Influenza Immunization Campaigns: Is an Ounce of Prevention Worth a Pound of Cure?

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INFLUENZA IMMUNIZATION CAMPAIGNS: IS AN OUNCE OF PREVENTION WORTH A POUND OF CURE? *

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Abstract

This study provides causal evidence on the health and economic consequences of a broad-scope vaccination program. The *Ontario Influenza Immunization Campaign* (introduced in 2001) expanded the scope of vaccine coverage to the full population. By using the timing of this campaign and exogenous variation in vaccine quality, I am able to causally link higher vaccination rates to decreases in lost work-time, hospitalization, and death. Results indicate that, when vaccine quality is high, the campaign resulted in higher gains for Ontario relative to other provinces and in short, an ounce of prevention is worth a pound of cure. Results also suggest significant positive health externalities for the elderly. Possible implications for the benefits of a flu vaccine specific to H1N1/09 flu are discussed.

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1 Introduction

In the early 20th century, pneumonia, influenza, and other respiratory infections accounted for more than a quarter of all deaths, and infectious diseases more generally were the principal cause of worldwide mortality. The subsequent decline in infectious disease coincided with an epidemiological transition that was in part characterized by the development and use of vaccines. This innovation led to extensive government action consisting of vaccination campaigns, regulatory measures, and education. Adoptions of such protocols continue for recently developed vaccines and are being considered for the newest form of influenza, the H1N1/09 strain or "swine flu."[1] Relying on standard arguments about the externality effects of preventing infectious disease, there is substantive motivation for public action. Nevertheless, public action in the form of immunization programs should rest on rigorous comparison of costs and benefits. Program evaluation of public campaigns for new and existing vaccines thus requires accurate evaluation of the health and economic consequences of such programs. Unfortunately, since there is little known about the true impact of vaccination campaigns it remains difficult to compare benefits to upfront costs.

This study focuses on a broad-based vaccination program targeted toward influenza (the flu). The Ontario Universal Influenza Immunization Campaign was introduced in 2001 and expanded delivery of free flu shots beyond the traditional target group to include all children and adults. Previous to 2001 only high-risk groups including the elderly and those with select chronic conditions were eligible to receive the vaccine and recommendations to vaccinate outside this target group continue to be controversial.[2] The program in Ontario is innovative on several dimensions: it not only recommends the flu shot for all age groups, but it also fully subsidizes the cost of the flu shot and its administration. I show that this highly advertised program has led to substantial increases in vaccination for the impacted group and has implied substantial increases in the overall level of vaccination within Ontario.

Since the Ontario campaign was successful at delivering flu shots, it offers a useful policy experiment to evaluate the impact of vaccinating children and younger adults against flu. Given that a simple before and after comparison for Ontario may incorrectly attribute all changes in outcomes to the flu shot campaign and even conventional difference-in-difference comparisons

[1] Other examples include: varicella, human papillomavirus, pneumococcal, meningococcal, and hepatitis vaccines.

[2] For instance, the United Kingdom's Department of Health offers flu shot coverage for the standard target group while deemphasizing the flu shot for others. Alternatively, the Centre for Disease Control and Prevention (CDC) in the U.S. has recently added children under 18 to the target group and is considering further changes to scope.

with other provinces may be confounded with differential trends, I instead develop an identification strategy that exploits variation in the match of the flu shot to the flu. This variation is plausibly exogenous. The composition of the flu shot is predetermined and fixed for each flu season and across all provinces, while the genetic composition of the flu is constantly changing. This implies that if there are benefits from vaccination, Ontario relative to the other provinces will have more to gain when the flu shot is a good match whereas it will have little to gain when it is not. By using this methodology, I am able to disentangle the causal impact of flu shots from alternative explanations for differences in outcomes such as advertising effects related to the program or any other associated differential trends.[3] Furthermore, since the match of the flu shot is unknown at the time of vaccination, changes in compensatory behaviors arising from immunization are unlikely correlated with the match and thus cannot explain the estimated impact.

Using weekly data for city-regions over an eleven-year period, I am able to estimate the causal impact of the flu shot campaign on work absences, hospitalization and other health outcomes. Estimates of the program effect imply that the sustained 9 percentage point relative increase in vaccination for Ontario post 2001 prevented 2 deaths per 100,000 people annually and led to a 67 percent decrease in overall flu admissions when the clinical match of the flu shot is perfect (a perfect match occurs in 1 out of every 2.2 seasons). The near elimination of flu admissions corresponds to predictions from a standard structural model of flu dynamics. Here, a vaccination rate above 31 percent combined with a perfectly matched vaccine is predicted to prevent a flu epidemic.[4] The Ontario campaign achieved a vaccination rate above 31 percent while average vaccination in other provinces remained below. This corroborates the large effects found for flu admissions, which were nearly eliminated in perfect match flu shot years, and may shed light on the possible benefits of a flu vaccine specifically matched to the H1N1/09 strain of flu.

I also find that the flu campaign has implications for labor force productivity. Using monthly labor force survey data, I find that during the flu season the program leads to a 22 percent decrease in worker illness absence in a perfect match year. These results are further supported by evidence for other measures of illness. There is a 34 percent decline in the weekly surveillance rate of lab tested flu, a 30 percent decline in bi-weekly bed illness and a 13 percent decline in

[3] An advertising effect is interesting in its own right. However, if decreases in illness are driven from program advertising about infectious disease and not from flu shot delivery this has alternative implications for program design.

[4] In effect, by reducing the size of the susceptible population, vaccination reduces the average number of infections caused by an infected individual. Given parameters regarding the infectiousness of flu; average infections will fall below the rate of one (meaning, an infection less than replaces itself) at a vaccination rate greater than 31 percent.

consumption of over-the-counter cold and flu medications.

The second stage of this paper focuses on estimating the effects for adults over the age of 65. The flu shot is covered for older adults in all provinces since the early 1990s. Hence, coverage status for this group is unchanged as a result of the Ontario campaign. This is reflected in relative vaccination patterns. For older adults, there is no difference in vaccination rates post program in Ontario when compared with other provinces. If we are willing to assume that this age group is unaffected by the vaccination of others, then within this age group, there should be little additional gain for Ontario in high match versus low match years. If there is a difference in the relative gain for older adults, such that illness declines more so in Ontario in perfect match years, it indicates that this age group was positively affected by relative increases in the vaccination of others. For older adults, I examine hospitalizations, bed illness, and cold/flu medications and find significant reductions in these illness outcomes. This suggests that there are external effects for this older group due to the increased vaccination of younger groups.

Relative to program costs, the implied aggregate benefits of the Ontario campaign, including spillover benefits to older adults, are substantial. Given the average cost of respiratory hospitalizations and the average wage, the impact of the flu shot campaign translates into best-case scenario cost savings of $174 million in a high match season. The expected cost savings (average cost savings multiplied by the expected match rate) yields a program benefit of $124 million. Program costs, on the other hand, are much less. The campaign delivers on average 6 million more vaccinations per season. This represents $19 million in additional administration costs and an extra $14 million in vaccine costs, totaling $33 million annually.

Estimates from this study are robust to using several definitions of the clinical match rate: a dichotomous definition (match versus no match), a continuous measure scaled by the proportion of unmatched flu strains in each province and year, or the log of this continuous measure to allow for nonlinearities in the effect of the match. It is not possible to completely rule out concurrent events that may be correlated with the effect of the flu shot match in Ontario post 2001 but such events are unlikely. For instance, a coinciding policy that was able to directly affect general immunity to disease could explain differences for Ontario in high match versus low match flu shot years. However, this is an unlikely explanation since health policies are typically (both before and after 2001) directed to treatment and not preventative care. Furthermore, such a policy, being related to general immunity, would have a general effect on health. However, I find no differences for other

types of hospitalizations besides those that involve flu or flu complications. Moreover, I find no effects on flu related illness measures in periods other than during high flu season.

This paper makes a number of contributions: (1) by using exogenous variation in the match of the flu shot to the flu and the novel immunization campaign in Ontario, I am able to estimate the causal impact of a program providing vaccines to all age groups, (2) by using a comprehensive dataset on all acute hospitalizations in Canada spanning a number of seasons across numerous well-defined geographical areas, I am able to use flexible specifications that include month, season and city-region fixed effects, analyze hospitalizations where flu was either the primary *or* secondary diagnosis, and analyze other types of diseases to rule out misspecification, (3) I am able to provide evidence of positive externality effects for the elderly from the vaccination of children and younger adults, and (4) by using labor force survey data, I am able to provide the first large-scale evidence of the effect of vaccination on worker productivity by looking at the impact on worker absenteeism.

This paper is organized as follows; Section 2 provides background information on the flu virus and vaccine, vaccination recommendations, provincial vaccination programs, and outlines a direction for the empirical approach. Section 3 outlines the identification strategy and Section 4 describes the data and presents descriptive statistics. Section 5 presents results. First, I present a main set of results for flu, pneumonia and worker absenteeism. Second, I explore effects for different age groups. Lastly, I provide further evidence on bi-weekly bed illness, monthly consumption of over-the-counter cold and flu medicines, laboratory confirmed flu rates and other hospital admissions for diseases such as heart disease, cancer and chronic respiratory disease. Section 6 provides interpretation and Section 7 concludes.

2 Background

2.1 The Flu

Influenza (or flu) is a common respiratory virus that is contagious through droplet spread.[5] The virus begins circulating in the fall and winter months and is usually the predominant cause of serious respiratory disease during this time (WHO 2003). In the U.S., the flu is estimated to be responsible for 100 million days of bed disability, 75 million days of work absenteeism, and 22

[5] Transmission occurs through spread of respiratory droplets from an infected source to the eyes, nose or mouth of a susceptible person. Further summary information on influenza and vaccination is available from the U.S. Center for Disease Control and Prevention (http://www.cdc.gov/flu/about/disease/index.htm) or the Canadian Immunization Guide published by the Public Health Agency of Canada (http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php)

million health care provider visits per year for those aged 18 to 64 (Benson, et al. 1998). For high-risk groups, flu and its related complications account for between 100,000 to 300,000 hospitalizations and between 20,000 to 40,000 deaths during each flu season (Thompson, et al. 2003, 2004). Research has also linked flu infection with added long-term effects. For instance, children in utero during the 1918 H1N1 flu pandemic displayed increased rates of physical disability and decreases in income and educational attainment in later life (Almond 2006).

Recovery from the acute effects of flu occurs within three to fourteen days. In some cases, the flu can lead to death, particularly if infection develops into pneumonia or is coupled with other complications such as asthma, heart disease or other conditions associated with immunosuppression (PHAC 2007). Infection risk begins prior to the onset of symptoms and continues for a number of days after recovery (CDC 2008). In addition, the virus can stay virulent on surfaces for a varying length of time. At body temperature, the virus is usually inactivated in less than a week whereas in cool dry temperatures the virus can last considerably longer (Zhang, et al. 2006). This is, in part, the reason why seasonal epidemics appear during winter months (WHO 2006).

There are many strains of the flu virus that are genetically differentiated or typed on the basis of surface antigens and the genetic structure of the virus is constantly changing over time through point mutations. This evolution results in antigenic drift and depending on antigenic changes, the cross-immunity to the new strain that was conferred by the previously circulating virus can be minimal (PHAC 2007).[6]

2.2 Vaccination

The flu shot was developed in the 1940s but was only more widely used following early 1990s initiatives by public health organizations emphasizing the shot for selected high-risk groups (Fedson et al. 1995). The flu shot provides protection against the flu by triggering an antibody producing immune response to targeted strains of flu. Because of this, protection depends on the match of the vaccine cocktail to circulating strains of flu. For instance, in a systematic review of evidence from randomized control trials, Jefferson et al. (2007) note that lower efficacy rates are estimated in studies whose timing corresponds to seasons where vaccine content is not well matched to circulating strains.

[6] This is particularly the case with the H1N1/09 strain, which has been described as an unusual re-assortment of existing H1N1 strains. Here, H1 represents the haemagglutinin antigen type and N1 represents the neuraminidase antigen type of Influenza A.

Vaccine protection usually begins within two weeks of receipt of the immunization and is sustained for six months or longer; however, if immune response is compromised (as is the case for those in low health or with weaker immune systems), then antibody levels may be below what is needed for full or sustained protection (CDC 2008). For instance, Jefferson et al. (2007) find a vaccine efficacy rate of 80 percent in healthy adults. Meanwhile, the results for children and older ages are lower: systematic review of the evidence yields an efficacy of 62 percent for children under 18 (Manzoli, et al. 2007) and an efficacy of 58 percent for adults over the age of 65 (Govaert, et al. 1994).

It is due to the constant genetic change in flu and the relevance of match to efficacy, that the flu vaccine is reformulated each year to account for changes in the antigenic composition of flu strains. The World Health Organization (WHO) closely monitors circulating flu viruses across the world and in early spring writes the annual vaccine recipe. The vaccine is constructed to target the most virulent strains in circulation and includes two subtypes of flu A (H3N2 and H1N1) and one flu B virus. Usually, one or two of the three virus strains in the vaccine are changed each year and the prescription is identical across the North American continent (WHO 2006).

Each year. Health Canada licenses the newly formulated inactivated flu vaccine for use.[7] Once licensed, the Government of Canada, through Public Works and Government Services Canada (PWGSC), purchases flu vaccines on behalf of the provinces and territories for distribution in late October early November.[8] The turn around period from the yearly WHO recommendation to availability of the vaccine is approximately 6 to 8 months depending on manufacturing conditions (Health Canada 2007).

2.3 Vaccination Programs in Canada

Provincial governments make flu vaccine available at public health clinics and doctor's offices in accordance with provincial influenza immunization programs.[9] Beginning in the early 1990s, all provinces developed vaccine programs covering the cost of vaccination for specific groups. The standard covered group included recipients less than 24 months or 65 years and older,

[7] To date, Health Canada has only licensed inactivated vaccines (containing killed virus strains) instead of live attenuated vaccines (containing weakened flu). It is thought that live attenuated vaccines are associated with adverse reactions that may not result from inactivated vaccines. However, since the virus has been killed, the immune response to an inactivated vaccine may be less than that of a live-attenuated vaccine.

[8] Administrative data from Ontario OHIP physician billings show that the majority of yearly vaccination takes place before December (Kwong and Manuel 2007). Similarly, survey data from the U.S. (the NPHS 2008) show that 91 percent of vaccinated respondents had received the current flu vaccine by December.

[9] Government approved flu vaccines are also available through private market contracts.

health care support staff, residents in care homes, and those with specific chronic conditions (Gao 2004).[10] Aside from minor changes to provincial programs, immunization targeting remained the same across all provinces with the exception of Ontario.[11] The provinces have otherwise similar health care systems, per capita health expenditures, physicians numbers and health resources (IHE 2006, 2008).

In July of 2000, the Government of Ontario announced the extension of vaccination coverage to all residents of the province through what it called the Universal Influenza Immunization Campaign (UIIC). The campaign was only one part of a larger ten-point plan to reduce emergency room wait times (Kurji 2004). The stated objective of the program was to ease pressure on health facilities and providers, in particular emergency rooms, by decreasing the impact of influenza during the flu season (MOHLC 2000). Even though the program targeted, by default, healthy prime age individuals, it was expected that this would afford protection for high-risk groups with already high rates of vaccination through an externality effect. Secondary objectives of the program were to decrease the economic impact of the flu during flu season and also to build infrastructure for delivery of flu or other vaccines in the event of a pandemic (Kurji 2004). In its first year, the program cost $31 million with 6 million vaccines administered (up from 2.1 million in the previous season) (Kurji 2004). The total program cost is a small portion of the overall health care budget of more than $30 billion annually and program funding is independent of hospital and physician budgets, which are determined separately through funding formulas and negotiations with the Ontario Medical Association.

2.4 Vaccination Recommendations and the Universal Influenza Immunization Campaign

The impact of flu vaccination on respiratory infection and mortality is a key issue in developing recommendations for the use of vaccines, and is valuable information for public health agencies that are unwilling to invest in programs that do not yield adequate benefits. Previous estimates of the impact of vaccination did not support policies of immunizing younger individuals outside of certain high-risk groups. For instance, based on meta-analysis of several randomized evaluations, Demicheli (2001) claims that the benefits to vaccinating healthy adults are small and

[10] Covered conditions include cardiac or pulmonary disease, asthma, diabetes, renal disease, liver disease, anaemia, HIV, and cancer.

[11] Quebec and New Brunswick made more recent changes to the coverage status of older adults. Quebec added 60 to 65 year olds to the standard covered group in 2001 and New Brunswick formally added coverage for ages 65 or older in 2002 (CPA 2007, 2003). The change in New Brunswick had no measurable effect on vaccination and due to data constraints in Quebec, this province cannot be included in the analysis (hospitals in Quebec did not submit to the national database for the full sample period).

"at odds with the conclusions reported in previous meta-analysis of evidence for the effect of immunization on elderly people, which showed greater clinical effectiveness, thus supporting the present worldwide policy of vaccinating only elderly people and other high-risk groups." Further to this, more recent surveys of cost benefit analysis indicate that evidence on the efficiency of vaccinating healthy adults or children continues to be mixed with no uniform prescription on the validity of recommending vaccination for these groups (Nichol 2003, 2008).

Yet evidence from these studies suffers several shortcomings that may lead to incorrect conclusions as to the benefits of vaccination, particularly as it applies to a broad based policy on immunization. First, study design of existing randomized evaluations is typically defined over one flu season for a particular group (workers at a firm, patients of a clinic, residents of a nursing home, *et cetera*). This makes it difficult to compare results across studies and has lead to inconclusive evidence on the impact of vaccination and the associated benefits for different groups. Furthermore, from the diversity in estimates and the specificity of the chosen sample, it is then unclear how these results extrapolate to a generalized population. Finally, since these studies typically isolate only one flu season, they cannot adequately account for the role of the flu vaccine match, which impacts the estimated benefits of vaccination systematically.

A second, possibly more important issue is that previous estimates are likely contaminated by treatment spillovers from the treated group to the control group. Specifically, these studies often randomize vaccination within a chosen sample and compare outcomes of treated and untreated groups. However, such methods fail to deal with benefits for the untreated group that accrue from vaccination of the treated, which may be large if the sample is chosen from, for instance, a specific locale or workplace. This difficulty has been shown in other contexts (Philipson 2000b; Miguel and Kremer 2004). Miguel and Kremer (2004) illustrate this concern in their seminal study of worms and deworming interventions. In their study, the authors evaluate a mass deworming program in Kenya that randomly phased in deworming interventions at the school level rather than within school (at the student level). Earlier studies based on within school randomization had found mixed evidence of the effect of deworming treatment on schooling outcomes but had failed to deal with the possibility of treatment spillovers. Because randomization took place at the school level in the Kenyan program, Miguel and Kremer are able to estimate the overall effect of the deworming intervention that is not contaminated by treatment spillovers. In contrast to previous evidence, the authors find that the deworming program had larger effects on

schooling outcomes than previously estimated and, notably, the program reduced school absenteeism by 25 percent in treatment schools. Further to this, by taking advantage of variation in the local density of treatment schools nearby, they also find evidence of cross-school treatment externalities, providing substantive evidence that children do benefit from treatment spillovers in the context of deworming interventions.

From the perspective of flu vaccination, if such externalities exist, evidence that fails to account for such spillovers will incorrectly estimate the effect of the vaccine. This is particularly a problem when establishing evidence based public health recommendations because the true impact of vaccination will always be understated if the untreated group experiences a decrease in illness due to treatment externalities and thus, estimates would cause one to conclude that vaccination is less beneficial than its true measure. It may be on these grounds that other jurisdictions had developed recommendations that were far more limited in scope than the Ontario program. The program, itself, was the first in North America to recommend and provide the flu shot to all groups and, in fact, a main criticism of the campaign was that it was not evidence based: previous estimates did not support a policy of mass immunization.

Yet by its nature, the Ontario program offers a good experiment to address whether such a policy is worthwhile. While previous evidence was only able to evaluate immunization for specific groups in specific contexts, evaluation of the Ontario campaign can assess the benefits of a broad public health campaign. Further, instead of comparing vaccinated and unvaccinated groups in Ontario, patterns in Ontario can be compared to patterns in provinces whose populations have similar baseline vaccination behaviors but that experienced no change in immunization programming. By comparing city-regions in Ontario to city-regions outside Ontario, estimates of the total impact will be free of the treatment externalities that would accrue post-program to unvaccinated groups in Ontario.

One remaining issue in detecting the true impact of the universal campaign is a careful accounting of differential trends among comparison provinces. For instance, Groll and Thompson (2006) find that there is a small relative *increase* in surveillance counts of laboratory confirmed flu for Ontario compared to other provinces at the introduction of the universal program. However, the authors fail to account for trends in the number of tests performed. Since surveillance testing increased more so post-program in Ontario, this would likely translate into higher counts of positive tests. Existence of such observed or unobserved differential trends can yield incorrect

estimates of the program impact and analyses that do not account for these differences may erroneously attribute them to the introduction of the campaign. For example, despite the fact that Kwong et al. (2008) find relative decreases in death, hospitalization, and emergency room visits at the introduction of the campaign, there is no way to know if these decreases are free from alternative explanations.

Similar problems arise in evaluating other public health interventions. Consider, for example, the Rockefeller Sanitary Commission eradication campaign waged against hookworm in the American South. Simple comparison of outcomes before and after the campaign cannot disentangle the effect of hookworm eradication from alternative explanations for trends in outcomes. Bleakley (2007) addresses this problem by comparing the pre-post impact of eradication for areas with higher levels of baseline hookworm (implying greater benefits from eradication) to areas with lower baseline levels of hookworm. Since pretreatment levels of hookworm were, arguably, exogenous (the campaign was motivated by innovations in knowledge regarding the presence of the disease itself), interpretation of the effect on child schooling outcomes is free of endogeneity problems that would be associated with alternative factors co-determining both hookworm infection levels and future growth.

To account for similar concerns in comparing outcomes among provinces before and after the vaccination campaign in Ontario, I compare the relative impact of the program in Ontario for flu seasons with higher vaccine match rates (implying greater benefits to the program) to seasons with lower vaccine match rates. Since mismatches are determined by random genetic mutation of flu strains as they relate to yearly vaccine content choices, mismatches can be thought of as exogenous. For example, I argue that mismatches are not related, for better or for worse, to program adoption in Ontario. In fact, vaccine content is identical across North America; preapproved by Health Canada across all provinces; and held fixed over each yearly flu season.

3 Identification Strategy

The purpose of the empirical work is to study the links between vaccination and health by identifying the impact, attributable to vaccination, of a broad scope immunization campaign. I start with an underlying model linking vaccination to health (broadly defined) with linear effects of vaccination:

$$h_{ijt} = \delta m_{jt} v_{ijt} + \gamma m_{jt} \bar{v}_{(i)jt} + X_{ijt}\Pi + \varepsilon_{ijt} \quad (1)$$

Here, h_{ijt} is a health measure for individual i residing in region j at time t, X_{ijt} is some vector of individual controls, and ε_{ijt} is an individual error term. The coefficient δ is meant to capture the individual effect of vaccination (denoted v_{ijt}) from person i's vaccination decision while the coefficient, γ, is meant to capture the effect of average vaccination excluding person i (denoted $\bar{v}_{(i)jt}$). In other words, it is the external effect of vaccination on the illness of person i arising from the vaccination behavior of others.

It is often the case that individual level data on vaccination and illness are unavailable. In this setting, the *total* effect of vaccination can be obtained from the aggregated model in (2):

$$\bar{h}_{jt} = \lambda m_{jt} \bar{v}_{jt} + \bar{X}_{jt}\Pi + \bar{\varepsilon}_{jt} \tag{2}$$

where $\bar{h}_{jt}$ is average health in region j at time t and where both own and external effects of vaccination are included in λ, the total effect of changes in average vaccination in region j at time t.[12] If vaccination prevents illness, then λ is assumed to be positive.

Estimation of λ presents a number of potential challenges. For instance, if lower baseline levels of average health are associated with higher vaccination levels, then this unobservable association will mitigate the relationship between vaccination and health and would bias estimates of the effect of vaccination downward. The data show that this is a probable concern. For instance, comparing vaccinated and unvaccinated groups, the data show a counterintuitive connection between vaccination and health during the summer season where the vaccine is unlikely to causally impact health. Specifically, in the summer months where flu is not in circulation, the rate of recent short-term bed illness for vaccinated individuals is 16 percent higher than that of unvaccinated individuals. This finding demonstrates selection into vaccination that is likely generated from heterogeneity in the return to immunization. Those in poorer health or with higher infection probabilities have higher returns to immunization and thus may be more likely to vaccinate. However, they are also more likely to experience negative health shocks, which may drive part of the relationship observed between health and vaccination.

Additionally, there may be other sources of selection that contribute to year by region variation in vaccination rates. For example, variation in incidence of other infectious diseases

[12] Here, λ is a function of the individual and external effects of vaccination and it enters linearly into the model in (1). The implications of decreasing returns to vaccination are discussed below and specifications capturing non-linearities in the response to vaccination and match are also explored in the reduced form counterpart to this model and are available upon request.

(colds, other respiratory viruses, *et cetera*) may be correlated with selection into vaccination and are also associated with health outcomes. In this case, the positive association between vaccination and health would be mitigated by this correlated effect. Furthermore, vaccination, itself, may be associated with other behaviors that affect health. For instance, hand washing or other prevention methods may increase after receiving the vaccine. If, for instance, a higher vaccination rate is associated with increased exposure to prevention information and increased prevention behaviors, then rates of illness may be lower regardless of receipt of the shot.

In the present study, there are several factors that contribute to identification of the effect of the broad scope Ontario immunization campaign. The first factor is time-region variation in a campaign that delivered vaccines free of charge to all age groups. The initiation of the campaign was unlikely motivated by higher levels of flu in Ontario: evidence indicates that, if anything, Ontario had marginally lower baseline surveillance rates of flu and flu hospitalizations. The second factor is that in different years and across provinces, there are different degrees of match between the flu shot and the flu. Furthermore, these mismatches are determined by random mutations in flu as they relate to yearly vaccine content, which is predetermined and fixed across North America and over each year. This means that, unknown to the recipient at the time of vaccination, the flu shot may offer a high degree of protection or it may offer a marginal degree of protection. Accordingly, areas with higher levels of vaccination will experience greater benefits if the flu shot is a good match and smaller benefits when it is not. These factors combined, suggest the following reduced form model:

$$y_{ajt} = \beta_1(Post_t * m_{jt}) + \beta_2(Post_t * Ont_j) + \beta_3(Ont_j * m_{jt}) + \beta_4(Post_t * Ont_j * m_{jt}) + X_{jt}\Pi + \mu_{ajt} \qquad (3)$$

where y_{ajt} is an illness outcome for age group a in region j at time t and X_{jt} is a vector of controls which may include, for example, surveillance counts of other respiratory disease to capture other possible changes in compensatory behavior; expenditures on health resources such as hospitals, physicians, and capital investments; the match rate in levels; and age, region, season and month fixed effects. The variable u_{ajt} is an error term with allowance for correlation at the province cluster level.[13]

Inclusion of region effects captures fixed features among regions and will account for

[13] All estimates of (3) are calculated using ordinary least squares (OLS). In the case of a dichotomous dependant variable, I also use logit or probit estimators. These results are not reported here but are available upon request.

unobservable region differences that are common across all seasons and all age groups. Similarly, by controlling for season and age effects, the model in (3) accounts for any fixed differences among seasons (across age and provinces) and age groups (across season and province). Remaining variation in illness is explained by factors that vary across age, region and season and will be determined by any number of sources. To detect that which is attributable to the immunization campaign and is due to changes in vaccination, I control for other unobservable differences occurring in Ontario post program and I also take into account that the match rate, in addition to impacting illness on its own, may have a differential impact among all provinces post program and a differential baseline impact in Ontario. These factors are captured by the coefficients β_1 to β_3. Explicitly, β_1 captures differences in the effect of the vaccine match post 2000 and hence controls for gains in the effect of the match that are common to all provinces; the coefficient β_2 captures unobservable differences in illness in Ontario versus other provinces post program; and the coefficient β_3 controls for baseline differences in the gain from the match that is different in Ontario versus the other provinces. After controlling for these factors and the factors in X_{jt}, the remaining variation in illness is captured by β_4, which summarizes the difference in the post program effect of the match for Ontario and captures the gain in illness prevention in good match years that is explained by the increase in vaccination attributable to the immunization campaign.

The identification strategy employed in (3) rests on the notion that the match rate directly affects the efficacy of vaccination. Aside from laboratory analysis on this relationship, the patterns observed in flu surveillance and previous literature on vaccination efficacy reveals that this is a reasonable conjecture. For instance, in a systematic review of randomized control studies for healthy adults, Jefferson, et al. (2007) find that the efficacy of vaccination for laboratory confirmed flu was 80 percent for studies performed in good match years while it was 50 percent in studies where there was a vaccine mismatch. Although these results should be interpreted with a degree of caution: there is considerable variability in study design and sample characteristics, it does indicate a basis for the argument that the match can impact the efficacy of the flu shot.

Since the research design is Equation (3) is not experimental, results should be interpreted within the context of the program studied. Specifically, since there is likely heterogeneity among individuals who received the shot after the program versus those that did not, the results are an average effect specific to this group of takers. On the other hand, since these types of selection

issues are likely to take place in a policy setting, this information may be of more use to policy makers than that which is based on random assignment of vaccine. This will be the case when broad policies replicating random assignment or strict mandated immunization are more difficult to implement than polices involving price incentives or promotion of the vaccine. A second caveat remains due to heterogeneity in the externality effect of such a program. Since there may be a distinction in the externality effect associated with different levels of vaccination, the effect found here is specific to these changes in vaccination relative to baseline levels. The effect found in this study will be smaller than the expected effect for jurisdictions with lower baseline levels of vaccination (assuming decreasing returns to vaccination).

This methodology can be modified to allow for differences in initial vaccination levels. This would be a possible way to investigate whether these results also reflect decreasing returns to vaccination that operate through differences in baseline average vaccination. Unfortunately, there is little variation in initial vaccination rates for regions in Ontario and regions elsewhere, making it difficult to examine this hypothesis. Alternatively, it also rules out this argument as a possible explanation for the effect that I find; the return to the immunization program, as it depends on initial vaccination levels, is not generated though regional differences in the returns to vaccination.

4 Data and Descriptive Statistics

The empirical analysis draws together information on health and economic outcomes, vaccination status, and the seasonal vaccine match. Table I contains information on the source and sample period of each data set.

4.1 Vaccination

I use master file health survey data from Statistics Canada in order to document the changes in flu vaccination and to provide supporting evidence of the impact of the immunization campaign on short-term health outcomes (bi-weekly bed illness and over the counter cold and flu medicines). There are four health surveys that contain questions relevant to flu vaccination: the National Population Health Survey (NPHS), Cycle 2 1996/1997 and the Canadian Community Health Survey (CCHS), Cycles 1.1 (2000/2001), 2.1 (2003) and 3.1 (2005).[14] These surveys are national, population-based surveys conducted on persons 12 years of age or older. In addition to

[14] The NPHS Cycle 3 (1998/1999) did not include a question on flu vaccination.

collecting demographic, socioeconomic and health information, these surveys also collect information on current and previous vaccination status. In each survey, the respondent is asked: "Have you ever had a flu shot?" and if the answer is affirmative, respondents are asked a follow up question: "When was your last flu shot?" Following the definition used by the Public Health Agency of Canada (PHAC) and the Center for Disease Control and Prevention (CDC), I define the flu season year to be the year starting in October and continuing to September of the following year. This is based on the timing of vaccination delivery in early fall and the seasonal pattern of flu circulation. Using this definition, I can determine coverage rates for each flu-season year by using the time of survey and current vaccination status for survey respondents.

Figure I shows vaccination rates for regions in and outside Ontario by age group over time. The figure shows increases in vaccination from 1996 to 2006 for all age groups and also shows that the young have lower vaccination rates than the old over the same time period. The figure also indicates that, while baseline vaccination rates for the young are not substantially different for regions in and outside Ontario, there are significant gains in vaccination for Ontario at the introduction of the program. Beginning in the 2000/01flu season and continuing to 2005/06, there is a 10 percent relative shift upward in vaccination for the young in Ontario. The same is not evident in the older age group. While the vaccination rate for ages 65 and older is greater for Ontario over the entire sample period, there is no relative change in vaccination at the introduction of the program.

To explore differences in program impact among sub groups, Table II gives a summary of vaccination rates pre and post October 2000. The table shows that, overall, vaccination rates have increased for all regions in the post period relative to previous rates. For instance, post program, there is a 20.8 percentage point increase in the vaccination rate for regions in Ontario and a 12.2 percentage point increase in regions outside Ontario, yielding a 8.7 percentage point relative increase in Ontario following the program. The relative gain in vaccination for Ontario post program is due to an increase of 10.8 percentage points for those under 65. Ages 65 or greater (who were not targeted by the coverage changes) have a small and insignificant relative increase of .4 percentage points. It is clear from these data, that the impact of the program is centered on the age group that was targeted by program incentives.

The remainder of Table II presents summary statistics for ages under 65 by selected characteristic. Baseline vaccination patterns for all provinces fall in line with previous research on

the determinants of vaccination (Mullahy 1999): females are more likely to vaccinate than males, vaccination is increasing in education (with the exception of those without secondary education), and is decreasing in income and time spent working. Underlying health may play a part in explaining these patterns as there are likely correlations between these factors and health characteristics. Meanwhile, health characteristics are also a likely determinant of vaccination. This is evident in the table, which shows substantial differences in baseline vaccination for different levels of self-rated health. These differences may reflect diversity in the expected cost of flu infection relative to costs of immunization: those who state excellent or very good health likely have lower expected costs of infection, while those with fair or poor health are likely have higher expected costs of infection. In the same vein, the data show that chronic conditions covered under provincial vaccination programs are associated with substantially higher baseline levels of vaccination.

Focusing on patterns pre-post, the relative increase in vaccination for regions in Ontario versus regions outside Ontario is similar across the sub groups indicated. The largest increases, in both absolute and relative terms, are among those not in the labor force (possibly reflecting smaller time costs of vaccination) and among those with lower income. The relative increase in Ontario post program is of similar magnitude regardless of having a covered chronic condition, and self-rated health status does not appear to be related to vaccination uptake pre-post program. In Ontario, there are increases of approximately 20 percentage points for all rankings of self rated health and relative to other provinces this reflects a 10 percentage point increase.[15]

4.2 Health Outcomes

Data on flu infections are obtained from surveillance counts of laboratory confirmed flu. The PHAC collects these data through its respiratory surveillance program. This program collects disease tests on a weekly basis from appointed sentinel physicians in a defined surveillance region (usually one per census division). The collected tests are sent to laboratories to be assessed for flu or other respiratory diseases. In the flu off-season, sentinels are still encouraged to collect tests. I use these data for two purposes; the first is to describe the impact of the coverage changes in Ontario on the rate of laboratory confirmed flu and the second is to define the period throughout

[15] Estimates of the relative increase in vaccination for each of the seven city-regions across Ontario obtained from regression analysis controlling for factors such as demographic, economic and health characteristics are consistent with results reported here and confirm that the relative increase in vaccination is similar across all seven city-regions in Ontario.

the year where flu is circulating. I use the flu season period as a conditioning variable for other illness outcomes such as hospitalizations and work absenteeism and I define it as the contained set of weeks starting from the first week the number of positive tests is greater than 5 percent of the season total until the last week it falls below 5 percent.[16] These data are presented graphically in Figure II. Panel B shows the laboratory confirmed flu rate (percent of collected tests that are positive for flu) and indicates the flu season period of each year. As a matter of construction, there will be limited laboratory flu during off-season. The same is not necessarily true for other illness measures such as hospitalizations and illness work absences, which may vary according to other factors related to health. However, to the extent that laboratory flu is a good measure of whether flu is circulating, we should expect that the program impact on health and productivity measures should be largest during the flu season (as it is defined here) and minimal during off-season. To explore this, I present results for both periods: off-season and flu-season. Further, I break the flu season into the period from the season start to peak and the period at season end in order to compare estimates among time periods where there is more or less information about the size of the yearly epidemic. It is worth pointing out that these periods do not always occur at the same time each year: there is variation in the timing of the epidemic. In order to take account of, for example, a "December effect" that systematically impacts illness during the month of December, I control for month effects in the empirical work.

Panel A of Figure II indicates the clinical match rate for each season. The pattern between match and the incidence of flu is apparent: a mismatch in the vaccine results in a more severe flu epidemic as measured by surveillance testing. To define the clinical match rate, I use strain isolation data from the PHAC along with reports on the cross-immunity of the yearly vaccine. I identify all flu strains observed by the PHAC as matched or not matched to the yearly vaccine. Reports on strain match are published each year in the Canadian Communicable Disease Report (CCDR). Additionally, I compare these findings with that of the U.S. Center of Disease Control and the vaccine recipe from the World Health Organization and find that they correspond. In order to get a measure of the match rate, I use data from the PHAC sample of strain isolated flu tests. During each flu season, the PHAC takes a sample of positive flu tests in each province and identifies individual flu strains. In the sample of tests, each test is categorized based on strain type,

[16] This is a standard definition is used in previous studies on influenza and it is used here for comparison of estimates throughout the season. In all subsequent analysis, results are reported for all separate periods during the year. An alternative definition of the flu season period used (but not reported here) is any week with positive surveillance tests.

which can be compared to the yearly CCDR report. The match rate is calculated as the proportion of strains in the sample that are a match (i.e. have cross immunity) with the current flu shot. Since the match rate is 100 percent for a number of seasons, I also examine a dichotomous definition of match that is 0 when there is at least one unmatched strain and 1 when there is not. The results are not presented here but are consistent with the results that use the continuous definition of match.

To investigate health consequences of flu vaccination, I use administrative data on hospitalizations from the Hospital Morbidity Database (HMDB) holdings of the Canadian Institute for Health Information. The HMDB data include complete records of hospital inpatient discharges for hospitals in Canada. Hospitals in Quebec and non-Winnipeg Manitoba started submitting to the HMDB after 2001 and are consequently excluded from the analysis. Each discharge abstract consists of information on patient age, sex and home postal code as well as detailed medical information: date of hospital admittance, whether the admittance is from care facility, date of discharge, discharge with death and detailed diagnosis information. Each abstract records one diagnosis labeled the most responsible diagnosis (MRD) and up to 15 co-diagnoses. Using this information, I am able to analyze hospitalizations where flu or pneumonia are listed as the MRD diagnosis or listed as one of the other 15 diagnoses. I study both flu and pneumonia diagnoses since an incidence of flu may be coded as viral pneumonia, a common complication of the flu. I also discuss results for other known complications of the flu such as: heart disease, other respiratory disease and, as a specification check other hospitalizations that do not contain any respiratory diagnosis.

I use diagnosis counts from the HMDB to construct weekly hospitalization rates for regions in Canada and I use the definition of economic regions defined by Statistics Canada. Each region is made up of a group of adjacent census divisions and is a standard geographic region meant to characterize regional economic activity. I use this definition instead of using census metropolitan areas since these regions will capture activity both including and surrounding cities and also allow for the entire geography of a province to be captured. Localized activity within these city-regions is likely to track patterns of flu transmission and by grouping admissions into well-defined regions, I am able to control for fixed regional characteristics such as density and other unobservables that impact illness. There are 76 regions in Canada, and for reasons of small cell size; I combine northern regions in each province leaving a total of 66 regions. Eight of these are dropped due to incomplete data for Quebec and non-Winnipeg Manitoba. Hospitalizations are

assigned to regions based on patient postal code. For each region, I construct rates for different age groups. Population counts for each group, region and year are used in the denominator of the weekly rates.

I am also able to observe admissions originating from care home facilities. With this information, I can calculate flu and pneumonia hospitalization rates for care home residents using provincial resident counts obtained from the Residential Care Facilities Survey conducted by Statistics Canada. From the early 1990s, vaccination has been covered for all residents of care facilities across all provinces, and vaccination rates have been high for this population.[17] A common argument for vaccinating healthier individuals in contact with care facility residents is that residents (with lower health and hence lower immune responses to vaccination) may benefit from the vaccination of contacts even if vaccination levels for this group are already high. I explore this possibility.

Flu shots may also have impacts along other dimensions. To investigate the effects for labor productivity, I use the Labor Force Survey (LFS). The LFS collects monthly information on the labor market and demographic variables for household members 15 years of age and older. Demographic characteristics include age, sex, marital status, educational attainment, and family characteristics. Labor force characteristics include employment information such as usual and actual hours of work, and hours and reasons absent in a reference week. I examine work absences "due to own illness" which do not include, for instance, maternity leave, care of children or elderly relatives, and vacations or holidays.

Summary statistics for hospitalization and illness absences are shown in Table III. In Panel A, the data show a visible pattern in health measures over different periods during the flu season. For flu, pneumonia and work absences, there are higher rates in the same weeks that that flu surveillance rates are highest. Meanwhile, there are no obvious differences across periods of the year for non-respiratory admissions. Rates for flu, pneumonia and work absences are also higher in seasons with a mis-match vaccine, while non-respiratory admissions show slightly higher rates in match seasons (possible reflecting shifts in resource use). The statistics show that in Ontario, hospital admissions are lower, while work absences are higher. Further, across all regions in the post-period, admissions decreased, while work absences rose (less so in matched seasons, however). There are also differences in underlying individual characteristics across mis-match and

[17] For instance the vaccination rate for care facility residents in Ontario was 93 percent before the UIIP program and 95 percent after the UIIP program (Clement and D'Cunha 2002) and Russell (2001) shows that Alberta rates in the 1990s were 91 percent.

match seasons (shown in Panel B). For instance, the average age among individuals admitted to hospital for flu and pneumonia is higher in mis-matched years. The same is evident for work absences but there is very little difference for non-respiratory admissions. This is likely explained by the fact that immunized groups are more sensitive to changes in the match rate than un-immunized groups. For instance, since older individuals have higher vaccination rates, they are underrepresented relative to younger groups when the match rate is high.

5 Results

5.1 Main Results

In this section, I investigate overall changes in health by estimating the reduced form version of Equation (2). As indicated by this equation, the relationship between health and the match rate is hypothesized to be positive: for a given vaccination rate, the match rate will influence health to the extent that the protection afforded by the vaccine depends on the quality of the match. A secondary prediction from Equation (2) is that this relationship is increasing in the vaccination rate: when the vaccination is higher, a higher proportion of individuals will yield the benefits of a good match.

To begin investigating the benefits arising from the immunization campaign for worker absenteeism, flu and pneumonia hospitalizations; I start with a graphical depiction of the flu hospitalization rate in Figure III, which reveals the patterns hypothesized by (2). The figure shows a scatter plot of average flu hospitalizations and vaccine match rates for each flu season-year. The linear regression of the average flu hospitalization rate against the match rate is also shown for each of four groupings: average flu hospitalizations for city regions outside of Ontario in both the pre and post period and average flu hospitalizations for city regions in Ontario, also in the pre and post period. As hypothesized in (2), the figure shows that the match has a negative effect on flu hospitalizations in both periods and over both city-region groupings. This is signified by the negative slope on the linear prediction in all four groups. The figure also shows a steeper slope for the higher vaccination levels occurring in the post period. The difference is only slight for city-regions outside of Ontario, but is evident for city-regions in Ontario (note that vaccination increased in all provinces but much more so in Ontario). This indicates that, to a much larger extent in Ontario, higher vaccine matches now decrease flu hospitalizations more substantially. Since this effect operates through variation in the match rate, it corresponds to the substantial

increases in vaccination that followed the immunization campaign.

It is worth noting the level shift down in the curve that occurs for city-regions outside Ontario in the pre versus post period. This shift down indicates that there is post period decreases in average admissions that are not explained by variation in the match rate. By comparison, the level shift down in Ontario is much smaller and these features outline the possible fallacy in simple comparisons of admissions pre-post for Ontario and other provinces. To see this, note that downward shifts in the curve indicate that there are other factors besides vaccines that lead to decreases in hospital admission rates. Further to this, differences in the magnitude of the shift indicate that the impact of these factors differs across region and time. Changes in hospital resources may be an example of one contributory factor where, for instance, the number of hospital beds in Ontario remained relatively constant over this period and declined 3 percent in other provinces (CIHI 2005).[18] Because of this, difference in difference comparisons among provinces will not yield the true effect of vaccination, but will be a combination of the impact of this and other correlated factors that change over region and time.

It is clear from Figure III that the match has a larger impact on flu admissions after the immunization program. Figure IV highlights the program match effect as each seasonal epidemic progresses over the year. On the top left side of the figure, the weekly flu hospitalization rate is shown for season-years with a mismatch in the vaccine. There is a clear decrease in flu admissions post program for all provinces but there are no obvious differences in the magnitude of the flu epidemic in Ontario versus the other provinces after program introduction. The top right side of the figure shows the flu hospitalization rate for season-years with a perfect match. In absolute terms, the flu rates are much smaller in these seasons relative to those in the plot on the left. This reflects the level effect of the match on admissions. The figure also shows decreases in flu post program for all provinces, but a more prominent decrease in Ontario. Post October 2000, flu admissions were almost eliminated in these season-years. There are similar patterns for pneumonia admissions given in the bottom of the figure. Here, the differences between Ontario and the other provinces are of a lesser degree.

Figure III illustrated the importance of controlling for other correlated factors explaining hospital admissions and Figure IV highlights differences in seasonal epidemics over region, time and match. In order to detect changes in hospitalizations that are causally linked to vaccination, I

[18] These numbers are determined through the author's calculation using source data from the Canadian Institute for Health Information: http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=AR150_2006data_e (accessed October 1, 2009)

examine changes in the effect of the match rate: an exogenous determinant of vaccine protection. By comparing the impact of the match on admissions over each of the four region-period groupings, I can control for other factors that "shift the curves" over season and region and additionally, I can control for baseline differences in the effect of the match that differ between city-regions. I formalize this by estimating the model in (3) and examining the variable of interest, Post*Ont*Match. Panel A of Table IV displays the coefficient for Post*Ont*Match in different periods during the season. The basic results show a substantial effect on flu admissions throughout the flu season. This is after controlling for month, age, city-region, and season fixed effects; the level effect of the match; all second level interactions (Post*Match, Post*Ont, and Ont*Match); government health expenditures on hospitals, physicians, and capital investments; diagnosis specific coding classifications changes (ICD10 versus ICD9); and the proportion of observed strains of each of H1N1, H3N3 and B in each season.

There is an apparent pattern in the program match effect over the flu season. The largest effect occurs in the season start to peak, with a smaller effect during the season end. During the season start to peak, the coefficient on Post*Ont*Match is -2.8 per week per 100,000 and the effect is -2.4 at the season end. There is little effect in the flu off-season: the point estimate is small and insignificant. These results indicate that, while a good flu shot match on its own will decrease flu hospitalizations, combined with the flu shot program in Ontario there are significant relative decreases that can only be explained by increases in vaccination. The mean match rate is 71 percent and using the numbers for the season start to peak, results imply that relative to an average match, a perfect match leads to a gain for Ontario of 0.9 less hospitalizations per week per 100,000 after introduction of the immunization campaign. In the season end, there is a gain of 0.7 less hospitalization per week. In the flu off-season there is no gain for Ontario arising from the immunization campaign.

I also estimate the impact on pneumonia hospitalizations, a frequent complication of the flu and a common diagnosis for a flu infection that becomes serious enough for hospital admission. These results are in column (3) of Table IV. Effects for pneumonia are smaller relative to baseline levels but significant decreases exist for Ontario when the flu shot is a match. In the season start to end and relative to an average match, a perfect match averts 1.4 hospitalizations for Ontario compared to other provinces. Again, the magnitude of the effect follows the seasonal pattern of flu; the largest effects occur during the flu season with little effect in the off-season. Note that this

is not by construction: except through the effects of the flu and the flu shot itself, there is little reason why the patterns we see for pneumonia hospitalizations should systematically follow the surveillance patterns of laboratory flu counts.

Work illness absences also exhibit a seasonal pattern following the seasonal pattern of flu surveillance. This is evident in Figure V, which shows average absence rates throughout different periods during the year. The top two panels of the figure show absence rates for months occurring in five different periods during the flu season: the fall (pre) season, season start, season peak, season end, and the summer (post) season. The bottom two panels show flu surveillance rates (fraction of tests positive for flu by each week). The peaks in work absences correspond to peaks in laboratory confirmed flu and are more severe when there is a mismatch in the vaccine. Moreover, despite the evident trend upward in work absences, there are mitigated increases for Ontario specific to good match flu shot years along with much more mitigated peaks in flu season periods. Column (4) in Table IV confirms these results. In the base specification, good flu shot years post-program in Ontario are associated with less work illness. Moreover, this is specific to the high flu season periods of the year. This pattern is found when controlling for differences over season-years, differences over regions, differences over age groups, differences over months and other controls (including: all base specification controls and education, marital status, sex, occupation and union status). In the season start to peak, there was a 0.5 percentage point decrease in worker illness. From a base of 2.7 percent this represents a 19 percent decrease when the flu shot is a perfect match and implies that relative to the average match rate, a perfect match decreases worker absences in Ontario by 0.2 percentage points (7 percent relative to base). I also explore several non-linear specifications, such as using the log of the match rate or probit/tobit models, to investigate diminishing marginal effects of the match. These results, not shown here, demonstrate similar patterns.

To test whether estimates are sensitive to a potential behavioral response to predicting or learning the match rate, I present results in Panel B that control for changes in circulation of other infectious disease. If individuals can accurately predict or learn the match for each season and residents of city-regions in Ontario are even better able or more responsive to these predictions after the immunization campaign, then it may bias results. In this case, in a bad match year, individuals can potentially compensate through other protective behaviors such as washing hands. If Ontario residents are more responsive specific to the introduction of the campaign, then results

will be underestimated. To assess whether this is the case, I use data on surveillance rates of other infectious disease collected by the PHAC. The diseases included are respiratory syncytial virus, parainfluenza, and adenovirus. These diseases are non-vaccine preventable respiratory viruses that are infectious through the same manner as the flu with similar symptoms. If compensatory behavior impacting flu circulation does exist in the manner described, then this behavior will also impact circulation of other infectious disease. In order to test this, I control for disease surveillance for other infectious disease and compare results to previous estimates. Panel B shows that point estimates are somewhat larger (in absolute terms), but the difference is negligible (in magnitude and significance). These results support the supposition that individuals are unable to predict and adjust behavior according to the match rate to a higher degree after the immunization campaign.

5.2 Impact on Lost Time to Illness

The immunization program had effects along other dimensions. Table V shows the effects for death, wait time in ER before admission, total hospital days and average length of stay. Results indicate that there are large effects for death; relative to the average match, a perfect match after the immunization campaign delayed 0.04 deaths per week per 100,000 for flu and 0.17 deaths per week from pneumonia. This represents a gain of almost 2 fewer deaths per 100,000 per season. There are also decreases in time spent waiting in the ER before admittance to acute care, although these results are not statistically significant.[19] There is a significant decrease in the number of hospital days per 100,000, an effect that is mainly due to fewer hospitalizations: average hospital length of stay increased when there was a good match post program in Ontario, although this effect is statistically indistinguishable from zero. These results along with the decreases in wait time from emergency to admittance may indicate a decreased crowding effect; less hospitalizations may mean more resources put towards other hospitalizations. I explore this further when looking at hospitalization rates for other diseases. The same pattern appears for work absences. The program match effect on time-spent ill is mainly due to decreased absences rather than due to shorter hours spent ill per illness. Similar to the results for hospital admissions, the length of time-spent absent is longer after the program in higher match seasons, although the effect is small and indistinguishable from zero.

[19] The results for emergency room wait time are around the same magnitude (10 minute decrease) for other types of hospital admissions, possibly indicating a slackening of resource constraints. Approximately 60 percent of all hospital admissions are admitted through the ER.

5.3 Impact for Age Groups

Table VI explores patterns among sub groups of the population. It is clear that the young and the oldest age groups had the most to gain from the flu shot program. This is true in absolute terms and relative to baseline average illness. Young children gain the most relative to baseline levels and because this group has the highest incidence of hospitalization for flu (next to those over 65), this translates into large savings in terms of hospital admits. For children under 5, relative to an average match, a perfect match brings a gain of 2.0 less hospitalizations per week per 100,000 for Ontario after the introduction of the flu shot campaign. There are smaller effects for middle age groups but the impact begins to increase in the elder age groups of 50 to 65. This group had a larger relative increase in vaccination of 12.9 percentage points and exhibits larger decreases in illness relative to the younger age group of 25 to 49.

Figure VI shows the program match effect over the full age distribution for flu and pneumonia admissions combined and also plots the percent decrease in admissions relative to baseline. The greatest percent decreases occur for children under 10 years of age with smaller decreases are apparent for prime-age individuals. The decline in hospitalization for ages over 65 is substantial both in number and relative to baseline even though there are no relative differences in the vaccination for older age. If older groups are unaffected by the vaccination of others, then there should be no difference in the relative gain for older adults when the flu shot is a good match in Ontario versus other provinces. However, as shown in the figure and in Table VI, there are negative effects for all outcomes among older age groups. Relative to baseline, the results are smaller than that for children under 18 but represent larger absolute decreases in hospitalization. For instance, in older adults, relative to an average match, a perfect match averts 3.5 flu hospitalizations for Ontario over and above city-regions in other provinces.

Further, I look at the hospitalizations of long-term care residents. Long-term care residents have had high vaccination rates since the early 1990s and are particularly at risk for complications associated with flu. It is often argued that even with high vaccination rates, this group could benefit from vaccination of others due to the low immune response and protection they can sustain from the flu shot personally. The program match effect for admissions from care homes, while imprecisely measured, indicates that there are large effects here as well: relative to an average match, a perfect match averts 16.7 flu hospitalizations per 100,000 residents per week during flu season. Relative to baseline levels this is a 27 percent decrease.

One possible explanation for differences in the post program match effect for older adults is that the effect may be driven by decreasing returns to vaccination. If there are diminishing returns to vaccination (as we might expect given the externality associated with vaccines) then there may be differences in illness that are generated solely by differences in baseline vaccination. In short, separate groups can have the same increase in flu vaccination but can expect different gains in health given current vaccination levels. In this context, this explanation does not explain the negative effects I find for older adults in Ontario. Assuming that there are no externality effects from other groups, with diminishing returns to vaccination, the gain for older adults in Ontario should be smaller compared to city-regions elsewhere. This is because while there were equal increases in vaccination in all provinces post program, baseline vaccination levels for these age groups are higher in Ontario. When vaccination exhibits diminishing returns, it would imply a positive post program match effect. Instead, there is a negative post program match effect, and the remaining explanation is that older groups in Ontario benefited from the externality associated with vaccination of younger groups. The effect may be even larger when baseline vaccination levels are more comparable to the other provinces.

5.4 Impact for Other Health Outcomes

It is clear that the flu shot program can affect the more serious health complications associated with hospital admission but I now explore impacts for less severe outcomes using health survey data. A subset of health surveys (summarized in Table I) include information on recent fluctuations in health. Each respondent is asked if they spent time in bed or reduced activity due to illness during the last two weeks. Respondents are also asked detailed questions about medications taken in the last month and these responses can be categorized by DIN number into different medicine types. Using this information, I generate a variables indicating reduced activity or bed illness and use of over-the-counter medications for cold or flu. Furthermore, by using the date of survey, I can divide the data into time spans during flu season and those during off-season. Unlike observations in the hospitalization data, these surveys are designed to be representative of the underlying population and can be used to analyze the general impact of the flu shot program. Results for these outcomes for full and sub samples are given in Table VII. For the full sample, there is a negative effect for both medications and bed illness. During flu season, a good match flu shot decreases medications for cold/flu by 10.2 percentage points for Ontario relative to the other

provinces.[20] There is a 3.0 percentage point fall in the rate of being recently in bed ill. This is compared to a 6.8 percentage point decrease in laboratory confirmed flu rate. The larger effect for laboratory flu rates may be explained by methods of testing. These lab tests are not collected through random sampling of the population but are instead collected from sentinel physicians and may have different sensitivities or specificities to true underlying flu. Likely, there is a higher proportion of flu incidence in this sample than in a random sample of the population. Furthermore, testing behaviors may be related to both the match rate and the immunization campaign, which could bias the result found here.

Patterns within age groups exhibit the same patterns as for work absences and hospitalizations: effects are largest for the youngest and oldest, with modest effects for those ages 25 to 64. Results for the sample of workers corroborates previous results from the Labour Force Survey. There is a 0.54 percentage point decrease in recent bed illness during the flu season for the sample of workers from the health surveys, which corresponds approximately to a 0.59 percentage point decrease in work absences for the same sub group using the Labour Force Survey.

5.5 Impact on Respiratory Versus Non-respiratory Admissions

Next I examine how other admissions are impacted by the flu shot program. Flu is known to cause complications for a number of diseases, for instance: heart diseases, chronic respiratory problems, cancer, disease of the nervous system and other conditions associated with immunosupression. To analyze the impact of the flu shot program on these diseases, I divide the admissions data into two categories: hospitalizations that contain a co-diagnosis of respiratory disease and hospitalizations that do not. Panel A in Table VIII shows results for respiratory diagnoses and indicates that respiratory hospitalizations are sensitive to the post program match effect. For instance, the average rate of hospitalization for respiratory disease is 32.2 per week during the flu season and is 24.8 in off-season. During the flu season, the program match effect is a decrease of 9.6 respiratory hospitalizations over and above city-regions outside Ontario, while the effect is small and statistically insignificant from zero in the off-season. Looking at other diseases, similar patterns emerge. Except for cancer, the post program match effect is largest during the flu season and small and indistinguishable from zero in the off-season. There is no effect on cancer patients in either the flu season or off-season. Panel B of the table reports results

[20] As a side note, there was no impact, positive or negative, on the use of antibiotics.

for hospitalizations that do not have a contributory diagnosis of respiratory disease. Here there are no visible patterns among diseases both during flu season and off flu season: all point estimates are small relative to the mean and indistinguishable from zero. This has two implications. First, there are no observable differences in patterns of health that are not associated with the flu or flu complications. We would expect that if general health were correlated in some way with the flu shot match specific to the time and place of the introduction of the immunization program, it would manifest in some other measures of health. The evidence shown here indicates that the impact of the program is specific to flu and its complications and moreover, follows the timing of elevated circulation of flu. Secondly, there seems to be no evidence that the flu shot program decreases crowd out of other disease admissions in any statistically significant way.

6 Interpretation

Are the estimates presented plausible for the effect of vaccination on flu incidence? Based on approximations of the transmission rate and duration rate of the flu, an infected individual mixing in a wholly unvaccinated population, would, on average, infect 1.44 before recovery (Hethcote 2000). A simple model of disease dynamics indicates that a fully protective vaccine and a vaccination rate greater than 31 percent will reduce the average infection number below one.[21] In other words, an infected individual will less than replace himself with a new infection and a flu epidemic will be prevented. Average vaccination rates in Ontario increased from 21 percent to 42 percent post program. Based on these numbers the expected effect of the immunization program should be large when the vaccine is of full protective value. Given a perfect vaccine match and the increases in vaccination following the immunization campaign, results show that the rate of flu hospitalizations decreased by 2.0 in flu season weeks. Relative to baseline levels, this is a 67 percent decrease. At the average match rate, this represents a 47 percent decrease. There is evidence that part of this effect is due to externalities from vaccination. For those 65 and older there was an 85 percent decrease (60 percent at average match) in hospitalizations relative to baseline levels. Illness absences for workers decreased 0.6 percentage points. Relative to the 10 percentage point increase in vaccination for this group, this implies that during the flu season when the flu shot is a good match, a vaccinated worker is 6 percent less likely to be absent from work

[21] This model is based on the Kermack and McKendrick Susceptible-Infective-Removed model of disease epidemics. Several variations of the model are shown in: Kremer and Snyder (2006), Geoffard and Philipson (1997), Francis (1997, 2004) and Boulier, et al. (2007).

for reasons of illness following the immunization campaign.

These results suggest that the flu shot may have substantial benefits in terms of hospitalization and lost work costs. For instance, estimates indicate that 9.6 respiratory hospitalizations per 100,000 are prevented per week during the flu season over the population of Ontario. This is a savings of 1,245 admissions per week. The length of the average flu season is 9.4 weeks and the cost of an average respiratory hospitalization is $8,629 (CIHI 2008). A back of the envelope calculation indicates a savings of $101m when the match is perfect. At the average match rate of 71 percent, this represents a savings of $72m. For illness absences, estimates indicate there was a 0.6 percentage point decrease in work absences over the working population of Ontario. This is a savings of 47,400 work absences per week. At an average hourly wage of $18 and average absence duration of 9.1 hours this translates into $73m in savings per season for Ontario in perfect match years ($52m at the average match). These saving are less than total program costs. As part of the program 6 million vaccinations were distributed in Ontario per season. This represented an average $19m in additional administration costs and an extra $14m in vaccine costs for a total additional cost of $33m per season.

7 Conclusion

I evaluate the health and economic consequences of a broad-scope immunization program: one of the first to recommend and provide the vaccine to all children and adults under 65. Since this program was one of the first of its kind, it provides novel evidence on the consequences of immunization for younger age groups and results reflect on the total impact for all groups and the externality effects for older age groups.

The study design benefits from a number of factors: (1) variation in the timing of a program that was pervasive and effective at increasing vaccination, (2) exogenous variation in the match of the flu shot that permits a treatment control design, and (3) comprehensive data on measures of health and productivity that span a number of seasons across numerous well-defined geographical areas. In contrast to existing literature that does not rule out other correlated effects, I find significant decreases in flu and pneumonia hospitalizations and provide evidence of the same for work absences and other health outcomes such as bi-weekly bed illness and monthly over the counter cold and flu medicines. Moreover, the research design implies that these results operate only through the impact of increased vaccination; the effect is identified through variation in the

efficacy of the flu shot whilst controlling for differences across time and region and differential effects of the match across time and province.

For those under 65, the impact was largest for children and the older age group of 50 to 65 years. This pattern is apparent in all outcomes studied and follows the pattern of vaccination uptake after program introduction. Further to this, significant effects were found for the hospitalizations of older adults (65 and older) and long-term care residents, both of whom experienced no significant relative increases in vaccination. I argue that this is evidence that these groups experienced external effects from the vaccination behavior of younger individuals living within the same geographical region. This is further supported by the negative effects for bi-weekly bed illness and monthly consumption of medicines for ages 65 and over. For the working population, there is a .6 percentage point decrease in work absences due to illness (22 percent decrease from baseline). This is corroborated by results from health surveys that indicate that decreases in recent bed illness for the same population were of the same magnitude.

This study contributes to two important questions. The first deals with the expected gains from vaccination of healthy children and younger adults; are there sufficient benefits from vaccination to recommend or even subsidize its use? I provide results that indicate that a flu shot with a good match can have a significant impact on the health and economic outcomes of these groups with still large benefits at the average match rate. This is true both for severe health outcomes such as hospitalization but also measures of productivity such as worker absenteeism. The second question deals with the expected gains for older groups; does vaccination of children and young adults impact the health of older individuals? I provide evidence of external effects of vaccination of younger groups on the health of older groups. The flu shot program led to significant benefits for older adults. This is true for all ages over 65 as well as long term care residents. Since these effects are substantial, in the very least, they imply that care must be taken to address possible treatment spillovers in other contexts.

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References

Almond, Douglas, "Is the 1918 Influenza Pandemic Over? Long-Term Effects of In Utero Influenza Exposure in the Post-1940 U.S. Population," *Journal of Political Economy*. 114 (2006), 672-712.

Almond, Douglas, and Bhashkar Mazumder, "The 1918 Influenza Pandemic and Subsequent Health Outcomes: An Analysis of SIPP Data," *American Economic Review*. 95 (2005), 258-262.

Angrist, Joshua D., and Jorn-Steffen Pischke, *Mostly Harmless Econometrics: An Empiricist's Companion*, (New York, NY: Princeton University Press)

Benson, V., and M. A. Marano, *Current Estimates From the National Health Interview Survey 1995*, (Hyattsville, Md: National Center for Health Statistics; Data From Vital Health and Health Statistics, 199, 1998)

Bleakley, Hoyt, "Disease and Development: Evidence from Hookworm Eradication in the American South," *Quarterly Journal of Economics*, 122 (2007), 73-117.

Bobonis, Gustavo, Edward Miguel, and Charu Puri Sharma, "Anemia and School Participation," *Journal of Human Resources,* 41 (2006), 692–721.

Boulier, Brian, Tejwant Datta, and Robert Goldfarb. 2007. "Vaccination Externalities." *The B.E. Journal of Economic Analysis and Policy*, 7 (2007), 71-25.

Canadian Institute for Health Information, *Hospital Trends in Canada. Results of a project to create a historical series of statistical and financial data for Canadian hospitals over twenty-seven years*, (Ottawa: Canadian Institute for Health Information, 2005)

Canadian Institute for Health Information, *The Cost of Acute Care Hospital Stays by Medical Condition in Canada,* 2004-2005, (Ottawa: Canadian Institute for Health Information, 2008)

Canadian Pharmacists Association, *The Flu: Influenza Immunization Guide for Pharmacist, (*Ottawa: Canadian Pharmacists Association, 2007)

Canadian Pharmacists Association, *The Flu: Influenza Immunization Guide for Pharmacists,* (Ottawa: Canadian Pharmacists Association 2003)

Centers for Disease Control and Prevention, "Recommendations of the Advisory Committee on Immunization Practices," *Morbidity and Mortality Weekly Report,* 57 (2008) 1-60.

Centers for Disease Control and Prevention, "Deaths: Final Data for 2004," *National Vital Statistics Reports*, 55 (2007), 1-120.

Clement, Tony, and Colin D'Cunha, "Snapshot of Ontario's Universal Influenza Immunization Program." (Geneva: Presentation at World Health Organization, November 2002).

Demicheli, Vittorio, "Mass influenza vaccination in Ontario: Is it worthwhile?" *Canadian Medical Association Journal,* 164 (2001), 38-39.

Fedson David S., Claude Hannoun, Jane Leese, Marc J. W. Sprenger, Alan W. Hampson, Klaus Bro-Jørgensen, Ann-Marie Ahlbom, Hanne Nøkleby, Martti Valle, Olafur Olafsson, Fracisco Salmeron Garcia, Richard Gugelman, Helena Rebelo de Andrade, René Snacken, Franz Ambrosch, and Isabella Donatelli, "Influenza vaccination in 18 developed countries, 1980-1992," *Vaccine*, 13 (1995), 623-627.

Francis, P. J., "Dynamic epidemiology and the market for vaccinations," *Journal of Public Economics*, 63 (1997), 383-406.

Francis, P. J., "Optimal tax/subsidy combinations for the flu season," *Journal of Economic Dynamics and Control*, 28 (2004), 2037-2054.

Gao, Ru-Nie, Helen Johansen, Luling Mao, Richard Marcoux, Cyril Nair, and Kathy Nguyen, "Influenza Vaccination," *Statistics Canada Health Reports*, 15 (2004), 33-43

Geoffard, P., and T. Philipson, "Disease Eradication: Private Versus Public Vaccination," *American Economic Review*, 87 (1997), 222-230.

Govaert, T., C. Thijs, N. Masurel, M. Sprenger, G. Dinant, and J. Knottnerus, "The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial," *Journal of the American Medical Association*. 272 (1994), 1661–1665.

Groll, D. L., and D. J. Thomson, "Incidence of influenza in Ontario following the Universal Influenza Immunization Campaign," *Vaccine,* 24 (2006), 5245–5250.

Health Canada, *Access To The Seasonal Flu Vaccine In Canada - How the flu shot makes its way from the laboratory to the doctor's office*, (Ottawa: Health Canada, 2007)

Hethcote, Herbert, "The Mathematics of Infectious Diseases" *SIAM Review*. 42 (2000), 599-653.

Institute for Health Economics, *IHE In Your Pocket 2008, 2006: A Handbook of Health Economic Statistics*, (Edmonton: Institute for Health Economics, 2008, 2006)

Jefferson T., D. Rivetti, C. Di Pietrantonj, A. Rivetti, and V. Demicheli, "Vaccines for preventing influenza in healthy adults," *Cochrane database of systematic reviews*. 2 (2007), CD001269.

Kermack, W.O. and A.G. McKendrick, "Contributions to the Mathematical theory of epidemics," *Proceedings of the Royal Society A*, 105 (1927), 700-721.

Kurji, Karim, 2004. "The Ontario Experience with Universal Vaccination" (Toronto: Ministry of Health and Long-Term Care, Presented at the National Influenza Vaccine Summit, Atlanta, U.S.A., April 2004)

Kwong, J. C., and D. Manuel, "Using OHIP Physician Billing Claims to Ascertain Individual Influenza Vaccination Status." *Vaccine*. 25 (2007), 1270-1274.

Kwong J., T. Stukel, J. Lim, and A. McGeer, R. Upshur, H. Johansen, C. Sambell, W. Thompson, D. Thiruchelvam, F. Marra, L. Svenson, D. Manuel, "The effect of universal influenza immunization on mortality and health care use," *Public Library of Science Medicine,* 5 (2008) e211.

Manzoli, L., F. Schioppa, A. Boccia, and P. Villari, "The efficacy of influenza vaccine for healthy children. A meta-analysis evaluating potential sources of variation in efficacy estimates including study quality," *Pediatric Infectious Disease Journal*, 26 (2007) 97–106.

Miguel, E. and M. Kremer, "Worms: Identifying Impacts on Education and Health in the Presence of Treatment Externalities," *Econometrica,* 72 (2004), 159-217.

Ministry of Health and Long Term Care, "Ontario invests $38 million to ease emergency room pressures with universal vaccination program" *Government of Ontario Press Releases*. July 25 (2000).

Mullahy, John, "It'll only hurt a second? Microeconomic determinants of who gets flu shots," *Health Economics*, 8 (1999), 9-24.

Nichol, Kristin, "Cost-Benefit Analysis of a Strategy to Vaccinate Healthy Working Adults Against Influenza," *Archives of Internal Medicine,* 161 (2001), 749-759.

Nichol, Kristin, "The efficacy, effectiveness and cost-effectiveness of inactivated influenza virus vaccines," *Vaccine,* 21 (2003), 1769-1775.

Nichol, Kristin, "Efficacy and effectiveness of influenza vaccination," *Vaccine,* 26 (2008), D17-D22.

Philipson, Tomas, 2000a. "Economic Epidemiology and Infectious Disease." In *Handbook of Health Economics*, A. J. Culyer and J. P. Newhouse, ed. (San Diego CA: Elsevier, 1B, 2000)

Philipson, Tomas, 2000b. "External Treatment Effects and Program Implementation Bias," Working Paper T0250. Cambridge, MA: National Bureau of Economic Research, 2000.

Public Health Agency of Canada, *Canadian Immunization Guide Seventh Edition* (Ottawa: Public Health Agency of Canada 2007)

Public Health Agency of Canada, (Benefits of Vaccines: http://www.phac-aspc.gc.ca/publicat/cig-gci/p01-02_e.html, accessed October 25, 2009).

Russell, Margaret, "Influenza Vaccination in Alberta Long Term Care Facilities*," Canadian Medical Association Journal,* 164 (2001), 1423-1427.

Thompson, William W., David K. Shay, Eric Weintraub, Lynnette Brammer, Nancy Cox, Larry J. Anderson, and Keiji Fukuda, "Mortality Associated With Influenza and Respiratory Syncytial Virus in the United States," *Journal of the American Medical Association*, 289 (2003), 179-186.

Thompson, William W., David K. Shay, Eric Weintraub, Lynnette Brammer, Carolyn B. Bridges, Nancy J. Cox, and Keiji Fukuda, "Influenza-Associated Hospitalizations in the United States," *Journal of the American Medical Association*, 292 (2004), 1333-1340.

Wooldridge, Jeffrey, Econometric Analysis of Cross Section and Panel Data (Cambridge, MA: MIT Press, 2002).

World Health Organization, *Influenza: report by the secretariat to the 56th World Health Assembly*, (Geneva, Switzerland: World Health Organization, A56/23, 2003)

Zhang, Gang, Dany Shoham, David Gilichinsky, Sergei Davydov, John D. Castello, and Scott O. Rogers, "Evidence of Influenza A Virus RNA in Siberian Lake Ice," *Journal of Virology,* 80 (2006), 12229-12235.

TABLE I

Summary of Data Sources

Variables	Data source	Time period	Frequency
Vaccination status	Statistics Canada: NPHS Cycle 2, CCHS Cycles 1.1, 2.1, 3.1***	1996-2006 (with gaps)	yearly
In bed due to illness	Statistics Canada: NPHS Cycles 1 - 3, CCHS Cycles 1.1, 2.1, 3.1	1994-2006 (with gaps)	bi-weekly
Over the counter cold/ flu medicines	Statistics Canada: NPHS Cycles 1 - 6	1994-2006 (with gaps)	monthly
Laboratory confirmed flu	Public Health Agency of Canada	1995-2006	weekly
Strain isolation of flu subtypes	Public Health Agency of Canada	1995-2006	yearly
Antigenic match: flu shot to strains of flu	Canadian Communicable Disease Report*	1995-2006	yearly
Hospitalizations	Canadian Institute for Health Information: Hospital Morbidity Database**	1996-2006	weekly
Worker absence	Statistics Canada: Labor Force Survey	1995-2006	monthly
Public health expenditure	Canadian Institute for Health Information: National Health Expenditure Database	1996-2006	yearly
Hospital bed counts	Canadian Institute for Health Information: Canadian MIS Database	1999-2006	yearly
Population counts	Statistics Canada: Population and Demography	1996-2006	yearly
Population in care facilities	Statistics Canada: Residential Care Facilities Survey	1996-2006	yearly

* Confirmed using data from the Center for Disease Control in the U.S. and the World Health Organization

** Quebec and rural Manitoba not included

*** NPHS = National Population Health Survey and CCHS = Canadian Community Health Survey

TABLE II

Flu Vaccination Rates by Selected Characteristic

	Ontario			Other regions			Relative change	Std. error
	Pre	Post	Change	Pre	Post	Change		
Panel A: Vaccination by age group								
Full Sample	0.208	0.417	0.209	0.170	0.291	0.122	0.087 ***	0.023
Under 65	0.120	0.333	0.213	0.092	0.197	0.105	0.108 ***	0.005
65 and over	0.609	0.737	0.128	0.521	0.645	0.124	0.004	0.029
Panel B: Vaccination under 65 by demographic characteristic and health status								
Male	0.111	0.292	0.181	0.076	0.169	0.093	0.088 ***	0.021
Female	0.128	0.369	0.241	0.107	0.222	0.115	0.127 ***	0.023
No secondary graduation	0.167	0.338	0.172	0.103	0.168	0.065	0.106 ***	0.025
Secondary graduation	0.101	0.308	0.207	0.075	0.162	0.087	0.120 ***	0.019
Some post-secondary	0.100	0.290	0.190	0.093	0.171	0.079	0.111 ***	0.021
Post-secondary graduation	0.113	0.346	0.233	0.097	0.231	0.135	0.098 ***	0.024
Income <$30K	0.130	0.350	0.220	0.101	0.186	0.085	0.135 ***	0.021
Income $30K-$50K	0.118	0.336	0.218	0.087	0.192	0.105	0.113 ***	0.022
Income >$50K	0.109	0.324	0.215	0.085	0.205	0.120	0.095 ***	0.024
Full time worker	0.096	0.301	0.205	0.079	0.187	0.108	0.097 ***	0.021
Part time worker	0.112	0.342	0.230	0.087	0.188	0.101	0.129 ***	0.021
Not in labor force	0.187	0.448	0.262	0.149	0.263	0.114	0.147 ***	0.023
No chronic conditions	0.085	0.267	0.182	0.061	0.143	0.082	0.100 ***	0.020
At least one condition	0.237	0.479	0.241	0.201	0.326	0.126	0.116 ***	0.028
SRH: excellent/very good	0.095	0.302	0.207	0.072	0.174	0.102	0.105 ***	0.023
SRH: good	0.138	0.356	0.217	0.103	0.209	0.106	0.112 ***	0.021
SRH: fair/poor	0.256	0.455	0.199	0.213	0.304	0.091	0.107 ***	0.024
Full sample obs.	40,012	119,294	159,306	31,824	144,774	176,598	335,904	

Statistics are calculated using the master files of the NPHS cycle 2 and CCHS cycles 1.1, 2.1, 3.1. Pre and post denote before and after October 2000. Vaccination rates for each sub-group are shown pre-post program in Ontario and other regions in Canada (excluding Quebec, rural Manitoba, and the Territoires). The relative change in vaccination for Ontario versus other regions is displayed in the second last column with robust standard errors clustered by province shown to the right of the estimate. Chronic conditions include Asthma, Heart Disease, High Blood Pressure, Diabetes, Cancer, Emphysema/Chronic Bronchitis. SRH stands for self-rated health. * p<0.10, ** p<0.05, *** p<0.001.

TABLE III

Summary Statistics

	Flu admissions		Pneumonia admissions		Non-respiratory admissions		Illness work absence	
	Mismatch	Match	Mismatch	Match	Mismatch	Match	Mismatch	Match
Panel A: Weekly incidence rate								
All weeks	0.524	0.450	9.451	9.339	60.237	62.387	0.0262	0.0221
	(0.015)	(0.012)	(0.046)	(0.052)	(0.175)	(0.208)	(0.0001)	(0.0001)
Season start to peak	2.280	1.572	13.359	13.204	58.354	62.818	0.0287	0.0238
	(0.102)	(0.073)	(0.187)	(0.207)	(0.517)	(0.656)	(0.0003)	(0.0003)
Season end	1.177	0.760	11.204	10.353	58.158	63.089	0.0289	0.0234
	(0.081)	(0.044)	(0.210)	(0.161)	(0.730)	(0.598)	(0.0003)	(0.0004)
Off-season weeks	0.245	0.266	8.805	8.715	60.647	62.243	0.0255	0.0217
	(0.006)	(0.007)	(0.043)	(0.050)	(0.192)	(0.236)	(0.0001)	(0.0001)
Post program	0.352	0.300	9.275	9.168	58.221	60.505	0.0299	0.0246
	(0.011)	(0.012)	(0.054)	(0.067)	(0.210)	(0.295)	(0.0001)	(0.0002)
Pre program	0.823	0.599	9.756	9.509	63.731	64.269	0.0193	0.0193
	(0.036)	(0.020)	(0.085)	(0.079)	(0.299)	(0.290)	(0.0001)	(0.0001)
Ontario	0.367	0.240	8.812	8.848	55.388	57.488	0.0284	0.0234
	(0.019)	(0.012)	(0.073)	(0.081)	(0.291)	(0.333)	(0.0002)	(0.0002)
Not Ontario	0.585	0.531	9.699	9.530	62.123	64.293	0.0251	0.0215
	(0.020)	(0.015)	(0.057)	(0.065)	(0.209)	(0.252)	(0.0001)	(0.0001)
Full sample size	64,575	46,350	64,575	46,350	64,575	46,350	2,851,884	1,963,596
Panel B: Individual characteristics								
Age	52.592	48.891	62.002	60.680	58.559	58.040	48.088	47.832
	(0.202)	(0.252)	(0.038)	(0.043)	(0.012)	(0.013)	(0.036)	(0.048)
Fraction male	0.446	0.431	0.532	0.538	0.519	0.518	0.319	0.330
	(0.003)	(0.004)	(0.001)	(0.001)	(0.000)	(0.000)	(0.002)	(0.002)
Duration	7.193	6.345	9.919	10.301	8.751	8.948	9.073	9.174
	(0.095)	(0.156)	(0.031)	(0.039)	(0.009)	(0.011)	(0.037)	(0.049)
Wait time in ER	4.878	4.969	4.774	4.823	4.244	4.654		
	(0.062)	(0.139)	(0.011)	(0.019)	(0.005)	(0.008)		
Fraction with death	0.038	0.022	0.139	0.142	0.043	0.045		
	(0.001)	(0.001)	(0.000)	(0.001)	(0.000)	(0.000)		
Care home resident	0.064	0.047	0.098	0.100	0.037	0.039		
	(0.002)	(0.002)	(0.000)	(0.000)	(0.000)	(0.000)		
Urban postal code	0.786	0.756	0.864	0.860	0.870	0.866		
	(0.003)	(0.003)	(0.000)	(0.001)	(0.000)	(0.000)		
Sample size	30,516	16,095	552,272	435,438	3,504,633	2,958,813	74,586	43,308
Source data:	HMDB; author's calculation						LFS; author's calculation	

Variable means displayed with standard error of the mean given in parentheses below. Hospitalization admission rates are calculated per 100,000 per week for different age groups across city-regions using data from the HMDB. Work absences are short term work absences for reasons of personal illness during a reference week and these data are collected from the LFS. Season periods are defined according to flu surveillance data from the PHAC. Non respiratory diagnoses include all hospitalizations that do not list a respiratory diagnosis as an MRD (most responsible diagnosis) or as a contributing diagnosis. Statistics are weighted by population cell size (HMDB) or survey weights (LFS). In Panel B, average characteristics of each illness incident are given. Average duration for hospital admissions is in days and average duration for work absences is in hours. Wait time in ER before admission is measured in hours.

TABLE IV

The Flu Immunization Campaign, Vaccine Match and Health Outcomes

Dependant Variables:	(1) Average duration	(2) Flu admissions	(3) Pneumonia admissions	(4) Illness work absence
		Panel A: Basic Results		
Season start to peak	5.3 weeks	-2.829 **	-4.693 *	-0.0050 *
		(0.750)	(2.461)	(0.0026)
		3.053	15.716	0.0267
Season end	4.1 weeks	-2.421 **	-4.917 **	-0.0079 *
		(0.661)	(1.615)	(0.0042)
		2.996	12.454	0.0276
Off season	42.6 weeks	-0.006	-0.336	-0.0009
		(0.032)	(0.204)	(0.0010)
		0.344	8.750	0.0249
Panel B: Account for behavioral response to match by controlling for circulation of other infectious disease				
Season start to peak		-2.835 **	-4.726 *	-0.0060 **
		(0.774)	(2.351)	(0.0023)
Season end		-2.440 **	-4.760 **	-0.0078 *
		(0.694)	(1.676)	(0.0042)
Off season		-0.009	-0.307	-0.0009
		(0.032)	(0.221)	(0.0010)

This table reports estimates of the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario. Table columns report results for different health outcomes and rows report results for three different periods during the year: the flu season start to peak, the flu season end, and the flu off-season. Column (1) shows the average duration of each different period. Each estimate shown in Column (2) to (4) is a separate regression. Robust standard errors are given in parentheses and are allowed to be correlated within province clusters (* $p<0.10$, ** $p<0.05$, *** $p<0.001$). The baseline mean of the dependent variable is given below the standard error of each estimate. The dependent variables are listed in the table headings. Flu admissions denote hospital admissions per 100,000, per week where flu was either the MRD (most responsible diagnosis) or other contributing diagnosis and pneumonia admissions denote hospital admissions per 100,000, per week where pneumonia was either the MRD or other contributing diagnosis (source data from the HMDB). Work absences are short term work absences for reasons of personal illness during a reference week (source data from the LFS). Regressions are weighted by cell size (admissions) or survey weight (absences). All regressions include the level effect of the match rate, month, age, season and city-region fixed effects as well as interactions of PostXMatch, PostXOntario, and OntarioXMatch. Regressions in columns (2) and (3) also control for public health expenditures on health care (hospitals, capital investments, physicians and other health professionals), diagnosis specific coding classifications changes (ICD10 versus ICD9) and the proportion of observed strains of each of H1N1, H3N3 and B in each season. Regressions in column (4) control for the same factors and for education, marital status, sex, occupation and union status. Results in Panel B control for surveillance rates of other infectious respiratory disease (respiratory syncytial virus, parainfluenza, and adenovirus).

TABLE V

The Flu Immunization Campaign, Vaccine Match and Time Lost to Illness

Dependant Variables:	(1) Flu admissions	(2) Pneumonia admissions	(3) Illness work absence
Death			
Flu season	-0.121 **	-0.560 **	
	(0.027)	(0.127)	
	0.122	1.459	
Off season	0.002	-0.042	
	(0.003)	(0.054)	
	0.006	1.098	
Wait time in ER			
Flu season	-0.161	-0.136	
	(0.240)	(0.588)	
	3.774	3.539	
Off season	0.000	-0.018	
	(0.026)	(0.029)	
	3.291	3.035	
Average duration			
Flu season	-15.365 **	-39.477 **	-0.0383 *
	(3.596)	(14.378)	(0.0189)
	23.232	124.024	0.1780
Off season	0.765	-3.366	0.0080
	(0.515)	(4.185)	(0.0076)
	2.314	94.444	0.1550
Duration per illness			
Flu season	3.769	1.751	0.7634
	(1.473)	(1.321)	(1.1668)
	7.674	9.562	8.9060
Off season	-0.966	-0.041	-0.1013
	(1.636)	(0.461)	(0.1838)
	6.596	10.519	9.2460

This table reports estimates of the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario. Table columns report results for different health outcomes and rows report results for death and different time factors associated with illness. Time spent ill is measured in days in the case of hospital admissions and hours in the case of work absences. Each estimate is a separate regression. Robust standard errors are given in parentheses and are allowed to be correlated within province clusters (* $p<0.10$, ** $p<0.05$, *** $p<0.001$). The baseline mean of the dependent variable is given below the standard error of each estimate. The dependent variables are listed in the table headings. Flu admissions denote hospital admissions per 100,000, per week where flu was either the MRD (most responsible diagnosis) or other contributing diagnosis and pneumonia admissions denote hospital admissions per 100,000, per week where pneumonia was either the MRD or other contributing diagnosis (source data from the HMDB). Work absences are short term work absences for reasons of personal illness during a reference week (source data from the LFS). Regressions are weighted by cell size (admissions) or survey weight (absences). All regressions include the level effect of the match rate, month, age, season and city-region fixed effects as well as interactions of PostXMatch, PostXOntario, and OntarioXMatch. Regressions in columns (1) and (2) also control for public health expenditures on health care (hospitals, capital investments, physicians and other health professionals), diagnosis specific coding classifications changes (ICD10 versus ICD9), the proportion of observed strains of each of H1N1, H3N3 and B in each season, and surveillance rates of other infectious respiratory disease (respiratory syncytial virus, parainfluenza, and adenovirus). Regressions in column (3) control for the same factors and for education, marital status, sex, occupation and union status.

TABLE VI

Results for Sub-groups During Flu Season

	(1) Flu admissions	(2) Pneumonia admissions	(3) Illness work absence	(4) Vaccination
Less than 5 years	-6.939 **	-14.012 **		
	(1.796)	(4.674)		
	6.155	25.443		
5 to 11 years	-1.180 **	-1.228 *		
	(0.482)	(0.642)		
	1.658	3.941		
12 to 19 years[1]	-0.450 *	-1.366 **	-0.0090	0.093 ***
	(0.196)	(0.508)	(0.0163)	(0.017)
	0.980	1.598	0.0250	0.167
20 to 24 years	-0.214	-1.073	-0.0179 **	0.085 ***
	(0.154)	(0.644)	(0.0068)	(0.011)
	0.823	1.680	0.0330	0.065
25 to 49 years	-0.513	-1.768 **	-0.0054 **	0.092 ***
	(0.297)	(0.389)	(0.0024)	(0.010)
	1.031	2.930	0.0320	0.076
50 to 64 years	-1.925 **	-4.380 **	-0.0076 ***	0.129 ***
	(0.565)	(0.936)	(0.0015)	(0.011)
	2.576	9.751	0.0140	0.256
65 or more years	-11.969 **	-21.283 **	-0.0036	0.004
	(3.577)	(6.794)	(0.0066)	(0.009)
	14.765	53.718	0.0090	0.609
Nursing home resident	-57.648	-157.831		
	(37.779)	(104.272)		
	62.008	137.309		
All ages	-2.006 **	-5.140 **	-0.0059 **	0.087 ***
	(0.546)	(1.138)	(0.0022)	-0.023
	3.016	10.914	0.0274	0.191

[1] This age group is 15 to 19 for work absences.

See notes for Table IV. Columns (1) to (3) report estimates of the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario for different sub-groups. Column (4) reports estimates of the interaction between a post October 2000 dummy and a dummy for city-regions in Ontario for the outcome of vaccination. Each estimate is a separate regression for the sub-group indicated. Regressions are weighted by cell population or survey weight. Robust standard errors are given in parentheses and are allowed to be correlated within province clusters (* p<0.10, ** p<0.05, *** p<0.001). The baseline mean of the dependent variable is given below the standard error of each estimate. The dependent variables are listed in the table headings.

TABLE VII

Results for Other Health Outcomes During Flu Season

Dependent variable:	(1) Weekly laboratory confirmed flu rate	(2) Cold or flu medicine in last month	(3) In bed due to illness in last two weeks	(4) Work absence due to illness in last week
All	-0.068	-0.102*	-0.030*	
	(0.064)	(0.052)	(0.017)	
Baseline mean	0.202	0.769	0.097	
Observations	1,197	18,981	72,974	
Workers		-0.105	-0.005	-0.006**
		(0.066)	(0.016)	(0.002)
Baseline mean		0.737	0.097	0.027
Observations		10,143	45,220	919,830
25 and younger		-0.105	-0.112***	
		(0.073)	(0.027)	
Baseline mean		0.841	0.130	
Observations		6,525	12,629	
25 to 64 years		-0.040	-0.010	
		(0.079)	(0.020)	
Baseline mean		0.740	0.100	
Observations		9,728	46,057	
65 and older		-0.368**	-0.055**	
		(0.156)	(0.018)	
Baseline mean		0.697	0.061	
Observations		2,728	14,288	
Data Source:	PHAC	NPHS:1-6	CCHS:1.1-3.1	LFS 1995-2006

See notes for Table IV. This table reports estimates of the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario for weeks during flu season. Table columns report results for different dependent variables and rows report results for different sub-groups. For laboratory confirmed flu rate (column [1]), regressions control for interactions of PostXMatch, PostXOntario, OntarioXMatch, season, province, age, and month effects, in addition to other base specification controls. Regressions for outcomes in columns (2) to (4) include interactions of PostXMatch, PostXOntario, OntarioXMatch, season, city-region, age, and month effects, in addition to other base specification controls. Each estimate is a separate regression. Regressions are weighted by cell population or survey weight. Robust standard errors are given in parentheses and are allowed to be correlated within province clusters (* p<0.10, ** p<0.05, *** p<0.001). The baseline mean of the dependent variable is given below the standard error of each estimate and sample size is given below the mean.

TABLE VIII

Results for Other Disease Outcomes

Dependent variable:	(1) Respiratory disease	(2) Heart disease	(3) Cancer	(4) Mental disease	(5) Disease of the nervous system
	Panel A: Admissions with co-diagnosis of respiratory disease				
Flu season	-9.579**	-2.756**	0.044	-1.605***	-0.212**
	(2.100)	(0.737)	(0.196)	(0.317)	(0.078)
	32.244	12.643	2.790	4.308	0.645
Off season	-1.796	-0.553	-0.021	-0.338	-0.030
	(1.354)	(0.349)	(0.124)	(0.216)	(0.020)
	24.847	10.208	2.626	3.500	0.500
	Panel B: Admissions without diagnosis of respiratory disease				
Flu season		0.280	0.474	-0.084	-0.077
		(1.185)	(0.324)	(0.543)	(0.087)
		25.342	9.264	13.347	1.045
Off season		0.725	0.209	-0.074	-0.077
		(0.457)	(0.135)	(0.325)	(0.057)
		25.469	9.627	13.293	1.060

See notes for Table IV. Columns (1) to (5) report estimates of the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario. Each estimate is a separate regression for the dependent variable and the time period indicated. Panel A includes admissions with a contributory diagnosis of respiratory disease and Panel B includes admissions without a contributory respiratory diagnosis. Regressions are weighted by cell population. Robust standard errors are given in parentheses and are allowed to be correlated within province clusters (* p<0.10, ** p<0.05, *** p<0.001). The baseline mean of the dependent variable is given below the standard error of each estimate.

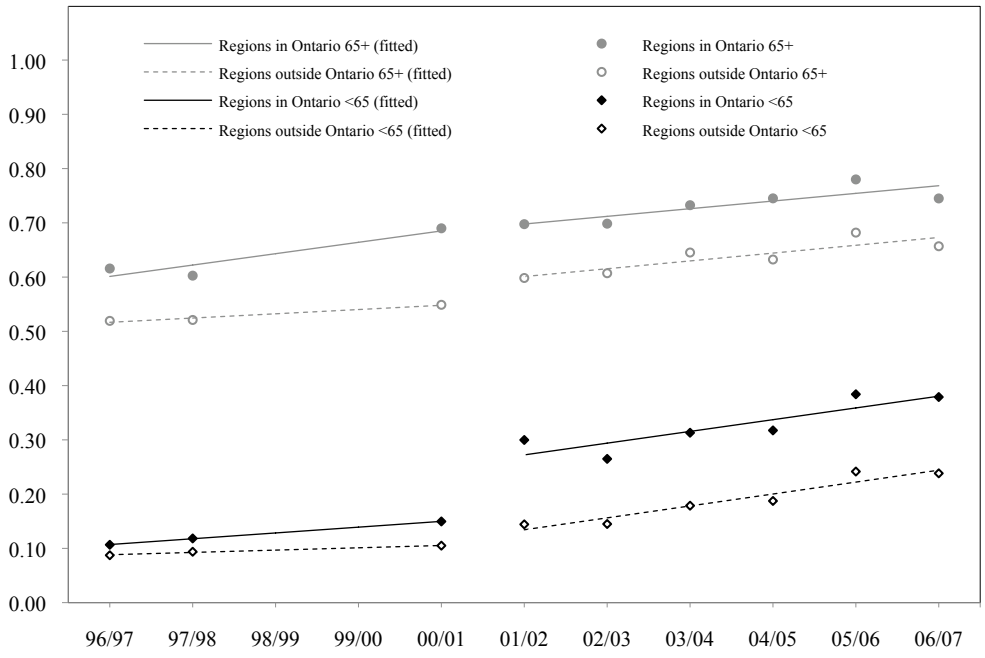

FIGURE I

Flu Vaccination for Flu Seasons 1996/1997 to 2006/2007

The y axis plots the average vaccination for each flu season-year based on master file data from the National Population Health Survey Cycle 2 and the Canadian Community Health Survey Cycles 1.1, 2.1, 3.1. Vaccination rates are given by age group for city-regions inside and outside Ontario. Solid lines show the fitted linear prediction for each age and region grouping.

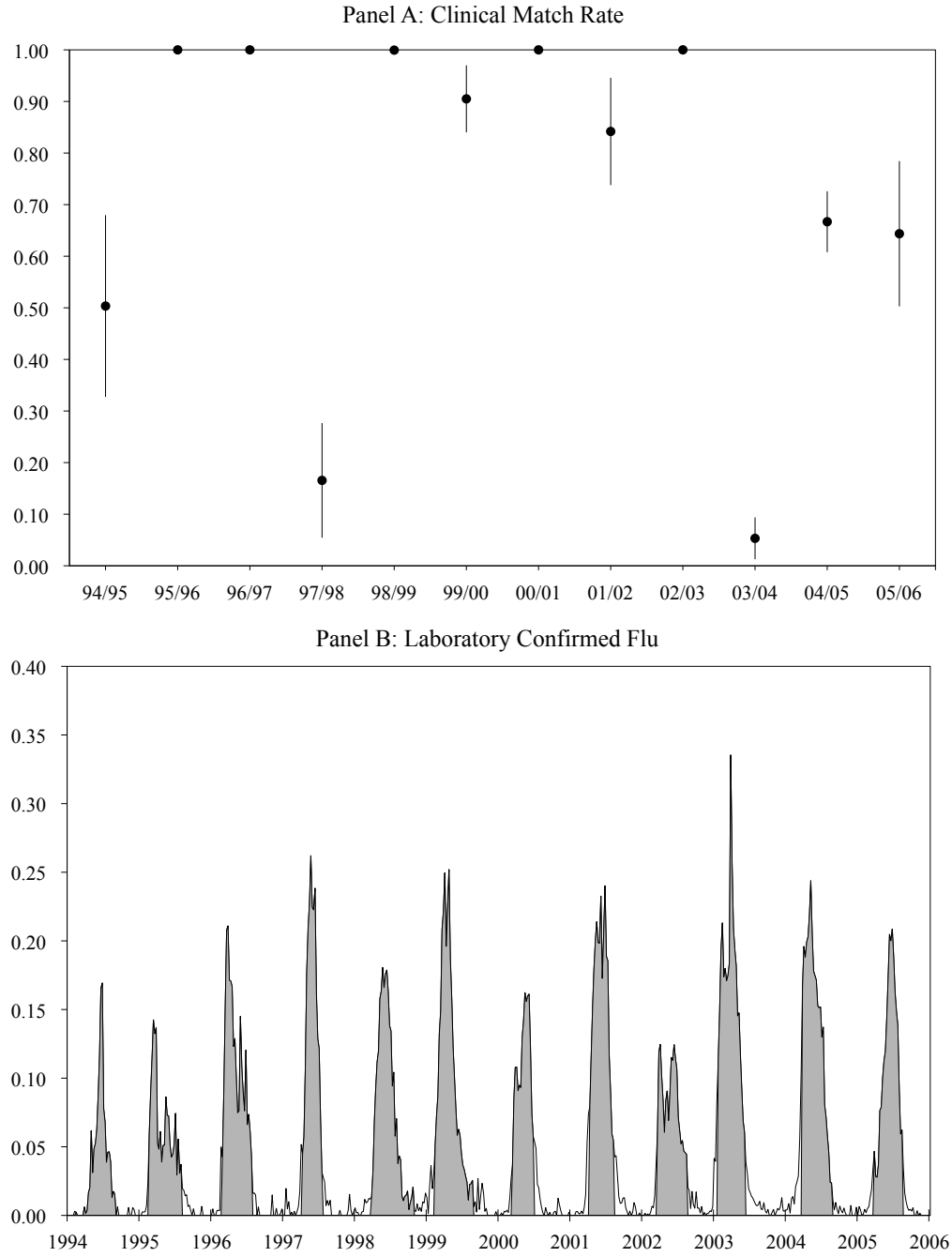

FIGURE II

Clinical Match Rate and Infectious Disease Surveillance

In Panel A, the average clinical match rate is shown for each season with error bars indicating two standard deviations from the mean (variaton is between province). The clinical match rate is calculated from the yearly Canadian Communicable Disease Report and strain isolation data from the PHAC. Panel B shows the average weekly fraction of infectious disease tests that are positive for flu. These data are collected through the disease surveillance program of the PHAC. For each year, week 40 (roughly the first week in October) is marked by a tick on the x axis. The period of high flu season is indicated by the shaded area and off-season is indicated by the un-shaded area.

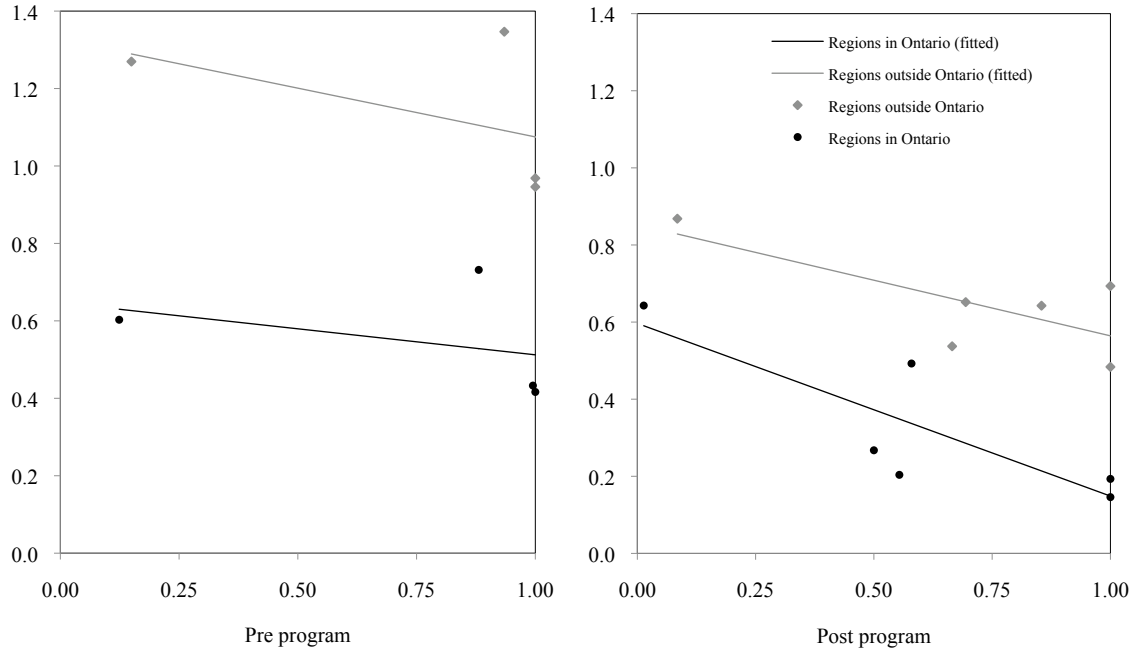

FIGURE III

Flu Hospital Admissions and the Clinical Vaccine Match

The y-axis plots the seasonal average flu hospital admission rate (per 100,000, per week) and the x-axis plots the seasonal clinical match rate for the flu vaccine. Data are calculated using the HMDB (for hospital admissions) and the PHAC and CCDR (for the match rate). Each point represents the year specific average flu admission rate and the corresponding average match rate for city-regions in and outside of Ontario. The lines are fitted values from regressions of the flu admission rate on the clinical match rate for each combination of pre-post, Ontario-not Ontario.

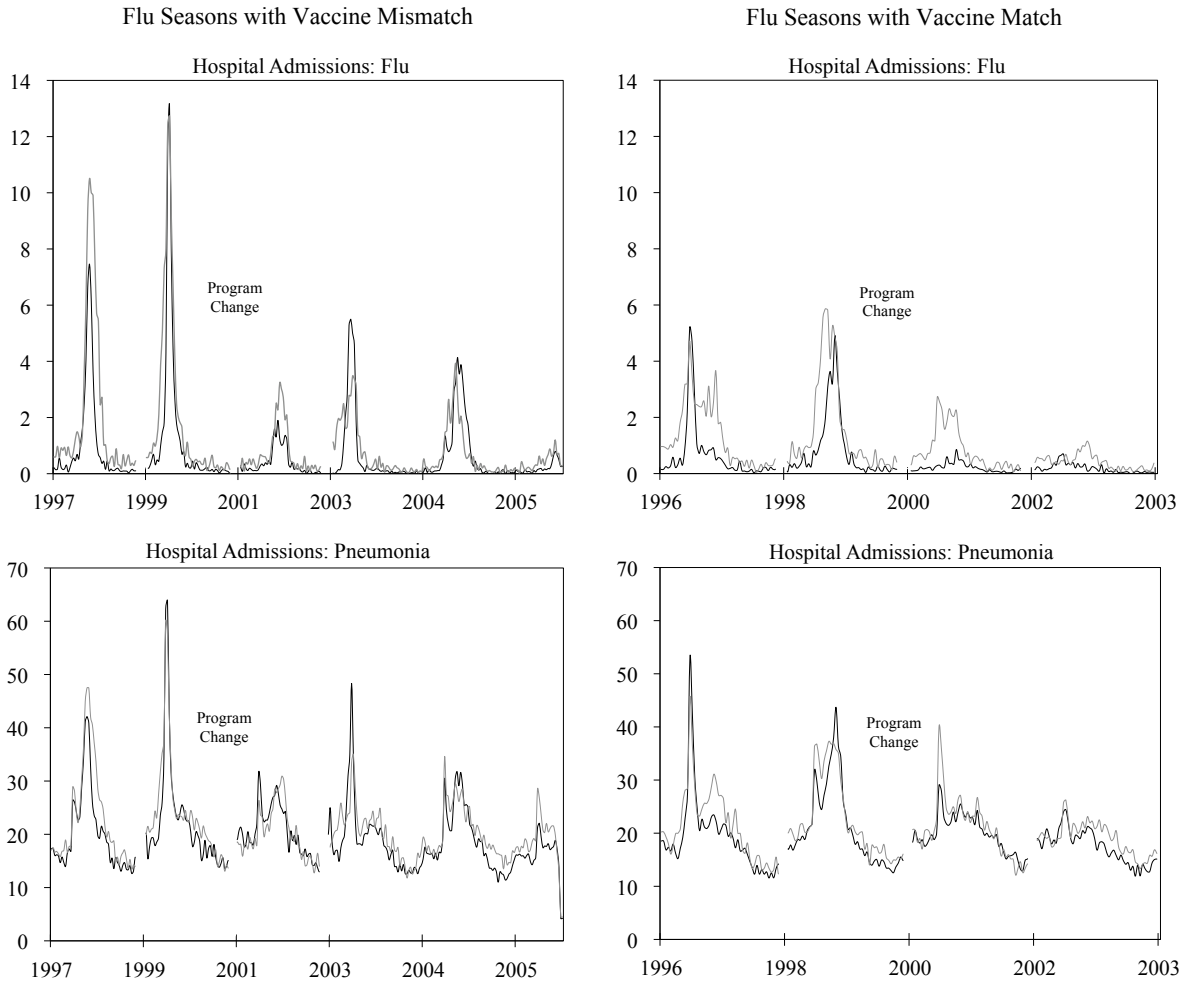

FIGURE IV

Weekly Hospital Admission Rate by Season and Vaccine Match

The top two graphs plot the average weekly hospital admission rate per 100,000 for flu and the bottom two plot the average weekly hospital admission rate for pneumonia (adjusted for ICD9 to ICD10 coding changes). Data are calculated using the HMDB. The dark line is the weekly average for city-regions in Ontario and the light line is the weekly average for city-regions in other provinces. The left side of the figure plots weekly rates for flu seasons with a mismatch in the flu vaccine and the right side of the figure plots weekly rates for seasons without a mismatch in the flu vaccine. For each year, week 40 (roughly the first week in October) is marked by a tick on the x axis. The immunization program in Ontario came into effect in week 40 of year 2000.

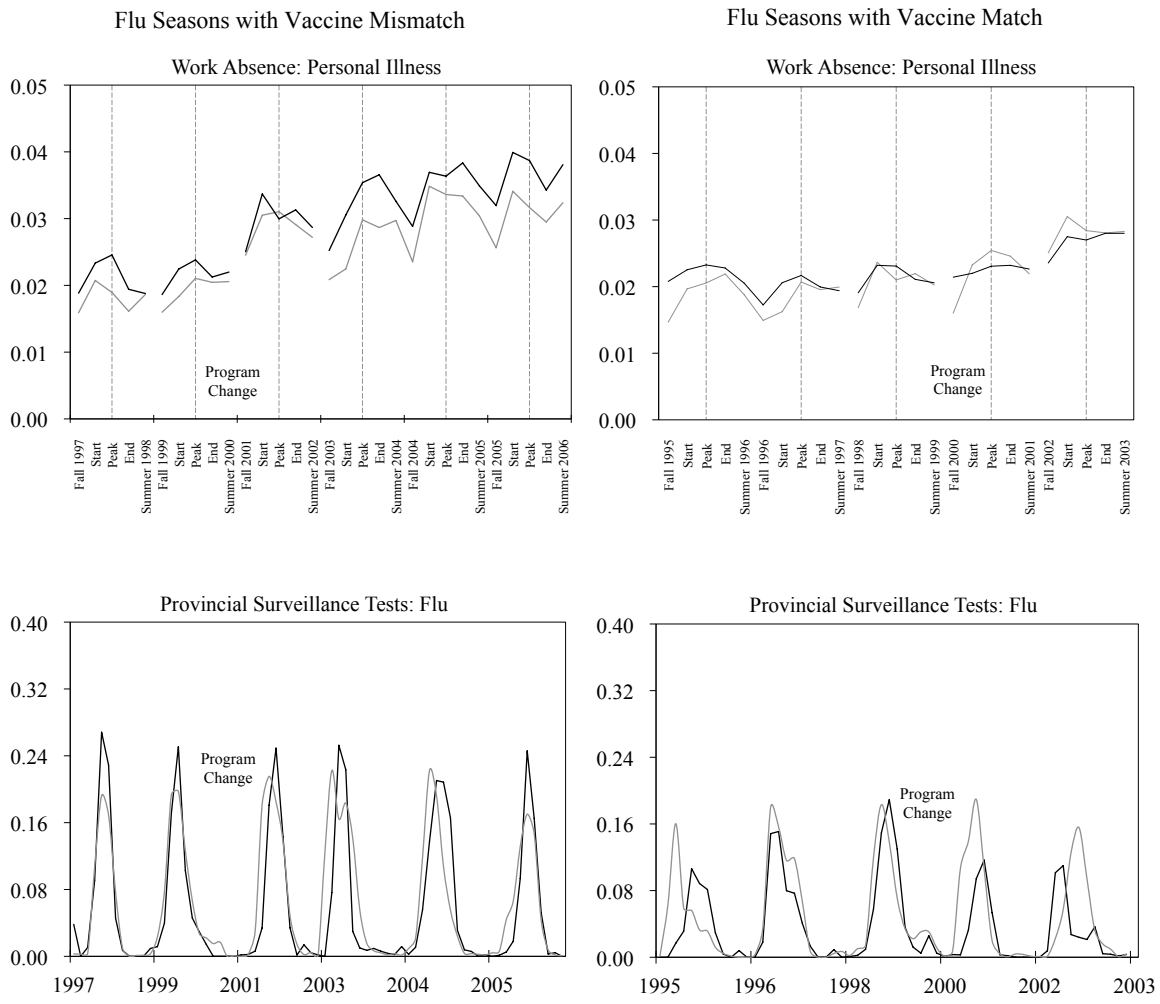

FIGURE V

Work Absenteeism and Flu Surveillance by Season and Vaccine Match

The top two graphs plot the average work absence rate for reasons of personal illness over months occurring in five different periods during the flu season: the fall (pre) season, season start, season peak, season end, and the summer (post) season. The dark line is the period average for workers in Ontario and the light line is the period average for workers in other provinces. Data are from successive months of the LFS. The y axis of the bottom two graphs plot the fraction of weekly surveillance tests that are positive for flu. These data are from the PHAC surveillance program. The dark line is the weekly flu surveillance rate in Ontario and the light line is the average weekly flu surveillance rate in the other provinces. For each year, week 40 (roughly the first week in October) is marked by a tick on the x axis. The left side of the figure plots work absence and flu surveillance rates for flu seasons with a mismatch in the flu vaccine and the right side of the figure plots weekly rates for seasons without a mismatch in the flu vaccine. The immunization program in Ontario came into effect in week 40 of year 2000.

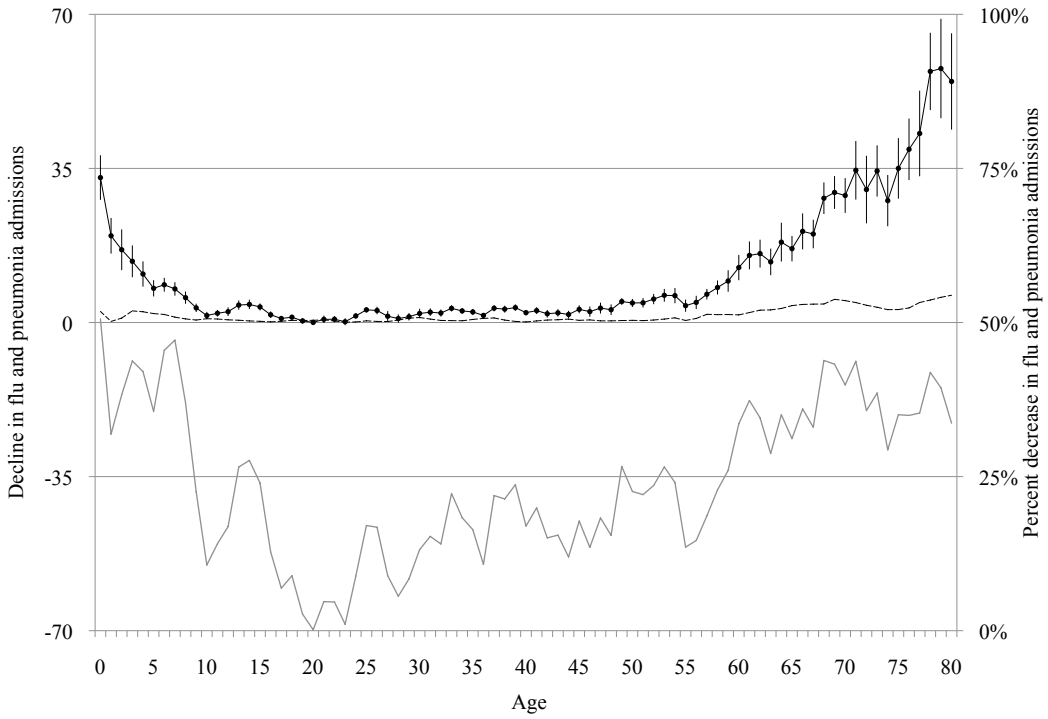

FIGURE VI

Vaccine Program Match Effect on Combined Flu and Pneumonia Admissions by Age Group

The y-axis on the left plots the age specific coefficients on the program match effect (the interaction of the clinical match rate, a post October 2000 dummy and a dummy for city-regions in Ontario) for flu and pneumonia admissions combined (rate per 100,000, per week). The dark solid line indicates the decline in admissions for each age group during the flu season with confidence intervals indicated by error bars for each coefficient estimate. For comparison, the dotted line shows the program match effect for each age group during the off-season period. The y-axis on the right shows the decline in admissions as a percent of the baseline admission rate and the light grey line shows the percent decline from baseline for each age group. Data are calculated using the HMDB.