Predictors of the Timing of Vaccination Uptake
The 2009 Influenza Pandemic (H1N1) in Montreal

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Background: In response to the 2009 H1N1 influenza pandemic, Canada undertook the largest vaccination campaign in its history. The effort mobilized thousands of healthcare workers, cost many hundreds of millions of dollars, and vaccinated more than 40% of the population. Despite the large investment in mass vaccination internationally, little is known about the factors that drive the timing of vaccination uptake.

Purpose: Data from 2009 were used to investigate three potential determinants of vaccination uptake in Montreal, Canada.

Methods: Poisson regression was used to analyze daily vaccination before and after a telephone intervention targeting households in 12 of the city's 29 health neighborhoods. The effect of an eligibility strategy based on risk groups, and of weather, on uptake was then estimated. Data were analyzed in 2013.

Results: Considerable variation in daily mass vaccination was observed, with the peak day (30,204 individuals) accounting for nearly five times the uptake of the slowest day (6298 individuals). No evidence was found that the telephone intervention led to a significant increase in vaccination. Daily vaccination was associated significantly with weather conditions, including mean temperature (relative risk [RR]=1.28, 95% CI=1.12, 1.46) and heavy precipitation (RR=0.63, 95% CI=0.45, 0.89), even after accounting for changes to eligibility, which also were associated with increased vaccination.

Conclusions: Considerable temporal variation in uptake can occur during mass vaccination efforts. Targeted interventions to increase vaccination should be evaluated further, as a large intervention had no observable effect. Mass vaccination campaigns should, however, attempt to optimize priority sequences and account for weather when estimating vaccine demand.
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Background

Although a recent economic analysis found that the H1N1 vaccination program was cost effective in at least one Canadian jurisdiction,[1] the hundreds of millions of dollars spent on the effort led to controversy and questions over the allocation of resources.[2] Moreover, simulation studies suggest that the timing of vaccination delivery can affect vaccination uptake and the spread of influenza.[3] Consequently, delays in delivery may detract from the benefits of prioritizing high-risk populations, a strategy that was employed in Canada and elsewhere.[4]

The 2009 provincial H1N1 immunization campaigns mobilized thousands of healthcare workers across Canada and lasted several weeks. Media reports suggested that uptake in Montreal was not constant over the campaign, with demand for vaccination varying substantially both over the 44 days of the campaign and geographically throughout the region.[5,6] Temporal variation in uptake during mass vaccination campaigns has received little attention in the literature. It is reasonable to expect, however, that the timing of uptake includes two components: (1) a secular trend, driven by relatively

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long-term changes to demand for vaccination at the population level, such as week-to-week perceptions of vaccine safety; (2) a shorter-term variation, driven by factors that change more rapidly among individuals considering vaccination, such as day-to-day perceptions of accessibility.

The tension between fear of infection and fear of vaccine side effects can lead to a "wait-and-see" behavior, where a considerable portion of the population delays vaccination while observing the effects on early adopters and the reports of disease severity.[7] Moreover, the success of vaccination efforts is, to a degree, self-limiting; effective efforts prevent the spread of infection, thereby reducing morbidity and mortality, which in turn decreases fear among the general population and decreases perceived need for vaccination among the unvaccinated. Thus one would expect that uptake in vaccination campaigns will initially increase and then decrease over the course of an epidemic. Overlaid on that longer-term pattern, short-term uptake may vary periodically (e.g., due to a day-of-week effect) or irregularly (e.g., due to changes to vaccination policy or weather).

An understanding of the factors that influence the timing of vaccine uptake is necessary to enable the development of interventions that can increase final vaccination coverage while reducing the total cost of the vaccination effort. However, little is known about the determinants of the temporal dynamics of mass vaccination. Work on vaccination timing and promotion largely precedes the 2009 H1N1 pandemic. Post-pandemic studies examining the wide range of local vaccination efforts have been mostly limited to surveys assessing the role of administrative strategies, logistic challenges, and perceived deterrents of vaccination.[8–12] The aim of the current study was to examine the association between daily rates of vaccination and clinic capacity, public health interventions, risk-group eligibility, and weather conditions.

Methods

Quebec Vaccination Campaign

The IRB at McGill University approved this study. Data were analyzed in 2013. The provincial vaccination strategy was to maximize coverage among those at high risk of serious outcomes by prioritizing subpopulations considered particularly vulnerable, such as the chronically ill. Prioritization was intended to reduce morbidity and mortality and to maximize the effects of the available supply of vaccine, which was limited in the first few weeks. Public health departments employed a multi-pronged strategy to optimize vaccination. Healthcare workers and hospital inpatients were vaccinated first. Temporary mass vaccination centers (MVCs) were organized to vaccinate the rest of the population efficiently. The provincial public health agency implemented a priority vaccination schedule at all MVCs, whereby specific high-risk subpopulations were sequentially eligible for vaccination before the general population. The eligibility groups and periods were set by the provincial public health director and the minister of emergency management; the Montreal public health director was allowed to adjust the start dates by 1 or 2 days according to the demand at the MVC.

The Montreal Public Health Department (Direction de Santé Publique, DSP) used TV, radio, newspapers, and governmental websites to keep the public informed of eligibility dates and the location of MVCs. On the Island of Montreal, MVCs were reserved for island residents; otherwise, access was not limited geographically. Public health personnel collected data on each person vaccinated using standard forms, and the data were subsequently entered into an electronic registry. At the end of the mass vaccination period, coverage was estimated to be 57% for the province of Quebec, and 50% for the Island of Montreal.[13] Although higher than the national coverage,[14] these rates fell short of the public health target for "herd immunity" (70%).[15]

Telephone Intervention

The DSP monitored vaccination uptake daily and observed that coverage rates were lower than expected in some neighborhoods. Toward the end of the mass vaccination period, the DSP implemented a telephone intervention to enhance uptake in these areas. The intervention used automatic-dialing technology to deliver a pre-recorded message from the DSP director urging recipients to get vaccinated. The intervention included three phases of calls. In each phase, an attempt was made to reach all households with home phones in four of the 29 health neighborhoods in Montreal. Intervention neighborhoods were selected based on neighborhood-wide low-coverage estimates.

Data Collection

The National Public Health Institute of Quebec (Institut national de santé publique du Québec) provided vaccination data for the study. These included, for all vaccinated individuals, the age and gender, risk-group status, residential address (converted to census tract to maintain confidentiality), and date and location of vaccination. Demographic and residence information was taken from provincial health records; risk-group status was self-reported at the time of vaccination. Vaccinations outside of Montreal's 18 MVCs and of healthcare workers (who were eligible for vaccination before the opening of the MVCs and were largely vaccinated at their place of work) were removed from the data set. Data on the at-risk population were obtained from the National Census.

The DSP provided data on the telephone intervention, risk-group eligibility, and MVC capacity. Intervention data included dates of the three phases and names of the targeted neighborhoods. Eligibility data included definitions for each risk group and start dates for each eligibility period. Capacity data included the official capacity for each MVC on the dates they were in operation.

Meteorologic data, obtained from the National Climate Data and Information Archive, included, for each day of the study period, mean daily temperature, and total daily snowfall and rainfall.[16]

Table 1. Descriptive statistics of vaccination, MVC capacity, and weather conditions, % unless otherwise noted

	Quarter[a]				
	First	Second	Third	Fourth	Overall
Coverage, cumulative[b]	15.3	28.9	42.7	49.9	49.9
Daily uptake, of unvaccinated (M [SD])	1.2 (0.4)	1.6 (0.5)	2.0 (0.4)	1.2 (0.2)	1.5 (0.5)
Daily MVC capacity (*n*, M [SD])	37,607 (2974)	43,265 (1518)	44,007 (121)	43,964 (97)	42,211 (3149)
Daily MVC use, of capacity (M [SD])	45.9 (15.0)	48.2 (14.1)	47.7 (11.6)	22.5 (4.2)	41.0 (15.9)
Daily temperature, min/max (°C)	1.6/11.5	1.3/7.4	−2.2/5.9	−17.6/−2.2	−17.6/11.5
Heavy rain, days >25 mm	0	0	1	0	1
Heavy snow, days >25 cm	0	0	0	1	1

[a]Quarters: November 5–15; November 16–26; November 27–December 7; December 8–18
[b]Includes all vaccinations (MVC and non-MVC)
MVC, mass vaccination center

Data Analysis

First, descriptive statistics were calculated, and time-series plots were used to compare daily variation of vaccination uptake and potential determinants. Second, Poisson regression was used to analyze the association between daily vaccination counts and the independent variables.

The first set of models compared vaccination before and after the telephone intervention with one model to assess the effectiveness of the three intervention phases. For each model, daily counts of vaccination in the intervention area (census tracts falling within the health neighborhoods targeted by that phase) were compared to counts in non-intervention areas (census tracts falling in the other 17 neighborhoods), by way of an interaction term between area and time period (pre- versus post-intervention).

A significant positive interaction would provide evidence that daily uptake had increased in response to the intervention. The model was fit seven times, varying the length of the "post" period, to test for effects over a range of days after each call. The models included the log of the daily remaining unvaccinated population as an offset term, to account for variation in the size of intervention areas and potential differences in the cumulative effects of uptake.

The second set of models looked at the relationship between daily vaccination counts and changes in eligibility and weather conditions. One model was fit for eligibility, where eligibility was measured as logged days since last change to eligibility. A second model was fit for weather conditions, including daily mean temperature and an indicator variable to account for days of heavy precipitation, defined as a day with >25 mm of rain or >25 cm of snow. A final model included both eligibility and weather variables. All models included the number of elapsed weeks since the opening of the MVC, to account for a possible secular trend in vaccination; the total daily MVC capacity, to account for the ramp-up of vaccination efforts in the first weeks of the campaign; and the daily remaining unvaccinated population (logged) as an offset term. The models included heteroskedastic and autocorrelation consistent (HAC) estimators to estimate the SEs for all regression coefficients.[17] Statistical analysis and plotting were completed using the R language (version 2.13.2), and the package *sandwich* (version 2.2-9) was used to calculate the HAC estimators.

Results

Overall

Confirming reports in the media, the results showed that daily and weekly demand for vaccination varied considerably during the vaccination effort (Table 1). This day-to-day variation would not have been apparent in a cumulative vaccine coverage plot, which is often used to display overall uptake and final level of coverage (Table 1, and Appendix A, available online at www.ajpmonline.org).

The daily uptake at the MVC ranged between 0.6% and 2.2% of remaining unvaccinated population. Uptake showed considerable variation in the first half of the campaign, peaking on November 25 and decreasing more or less smoothly until the mass vaccination effort was terminated, on December 18, by decision of the provincial minister of health based on the trend of overall demand. Compared to individuals vaccinated at MVCs, individuals vaccinated outside of MVCs were older (aged ≥65 years: 32.2% vs 17.8%) and more likely to be female (62.8% vs 52.9%), perhaps because of their considerably higher proportion of healthcare workers (35.7% vs 2.0%).

Capacity

The vaccination program had the capacity to vaccinate the entire population of the Island of Montreal in 43 days. This interval dropped to 40 days after omitting the 153,017 individuals vaccinated outside of MVCs. Overall capacity was relatively stable for the period of MVC operation. Capacity was lowest in the first 3 days of MVC operation (<40,000 vaccinations a day) but quickly increased to reach maximum capacity by November 16, after which it remained stable at just under 44,000 vaccinations a day (Appendix B, available online at www.ajpmonline.org).

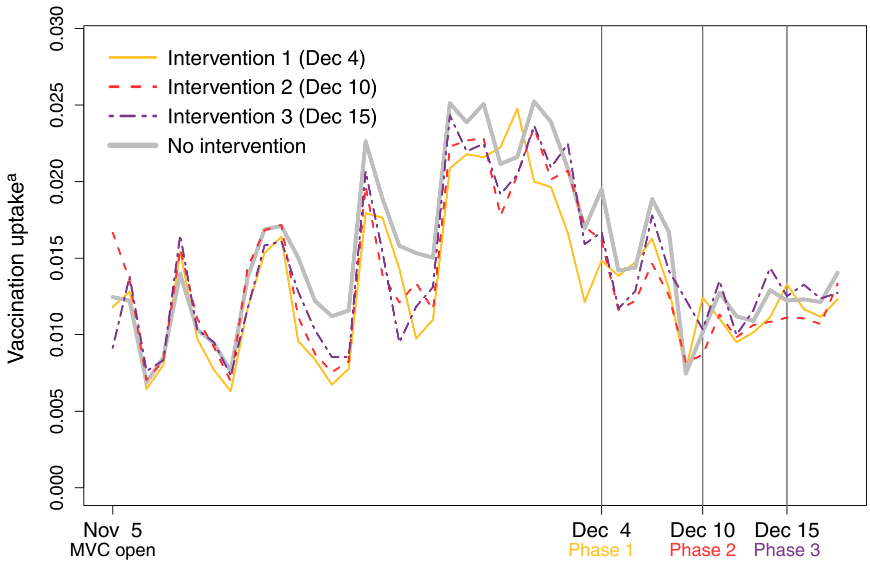

Figure 1. Vaccination uptake before and after telephone intervention, by area (MVC and non-MVC vaccinations)
[a]As a proportion of the remaining unvaccinated population
Dec, December; MVC, mass vaccination center; Nov, November

Telephone Intervention

The territory covered by the intervention included almost half the island population. Final coverage for the three intervention areas was marginally lower than for the remaining non-intervention (47.9% vs 51.2%). Compared to the difference observed between intervention areas (Figure 1), changes in daily uptake following the intervention were small (0.6% change to daily uptake for the 2 days following compared to the 2 days preceding the phone calls).

None of the interaction terms in the intervention models was significant. The associations between the interaction terms and daily vaccination counts were highest in the 2 days after each intervention (from a low of relative risk [RR]=1.01, SD=0.73–1.41, for Phase 2 to a high of RR=1.14, SD=0.80–1.73, for Phase 1). Longer post-periods decreased the effect sizes (Appendix C, available online at www.ajpmonline.org). When comparing neighborhoods targeted and not targeted by the phone intervention, there were no obvious differences in the distribution of gender, age, or risk groups, either among vaccinated residents or the neighborhoods themselves.

Priority Group Eligibility

Changes to eligibility were correlated with rapid increases in vaccine uptake (Figure 2). Vaccination within priority groups peaked on the second or third day of each eligibility period and decreased monotonically thereafter. Uptake in the general population peaked on the first day of eligibility, and then decreased more or less smoothly until December 9 when it increased moderately and remained stable until the end of MVC operation. Priority groups accounted for one third of the total population; final coverage varied notably between groups: 37.3% of chronically ill aged <65 years, 43.4% of pregnant women, 62.7% of adults aged >64 years, and 69.7% of children aged <5 years (Appendix D, available online at www.ajpmonline.org).

The logged number of elapsed days since last change of eligibility was significantly and negatively associated with daily vaccination rates, when controlling for total MVC capacity and the number of weeks elapsed since the beginning of the mass vaccination efforts (Table 2). For all vaccine recipients, compared to the first day of eligibility, the relative risk of vaccination was 0.80 (95% CI=0.74, 0.86) on Day 2 of eligibility; 0.53 (95% CI=0.44, 0.66) on Day 7; and 0.43 (95% CI=0.32, 0.57) on Day 14. The effect of time since the beginning of eligibility was decreased slightly after controlling for weather (RR=0.86, 95%CI=0.79, 0.95; RR=0.66, 95% CI=0.51, 0.86; RR=0.57, 95% CI=0.40, 0.81, on Days 2, 7, and 14, respectively).

Weather Conditions

Peaks in daily vaccine uptake appeared to match peaks in daily mean temperature (Figure 2). This association continued after vaccination was extended to the general public on November 25. Days of heavy rain (December 3) and heavy snow (December 9) corresponded to drops in uptake. The associations between weather conditions and vaccination were relatively strong and significant when controlling for total MVC capacity and duration of the

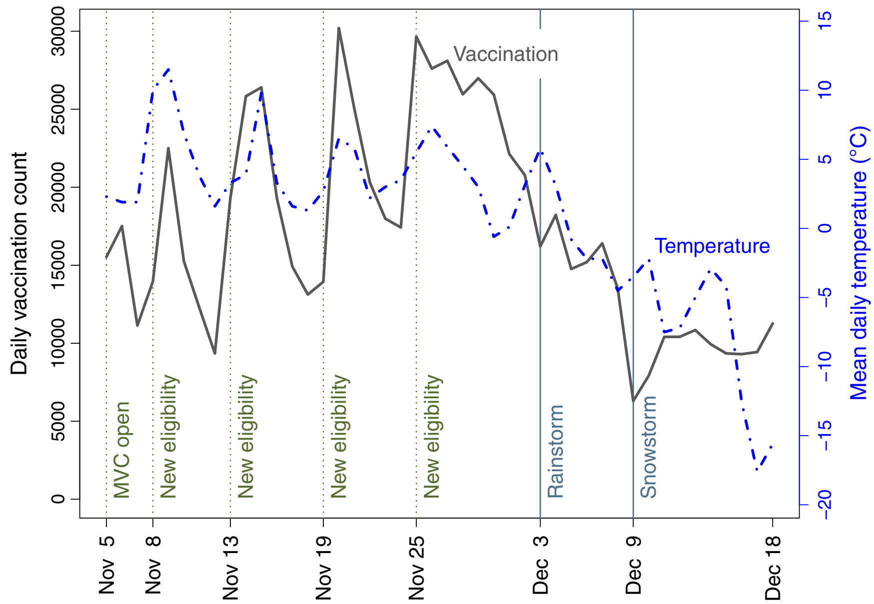

Figure 2. Daily uptake at MVCs compared to eligibility start dates and weather conditions
Dec, December; MVC, mass vaccination center; Nov, November

campaign (Table 2). Mean temperature had a positive association with daily vaccination rates (RR=1.36, 95% CI=1.19, 1.55); vaccination was negatively associated with days of heavy precipitation (RR=0.58, 95% CI=0.43, 0.79). The strength of these associations decreased slightly after controlling for eligibility (RR=1.28, 95% CI=1.12, 1.46, for temperature and RR=0.63, 95% CI=0.45, 0.89, for precipitation). No significant day-of-week effect on uptake was observed in multivariable analysis (results not shown).

Discussion

An analysis of daily vaccination uptake in Montreal showed that the temporal distribution among priority groups peaked early, decreased monotonically thereafter, and was largely a function of date of first eligibility. A telephone intervention showed no significant effect on uptake in areas with low vaccine coverage, but some variation in daily uptake was explained by changes to temperature and heavy precipitation. The association between weather conditions and vaccination persisted even after controlling for the effects of eligibility.

The capacity of the MVCs did not appear to limit uptake. Long wait-times were reported at certain MVCs, though almost exclusively at the beginning of the campaign. Efforts to manage wait-times and more generally increase uptake included enforcing the eligibility requirement, improving communication of eligibility criteria, opening additional MVCs, and providing "tickets" for pre-specified time-slots to minimize time spent standing in line.

The reason for the association between uneven and non-significant increases in vaccinations with the telephone intervention is not clear. Published research has

Table 2. Model results for multivariate regression on changes to eligibility and weather conditions, relative risk (95% CI)

	Eligibility	Weather	Eligibility + weather
Days since change to eligibility (logged)	0.73 (0.65, 0.81)	—	0.81 (0.71, 0.92)
Temperature (per 5°C increase)	—	1.36 (1.19, 1.55)	1.28 (1.12, 1.46)
Heavy precipitation (ref: no heavy precipitation)	—	0.58 (0.43, 0.79)	0.63 (0.45, 0.89)
MVC capacity (5000 vaccinations/day)	1.23 (1.00, 1.51)	1.09 (0.86, 1.37)	1.05 (0.89, 1.24)
Weeks since opening of MVCs	1.14 (1.06, 1.24)	1.19 (1.04, 1.36)	1.28 (1.16, 1.42)

Note: All models included daily remaining unvaccinated population (logged) as offset term. CIs were calculated using sandwich estimators heteroskedastic and autocorrelation consistent. Heavy precipitation was defined as >25 mm of rain per day or >25 cm of snow per day.
MVC, mass vaccination center

yet to evaluate the effectiveness of using automated calling to promote vaccination. However, recent work evaluating text messaging did find evidence of increased vaccination in areas of low uptake in the U.S.,[18,19] but findings from France suggested that promotional mailings did not.[20] Data on the number of completed telephone calls were not available, but the limited evidence of an effect of the intervention may be at least partially attributable to calls not being received.

Eligibility had a strong influence on uptake in the first half of the vaccination effort. The results suggest that individuals in newly eligible risk groups (based on start dates) rushed to get vaccinated but that the pool of vaccination seekers was depleted relatively quickly. This pattern makes sense, but no published reports of a similar pattern in other campaigns could be found.

The simultaneous occurrence of warmer temperatures and changes to eligibility complicates interpretation of the findings. Weather conditions did not influence decisions regarding eligibility periods, but the response (change to uptake) could be due to changes to eligibility, temperature, or a combination of both factors. Published research has yet to examine the effects of weather on mass vaccination. However, two observations support the conclusion that temperature had an independent effect on eligibility. First, uptake continued to track temperature even after the last change to eligibility. Second, with one exception, uptake peaked 1 or 2 days after the start of eligibility. The decrease in the daily vaccination rate after the midpoint of the campaign, together with the absence of an increase in the vaccination rate at the end, suggests that some of those who delayed vaccination ultimately may not have been vaccinated, which is in keeping with evidence that intention to vaccinate decreased during the pandemic.[21]

Limitations

Montreal is subject to extreme variations in temperature; the effects observed here may not apply to locations with milder weather. Clinic vaccination capacity was measured using official estimates of vaccination throughput based on staffing levels at each MVC. It did not account for availability of vaccine, which was limited in the initial weeks of mass vaccination. Actual capacity may have been overestimated for those weeks. A consideration of media reports of pandemic mortality and morbidity was beyond the study scope. Anecdotal evidence suggests that reports of deaths due to influenza can provide strong motivation to get vaccinated, yet it seems unlikely that media reports were confounded with weather, eligibility, or the telephone campaign and thus biased the findings.

Conclusion

The findings have direct implications for public health practice during future campaigns. First, public health agencies should attempt to limit the effect of inclement weather on access to vaccination by, for example, providing indoor waiting areas or assistance with transport to vaccination centers. Second, a large telephone intervention to increase vaccination was not effective during the pandemic in Montreal. Further research is required to understand the determinants of success of this type of intervention.

Although the cumulative vaccine coverage increases monotonically throughout a campaign, the study has demonstrated that the daily vaccination rate can fluctuate considerably because of factors such as eligibility groups and weather. In future mass vaccination efforts, public health agencies should be aware of these factors and should put in place systems to monitor vaccination coverage so that they can take measures to ensure the full utilization of vaccination resources. Examining the "front-loading" of efforts and greater local-level flexibility in setting eligibility periods appear to be promising avenues of investigation.

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Appendix

Supplementary data

Supplementary data associated with this article can be found, in the online version at, http://dx.doi.org/10.1016/j.amepre.2013.06.016.