

Running Head: Preferences COVID-19 vaccine

Preferences for COVID-19 vaccination in people with chronic immune-mediated inflammatory diseases

Glen S. Hazlewood^{1,2,3} (ORCID: 0000-0001-7709-3741), Ines Colmegna⁴, Carol Hitchon⁵ (ORCID: 0000-0001-5547-3268), Paul R. Fortin^{6,7} (ORCID: 0000-0002-7278-2596), Sasha Bernatsky⁴, Ann E. Clarke^{1,2,3} (ORCID: 0000-0002-3112-9646), Dianne Mosher^{1,2,3}, Todd Wilson², Megan Thomas^{3,8}, Claire Barber^{1,2,3} (ORCID: 0000-0002-3062-5488), Mark Harrison^{3,8, 9, 10} (ORCID: 0000-0002-2115-2447), Nick Bansback^{3,9,10}, Laurie Proulx¹¹, Dawn P. Richards¹¹ (ORCID: 0000-0003-1151-0826), Gilaad G. Kaplan^{1,2} (ORCID: 0000-0003-2719-0556)

Name of Departments and Institutions to which the work should be attributed:

¹Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Canada

²Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Canada

³Arthritis Research Canada, Vancouver, British Columbia, Canada

⁴The Research Institute of the McGill University Health Centre, McGill University, Montreal, Quebec, Canada

⁵Department of Internal Medicine, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

⁶Division de Rhumatologie, Département de Médecine, CHU de Québec - Université Laval, Québec City, Québec, Canada

⁷Centre de Recherche ARThrite - Arthrite, Recherche et Traitements, Université Laval, Québec City, Québec, Canada

⁸Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada

⁹School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada

¹⁰Centre for Health Evaluation and Outcome Sciences, St. Paul's Hospital, Vancouver, British Columbia, Canada

¹¹Canadian Arthritis Patient Alliance, Ontario, Canada

Sources of support: This work was supported by the Canadian Rheumatology Association; a Canadian Institutes of Health Research Operating Grant: COVID-19 Rapid Research Funding Opportunity [Funding Reference number VR5-172684]; and the Public Health Agency of Canada through the Vaccine Surveillance Reference Group (VSRG) and the COVID-19 Immunity Task Force (CITY). Dr. Hazlewood is supported by a Canadian Institutes of Health Research New Investigator Award. Dr Fortin holds a tier 1 Canada Research Chair on Systemic Autoimmune Rheumatic Diseases. Dr. Clarke holds The Arthritis Society Chair in Rheumatic Diseases at the University of Calgary. Dr. Harrison received salary support through a 2017 Scholar Award from the Michael Smith Foundation for Health Services Research.

Initials, surnames, appointments, and highest academic degrees of all authors:

GS Hazlewood, MD PhD, Associate Professor of Medicine

I Colmegna, MD, Associate Professor of Medicine

C Hitchon, MD MSc, Associate Professor of Medicine

PR Fortin, MD, Professor of Medicine

S Bernatsky, MD, PhD, Professor of Medicine

AE Clarke, MD, Professor of Medicine

D Mosher, MD, Professor of Medicine,

T Wilson, PhD, Research Assistant

M Thomas, MSc

CEH Barber, MD PhD, Associate Professor of Medicine

M Harrison, PhD, Associate Professor of Medicine

N Bansback, PhD, Associate Professor of Medicine

L Proulx, B.Com

DP Richards, PhD

G Kaplan, MD, MPH, Professor of Medicine

Conflicts of interests:

GSH: None

IC: None

CH: unrelated research funding from Pfizer Canada; Advisory board for Astra-Zeneca

PRF: Advisory board for Astra-Zeneca, AbbVie and GSK.

SB: None

AC: Consulting fees from AstraZeneca/MedImmune, BristolMyersSquibb, Exagen Diagnostics, and GlaxoSmithKline .

DM: unrelated research funding from Pfizer Canada

TW: None

MT: None

CB: None

MH: None

NB: None

LP: Has received honoraria for speaking about arthritis patient organizations at a Lilly ad board meeting. Is a volunteer vice president of the Canadian Arthritis Patient Alliance which receives independent grants from pharmaceutical companies.

DR: Has received honoraria for speaking about arthritis patient organizations at a Lilly ad board meeting. Is a volunteer vice president of the Canadian Arthritis Patient Alliance which receives independent grants from pharmaceutical companies.

GK: Dr. Kaplan has received honoraria for speaking or consultancy from AbbVie, Janssen, Pfizer, Amgen, and Takeda. He has received research support from Ferring, Janssen, AbbVie, GlaxoSmith Kline, Merck, and Shire. He has been a consultant for Gilead. He shares ownership of a patent: TREATMENT OF INFLAMMATORY DISORDERS, AUTOIMMUNE DISEASE, AND PBC. UTI Limited Partnership, assignee. Patent WO2019046959A1. PCT/CA2018/051098. 7 Sept. 2018

Correspondence to: Glen S Hazlewood, Departments of Medicine and Community Health Sciences, Cumming School of Medicine, University of Calgary, 3280 Hospital Drive NW, Calgary, T2N 4Z6, Canada. E-mail: gshazlew@ucalgary.ca. Phone: +1-403-220-5903

Key indexing terms (MeSH): patient preference, autoimmune diseases, rheumatoid arthritis, inflammatory bowel diseases, Systemic Lupus Erythematosus, COVID-19 vaccines

Word count: 3366

ABSTRACT

Objectives: To understand how people with chronic immune-mediated inflammatory diseases (IMIDs) trade-off the benefits and risks of COVID-19 vaccine options.

Methods: We conducted an online discrete-choice experiment in people with IMIDs to quantify the relative importance of attributes relevant to COVID-19 vaccination. Participants were recruited between May-Aug 2021 through patient groups and clinics in Canada and completed 10 choices where they selected one of 2 hypothetical vaccine options or no vaccine. The relative importance (RI) of each attribute was estimated and heterogeneity was explored through latent class analysis.

Results: The survey was completed by 551 people (89% female, mean age 46 years) with a range of IMIDs (48% IBD, 38% RA, 16% SLE). Most had received one (94%) or two (64%) vaccines. Across the ranges of levels considered, vaccine effectiveness was most important (RI = 66%), followed by disease flare (21%), rare but serious risks (9%) and number/timing of shots (4%). Patients would accept a risk of disease flare requiring a treatment change of 8.8% or less, for a vaccine with a small absolute increase in effectiveness (10%). Of the three latent classes, the group with the greatest aversion to disease flare were more likely to be male and have lower incomes, but this group still valued effectiveness higher than other attributes.

Conclusion: Patients perceived the benefits of COVID-19 vaccination to outweigh rare serious risks and disease flare. This supports COVID-19 vaccine strategies that maximize effectiveness, while recognizing the heterogeneity in preferences that exists.

INTRODUCTION

COVID-19 vaccines have had a remarkable impact on preventing infection and severe outcomes from the SARS-CoV-2 virus. When these vaccines were introduced, there was hesitation amongst some public health agencies in vaccinating patients with chronic immune-mediated inflammatory diseases (IMID), as those individuals were excluded from the vaccine clinical trials (1). Vaccines have been rarely associated with autoimmune events (2), and there was a concern that these vaccines could trigger flares of pre-existing autoimmune diseases. IMID societies and patient groups, however, were unanimous in their support and recommendation for vaccination (3-6). The key argument, even in the initial stages, was that the benefits from vaccination - even if somewhat reduced in people with autoimmune diseases on immune suppressing therapy, outweighed any known rare risks and theoretical risks of disease flare. Since then, trade-offs between vaccine efficacy and a theoretical risk of disease flare continue to be relevant for decisions such as whether to hold medications at the time of vaccination, the administration of booster vaccines, and second-generation COVID-19 vaccines for COVID-19 variants that are in development.

Patient preferences can be quantified using discrete-choice experiments (DCEs) (7,8). In a DCE, people choose between 2 or more different options, that vary in terms of their attributes or properties. By varying the choices presented across a series of choice tasks, and analyzing which options patients select, the preference weight of each attribute level can be calculated. These preference weights can then be compared to estimate the relative importance of any 2 attributes and to quantify the rates at which patients are willing to trade-off one attribute for

another (7). In the case of COVID-19 vaccination, patients' willingness to accept a disease flare or potential rare risks of vaccination can be quantified in terms of vaccine benefits.

The objective of this study was to measure the preferences of people with chronic IMIDs for COVID-19 vaccines. In particular, we were interested in how patients would trade-off between vaccine effectiveness and a hypothetical increased risk of a flare of their disease.

MATERIALS AND METHODS

Survey design

We designed a DCE to quantify trade-offs relevant to the choice of available COVID-19 vaccines.

The DCE was designed as an online survey, using Sawtooth Software, and followed best practices for the development of DCEs (7). A draft survey was developed by the research team

that included clinicians, researchers, vaccine experts and patients. The selection of attributes

and levels was informed by work from our team on guidelines for COVID-19 vaccination in

people with autoimmune rheumatic diseases (4). During guideline development, vaccine

effectiveness, the theoretical risk of diseases flare, and potential rare risks were judged to be

key trade-offs relevant to decision-making. Vaccine dosing was included as an additional

attribute, as the guideline panel had felt that this was potentially important to some patients.

The levels for each attribute were derived from the plausible values, again informed by work on

clinical practice guidelines (4). The plausible levels for disease flare were chosen by expert

consensus, as no data existed for COVID-19 vaccines.

The draft survey was then piloted in March-April 2021 in 1-on-1 'think-aloud' interviews with four patients conducted using Zoom® by a research assistant with prior experience piloting DCEs. In addition to feedback on the overall readability, clarity of attribute descriptions, survey design and flow, we sought feedback on the framing of the vaccine effectiveness attribute and the inclusion of a 'no vaccine' option (opt-out). Participants favoured describing vaccine effectiveness in terms of preventing symptomatic COVID-19 infection, rather than severe COVID-19 infection. For prevention of severe COVID-19, it was challenging to choose a range of plausible values that would apply to all patients, given the risk of severe disease varies so much with age and other factors. Including both severe and symptomatic COVID-19 infection as separate attributes in the same choice task led to confusion when an option had discordant protection for symptomatic and severe disease (e.g., 95% protection for symptomatic COVID-19, but only 30% against severe infection). Participants preferred framing the effectiveness as a percent value (e.g., 95% protection), rather than an absolute risk, as this was the way vaccines were being discussed in the media, and the latter was more challenging to understand. Participants favoured having a no vaccine option in each choice set (opt-out), rather than as an additional question after patients were forced to choose between vaccine options.

Following the piloting, the survey was pre-tested by sending an invitation to members of the Canadian Arthritis Patient Alliance (CAPA). The responses were monitored and after 37 participants, the survey was paused when the number of flares reported by participants over the past year (an additional question at the end of survey) was much higher than expected. We realized that the initial description of a flare was vague. The definition was modified to indicate

that flares were those that required treatment and occurred within one month after vaccination. This better aligned with the outcome of interest, and how flare has been measured in clinical studies. The survey was then launched again, and no further issues were identified. Data from the patients in the pre-testing group was not included in the final sample, but we e-mailed those participants that had provided their e-mail address, explained the update, and re-invited them to participate in the final survey.

The final survey included 10 choice tasks, in which participants chose between 2 hypothetical vaccine options or no vaccine (Figure 1). The full list of attributes and levels is presented in Table 1. The order of the four attributes was the same for a participant but was varied randomly between participants. We randomly assigned patients 1 of 100 different sets of choice tasks that were generated using a balanced-overlap fractional factorial design in Sawtooth Software (Orem, UT, USA), which follows principles of efficient design including orthogonality and level balance (9). Prior to the DCE choice tasks, the survey included additional questions regarding the perceived benefits and risks of vaccination and descriptions of the tasks and attributes (see full survey in Supplementary material). The final page of the survey included demographic questions.

Recruitment and consent

The eligibility criteria were adults (age >18) with an autoimmune condition. Participants were recruited from clinical cohorts and patient groups between May-Aug 2021. Clinical cohorts included rheumatoid arthritis (10) and lupus cohorts in Calgary, Alberta, and a general

rheumatology clinic in Montreal, Quebec. For each of these cohorts, patients were recruited at the time of their clinic visit or through e-mail invitation if they had consented to be contacted about other research studies. Patient groups included CAPA, The Arthritis Research Canada's Arthritis Patient Advisory Board, Crohn's and Colitis Canada, and Rheumatoid Arthritis Facebook Canada. These groups disseminated the invitation to their members through e-mail lists, social media and posting on websites. Participants viewed the consent form on the first page of the survey and implied consent was obtained on completion of the survey. Participants in the pre-testing provided informed consent at the time of the interview. The study was approved through the University of Calgary Conjoint Research Ethics Board (REB#21-0080).

Data analysis

Demographics and Internal validity

Demographic characteristics were summarized descriptively. We conducted several tests of internal validity following published guidance and compared the results to normative values (see Supplementary material for details) (11).

DCE results

We estimated the value for each attribute level using a main-effects multinomial logit model, with an alternative specific constant for the no vaccine option (12). The risk attributes (vaccine effectiveness, flare, rare risks) were first modelled as categorical (effects coded (13)), then as linear, after visually confirming a linear relationship and comparing the Akaike Information Criterion (AIC) between the categorical and linear models. In the linear model, we assigned the

level of “less than 1%” for the flare attribute a value of 0.5%. To understand preference heterogeneity, we conducted latent class analysis, comparing the model fit (adjusted Bayesian information criterion and consistent AIC) of 2, 3 and 4 group solutions. In exploratory analyses, we evaluated whether there was an association between patient characteristics and group membership through univariate and multivariable logistic regression. The multivariable model included age and gender, and any variable with a *P*-value of <0.20 in univariate analyses. A *P*-value of <0.05 was considered statistically significant.

To aid in the interpretation of the results, we calculated the relative importance (RI) of each attribute by scaling the preference weight of each attribute (difference between highest and lowest levels), so that the four attributes summed to 100. We also calculated the maximum acceptable risk (MAR) of disease flare that patients would accept for a vaccine with a given increase in effectiveness. We considered a 10% absolute increase in effectiveness to be a marginal gain, but plotted the MAR of disease flare across the range of levels included in the DCE. All analyses were conducted using R version 4.1.2 (<http://www.r-project.org>), SSI Web version 9.12.1 (Sawtooth Software), and Stata 17 (StataCorp).

Patient involvement

Two patient partners (DPR, LP) were involved throughout the study, including with survey development, interpretation of findings and reviewing the manuscript. Patient groups assisted with recruitment, as described above.

RESULTS

Sample population

Of the 747 people who started the survey, 551 (74%) completed it. Demographics of the participants are presented in Table 2. The median age of respondents was 46 years and 89% were female. Most people had inflammatory bowel disease (48%), rheumatoid arthritis (38%), or systemic lupus erythematosus (16%). Nearly all participants (94%) had received at least one dose of the vaccine at the time of completing the survey and 64% had received two.

Participants were on a wide range of medications. Most participants (82%) did not hold their medication around the time of the vaccine, although this varied by drug (see Supplementary Table S1).

Perceived benefits and concerns of COVID-19 vaccination

Participants reported high concern for many aspects of COVID-19 infection (Supplementary Table S2). Passing infection on to their family and friends was the highest rated concern (median 9, 0=not concerned; 10=very concerned), and death due to COVID-19 the lowest (median 6). Nearly all patients identified a wide range of benefits of COVID-19 vaccination. Patients were most concerned about both the known (45% of patients) and unknown side effects (50%), the potential lack of effectiveness in them (48%), and the possibility of causing their autoimmune condition to worsen (47%). Most participants stated that prior to receiving their vaccine, they preferred an mRNA vaccine (75%), with 20% stating they had no preference.

Discrete-choice experiment

Main results

The tests of internal validity were in line with published values for DCEs (Supplementary Table S3) (11). The results of the main model DCE estimates for both the categorical and linear models are presented in Table 3. The linear model had improved model fit. The opt-out (no vaccine), was chosen in 683/5,840 (12%) choice sets, and had a value of -1.18 in the linear model, which was low in magnitude compared to vaccine effectiveness, meaning patients, would, on average, accept a vaccine with marginal benefits. For example, consider a 2-dose vaccine 1 month apart (value 0.15 in the linear model), with a 1/100,000 rare but serious risk (value = $-0.06 \times 10 = -0.6$) and a 2% risk of flare (value = $-0.08 \times 2 = -0.16$), which evidence suggests is the true risk of flare (14,15). This vaccine would be preferred on average to no vaccine, even if the effectiveness was only 30% (value = $0.07 \times 30 = 2.1$) - the lowest level considered, as the total value of this vaccine ($0.15 - 0.6 - 0.16 + 2.1 = 1.49$) would more than offset the negative value of the opt-out.

When comparing the relative importance of the attributes, vaccine effectiveness was the most important attribute across the range of levels considered, followed by flare, rare but serious risks and the number of shots (Table 3 and Figure 2). In comparing vaccine effectiveness and disease flare, participants would accept a marginal gain in vaccine effectiveness of 10% provided the risk of disease flare requiring a treatment change was less than 8.8% (Figure 3, presented alongside the latent class analysis findings discussed below). If the risk of disease flare is 2% or less (14,15), a vaccine would only need to provide an absolute gain in effectiveness of 2.3%.

Latent class analyses

The relative importance of the attributes in the three-group latent class analysis solution, which had improved model fit over the 2 and 4-group solutions, are presented in Figure 2. In all three groups, vaccine effectiveness was still the most important attribute, and the importance placed on rare risks and number of doses was quite consistent between groups. However, the willingness to trade-off between vaccine effectiveness and disease flare varied across the groups. For the most risk tolerant group (Group 3 in Figure 2), which included 52% of participants, a 10% absolute gain in vaccine effectiveness would be accepted, provided the risk of flare was less than 14.1% (Figure 3). This threshold decreased to 7.6% and 3.7% for the more risk averse groups, which included 28% and 20% of patients respectively.

Results of the regression analyses evaluating the association between participant characteristics and latent class membership are presented in Supplementary Table 4. The results compare group 1 (the most risk averse group) to groups 2 and 3 combined. In univariate analyses, participants in the most risk averse group had a statistically significant lower likelihood of being Caucasian (82% versus 90%, P -value = 0.016), or having an income greater than \$100,000 (28% versus 44%, P -value = 0.003), and a statistically significant higher likelihood of having been recruited from a clinical cohort (37% versus 23%, P -value = 0.003). There was a non-statistically significant trend towards the more risk averse group having fewer females (84% versus 90%), fewer people with inflammatory bowel disease (39% versus 48%), and more people who were taking rituximab or mycophenolate mofetil (9% versus 4.5%). In multivariable

analyses, only an income greater than \$100,000 remained statistically significantly associated with a lower odds of being in the risk averse group [odds ratio (95% confidence intervals): 0.46 (0.28, 0.76)], while female gender became statistically significant with a lower odds of being in the risk averse group [odds ratio (95% confidence interval): 0.47 (0.24, 0.91)].

DISCUSSION

Our results provide quantified preferences for people with IMID for trade-offs related to COVID-19 vaccination. Importantly, we found that patients in our sample, when asked early in the vaccine roll-out, valued the benefits of vaccination as the most important attribute. Smaller groups of patients were more averse to a potential risk of a serious flare, although even for these patients, vaccine effectiveness was still the most important attribute. Overall, our results support vaccination strategies that maximize vaccine effectiveness.

While our questions focused on the preferences for the initial 2-dose COVID-19 vaccination series, the trade-offs between vaccine efficacy and potential disease flare remain relevant for many decisions regarding vaccination. As the risk of flares requiring treatment changes following vaccination has been shown to be very low (<2%) (14,15), our results suggest that most patients would accept third and fourth vaccine doses for very small gains in effectiveness. As new vaccines for variants are developed, and alternative vaccination approaches are tried (e.g. mixing vaccine types), our results suggest that vaccine approaches with a marginal absolute gain in efficacy (10%) will be preferred by the majority, provided the risk of a flare is <9%. Studies could potentially use this to inform a maximum acceptable threshold for flare in

sample size calculations (16,17); demonstrating the upper bound of the 95% confidence interval for the risk of flare is below this threshold would support the benefit/risk profile of the vaccine. We present a figure (Figure 3) that shows how this threshold would vary according to the expected effectiveness of the vaccine and the risk tolerance of the patient subgroup, according to the latent classes we identified.

Our results support a shared decision when deciding between continuing or pausing medications to optimize antibody response to a vaccine, as holding medications to treat an IMID may trigger a flare. A recent randomized trial found that patients with RA who held methotrexate around the time of their vaccine had higher rates of flares after the second dose (18). Consequently, continuing treatment will be best for patients at higher risk of flare or serious consequences from flares, and in patients with stronger preferences for avoiding flares. For patients where additional efficacy is highly desired and flares are less of a concern, holding medications may be considered. Current recommendations on holding medications in people with IMIDs around the time of COVID-19 vaccination vary. The American College of Rheumatology (ACR) recommends holding certain medications around the time of vaccination (19), whereas the European League Against Rheumatism (EULAR) and other groups recommend against the routine interruption of therapy (4,20,21). All groups though recognize the importance of tailoring the decision to the patient.

The latent class analyses demonstrated preference heterogeneity in terms of aversion to flare, which was associated with sociodemographic variables. It is common that patient preferences,

including inflammatory arthritis, are more often associated with sociodemographic characteristics, rather than disease characteristics (22). Patient preferences are shaped by their environment, peer groups, life roles and past experiences (23,24). Respectful, open communication around vaccines will help providers understand their patients' preferences, and address concerns.

Strengths of our study include the quantification of patient preferences, diverse sample of different diseases, and the relatively large sample size relative to typical DCEs (25). Patients were involved throughout the study, and the survey was pre-tested, then piloted prior to implementation, which allowed us to refine the survey prior to full administration. The results were in the expected direction of effect, and the tests of internal validity were in line or better than published DCE values.

Our survey has limitations. The sample is skewed towards people who are largely accepting of vaccines, as 94% of patients in our sample had already been vaccinated. While this is in line with high rates of vaccination in Canada, where ~90% have received 2 doses (26), and even higher rates in Canadian patients with IMID disorders (27), our results would not be applicable to the small percentage of people who have strong aversions to vaccination, either in general, or specifically to COVID-19 vaccines (28). It is likely that additional factors, beyond risk/benefit trade-offs related to their disease, are the main drivers of their preferences. While our multi-faceted recruitment approach allowed us to sample patients with a range of IMID conditions including autoimmune rheumatic disease and IBD from across Canada, recruitment through

Accepted Article

online channels, the English-only survey, and online nature of the survey mean that we did not capture the preferences of some populations who may be at greater risk of inequities. As our latent class analysis found some of these characteristics were associated with greater aversion to flare, the average population value estimates in our paper may overestimate the willingness to accept flare in the general population of patients with IMID conditions. Nevertheless, even the most risk averse group we identified was willing to accept vaccines with relatively low absolute gains in efficacy, given the known low risk of flare. Although not feasible in this study, recruitment strategies to target under-represented groups, such as clinic-based collection in underserved areas, purposive sampling, and translation to other languages, would help ensure the representativeness of preference studies in the future.

Studies to date have demonstrated relatively high rates of COVID-19 vaccine acceptance in people with IMIDs, which has improved over time (27,29). Our findings on the perceived benefits and concerns of COVID-19 vaccination align with other studies (29-31). Our results add to this literature, by quantifying the relative importance of considerations relevant to COVID-19 vaccination. We are not aware of other preference studies for other vaccines in patients with chronic IMID. These same principles are likely relevant for the acceptance of other vaccines, although our results would not directly translate, given the real or perceived difference in risk/benefit trade-offs for COVID-19 vaccination compared to vaccination against other infectious diseases.

In summary, our results quantify the risk/benefit trade-offs for COVID-19 vaccination, from the patients' perspective. Overall, the results are supportive of ongoing approaches to maximize vaccine effectiveness, while at the same time, being aware of individual differences, and highlighting the importance of shared decision-making.

ACKNOWLEDGEMENTS

The authors thank the Canadian Arthritis Patient Alliance (CAPA) for its assistance with developing and reviewing the survey used in this study and its help with recruiting participants. A number of other patient organisations in Canada also supported recruitment, for which the authors are very grateful. They are CAPA, Arthritis Research Canada (ARC)'s Arthritis Patient Advisory Board (APAB), Crohn's and Colitis Canada, and the Facebook group Rheumatoid Arthritis Canada. Clinical cohorts that participated in recruitment included the Rheum4U Precision Health Registry Cohort (Rheum4U). Rheum4U was established by Drs. Dianne Mosher, Claire Barber, Susanne Benseler, Paul MacMullan, Deborah Marshall, Marinka Twilt and is supported by Inelda Gjata, Namneet Sandhu, Martina Stevenson. Rheum4U would like to thank participating physicians and patients who contributed data to the cohort, as well as clinic staff, allied health professionals and registered nurses at the Richmond Road Diagnostic and Treatment Center and South Health Campus Hospital.

REFERENCES

FIGURE LEGENDS

Figure 1. Screenshot of choice task

Figure 2. Relative importance of attributes for the overall model and three group latent class analyses

Figure 3. Willingness to trade-off between vaccine effectiveness and disease flare. For any given increase in the absolute effectiveness of a vaccine (y-axis), the risk of flare that patients would be willing to accept (x-axis) can be estimated for the overall group and each identified latent class. The horizontal dashed line shows a hypothetical vaccine that provides a 10% absolute increase in effectiveness.

1. National Advisory Committee on Immunization (NACI). Recommendations on the use of COVID-19 vaccines. [Internet. Accessed Sept 23, 2022.] Available from: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html>.
2. Wraith DC, Goldman M, Lambert PH. Vaccination and autoimmune disease: what is the evidence? *Lancet* 2003;362:1659-66.
3. Curtis JR, Johnson SR, Anthony DD, et al. American College of Rheumatology Guidance for COVID-19 Vaccination in Patients With Rheumatic and Musculoskeletal Diseases: Version 1. *Arthritis Rheumatol* 2021;73:1093-107.

4. Hazlewood GS, Pardo JP, Barnabe C, et al. Canadian Rheumatology Association Recommendation for the Use of COVID-19 Vaccination for Patients With Autoimmune Rheumatic Diseases. *J Rheumatol* 2021;48:1330-9.
5. Murthy SK, Kuenzig ME, Windsor JW, et al. Crohn's and Colitis Canada's 2021 Impact of COVID-19 and Inflammatory Bowel Disease in Canada: COVID-19 Vaccines-Biology, Current Evidence and Recommendations. *J Can Assoc Gastroenterol* 2021;4:S54-S60.
6. Landewe RBM, Kroon FPB, Alunno A, et al. EULAR recommendations for the management and vaccination of people with rheumatic and musculoskeletal diseases in the context of SARS-CoV-2: the November 2021 update. *Ann Rheum Dis* (Epub ahead of print).
7. Bridges JF, Hauber AB, Marshall D, et al. Conjoint analysis applications in health--a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value Health* 2011;14:403-13.
8. Hazlewood GS. Measuring Patient Preferences: An Overview of Methods with a Focus on Discrete Choice Experiments. *Rheum Dis Clin North Am* 2018;44:337-47.
9. Reed Johnson F, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. *Value Health* 2013;16:3-13.
10. Barber CEH, Sandhu N, Rankin JA, et al. Rheum4U: Development and testing of a web-based tool for improving the quality of care for patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2019;37:385-92.

11. Johnson FR, Yang JC, Reed SD. The Internal Validity of Discrete Choice Experiment Data: A Testing Tool for Quantitative Assessments. *Value Health* 2019;22:157-60.
12. Campbell D, Erdem S. Including Opt-Out Options in Discrete Choice Experiments: Issues to Consider. *Patient* 2019;12:1-14.
13. Bech M, Gyrd-Hansen D. Effects coding in discrete choice experiments. *Health Econ* 2005;14:1079-83.
14. Machado PM, Lawson-Tovey S, Strangfeld A, et al. Safety of vaccination against SARS-CoV-2 in people with rheumatic and musculoskeletal diseases: results from the EULAR Coronavirus Vaccine (COVAX) physician-reported registry. *Ann Rheum Dis* 2022;81:695-709.
15. Weaver KN, Zhang X, Dai X, et al. Impact of SARS-CoV-2 Vaccination on Inflammatory Bowel Disease Activity and Development of Vaccine-Related Adverse Events: Results From PREVENT-COVID. *Inflamm Bowel Dis* (Epub ahead of print).
16. Ferreira ML, Herbert RD, Ferreira PH, et al. A critical review of methods used to determine the smallest worthwhile effect of interventions for low back pain. *J Clin Epidemiol* 2012;65:253-61.
17. Thomas M, Marshall DA, Choudhary D, Bartlett SJ, Sanchez AL, Hazlewood GS. The Application of Preference Elicitation Methods in Clinical Trial Design to Quantify Trade-Offs: A Scoping Review. *Patient* 2022;15:423-34.
18. Araujo CSR, Medeiros-Ribeiro AC, Saad CGS, et al. Two-week methotrexate discontinuation in patients with rheumatoid arthritis vaccinated with inactivated SARS-CoV-2 vaccine: a randomised clinical trial. *Ann Rheum Dis* 2022;81:889-97.

19. Curtis JR, Johnson SR, Anthony DD, et al. American College of Rheumatology Guidance for COVID-19 Vaccination in Patients With Rheumatic and Musculoskeletal Diseases: Version 3. *Arthritis Rheumatol* 2021;73:e60-e75.
20. Bijlsma JW, Force EC-T. EULAR 2021 updated viewpoints on SARS-CoV-2 vaccination in patients with RMDs: a guidance to answer patients' questions. *Ann Rheum Dis* 2022;81:786-8.
21. Siegel CA, Melmed GY, McGovern DP, et al. SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting. *Gut* 2021;70:635-40.
22. Durand C, Eldoma M, Marshall DA, Bansback N, Hazlewood GS. Patient Preferences for Disease-modifying Antirheumatic Drug Treatment in Rheumatoid Arthritis: A Systematic Review. *J Rheumatol* 2020;47:176-87.
23. Hazlewood GS, Loyola-Sanchez A, Bykerk V, et al. Patient and rheumatologist perspectives on tapering DMARDs in rheumatoid arthritis: a qualitative study. *Rheumatology (Oxford)* 2022;61:606-16.
24. Landgren E, Bremander A, Lindqvist E, Nylander M, Van der Elst K, Larsson I. "Mastering a New Life Situation" - Patients' Preferences of Treatment Outcomes in Early Rheumatoid Arthritis - A Longitudinal Qualitative Study. *Patient Prefer Adherence* 2020;14:1421-33.
25. Marshall D, Bridges JF, Hauber B, et al. Conjoint Analysis Applications in Health - How are Studies being Designed and Reported?: An Update on Current Practice in the Published Literature between 2005 and 2008. *Patient* 2010;3:249-56.

26. Public Health Agency of Canada. Canadian COVID-19 vaccination coverage report. Ottawa: Public Health Agency of Canada. [Internet. Accessed Sept 23, 2022.] Available from: <https://health-infobase.canada.ca/covid-19/vaccination-coverage/>.
27. Widdifield J, Eder L, Chen S, et al. COVID-19 Vaccination Uptake Among Individuals With Immune-mediated Inflammatory Diseases in Ontario, Canada, Between December 2020 and October 2021: A Population-based Analysis. *J Rheumatol* 2022;49:531-6.
28. Putman M, Kennedy K, Sirotich E, et al. COVID-19 vaccine perceptions and uptake: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey. *Lancet Rheumatol* 2022;4:e237-e40.
29. Boekel L, Hooijberg F, Besten YR, et al. COVID-19 vaccine acceptance over time in patients with immune-mediated inflammatory rheumatic diseases. *Lancet Rheumatol* 2022;4:e310-e3.
30. Gaur P, Agrawat H, Shukla A. COVID-19 vaccine hesitancy in patients with systemic autoimmune rheumatic disease: an interview-based survey. *Rheumatol Int* 2021;41:1601-5.
31. Ko T, Dendle C, Woolley I, Morand E, Antony A. SARS-COV-2 vaccine acceptance in patients with rheumatic diseases: a cross-sectional study. *Hum Vaccin Immunother* 2021;17:4048-56.

Table 1. Attributes and levels included in DCE

Attribute	Levels
Number of shots	One shot
	Two shots (separated by 1 month, as tested in the trials)
	Two shots (separated by 4 months, longer than tested in the trials)
Vaccine effectiveness after full dose (preventing symptomatic COVID-19 infection)	30%
	50%
	75%
	95%
Likelihood of having a flare of your autoimmune condition in the month after having the vaccine	< 1%
	1%
	2%
	5%
	10%
	20%
Rare but serious risks	None identified
	1 out of 1,000,000
	5 out of 1,000,000
	10 out of 1,000,000

TABLE 2. Patient characteristics

Age, years, median (25 th , 75 th percentile)	46 (36, 58)
Gender, n (%)	
Male	59 (10.7)
Female	488 (88.6)
Non-binary / third gender	1 (0.2)
Prefer not to answer	3 (0.5)
Ethnicity, n (%)	
Asian	33 (6.0)
Black	4 (0.7)
Caucasian	488 (88.6)
First Nations	9 (1.6)
Hispanic	5 (0.9)
South Asian	8 (1.5)
Other	18 (3.3)
Prefer not to answer	4 (0.7)
Highest level of education, n (%)	
Elementary school	3 (0.5)
High school	38 (6.9)
Some postsecondary	47 (8.5)
Postsecondary certificate or diploma	164 (29.8)

University bachelor's degree	174 (31.6)
Above university bachelor's degree	116 (21.1)
Prefer not to answer	9 (1.6)
Annual household income, n (%)	
<\$20,000	18 (3.3)
\$20,000-\$49,999	45 (8.2)
\$50,000-\$99,999	149 (27.0)
\$100,000-\$249,000	197 (35.8)
>\$250,000	26 (4.7)
Prefer not to answer	116 (21.1)
Employment status, n (%)	
Working from home	193 (35.0)
Working outside home	164 (29.8)
Not currently working	184 (33.4)
Prefer not to answer	10 (1.8)
Immune Mediated Inflammatory Disease, n (%)	
Ankylosing spondylitis / spondyloarthritis	21 (3.8)
Inflammatory bowel disease	263 (47.7)
Myositis	2 (0.4)
Multiple sclerosis	2 (0.4)
Polymyalgia rheumatica	2 (0.4)

Psoriasis	27 (4.9)
Psoriatic arthritis	15 (2.7)
Reactive arthritis	4 (0.7)
Rheumatoid arthritis	207 (37.6)
Scleroderma	4 (0.7)
Sjogren's syndrome	22 (4.0)
Systemic lupus erythematosus	88 (16.0)
Vasculitis	8 (1.5)
Other	52 (9.4)
Medications, n (%)	
TNF inhibitors	163 (29.6)
Rituximab	11 (2.0)
Vedolizumab	31 (5.6)
Other biologic DMARDS	62 (11.3)
JAK Inhibitors	25 (4.5)
Methotrexate	152 (27.6)
Azathioprine (Imuran) or 6-mercaptopurine	56 (10.2)
Hydroxychloroquine (Plaquenil)	152 (27.6)
Leflunomide (Arava)	18 (3.3)
Sulfasalazine	44 (8.0)
Mycophenolate mofetil (CellCept)	21 (3.8)

Calcineurin inhibitors	6 (1.1)
Prednisone (20mg per day or less)	36 (6.5)
Prednisone (more than 20mg per day)	3 (0.5)
Other	56 (10.2)
None	34 (6.2)
Patient global assessment of disease activity (scale 0 to 10), median (25 th , 75 th percentile)	3 (2, 6)
Flares requiring a change in treatment in the past year, median (25 th , 75 th percentile)	1 (0, 3)
Comorbidities, n (%)	
Lung Disease	57 (10.3)
Heart Disease	19 (3.4)
High Blood Pressure (Hypertension)	102 (18.5)
Diabetes	24 (4.4)
Kidney Disease	23 (4.2)
Liver Disease	15 (2.7)
Dementia	0 (0.0)
Stroke	8 (1.5)
Cancer	11 (2.0)
Current smoking, n (%)	
Yes	25 (4.5)

Prefer not to answer	5 (0.9)
Prior Covid-19 infection, n (%)	
Yes	6 (2.2)
Prefer Not to Say	1 (0.2)
Doses Covid-19 vaccine, n (%)	
0	32 (5.8)
1	165 (29.9)
2	354 (64.2)
Covid-19 vaccine received, n (%)*	
AstraZeneca-Oxford	20 (3.6)
Johnson & Johnson	0 (0.0)
Moderna	102 (18.5)
Pfizer-BioNTech	381 (69.1)
Mixed	16 (3.1)
Recruited through a clinical cohort	142 (26)

Table 3. Results of discrete-choice experiment

Attribute and Level	Value (coefficient)*, mean (95% CI)	Relative importance
Categorical model		
Dosing		3.6%
One dose	-0.06 (-0.13, 0.01)	
Two doses one month apart	0.15 (0.08, 0.22)	
Two doses four months apart	-0.09 (-0.16, -0.02)	
Vaccine Effectiveness		66.4%
30%	-2.34 (-2.47, -2.21)	
50%	-0.65 (-0.74, -0.57)	
75%	0.84 (0.76, 0.92)	
95%	2.16 (2.05, 2.26)	
Likelihood of having a flare		21.4%
<1%	0.45 (0.33, 0.57)	
1%	0.43 (0.31, 0.54)	
2%	0.33 (0.22, 0.44)	
5%	0.12 (0.00, 0.23)	
10%	-0.33 (-0.45, -0.21)	
20%	-1.00 (-1.12, -0.87)	
Rare but serious risks		8.9%

None identified	0.21 (0.13, 0.30)	
1 out of 1,000,000	0.18 (0.09, 0.27)	
5 out of 1,000,000	-0.03 (-0.12, 0.06)	
10 out of 1,000,000	-0.37 (-0.46, -0.27)	
No vaccine (opt-out)	-1.14 (-1.23, -1.05)	
Linear model		
Dosing		3.7%
One dose	-0.07 (-0.14, 0.01)	
Two doses one month apart	0.15 (0.08, 0.22)	
Two doses four months apart	-0.09 (-0.16, -0.02)	
Vaccine effectiveness (per 1% increase from 30% to 95%)	0.07 (0.06, 0.07)	64.8%
Likelihood of flare (per 1% increase from <1% to 20%)	-0.08 (-0.08, -0.07)	22.6%
Rare but serious risks (per increase of 1/1,000,000 from none to 10/1,000,000)	-0.06 (-0.07, -0.05)	8.9%
No vaccine (opt-out)	-1.18 (-1.27, -1.09)	

*Value estimates are the coefficients from a main-effects multinomial logit model. Estimates are effects-coded, meaning that for categorical attributes, the estimates of the levels for any given attribute are centered on zero. Model fit: Bayesian Information Criteria for categorical model: 6,533; Bayesian Information Criteria for continuous model: 6,485

Accepted Article

Abbreviations: CI, confidence interval

If these were your COVID-19 vaccine options, which one would you choose?

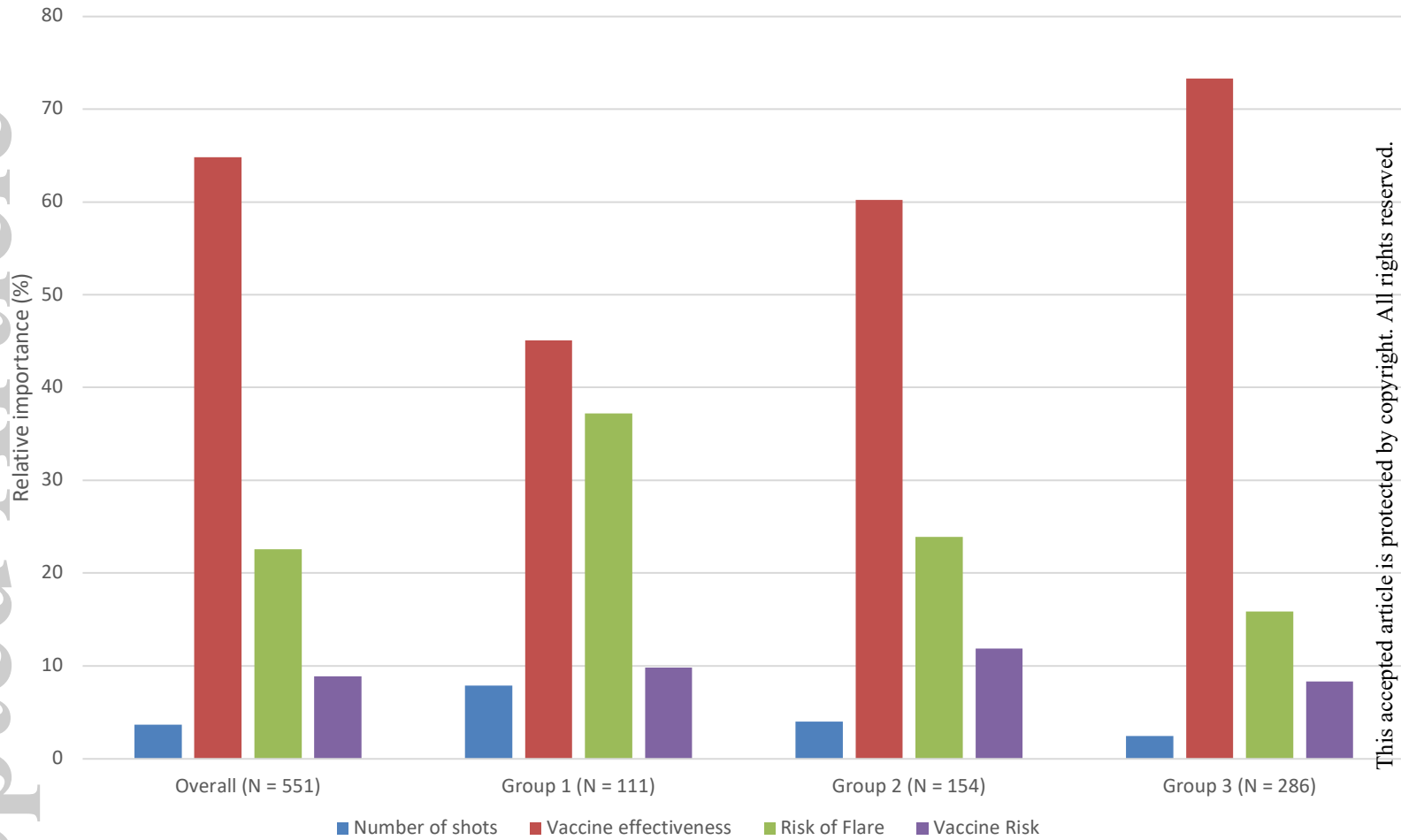
Important: If you have already had a COVID-19 vaccine, please respond as though you haven't yet.
(3 of 10)

	Vaccine 1	Vaccine 2	None
Vaccine effectiveness after full dose (preventing symptomatic COVID-19)	75%	95%	I would not have either of these vaccines
Likelihood your autoimmune condition will flare in the month after having the vaccine	2%	20%	
Rare but serious risks	10 out of 1,000,000	5 out of 1,000,000	
Number of shots	Two shots (separated by 1 month, as tested in the trials)	1 shot (as tested in the trials)	
	Select	Select	Select

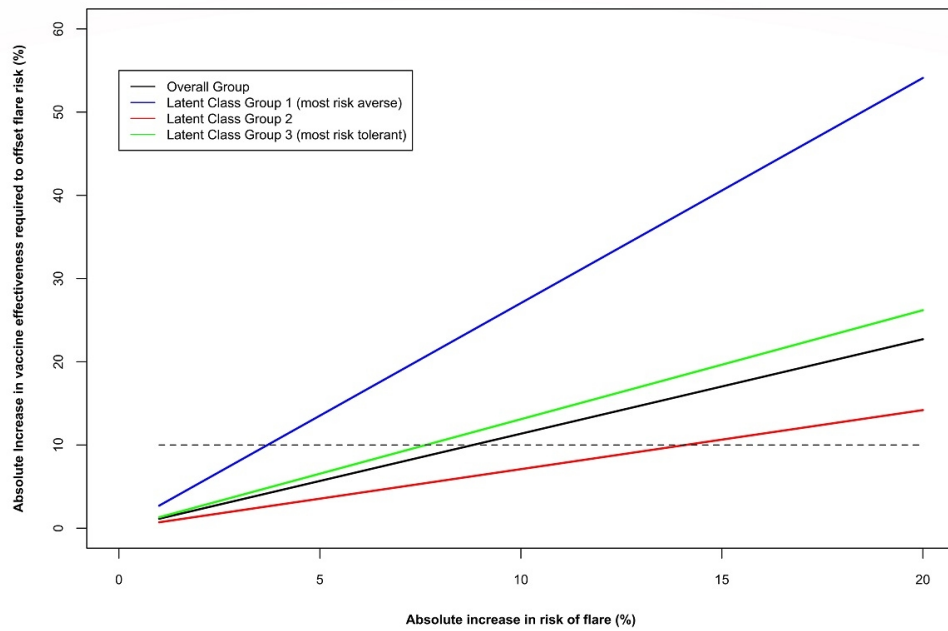
Figure 1. Screenshot of choice task

523x340mm (144 x 144 DPI)

Accepted Article



This accepted article is protected by copyright. All rights reserved.



317x221mm (96 x 96 DPI)