Determinants of 2009 Pandemic A/H1N1 Influenza Vaccination in Montreal

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August 2011

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Master of Science

ABSTRACT

To develop successful vaccination programs for influenza pandemics, it is essential to understand the neighborhood-level factors that influence vaccination. Few studies have used an immunization registry to examine the neighborhood determinants of pandemic influenza vaccination among the general population. Using individual-level vaccination data and census, survey and administrative data to estimate the population at risk, an ecological study of the neighborhood determinants of 2009 pandemic A/H1N1 influenza vaccination in Montreal was conducted. Using logistic regression, accounting for spatial autocorrelation, the neighborhood socioeconomic and demographic determinants of pandemic influenza vaccination were identified among the total population and stratified by priority group. In Montreal, 918,733 (49.9%) residents were vaccinated against pandemic A/H1N1 influenza. Coverage was greater among females compared to males and varied by age with greatest coverage among infants. Coverage also differed by priority group with greatest coverage among healthcare workers. Neighborhood variation in coverage was observed and ranged from 33.6% to 71.0%, with low coverage clustered in neighborhoods in Eastern Montreal. Among the total population, high neighborhood proportions of immigrants and material deprivation were significantly associated with lower neighborhood vaccine coverage. These results will help public health authorities implement priority group specific vaccination strategies to increase vaccination during future influenza pandemics.

ABRÉGÉ

Pour bien développer des programmes de vaccination contre les pandémies de grippe, la compréhension des éléments de voisinage qui influence la vaccination est essentielle. Très peu d'études ont été effectuées en utilisant un registre d'immunisation dans le but d'explorer les déterminants du voisinage relatifs à la vaccination. En utilisant des données individuelles, des données de recensement, de sondages et des données administratives pour estimer la population à risque, une étude écologique des déterminants de voisinage lors de la vaccination de la grippe pandémique A/H1N1 fut effectuée. En utilisant la régression logistique, en tenant compte de l'autocorrélation spatiale, les déterminants socio-économiques et démographiques pour la vaccination ont été identifiés et classés par groupe de priorité. À Montréal, un total de 918,733 (49,9%) habitants furent vaccinés contre la grippe A/H1N1. Le taux de vaccination était plus important parmi les femmes comparativement aux hommes. Il a varié selon l'âge, le plus haut taux était parmi les enfants de moins de cinq ans. Le taux a aussi vu une croissance parmi les gens travaillant dans le secteur des soins de santé. Dans les différents quartiers de Montréal, les taux de vaccination ont variés de 33,6% à 71,0%. Les taux les plus bas furent retrouvés dans les quartiers de l'Est de Montréal. Dans la population générale, l'immigration et les milieux défavorisés ont été des facteurs significatifs associés aux bas taux de vaccination. Ces résultats vont aider les autorités des soins de santé à implanter des stratégies spécifiques aux divers groupes de priorité lors des futures pandémies de grippe.

Preface

This thesis contains four chapters. Chapter one, the introduction, provides the background, rationale and objectives of the thesis. Chapter two reviews the literature on the determinants of pandemic influenza vaccination. Chapter three includes the methods used to address the thesis objectives and presents the results on pandemic influenza vaccine coverage in Montreal and neighborhood determinants of vaccination. Chapter four summarizes the overall findings.

Chapters two and three are formatted as manuscripts for submission to peer-reviewed journals. Each manuscript is preceded by a short introduction and formatted according to the intended journal's specifications. The tables, figures and references for each manuscript are provided at the end of their respective chapters. A full reference list is also provided at the end of the thesis. This thesis conforms to the guidelines and requirements of a manuscript-based thesis at McGill University.

Contribution of Authors

As a first author, I contributed to the conception and planning of the study design, conducted the literature search, study selection and data extraction, conducted a large majority of the data manipulation, all analyses, interpreted the results, wrote a first draft of both manuscripts, and incorporated other authors' revisions. My thesis supervisor, David Buckeridge, contributed to all stages of the research, from conceiving the study design, to providing thoughtful discussion of the results and revising the manuscripts. Jeff Kwong, a member of my thesis supervisory committee, provided helpful feedback on the study design, the interpretation of the results and edited the manuscripts. Katia Charland provided guidance and feedback on the statistical analyses and revised the second manuscript. Aman Verma provided computational assistance in identifying the number of pregnant women in Montreal and edited the second manuscript.

ACKNOWLEDGEMENTS

During my studies, I received a Graduate Student Scholarship from the Public Health Agency of Canada and Canadian Institutes of Health Research Influenza Research Network (PCIRN) for years 2010 and 2011 and a Studentship award for years 2009 to 2011 from the Canadian Institutes of Health Research.

There are many people I would like to thank and acknowledge for their assistance and encouragement as I near the completion of my Master's thesis. First I would like to thank my supervisor, David Buckeridge for his support, always insightful and helpful advice, and encouragement. I would also like to thank him for giving me the freedom to work independently at my own pace and always being available when I needed his input. I would also like to thank Jeff Kwong, my thesis committee member, who always provided timely and insightful advice regarding my project. I would sincerely like to thank David and Jeff for their patience, support, guidance and opportunity to learn from their expertise. I would also like to thank them for introducing me to the PCIRN Vaccine Coverage Group, which opened doors to many new, exciting opportunities. I am truly thankful to have worked with such knowledgeable, supportive supervisors.

I would like to thank the members of the McGill Surveillance Lab, whom I have worked closely with during the past year, for their guidance and support. I would first like to thank Katia Charland, for always providing kind and thorough advice concerning all my biostatistical problems. Katia always went out of her way to help me and I truly appreciate her effort. I would like to thank Aman Verma who answered all my questions and requests regarding the identification of pregnant women using administrative data. I would like to thank Luc de Montigny for introducing me to GIS software, answering all my GIS questions, and giving me advice on how to make maps. I would like to thank all other members of the McGill Surveillance Lab for providing thoughtful comments during my lab meeting presentations. It has been wonderful to have worked with such a collaborative and helpful group and I will truly miss them as I move on to the next chapter in my life.

I would also like to thank the support staff at the McGill Clinical and Health Informatics Research Group. I would like to thank Patricia Plouffe for being so helpful while scheduling my many meetings with David. I would like to thank Rosalba Pupo for being so patient and reliable while dealing with the administrative tasks regarding the payment of my scholarship.

Finally I would like to thank my parents, Sharon and Sylvain, my brothers, Steven and Shane, my boyfriend, Chris, and my friends for all their support, love and encouragement for without them I could not have accomplished this goal.

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LIST OF ABBREVIATIONS

CI, Confidence interval (Frequentist), Credible interval (Bayesian)

DA, Dissemination area

ICD-9, International Classification of Diseases, Ninth Revision

MED-ECHO, Maintenance et exploitation des données pour l’étude de la clientèle hospitalière

NPHS, National Population Health Survey

OR, Odds ratio

Q1, First quartile

Q3, Third quartile

RAMQ, Régie de l'assurance maladie du Québec

CHAPTER 1

Introduction

Background

The first influenza pandemic of the 21st century was declared on June11th, 2009 (World Health Organization, 11 June 2009) in response to the identification of a novel A/H1N1 influenza strain which at the time had spread to 74 countries and territories (World Health Organization, 11 June 2009). In the following months, the virus had spread to a total of 214 countries, resulting in 18,449 deaths (World Health Organization, 6 August 2010). In an attempt to mitigate the effects of the pandemic, public health authorities worldwide set out to organize mass vaccination campaigns as vaccination is the most effective measure implemented to prevent infection and contain transmission of the virus (Centers for Disease Control and Prevention, 1 August 2009).

Rationale

To develop a successful vaccination program it is essential to understand the factors that influence pandemic influenza vaccination. Of particular interest are factors that can be measured at the population-level and targeted by public health programs. To monitor and evaluate the success of a vaccination campaign, accurate and reliable influenza vaccine coverage estimates are required. Often vaccine coverage has been estimated using survey methodology and the determinants of vaccination have been identified at the individual-level. Although such methods provide valuable information for public health planners, there are limitations to this approach. For example, survey data are subject to selection bias, poor recall, and reliance on self-report. Additionally, as the delivery of health services is often conducted at the local level, understanding neighborhood determinants of vaccination may be more informative than individual determinants from a public health perspective.

Little attention has been given to examining determinants of pandemic influenza vaccination using an immunization registry, which provides numerator data not subject to many of the biases that influence survey results. Nor have studies identified the determinants of vaccination at a neighborhood-level, which would provide public health officials with an evidence-based strategy to plan for pandemic influenza vaccination campaigns.

Objectives

The objectives of this thesis were:

1) To conduct a systematic review:

A) To identify and summarize studies examining the determinants of pandemic influenza vaccination, focusing primarily on socioeconomic and demographic factors;

B) To summarize the methods used to identify the determinants of pandemic influenza vaccination;

2) To estimate population counts by Montreal neighborhood for priority groups recommended to receive the A/H1N1 influenza vaccine;

3) To describe pandemic influenza vaccine coverage in Montreal overall and by sex, age group, priority group, date of vaccination and neighborhood using a vaccination registry;

4) To identify the neighborhood socioeconomic and demographic determinants of pandemic influenza vaccination in Montreal among the total population and priority groups.

CHAPTER 2

Literature Review

The following manuscript summarizes the current knowledge regarding the determinants of pandemic influenza vaccination. A literature review was conducted, including studies examining actual receipt of vaccine and associated factors. This manuscript focuses mainly on the determinants that can be measured at a neighborhood-level, to provide public health officials with information needed to design and implement effective mass vaccination campaigns for pandemic influenza. The paper also summarizes the methods used to identify the determinants of pandemic influenza vaccination and the gaps in the literature, which helped to formulate the objectives and methods of this thesis. This manuscript will be submitted for publication to Vaccine and has been formatted according to the Journal's specifications.

Title: The determinants of 2009 pandemic A/H1N1 influenza vaccination: A systematic review

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Abstract

Introduction: Pandemic A/H1N1 influenza vaccine coverage varied widely across countries. To understand the factors influencing pandemic influenza vaccination and to guide the development of successful vaccination programs for future influenza pandemics, we identified and summarized studies examining the determinants of vaccination during the 2009 influenza pandemic.

Methods: We performed a systematic literature review using the PubMED electronic database from June 2009 to February 2011. We included studies examining an association between a possible predictive variable and actual receipt of the pandemic A/H1N1 influenza vaccine. We excluded studies examining intention or willingness to receive the vaccine.

Results: Twenty-seven studies were identified from twelve countries. Pandemic influenza vaccine coverage varied from 4.8% to 92%. Coverage varied by population sub-group, country, and assessment method used. Most studies used questionnaires to estimate vaccine coverage, however seven (26%) used a vaccination registry. Factors that positively influenced pandemic influenza vaccination were: male sex, younger age, higher education, being a doctor, being in a priority group for which vaccination was recommended, receiving a prior seasonal influenza vaccination, believing the vaccine to be safe and/or effective, and obtaining information from official medical sources.

Conclusion: Vaccine coverage during the pandemic varied widely across countries and population sub-groups. While we identified some consistent determinants of this variation, further research is needed to identify determinants of pandemic influenza vaccination that could be easily targeted at a population level to increase coverage during future influenza pandemics.

Key words: pandemic, influenza, vaccination, coverage

1. Introduction

On June 11th, 2009, the World Health Organization declared the beginning of the first influenza pandemic of the 21st century [1]. This statement was issued in response to the identification of a novel A/H1N1 influenza strain, which at the time had spread to 74 countries [1]. By August 1st, 2010, the World Health Organization had confirmed 18,449 deaths worldwide due to the influenza A/H1N1 strain in 214 countries and territories [2].

During the second wave of the pandemic, public health authorities attempted to mitigate the effects of the pandemic by initiating mass vaccination campaigns. These campaigns met with variable success, possibly due to limited knowledge of the factors that influence pandemic influenza vaccination. To develop successful vaccination programs for future influenza pandemics, it is essential to understand the factors that influenced vaccination during the pandemic. Of particular interest are factors that can be measured at the population-level and targeted by public health programs.

To our knowledge, a review of the literature on the determinants of pandemic influenza vaccination focusing solely on actual receipt of the pandemic influenza vaccine has not been conducted. One review was recently published examining the psychological and demographic determinants of intention to vaccinate and actual vaccination [3]. However the determinants of intention to vaccinate may differ from actual behaviour as estimates of vaccine intention were reported to be much greater than actual vaccine coverage estimates [4-11]. The objectives of this review were: 1) to identify and summarize studies examining the determinants of pandemic influenza vaccination, focusing primarily on socioeconomic and demographic factors; and 2) to summarize the methods used to identify the determinants of pandemic influenza vaccination.

2. Methods

2.1. Search Strategy

We performed a search of the literature using the PubMED electronic database to obtain studies examining the determinants of pandemic A/H1N1 influenza vaccination. We used the following terms: "Influenza, Human", "Immunization" and key words: coverage, accept*, uptake, pandemic, H1N1, influenza, immuniz*, vaccin*.

2.2. Inclusion/Exclusion Criteria

Studies were screened by reviewing the title and abstract. Studies were included in the review if they examined an association between possible predictive variables (socioeconomic, demographic, health status and behaviours, attitudes, perceptions, beliefs, knowledge, information source, etc.) and pandemic A/H1N1 influenza vaccination. We included studies examining any population group as long as they defined the outcome as previous receipt of the pandemic A/H1N1 influenza vaccine and were published in press or electronically between June 1, 2009 and January 31, 2011. We excluded studies if the outcome included intention or willingness to receive the pandemic A/H1N1 influenza vaccine. Studies that examined characteristics of the vaccinated group only, studies that were written in a language other than English, and reviews, letters, editorials or case reports were excluded.

2.3. Data Extraction

From the studies included in our review we extracted the following data: study location/setting/period, study population, sample size, data collection methods and instrumentation, study outcome, data analysis, vaccine coverage achieved, and the variables associated with vaccination that were found to be statistically significant in a univariate or multivariate analysis. Several studies did not report confidence intervals along with coverage estimates, and we estimated confidence intervals where possible.

3. Results

3.1. Summary of Included Studies

Twenty-seven studies were included in the review. In Table 1 we summarize the main characteristics of these studies. Nine studies examined the determinants of vaccination among the general population[1] [6, 8, 11-17], four focused specifically on children or adults with chronic conditions [18-21], three studied pregnant women [22-24], and eleven examined determinants of vaccination among healthcare workers[2] [4, 25-34]. Pandemic influenza vaccine coverage was examined in a wide range of regions including: United States [6, 13-14, 16, 22, 26], Turkey [15, 24, 30, 32-33], France [11-12, 25, 28], Greece [18, 20, 27], Madrid, Spain [19, 34], South Korea [29], Sherbrooke, Québec, Canada [23], Beijing, China [31], Sicily, Italy [4], Israel [17], Germany [21], and Western Australia, Australia [8]. The studies were conducted between May 2009 and April 2010. The sample sizes of the selected studies varied greatly and ranged from 64 [18] to 64,942,414 [12].

3.2. Pandemic A/H1N1 Influenza Vaccine Coverage

Pandemic A/H1N1 influenza vaccine coverage for each study is shown in Table 1 and summarized by population sub-group in Table 2. Overall, median pandemic influenza vaccine coverage was 21.2%. The lowest coverage reported was 4.8% [15], for the household

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[1] May include priority groups within the population.
[2] Includes employees with healthcare (e.g. physician, nurse) and non-healthcare occupations (e.g. administrative assistants) working in a healthcare setting.

adult population of Turkey. The highest coverage was observed in South Korea in a sample of hospital employees at 91.7% [29]. Across population groups, vaccine coverage was generally greater among adults and children with a chronic condition, followed by pregnant women, healthcare workers, and finally the general population. Coverage also varied by geographical region, with coverage being higher in the United States (20.3%) [6] compared to France (11.1%) [11], when considering studies among the general population.

Coverage also differed by the data collection method used, with studies using a vaccination registry[3] generally reporting lower coverage estimates compared to studies using a questionnaire. For example, Nougairède et al. estimated coverage at 30.1%, 95% CI: (28.6-31.7%) among French hospital workers using a registry whereas Barrière et al. estimated coverage to be 51.4%, 95% CI: (47.0-55.7%) among a similar population using a survey. Bone et al. and Vaux et al. estimated vaccine coverage among the general population of France using a registry and a survey, respectively. A statistically significant lower estimate was reported from the registry (7.95%) compared to the survey (11.1%).

3.3. Summary of Methodologies to Identify the Determinants of Pandemic Influenza Vaccination

Two methods were used to identify the determinants of pandemic influenza vaccination. Nine (33.3%) studies conducted descriptive analyses, estimating vaccine coverage by different characteristics and testing whether differences in coverage by various characteristics were statistically significant [6, 8, 12-13, 16, 18, 21-22, 26]. Eighteen (66.7%) of the studies modelled vaccination using regression [4, 11, 15, 17, 19-20, 23-25, 27-34],

[3] Registry refers to any form of data collection in which vaccination data was collected by any means other than self-report and was collected during the receipt of the vaccination or during the campaign.

including each potential determinant as a covariate in the model to assess its effect on the reported coverage estimates.

To estimate vaccine coverage by demographic characteristics and risk factors, a numerator and denominator are required, with both stratified by levels of demographic characteristics and risk factors. The numerator is the number vaccinated and the denominator is the population at risk. Twenty (74.1%) studies used surveys, conducted as either self-administered questionnaires [14-16, 18, 22-23, 25-27, 30-34], or by telephone [6, 11, 13, 17, 21] or as face-to face interviews [24] to estimate the numerator and the denominator from survey respondents (Table 1). The remaining six (22.2%) studies [4, 12, 19-20, 28-29] used a vaccination registry and one study used both a telephone survey and a registry [8].

The studies using registries estimated the numerator from registry data. The denominators in these studies were estimated from demographic and risk factor data at the individual [4, 12, 19-20, 28-29] or aggregate level [8] obtained from administrative records of hospital employees [4, 28-29], face-to-face interviews and patients' medical files [20], computerized clinical history records [19], State Health insurance records [12], population projections, data provided by personal communication, or survey data [8].

Among the studies in this review that identified determinants of pandemic influenza vaccination using regression modelling, all were conducted at the individual-level. This method requires knowledge of the vaccination status of each individual within the study population and individual-level demographic and risk factor data. Fifteen (55.6%) of the studies analyzed multiple predictors concurrently in the same model [4, 11, 14-15, 17, 19, 23-25, 27, 29-30, 32-34] whereas three (11.1%) studies examined candidate predictors in separate bivariate models using logistic regression [20, 28, 31]. Twenty-three (85.2%) of the studies examined previous receipt of the pandemic A/H1N1 influenza vaccine as the outcome and four examined refusal to vaccinate [4, 25, 32, 34].

3.4. Determinants of Pandemic Influenza Vaccination

The determinants of pandemic A/H1N1 influenza vaccination can be divided into five major categories: 1) socioeconomic and demographic factors; 2) regional and household characteristics; 3) health status and behaviours; 4) beliefs and perceptions; and 5) information, knowledge and advice.

Socioeconomic and Demographic Factors

The socioeconomic and demographic determinants that were most often found to be statistically significant predictors of vaccination were sex, age, ethnicity, occupation, and education level.

Fourteen studies [4, 8, 11-12, 17, 19-20, 25, 27, 29-30, 32-34] examined the effect of sex on vaccination. Six found that males [4, 17, 19, 32-34] and two found that females [8, 29] were more likely to receive the pandemic vaccine. Interestingly, Bone et al. found that younger females, aged 25 to 44 years, and older males, 45 years of age or older, were more likely to receive the vaccine.

Out of the seventeen studies [4, 6, 8, 11-13, 15, 17-20, 23-25, 29, 32, 34] examining age as a determinant of pandemic influenza vaccination, seven found that older age groups [4, 8, 17, 19, 25, 29, 32] and three found that younger age groups [6, 11-12] were more likely to receive the vaccine. Although coverage was observed to be high among older age groups in most studies, young children were excluded from the analysis in many of these studies [4, 8, 15, 17, 20, 23-25, 29, 32, 34]. Among the studies including all age groups (6 months of age or older) [6, 11-13, 19], coverage was higher among younger individuals [6, 11-12]. In addition, a study conducted by the CDC reported coverage for different age groups at the state level, and although statistical significance was not assessed, state-specific coverage was generally greater among children 6 months to 17 years of age [13].

Four studies explored the effect of ethnic origin on pandemic influenza vaccination [6, 8, 17, 19], however a clear pattern was not identified. One study found that vaccination rates were higher among non-Hispanic whites compared to non-Hispanic blacks for adults aged 25 to 64 with a high-risk condition and for healthcare workers [6]. Studies also found that being an immigrant [19], Jewish [17] or an Aboriginal and/or Torres Strait Islander [8] was associated with higher rates of vaccination.

Occupation category or status was observed to be significantly associated with pandemic influenza vaccination. Being a professional, a manager, a farmer or a retired person were all significantly associated with receiving the pandemic vaccine [11]. Among pregnant women, Ozer et al. found that women working outside the home were more likely to receive the vaccine compared to women who were not employed outside of the home. Among the studies examining the determinants of pandemic influenza vaccination in healthcare workers [4, 25-26, 28-29, 31-34], being a physician [4, 25, 28, 31-34] was most often associated with receiving the vaccine, compared to nurses, administrative staff or technicians.

Of the seven studies that investigated education as a determinant of pandemic influenza vaccination [11, 17-18, 23-24, 26-27], five found that higher education (i.e., either having a college/university degree [11, 18, 23, 26] or clinical education [27]) was significantly associated with receiving the vaccine. Income was also examined as a predictor of vaccination in two studies [17, 23], however results were not consistent.

Regional and Household Characteristics

Several regional and household characteristics were found to be associated with pandemic influenza vaccination. Some studies in this review examined pandemic influenza vaccination by region or residence [12-13, 24]. Bone et al. and a study conducted by the CDC, reported that coverage varied by region, ranging from approximately 6% to 12% and 13% to 39%, respectively [12-13]. These studies did not investigate the heterogeneity further. Ozer et al. were not able to conclude a statistically significant association between region of residence and vaccination.

Three studies [11, 24, 32] examined the effect of the number of individuals living in the household on vaccination. Two children [24] or more than one child under 5 years of age [11] living in the household was significantly associated with higher vaccination rates. Vaux et al. also found that living in a household with three or more individuals increased the likelihood of vaccination.

Health Status and Behaviours

All of the studies examining the influence of seasonal influenza vaccination receipt in the past 1-3 years on pandemic influenza vaccination found that prior seasonal vaccination was positively associated with receipt of the pandemic vaccine [4, 11, 18-20, 25, 31-34].

Most of the studies concluded that being in a priority group for which pandemic influenza vaccination is recommend (chronically ill, pregnant women, or healthcare worker) increased the likelihood of receiving the vaccine [8, 11-13, 15, 34]. Rodríquez-Rieiro et al. concluded that the number of chronic conditions was positively associated with vaccine coverage.

Belief and Perceptions

There were four major beliefs and perceptions regarding the vaccine and the pandemic that were significantly associated with receipt of the vaccine: 1) believing that the vaccine was safe or without risk of side effects [14-15, 23-24, 30, 32-33]; 2) believing in the efficacy/effectiveness of the vaccine and its benefits [14-15, 23, 30-33]; 3) a perception of susceptibility to infection [23, 32]; and 4) a perception that pandemic influenza infection is severe [30].

Information, Knowledge and Advice

Having the correct knowledge regarding pandemic influenza vaccination or being informed and aware of the recommendations for vaccination was related to vaccine receipt [23, 27]. Obtaining information from official sources such as the medical literature, government information campaigns, the WHO or CDC, a local health department, or a physician increased the likelihood of vaccination [16, 21, 23, 25, 27, 32-33]. In addition, receiving a recommendation or advice from a health professional [14, 21-23], an employer/co-worker [14, 25-26] or a spouse/family/friend [14, 23] increased vaccine receipt.

4. Discussion

Among the 27 studies included in this review, a wide range of pandemic influenza vaccine coverage was observed. Coverage was greatest among the chronically ill, followed by pregnant women, healthcare workers, and finally the general population. Coverage varied by region and by assessment method. The most often cited determinants of pandemic influenza vaccination were male sex, younger age, higher education, being a doctor, belonging to a priority group for which vaccination is recommended, receiving a prior seasonal influenza vaccination, believing that the vaccine is safe without risk of side effects, believing in the efficacy/effectiveness of the vaccine and its benefits, and obtaining information from official medical sources.

Reviews on the determinants of intention and receipt of pandemic influenza vaccination [3] and seasonal influenza vaccination among healthy adults [35], elderly [36-37], high-risk individuals [35], and healthcare workers [35, 38] have reported similar results as our review. Among these studies the most commonly cited socioeconomic and demographic variables associated with increased pandemic or seasonal influenza vaccination were higher socioeconomic status [35-37], living in a suburban, less deprived area [36] and living in larger households [37], as we observed in our review. Having a chronic illness [3, 35-37] and receiving a previous seasonal influenza vaccination [3, 35, 38] have been shown to be associated with receiving a seasonal or pandemic influenza vaccine. Perceptions regarding susceptibility to infection [3, 35-36, 38], severity of illness [3, 35, 38], benefits/effectiveness of the vaccine [3, 35-36, 38], and not perceiving barriers to vaccination such as safety of the vaccine [3, 35-36, 38] were also positively associated with receiving the vaccine. Receiving a recommendation to be vaccinated was also often associated with vaccination [3, 35-36, 38].

Although this review outlines the main patterns observed among the identified studies, we did note some inconsistencies. Since studies were conducted between May 2009 and April 2010, and events modifying the perceived severity of the pandemic occurred throughout this period, the results may have been influenced by when the data were collected. In addition, local and cultural differences may also have led to the variability in coverage as some regions did not emphasize the importance of vaccination as much as others. Additionally, different priority groups and vaccination strategies were established in different geographical regions. These discrepancies could have affected the differences observed among the vaccine coverage rates.

The lack of consistency observed among determinants suggests that future research on this topic is required. Most of the studies included in this review examined the determinants of pandemic A/H1N1 influenza using survey methodology. This method is subject to many biases such as selection bias, poor recall, and reliance on self-report. We also observed that surveys tended to overestimate coverage rates when compared with results using registry data. It is likely that individuals who respond to surveys are more likely to also be vaccinated. Using a vaccination registry to estimate coverage provides numerator data not subject to many of the biases that influence survey results. However, using a registry requires a method to estimate the denominator data. The methods used to estimate a denominator among the identified studies lacked consistency and precision. Estimating precise denominators is important as imprecise denominator estimates can affect coverage estimates, as shown in the study conducted by Bone et al. which reported different estimates by age depending on the denominator estimates used. Standard methods for denominator estimation that are reliable, valid and can be applied easily to estimate coverage in a timely fashion should be used. The existence of such methods would aid public health officials in planning and evaluating the progress of a vaccination campaign.

Most of the included studies used individuals as the unit of analysis. Only two studies examined coverage at a regional level [12-13]. As the delivery of health services is often conducted at the local level, understanding the neighborhood differences in vaccine coverage is informative from a public health perspective. Furthermore, understanding the reason for this heterogeneity may help to further elucidate the barriers and determinants related to decreased vaccine coverage and allow public health officials to target their efforts more effectively.

There are several limitations to our review. We did not focus on the reasons for acceptance or refusal of the vaccine; doing so may have helped to explain the importance of some determinants, however this was not the purpose of the review. We also did not distinguish between univariate and multivariate analysis when commenting on the determinants of pandemic influenza vaccination; however the results did not appear to be systematically different. We only included studies published between June 2009 and February 2011. More studies will likely be published following this period, perhaps providing more data on the determinants of vaccination. Nonetheless, our review included a large number of studies. We did not conduct a meta-analysis as the studies were too heterogeneous and different outcomes were used. For example, some studies reported only coverage estimates or odds ratios for receiving or refusing the vaccine. Additionally, the independent variables included in the studies were not consistent. Finally we excluded studies written in languages other than English, possibly excluding some relevant studies.

The decision to receive the pandemic influenza vaccination is influenced by many factors. Recognizing and understanding the factors that influence pandemic influenza vaccination can help to devise effective immunization strategies. To further aid public health officials, future studies are needed to identify the determinants of pandemic influenza vaccination at the population level using simple and reliable population estimates.

Acknowledgements

This research was supported by a Graduate Student Scholarship from the Public Health Agency of Canada and Canadian Institutes of Health Research Influenza Research Network (PCIRN) and a Studentship award from the Canadian Institutes of Health Research.

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Tables

Table 1

Summary of included studies examining the determinants of pandemic A/H1N1 influenza vaccination, ordered in descending vaccine coverage by study location

Author, Year	Study Location, Setting and Period	Sample Population and Size	Data Collection and Instrumentation	Vaccine Coverage, % (95% CI)	Statistically Significant Findings Positively Associated with Pandemic Influenza Vaccination
Park et al., 2010[29]	South Korea, Seven university-affiliated hospitals, October 2009 to December 2009	Hospital workers n=11,497	Collected vaccination data prospectively during the vaccination campaign from all registered hospital employees	91.7% (91.2-92.2%)	Female sex, older age (40 to 49 years), all healthcare occupations other than physician
Fabry et al., 2011[23]	Sherbrooke, Quebec, Canada, University Hospital Centre, February 15 to 24, 2010	Pregnant and early post-partum women n=250	Self-administered questionnaire distributed to women present in the hospital for a hospitalization or a consultation during the study period	76.0% (70.3-80.9%)	Higher education level (college and university), being in the third trimester or post-partum stage of pregnancy, obtained information from Pandémie Québec, belief that the vaccine is protective, not fearful of vaccine safety, belief that advice from a health professional or spouse is important, belief that the vaccine has been tested adequately, perceived a risk of infection, correct knowledge regarding the vaccine
Stavroulopoulos et al., 2010[20]	Athens, Greece, Hemodialysis Unit, November 25, 2009 to December 4, 2009	Patients with chronic renal disease on hemodialysis n=161	Collected vaccination data prospectively during the vaccination campaign from all patients present at the hemodialysis unit during the study period. Collected data on the study population from interviews and medical files	68.0% (60.1-74.4%)	Received the seasonal influenza vaccine, received the pneumococcus vaccine, clinical findings (higher hemoglobin blood levels, lower white blood cell count, higher albumin blood levels)
Printza et al., 2010[18]	Greece, Pediatric Nephrology Department, February 2010	Children with chronic renal diseases n=64	Self-administered questionnaire distributed to all patients in the department during the vaccination campaign	43.8% (32.3-55.9%)	Patient group (transplant patients), higher parental education (university), received the seasonal influenza vaccine
Mavros et al., 2010[27]	Athens, Greece, University of Athens, School of Medicine, December 10 to 16, 2009	Medical students n=922	Self-administered questionnaire distributed to students during mandatory classes hours and to students in teaching hospitals using non-probability sampling	8.0% (6.2-9.7%)	Higher education (4-6 years of medical school), being informed and aware of recommendation for vaccination, obtaining information from official medical sources

Table 1, continued

Author, Year	Study Location, Setting and Period	Sample Population and Size	Data Collection and Instrumentation	Vaccine Coverage, % (95% CI)	Statistically Significant Findings Positively Associated with Vaccination
Goldschmidt et al., 2011[21]	Germany, Hanover Medical School Children's Hospital, February 2010	Pediatric liver transplant recipients n=127	Telephone survey given to all patients that underwent transplantation before October 1, 2008, and were receiving follow-up care during the study. Collected clinical data from patient files	56.7% (48.0-65.0%)	Received a recommendation from the pediatric liver transplant unit or local paediatrician, parent telephone inquiries to clinic regarding H1N1 vaccination
Barrière et al., 2010[25]	Paris and Nice, France, Cancer centres, December 20, 2009 to January 25, 2010	Hospital workers n=506	Mailed and emailed a questionnaire created by authors based on a review of the literature to employees of two cancer centers	Survey Respondents: 51.4% (47.0-55.7%) All Hospital workers: 30.7% (28.6-32.8%)	Older age (more than 35), being a physician, received prior seasonal influenza vaccines, colleagues' advice and institutional campaign as the main source of information, wish to have family vaccinated
Nougairède et al., 2010[28]	Marseille, France, La Conception Public Hospital October 20, 2009 to December 4, 2009	Hospital workers n=3,315	Collected vaccination data during the vaccination campaign. Used administrative records to define the study population	30.1% (28.6-31.7%)	Received the vaccination at mobile vaccination facility, being part of the medical staff, being vaccinated after November 21
Vaux et al., 2011[11]	France, May 2009 to April 2010	Household population, all ages n=10,091	Telephone survey of a random sample of household selected from the telephone directory. Two participants from each household, below and above 5 years of age were selected	11.1% (9.8-12.4%)	Under 5 and 30-64 years of age, being in a risk group, being 0 to 4 years of age or younger than 64 years of age and in a risk group, children living in the household, more than 3 people living in the household, higher education (more than 2 years of university), being a healthcare worker, having an occupation such as professional/managerial, self-employed, intermediate or retired, received the seasonal influenza vaccine
Bone et al., 2010[12]	France, October 18, 2009 to February 20, 2010	General population, 6 months of age or older n=64,942,414	Collected vaccination data during the campaign using vaccination coupons sent to the entire population with a registered address within the State Health insurance system	7.95% (7.949-7.951%)	Young women (25 to 44 years), older men (45+ years). Descriptive results (statistical significance not reported): Coverage highest among children 6 to 23 months of age, decreased with age, reaching lowest coverage in adults 18 to 24 years of age then increased in older adults, regional variations observed, being pregnant or having a chronic condition

Table 1, continued

Author, Year	Study Location, Setting and Period	Sample Population and Size	Data Collection and Instrumentation	Vaccine Coverage, % (95% CI)	Statistically Significant Findings Positively Associated with Vaccination
Centers for Disease Control and Prevention, 2010[22]	United States, October 1, 2009 to March 12, 2010	Pregnant women n=5,112	Participants with recent live births from October 1, 2009 to March 12, 2010, selected by stratified random sampling from State birth certificate registries. Participants mailed a questionnaire after delivery	46.6% (44.7-48.4%)	Vaccination offered or recommended by their health-care provider, received the vaccination at the obstetrician/gynecologist office, health department/community clinic, family physician office, work/school compared to pharmacy
Centers for Disease Control and Prevention, 2010[26]	United States, January 2010	Hospital workers n=1,417	Participants recruited using address-based sampling and random digit dialling. Internet survey administered to participants	37.1% (33.1-41.2%)	Employer requirement or recommendation, workplace (hospital), unit (intensive care, burn or obstetric units or around seriously ill patients), education (bachelor's degree or higher)
Centers for Disease Control and Prevention, 2010[13]	United States, November 2009 to February 2010	Household population, 6 months of age or older n=214,316 47 States	Two telephone surveys administered to the non-institutionalized, U.S. civilian population selected by random-digit dialling	23.9%[a] (12.9-38.8%)[b]	Descriptive results (statistical significance not reported): Children and adult state coverage were highly correlated. Large variation in state coverage observed overall, and by age and priority groups
Gargano et al., 2011[14]	Georgia, United States, Mid- and high schools in two rural counties, September 11, 2009 to May 2010	Teachers and staff members n=66	Sampled all staff from schools participating in an ongoing seasonal influenza vaccination intervention. Data collected by self-administered questionnaire.	21.2% (13.1-32.5%)	Do not perceive any barriers (regarding vaccine safety and effectiveness) to receiving the vaccine, perceive receiving the vaccine to be a social norm (influenced by doctor's, coworkers' and family's advice)
Centers for Disease Control and Prevention, 2010[6]	United States, December 1, 2009 to January 2, 2010	Household population, 6 months of age or over n=3,023	Two telephone surveys administered to the non-institutionalized U.S. civilian population selected by random-digit dialling	20.3% (17.2-23.4%)	Being a non-Hispanic white among those aged 25 to 64 with a high-risk condition and healthcare workers, being in the initial target group or limited vaccine subset, younger age (less than 19 years), being a pregnant woman
Maurer et al., 2010[16]	United States, March 4 to 24, 2010	Household population, adults aged 18 or over n=3,917	Survey administered via the internet. Households selected from a previously defined research panel by random digit dialling and address-based sampling	20.0% (17.8-22.1%)	Information source (employer, healthcare provider or CDC/local health department)

Table 1, continued

Author, Year	Study Location, Setting and Period	Sample Population and Size	Data Collection and Instrumentation	Vaccine Coverage, % (95% CI)	Statistically Significant Findings Positively Associated with Vaccination
Torun et al., 2010[33]	Istanbul, Turkey, Umraniye Research and Training Hospital, December 7 to 22, 2009	Hospital workers: Parents of children 6 months to 18 years old n=389	Self-administered questionnaire distributed to all persons employed in the hospital that are parents of children 6 months to 18 years of age	27.0% (22.8-31.6%)	Male sex, occupation (doctor), self receipt of pandemic influenza vaccine, obtained information from sources other than the media, belief that the pandemic vaccine is safe, belief that the vaccine is effective, trust in Ministry of Health
Torun et al., 2010[32]	Istanbul, Turkey, Umraniye Research and Training Hospital, December 7 to 22, 2009	Hospital workers n=718	Self-administered questionnaire distributed to all persons employed in the hospital	23.1% (20.2-26.3%)	Male sex, older age (40+ years), being a doctor, received the 2009 seasonal influenza vaccine, anxious about personal infection, information source (WHO, CDC, doctors, or Ministry of Health), trust in the Ministry of Health, belief that the vaccine is effective and safe, belief that the vaccination benefits outweigh the risks, belief that healthcare workers have a professional responsibility, do not believe the media exaggerates the situation, are not confused about the pandemic
Savas et al., 2010[30]	Turkey, University and State Hospital, November 23, 2009 to December 4, 2009	Hospital workers n=300	Self-administered questionnaire distributed via convenience sampling to hospital employees	12.7% (9.4-16.9%)	Belief that the swine flu is a serious outbreak, belief that the vaccine is protective, belief that the vaccine is safe, plan on vaccinating children
Ozer et al., 2010[24]	Kahramanmaras, Turkey, Kahramanmaras Sutcuimam University, Antenatal clinic, December 23, 2009 to February 1, 2010	Pregnant women n=314	Face-to-face questionnaire administered to all pregnant women at the clinic during the study period	8.9% (6.2-12.6%)	Has an occupation, correct knowledge regarding the H1N1 vaccine and side effects during pregnancy, has, two children
Gaygisiz et al., 2011[15]	Turkey, January 5 to 17, 2010	Household population, adults n=1,137	Self-administered survey distributed by non-probability sampling to households in the neighbourhoods' of data collectors (60 students)	4.8% (3.7-6.2%)	Belief that there is a swine flu epidemic, trust in the effectiveness of the vaccine, do not perceive risk of side effects from the vaccine, perceive a benefit for receiving the vaccine, chronically ill

Table 1, continued

Author, Year	Study Location, Setting and Period	Sample Population and Size	Data Collection and Instrumentation	Vaccine Coverage, % (95% CI)	Statistically Significant Findings Positively Associated with Vaccination
Seale et al., 2011[31]	Beijing, China, 19 Public hospitals, January 2010	Hospital workers n=1,657	Self-administered survey distributed to previously selected participants of a randomized control trial	24.7% (22.7-26.9%)	Received the seasonal influenza vaccine for the 2009/2010 season, being a doctor, belief that the vaccine will protect against the flu
Amodio et al., 2011[4]	Sicily, Italy, University hospital, Azienda Ospedaliera Universitaria Policlinico of Palermo, November 2009 to February 2010	Hospital workers n=2,267	Collected vaccination and covariate data during the vaccination campaign using a self-administered questionnaire and administrative records	18.0% (16.5-19.6%)	Higher mean age, male sex, being a doctor or biologist, having clinical duties, having a full-time job, received the seasonal influenza vaccine last year
Velan et al., 2010[17]	Israel, March 15 to 16, 2010	Household population, aged 18 years or over n=501	Telephone survey of households randomly selected from official statistical units using probabilistic stratified sampling	17.0% (13.9-20.5%)	Male sex, older age (more than 39 years), non-disclosed income, Jewish ethnicity
Vírseda et al., 2010[34]	Madrid, Spain, University Hospital 12 de Octubre, December 23, 2009 to January 13, 2010	Hospital workers n=527	Mailed self-administered questionnaire to healthcare workers selected from the hospital staff roster using systematic random sampling	16.5% (13.6-19.9 %)	Male sex, having regular patient contact, received the 2008-2009 and 2009-2010 seasonal influenza vaccine, being a physician, not being in a priority group for pandemic influenza, being in a priority group for seasonal influenza
Rodríquez-Rieiro et al., 2010[19]	Madrid, Spain, November 16, 2009 to March 22, 2010	Individuals with a chronic condition, ages 6 months or above n=1,114,632	Collected vaccination data from all individuals vaccinated during the campaign. Used computerized clinical history records and other information systems to define the study population	14.6% (14.5-14.7%)	Male sex, older age (45+), increasing number of indications, general/pensioner medical card, received the 2009 seasonal influenza vaccine, immigrant origin
Mak et al., 2010[8]	Western Australia, Australia, September 30, 2009 to January 31, 2010	General population, 10 years of age or over n=550 (survey) 1,908,767 (database)	Collected vaccination, demographic and risk factor data during the campaign. Estimated the population at risk using population projections and personal communication. Also collected data using a telephone survey. Participants were selected by stratified random sampling from the telephone directory	Registry: 9.0% (8.96-9.04%) Survey: 14.5% (12.6-16.6%)	Older age (40+), female sex, has a medical condition, Descriptive results (statistical significance not assessed): being an aboriginal and/or Torres Strait Islander, being a healthcare worker compared to being a pregnant women

[a] Median.
[b] Range.

Table 2
Summary of pandemic A/H1N1 influenza vaccine coverage among included studies, overall and by population sub-group

Population	n	Median[a]	Range[a]
Overall	27	21.1%	4.8-91.7%
Individuals with a chronic condition	4	50.3%	14.6-68.0%
Pregnant women	3	46.6%	8.9-76.0%
Healthcare workers[b]	11	24.7%	8.0-91.7%
General population[c]	9	17.0%	4.8-23.9%

[a] Values include the coverage value obtained from the registry data [8] and median overall coverage [13].

[b] Includes employees with healthcare (e.g. physician, nurse) and non-healthcare occupations (e.g. administrative assistants) working in a healthcare setting and medical students.

[c] Includes different age groups and may include priority groups.

CHAPTER 3

Methods and Results

The following manuscript uses the knowledge gained from the literature review to inform the design of a study intended to be relevant to public health officials when planning for future pandemic influenza vaccination campaigns.

Most studies have used surveys to estimate vaccine coverage at the national-level and have identified the determinants of vaccination at the individual-level. As the delivery of health services is conducted at a local-level, it is important from a public health perspective to estimate vaccine coverage at the neighborhood-level. Few ecologic studies have been conducted to identify the determinants of vaccination, and none have examined the determinants of pandemic influenza vaccination. This manuscript aims to identify the neighborhood determinants of pandemic influenza vaccination.

The following manuscript details the methods and the results of this research. The manuscript includes an appendix which provides additional results and detailed information on the models used in the analysis. This manuscript will be submitted for publication to the American Journal of Epidemiology and has been formatted according to the Journal's specifications.

TITLE:

Pandemic influenza vaccine coverage and neighborhood determinants of vaccination

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Abbreviations:

CCHS, Canadian Community Health Survey;

DA, Dissemination area;

ICD-9, International Classification of Diseases, Ninth Revision

NPHS, National Population Health Survey;

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ABSTRACT

Accurate neighborhood-level estimates of vaccine coverage are essential for directing and evaluating mass vaccination campaigns. In addition, neighborhood-level coverage data can be used to identify determinants of vaccination that should be considered in planning for future influenza pandemics. Immunization registries are an ideal source of data for estimating neighborhood-level coverage, but few studies have examined the determinants of pandemic influenza vaccination among the general population using a registry. Using individual-level vaccination data, we described pandemic A/H1N1 influenza vaccine coverage in Montreal using census, survey and administrative data to estimate the population at risk. The neighborhood socioeconomic and demographic determinants of pandemic influenza vaccination were identified using logistic regression, accounting for spatial autocorrelation. A total of 918,733 (49.9%) Montreal residents were vaccinated against pandemic A/H1N1 influenza between October 22, 2009, and April 8, 2010. Coverage was greater among females, children less than 5 years of age, and healthcare workers. Neighborhood vaccine coverage ranged from 33.6% to 71.0%, with lower coverage clustering in urban regions of Montreal. High proportions of neighborhood immigration and material deprivation were significantly associated with lower neighborhood vaccine coverage. These results should help public health officials implement priority-group specific vaccination strategies to increase vaccination during future influenza pandemics.

Keywords: Pandemics; Influenza, Human; Immunization

Abstract word count: 200 words

On June 11th, 2009, the World Health Organization declared the beginning of the first influenza pandemic of the 21st century (1). The first case of 2009 A/H1N1 influenza virus in Quebec, Canada was confirmed on April 30th, 2009, in Montreal (2). The number of laboratory-confirmed cases in Quebec totaled 10,889, with 2492 hospitalized cases and 83 deaths (3). Fourteen percent of hospitalized cases and 14% of deaths occurred in Montreal (3), which accounts for 25% of the provincial population (4).

On October 26th, 2009, Quebec launched a mass pandemic influenza vaccination campaign to prevent infection and protect susceptible populations from severe disease. Measuring vaccine coverage accurately is necessary for evaluating campaign effectiveness. Identifying neighborhoods and population subgroups with low vaccination rates is also crucial so that public health officials can identify inconsistencies in program delivery possibly leading to target intervention strategies to enhance vaccination in vulnerable populations.

A number of studies have examined the determinants of pandemic influenza vaccination in the general population (5-13), but only two used a vaccination registry (5, 10). The remainder used surveys (6-9, 11-13), which can be susceptible to selection bias and a variety of biases associated with self-reporting such as social desirability bias. As a result, surveys tend to overestimate coverage compared to registries (5, 12, 14, 15).

Using registries to assess vaccine coverage requires a method to estimate the at-risk population. Published methods have varied in terms of complexity and accuracy (5, 10, 15-19). Estimating precise denominators is important to avoid potential bias in coverage estimates (5). Standard denominator estimation methods that are reliable, valid and can be rapidly applied are needed.

Few studies examining the determinants of pandemic influenza vaccination have reported regional coverage estimates (5, 6). Geographic variation was noted in these studies, but was not investigated further. Understanding the reasons for this heterogeneity may help to elucidate the barriers and determinants of pandemic influenza vaccination. Furthermore, understanding local determinants of vaccination is beneficial from a public health perspective because health services are delivered locally.

The objectives of this study were: 1) to estimate by Montreal neighborhood the population of priority groups for which pandemic A/H1N1 influenza vaccination was recommended; 2) to describe pandemic influenza vaccine coverage in Montreal by sex, age group, priority group, date of vaccination, and neighborhood using a vaccination registry; and 3) to identify the neighborhood socioeconomic and demographic determinants of pandemic influenza vaccination in Montreal among the total population and priority groups.

MATERIALS AND METHODS

Setting

Montreal is the cosmopolitan economic capital of the Canadian province of Quebec, with a population of 1,854,442, representing 25% of the provincial population in the 2006 census (4). The public health department of the health and social services agency of Montreal divided the Island of Montreal into 111 neighborhoods by aggregating the 522 census tracts in a way that attempted to maintain within-neighborhood homogeneity with respect to socio-demographic factors (20). A census tract is a small statistical area in an urban area with between 2,500 to 8,000 individuals (21).

The pandemic influenza vaccination campaign in Montreal began on October 26th, 2009, during the peak of the second wave. The vaccines were administered free-of-charge in priority sequence (Appendix Table 1) at twelve mass vaccination clinics located throughout the Island. Following the closure of these clinics on December 18th, 2009, individuals could obtain the vaccine at local community health centers. Throughout the campaign, federal and provincial authorities conducted extensive media campaigns informing the public of the benefits of vaccination.

Study Design

We conducted an ecological study to identify neighborhood determinants of pandemic influenza vaccination. The study population included all Island of Montreal residents aged 6 months or older. This study was approved by the McGill University Institutional Review Board and use of the vaccination registry data was approved by the Quebec Information Access Commission (Commission d'accès à l'information du Québec).

Data Sources

Vaccination Data. Vaccination data were recorded at the point of care throughout the campaign and subsequently entered in a central registry, which was established in 2009 for the sole purpose of collecting pandemic influenza vaccination data in Quebec. We obtained records of vaccination from the National Public Health Institute of Quebec (Institut national de santé publique du Québec) for all individuals vaccinated on the Island of Montreal. For our study we obtained age group, sex, date of vaccination, census tract of residence, and self-reported priority group status (healthcare worker, chronically ill, pregnant women) for each vaccinated individual. We restricted our analysis to Island of Montreal residents.

Healthcare Utilization Data. Healthcare utilization data were obtained from the Régie de l'assurance maladie du Québec (RAMQ), and the Maintenance et exploitation des données pour l'étude de la clientèle hospitalière (MED-ECHO) administrative databases to estimate the number of pregnant women. These databases contain information on medical services and hospitalizations, respectively, for all Quebec residents. Previous studies have used these databases to identify pregnant women (22-24). Data on mother's age, census tract of residence, and International Classification of Diseases, 9th Revision (ICD-9) diagnostic code were provided for each record.

Census Data. Data from the 2006 Census were obtained from Statistics Canada to estimate the population by age and sex, the number of healthcare workers, and covariates (% immigrants, material and social deprivation).

Survey Data. Survey data were obtained from the 2007/2008 Canadian Community Health Survey (CCHS), and the 1998/1999 National Population Health Survey (NPHS) to estimate numbers of individuals with chronic illnesses. These national, population-based surveys collect data related to the health and socio-demographics of the Canadian population. We used the Public Use Microdata Files, which contain anonymized individual-level data on sex, age group, presence of chronic conditions, and geographical region.

Estimation of Denominators

To estimate vaccine coverage, numerator and denominator data are required. Unlike surveys, which capture numerator and denominator data from survey respondents, registries collect only numerator data. We sought to estimate the denominator, in other words the population of Montreal, by age, sex and priority group status, for the entire city and by neighborhood. Data on priority groups by Montreal neighborhoods are not readily available. Consequently, we employed several previously developed data sources and methods to estimate the required denominators.

Population count. We used 2006 Census data as an approximation of the population in 2009. We obtained counts for each age-sex stratum for each census tract on the Island of Montreal.

Pregnant Women. We identified pregnant women using healthcare utilization data and the ICD-9 codes listed in Appendix Table 2 (25). These codes were developed for the Canadian Chronic Disease Surveillance System to exclude women with gestational diabetes and pregnancy-induced hypertension when estimating the prevalence and incidence of diabetes in the Canadian population (25, 26). These codes describe pregnancy-related procedures and outcomes.

To determine the number of pregnant women in each neighborhood during the study period, we identified women with at least one ICD-9 code from the set during the 2006 calendar year. Women with multiple codes were only considered once. Previous studies used yearly estimates to determine the number of pregnant women during pandemic or seasonal influenza seasons (10, 27, 28).

Chronic Illness. The CCHS and NPHS defined the presence of a chronic condition as a "long-term condition that had lasted or was expected to last six months or more and that had been diagnosed by a health professional" (29, 30). Those who reported having asthma, diabetes, heart disease, cancer, effects of stroke, or chronic bronchitis/emphysema were considered to have a chronic illness for which influenza vaccination is recommended. These variables have been described previously (31, 32).

We calculated the proportion of persons with one or more chronic conditions by age group, region, and year (Appendix Table 3). Estimates were calculated and reported according to Statistics Canada guidelines (33). Proportions for children under 19 years of age were calculated using the NPHS for Quebec since the CCHS is restricted to individuals 12 years or older and NPHS estimates for Montreal were too unstable. This method slightly underestimates the proportion of children with a chronic illness in Montreal, but the difference is not statistically significant (Appendix Table 4).

To estimate the population of individuals with a chronic illness less than 65 years of age, we applied the age-specific proportions to the corresponding age distribution of each neighborhood. We then took the sum of the stratum-specific numbers. This method of denominator estimation has been previously described (34, 35).

Healthcare Workers. The number of healthcare workers was estimated using Census data. We used a variable from the Census describing “the general nature of the business carried out in the establishment where the person worked” (21). To estimate the number of healthcare workers in a neighborhood we obtained the count of individuals identifying their industry to be described as “Health care and social assistance” for each census tract. This includes healthcare workers such as physicians and nurses as well as non-healthcare workers such as administrative personnel, a definition used previously (14-17, 36-40).

Covariates

The independent variables included in this study were determined from a literature review on the determinants of pandemic influenza vaccination. The socioeconomic and demographic determinants identified to significantly predict pandemic influenza vaccination were: age, gender, priority group status, ethnicity/immigration status, education, occupation, income, and number of children/people living in the household. Rather than include all variables in the analysis we used indices of material and social deprivation, and % immigrants, as these variables encompass all categories mentioned above and avoid the problem of multi-collinearity that arises when including highly correlated covariates in the analysis.

Deprivation indices. Indices of material and social deprivation were constructed by Pampalon and Raymond (41) in Quebec to estimate an individual's socioeconomic status by using the neighborhood-level socioeconomic status as a proxy (42). Each index is composed of three census variables that are intended to reflect the deprivation of individuals in the area relative to the population being studied. Material deprivation measures the lack of access to goods and services and includes the proportion of persons lacking a high school diploma, employment-to-population ratio, and average income. Social deprivation measures the lack of social support and involvement and includes the proportion of persons living alone, the proportion of persons separated, divorced or widowed, and the proportion of single-parent families. These indices have been used extensively to examine determinants of health in Quebec (43-48).

We obtained the deprivation score for each dissemination area (DA), the smallest geographic area for which Census data are available, in Montreal (21). From these values, quintiles of deprivation for Montreal were determined. As each neighborhood comprises several DAs, we calculated the average DA deprivation value for each neighborhood. We then grouped the neighborhood DA values into quintiles, with a value of five representing the highest deprivation level.

Immigrants. Using Census data, we estimated the number of recent immigrants in each neighborhood by including those who immigrated between 2001 and 2006. The number of immigrants in each neighborhood was divided by the total population of the neighborhood to obtain the proportion of immigrants.

Statistical analysis

Vaccine coverage and 95% confidence intervals were calculated overall and by sex, age group, priority group, and neighborhood. Cumulative coverage was calculated by date of vaccination among priority and age groups. Choropleth maps were constructed of the dependent variables (vaccine coverage overall and by priority group) and independent variables (% immigrants, material and social deprivation). We excluded observations with missing data.

To identify the neighborhood determinants of pandemic influenza vaccination we used a Bayesian ecological logistic regression model accounting for spatially unstructured and structured variation in vaccine coverage (49-51).

We fit our models using three chains each with different initial values. To improve convergence we centered all covariates. Convergence was assessed by visual inspection of Gelman-Rubin diagnostic plots. Once convergence was achieved, we ran an additional 20,000 iterations to obtain the posterior distributions. We investigated the influence of the different choices of hyperpriors on our results through sensitivity analyses.

We undertook separate analyses for the total population, pregnant women, chronically ill, and healthcare workers. The independent variables were % immigrants and material and social deprivation, and the potential confounders were age group, sex and priority group status as a percentage of the neighborhood population. The determinants of pandemic influenza vaccination were investigated using univariable and multivariable analyses. We included all variables in the multivariable model regardless of significance as all variables are relevant from a public health perspective. We calculated univariable and multivariable odds ratios and 95% credible intervals. For six (1.4%) neighborhoods with proportions greater than one, we changed the numerator value to equal the denominator value. To investigate the influence of changing the numerator value on our results, we conducted sensitivity analyses in which we changed the denominator to equal the numerator value and we excluded the numerator value (i.e., assumed that the neighborhood's value was missing). Data were analyzed using Stata/SE 9.2 and WinBUGS 1.4. Maps were constructed using ArcMap 9.3.

RESULTS

A total of 1,015,068 individuals aged six months or older were vaccinated on the Island of Montreal during the study interval (Figure 1). We excluded 94,923 (9.4%) vaccinations of non-residents. An additional 1,371 (0.15%) records were excluded because they were for residents of census tracts with missing or suppressed population data (n=1,339) (52) or were missing age or sex data (n=32).

Among our study population, a total of 918,733 (49.9%) Montreal residents were vaccinated against pandemic influenza during the study period (Table 1). Statistically significant differences in coverage were observed by sex, age group, and priority group. Coverage was highest among females (52.4%), children aged 6 months to 4 years (70.0%) and healthcare workers (66.8%).

Vaccinations took place between October 22, 2009, and April 8, 2010. Most (95%) of the vaccinations occurred before December 16th. Vaccine coverage rose rapidly among healthcare workers, pregnant women, and young children once these groups were eligible to receive the vaccine (Figure 2). Vaccine coverage changed little after December 18th, corresponding to the closure of the mass vaccination clinics.

Neighborhood vaccine coverage varied overall and by sex, age, and priority group (Figure 3). Variation in coverage by neighborhood was lowest among 20 to 64 year olds and greatest among pregnant women. The geographic distribution of vaccine coverage varied overall and when stratified by priority group (Figure 4). Among the overall population, areas of low coverage were clustered in the North and Eastern neighborhoods of Montreal, coinciding with higher deprivation scores and greater proportions of immigrants (Figure 5).

Univariable analyses showed that the proportion of immigrants and material and social deprivation were negatively associated with neighborhood pandemic influenza vaccine coverage among the total population (Table 2). Among priority groups, material deprivation was negatively associated with vaccine coverage among pregnant women and healthcare workers, and the proportion of immigrants was negatively associated with vaccine coverage among the chronically ill.

After adjusting for age, sex, and priority group status, neighborhood material deprivation and the proportion of immigrants remained negatively associated with neighborhood vaccine coverage. After adjusting for the effects of other variables, an increase of one quintile in neighborhood material deprivation resulted in approximately a 7%, 15%, and 17% decrease in the odds of neighborhood vaccination among the total population, healthcare workers, and pregnant women, respectively (Table 3). A 10% and 17% decrease in the odds of neighborhood vaccination was observed for every 5% increase in neighborhood percentage of immigrants among the total population and the chronically ill under 65, respectively, after adjusting for the effects of other variables (Table 3). There did not appear to be a statistically significant relationship between social deprivation and vaccine coverage in the multivariable analysis for all populations analyzed.

Our results were sensitive to neither our choice of hyperpriors (Appendix Tables 5 to 8) nor the method used to correct neighborhoods with vaccine coverage greater than 100% (Appendix Tables 9 and 10).

DISCUSSION

Using a large, population-based immunization registry to estimate events, and census, survey, and administrative records to estimate the population at risk, we calculated pandemic influenza vaccine coverage for an urban area at a higher geographical resolution than any estimates previously published. Overall pandemic influenza vaccine coverage in Montreal was 50%; however, we observed considerable variation by population sub-group and geographic region. Females, younger individuals, and healthcare workers were more likely to receive the vaccine. We found that neighborhoods with higher proportions of immigrants and more material deprivation had lower vaccine coverage.

Neighborhoods with low vaccine coverage, particularly those with vulnerable populations, can contribute to the spread of outbreaks; to prevent transmission, coverage must be high not just overall, but also among neighborhoods within a region. Interventions are needed to reduce the observed variations in coverage. Using the methods described in this study, public health officials can estimate coverage among neighborhoods, assess variations in coverage, and target regions of lower coverage. To our knowledge this is the first study to identify the neighborhood determinants of pandemic influenza vaccination for the total population and priority groups. Using the population-level determinants of vaccination we identified, public health officials will be able to identify and target neighborhoods likely to have lower vaccine coverage in real-time, and implement priority-group specific vaccination strategies such as telephone or mailed reminders to increase vaccination during future influenza pandemics.

Our overall coverage estimate is similar to other estimates of Montreal (50.4%) (3), and greater than estimates reported for many other regions (Range: 4.8% to 20.3%) (7, 9, 10, 12, 13). Our results are similar to other studies in which females (32, 53), children (5, 7, 12), and healthcare workers (10, 12) were more likely to receive the vaccine.

The geographic variability we observed among population groups was partially explained by neighborhood material deprivation and the proportion of immigrants. Our results are comparable to other epidemiologic studies on the determinants of pandemic influenza vaccination in which ethnic origin (7, 10, 13, 18), income (18), occupation (12, 54), and education (12, 36, 55-57) predicted vaccination. In one review of seasonal influenza vaccination determinants, vaccination rates were lower among racial and ethnic minorities and those living in poverty (58). The possible reasons for lower coverage in areas with greater proportions of immigrants may be due to barriers in access to health care, transportation, knowledge, and language (59-63). Possible reasons for lower coverage in areas with more material deprivation may be related to poor understanding and lower sensitivity to public health messages, leading to decreased health awareness and the adoption of fewer public health interventions (64). We did observe differences in determinants by priority group where material deprivation was negatively associated with vaccination among pregnant women and healthcare workers and the proportion of immigrants was negatively associated with vaccination among the chronically ill, indicating that the neighborhood factors that influence the decision to receive the vaccine likely differ by priority group.

Due to the large neighborhood variability observed, our results suggest that coverage should ideally be measured at the neighborhood-level. Furthermore neighborhood estimates of coverage are essential for public health officials to make informed decisions during vaccination campaigns. Using registry data, we were able to calculate estimates of vaccine coverage at a higher resolution than any estimates previously published using traditional survey methodology. However, estimating denominators for priority groups for small areas is a challenge as data describing individuals within priority groups are not readily available at the neighborhood-level. Therefore we applied a simple approach to estimate denominators that can be applied using data that are readily available to public health officials. Although our method of estimation has not been validated for small areas, our results are similar to those from other studies. We observed six regions with coverage over 100%, a small percentage of observations (1.4%). Although we cannot verify if this finding reflects an issue with numerator (possibly due to self-reported priority group status which was not verified at point of care and therefore over-reported) or denominator data (errors in estimation leading to under-estimation), our sensitivity analyses indicated that these observations did not affect our results. When estimating the number of individuals with a chronic illness, we could have stratified our proportions by socioeconomic status, to obtain more precise estimates. However as we did not observe any neighborhoods with over 100% coverage, we can assume our method of estimation is reasonably accurate.

There were several other limitations of our study, unrelated to our method of estimation. Our data were restricted to vaccinations that took place on the Island of Montreal among residents. We were missing 1% of vaccinations among residents that took place off the Island. However these were mainly healthcare workers who were vaccinated at their workplace off the island. As we studied the determinants of vaccination at the neighborhood-level we cannot extrapolate our findings to the individual, although our neighborhood perspective compliments the results of individual-level studies for guiding public health interventions.

This study highlights the importance of measuring vaccine coverage at the neighborhood-level and provides the methods to estimate at risk populations for small areas.

We identified population-level characteristics that can be used by public health officials to strategically plan for future influenza pandemics.

ACKNOWLEDGEMENTS

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This work was supported by the Public Health Agency of Canada and Canadian Institutes of Health Research Influenza Research Network (Graduate Student Scholarship award to S.B.); and the Canadian Institutes of Health Research (Grants HIN-218590 and PAN-83152 to D.B.).

Part of this work was presented at the Epidemiology, Biostatistics and Occupational Health Student Society (EBOSS) 7th Annual Student Research Day on April 27, 2011, in Montreal, Quebec, the PHAC/CIHR Influenza Research Network (PCIRN) Annual General Meeting on April 20, 2011, in Ottawa, Ontario and the Canadian Society for Epidemiology and Biostatistics (CSEB) 2011 Student Conference on June 20, 2011, in Montreal, Quebec.

Conflict of interest: None declared.

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FIGURE LEGENDS

Figure 1. Flow diagram of vaccinations administered in Montreal and vaccinations among residents of Montreal included in this study, October 2009 to April 2010.

Figure 2. Cumulative pandemic A/H1N1 influenza vaccine coverage, by date of vaccination, from October 22, 2009, to December 31, 2009, among priority groups (A), and age groups (B), where vertical bars indicate vaccination eligibility dates.

Figure 3. Box plots of neighborhood (n=111) pandemic A/H1N1 influenza vaccine coverage in Montreal, by characteristic, October 2009 to April 2010. Neighborhoods with >100% coverage were coded as 100% among 5 to 19 year olds (n=1), pregnant women (n=1) and healthcare workers (n=5).

Figure 4. Choropleth maps of neighborhood pandemic A/H1N1 influenza vaccine coverage in Montreal among the total population (A), pregnant women (B), chronically ill under 65 (C), and healthcare workers (D), October 2009 to April 2010.

Figure 5. Choropleth map of neighborhood variables of Montreal: material deprivation (A), social deprivation (B), % immigrants (C), 2006.

TABLES AND FIGURES

Figure 1.

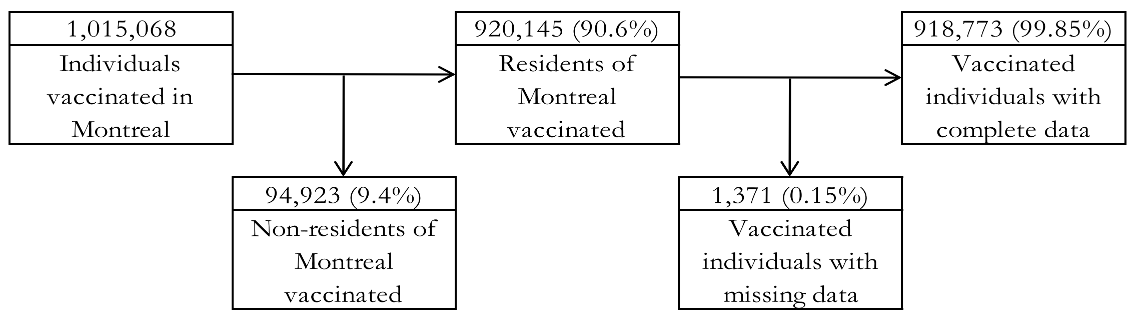


Table 1. Characteristics of Montreal Population, Overall and by Neighborhood (n=111) and Pandemic A/H1N1 Influenza Vaccine Coverage, October 2009 to April 2010.

Characteristic	Overall					Neighborhood, % total population					
	Study population		Vaccinated			Min	Q1	Median	Mean	Q3	Max
	N	%	N	%	95% CI						
Total population (N)	1,842,897		918,773	49.9	49.8, 50.0	1,958	10,099	15,734	16,603	20,543	62,963
Sex											
Female	956,342	51.9	501,300	52.4	52.3, 52.5	39.0	51.1	52.2	51.7	53.3	56.6
Male	886,555	48.1	417,473	47.1	47.0, 47.2	43.4	46.7	47.8	48.3	48.9	61.1
Age groups											
6 months to 4 years	84,452	4.6	59,077	70.0	69.6, 70.3	2.1	4.0	4.5	4.5	5.1	8.0
5 to 19 years	292,950	15.9	164,333	56.1	55.9, 56.3	6.9	13.1	16.2	16.1	18.7	24.9
20 to 64 years	1,179,125	64.0	510,447	43.3	43.2, 43.4	48.2	59.9	62.6	63.9	66.6	81.7
65 years and over	286,370	15.5	184,916	64.6	64.4, 64.7	7.1	12.0	15.1	15.4	18.3	32.3
Priority groups											
Healthcare workers	103,490	5.6	69,086	66.8	66.5, 67.0	2.3	4.9	5.7	5.6	6.5	8.4
Female[a]	77,935	75.3	48,388	62.1	61.7, 62.4	54.3	72.8	76.8	76.0	80.7	100.0
Male[a]	25,555	24.7	20,698	81.0	80.5, 81.5	0.0	19.3	23.2	24.0	27.2	45.7
Pregnant women	19,490	1.1	9,622	49.4	48.7, 50.1	0.5	0.9	1.0	1.1	1.2	2.5
Less than 20 years[b]	399	2.0	160	40.1	35.4, 45.0	0.0	0.8	1.6	2.1	3.2	13.3
20 to 44 years[b]	17,095	87.7	8,985	52.6	51.8, 53.3	68.3	84.0	87.7	86.8	90.2	95.7
45 years and over[b]	1,996	10.2	477	23.9	22.1, 25.8	1.8	7.7	10.1	11.1	14.1	31.7
Chronically ill < 65 years	240,830	13.1	93,724	38.9	38.7, 39.1	11.3	12.7	13.1	13.1	13.6	15.1
Less than 20 years[c]	41,475	17.2	13,697	33.0	32.6, 33.5	7.3	14.6	17.5	17.3	20.4	25.6
20 to 39 years[c]	58,856	24.4	16,628	28.3	27.9, 28.6	12.7	20.1	22.7	23.8	26.4	43.3
40 to 64 years[c]	140,499	58.3	63,399	45.1	44.9, 45.4	47.6	55.8	59.4	58.9	62.6	68.4
Neighborhood characteristics											
Immigrants	137,762	7.5				1.1	4.1	6.2	7.0	8.4	21.9
Material deprivation index						1.0	2.1	3.2	3.0	3.9	5.0
Social deprivation index						1.1	2.9	3.6	3.5	4.1	4.9

Abbreviations: CI, Confidence interval; Q1, First quartile; Q3, Third quartile.

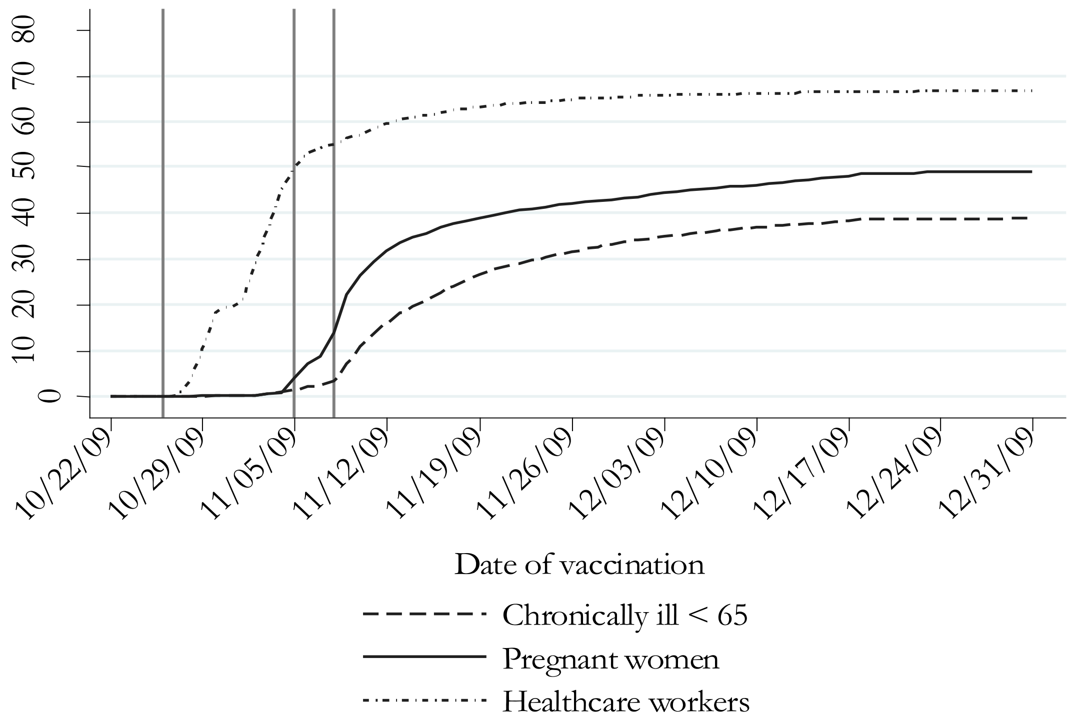
[a] Percentage among healthcare workers.

[b] Percentage among pregnant women.

[c] Percentage among the chronically ill < 65 years.

Figure 2.

A)


0
10
20
30
40
50
60
70
80
10/22/09
10/29/09
11/05/09
11/12/09
11/19/09
11/26/09
12/03/09
12/10/09
12/17/09
12/24/09
12/31/09
Date of vaccination
Chronically ill < 65
Pregnant women
Healthcare workers

B)

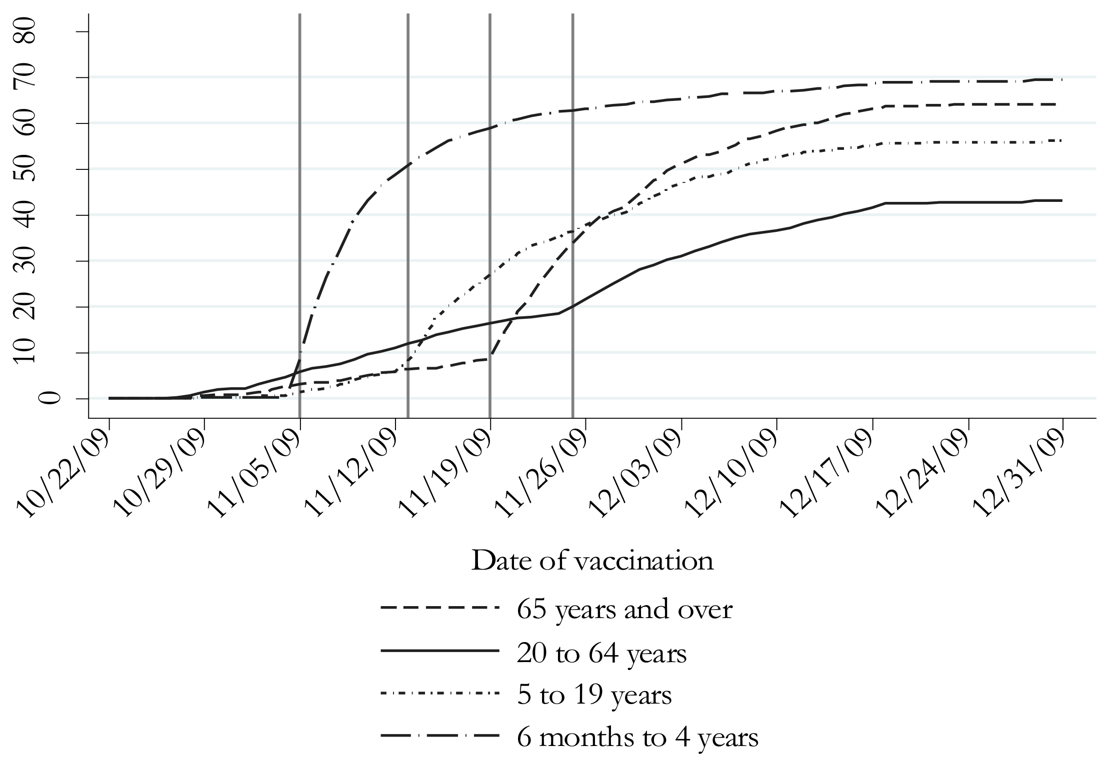

0
10
20
30
40
50
60
70
80
10/22/09
10/29/09
11/05/09
11/12/09
11/19/09
11/26/09
12/03/09
12/10/09
12/17/09
12/24/09
12/31/09
Date of vaccination
65 years and over
20 to 64 years
5 to 19 years
6 months to 4 years

Figure 3.

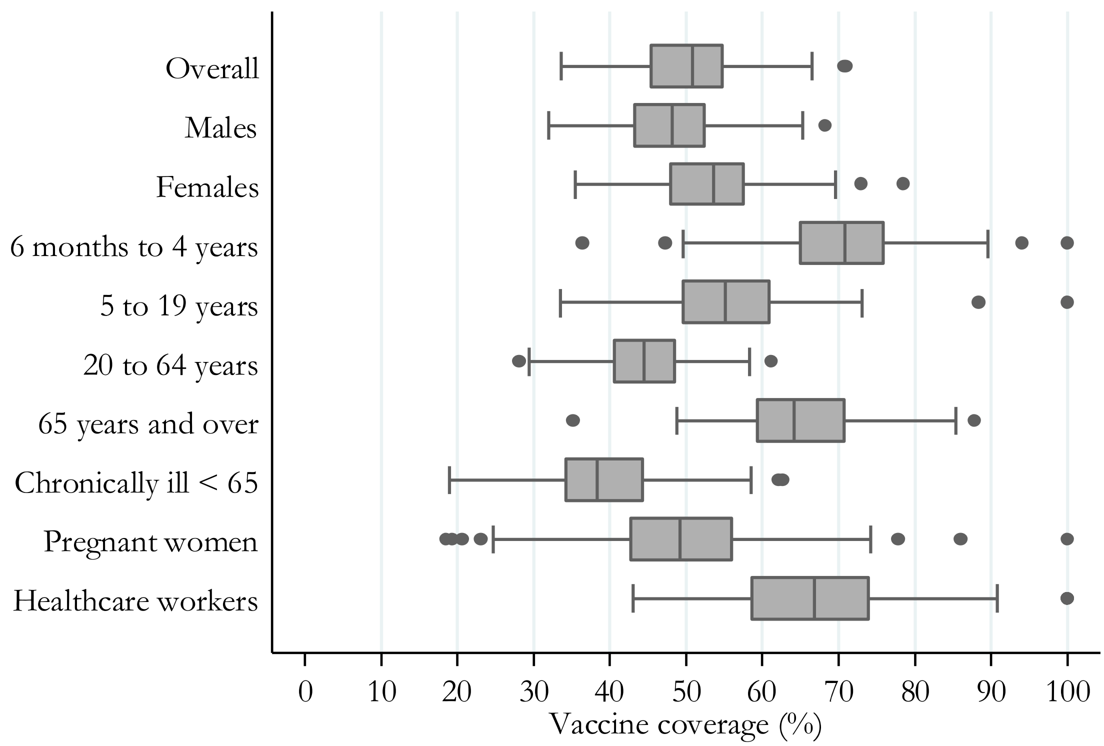

Overall
Males
Females
6 months to 4 years
5 to 19 years
20 to 64 years
65 years and over
Chronically ill < 65
Pregnant women
Healthcare workers
0
10
20
30
40
50
60
70
80
90
100
Vaccine coverage (%)

Figure 4.

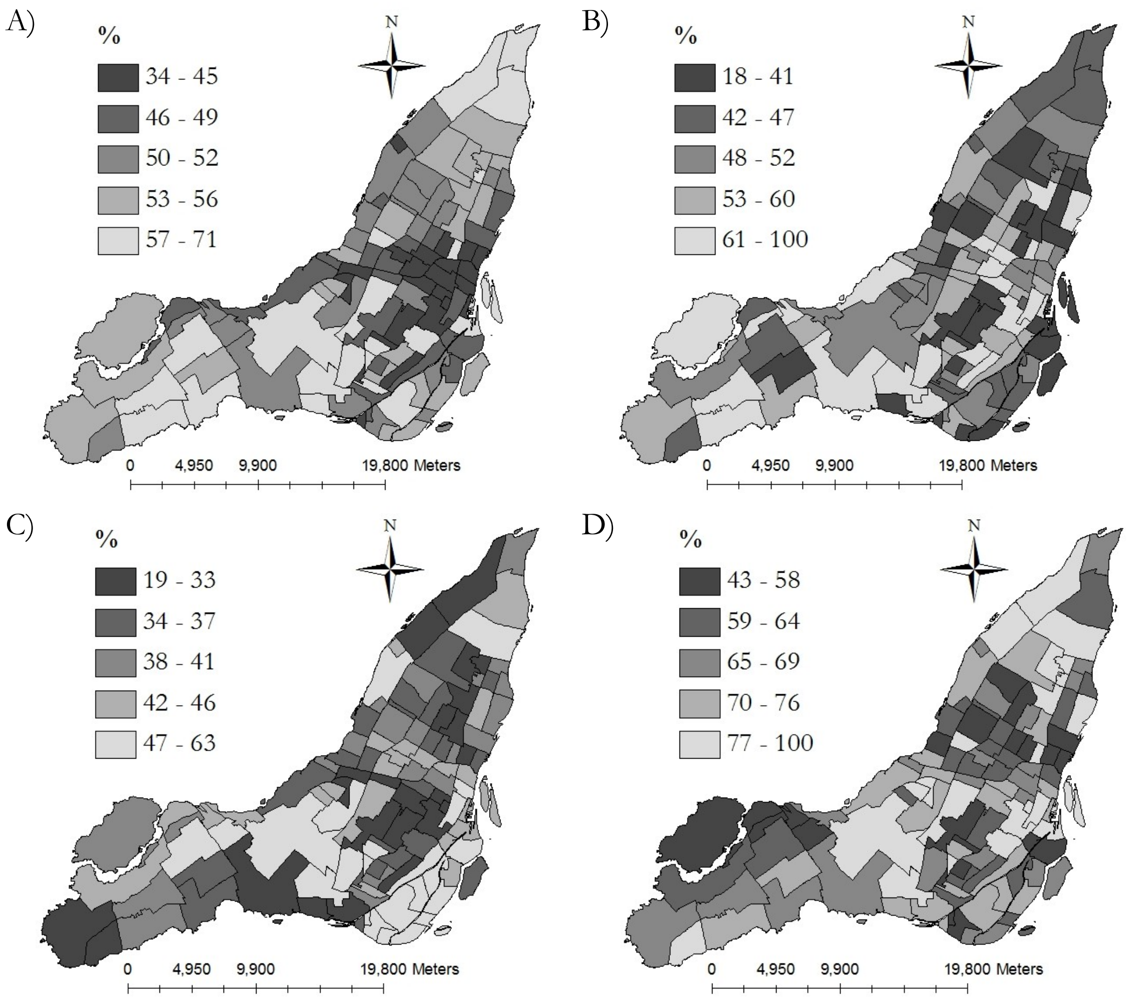

A)
%
34 - 45
46 - 49
50 - 52
53 - 56
57 - 71
N
0
4,950
9,900
19,800 Meters
B)
%
18 - 41
42 - 47
48 - 52
53 - 60
61 - 100
N
0
4,950
9,900
19,800 Meters
C)
%
19 - 33
34 - 37
38 - 41
42 - 46
47 - 63
N
0
4,950
9,900
19,800 Meters
D)
%
43 - 58
59 - 64
65 - 69
70 - 76
77 - 100
N
0
4,950
9,900
19,800 Meters

Figure 5.

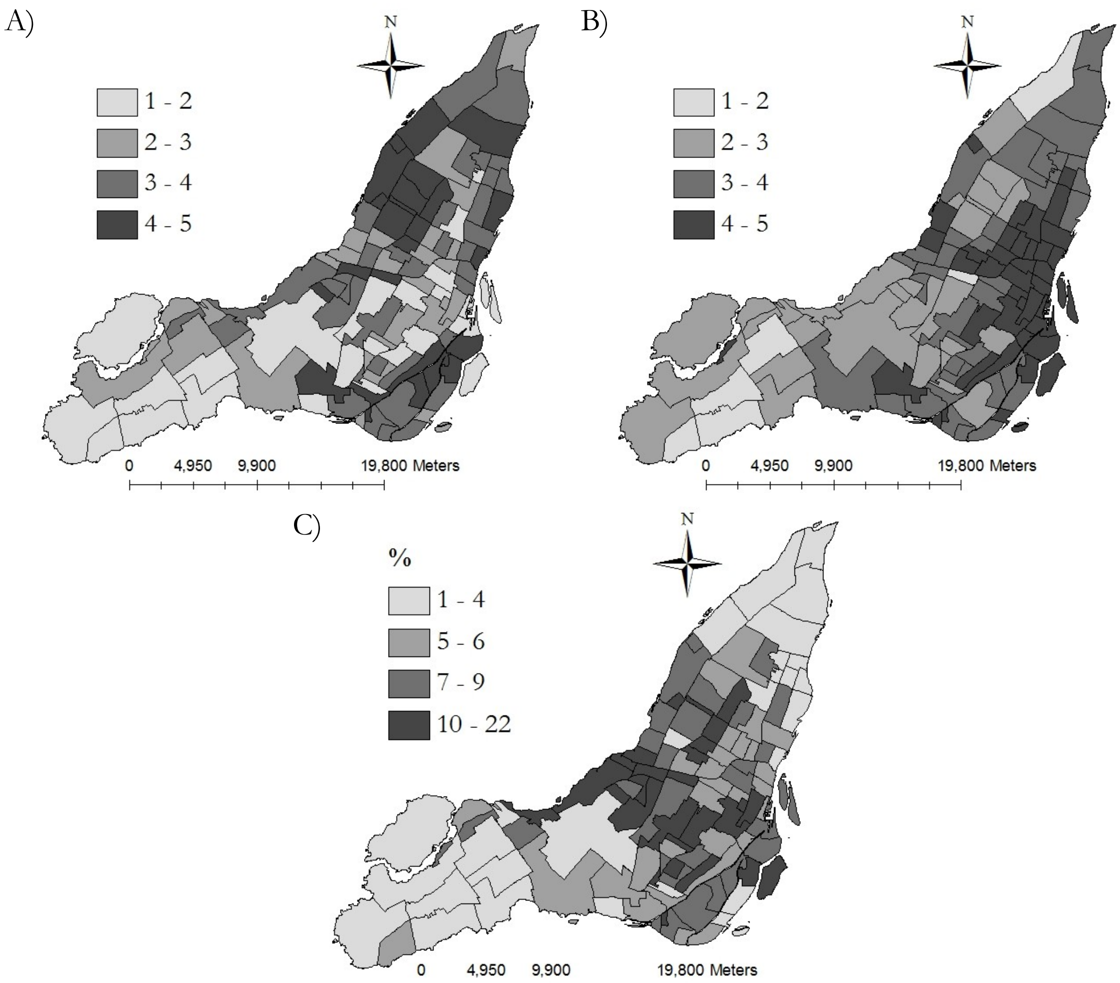

A)
N
1 - 2
2 - 3
3 - 4
4 - 5
0 4,950 9,900 19,800 Meters
B)
N
1 - 2
2 - 3
3 - 4
4 - 5
0 4,950 9,900 19,800 Meters
C)
N
%
1 - 4
5 - 6
7 - 9
10 - 22
0 4,950 9,900 19,800 Meters

Table 2. Neighborhood Determinants of Pandemic A/H1N1 Vaccination in Montreal, October 2009 to April 2010. Univariable Odds Ratios and 95% Credible Intervals.

Determinants	Total population		Pregnant women		Chronically ill <65		Healthcare workers	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Material deprivation[a]	0.918	0.876, 0.963	0.897	0.821, 0.977	1.012	0.957, 1.078	0.866	0.732, 0.998
% Immigrants[b]	0.855	0.808, 0.902	0.979	0.874, 1.090	0.848	0.786, 0.912	0.921	0.761, 1.109
Social deprivation[a]	0.887	0.834, 0.951	1.022	0.923, 1.136	0.969	0.892, 1.049	0.998	0.840, 1.175

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Estimates given per quintile increments.

[b] Estimates given per 5% increments.

Table 3. Neighborhood Determinants of Pandemic A/H1N1 Vaccination in Montreal, October 2009 to April 2010. Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Total population[a]		Pregnant women[b]		Chronically ill <65[c]		Healthcare workers[d]	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Material deprivation[e]	0.931	0.882, 0.976	0.831	0.737, 0.931	1.093	1.015, 1.170	0.852	0.699, 0.991
% Immigrants[f]	0.903	0.856, 0.954	1.076	0.953, 1.211	0.830	0.756, 0.906	0.994	0.807, 1.217
Social deprivation[e]	1.003	0.938, 1.073	0.983	0.874, 1.095	0.993	0.911, 1.085	0.993	0.849, 1.169

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % female, % 20 to 64 years, % 65 years and over, % pregnant women, % chronically ill under 65, % healthcare workers.

[b] Adjusted for % pregnant women 20 to 44 years, % pregnant women 45 years and over.

[c] Adjusted for % chronically ill 20 to 39 years, % chronically ill 40 to 64 years.

[d] Adjusted for % female healthcare workers.

[e] Estimates given per quintile increments.

[f] Estimates given per 5% increments.

APPENDIX

Appendix Table 1. Priority Groups Defined in This Study for Which Pandemic A/H1N1 Influenza Vaccination was Recommended and Vaccine Eligibility Schedule in Montreal, 2009[a].

Date	Risk Group
October 26th	Healthcare workers
November 5th	Pregnant women
November 5th	Children 6 months to 5 years of age
November 8th	Chronically ill under 65 years of age
November 13th	Children 5 to 19 years of age
November 19th	Adults 65 years and over
November 24th	Adults 20 to 64 years of age

[a] Information provided by the health and social services agency of Montreal.

Appendix Table 2. The Set of ICD-9 Codes Used to Identify Pregnant Women in Montreal[a].

Code	Description
641	Antepartum hemorrhage abruptio placentae and placenta previa
642	Hypertension complicating pregnancy, childbirth, and the puerperium
643	Excessive vomiting in pregnancy
644	Early or threatened labor
645	Prolonged pregnancy
646	Other complications of pregnancy, not elsewhere classified
647	Infectious and parasitic conditions in the mother classifiable elsewhere but complicating pregnancy childbirth or the puerperium
648	Other current conditions in the mother classifiable but complicating pregnancy childbirth or the puerperium
649	Other conditions or status of the mother complicating pregnancy, childbirth, or the puerperium
650	Normal delivery
651	Multiple gestation
652	Malposition and malpresentation of fetus
653	Disproportion in pregnancy labor and delivery
654	Abnormality of organs and soft tissues of pelvis
655	Known or suspected fetal abnormality affecting management of mother
656	Other fetal and placental problems affecting management of mother
657	Polyhydramnios
658	Other problems associated with amniotic cavity and membranes
659	Other indications for care or intervention related to labor and delivery not elsewhere classified
660	Obstructed labor
661	Abnormality of forces of labor
662	Long labor
663	Umbilical cord complications during labor and delivery
664	Trauma to perineum and vulva during delivery
665	Other obstetrical trauma
666	Postpartum hemorrhage
667	Retained placenta or membranes, without hemorrhage
668	Complications of the administration of anesthetic or other sedation in labor and delivery
669	Other complications of labor and delivery, not elsewhere classified
670	Major puerperal infection, unspecified
671	Venous complications in pregnancy and the puerperium
672	Pyrexia of unknown origin during the puerperium
673	Obstetrical pulmonary embolism
674	Other and unspecified complications of the puerperium not elsewhere classified
675	Infections of the breast and nipple associated with childbirth
676	Other disorders of the breast associated with childbirth and disorders of lactation
V27	Outcome of delivery

Abbreviation: ICD-9, International Classification of Diseases, Ninth Revision.

[a] Canadian Chronic Disease Surveillance System Methods Documentation, 2010.

Appendix Table 3. Proportion of Children and Adults with One or More Chronic Conditions[a] for Which Influenza Vaccination is Recommended, for Quebec and Montreal. Estimated From the 1998/1999 NPHS and 2007/2008 CCHS.

Age Group	Region	Cycle	%	95% CI
Children				
0 to 9 years	Quebec	1998/1999	9.5	6.9, 12.1
10 to 19 years	Quebec	1998/1999	12.3	9.4, 15.3
Adults				
20 to 39 years	Montreal	2007/2008	10.5	7.9, 13.9
40 to 54 years	Montreal	2007/2008	19.1	15.1, 23.9
55 to 64 years	Montreal	2007/2008	30.0	23.4, 36.7

Abbreviations: CI, Confidence interval; CCHS, Canadian Community Health survey; NPHS, National Population Health Survey.

[a] Asthma, emphysema or chronic bronchitis, diabetes, heart disease, cancer and effects of stroke.

Appendix Table 4. Comparison of the Proportion of Children and Adults with One or More Chronic Conditions[a] for Which Influenza Vaccination is Recommended, by Region and Year. Estimated from the 1998/1999 NPHS and 2007/2008 CCHS.

Age Group	Region	Cycle	%	95% CI
12 to 19 years	Montreal	2007/2008	14.0	8.0, 19.9
	Quebec	1998/1999	12.8	9.6, 15.9
		2007/2008	11.9	9.0, 14.7
20 to 64 years	Montreal	2007/2008	16.8	14.6, 19.1
	Quebec	1998/1999	12.1	10.8, 13.4
		2007/2008	16.8	15.5, 18.1

Abbreviations: CI, Confidence interval; CCHS, Canadian Community Health survey; NPHS, National Population Health Survey.

[a] Asthma, emphysema or chronic bronchitis, diabetes, heart disease, cancer and effects of stroke.

Appendix Table 5. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among the Total Population in Montreal, October 2009 to April 2010, With Different Hyperpriors. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	0.916	0.875, 0.965	0.921	0.878, 0.968	0.930	0.882, 0.986	0.937	0.894, 0.989
% Immigrants[e]	0.853	0.800, 0.908	0.856	0.808, 0.912	0.901	0.857, 0.944	0.898	0.846, 0.947
Social deprivation[d]	0.884	0.823, 0.950	0.891	0.831, 0.970	0.997	0.930, 1.075	0.995	0.942, 1.050

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % female, % 20 to 64 years, % 65 years and over, % pregnant women, % chronically ill under 65, % healthcare workers.

[b] Hyperpriors: Gamma (0.1, 0.001)

[c] Hyperpriors: Gamma (0.01, 0.0001)

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

Appendix Table 6. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among Pregnant Women in Montreal, October 2009 to April 2010, With Different Hyperpriors. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	0.898	0.818, 0.981	0.902	0.820, 0.995	0.833	0.738, 0.944	0.850	0.751, 0.961
% Immigrants[e]	0.980	0.878, 1.008	0.983	0.888, 1.084	1.072	0.941, 1.213	1.053	0.944, 1.189
Social deprivation[d]	1.018	0.922, 1.132	1.013	0.929, 1.125	0.986	0.879, 1.091	0.993	0.895, 1.084

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % pregnant women 20 to 44 years, % pregnant women 45 years and over.

[b] Hyperpriors: Gamma (0.1, 0.001)

[c] Hyperpriors: Gamma (0.01, 0.0001)

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

[f] For neighborhoods with coverage >100% (n=1), the numerator value was changed to the denominator value.

Appendix Table 7. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among Chronically Ill Under 65 Years in Montreal, October 2009 to April 2010, With Different Hyperpriors. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	1.009	0.954, 1.068	1.006	0.959, 1.060	1.091	1.017, 1.177	1.080	1.001, 1.165
% Immigrants[e]	0.851	0.787, 0.918	0.852	0.793, 0.916	0.829	0.764, 0.894	0.833	0.762, 0.904
Social deprivation[d]	0.970	0.896, 1.046	0.977	0.898, 1.033	0.998	0.913, 1.079	0.995	0.919, 1.077

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % chronically ill 20 to 39 years, % chronically ill 40 to 64 years.

[b] Hyperpriors: Gamma (0.1, 0.001)

[c] Hyperpriors: Gamma (0.01, 0.0001)

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

Appendix Table 8. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among Healthcare Workers in Montreal, October 2009 to April 2010, With Different Hyperpriors. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	0.849	0.727, 0.990	0.862	0.733, 1.004	0.845	0.679, 1.005	0.853	0.691, 1.010
% Immigrants[e]	0.920	0.764, 1.110	0.938	0.785, 1.086	0.994	0.809, 1.217	0.997	0.836, 1.179
Social deprivation[d]	0.992	0.855, 1.129	0.993	0.835, 1.139	0.995	0.850, 1.141	0.992	0.840, 1.126

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % female healthcare workers.

[b] Hyperpriors: Gamma (0.1, 0.001)

[c] Hyperpriors: Gamma (0.01, 0.0001)

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

[f] For neighborhoods with coverage >100% (n=5), the numerator value was changed to the denominator value.

Appendix Table 9. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among Pregnant Women in Montreal, October 2009 to April 2010, Changing the Denominator or Numerator Value for Neighborhoods with over 100% Coverage. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	0.903	0.826, 0.983	0.882	0.809, 0.961	0.828	0.734, 0.932	0.841	0.746, 0.941
% Immigrants[e]	0.983	0.876, 1.099	0.966	0.863, 1.076	1.084	0.954, 1.222	1.048	0.922, 1.179
Social deprivation[d]	1.020	0.915, 1.136	1.012	0.910, 1.122	0.984	0.877, 1.097	0.980	0.878, 1.088

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % pregnant women 20 to 44 years, % pregnant women 45 years and over.

[b] For neighborhoods with coverage >100% (n=1), the denominator value was changed to the numerator value.

[c] For neighborhoods with coverage >100% (n=1), the numerator value was changed to a missing value.

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

Appendix Table 10. Sensitivity Analysis of Neighborhood Determinants of Pandemic A/H1N1 Vaccination Among Healthcare Workers in Montreal, October 2009 to April 2010, Changing the Denominator or Numerator Value for Neighborhoods with over 100% Coverage. Univariable and Multivariable Odds Ratios and 95% Credible Intervals.

Determinants	Univariable				Multivariable[a]			
	Model 1[b]		Model 2[c]		Model 1[b]		Model 2[c]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Material deprivation[d]	0.869	0.745, 1.003	0.874	0.793, 0.959	0.843	0.702, 0.992	0.881	0.780, 0.985
% Immigrants[e]	0.919	0.743, 1.105	0.896	0.797, 1.007	0.992	0.789, 1.227	0.965	0.850, 1.099
Social deprivation[d]	0.999	0.843, 1.173	0.907	0.796, 1.020	1.007	0.865, 1.185	0.907	0.795, 1.018

Abbreviations: CI, Credible interval; OR, Odds ratio.

[a] Adjusted for % female healthcare workers.

[b] For neighborhoods with coverage >100% (n=5), the denominator value was changed to the numerator value.

[c] For neighborhoods with coverage >100% (n=5), the numerator value was changed to a missing value.

[d] Estimates given per quintile increments.

[e] Estimates given per 5% increments.

Appendix 11. Additional Model Details

We assumed

$$y_i \sim \text{binomial}\,(n_i, p_i).$$

where y_i represents the number of vaccinated individuals in neighborhood i and n_i the total population in neighborhood i, where i=1,..., 111. The probability of vaccination p_i in neighborhood i is given by

$$\text{logit}(p_i) = \alpha + \beta_1 \cdot x_{1i} + \ldots + \beta_k \cdot x_{ki} + u_i + v_i$$

where x_{1i},..., x_{ki} indicates the value for covariate *1,..., k* for neighborhood i, and u_i and v_i are random effects.

The random effects were decomposed into two components: u_i accounts for extra-variation that displays spatial dependence and v_i represents unstructured variation. The v_i were assigned a conditional autoregressive (CAR) prior with the inherent assumption that rates of neighboring areas are similar (53). Neighbors were defined as areas sharing a border.

Appendix 12. Models

Total population

y_i = number vaccinated in neighborhood i
n_i = total population in neighborhood i
fem_i = proportion female for neighborhood i
$age2_i$ = proportion 20 to 64 years of age for neighborhood i
$age3_i$ = proportion 65 years of age and over for neighborhood i
$preg_i$ = proportion pregnant for neighborhood i
$chronic_i$ = proportion chronically ill<65 for neighborhood i
hcw_i = proportion healthcare workers for neighborhood i
$material_i$ = material deprivation score for neighborhood i
$social_i$ = social deprivation score for neighborhood i
$immigrant_i$ = proportion immigrants for neighborhood i

then to estimate neighborhood vaccination rate we use a logistic model:

$$\operatorname{logit}\left(\frac{yi}{ni}\right) = \alpha + \beta_1 \times fem_i + \beta_2 \times age1_i + \beta_3 \times age2_i + \beta_4 \times age3_i + \beta_5 \times age4_i + \beta_6 \times preg_i + \beta_7 \times chronic_i + \beta_8 \times hcw_i + \beta_9 \times material_i + \beta_{10} \times social_i + \beta_{11} \times immigrant_i + u_i + v_i$$

Where u_i and v_i are the spatially-correlated and uncorrelated heterogeneity random effects.

Pregnant women

y_i = number pregnant women vaccinated in neighborhood i
n_i = total number of pregnant women in neighborhood i
$age2_i$ = proportion pregnant women 20 to 39 years of age per pregnant women for neighborhood i
$age3_i$ = proportion pregnant women 40 to 64 years of age per pregnant women for neighborhood i
$material_i$ = material deprivation score for neighborhood i
$social_i$ = social deprivation score for neighborhood i
$immigrant_i$ = proportion immigrants for neighborhood i

then to estimate neighborhood vaccination rate we use a logistic model:

$$\operatorname{logit}\left(\frac{yi}{ni}\right) = \alpha + \beta_1 \times age2_i + \beta_2 \times age3_i + \beta_3 \times material_i + \beta_4 \times social_i + \beta_5 \times immigrant_i + u_i + v_i$$

Where u_i and v_i are the spatially-correlated and uncorrelated heterogeneity random effects.

Chronically ill <65

y_i = number chronically ill <65 vaccinated in neighborhood i
n_i = total number of chronically ill <65 in neighborhood i
$age2_i$ = proportion chronically ill 20 to39 years of age per chronically ill < 65 for neighborhood i
$age3_i$ = proportion chronically ill 40 to 64 years of age per chronically ill < 65 for neighborhood i
$material_i$ = material deprivation score for neighborhood i
$social_i$ = social deprivation score for neighborhood i
$immigrant_i$ = proportion immigrants for neighborhood i

then to estimate neighborhood vaccination rate we use a logistic model:

$$\text{logit}\left(\frac{yi}{ni}\right) = \alpha + \beta_1 \times age2_i + \beta_2 \times age3_i + \beta_3 \times material_i + \beta_4 \times social_i + \beta_5 \times immigrant_i + u_i + v_i$$

Where u_i and v_i are the spatially-correlated and uncorrelated heterogeneity random effects.

Healthcare workers

y_i = number healthcare workers vaccinated in neighborhood i
n_i = total number of healthcare workers in neighborhood i
fem_i = proportion female healthcare workers per healthcare workers for neighborhood i
$material_i$ = material deprivation score for neighborhood i
$social_i$ = social deprivation score for neighborhood i
$immigrant_i$ = proportion immigrants for neighborhood i

then to estimate neighborhood vaccination rate we use a logistic model:

$$\text{logit}\left(\frac{yi}{ni}\right) = \alpha + \beta_1 \times fem_i + \beta_2 \times material_i + \beta_3 \times social_i + \beta_4 \times immigrant_i + u_i + v_i$$

Where u_i and v_i are the spatially-correlated and uncorrelated heterogeneity random effects.

Appendix 13. Example of WinBUGS Code

model
{
for (i in 1:N)
	The number of neighborhoods included in the study (N).

{	
y[i]~dbin(p[i],n[i])	Neighborhood counts of vaccination, binomially distributed.
logit(p[i])<-alpha+beta*(x[i]-x.bar)+u[i]+v[i]	Logistic regression equation, centering covariates.
v[i] ~ dnorm(0, tau.v)	Prior distribution of heterogeneity component, assumed to be normally distributed with mean zero and variance of tau.v.
}	
u[1:N] ~ car.normal(adj[], weights[], num[], tau.v) for(k in 1:sumNumNeigh) {	Prior distribution of clustering component: Normally distributed with mean equal to the average of its neighbors, and variance inversely proportional to the number of neighbors.
weights[k] <- 1	Weight for CAR normal distribution where adjacent neighborhoods are assigned a weight of one.
}	
alpha~dflat()	Improper uniform prior distribution of intercept.
beta~ dnorm(0.0, tau.beta)	Prior distribution of slope, assumed to be normally distributed with mean zero and variance of tau.beta.
tau.u~dgamma(0.5, 0.005) tau.v~dgamma(0.5, 0.005) tau.beta dgamma(0.5, 0.005)	Hyperprior distribution of variance of assumed to be gamma distributed with scale 0.5 and shape 0.005.
x.bar<-mean(x[]) }	Mean of covariate.

CHAPTER 4

Conclusion

In this thesis a literature review of the determinants of pandemic influenza vaccination was conducted, focusing on neighborhood-level factors. The results of this review suggested that male sex, younger age, higher education, being a doctor, being in a priority group were the factors most consistently associated with receiving the pandemic influenza vaccine. In the second part of the thesis, pandemic influenza vaccine coverage was estimated for an urban area, at high resolution using a large, population-based vaccination registry. Different data sources such as census, survey and administrative records were used to estimate the population at risk for neighborhoods of Montreal. Vaccine coverage was estimated overall and by different socio demographic and health status characteristic. The neighborhood socioeconomic and demographic determinants of vaccination were then identified among the total population and priority groups. Overall pandemic influenza vaccine coverage was relatively high in Montreal; however considerable variation was observed by population sub-group and neighborhood. The results of the ecologic study suggested that neighborhoods with a higher composition of immigrants and with lower socioeconomic status had lower vaccine coverage.

While the results of this thesis are similar in many respects to those of other studies, the results of our ecological study regarding the influence of sex on pandemic influenza vaccination differ from results of previous studies. The discrepancy observed may be due to the fact that the influence of sex differs by population group examined. For example, in the ecological study, higher vaccination rates were observed among females overall, yet higher coverage was observed among male healthcare workers. In contrast, in the literature review the results suggested that males were more likely to receive the vaccine. However most of the studies examining the effect of sex on vaccination were conducted among healthcare workers. In fact, four studies (Amodio, et al., 2011; Torun & Torun, 2010; Torun, et al., 2010; Virseda, et al., 2010) observed higher vaccination rates among males healthcare workers as compared to one study that observed higher rates among female healthcare workers (Park, et al., 2011). Unfortunately, among the studies included in the literature review, there were too few studies examining other population groups to make further comparisons.

We also noted a methodological concern when attempting to determine the influence of age on the receipt of the pandemic influenza vaccine. In the ecological study, individuals of all ages were included and higher coverage was observed among children. Similarly, in the literature review, studies including all age groups observed higher coverage among children (Bone, et al., 2010; Centers for Disease Control and Prevention, 2010b, 2010c; Vaux, et al., 2011). However, when young children were excluded from the analysis, studies found higher coverage among older age groups (Amodio, et al., 2011; Barriere, et al., 2010; Fabry, et al., 2011; Gaygisiz, et al., 2010; Ozer, et al., 2010; Park, et al., 2011; Stavroulopoulos, et al., 2010; Torun & Torun, 2010; Velan, et al., 2011; Virseda, et al., 2010). This discrepancy highlights the need to include all ages in the analysis so as to make accurate conclusions.

Further research is necessary to fully understand the determinants of pandemic influenza vaccination. As the determinants of pandemic influenza vaccination differ by population group, future reviews should attempt to differentiate between these groups when reporting results. Furthermore it is necessary to include all age groups as excluding certain age groups influences the results. Future research should focus on using a registry to estimate coverage in order to obtain accurate, precise estimates which are not subject to biases present in studies using survey methodology.

The development of a successful vaccination program against pandemic influenza requires an understanding of the factors that influence vaccination. The methods and results of this research can aid public health officials in the process of planning for future influenza pandemics. Using the methods described to estimate the population at risk, public health officials can estimate the vulnerable population sizes for small areas. Officials can also estimate coverage at a high resolution, at the neighborhood-level, which has not been previously reported in the pandemic influenza literature. Through the use of a large population-based vaccination registry public health officials can to identify areas of low coverage and direct resources appropriately. Additionally, public health officials can strategically plan a vaccination campaign based on the population level constructs and characteristics identified in this thesis.

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