration of consultations, limited ability of the system to educate patients and offer follow-up, and absence of knowledge about adherence and of

effective interventions for enhancing it); 3) condition-related factors (which includes: symptoms, severity, progression of disease, and availability of effective treatment); 4) therapy-related factors (which includes: accessibility of the drug, side effects, drug regimen, frequent changes, treatment duration, and previous treatment failures); and 5) patient-related factors (which includes: forgetfulness to take medication, knowledge, beliefs, perception, and low self-efficacy).[9] Although the WHO model aims to include all possible determinants for non-adherence, it must be noted that some factors affect adherence in multiple ways. For instance, accessibility of medication can be assessed by the availability of the drug in a certain residential area; and it can also be assessed by whether the patient is able to afford purchasing that drug. Financial support systems, such as prescription medication cost coverage (PMCC), are important enablers that insure patients can afford purchasing the drug of interest.

1.9. Medication cost and non-adherence

Medication cost is one of the barriers that prevents medication adherence.[68-70] This has been shown repeatedly in the literature. For example, in one study, high medication cost was selected by 17% of the study population as the most common reason for non-adherence.[71] PMCC can help those who are non-adherent because of the high medication cost and can assist in overcoming the cost barrier. In a population of patients that had Medicare benefits (a US national social insurance program), 55.5% of patients did not fill at least one prescription medication because they "thought it would cost too much" and 20.2% of patients chose not to fill a prescription because the "medicine [was] not covered by insurance".[72] Notably, cardiovascular medications accounted for 18%, while endocrine/metabolic agents represented 7% of unfilled prescription medications in this study.[72] These studies suggest that relieving

chronic disease patients from their high medication cost can help prevent non-adherence and overcome the high medication cost barrier.

Canada's drug-related health problems due to non-adherence constitute around an average of 35% of medication spending.[73] This spending accounts for 140,000 hospital admissions and 35,000 deaths that occur every year due to non-adherence.[74] Moreover, with the increase of drug costs (at an annual rate of 9%), the estimated cost of non-adherence-which is following suit - is estimated to grow to a staggering $14 billion in Canada.[73-75]

1.10. Drug insurance coverage in Canada

Canada is the only developed country that has a universal health insurance system, yet it does not offer universal coverage for medications.[76] The *Canada Health Act* requires provinces to cover hospital, physician, and most medical laboratory testing services.[77] This universal coverage does not include prescription medication use outside of hospitals. PMCC is certainly a patchwork of federal and provincial effort to include populations viewed as most in need for PMCC.[78,79] The federal government covers the cost of prescription drugs for approximately 2% of the Canadian population including some Aboriginal populations, armed forces, Royal Canadian Mounted Police, veterans, and federal penitentiaries inmates.[80] Provinces therefore have developed different public PMCC plans for some groups of the population such as senior citizens, persons with low income and patients who face prescription medication costs that exceed a set percentage (for example 4%) of their household income. The latter discussed type of coverage is also known as catastrophic drug coverage.[81] Most Canadian employers, on the other hand, do offer various levels of private PMCC plans for medication

coverage for their employees.[80] Lastly, Canadians may opt to purchase their own private PMCC plan.

Because of medication coverage gaps within the Canadian population, it comes as no surprise that a significant number of Canadians do not have the needed support for cost coverage of their prescription medication.[82-84] It is estimated that about 66% of Canadian households address out-of-pocket expenses for their prescription medication.[37] In fact, when a cross-sectional study approach was used to determine the national proportion of cost-related non-adherence in Canada, about 1 in 10 people were found to have reported that their non-adherence was cost-related.[37] A similar study looked at only one chronic disease (HTN) in one year.[85] However, because answers to "cost" as reasons for not taking medication were too few, reliable estimates could not be produced.

Cost can be a barrier even with the availability of PMCC. In Quebec, thanks to provincial legislation, all residents are obligated to have PMCC.[86] The provincial insurance agency (Régie de l'Assurance Maladie du Québec or RAMQ) provides drug insurance to approximately 50% of Québec residents which includes seniors, social assistance recipients, and those without private PMCC plans.[86] The other 50% of residents have private PMCC insurance plans either because of their employment or they purchased PMCC independently. PMCC plans can either fully or partially cover drug costs. When partially covered, the patient pays part of the cost in the form of copayments. Though all residents have some kind of PMCC, a study showed that high medication copayment was still significantly associated with non-adherence.[62] Compared with those who do not pay for their prescription medication, there was a 37% increase in the odds of non-adherence among patients who had the maximum copayment.[62] As significant and useful

as these results were, they could not convey the actual prevalence and impact of the absence of PMCC for patients across Canada. Provincial law in Quebec is very different from the rest of the provinces in Canada and results could not be generalized across the population.

Chapter 2: The Literature Gap and Study Objectives

I found quite a number of published studies on PMCC-related non-adherence to medications.[64] Nevertheless, the obvious limitation observed was that most studies had looked at insurance coverage outside Canada. Even for studies carried out in Canada, researchers either focused on one province, or a particular year in time, or were not able to address insurance as a factor for non-adherence due to study limitations.[37,85,87-89] I was not able to find a recent study that had measured the time-trend and impact of PMCC on optimal adherence specifically to HTN and DM medications. Among all chronic diseases, HTN and DM are causing the most significant preventable cardiovascular outcomes in Canada; and optimizing the care for patients with those two disease states is a dire obligation for the whole nation. Accordingly, there is a need to address the trend of the PMCC impact on non-adherence in a representative sample of the general Canadian population who has HTN and DM. Thus, my research objective is to measure the time-trend and impact of the association between absence of PMCC and medication non-adherence in people with HTN and/or DM. It is carried out through a repeated cross-sectional study design.

The Canadian Pharmacists Association has called government and policy makers to assess evidence for gaining a clear understanding as to the reasons of financial barriers to optimal health outcomes.[90] Measuring the magnitude of association between PMCC and non-adherence will help us understand whether lacking insurance is causing a significant impact on Canadians and their medication adherence behaviour. Shedding light on this association in this way will quantify the burden of absence of PMCC on non-adherence to medications for HTN and DM. The study results can help policy makers and administrators in assessing the need for

action towards improvement of medication adherence. The results also distinguish the characteristics within the population most likely to be at a disadvantage from the lack of PMCC.[91]

Chapter 3: Methodology

3.1 Study Design

Repeated cross-sectional study design

3.2 Study aim / objective

To measure the trend and determinants of the association between absence of prescription medication cost coverage (PMCC) and non-adherence to oral HTN and DM medications among adults in Canada.

3.3 Hypothesis

The percentage of Canadians with PMCC has decreased over the study period and it is associated with a significant increase of non-adherence to oral HTN and DM medications.

3.4 Data Source

The Canadian Community Health Survey (CCHS) cycles 2007-2008, 2013, 2014 is the data source for this study.[92] CCHS is a cross-sectional survey of a representative sample of 12 years of age and older in all Canadian provinces and territories. The survey excludes populations living on reserves and other Aboriginal settlements in the provinces, full-time members of the Canadian Armed Forces, people that are placed in institutions, and persons living in the Inuit and Cree regions of Quebec (namely, Québec health regions of Région du Nunavik and Région des Terres-Cries-de-la-Baie-James).[92] Altogether, these excluded populations account for about less than 3% of the representative Canadian population. This survey targets the Canadian population at a sub-provincial level (by health region or combined

health regions) and collects information related to health statuses, determinants, and health care utilization. The CCHS collects data on an ongoing basis where one year corresponds to one cycle - and targets the Canadian population as a whole. The survey is collected each year during the months of January to December and can be referred to as a "cycle". Across two cycles, the collection is divided into 12 two-month collection periods. This facilitates the option of combining cycles. The CCHS collection years are combinable to facilitate examining the time trend.[92] Samples drawn constitute a representative number of households in the population.

Since the year 2007, the survey has been carried out annually instead of once every two years. Every year, a simple random sample of around 65,000 participants is selected across all Canadian provinces and territories. The sample collected comes from three different sample frames: 58.5% of the sample is selected from a frame of the list of telephone numbers, 40.5% is from an area frame, and 1% is from the Random Digit Dialling sampling frame. These respondents provide reliable estimates to the 110 health regions. The multi-stage sample allocation strategy carried out by CCHS treats relatively all health regions and provinces with equal importance.

There are three question content types in the CCHS questionnaire: core, optional and rapid response contents.[93] Core content questions target all provinces during every collection period. Optional content includes questions that are selectively chosen by some provinces to be provided to their residents that are included in the survey. Rapid response content questions are asked during a single collection period (which is two months) to the targeted study population as a whole across Canada.

3.5 Validity of CCHS

Multiple steps are taken to perform data validation in CCHS.[92] First, the CCHS team uses a validation program that compares estimates of the common content health indicators with that of the previous year. These estimates are taken at various geographic levels, in addition to using age and sex as estimates of comparison. Surveys which collect CCHS variables, other than Statistics Canada, are compared with CCHS results. The CCHS team searches for important differences between the surveys. This is done to check if there are any anomalies in the data. If the differences are significant, CCHS team investigates and documents the possible causes. Second, CCHS analysts look at many variables in-depth and publish analytical articles on specific themes carried out in the survey. In doing this, the analysts effectively identify errors in which variables may be holding. This practice increases the possibility of error detection and adds to the validation of the CCHS. Lastly, as an external validation measure, prior to release of the collected data, shared files are sent for a two-week review period to provincial and federal partners. These partners examine, scrutinize, and advise Statistics Canada on any concerns or abnormalities related to data quality.

The validity of CCHS survey answers related to oral DM and HTN prescription medications has been studied by cross-examining the self-response of participants with prescription claim databases.[94] Using Cohen's kappa coefficient as measure of agreement, answers for oral diabetic medication were found to have good to very good agreement [Kappa was found to be 0.79 in 2001; (95%CI 0.76-0.82) and 0.87 in 2005 (95%CI 0.85-0.89)] and that responses related to hypertension medication had a moderate agreement [Kappa was found to be 0.46 in 2001; (95%CI 0.43-0.48) and 0.55 in 2005 (95%CI 0.53-0.57)].[94] Other studies, mentioned previously

here, have supported the finding that self-reported adherence is a valid measure to use in surveys.[38-40]

3.6 Weighting in CCHS surveys

The weighting technique in CCHS ensures generalizability on a level from which the samples have originated. In other words, if a study sample with specific characteristics came from a province such as Ontario, then the inferences made from this study sample are generalizable and representative of people with similar characteristics in Ontario. The technique followed in weighting is a multi-step complex technique.[95] Sarafin *et al.* has reviewed this technique explicitly.[96] Households are selected according to the national prevalence of family size and age. For example, the prevalence of households with at least one "child" is 20% and therefore CCHS targets 20% of the households that have at least one child. To achieve this target, 7 steps are performed: 1. Removal of out-of-scope units that cannot be practically reached such as a demolished building or an institution, 2. Calculating household-level nonresponse weights within targeted population and redistributing those weights within the remaining population, 3. Combining the weights from the telephone and area sample frames and integrating them to avoid bias that might occur (this step is performed to avoid under-coverage of the telephone sample frame), 4. Adjusting the household-level weights are adjusted using the inverse person-level selection probabilities for calculating person-level weights based on household size and age of household members,[95] 5. The interview process occurs in two steps. First, the interviewer contacts the household to complete the list of household's members. Then, one person is selected for the interview and is contacted. If the person selected refuses to be interviewed, person-level nonresponse adjustment is carried out.

This is when the fifth step for adjusting person-level weight comes in. Person-level nonresponse is treated the same way as household-level nonresponse in step number two, 6. Reducing variance of the estimates by 'Winsorization'.[97] Because weighting is carried out through multiple steps, some units end up with extreme weights. While potentially introducing a small bias, Winsorization reduces the variance estimates as a correction measure by applying lower weight values to outliers, and 7. Calibration to confirm the final weights' total, indicating the population estimates that were initially defined at the household response level. The resulted weights of these steps are used to produce a representative sample of males and females within the age groups of the population. Variances in CCHS estimates are calculated using the bootstrapping method.[98] Bootstrapping is: "a technique for estimating the variance and bias of an estimated parameter by repeatedly drawing random samples with replacement from the observations at hand, with the resamples having the same size as the original sample". [99] For higher accuracy in this study, results were produced using bootstrap weights. Please see the CCHS user guides for further information on the weighting strategy.[92,93,100-102]

3.7 Rationale for choice of survey

In comparison to other available surveys that are similarly health-oriented, the CCHS is unique because it has a specific set of questions that are of interest for my study. Additionally, CCHS is carried out annually. To the best of my knowledge, of all the surveys available at the Research Data Centre (RDC) at the University of Waterloo, only the Joint Canada/United States Survey of Health[103] contains very similar questions that are of interest.[104] However, this particular survey was only carried out once in 2004 and was a joint study with the US targeting a smaller number of Canadian participants in the sample.

3.8 Cycle year selection

The sample was drawn from 260,269 respondents that were included in cycles 2007-2008, 2013, and 2014.The availability of the medication cost coverage question (which was an optional content question) was the main reason for choosing each cycle year. Therefore, to facilitate comparison across the years, provinces had to include the optional content PMCC question in their survey across at least two years. Ontario and New Brunswick were chosen because these provinces included the PMCC question and over several cycle years.

3.9 Study participants

Respondents were included in this study if they were 18 years of age or older on the date of the survey, had DM type II (DM II), or HTN, and have answered the questions about oral medication use and PMCC status. Excluded participants were either those who were pregnant upon diagnosis with HTN or DM II, had Alzheimer's disease, had incomplete data about having HTN or having DM II or the status of their prescription medication cost coverage.[100,105]

3.10 Exposure assessment:

Exposure is the status of not having any kind of PMCC that paid all or part of the cost of respondents' medications. This was assessed using the question: "Do you have insurance that covers all or part of the cost of your prescription medications?"

3.11 Outcome assessment:

The outcome is adherence to HTN and DM II medications. Adherence to medication was assessed using the following question for HTN "In the past month, have you taken any medicine for your high blood pressure?" for respondents who have HTN only. Respondents who

answered “No” to this question were considered to be non-adherent. The question for DM was “In the past month, did you take pills to control your blood sugar?”, asked to respondents who have DM only. Respondents who answered “No” to this question were considered to be non-adherent. For respondents who had both HTN and DM, answering at least one of the two questions with “no” was considered as non-adherence. To examine the robustness of this consideration among respondents with HTN and DM, I performed a sensitivity analysis by requiring the answer to both questions with “no” to consider the respondent as non-adherent.

3.12 Confounders and Effect modifiers

Factors that were considered as confounding variables were chosen based on the discussed WHO’s theoretical framework that conceptualized five main adherence domains.[9] Twenty-four variables available in the CCHS survey were examined for inclusion in the model as confounders. **Error! Not a valid bookmark self-reference.** shows the definition of each variable and the corresponding CCHS coding considered for addition in the model.

These variables were available for all participants regardless which year the respondent participated in and regardless of the respondent’s background. Therefore, questions that were not applicable to be asked to some respondents were not included as confounders in the model as they were not available for all participants.

Table 1 CCHS variables that were considered in building the final model.

Definition	Variable Code
Social and economic factors	
Derived variable for education level	EDUDR04
General health perception	GEN_01
Distribution of household income - National level (quintiles)	INCDRCA
Main source of Household income	INC_2
Health-care team and system-related factors	
Year	_
Province	GEO_PRV
Having a regular doctor	HCU_1AA
Condition-related factors	
Cardiovascular Disease (stroke, heart disease)	CCC_121, CCC_151, both
Hypertension, DM, both	CCC_073, CCC_101, both
Therapy-related factors	
Asthma	CCC_031
Arthritis (arthritis, excluding fibromyalgia)	CCC_051
Back Problems	CCC_061
Migraine	CCC_081
Cancer	CCC_031, CCC_031A
Gastrointestinal: ulcer or have a bowel disorder such as Crohn's Disease, ulcerative colitis, Irritable Bowel	CCC_171, CCC_141
Syndrome or bowel incontinence	CCC_280, CCC_290
Patient-related factors	
Age	DHH_AGE
SEX	DHH_SEX
Number of chronic diseases	CCC_073 or CCC_101, or both
Race	SDC_
Smoking status: derived variable	SMKDSTY
Alcohol consumption: derived variable	ALCDTTM
Staying overnight in hospital, nursing home or convalescent home	HCU_01 (in 2007-2008) or CHP_01 (in 2013-2014)
Has taken flu shot	FLU_160

Model building was done following the forward method. I performed the likelihood ratio test on each variable added to assess the model's goodness of fit. Some variables, such as province, year, household income, were forced into the model to control for potential confounding imposed by geographical, time, and income factors. Other variables were excluded if they did not maximize the log-likelihood function of the full model compared to the current model.

3.13 Statistical Analyses

Data from included respondents were stratified according to PMCC status to respondents with or without PMCC. The descriptive statistics of the differences in characteristics of these two groups were assessed using Chi-square test of univariate analysis of significance on all bootstrapped weighted and unweighted variables of interest and t-test for continuous variables. Then, a bootstrapped weighted multivariate logistic model was constructed following the stepwise forward selection method approach. All variables of interest were categorical variables. The variables were constructed using the CCHS's data dictionaries as well as the CCHS's Annual Component of Derived Variable (DV) Specifications.[93,100,101,106,107] I could not use the derived variable constructed by CCHS to identify DM type I and DM type II. This is because I was including cycle years before the time CCHS had constructed these derived variables. Instead, I followed the same algorithm CCHS had used to derive respondents with type I and type II.[108]

To use total household income as a potential confounder, it was important to include a variable that accounted for change in time since the monetary value over time certainly would not have remained the same across the 7 years. Therefore, I used the imputed and derived

national level deciles variable which provides a relative measure of respondent's household income to the household income of all other respondents, and is adjusted each year based on the consumer product index.[100,109,110] The derived variable is produced in three steps. First, the low income cut-offs for each respondent's family and community size is determined using the Survey of Labour and income.[100] Second, individual ratios of reported or imputed household income to the low income cut-off -corresponding to respondent's household and community size- are caluclated.[100] Then, each respondent's ratio is assigned a decile within the whole national data of ration.[100] I collapsed each consecutive decile to form a quintile, in order to simplify statistical analyses and inferences. For example decile 1, which is the lowest 10% of household incomes, was combined with decile 2, the second 10%, to form the 1st 20% level of lowest household income amongst 4 other quintiles.

The year of survey variable consisted of 2007 to 2008 (combined), 2013, and 2014. While New Brunswick included the PMCC question in all years, Ontario only included the PMCC question starting 2008. Therefore, since 2007 only included respondents from New Brunswick, I combined years 2007 and 2008 to have a sample size that is comparable to 2013 and 2014.

It is common and feasible to combine CCHS cycles; and the risk of participants' re-inclusion is low.[111] To protect participants' confidentiality, identifying respondents across the years to remove any possible re-inclusion of an individual is not allowed. However, CCHS does not include respondents more than once over a period of five years.[95] Since I was including cycles that span over seven years, the CCHS focal point and CCHS subject matter experts from Statistics Canada addressed my concern of possible re-inclusion, by responding that "The likelihood of an individual being a respondent in more than one cycle is very low" and that "The

CCHS does not have an estimate of the proportion of respondents in the annual files who have previously been a respondent to the CCHS annual component" and that “this proportion could be higher in rural low-density areas and lower in urban high-density areas”. This confirms that re-inclusion of individuals will not be a significant concern in this study.

A P-value less than 0.05 was considered statistically significant in the analysis. Variables that were significant in the univariate analyses tests were retained in the final model if they were significant in the likelihood ratio test (using Wald’s t-test); and increased the fitness of the model as assessed by the Akaike information criterion. Year of survey, province of residence, and total household income, regardless of statistical significance, were forced into the model to account for geographical differences, policy differences in PMCC in the two provinces, as well as if any policy change had occurred over time.

To test for potential effect modifiers, interaction terms were introduced in the model. Age, sex, income, and cancer (i.e. diagnosed with cancer or previously had cancer) variables were tested for effect modification.[112,113] Additionally, testing for effect modification was also done by stratifying the study group by age, sex, income, and cancer and comparing the odds ratios (ORs) to the overall model.

Multicollinearity, between variables included in the final model, was tested using Spearman’s rank correlation coefficient.[114] This method, unlike the Variance inflation factor, can be used to measure collinearity between independent variables that are not only binary but also for multi-level ordinal variables. Spearman’s rank correlation coefficient, unlike Pearson’s r-correlation, is able to measure collinearity when variables may not necessarily have a linear relationship but rather a non-parametric one. The cutoff I used was more than 0.7.[115]

SAS®, version 9.4 (SAS Institute Inc, Cary, NC) was used to perform the statistical analysis. Main model outputs of point estimates and ORs were compared using STATA® version 14. The results were exact to the hundredth decimal point in both statistical programs.

3.14 Missingness in data

Because the pattern of missingness was arbitrary, I followed the Fully Conditional Specification method (FCS) available in SAS®.[116] The FCS method provides the possibility to factor in the complex sample selection design of strata and clusters. However, due to confidentiality reasons, analysts using the CCHS data are blinded from obtaining these strata and clusters of which the CCHS randomly selected the sample from. Instead, we are provided with bootstrap weights that are generated 500 times with replacement. To overcome this limitation, I was able to apply the bootstrap weights the CCHS has provided us with, instead of the strata and clusters needed for the FCS procedure. I confirmed the robustness of my method with a specialist from the Data Analysis Resource Centre at Statistics Canada who confirmed that my proposed procedure was reasonable provided that the imputation is capturing the variability due to imputation, which it did.

Chapter 4: Results

4.1 Study sample:

The steps of extracting the sample are illustrated in Figure 5 (unweighted) and Figure 6 (weighted) that are available in Appendix A. The unweighted study population consisted of 23,215 participants. The weighted bootstrapped total number of participants was equal to 8,696,520.

4.2 Descriptive statistics

Table 12 and Table 13 (Appendix B) describe the characteristics among those with and without PMCC. Almost one third (31.2%) of participants were from years 2007-2008 while years, 2013 and 2014, consisted of 34.3% and 34.4% of the total participant population respectively. Over half of the study population were female (51%), and 48% were 65 years of age or older. The full descriptive statistic results are provided in Table 12 and Table 13. Over the study period, the characteristics of respondents were similar. Figure 7 (Appendix B) illustrates the time-trend of respondents demographics. Figure 7 shows the trend of the percentage of people with both HT and DM over the study period. The prevalence of DM and HTN and people with both HT and DM increased over time.

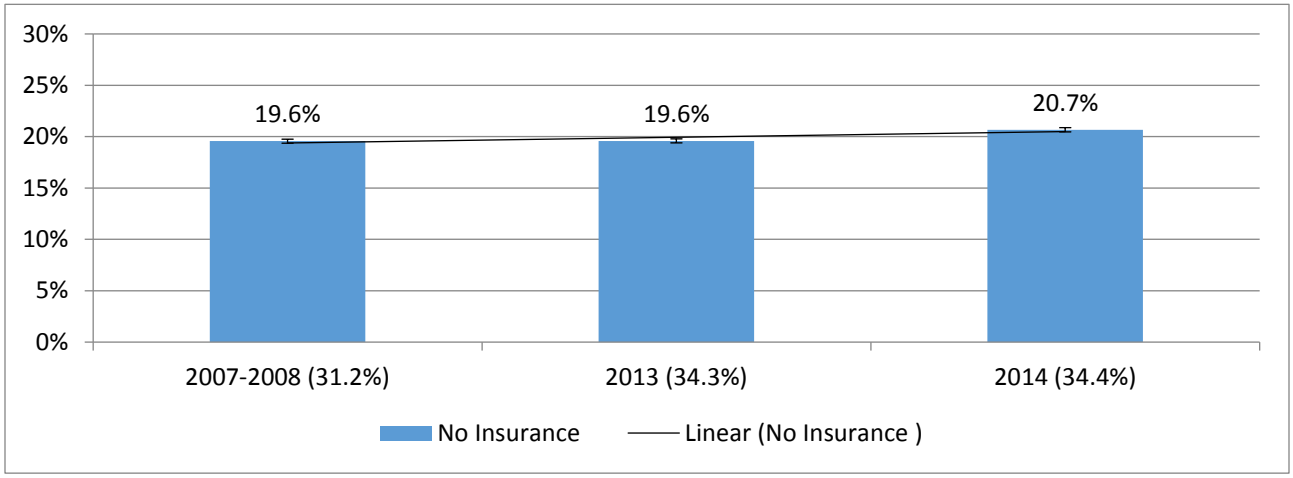
Overall, 20% of the study population indicated that they did not have any drug insurance that covered all or part of the cost of their prescription medication. The majority without insurance were middle aged (45-64) and this percentage increased slightly over the study period by 0.8%. Mainly, 28% of Canadians were non-adherent to either DM or HTN oral

medication. Specifically, 34.6% of those who do not have insurance were non-adherent while 22.6% of those who have insurance were non-adherent.

4.3 Time trend

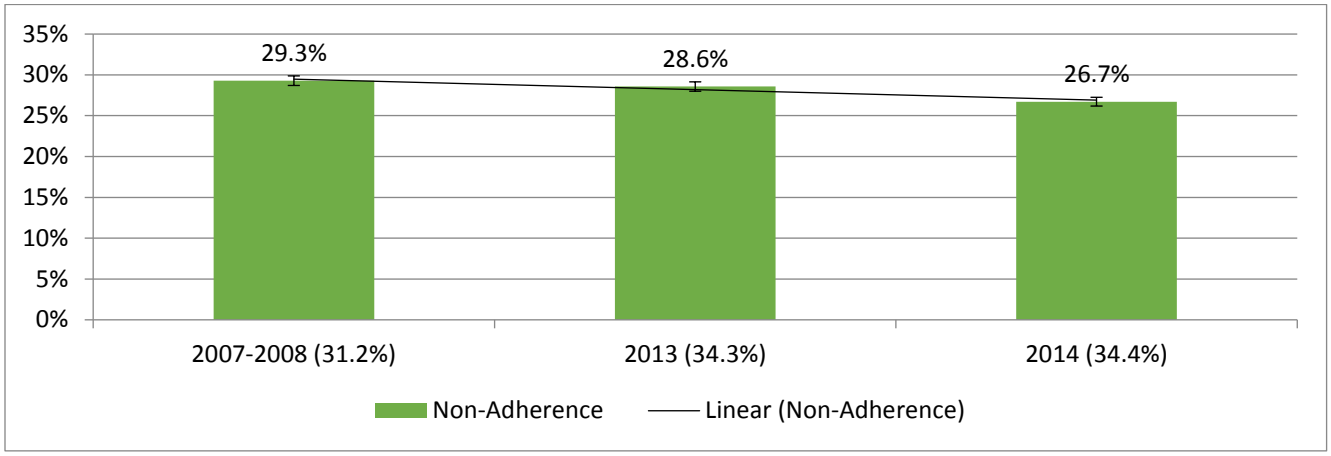
Overtime, the proportion of the participants who do not have PMCC increased slightly. When comparing between years 2007-2008 and year 2013, the proportion of people without insurance did not change (19.6%). However, this percentage increased slightly by 5% (or 1% in absolute terms) to 20.7% in 2014 [**Figure 1].**

Figure 1: Weighted percentage of Canadians who do not have medication insurance from 2007 to 2014



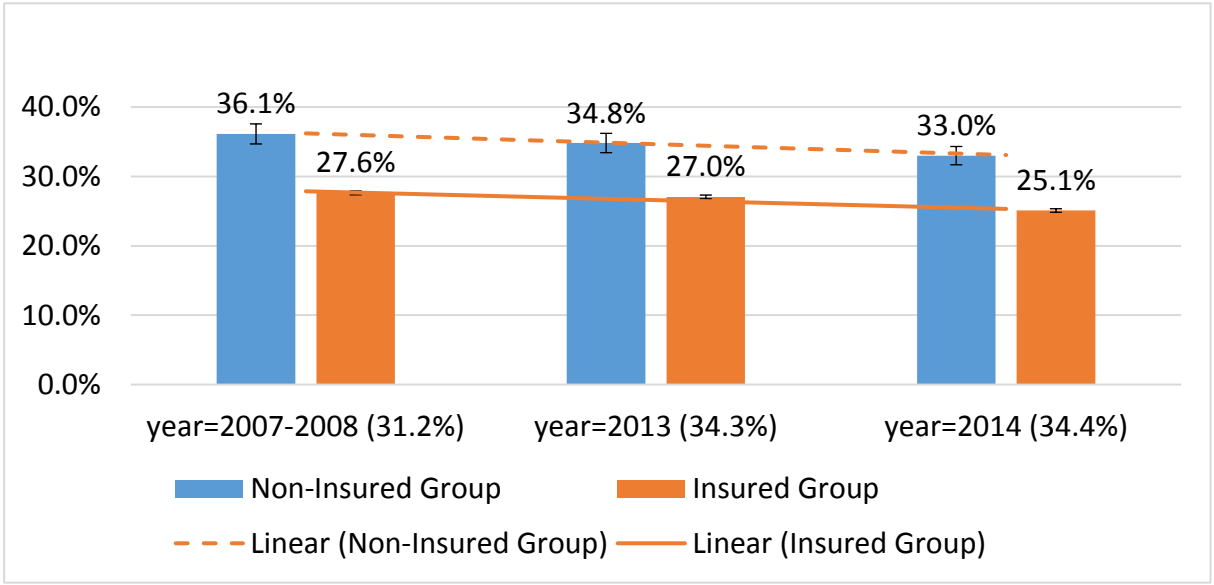
Overall, the percentage of non-adherent patients decreased significantly by 8.9% (or 2.6% in absolute terms) over the study period from 29.3% to 26.7% (**Figure 2**).

Figure 2 Weighted percentage of Canadians who are not adherent to oral medications of either diabetes or hypertension from 2007 to 2014



While the percentage of non-adherence decreased across all groups (with or without PMCC) by 8.9%, those without insurance, showed less profound improvement in their adherence (8.3%) compared to those who had insurance (10.8%) (***Figure 3***).

Figure 3: Weighted percentage of Canadians who are not adherent to oral medications of either diabetes or hypertension stratified by PMCC from 2007 to 2014



When expressing the association between PMCC and adherence in absolute risk reduction (ARR) term (the difference between the percentage of non-adherent cases of the PMCC group from the percentage of non-adherent cases of the control group), the impact of PMCC on adherence did not change over the study years and remained at 8% (**Table 2**). The relative risk reduction (RRR) (that is ARR divided by baseline adherence rate), also did not substantially change over the years. The number needed to treat (NNT) (i.e. the number needed to provide insurance to in order to avoid one case of non-adherence-assuming a causation relationship does exist) was 13 (**Table 2**).

Table 2 Relative, absolute risk reduction and numbers needed to treat (with providing insurance) for each year.

Year	Absolute Risk Reduction (ARR)	Relative Risk Reduction (RRR)	Numbers Needed to treat (NNT)
2007-2008	8%	13%	13
2013	8%	12%	13
2014	8%	12%	13

4.4 Model Building

The final number of confounding variables included in the model was twelve and included: Respondents' socio-demographic characteristics (age, sex, household income, and respondent's highest acquired level of education), condition and therapy related factors (diagnosed with cancer or having suffered previously from cancer, had a cardiovascular disease such as stroke or heart disease or had either HTN or DM or both, other CDs could not be used in the final model due to inconsistencies of data availability, statistical non-significance, or non-improvement when testing for goodness of fit and because my observational study measured self-reported responses, respondents with dementia were excluded to avoid jeopardizing the

integrity of responses, as these responses depended on memory) patient-related factors (smoking status and flu shot usage), and health care resource use (had a regular medical doctor, the province of residence, and the year the survey was taken).[37,117-119] Four variables were ordinal including: education attainment (less than secondary school, secondary school, and post-secondary), year of survey (2007-2008, 2013, and 2014), age (18-29, 30-44, 45-64, and 65 and above), and household income (quintiles of income within the whole population). The remaining nine variables were binary. Correlation between all variables of interest was well below 0.7.

4.5 Multivariate logistic regression

Participants who did not have insurance had an estimated crude odds ratio (OR) of 0.69 for adherence to either DM or HTN oral medications, compared to those who did have insurance. After adjusting for possible confounding factors, the odds of adherence increased to 0.77. The OR estimates along with corresponding 95% Confidence Intervals (95%CI) both from the crude and full model outputs are illustrated in **Table 3**. The full model output is illustrated in Table 14 in Appendix C.

Table 3: Odds ratios of adherence among people without insurance vs. people with insurance in crude and full models

Model	Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
			Lower	Upper
Crude Model	**No Insurance vs. Insurance**	0.685	0.589	0.796
Full Model		0.774	0.657	0.911

4.6 Testing for effect modification

In comparison to the full model, the model fitness did not increase substantially when the interaction terms were introduced (table 4). The results of both effect-modification analyses (introducing interaction terms and performing stratified analysis) are displayed in Table 5. When the interaction between insurance and age, insurance and sex, insurance and cancer, and insurance and income were added, the OR remained around 0.7 (**Table 5**).

Table 4 Model Fit Statistics

Testing for Effect Modification		**Parameter Effect**	**Intercept and Covariates**	**Difference (interaction – Full model)**	**Association of Predicted Probabilities and Observed Responses C-statistic**
			-2 Log L		
Full model		No Insurance vs. Insurance	9086069		0.692
Interaction	Insurance * Age		9084605	-1463.9	0.691
	Insurance *Sex		9086068	-0.7	0.691
	Insurance *Cancer		9085539	-530	0.691
	Insurance * Income		9083968.3	-2100.7	0.691

When stratifying the analysis by age, absence of PMCC showed higher OR for adherence among older individuals (≥65) compared to younger individuals (<65) and people with no cancer compared to those who had a history of the disease. Stratification by sex or income, on the other hand, did not change significantly the association between PMCC and adherence [Table 5].

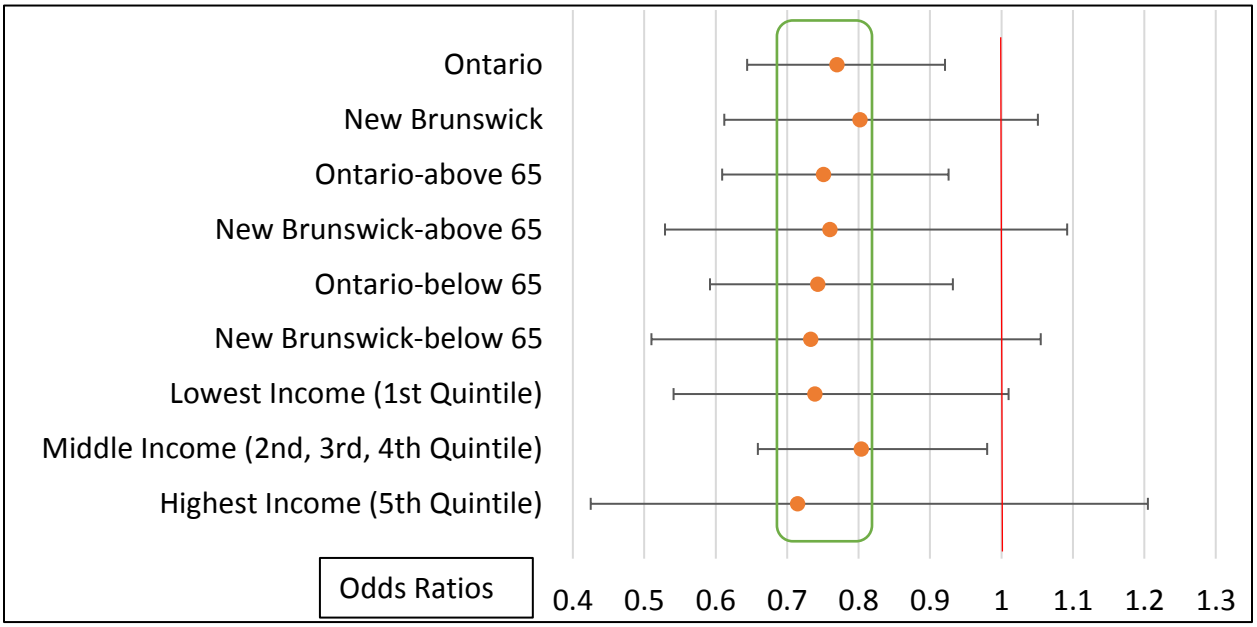
Table 5 Results for testing variables age, sex, cancer and income as potential effect modifiers.

Testing for Effect Modification			Parameter Effect	Odds Ratio Point Estimates	95% Wald Confidence Limits	
					Lower	Upper
Full model			No Insurance vs. Insurance	0.774	0.657	0.911
Introducing interaction term	Insurance * Age			0.692	0.636	1.743
	Insurance *Sex			0.771	0.883	0.995
	Insurance *Cancer			0.683	0.790	1.105
	Insurance * Income			0.785	0.849	1.096
Stratified analysis	By age	≥65		0.870	0.705	1.073
		< 65		0.751	0.620	0.910
	By Sex	Males		0.769	0.596	0.991
		Females		0.763	0.617	0.945
	By Cancer	Cancer		0.661	0.402	1.085
		No Cancer		0.789	0.666	0.936
	Income	Low Income		0.739	0.541	1.01
		Middle and high income		0.782	0.653	0.936

4.7 Subgroup Analyses

The subgroups analyses yielded ORs for adherence ranging from 0.7-0.8 as shown below in **Figure 4**. This figure illustrates the ORs (in orange dots) of adherence when PMCC is absent. Each orange dot represents the estimation point of the OR of each subgroup analysis carried out-along with corresponding 95%CI. The association between insurance and adherence did not change significantly when patients who shared the same province of residence, same age group, or both province and age were analyzed separately.

Figure 4: Odds Ratios of Adherence with No PMCC in Subgroups with 95% Confidence Intervals.



Additionally**, Figure 9 and Table 15 in** Appendix D illustrate the OR estimates of adherence when PMCC is not present in further subgroups tested. Interestingly, no PMCC among high-income patients in New Brunswick who are less than 65 years of age increased the odds for adherence by 12% (i.e. no PMCC had a protective effect) as compared to those who had PMCC-albeit this association was not significant (**Table 15**). Similarly, no PMCC showed a protective effect among patients who have been using insulin for 10 years or more, where the OR for non-adherence was 1.09 (95%CI 0.62 to 1.94) (**Table 15**). On the other hand, the OR of the association between PMCC and adherence in patients who have been using insulin along with their oral anti-diabetic for less than 10 years was 0.5, (95% CI 0.16 to 1.52). When I performed subgroup analyses depending on having DM only, HTN only, and both HTN and DM, the association between not having insurance and adherence was the most profound among

patients who had only HTN (OR=0.72, 95%CI 0.59 to 0.88) and was not significant among patients with DM only or with both HTN and DM (Table 6).

Table 6 Subgroup analysis for DM only, HTN only, and DM&HTN together

Number of participants	Subgroup	Parameter Effect	Odds Ratio	95% Wald Confidence Limits	
1735	DM only	No Insurance vs. Insurance	0.908	0.539	1.529
17084	HTN only		0.721	0.592	0.878
4396	HTN with DM		0.999	0.726	1.374

Among Ontarians who were 65 years of age or older, the estimated OR of adherence with not having PMCC for this subgroup was 0.75 (95%CI 0.61 to 0.93). Remarkably, 17.1% (n=1819) of those patients answered “no” to having PMCC, in spite of having an automatic PMCC through the Ontario provincial plan.[120] Those patients represent 6.2% of the total study population who were classified to having no PMCC. In Ontario, once a resident turns 65, they become automatically covered by the Ontario Drug Benefit plan.[120] According to their income status, they may be exempted from paying the $100 annual deductible.[120] Additionally, should their household circumstances meet the criteria and their income is below the specified amount, the co-payment for every prescription that they receive is reduced from $6.11 to $2.00.[120] As for people from New Brunswick, I was not able to quantify the potential misclassification since New Brunswick's drug coverage plan is quite different from that of Ontario's. In New Brunswick, seniors that turn 65 years or are older have a 60 days notice which they receive through the mail that they have to apply for to obtain provincial coverage for prescription medication.[121] This provincial coverage strictly depends upon income status. Those meeting the conditions, do not have a deductible but have a copayment of $9.05 for each

prescription, which is capped up to an annual of $500 of prescription co-payments.[122] Those that do not meet the low-income criteria have the option to purchase a premium through the province.[122] This type of premium is also strictly dependent upon their gross annual income and number of household members.[122] The premiums and copayments increase with increasing gross income levels and is different for individuals and couples with or without children.[122] I was not able to find previous literature that tried to estimate the number of patients who access provincial prescription plans in New Brunswick.

A subgroup analysis was carried out for those who had PMCC (**Table 7**), depending on the type of insurance. The type of insurance did not impact significantly adherence to DM and HTN medications. The OR for those who had employer or private insurance versus governmental insurance was found to be 1.10 (95%CI 0.91 to 1.32). On the other hand, having more than one plan was associated with better adherence. Those who had more than one type of insurance had higher odds of adherence (OR=1.44, 95%CI 1.12 to 1.86) as compared with having only governmental insurance.

Table 7:Odds Ratios of Adherence with Insurance type among insurance subgroup in 95% Confidence Intervals.

Subgroups	Odds Ratio Estimates	95% Wald Confidence Limits	
Employer/Private vs. Governmental insurance	1.095	0.908	1.319
Mixed plans (more than 1 type) vs. Governmental insurance	1.442	1.117	1.862

4.8 Sensitivity analyses

Unlike the main analysis, where participants who had both HTN and DM had to have answered yes to both medications to be classified as adherent, I carried out sensitivity analyses with four different scenarios to consider participants as adherent to test the robustness of my definition of adherence (Models #2-5, **Table 8**). None of the sensitivity analysis caused a large change in the OR in all of the studied scenarios.[123]

Table 8 Comparison of four different adherence definition scenarios to the main analysis, when patients have both HTN and DM

Model #	Criteria when having both HTN and DM	Parameter Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
1: Main analysis	Adherent if response to both medications = yes	No Insurance vs. Insurance	0.774	0.657	0.911
2	Adherent if response to either medication = yes.		0.739	0.618	0.883
3	Adherent if answered yes to at least one medication. It is allowed for the other medication's answer to be: "don't know/ missing".		0.773	0.656	0.911
4	Adherent if answered yes to at least one medication. It is allowed for the other disease's answer to be: "no/don't know/ missing".		0.738	0.616	0.883
5	Patient was considered non-adherent, if the answer was confirmed to be "no" to adherence question. Patients were only considered to be non-adherent if responded no to the first disease and don't have the other disease; or if they answered "no" to both.		0.736	0.615	0.881

I carried out sensitivity analyses by changing the answer of Ontario seniors and all seniors, and the odds did not shift substantially. The results of this analysis are illustrated in Table 9.

Table 9 Sensitivity Analyses for changing senior's response to having insurance

Number of participant included	Criteria	Parameter Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
23215	Full model from main analysis	No Insurance vs. Insurance	0.774	0.657	0.911
23215	Assuming all senior Ontarians have insurance		0.744	0.609	0.908
23215	Assuming all seniors have insurance		0.743	0.604	0.914

Misclassification of DM type I patients as type II was suspected when some diabetic participants were found to be using insulin early on in their lives, at a very young age, but also answered questions about adherence to their oral medication. I observed that all participants who have answered “yes” to having diabetes, were provided with the question for adhering to oral medication for diabetes, and the question was not restricted to those who had DM type II. Statistics Canada’s algorithm that aimed to differentiate DM type II from type I, classified respondents who have answered “yes” to adhering to oral anti-diabetic medications as being type II. Though, evidently, some type I individuals seemed to have answered “yes” to adhering to oral medications. Thus, this may have been the reason for some patients with DM type I to be included in the study. This misclassification was found to affect 1% (289) of the study population. I performed sensitivity analyses by removing those diagnosed with DM at an age

less than 30. Estimated ORs were very similar after the removal of those patients, when compared to the main analysis. Table 10 shows the odds before and after this removal.

Table 10 Sensitivity analyses for removing suspicious DM type I participants

Number of participant included	Criteria	Parameter Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
23215	Full model of the main analysis	No Insurance vs. Insurance	0.774	0.657	0.911
22987	After removing patients who were diagnosed with DM at age less than 30		0.784	0.664	0.926
1735	DM respondents only		0.908	0.539	1.529
1641	DM participants after removing those diagnosed at age less than 30		0.914	0.537	1.558

4.9 Handling Missingness in Data

About 5% (1,153) of respondents had missingness in one or more covariate-other than the exposure and outcome. I managed missingness in the data by implementing three strategies. First, in the main analysis, since missingness in the data did not exceed 5%, I concluded that the size of missingness was small to a relatively large sample size, I followed the educated-guessing approach as the form of imputation of any missing data.[124] Hence, when a variable had a missing value, I assumed that the answer to this question was "no" (i.e. variable value=0). For example, for those who did not answer the smoking status question, the initial assumption was that they were non-smokers. When the variable was multileveled, I assumed that the missing value was the lowest value. For example, for missing education level, I

assumed the participant had the lowest level of education achievable. By not following the mean/modal imputation approach (that is choosing to replace missing values according to the modal category), I was able to avoid this recently un-preferred approach as it has gained a growing concern for its cause of reduction of data variablility.[125]

Second, I managed missingness by removing participants with missing value in at least one variable. In this case, the OR produced did not differ substantially (0.77, 95%CI 0.60 to 0.99) as compared to the main analysis (0.77, 95%CI 0.66 to 0.91). The results before and after the removal of missing values are displayed in Table 11. Third, I carried out 5 multiple imputations by fitting a logistic regression to predict the missing variable's value by using all other covariates (Models #3 to 7,Table 11) following the assumption that missingness occurred at random. The 5 different imputations in Table 11 produced very similar ORs to the main analysis (Model #1).

Table 11: Missingness Diagnostics

Model #	Criteria	Parameter Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
1: Main analysis	Initial Assumption for missingness to apply lowest level	No Insurance vs. Insurance	0.774	0.657	0.911
2	Removing missing data- (1212 observations were removed)		0.769	0.596	0.991
3	Imputation Number=1		0.777	0.659	0.915
4	Imputation Number=2		0.777	0.660	0.915
5	Imputation Number=3		0.775	0.658	0.913
6	Imputation Number=4		0.776	0.659	0.914
7	Imputation Number=5		0.773	0.656	0.910

Chapter 5:

5.1 Discussion

Over the study period, the percentage of participants without PMCC in Canada increased slightly from 19.6% in 2007-2008 to 20.7% in 2014. Absence of PMCC is associated with 23% relative decrease in adherence to oral DM and HTN medications in comparison to those who had PMCC (OR 0.77, 95%CI 0.66 to 0.91). Correspondingly, the absence of PMCC is associated with an 8% absolute decrease in adherence to oral DM and HTN medications. This means that with assuming a causation relationship, providing PMCC to 13 patients, may help in preventing one case of non-adherence. In a subgroup analysis, for those who had PMCC, I found that having more than one type of insurance increases the odds of adherence.

The percentage increase of 1% in the absence of PMCC represents a substantial number of Canadians without insurance. Numerically speaking, if we were to extrapolate these findings in 2016, a 1% increase would mean that around 360,000 additional Canadians are without PMCC. According to reports on National Health Expenditure Trends reported by the Canadian Institute for Health Information (CIHI), the percentage of out-of-pocket costs for drug expenditures increased from 33% in 2007 to 39.6% in 2012.[126-128] Absence of PMCC in my study may explain some of the increase in out-of-pocket expenditure of medications in Canada observed in the CIHI study.

PMCC in Canada is closely related to the economy.[129] A study found that over the time-period between 1997 and 2009, Canadians were facing increasing out-of-pocket expenses.[129] Additionally, the first and second lowest household income quintiles were found to have higher

out-of-pocket expenses in comparison to the remaining quintiles (that is third, fourth, and fifth household income quintiles). In my study, almost one half (47%) of the study population came from the first and second lowest household income quintiles; and hence absence of PMCC, that is more profound among this strata of the population, may explain the increase in non-adherence over time. It can be speculated that the economic crises of 2008, which was associated with increased unemployment rates, has caused this increase in the absence of PMCC percentage. Additionally, with the changing economic landscape post-crisis, employer-offered medication insurance may have been restricted to a lower number of employees, with a less-generous coverage, by comparison to the pre-2008 era.

Previous research has shown that financial burden is a major obstacle that prevents patients from adhering to their medications.[130] My study demonstrated that absence of PMCC is associated with a significant proportion of non-adherence to specifically two of the most devastating chronic diseases (i.e. DM and HT), even after controlling for all other patient, disease and health-care system characteristics. The results of my study provide the empirical evidence that offering PMCC to Canadians is essential to help more patients adhere to their medications. This would be far overarching important results for public health in Canada and would potentially lead to cost-saving for the Canadian health care system.[76]

My study's results also showed that having a cardiovascular disease (heart disease or stroke) is associated with higher odds of adherence, in comparison to those who do not have this comorbidity.[131] This finding agrees with previous research which indicates that those who have comorbidities have a higher probability of adhering to their medication.[132] Patients who suffer from multiple CDs usually see more health care professionals and have a higher

realization of the devastating consequences of their diseases.[132] This may partly explain the results of my studies. On the other hand, respondents with a history of cancer or those with both HTN and DM showed lower odds for adherence. According to previous research, cancer survivors and hypertensive people with comorbidities show lower rates of adherence.[133,134] It seems that different comorbidities are associated with adherence differently, where some may decrease the odds of adherence such as having a history of cancer, or having both DM and HT; while others increase the odds such as suffering from stroke or heart disease. This should raise concerns that some, but not all comorbidities, may reduce adherence.

My results showed a significant improvement in adherence to DM and HTN medications. This is consistent with the significant improvement of medication adherence that was noted over time in the literature - both among new users and prevalent users.[135] For example, a large study included 33,646 patients that were discharged post-myocardial infarction. Over the eight-year study period (1995-2003), adherence rate increased from 38.6% in 1995 to 56.2% in 2003 amongst those who were prescribed statins (p value <0.001).[135] This improvement can be explained in two ways. First, we have an aging population in Canada; and studies have shown that older people are more adherent to medication than younger counterparts.[119] In fact, in my model, increased age was associated with increased odds of adherence. Second, aside from aging, there is an increase in chronic disease burden in the Canadian population which is generally associated with the increase of adherence over time.[136] My study has shown that people who had cardiovascular diseases (such as heart disease or stroke) were at higher odds for adhering to their medication. Thus, the increase in age and CD burden over time may then explain increased adherence.

Lack of PMCC may have deprived patients from taking full advantage of this phenomenon of improving adherence across patients groups. In my study, although there was a trend of improvement of adherence over time, the extent of improvement amongst those uninsured may have been hindered because of absence of insurance. Thus, those without insurance were at a lower advantage for adhering to their medication.[137] This was confirmed when I carried out the subgroup analysis for those who had PMCC. Here, I found that having two types of insurance, as compared to one type, increased the odds for adherence. This confirms a dose-response or exposure-response relationship. That is, an increase in insurance coverage increases the odds for adherence.

5.2 Advantages and strengths of Study

A repeated cross-sectional study method for answering the question of interest is of advantage over other designs.[138] First, the design provides a valuable glimpse of the real-world association between no PMCC and adherence in the Canadian population with DM II and HTN at multiple points in time. Second, this design also provides a clear examination of the time-trend of the impact of lack of PMCC on medication adherence to two of the most important chronic diseases in Canada. And third, this study examines a relatively large sample that is representative of the Canadian population.

5.3 Limitations

In addition to the fundamental limitations of observational studies, several specific limitations can be noted in my study. First, a misclassification occurred when senior Ontarians denied having PMCC, in spite of the fact that, in Ontario, PMCC for seniors is automatic and

activated upon showing a valid health card to the pharmacy while picking up prescription medication after a patient's 65th birthday. Due to the presence of a deductible in Ontario, a misunderstanding may have occurred, in which some study participants may have not considered this kind of insurance as PMCC.[139] Because my results did not change when this group was removed, it seems that seniors with the wrong perception of not having insurance when they are clearly eligible are at the same risk of non-adherence. Thus, misperception about PMCC is comparable to not having PMCC and is associated with non-adherence. A previous study published in Statistics Canada's Health Report Catalogue, found that 49% of seniors in 1996/1997 did not report acquiring PMCC when being surveyed, although they were eligible for provincial benefits.[139] The study also found that provinces that did not impose deductibles were less likely to underreport their insurance status.[139] In my study, this percentage was not substantial (6.8% of eligible Ontarians) and numerous subgroup analyses were carried out to quantify the odds of adherence in the absence of PMCC while controlling for age. A similar argument can be put forward for seniors in New Brunswick, regardless of the difference in coverage in that province.

Another unavoidable misclassification may be the inclusion of participants with DM type I. A very small proportion of the study participants were found to have type I diabetes instead of type II because the algorithm that was developed by Statistics Canada, indiscriminately allowed participants that had answered "yes" to adhering to oral medication to remain in the study although they were diagnosed with DM early on in their lives (for example at 2 years old). The proportion of individuals that may be inadvertently included in my study in spite of having

DM type I, was found to be low and the sensitivity analyses illustrated that this misclassification did not change the results significantly.

Third, a misclassification may have occurred if participants answered incorrectly and overestimated their adherence to medication. Arguably, overestimating non-adherence is highly unlikely. The one month cut off is a very high threshold for not adhering to medication. Hence, flagging non-adherence is most likely an underestimation in this study. Since some patients may not have been using their medication for some time yet never reached one month for becoming considered as non-adherent.

Fourth, respondents were considered to be receiving an antihypertensive medication if they self-reported having high blood pressure or having been diagnosed with high blood pressure by a medical doctor. There is a possibility that some patients may have had hypertension but were never prescribed an antihypertensive medication. Similarly, some patients may have been diagnosed with DM type II but were never put on antidiabetic medication. Due to the limitations of the data, the extent of this possibility could not have been sought out. A recent update about the epidemiology of hypertension in Canada found that about 90% of respondents who self-reported having high blood pressure also indicated that they were receiving treatment.[140] Hence, it can be speculated that 10% of patients who were classified as non-adherent in fact were not prescribed medication for their condition. However, this misclassification could not affect patients with PMCC differently from patients without PMCC. The decision made by prescribers to prescribe is probably not affected by patient's insurance status. Thus, even if this misclassification does exist, it is mostly non-differential, and hence could not have affected the estimated OR of the association between PMCC and

adherence to HTN and diabetes medications. On the other hand, even if this misclassification is differential, it would have resulted in underestimation of the true association between PMCC and adherence. In this case, patients who have insurance are more likely to receive a prescription, as they might visit with their physicians more frequently. This would mean that a larger percentage among patients with PMCC is misclassified as non-adherent when compared to patients without PMCC. This would have yielded an OR that is closer to the null hypothesis than the "true" OR. Hence, the original calculated odds in my study would be an underestimation to the actual odds if this misclassification is for example illustrated in fact differential.

Lastly, generalizability across Canada should be taken cautiously. This is because the data source was limited to Ontario and New Brunswick participants. However, the population in those two provinces makes up nearly 40% of the Canadian population.[141]

Chapter 6

6.1 Implications and further research

This study examined and quantified the impact of not having PMCC on adherence in Canada overtime. The study assists in filling the knowledge gap for identifying if the absence of PMCC is associated with medication non-adherence among patients with HTN and DM type II. The results help in understanding the size of the "access gap" Canadians experience when they are unable to afford their chronic disease medications due to the absence of insurance to cover their prescription medication cost.[37]

Because this study could use data from Ontario and New Brunswick only, further research is needed for a Canada-wide inclusion. What is now required is a longitudinal study involving this study's participants to assess the change of adherence within the same individuals in order to examine the consistency of the current study's findings. Moreover, a longitudinal study is also needed to measure the hazard of exposure to not having PMCC on facing clinical outcomes.

This research has raised many questions in need of further investigation. Studies have found that people sometimes under-report their insurance status.[139] It would be interesting to find out why seniors in Ontario have answered "no" to having PMCC. Finally, Ontario has recently introduced a new drug coverage policy. Effective January 2018, residents aged less than 25 years have been included in the provincial coverage plan, similar to the seniors' plan. It is important to study the effect of policy implementation to measure the benefit of new

coverage and whether it will cause improvement in their parents' medication adherence for HT and DM.

6.2 Conclusion

The purpose of the current study was to investigate the trend and impact of not having PMCC on adherence to oral medication for hypertension and diabetes mellitus. Absence of PMCC increased slightly over the study period in Canada and the analysis revealed that absence of PMCC reduces the odds of adherence by 23%. This percentage reduction is consistent with previous research.[137] However, the current study provides specific evidence about the impact of PMCC on adherence to the most devastating chronic diseases in Canada. This study also found that adherence improved over time in Canada, despite the increase of the proportion of people without PMCC. However, patients without PMCC did not take the full advantage of adherence improvement.

One of the significant findings of this study is that the OR of adherence without PMCC remained fairly in between 0.7-0.8, even in subgroups stratified by age, by province, and by household income level. The evidence from this study also suggests that having more than one PMCC can improve adherence further by 44%. Overall, this study provides the necessary real-world evidence for the argument that PMCC is indeed needed for the improvement of adherence to oral hypertension and diabetes oral medications. The trend in this study also establishes that absence of PMCC still persists as a barrier hindering proper adherence to medications.

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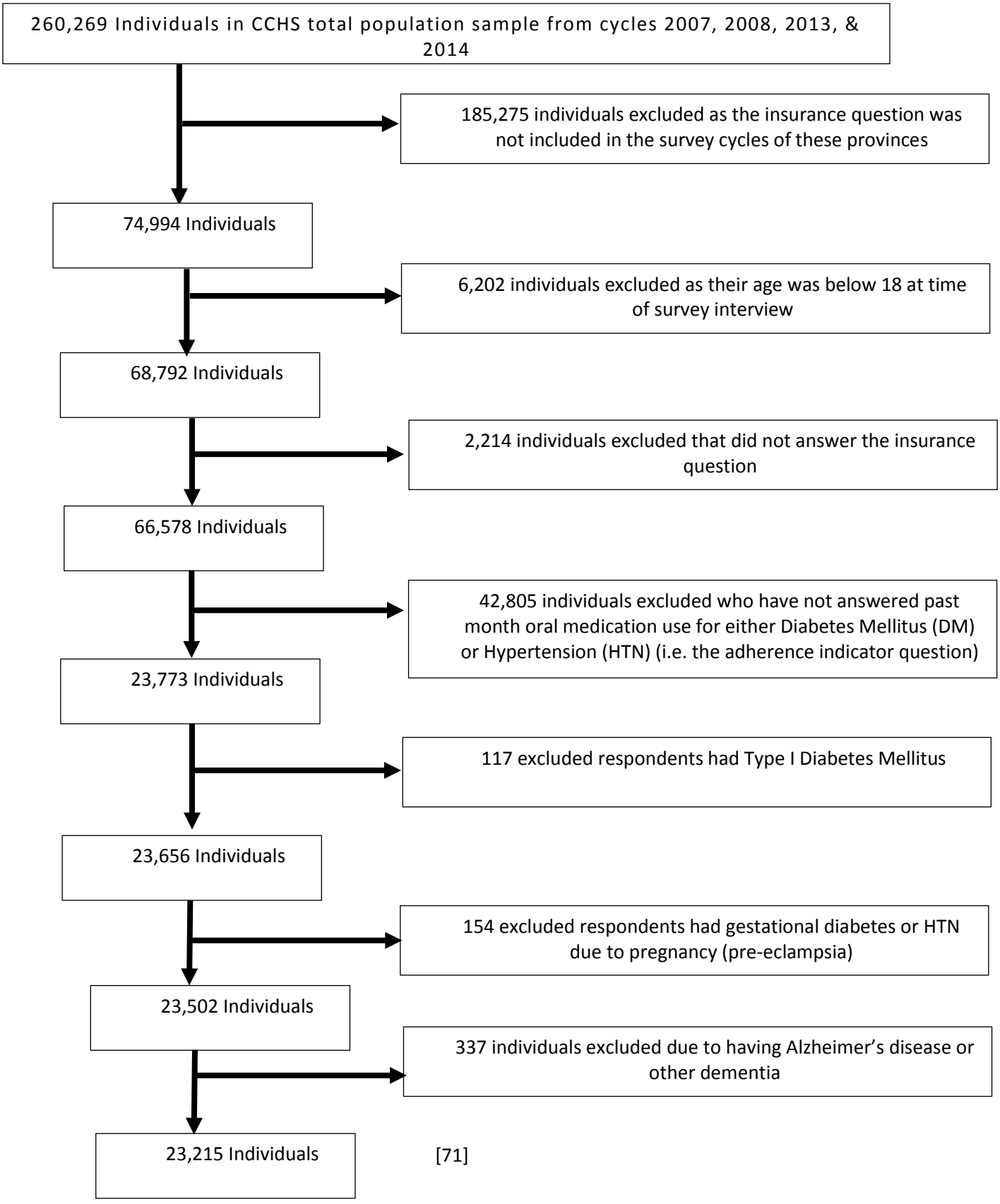
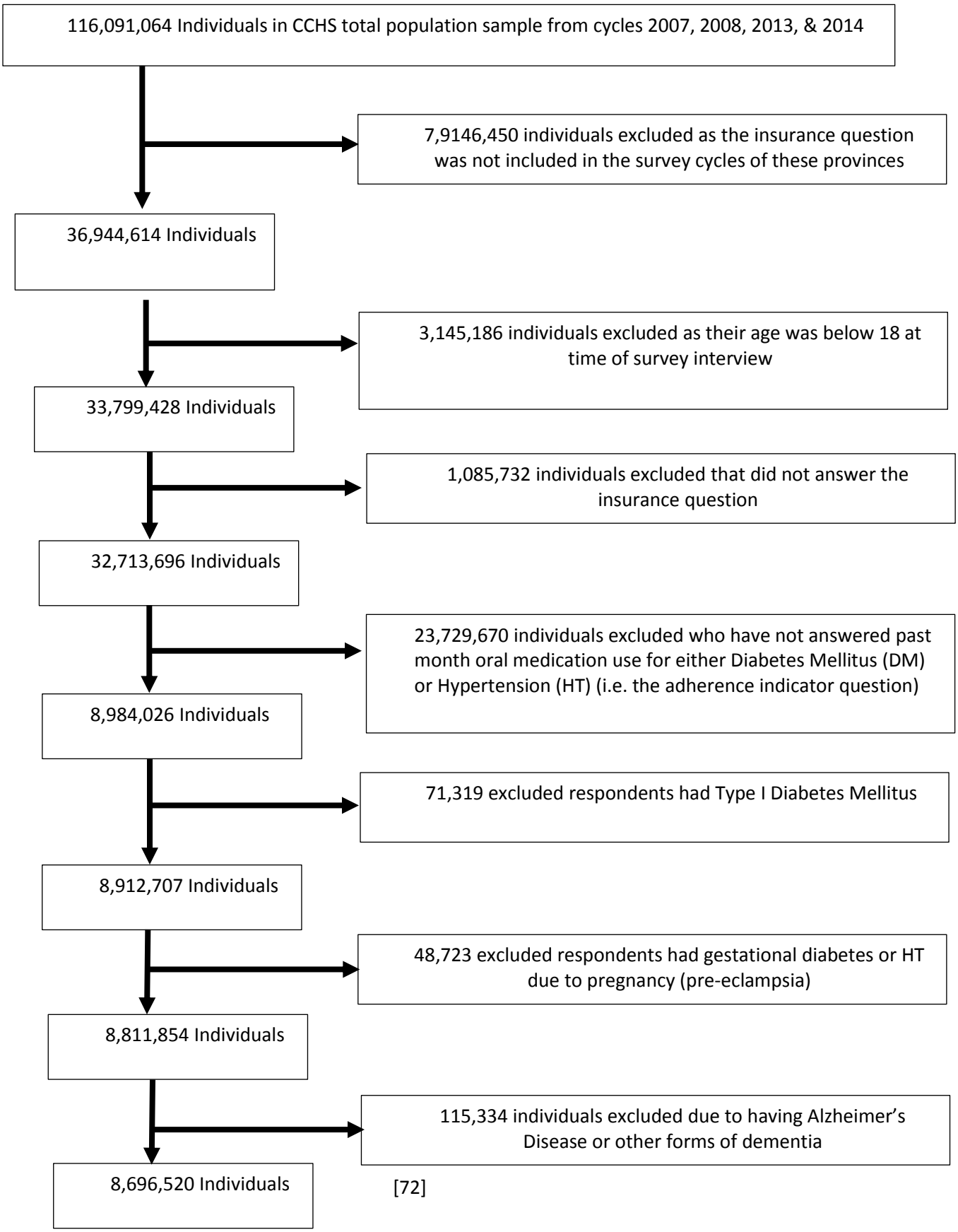
Appendix A

Figure 5: Steps taken to achieve study participants (unweighted).



[71]

Figure 6: Steps taken to achieve study participants (weighted).



[72]

Appendix B

Table 12-Characteristics of respondents in study

Variable Name	Categories	No Insurance (n=4329)		Insurance (n=18886)		Total (n=23215)		P-Value from Chi-Square or t-test
		n	%	n	%	n	%	
Adherence (Outcome)	Yes	3037	70.15	14616	77.39	17653	76.04	<0.0001
	No	1292	29.85	4270	22.61	5562	23.96	
	Total	4329	100.00	18886	100.00	23215	100.00	
Year	2007 or 2008	1547	35.74	6472	34.27	8019	34.54	0.0994
	2013	1418	32.76	6180	32.72	7598	32.73	
	2014	1364	31.51	6234	33.01	7598	32.73	
	Total	4329	100.00	18886	100.00	23215	100.00	
Age	Mean (SD)	63.81 (14.865)		64.98 (13.77)		64.76 (13.99)		<0.0001
	18-29	141	3.26	272	1.44	413	1.78	<0.0001
	30-44	328	7.58	1357	7.19	1685	7.26	
	45-64	1707	39.43	6865	36.35	8572	36.92	
	65+	2153	49.73	10392	55.02	12545	54.04	
	Total	4329	100.00	18886	100.00	23215	100.00	
	Minimum Age	18						
	Maximum Age	102		104				
SEX	Male	1841	42.53	8420	44.58	10261	44.20	0.0140
	Female	2488	57.47	10466	55.42	12954	55.80	
	Total		100.00		100.00	23215	100.00	
Education Level	Less than Secondary School graduation	1421	32.83	5029	26.63	6450	27.78	<0.0001
	Secondary School Graduation	880	20.33	3852	20.40	4732	20.38	
	Secondary School Graduation	2028	46.85	10005	52.98	12033	51.83	

Variable Name	Categories	No Insurance (n=4329)		Insurance (n=18886)		Total (n=23215)		P-Value from Chi-Square or t-test
	Total	4329	100.00	18886	100.00	23215	100.00	
Household Income (National level quintiles)	First 20% (Lowest Income)	1410	32.57	3866	20.47	5276	22.73	<0.0001
	Second 20%	1373	31.72	4466	23.65	5839	25.15	
	Third 20%	746	17.23	3898	20.64	4644	20.00	
	Fourth 20%	451	10.42	3507	18.57	3958	17.05	
	Fifth 20%(Highest Income)	349	8.06	3149	16.67	3498	15.07	
	Total	4329	100.00	18886	100.00	23215	100.00	
Number of chronic diseases	Hypertension or diabetes	3596	83.07	15223	80.60	18819	81.06	0.0002
	Hypertension and diabetes	733	16.93	3663	19.40	4396	18.94	
	Total	4329	100.00	18886	100.00	23215	100.00	
Province	Ontario	3541	81.80	16073	85.11	19614	84.49	<.0001
	New Brunswick	788	18.20	2813	14.89	3601	15.51	
	Total	4329	100.00	18886	100.00	23215	100.00	
Race	Aboriginal	113	2.61	589	3.12	702	3.02	<0.0001
	White	3807	87.94	17058	90.32	20865	89.88	
	Other	409	9.45	1239	6.56	1648	7.10	
	Total	4329	100.00	18886	100.00	23215	100.00	
Smoking status	Smoker	852	19.68	2952	15.63	3804	16.39	<0.0001
	Non-smoker	3477	80.32	15934	84.37	19411	83.61	
	Total	4329	100.00	18886	100.00	23215	100.00	
Alcohol consumption	Regular drinker	2120	48.97	9873	52.28	11993	51.66	<0.0001
	Occasional drinker	835	19.29	3637	19.26	4472	19.26	
	Did not drink in the last 12 months	1374	31.74	5376	28.47	6750	29.08	
	Total	4329	100.00	18886	100.00	23215	100.00	
	Hypertension	3262	75.35	13822	73.19	17084	73.59	0.0009

Variable Name	Categories	No Insurance (n=4329)		Insurance (n=18886)		Total (n=23215)		P-Value from Chi-Square or t-test
Disease of interest	Diabetes	334	7.72	1401	7.42	1735	7.47	
	Both DM and HTN	733	16.93	3663	19.40	4396	18.94	
	Total	4329	100.00	18886	100.00	23215	100.00	
Asthma	Yes	377	8.71	1745	9.24	2122	9.14	0.2742
	No	3952	91.29	17141	90.76	21093	90.86	
	Total	4329	100.00	18886	100.00	23215	100.00	
Arthritis (arthritis, excluding fibromyalgia)	Yes	1725	39.85	8247	43.67	9972	42.95	<.0001
	No	2604	60.15	10639	56.33	13243	57.05	
	Total	4329	100.00	18886	100.00	23215	100.00	
Back Problems	Yes	1297	29.96	5858	31.02	7155	30.82	0.1743
	No	3032	70.04	13028	68.98	16060	69.18	
	Total	4329	100.00	18886	100.00	23215	100.00	
Migraine	Yes	408	9.42	1684	8.92	2092	9.01	0.2923
	No	3921	90.58	17202	91.08	21123	90.99	
	Total	4329	100.00	18886	100.00	23215	100.00	
Cardiovascular Disease (Heart disease/stroke)	Yes	720	16.63	3747	19.84	4467	19.24	<.0001
	No	3609	83.37	15139	80.16	18748	80.76	
	Total	4329	100.00	18886	100.00	23215	100.00	
Cancer	Yes	643	14.85	3220	17.05	3863	16.64	0.0005
	No	3686	85.15	15666	82.95	19352	83.36	
	Total	4329	100.00	18886	100.00	23215	100.00	
Gastrointestinal: ulcer or have a bowel disorder such as Crohn's Disease, ulcerative colitis, Irritable Bowel Syndrome or	Yes	503	11.62	2082	11.02	2585	11.14	0.2614
	No	3826	88.38	16804	88.98	20630	88.86	
	Total	4329	100.00	18886	100.00	23215	100.00	

Variable Name	Categories	No Insurance (n=4329)		Insurance (n=18886)		Total (n=23215)		P-Value from Chi-Square or t-test
bowel incontinence								
Mental health	YES	588	13.58	2845	15.06	3433	14.79	0.0133
	NO	3741	86.42	16041	84.94	19782	85.21	
	Total	4329	100.00	18886	100.00	23215	100.00	
Staying overnight in hospital, nursing home or convalescent home	Yes	517	2.23	2552	13.51	3069	13.22	0.0059
	No	3812	88.06	16334	86.49	20146	86.78	
	Total	4329	90.28	18886	100.00	23215	100.00	
Main source of Household income	Employment (history)	3369	77.82	15481	81.97	18850	81.20	<.0001
	Governmental support	427	9.86	1696	8.98	2123	9.14	
	Other	525	12.13	1696	8.98	2221	9.57	
	Total	4321	99.82	18873	99.93	23194	99.91	
General health perception	Good	3210	74.15	13936	73.79	17146	73.86	0.2157
	fair	767	17.72	3519	18.63	4286	18.46	
	poor	352	8.13	1431	7.58	1783	7.68	
	Total	4329	100.00	18886	100.00	23215	100.00	
Has taken flu shot	Yes	3085	71.26	14833	78.54	17918	77.18	<.0001
	No	1244	28.74	4053	21.46	5297	22.82	
	Total	4329	100.00	18886	100.00	23215	100.00	
Has regular medical doctor	Yes	4075	94.13	18165	96.18	22240	95.80	<.0001
	No	254	5.87	721	3.82	975	4.20	
	Total	4329	100.00	18886	100.00	23215	100.00	
SUB SAMPLE: Health insurance plan type	Government	_	_	7282	38.56	7282	31.37	<.0001
	Employer/private	_	_	10310	54.59	10310	44.41	
	Mixed	_	_	1215	6.43	1215	5.23	
	Total			18807	99.58	18807	81.01	

Table 13 Characteristics of study sample (Weighted)

Variable Name	Categories	No Insurance (n=1735362)		Insurance (n=6961158)		Total (n=8696520)		P-Value from Chi-Square or t-test
		n	%	n	%	n	%	
Adherence (Outcome)	Yes	1135543	65.44	5112279	73.44	6247822	71.84	<0.0001
	No	599818	34.56	1848880	26.56	2448698	28.16	
	Total	1735361	100	6961159	100	8696520	100	
Year	2007 or 2008	530789	30.59	2182171	31.35	2712960	31.20	0.0994
	2013	585180	33.72	2401508	34.50	2986688	34.34	
	2014	619393	35.69	2377479	34.15	2996872	34.46	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Age	Mean (SD)	58.34 (2829429)		60.5 (4874214)		60.07 (5328763)		<0.0001
	18-29	81559	4.70	169245	2.43	250804	2.88	
	30-44	232957	13.42	797236	11.45	1030193	11.85	
	45-64	828879	47.76	3135195	45.04	3964074	45.58	
	65+	591967	34.11	2859482	41.08	3451449	39.69	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
	Minimum Age	18						
	Maximum Age	102		104				
SEX	Male	862618	49.71	3588107	51.54	4450725	51.18	0.2725
	Female	872744	50.29	3373051	48.46	4245795	48.82	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Education Level	Less than Secondary School graduation	491818	28.34	1549046	22.25	2040864	23.47	0.0001
	Secondary School Graduation	330784	19.06	1441849	20.71	1772633	20.38	
	Secondary School Graduation	912759	52.60	3970263	57.03	4883022	56.15	

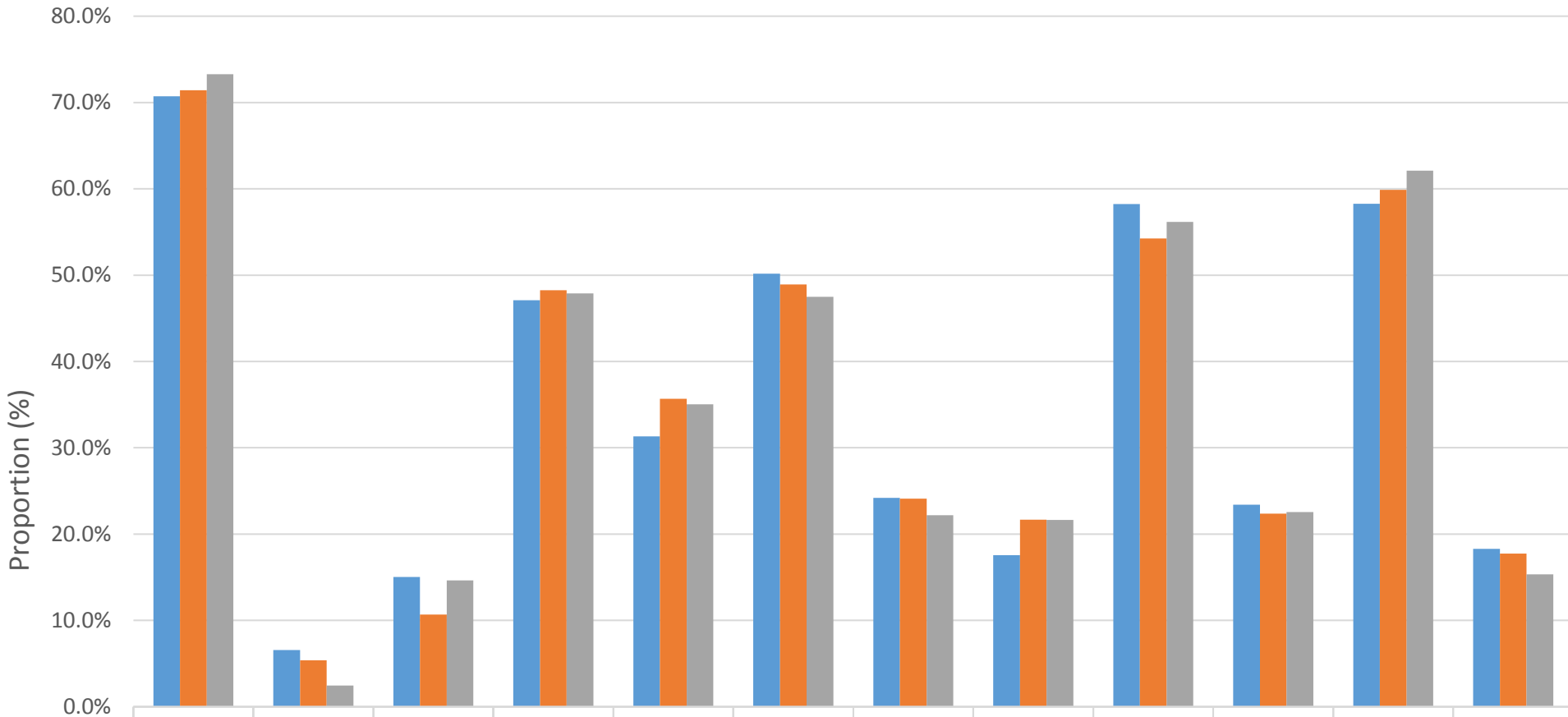
Variable Name	Categories	No Insurance (n=1735362)		Insurance (n=6961158)		Total (n=8696520)		P-Value from Chi-Square or t-test
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Household Income (National level quintiles)	First 20% (Lowest Income)	620885	35.78	1358475	19.52	1979360	22.76	<0.0001
	Second 20%	497474	28.67	1472436	21.15	1969910	22.65	
	Third 20%	274700	15.83	1402885	20.15	1677585	19.29	
	Fourth 20%	188737	10.88	1394726	20.04	1583463	18.21	
	Fifth 20%(Highest Income)	153565	8.85	1332636	19.14	1486201	17.09	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Number of chronic diseases	Hypertension or diabetes	1492682	86.02	5714627	82.09	7207309	82.88	0.0001
	Having both Hypertension and diabetes	242680	13.98	1246531	17.91	1489211	17.12	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Province	Ontario	1579895	91.04	6382477	91.69	7962372	91.56	0.2310
	New Brunswick	155467	8.96	578681	8.31	734148	8.44	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Race	Aboriginal	38156	2.20	182038	2.62	220194	2.53	<0.0001
	White	1217862	70.18	5545839	79.67	6763701	77.77	
	Other	479344	27.62	1233281	17.72	1712625	19.69	

Variable Name	Categories	No Insurance (n=1735362)		Insurance (n=6961158)		Total (n=8696520)		P-Value from Chi-Square or t-test
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Smoking status	Smoker	356442	20.54	1160917	16.68	1517359	17.45	0.0017
	Non-smoker	1378920	79.46	5800242	83.32	7179162	82.55	
	Total	1735362	100.00	6961159	100.00	8696521	100.00	
Alcohol consumption	Regular drinker	850563	49.01	3703465	53.20	4554028	52.37	0.0063
	Occasional drinker	307775	17.74	1286596	18.48	1594371	18.33	
	Did not drink in the last 12 months	577024	33.25	1971097	28.32	2548121	29.30	
	Total	1735362	100.00	6961158	100.00	8696520	100.00	
Disease of interest	Hypertension	1317199	75.90	5129435	73.69	6446634	74.13	0.0043
	Diabetes	175482	10.11	585192	8.41	760674	8.75	
	Both DM and HTN	242680	13.98	1246531	17.91	1489211	17.12	
	Total	1735361	100.00	6961158	100.00	8696519	100.00	
Asthma	Yes	133295	7.68	637085	9.15	770380	8.86	0.0615
	No	1602067	92.32	6324074	90.85	7926141	91.14	
	Total	1735362	100.00	6961159	100	8696521	100.00	
Arthritis (arthritis, excluding fibromyalgia)	Yes	538656	31.04	2546995	36.59	3085651	35.48	0.0002
	No	1196706	68.96	4414163	63.41	5610869	64.52	
	Total	1735362	100.00	6961158	100	8696520	100.00	
Back Problems	Yes	482083	27.78	2009494	28.87	2491577	28.65	0.4609
	No	1253279	72.22	4951664	71.13	6204943	71.35	
	Total	1735362	100.00	6961158	100	8696520	100.00	
Migraine	Yes	174859	10.08	715959	10.29	890818	10.24	0.8223
	No	1560503	89.92	6245199	89.71	7805702	89.76	
	Total	1735362	100.00	6961158	100	8696520	100.00	
	Yes	216279	12.46	1175563	16.89	1391842	16.00	<.0001

Variable Name	Categories	No Insurance (n=1735362)		Insurance (n=6961158)		Total (n=8696520)		P-Value from Chi-Square or t-test
Cardiovascular Disease (Heart disease/stroke)	No	1519082	87.54	5785596	83.11	7304678	84.00	
	Total	1735361	100.00	6961159	100	8696520	100.00	
Cancer	Yes	184295	10.62	888076	12.76	1072371	12.33	0.0532
	No	1551066	89.38	6073082	87.24	7624148	87.67	
	Total	1735361	100.00	6961158	100	8696519	100.00	
Gastrointestinal: ulcer or have a bowel disorder such as Crohn's Disease, ulcerative colitis, Irritable Bowel Syndrome or bowel incontinence	Yes	168173	9.69	717267	10.30	885440	10.18	0.5456
	No	1567189	90.31	6243892	89.70	7811081	89.82	
	Total	1735362	100.00	6961159	100	8696521	100.00	
Mental health	YES	235704	13.58	1083352	15.56	1319056	15.17	0.1145
	NO	1499658	86.42	5877806	84.44	7377464	84.83	
	Total	1735362	100.00	6961158	100	8696520	100.00	
Staying overnight in hospital, nursing home or convalescent home	Yes	180599	10.41	803680	11.55	984279	11.32	0.2878
	No	1554763	89.59	6157478	88.45	7712241	88.68	
	Total	1735362	100.00	6961158	100	8696520	100.00	
Main source of Household income	Employment (history)	1418460	81.74	5930548	85.19	7349008	84.51	0.0107
	Governmental support	144371	8.32	491159	7.06	635530	7.31	

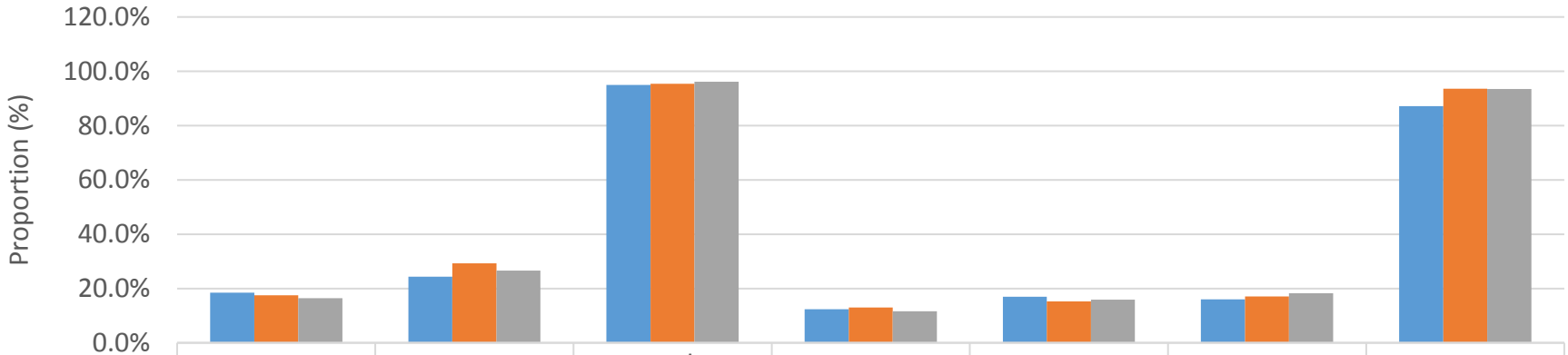
Variable Name	Categories	No Insurance (n=1735362)		Insurance (n=6961158)		Total (n=8696520)		P-Value from Chi-Square or t-test
	Other	171234	9.87	532488	7.65	703722	8.09	
	Total	1734065.00	99.93	6954195	99.90	8688260	99.91	
General health perception	Good	1277430	73.61	5208613	74.82	6486043	74.58	0.4264
	fair	298529	17.20	1203994	17.30	1502523	17.28	
	poor	159403	9.19	548552	7.88	707955	8.14	
	Total	1735362	100.00	6961159	100.00	8696521	100.00	
Has taken flu shot	Yes	1147902	66.15	5215517	74.92	6363419	73.17	<.0001
	No	587460	33.85	1745641	25.08	2333101	26.83	
	Total	1735362	100.00	6961158	100	8696520	100.00	
Has regular medical doctor	Yes	1613692	92.99	6692340	96.14	8306032	95.51	<.0001
	No	121670	7.01	268818	3.86	390488	4.49	
	Total	1735362	100.00	6961158	100	8696520	100.00	
SUB SAMPLE: Health insurance plan	Government-sponsored	_	_	2269571	32.60	2269571	26.10	<.0001
	Employer/private-sponsored	_	_	4321788	62.08	4321788	49.70	
	Mixed	_	_	350227	5.03	350227	4.03	
	Total			6941586	99.72	6941586	79.82	

Figure 7 Characteristics among respondents to the CCHS in 2007-2008, 2013, 2014



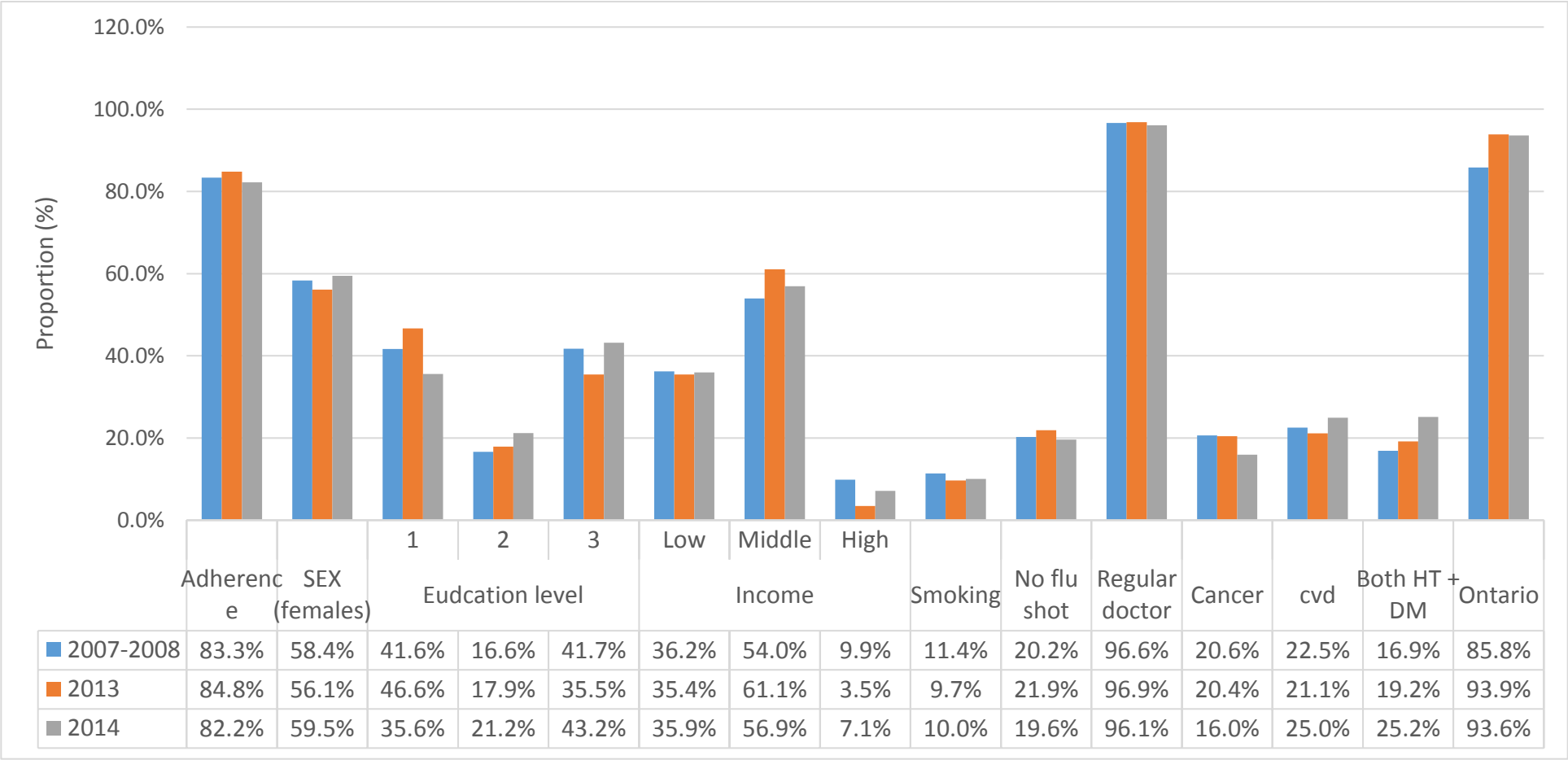
	Adherence	No Insurance in Age Group				SEX (females)	Eudcation level			Income status		
		1	2	3	4		1	2	3	Low Income	Middle Income	High Income
2007-2008	70.7%	6.6%	15.0%	47.1%	31.3%	50.2%	24.2%	17.6%	58.2%	23.4%	58.3%	18.3%
2013	71.4%	5.4%	10.7%	48.2%	35.7%	48.9%	24.1%	21.7%	54.2%	22.4%	59.9%	17.7%
2014	73.3%	2.5%	14.6%	47.9%	35.0%	47.5%	22.2%	21.6%	56.2%	22.5%	62.1%	15.4%

Figure 7 (Cont.)Characteristics among respondents to the CCHS in 2007-2008, 2013, 2014



	Smoking	No flu shot	Regular doctor	Cancer	CVD	Both HT + DM	Ontario
2007-2008	18.5%	24.4%	94.9%	12.4%	16.9%	16.0%	87.2%
2013	17.5%	29.3%	95.4%	13.0%	15.2%	17.1%	93.6%
2014	16.5%	26.6%	96.1%	11.6%	15.9%	18.2%	93.5%

Figure 8 Characteristics among senior respondents with wrong perception of not having insurance in the CCHS in 2007-2008, 2013, 2014



	Adherence	SEX (females)	Eudcation level			Income			Smoking	No flu shot	Regular doctor	Cancer	cvd	Both HT + DM	Ontario
			1	2	3	Low	Middle	High							
2007-2008	83.3%	58.4%	41.6%	16.6%	41.7%	36.2%	54.0%	9.9%	11.4%	20.2%	96.6%	20.6%	22.5%	16.9%	85.8%
2013	84.8%	56.1%	46.6%	17.9%	35.5%	35.4%	61.1%	3.5%	9.7%	21.9%	96.9%	20.4%	21.1%	19.2%	93.9%
2014	82.2%	59.5%	35.6%	21.2%	43.2%	35.9%	56.9%	7.1%	10.0%	19.6%	96.1%	16.0%	25.0%	25.2%	93.6%

Appendix C

Table 14: Results of full model output

Effect	Odds Ratio Estimates	95% Wald Confidence Limits	
No Insurance vs. Insurance	0.774	0.657	0.911
Ontario vs New Brunswick	1.016	0.891	1.159
Female vs. male	0.844	0.742	0.96
2013 vs. 2007-2008	0.998	0.844	1.18
2014 vs. 2007-2008	1.053	0.908	1.221
Secondary education vs. lower	1.131	0.922	1.388
Post Secondary education vs. lower than secondary	0.829	0.693	0.992
30-44 vs 18-29	4.449	2.575	7.689
45-64 vs 18-29	12.795	7.595	21.556
65+ vs 18-29	25.479	15.078	43.056
2nd vs. 1st quintile	1.150	0.953	1.388
3rd vs. 1st quintile	1.012	0.817	1.255
4th vs. 1st quintile	0.896	0.71	1.132
5th vs. 1st quintile	0.984	0.791	1.225
Smoking vs nonsmoking	0.696	0.586	0.827
No flu shot vs. flu shot	0.725	0.625	0.841
No regular doctor. vs. regular doctor	0.486	0.364	0.649
1 disease (HTN/DM) vs. both	1.273	1.071	1.513
No cancer vs cancer	1.205	1.021	1.423
No cardiovascular disease vs. cardiovascular	0.601	0.509	0.709

Appendix D

Figure 9: Odds Ratios of Adherence with No Insurance in Subgroups in 95% Confidence Intervals

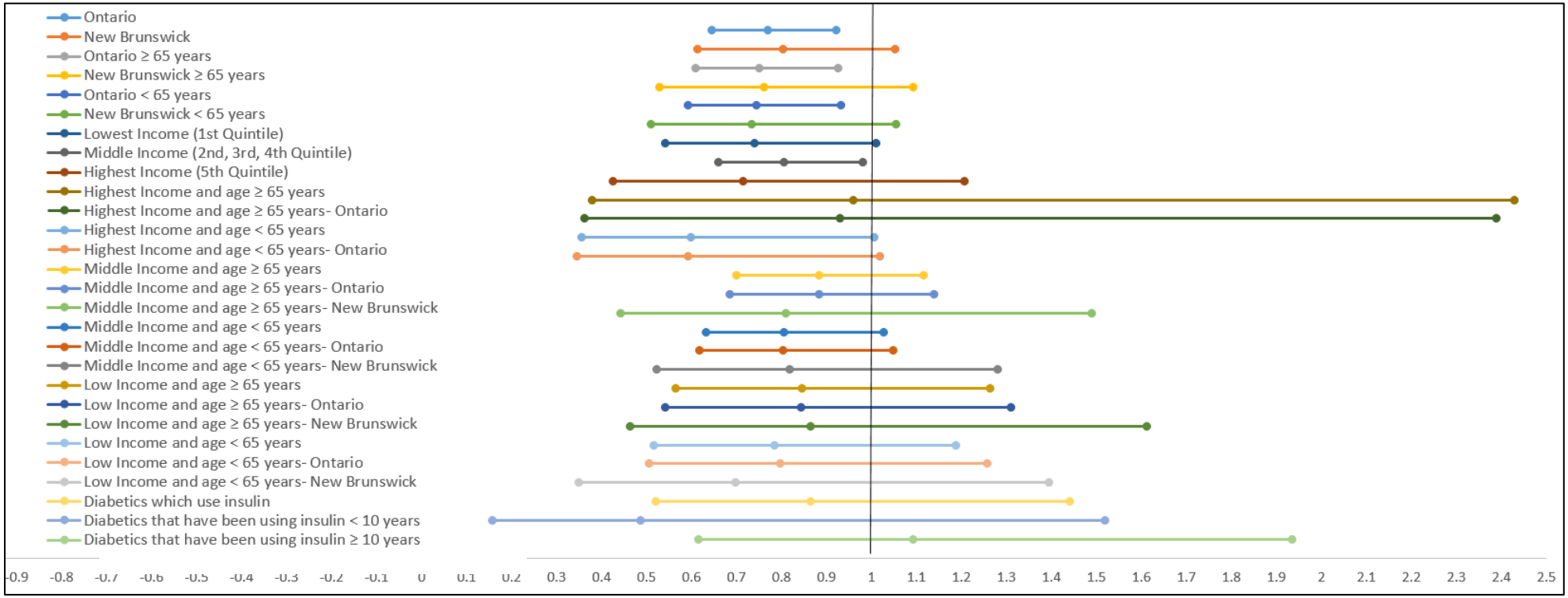


Table 15: Odds Ratios of Adherence with No Insurance in Subgroups in 95% Confidence Intervals.

No Insurance vs. Insurance Subgroups	Odds Ratio Estimates	95% Wald Confidence Limits	
Ontario	0.774	0.644	0.921
New Brunswick	0.802	0.612	1.051
Ontario ≥ 65	0.751	0.609	0.926
New Brunswick ≥ 65	0.76	0.529	1.092
Ontario-below 65	0.743	0.592	0.932
New Brunswick-below 65	0.733	0.51	1.055
Lowest Income (1st Quintile)	0.739	0.541	1.01
Middle Income (2nd, 3rd, 4th Quintile)	0.804	0.659	0.980
Highest Income (5th Quintile)	0.715	0.425	1.205
Highest Income and age ≥ 65 years	0.958	0.378	2.428
Highest Income and age ≥ 65 years- Ontario	0.930	0.362	2.388
Highest Income and age < 65 years	0.599	0.356	1.006
Highest Income and age < 65 years- Ontario	0.592	0.344	1.019
Highest Income and age < 65 years- New Brunswick	1.121	0.075	16.775
Middle Income and age ≥ 65 years	0.883	0.699	1.115
Middle Income and age ≥ 65 years- Ontario	0.883	0.685	1.138
Middle Income and age ≥ 65 years- New Brunswick	0.810	0.441	1.489
Middle Income and age < 65 years	0.805	0.632	1.026
Middle Income and age < 65 years- Ontario	0.803	0.616	1.047
Middle Income and age < 65 years- New Brunswick	0.817	0.521	1.280
Low Income and age ≥ 65 years	0.844	0.564	1.264
Low Income and age ≥ 65 years- Ontario	0.842	0.542	1.310
Low Income and age ≥ 65 years- New Brunswick	0.864	0.463	1.612
Low Income and age < 65 years	0.783	0.516	1.187
Low Income and age < 65 years- Ontario	0.796	0.505	1.256
Low Income and age < 65 years- New Brunswick	0.697	0.349	1.394
Diabetics which use insulin	0.864	0.519	1.440
Diabetics that have been using insulin < 10 years	0.486	0.156	1.519
Diabetics that have been using insulin ≥ 10 years	1.091	0.615	1.935
Odds after removing seniors, respondents with cancer history, and low income class	0.795	0.635	0.995
Odds after removing Ontario seniors that denied having insurance	0.738	0.604	0.902