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Title	Uptake of influenza vaccination in inflammatory bowel disease, multiple sclerosis and rheumatoid arthritis: a cohort study
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Reviewer 1	Ali Elbeddini
Institution	Winchester District Memorial Hospital, Winchester, Ont.
General comments (author response in bold)	<p>1. I enjoyed reviewing the manuscript. I find the results are very interesting. I learned that psychiatric disorders are associated with lower uptake of preventative healthcare such as vaccination. Thank you for the supportive comments.</p> <p>However, I would like to share few comments that may need clarification which are:</p> <p>2. Title: I find it broad with mentioning Immune mediated diseases especially authors only looked at MS, RA and IBD and they didn't mention any other Immune mediated disease such as Lupus, Psoriasis and Guillian-Barre syndrome. I would suggest to modify the tile to" "Studying the association of immune-mediated inflammatory diseases (IBD,MS,RA) , psychiatric comorbidities and uptake of influenza vaccine: A retrospective study" or something around this line. My suggestion with title may seem bit long but The point is to be specific with selecting the targeted population. Thank you We have modified the title to specify the study populations as suggested: Uptake of Influenza Vaccination in Inflammatory Bowel Disease, Multiple Sclerosis and Rheumatoid Arthritis: A Cohort Study</p> <p>3. Great work on the literature review analysis in the discussion section. Wonderful job in looking at the bigger population in other countries (Norway, Poland, Israel, ... etc). Thank you for the supportive comments</p> <p>4. if you could elaborate on: reason why number of female in study was 2/3 compared to male?, does this have anything to do with MS is more predominant in females?. Thank you MS and RA are both more common in females than males. The sex distribution of IBD varies by age of onset, and across studies. We have modified the discussion of study strengths and limitations (limitations paragraph, page 11): The female predominance and age distribution of our cohorts are consistent with the epidemiology of the diseases studied.</p>
Reviewer 2	Sanal Girija
Institution	Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India
General comments (author response in bold)	1. The study is satisfactory. The authors may define "vaccination uptake". It is obvious that 'vaccination uptake increased over the thirty-year study period'- however what is he right way to make the comparison across 3 decades? The

vaccine, vaccine programs, access, awareness, economy, policy, polity, society has changed over the time. The Manitoban vaccination coverage is better than many developing nations.

In the first paragraph of the introduction we have clarified what we mean by vaccination uptake:

Effective implementation of influenza vaccination strategies require knowledge of vaccine uptake (use), and how this varies across population subgroups.

The regression analysis was limited to a 10 year period to address the issue of temporal changes and best reflect the current state as indicated in methods:

“Although we accessed data for the period April 1, 1984-March 31, 2016 initially, for regression analyses, we limited the time period to 2006-2016 to reduce secular trends.”

We also acknowledged the changes in policy that had occurred in Manitoba in the first paragraph of the discussion:

“In this population-based study, vaccination uptake increased over the thirty-year study period in three immune-mediated inflammatory disease cohorts, and a matched cohort without immune-mediated inflammatory disease, in concert with programmatic changes. In 1999, vaccinations became publicly funded for Manitobans aged ≥ 65 years, those with some chronic conditions, and health care workers. In 2005, funding was extended to chronic respiratory disease. However, despite universal vaccination coverage as of 2010, and access via pharmacists as of 2014, vaccination rates in all populations remain much lower than desired.”

While vaccination coverage may be better than in the developing countries it is nonetheless below recommended public health targets, and influenza causes numerous hospitalizations, and deaths in Manitoba each year. Therefore we believe that the findings are important.

2. The vaccination cover of IMID families and contacts are also important-herd immunity-which is not covered in this study. When susceptible patients attend the clinic for follow-up visits/refills, they are not specially advised for vaccination? Or is it about patient compliance? If vaccination is free, then what prevents them from getting vaccinated? Is it because of anti-vaccine campaigns? At the global vaccine summit the EU Commission and WHO (Brussels) unveiled 10 “actions towards vaccination for all.” (Refer BMJ 2019;366:l5576).

Using administrative data we cannot address the reasons why uptake of vaccination was inadequate, and this was not the focus of the present study. A detailed discussion of the literature regarding the factors contribution to low vaccination rates is limited by the word restrictions, but we have added the following sentence to the discussion (page 10), and then cited relevant literature from Canada, and in immune-mediated inflammatory disease populations.

Factors contributing to low vaccination rates include a lack of perceived susceptibility to influenza, lack of perceived severity of infection, and not believing in the vaccine’s effectiveness.^{9,10,52-54}

3. I would appreciate if the authors could convert some of the table content to pictures/graphs.

	We have included 2 figures and 1 supplemental figure in the manuscript. Given the rather lengthy additions to the supplemental materials, and the difficulty of representing the full multivariable model results in figures, we have not converted tables to figures.
Reviewer 3	John Marshall
Institution	Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ont.
General comments (author response in bold)	<p>Marrie et al report an analysis of influenza vaccine uptake in a population-based cohort of IMID patients and matched controls in Manitoba. The research question is important and points to a gap in care. The paper is well-written, and the analysis fairly straightforward.</p> <p>Thank you for the supportive comments.</p> <p>I have a few points of clarification:</p> <p>1. The authors note in their Discussion that pharmacists can administer the vaccine since 2014, but vaccine delivery is tracked using tariff codes. Can the authors confirm that pharmacists would have used the same codes, and can they confirm that no other pathways to vaccination (e.g. workplace or campus health offices) were available during the study interval?</p> <p>Pharmacists use the same tariff codes as physicians as noted in the methods:</p> <p>“...we identified influenza vaccinations using tariff codes 8791, 8792 or 8799, which are used by primary care and pharmacy providers to bill for their services”.</p> <p>Vaccinations in private (not public) workplaces may not have been captured. We have modified the discussion of study limits to be more explicit about this potential source of underascertainment. Notably, the proportion of our matched cohort vaccinated in 2013 is consistent with self-reports through the CCHS in 2013, suggesting our estimates are valid. We modified the limitations paragraph (page 11) to note this:</p> <p>We may not have identified all vaccinations administered as <i>vaccinations in private workplaces would not be captured</i>, but under-ascertainment is likely to be non-differential between cohorts, and would be insufficient to fully account for our findings. Reassuringly, the proportion of Manitobans reporting influenza vaccinations in the Canadian Community Health Survey (30%) was consistent with the proportion in our control cohort.⁵²</p> <p>2. Can the authors identify which physician administered the vaccine? Was it done in primary care or by the IMID specialty team?</p> <p>In Manitoba, IMID specialty teams are generally not involved in the administration of vaccinations. Vaccinations are administered by primary care providers, pharmacists and public health nurses.</p> <p>3. Do the authors have information on healthcare visit frequency? As much vaccination is done opportunistically, the frequency of visits to primary care providers could be an important predictor. Primary care visits could be hypothesized to occur more or less often in patients seeing specialists regularly for IMID care.</p> <p>We have added information about the frequency of physician visits in the year before the index date to Table 1. We added a complementary analysis in</p>

	<p>which we adjusted for the annual number of physician visits in the year prior to vaccination. Our findings were generally similar to those of the primary analysis, which we now show in Table e9.</p> <p>Given that specialist care for immune-mediated inflammatory diseases does not apply to the control cohort(s), we did not include specialist visits as a separate variable. The total physician visits provides an index of health care access/use and opportunities to receive the vaccine or to be reminded about the vaccine.</p>
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