Article ID: 2022-0242

Article title: Impact of a vaccine passport on first-dose COVID-19 vaccine coverage by age and area-level social determinants in the Canadian provinces of Québec and Ontario: an interrupted time-series analysis

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Reviewer 1: Dr. Dena Schanzer, Public Health Agency of Canada

In this manuscript, the authors aim to estimate the impact of the COVID-19 vaccine passport on the coverage of first-dose COVID-19 vaccine doses by estimating the excess rate of 1st doses among eligible persons (unvaccinated) following the announcement of provincial proof of vaccination requirements. Hopefully there will be an extensive review of the impact of the various policy decisions made during the Covid-19 pandemic, so this research topic is of considerable interest.

However, I found the manuscript challenging to interpret and assess, whether one considers the study design an observational study or modelling study. As an observational study, there is a high risk of bias due to many missing confounders and extremely short study period. As a modelling study, the authors have omitted to identity the assumptions inherent in their model, and the sensitivity analysis is lacking the important assumptions (see CHEERS Equator Network Reporting guidelines).

The study results seem to be highly dependent on various assumptions, for a few examples,

1) that the impact (increase in the rate of 1st doses given due to the mandate) lasted only 6 weeks after the announcement of the mandate (and 3 weeks after the effective date for Ontario);

2) that all of the excess doses were attributed to the mandate;

3) that 2nd doses were not impacted by the proof of vaccination mandate.

The “post-intervention” period actually did not occur until March 2022 when Ontario lifted the proof of vaccination requirements for all settings. The full time-series of 1st doses per eligible population from Jan 2021 to Dec 2022 should be provided so readers can see the strong drop in 1st doses following the lifting of the mandate and other periods of increase in vaccine uptake.

By looking at the full time-series, one will also note subsequent increases in 1st doses associated with subsequent waves. For example, as of mid-Aug 2021, cases started to trend upward as the Delta variant emerged internationally, and in Dec 2021/Jan 2022, the highly transmissible Omicron variant emerged in Ontario. One would also expect a similar impact from the vaccination mandate on 2nd doses per eligible population (8 weeks post 1st dose). This time-series should also be plotted along with the trends in cases and/or hospitalizations. The stated aim of the Ontario announcement was to protect the unvaccinated population of Ontario from the worse of the Delta-driven fourth wave. This context is important, as the announcement comes shortly after an increase in cases towards the end of August, which could have been influenced by evidence a potentially severe Delta-driven wave. The interpretation of your study results should be put into the broader context of all relevant data. Lack of vaccine appointments outside hotspots and other omitted context or potential confounders:

The authors' choice of study period is rather short, and, at least in Ontario, there were other events that would likely have had an influence of the timing of 1st doses. The number of weekly 1st doses peaked in May, in part because 2nd doses for the elderly became an urgent priority at this time. As vaccine was in short supply, the age-based prioritization resulted in delays in eligibility for younger age groups, thus delaying their 1st dose eligibility, and as expected, the number of 1st doses declined quickly, reaching a nadir in mid August. When Hot spots were prioritized, it was challenge to get a vaccine appointment outside the hot spots (Toronto). In late August, the public health messaging changed. There were announcements that vaccine appointments were available, and there would be enough vaccine for everyone by September. As well, the lull in Covid activity over the summer was over, and cases started to increase in mid-August. At this time, there was concern about the level of severity of the Delta variant internationally (in India for example). Over the summer, proof of vaccination was also required to avoid a 14-day quarantine on return to Canada from international travel (a federal mandate). There were also employer mandates for proof of vaccination. It is hard to say how much of the increase in the weekly number of 1st doses from mid August to early October was due to provincial mandates (for access to bars, gyms, restaurants). By October, case counts were slowing declining again, only to pick-up again in November with increasing local transmission of Delta, and then in late December Omicron. By looking at a longer time-series available from https://data.ontario.ca/en/dataset/covid-19-vaccine-data-in-ontario for the Ontario data, and comparing trends in case rates (also available from Ontario Public Health) and 1st doses rates (per unvaccinated population) it would appear that public health messages related to risk (case count trends), vaccine effectiveness, and insufficient vaccine supply, played a role in the trends of 1st doses. Even after the first wave of Omicron, when a large portion of the population were infected, we are still seeing some uptake of 1st doses.

In assessing the plausibility of when vaccine passports would likely have an impact on 1st dose rates, restrictions on the timing between 1st and 2nd doses should be considered. (I seem to recall that there was an 8-week wait between doses plus 2 weeks to be considered fully vaccinated?) Anecdotal evidence suggests that many people timed their vaccination to correspond to travel (airline restrictions requiring proof of vaccination for a domestic flight in November would require initiating the 1st dose in mid August, and flying home for Christmas would require initiating the 1st dose before October). It seems plausible that the impact of proof of vaccination mandates lasted longer than 6 weeks.

**When revising the manuscript, I'd suggest the authors avoid over generalizing results. It is import to report the results in a fashion that is consistent with the principle that "correlation is not causation". Sufficient context should be added to remind readers of the many issues that could have also contributed to the rather consistent increase in 1st doses in September (prior vaccine shortage, anticipation of another wave due to a new variant (Delta), federal mandates related to travel and employer mandates). As per the STROBE reporting guidelines, additional context is needed to discuss the potential risk of bias and omitted confounders (delays in 1st doses due to vaccine shortages, increased risk posed by the threat of a severe Delta wave, or simply an increasing trend in the number of new cases, timing of eligibility by age group and location of Hot spots in Ontario, and other federal vaccine mandates); timing of eligibility for a 1st dose appointment and availability of appointments (it may have taken a week or more to get an appointment); the rational for the specific 6-week impact period, and the short overall study period, timing of the proof of vaccine announcement (Sept1 in Ontario), and the effective start date (3 weeks later); time in weeks required to become fully vaccinated; and the actual end of the provincial proof of vaccination mandate, and the date it was lifted. Could you compare the update of 1st doses by age groups between hot-spots (Toronto) and other areas?

For a study with modelled output, the CHEERS reporting guideline is recommended (see for example JAMA author guidelines https://jamanetwork.com/journals/jamanetworkopen/pages/instructions-for-authors) and for a quality of evidence evaluation for policy, the overview GRADE guideline (https://doi.org/https://doi.org/10.1016/j.jclinepi.2020.09.018) provides a good background. The most salient points are to provide a detailed list of all assumptions, both assumptions explicit in the choice of model parameters and any assumptions implicit in the structure of the model or its induced constraints. Confidence intervals are usually replaced with the results of a much broader sensitivity analysis. (There is overlap the discussion of potential confounders for an observational study, and the list of assumptions in a modelling study).

We thank the reviewer for the thorough feedback on the manuscript and the opportunity to clarify misconceptions about vaccine passports, our methods, and our statistical approach. Below we address each of the comments by paragraph.

We are using standard epidemiological methods that are well-established for observational data analyses. These methods are part of the basic epidemiological toolkit (i.e., regression). To be clear, this is not a modeling study. It is an observational interrupted-time series (ITS) study (Lopez Bernal et al., 2017, 2018). The CHEERS guidelines are used for economic evaluations studies and are therefore not applicable to our study.

We disagree with the statement "as an observational study, there is a high risk of bias due to many missing confounders and extremely short study period." First, we did control for important confounders. Second, ITS is a robust study design that can be used to estimate causal effects (Lopez Bernal et al., 2017). Second, there is simply no alternative to an observational study to answer our research question. Third, given the context of our study (a mass vaccination campaign), long-term trends are expected to change throughout different stages of the campaign, and therefore a shorter study period is optimal. The short study period is in this context a strength of our approach, as it excludes potential impacts of other policies or events on our estimate (i.e., reduce the risk of confounding) while still allowing the estimation of the temporal trend. Indeed, such a short-term study period (10 weeks) has been recently used by PHAC (Maquiling et al., 2023) to assess the impact of vaccine-passports on first-dose vaccine coverage. However, contrary to us, they found no impact of vaccine passports in Ontario and Québec. As we have access to more detailed DA-level vaccination coverage information, our conclusions are more nuanced (i.e., there is an impact), robust (i.e., DA-level data

prevents residual confounding), and can help inform mitigation of intervention-generated health inequalities (i.e., policy-actionable results).

Our study results are not "highly dependent on various assumptions" and we conducted several sensitivity analyses and robustness checks to validate this claim. We address our main assumptions below:

1) We tested alternative lengths of impact (5 and 7 weeks), which only slightly change the effect estimates and do not qualitatively affect conclusions regarding the relative trends observed (see Supplementary Figure S8 in the Supplementary and Figure R5 here).

2) This assumption is reasonable given that no other major policies were in place. As discussed above, this is why we restrict our study period to after vaccination rates stabilized but before other major events or policies took place. Moreover, the Limitations section already highlights that other factors that could have hypothetically increased vaccine uptake (university-/college-based mandates in Ontario, vaccine lottery in Québec) would have had minimal or very limited impacts.

3) Our study does not make any statement regarding lack of impact on second doses — we focus on first doses. As stated in our Methods section (p. 5), any effect of vaccine passports on second-dose vaccinations will be harder to estimate given the influence of time since first vaccination and changes in interval recommendations. We focus on first-dose vaccinations because they are a clearer outcome of the vaccine passport policy. Whether vaccine passport policies have an effect or not on second doses is not relevant for their impact on first doses.

We disagree on methodological and conceptual grounds that the study period should have been extended to March 2022 (see responses to the editorial team above). Further, it is factually incorrect to state that first- dose vaccinations decreased following the lifting of mandates. In both provinces, first-dose vaccinations were decreasing before governments announced that vaccine passports would be lifted (Figure R2).

Regarding the link between case increases and vaccinations, Figure R1 shows that increases in August–October 2021 (1st Delta wave) were rather small compared to the number of cases that had been observed in previous waves. Moreover, despite the unprecedented Omicron wave in December 2021–January 2022, increases were much smaller — vaccination rates were 6 to 8 times lower than those observed immediately after the announcement of vaccine passports. Additionally, the increase was more marked in Québec than Ontario, where the vaccine passport was extended to liquor, cannabis, and big-box stores in January 2022 (Ministère de la Santé et des Services sociaux, 2022). Therefore, comparing these increases actually further supports the idea that vaccination increases in fall 2021 were due to vaccine passport policies.

As discussed above, the study period is relatively short precisely to (1) estimate a valid temporal trend and (2) prevent the effect estimate of vaccine passports from being confounded by other events:

Age-based prioritization: this is not relevant for our study period since all people 12 and over had been eligible for a first dose for over 5 weeks before the start of our study (Ministère de la Santé et des Services sociaux, 2021a; Ministry of Health, 2021).

Impact of hotspot strategy: we discuss in the Interpretation that the hotspot strategy likely resulted in the lack of vaccination disparities by racialized proportion in Ontario (as compared to Québec). However, given that this policy of prioritizing vaccine doses to hard-hit neighbourhoods was only implemented between April and June 2021, it is not relevant for our study period which starts in July 2021. We have added a section in the Supplementary to clarify that the study period was chosen to avoid including the impact of the hotspot strategy in the pre-intervention trend, as this would have biased results.

Impact of case increases and Delta variant: as already discussed above in link between case increases and vaccinations, case increases before vaccine passports were announced were too small relative to prior waves to have caused meaningful vaccination uptake during our study period (Figure R1). We have also added a supplementary analysis including weekly log cases in the regression, which gives identical point estimates (Supplementary Figure S11 and Supplementary Table S4).

Impact of proof of vaccination for travel: the changes were announced in June 2021 and took effect July 2021, making it unlikely that they affected our impact estimates (Public Health Agency of Canada, 2021). Moreover, the monthly number of returning Canadian residents was still four times lower than pre-pandemic, making it also unlikely to have affected the pre-announcement temporal trend (Figure R4).

Impact of employer mandates: employers were asked to delay the return to offices in August 2021 and the governmental recommendation to prioritize remote work only ended in November 2021, after our study period ends (Ministère de la Santé et des Services sociaux, 2021b, 2021c).

Insufficient vaccine supply: as shown in Figure R3, vaccine supply stopped being a constraint in the vaccination campaign of Québec and Ontario in late June 2021, after which the number of doses distributed vastly outpaced the number of doses administered. This factor is thus not a consideration for our study period (July–November 2021).

Interval between first and second dose: while the interval between doses would be strong determinant for the second dose, this has no implications for the impact of vaccine passports on first doses: the reviewer is discussing events that occurs after our outcome (i.e., first dose) and it would be scientifically unsound to control for 2nd dose vaccination intervals.

Impact of proof of vaccination for travel: discussed above. Additionally, there is no representative evidence that a sizeable part of the population timed their vaccination solely based on travel plans.

Impact of passports beyond 6 weeks: there is strong evidence from other jurisdictions in Canada and Europe that proof-of-vaccination policies lead to transient increases in vaccination rates — e.g., Fig 1 in (Karaivanov et al., 2022) and Fig 1 in (Mills &

Rüttenauer, 2022). This was also the assumptions adopted by PHAC (Maquiling et al., 2023) for their evaluation of vaccine passport policies. Additionally, we have added this potential limitation in the Limitations section.

We conducted a carefully constructed interrupted time-series analysis, leveraging the most detailed vaccination data available. We estimated an appropriate counterfactual scenario and reported robust impact measures of the vaccine passport, along with their uncertainty. In our response above (to the editorial team and this reviewer), we have refuted all concerns raised, from age-based prioritization (already controlled for) to the time periods (in line with the scholarship on the subject), to variants and case counts (sensitivity analysis), to second-dose vaccination (irrelevant for our outcome). The "modeled" outputs are simply obtained using regressions. As such, this is an observational interrupted-time series (ITS) study (Lopez Bernal et al., 2017, 2018), not a modelling study, so the CHEERS guidelines are not applicable since they refer to economic evaluations.

Finally, our assumptions, sensitivity analyses, and robustness checks are detailed in the Supplemental Materials. The suggestion to replace confidence intervals with those for sensitivity analyses is not in line with best practices and has no basis in statistical theory.

Specific comments:

1)Abstract: An increase of 1 p.p vaccine coverage from 82 to 83% vaccinated would correspond to a 1.2% increase in the number vaccinated, or equivalently a 1 p.p. decline from 18% to 17% in unvaccinated, would correspond to a 5% reduction in the number of unvaccinated persons (over 6 weeks). Something is amiss with the following statement "In relative terms, these correspond to 23% (95%CI:10-36%) and 19% (95%CI:15-22%) more vaccinations." I'd suggest rewording the statement. 20% more vaccinations compared to what (2nd doses outnumber 1st during the "impact period")? And only for the 6-week period? Perhaps you could say that this estimate implies an increase of 20% in the number of 1st dose vaccines given during the 6 weeks follow the provincial vaccine passport announcement. I'm not sure what you are getting at, as I would expect the impact of the proof of vaccination requirement to decline over time, not stop abruptly.

Thank you for the opportunity to clarify this statement. We are referring here to the increase in number of doses administered over the 11-week post-announcement period.

Regarding whether the impact of proof-of-vaccination requirements would decline over time, data from Canada and other countries supports a temporary effect of vaccine passport policies. In Québec, surveys conducted by the provincial public health institute have consistently shown that the proportion of people who have no intention to be vaccinated has remained unchanged at 4–7% since June 2021 (Dionne et al., 2022, 2023). This underscores that there is a fraction of the population that will not be convinced to be vaccinated through proof-of-vaccination policies. In light of this, it is reasonable to assume that once those who can be convinced by vaccine passport policies get vaccinated, vaccination rates would return to the pre-intervention trend.

2) Re: “The impact was larger among people aged 12-39 (1-2 p.p.)” When comparing rates for two groups, the 95%CI or other measure of statistical significance for the difference should be included. What is the range given here?

Given other suggestions to the abstract, we have prioritized giving more context in the abstract and —given word-count constraints—have only left the qualitative statement regarding the age gradient in the impact of vaccine passports.

3) Study design. Please provide the date of the announcement, the date of effect for the vaccine mandate, and the date that the mandate was lifted. Please include the time required to become fully vaccinated (8-weeks between doses plus 2 weeks after the 2nd dose?). A rationale for the 6-week “impact period” should also be given. I would expect the impact to be the strongest when announced, then decline their after. It seems that it will take at least 10 weeks from the date of the 1st dose to obtain proof of vaccination, and people were only given 3 weeks from the announcement to effective date to comply.

Thank you for this suggestion. We have added the implementation and lifting dates in the abstract, and the announcement and implementation dates are already provided in the *Methods* section, first paragraph. The selection of the 6-week impact period is explained in the Supplementary materials, and we have added a sentence in the main text to indicate that this was based on goodness-of-fit comparisons.
Regarding the comment about the required intervals between the first and second doses, it is not relevant to our study objectives and methods.

4) Sensitivity analysis: The sensitivity analysis seems rather restrictive. I’d suggest taking into account a longer time-series, at least including the full period of the proof of vaccination mandate, plus a proper post-intervention period. I’d expect to see gradual tapering of the estimated impact over time. There was a similar increase in %1st doses in January 2022 with the first major Omicron wave. This period of increase should be included in your modelling. As I understand your model, I suspect you would get a similar estimate of excess in doses using your method over the Jan 2022 increase in vaccine uptake, even though there were no new restrictions.

As discussed above in points 10 and 20 to the editor, extending the timeframe of our study would risk increasing bias because of other events that could have also influenced uptake. As stated earlier, this is consistent with PHAC’s approach. We focus our study on a relatively short timeframe (during which no other major policies were enacted) to ensure that we can attribute vaccination increases to the vaccine passport announcement, making the timeframe restriction a strength of this approach. We have detailed our rationale for the length of the study period in the Supplementary.

The fact that one could estimate increases in vaccinations in January 2022 is not relevant to our estimate of the impact of the vaccine passport announcement because the foundation of the interrupted-time series approach is identifying a context in which (1) no other major concurrent events can impact the outcome and (2) pre-intervention time trends can be used to estimate a counterfactual.

5) Results. Replace “by the end of the study period” with the number of weeks over which the coverage rate increased 5 p.p.

6) Re: “Prior to the announcement of vaccine passports, weekly first-dose vaccination rates were stable in Québec and declining in all age groups in Ontario.” It looks to me that 1st dose rates increased in Ontario from about 2.5% per week in Mid August to 3% at the end of August. This increase gives your counterfactual trend a short upward trend in most figures, and corresponds to public health announcements about recent increases in case counts and concern about a severe Delta wave. Perhaps, a scenario with the start of the pre-announcement period in mid August rather than July 1st could be included as part of the sensitivity analysis, as this date would correspond to the actual motivation for the passport. The Ontario announcement clearly states that this increase in cases and risk of a Delta-driven wave was the motivation for the mandate. Increase in 1st doses in August could also have been due to vaccine mandates for travel (airline or international, check dates for federal mandates against time to become fully vaccinated).

7) Sensitivity analyses: How do the results from the sensitivity analysis compare to the 95% confidence intervals?

We have made this change in the text to clarify the timeframe (*Results*, pp. 8 and 11).

It is true that rates were more variable in the pre-announcement period in Ontario than Québec, but this is addressed by our use of a spline to model the temporal trend. It is unlikely that this increase was a consequence of the Delta variant since it was already dominant at that time in both provinces. Moreover, our sensitivity analysis exploring alternative model specifications partially address this concern by fitting a log-linear model with a quadratic term for time and different intercept and slope coefficients for July (Supplementary Figures S8 and S9). This model allows for a change in the level and slope of the vaccination rates between July and August in Ontario. While this model specification results in slightly lower estimates of impact (Figure R5), these estimates are still captured by the 95% CIs of our main analysis for 5/6 age groups.

Broadly speaking, the 95% CIs of the main model captured most of the age-specific point estimate of the sensitivity analyses results (Figure R5). When this was not the case, it was usually because the objective of the sensitivity analysis was to show that the alternative model specification was not appropriate (i.e., it fit the data poorly).

Changing the start of the timeseries: in Québec, the effect estimates are not sensitive to changing start of time series (very little change in point estimate). In Ontario, estimates are more sensitive but mostly fall within the 95% CIs, and conclusions regarding the age patterns are not affected.
Changing the length of the vaccine passport impact period: in both provinces, the effect estimate is lower with a 5-week impact period (but still mostly falls within the CIs). When using a longer impact period, the estimates are slightly decreased (Québec) or increased (Ontario), almost all fall within CI.

Changing the model specification for the temporal trend: for Québec, the best-fitting non-spline model either increases or slightly decreases the estimates, but they all fall within the 95% CI, meaning that the changes are relatively small. For Ontario, the best-fitting non-spline model slightly decreases estimates, and the effects all fall within CI except for

12–17 age group. Almost all estimates from the log-linear model were high and fell mostly outside of the CI, but as mentioned in the *Sensitivity analysis* part of the *Results* (last paragraph; see also Supplementary Figure S9, C & F) this is not an appropriate way to model the counterfactual trend.

8) A broader sensitivity analysis is needed, one that includes all assumptions. For example, your sensitivity analysis looked at varying the length of the impact week from 5 to 7, without much change. I'd recommend including an analysis using the full mandate period (Sept 2021 to March 2022), and data after the lifting of the mandate as the post-passport period. Perhaps you could also include infection rates or hospitalization rates as another explanatory variable, as the 1st dose rate seems to react to trends in cases.

As previously discussed (see #4 here, and #10 and 20 to the editor), a longer timeframe is not appropriate. We have clarified this in the Supplementary.
Including the number of weekly reported cases at the public health unit level (*région sociosanitaire* in Québec) did not meaningfully change our results. This has been added in pp. 7, 16 in the main text.

The methods are explained in detail in the Supplementary material and results are presented in Supplementary Figure S11 and Supplementary Table S4. We do not conduct this analysis for Ontario given the time constraints in obtaining the required data within our assigned response window.

9) Interpretation: How would the statement "This translates to relative increases of 23% (Québec) and 19% (Ontario) in vaccinations among people without a first dose" be interpreted by readers in 2023? Are you intending that they generalize past the specific 6-week period, ie 20% of first doses given during the full proof of vaccine mandate period from Sept 2021 to March 2022? How would the statement "Vaccine passports increased COVID-19 first-dose vaccine coverage by approximately 1 p.p. in both Québec and Ontario" be interpreted today? I note that 1st dose coverage for Adults increased from 83% at the time of the announcement to 92% at the end of the mandate in March 2022 and is now 94%? The two quoted statements should be revised so that they will more likely be correctly interpreted if quoted by others (media or other researchers).

We have clarified the timeframe in the first paragraph of the *Interpretation* and have made similar changes in the *Results* where relevant.

Reviewer 2: Dr. Kevin Bardosh, University of Florida

This is a well-designed and reported paper on an important topic of wide scholarly interest. It uses a strong methodological approach.

The only substantial comment I have regards the use of the term 'racialized'. This term is typically used to denote individuals subject to racism (although it is used in different ways). I would recommend that the authors use the more neutral term 'racial minority' or 'ethnic minority.' There are also two studies that I think may be of interest to the authors to cite, regarding lower vaccine uptake in Canada. It may useful to reference these.

Smylie, J., McConkey, S., Rachlis, B., Avery, L., Mecredy, G., Brar, R., ... & Rotondi, M. A. (2022). Uncovering SARS-COV-2 vaccine uptake and COVID-19 impacts among First Nations, Inuit and Métis Peoples living in Toronto and London, Ontario. CMAJ, 194(29), E1018-E1026.

Cénat, J. M., Noorishad, P. G., Moshirian Farahi, S. M. M., Darius, W. P., Mesbahi El Aouame, A., Onesi, O., ... & Labelle, P. R. (2022). Prevalence and factors related to COVID-19 vaccine hesitancy and unwillingness in Canada: A systematic review and meta-analysis. Journal of Medical Virology.

We thank the reviewer for the positive feedback on this manuscript.

We use the term racialized here to refer to individuals who are coded as non-white (white being the dominant/majority group in Canada). This term is better understood by audiences outside of Canada than the term "visible minority," which is the term used in the census questionnaire.

We have included these two relevant references in the last paragraph of the *Interpretation* section .We thank the reviewer for these suggestions.

Reviewer 3: Dr. Affan Shoukat, Yale University

The authors conclude that proof of vaccination policies led to increases in vaccination of 23% and 19% in Quebec and Ontario. This seems plausible and I see a strong correlation in the data. However, it might be beneficial to mention that that there were no other ongoing 'dynamics' that coincided with proof-of-vaccination policies that could've caused a sharp increase. Examples include: a large influx of supply of vaccines around that date that may have increased uptake, an emerging variant that scared the population, or that companies/workplaces were trying to get rid of WFH policies. The authors can conclude that these dynamics were likely NOT a part of the increased coverage, and it was indeed the policies that drove the demand.

We have included a sensitivity analysis that shows that including case counts in the statistical model does not change our results (Supplementary Figure S11 and Supplementary Table S4).

Regarding vaccine influx, vaccine supply certainly affected uptake early on, but supply was sufficient and consistent throughout the study period and is therefore not a concern. For the other dynamics, we have added a section in the Supplementary materials (*Length of study period*) to explain that the chosen study period was meant to reduce the risk of confounding by excluding the other events mentioned.