

Vaccine Hesitancy: The Next Challenge in the Fight Against COVID-19

Amiel A. Dror (✉ amielror@gmail.com)

Department of Otolaryngology, Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel <https://orcid.org/0000-0002-7178-6771>

Netanel Eisenbach

Department of Otolaryngology, Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

Shahar Taiber

Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Nicole G. Morozov

Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Matti Mizrachi

Department of Otolaryngology, Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

Asaf Zigran

Oral and Maxillofacial Department, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

Samer Srouji

Oral and Maxillofacial Department, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

Eyal Sela

Department of Otolaryngology, Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel; The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel

Research Article

Keywords: COVID-19, SARS-CoV-2 vaccine, vaccine hesitancy, healthcare staff, vaccine safety, Israel

Posted Date: June 17th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-35372/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published on August 12th, 2020. See the published version at <https://doi.org/10.1007/s10654-020-00671-y>.

Abstract

Vaccine hesitancy remains a barrier to full population inoculation against highly infectious diseases. With rapid developments in a potential COVID-19 vaccine by scientists across the globe, public concerns over the safety and side effects of such a vaccine may contribute to vaccine hesitancy. We analyzed anonymous questionnaire answers regarding acceptance of a potential COVID-19 vaccine posed to healthcare workers and the general population throughout Israel with a total respondent count of 1941. Our results demonstrate higher rates of COVID-19 vaccine hesitancy among various groups: parents, nurses, and medical workers not caring for SARS-CoV-2 positive patients. Healthcare staff involved in the care of COVID-19 positive patients and individuals who consider themselves at higher risk of disease were more likely to self-report acquiescence to obtain a COVID-19 vaccine if and when it becomes available. Interventional educational campaigns targeted towards populations at risk of vaccine hesitancy, therefore, are urgently needed to combat misinformation and resultant low inoculation rates.

Introduction

The rapidly evolving COVID-19 pandemic is in some ways a global unifier: countries across the world are unanimously challenged to contain the spread of SARS-CoV-2. The World Health Organization (WHO) is navigating a global campaign in prevention, early diagnosis, and medical treatment around the world. Parallel to ongoing efforts to flatten the curve of infection, there are massive organizational efforts to quickly develop a vaccine to prevent future infections with this deadly disease, a crowning achievement for global health organizations. Many clinical vaccine trials are in progress and the eventual public distribution of a safe and effective vaccine is estimated to be between six to 18 months [1]. As previously demonstrated, even vaccine availability does not guarantee sufficient population vaccination as evidenced by vaccine hesitancy [2]. Insufficient vaccination can lead to continued disease outbreaks [3]. While ensuring the vaccine will be accessible and affordable to all is a primary goal, prior research indicates that vaccine compliance is variable and inconsistent, demonstrating the need for continued public educational campaigns about the safety and efficacy of vaccination.

To evaluate the current vaccination compliance rate among the Israeli populations, we distributed a multicenter anonymous questionnaire to medical staff and civilians across the country, asking if they would agree to receive a SARS-CoV-2 vaccine once available. We analyzed the 1941 responses based on occupation, exposure to either suspected or confirmed SARS-CoV-2 patients, and history of vaccinations to influenza strains prior to the COVID-19 epidemic. The responses of the 829 healthcare staff were compared with 1112 responders of the general population. All questionnaires were filled out during the mandatory quarantine period in Israel. We hypothesized that a higher rate of vaccine compliance would be observed among medical staff members who stand at the forefront of the COVID-19 crisis.

Surprisingly, we witnessed a high rate of vaccine skepticism among medical staff who normally advocate for community vaccination. Moreover, most of the responders who are noncompliant with recommended vaccinations expressed concerns regarding the safety of a rapidly-developed vaccine. Our data also show

that individuals who consider themselves to be at a higher risk of the disease have a higher compliance to vaccination.

Our study highlights the necessity of early educational campaigns produced and disseminated by institutions such as the WHO and health institutions on a country level specifically directed at medical staff, given their role as advocates for widespread vaccination, highlighting the safety and efficacy of vaccination. Taken together, these results imply that vaccination compliance relies on a personal risk-benefit perception that may be influenced by misinformation regarding vaccine safety. Because one of the main concerns described by study participants is the speed at which the COVID-19 vaccine is being developed, educational campaigns should focus on alleviating this apprehension in particular.

Methods

Study design

Ethical approval was granted by the Research Ethics Committee of the Galilee Medical Center before the initiation of this study. Informed consent was provided to responders within the introductory web page prior to the survey enrollment. The web-based survey followed the American Association for Public Opinion Research (AAPOR) reporting guideline. The survey was anonymous, and confidentiality of information was assured. Participants were permitted to terminate the survey at any time point. The survey was conducted by regions and stratified for the health care team and for the general population. The survey was distributed one week after the first social distancing and quarantine regulations went into effect in Israel (March 19, 2020). The survey was distributed electronically via Qualtrics health care professionals at academic medical centers across Israel and in parallel to the general population over a 2-week period.

Data collection

Demographic data were self-reported by the participants and included classifications such as sex (male or female), age (18-25, 26-30, 31-40, 41-50, 51-60 or >60 years), geographic location, a region of residence (urban or rural), marital status and having children. Participants were asked whether they vaccinate themselves or their children (if applicable) for the seasonal influenza vaccine and if they are willing to accept future COVID-19 vaccination (either for themselves and for their children, if applicable).

Responders avoiding the COVID-19 vaccine option were presented with specific questions regarding the reasons for vaccine hesitancy.

Additional specific questions for the health care team included occupation (e.g. physician, nurse, technician, or other health care professionals), place of work (e.g. hospital, ambulatory, or community), medical discipline (e.g. internal medicine, general surgery, intensive care unit, anesthesiologist, imaging, etc.), and whether they directly engaged with diagnosing, treating, or providing nursing care to patients with either suspected or confirmed positive SARS-CoV-2. Specific questions for the general population included the occupation status during the COVID 19 crisis (e.g. working as usual, temporary

unemployment, lost job), and educational level for the general population (\leq undergraduate or \geq postgraduate)

Statistical analysis

To isolate predictors of vaccine compliance we performed a multivariate logistic regression. The variables that were included in our model were: age, gender, subjective personal risk, having infected relatives, being a healthcare worker, and parental status. We did not include other variables to which we had a high rate of missing data, such as economic status, area of residence, education, and others. Whenever multiple comparisons were performed, Dunn, Tukey or Bonferroni were used to adjust P values. We used IBM SPSS Statistics (IBM Corporation, Armonk, New York, USA) and GraphPad Prism version 8 (GraphPad Software, La Jolla, CA, USA) for all statistical analysis.

Results

Surprisingly, our findings suggest that employment within the healthcare sector does not significantly influence the respondents' acceptance or rejection of a potential COVID-19 vaccine (Fig 1).

Comparative analysis between varying adoption rates for future COVID-19 vaccine and current influenza vaccination status reveals an interesting observation: the rate of acceptance for a COVID-19 vaccine among physicians and nurses overall is lower compared to their acceptance rates of seasonal influenza vaccination. Further analysis of the subdivisions with healthcare workers (Fig 2) reveals that vaccine acceptance among doctors (78%) is significantly higher than nurses (61%; $p < 0.01$), but is indiscriminate to the rate observed by the entire population (75%). Lower vaccination acceptance rates among nurses may potentially lead to a decrease in future vaccination compliance of individuals who coincidentally engage with vaccine-hesitant nurses on a professional or personal level. When comparing subspecialties (Fig 3), healthcare workers in internal medicine departments have a prominently higher vaccine acceptance rate (91%) compared to those working in general surgery departments (75%; $P < 0.01$). As expected, medical teams in COVID19 related departments (94%) show higher acceptance rates compared to those in non-COVID-19 departments (77%; $P < 0.01$).

According to our survey, the most significant positive predictor for people to accept a potential COVID-19 vaccine is their current influenza vaccination status. People willing to receive influenza vaccinations in ordinary years have a strong tendency to accept a future COVID-19 vaccine. Our survey demonstrates a significantly higher compliance for potential future vaccination among responders who lost their job during the crisis (96%) as compared to those who continued working (72%; $P < 0.01$) (via essential occupations) or those who stayed home but were confident about their returns to work when possible (75%; $P < 0.01$) (Fig. 4).

Another positive predicting factor to accept the future vaccine is the self-perception of individuals who categorize themselves under high-risk for severe COVID19 infection. Interestingly, respondents do not consider age to be a factor in the 'high-risk' category. In other words, healthy people in their 70's with no

clinical history do not consider their age as a contributing factor to whether or not they acquire future vaccination. Of note, a positive predicting factor for vaccine acceptance is related to respondents' sex; males are more likely to accept the potential COVID-19 vaccine.

Regardless of occupation, the difference in vaccination acceptance between parent and non-parent population populations is apparent. Interestingly, the prominent trend amongst respondents with children shows that having a child is a negative predictor for accepting future vaccination (Fig, 1).

Discussion

The COVID-19 pandemic has dramatically affected the lives of people worldwide. Countries' efforts to fight the pandemic have included a variety of strict measurements including intermittent lockdowns of regions and countries [4]. Despite the disease's deadliness, the healthcare sector has become one of the most important leaders in efforts against COVID-19; it responded immediately despite shortages of critical protective equipment and resources that has directly affected survival rates of patients flooding COVID-19 departments. Hence, we hypothesized that the current COVID-19 pandemic would increase compliance with future vaccinations, especially among healthcare workers. The data demonstrate several positive predictors for vaccination: status as a physician, employment in a healthcare setting caring specifically for SARS-CoV-2 positive patients, unemployment during the quarantine period, and sex-specifically male, with negative predictors including: status as a nurse and parenthood.

Our results indicate that healthcare providers not caring for COVID-19 positive patients appeared to be less trustful of a COVID-19 vaccine than the general population. Nurses, in addition, tend to be more vaccine hesitant than physicians. Though nurses have slightly higher rates of annual influenza vaccination than the general population, nurses remain much more hesitant about COVID-19 inoculation than the general population. This discovery is of major concern because healthcare workers represent the most reliable social resource to encourage vaccination among the general population.

We presumed that the devastating economic consequences of COVID-19-related restrictions would lead to an increase in compliance rates for potential future vaccines among the general population due to a desire to prevent catastrophic lay-offs, high underemployment levels, and school closures.

Unemployment and job insecurity is a positive predictor for acceptance of COVID-19 vaccination, contrasting with parenthood as a negative predictor. A possible explanation for the observation that parenthood is a negative predictor of vaccination is that parents have heightened concerns for their own safety; potentially deleterious effects of a vaccine could compromise their ability to care for their children. Future research should elucidate the reasons underlying this intriguing association between parenthood and self-avoidance of vaccination.

There is a positive association for male acceptance of COVID-19 vaccination. Several independent reports demonstrate higher risks for severe COVID-19 infection, complications, and death among males [4]. While other sex-based health disparities have been extensively reviewed in public media, such as cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer[5], the sex-based

difference in COVID-19 mortality can be an area of vaccine targeting towards men. This observation is of particular note because women tend to have higher influenza vaccination rates than men [6].

While “herd immunity” is achieved by high rates of vaccination dispersed homogeneously throughout a population [7], even higher vaccination rates are necessary among communities containing individuals at higher disease risk [8]. Sustained encouragement of people with greater health risks to accept the future COVID-19 vaccine could lead to reduced morbidity and mortality while at the same time releasing valuable resources of the healthcare system to deliver equally important ambulatory activity.

Government mandated social isolation techniques to avoid viral transmission have led to rising unemployment rates and school suspensions [9], leaving workers with tenuous economic situations and parents struggling to provide a residual educational framework at home. Additional emotional distress in the face of extensive media coverage of the rising numbers of casualties, overburdened health systems, and insufficient government responses to COVID-19 has perhaps risen communal anxieties and distrust in healthcare systems and state actors [10]. These fears could also be contributing to wariness of the safety of a potential COVID-19 vaccine among the general public.

Concerns among responders regarding potential COVID-19 vaccines provide an important perspective for possible interventional educational programs to enhance vaccination rates. Of greatest concern to Israeli healthcare and civilian respondents were issues related to quality control, side effects, and efficacy of the vaccine. While current literature covers extensively vaccine efficacy and safety [11,12], the vast majority of the responders’ concerns, both among healthcare workers and non-healthcare workers alike, are due to public uncertainty of the COVID-19 vaccine’s rapid development. These concerns could hamper the achievements of the scientific community and its attempts to disseminate the vaccine. While scaled-up vaccine-manufacturing capacities and strategies assure that vaccines will be affordable to most people, we as a scientific community must act to educate, inform, and intervene to increase COVID-19 compliance rates of the entire population.

Declarations

Competing interests: The authors declare no competing interests.

References

1. Callaway E. The race for coronavirus vaccines: a graphical guide. *Nature*. 2020;580:576–7.
2. Omer SB, Salmon DA, Orenstein WA, DeHart MP, Halsey N. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. *N Engl J Med*. 2009;360:1981–8. Available from: doi:10.1056/NEJMSa0806477
3. Bankamp B, Hickman C, Icenogle JP, Rota. Successes and challenges for preventing measles, mumps and rubella by vaccination. *Curr. Opin. Virol*. Elsevier B.V.; 2019. p. 110–6.

4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395:507–13.
5. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ*. 2020. p.
6. Buchan SA, Kwong JC. Trends in influenza vaccine coverage and vaccine hesitancy in Canada, 2006/07 to 2013/14: results from cross-sectional survey data. *C open*. 2016;4:E455–62.
7. Rashid H, Khandaker G, Booy R. Vaccination and herd immunity: what more do we know? *Curr Opin Infect Dis*. 2012;25:243–9.
8. Wateska AR, Nowalk MP, Lin CJ, Harrison LH, Schaffner W, Zimmerman RK, et al. An intervention to improve pneumococcal vaccination uptake in high risk 50-64 year olds vs. expanded age-based recommendations: an exploratory cost-effectiveness analysis. *Hum Vaccin Immunother*. 2019;15:863–72.
9. Lee J. Mental health effects of school closures during COVID-19. *Lancet Child Adolesc Heal*. 2020;
10. Gunnell D, Appleby L, Arensman E, Hawton K, John A, Kapur N, et al. Suicide risk and prevention during the COVID-19 pandemic. *The lancet Psychiatry*. 2020;
11. Dean NE, Gsell P-S, Brookmeyer R, De Gruttola V, Donnelly CA, Halloran ME, et al. Design of vaccine efficacy trials during public health emergencies. *Sci Transl Med*. 2019;11.
12. Corey BL, Mascola JR, Fauci AS, Collins FS. A strategic approach to COVID-19 vaccine R&D. 2020;

Figures

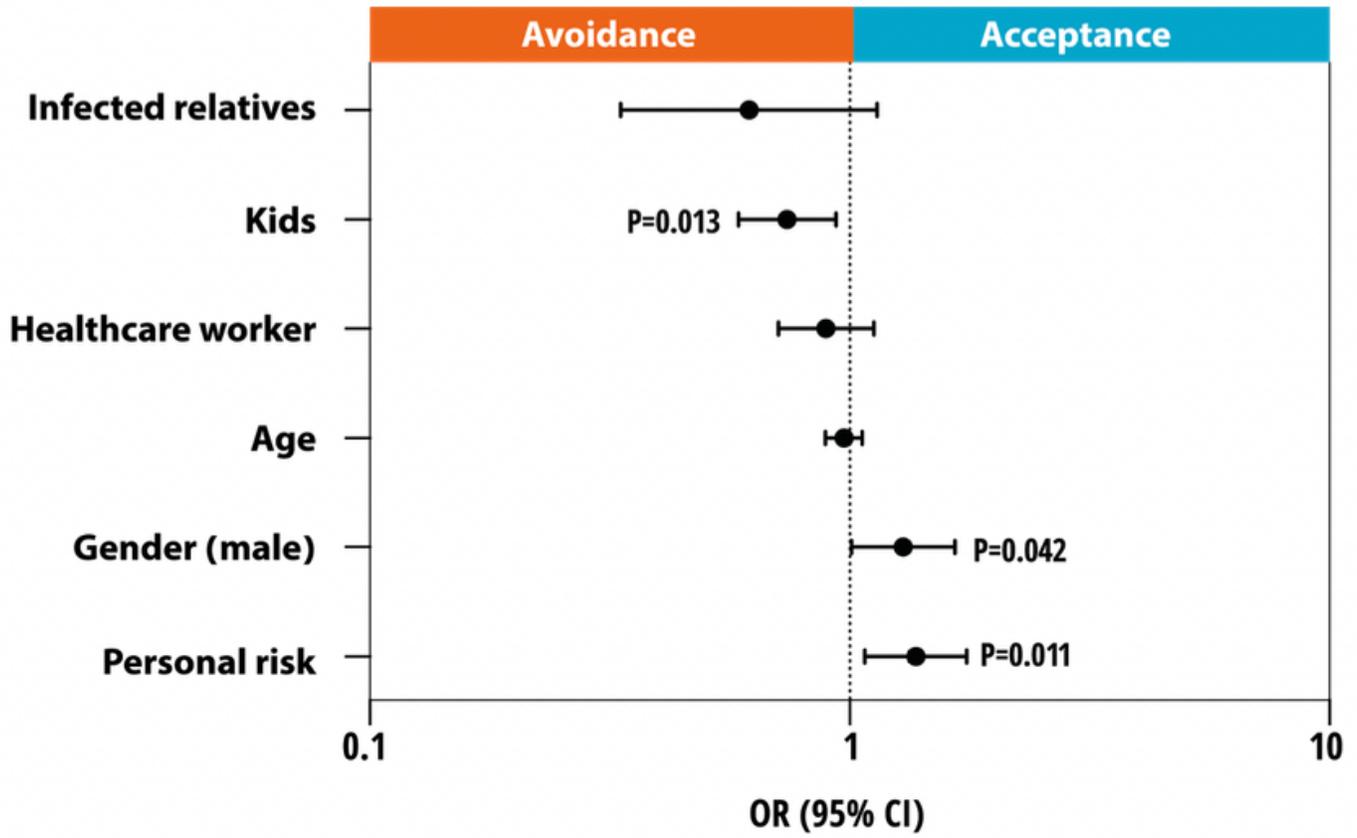


Figure 1

Forrest plot demonstrates the degree to which respondents' demographics affect future vaccine acceptance among responders. Combined data analysis of 1941 respondents lists the different parameters plotted with overlap. Having children is the strongest negative predictor for acceptance of potential COVID-19 vaccination among responders. Positive predictors include sex (male) and the self-perception of disease risk among responders. Other characteristics such as age and occupation within the healthcare system does not have a significant influence on responders' decision whether to accept vaccination or not.

Acceptance rates for future COVID-19 vaccination
(healthcare professional compared with the general population)

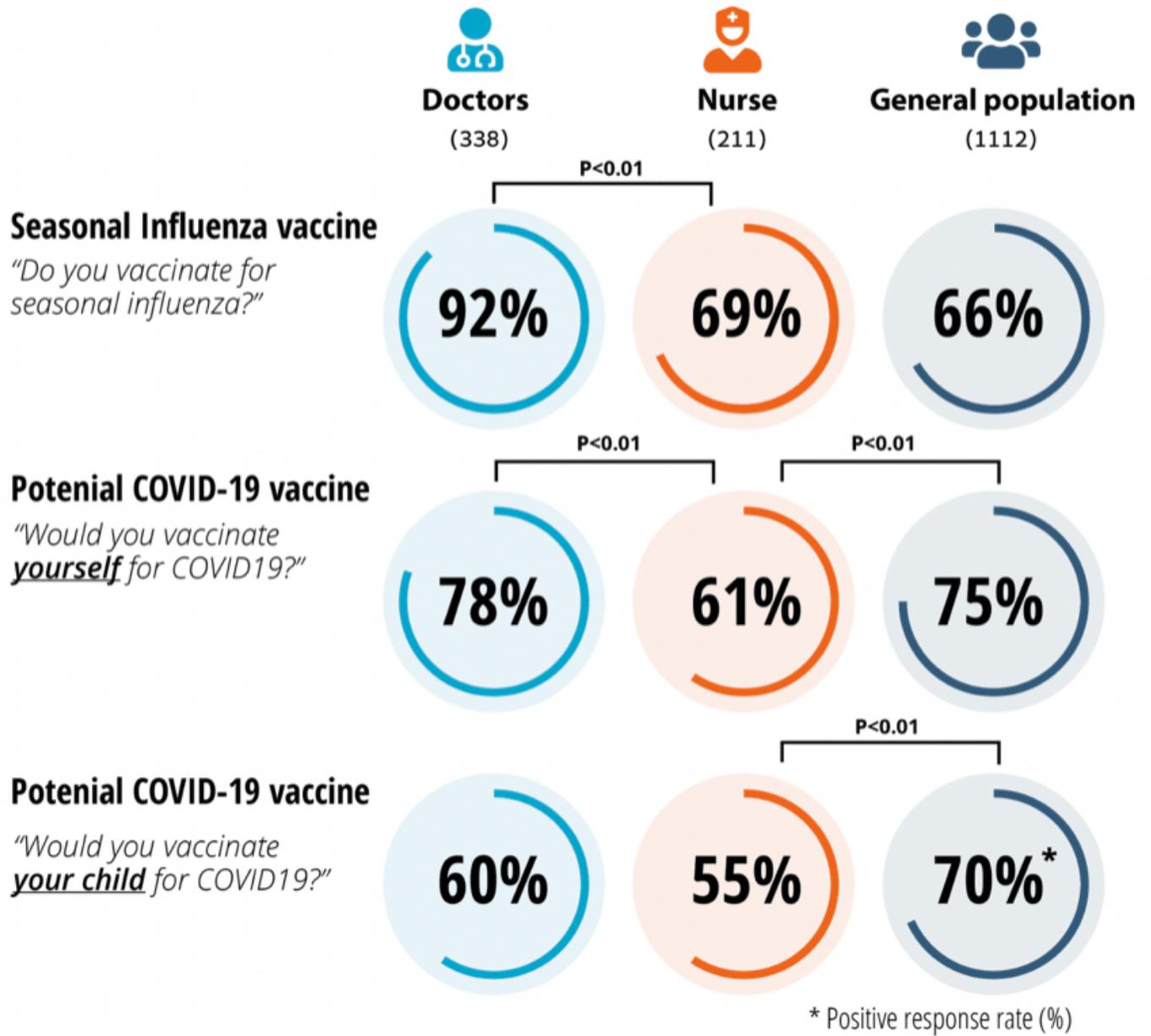


Figure 2

Association between compliance for seasonal influenza vaccination and for potential COVID-19 vaccination.

Acceptance rates for future COVID-19 vaccination
(according to clinical disciplines and exposure to COVID-19 departments)

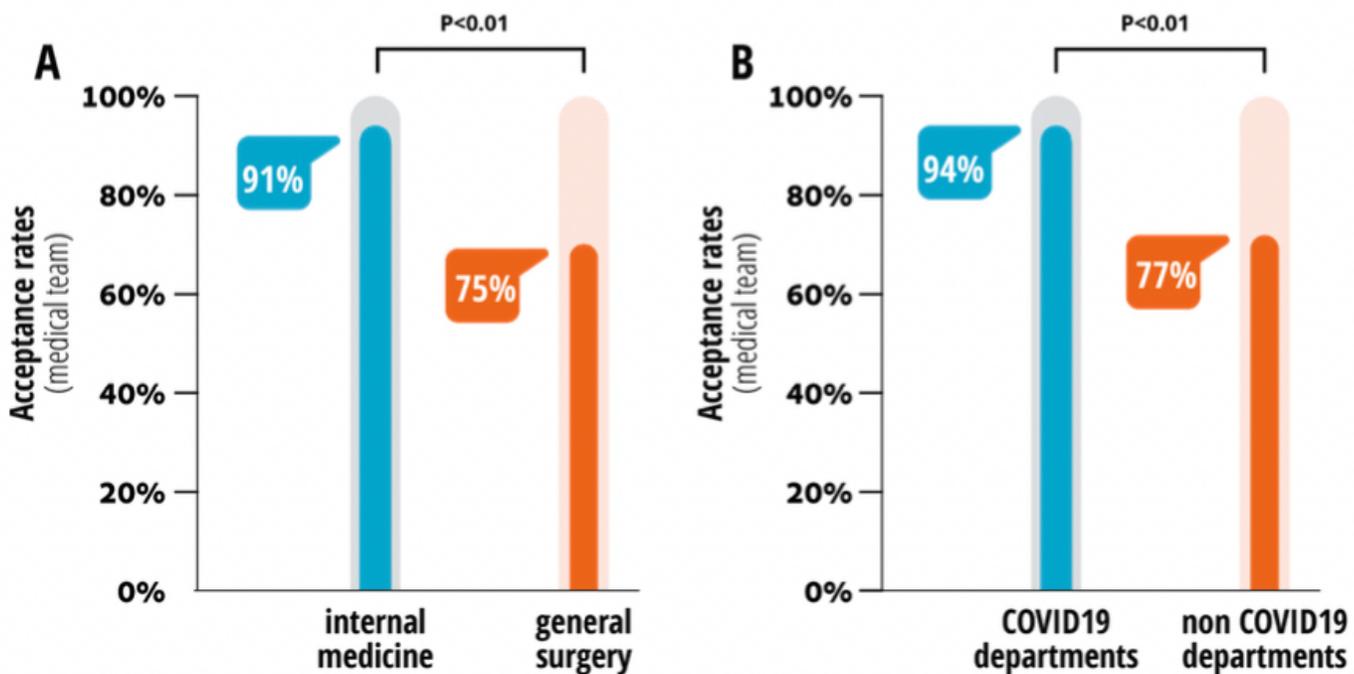


Figure 3

Rate of vaccine acceptance is significantly higher among health workers within internal medicine and COVID-19 dedicated departments.

Acceptance rates for future COVID-19 vaccination (according to occupational status during the crisis)

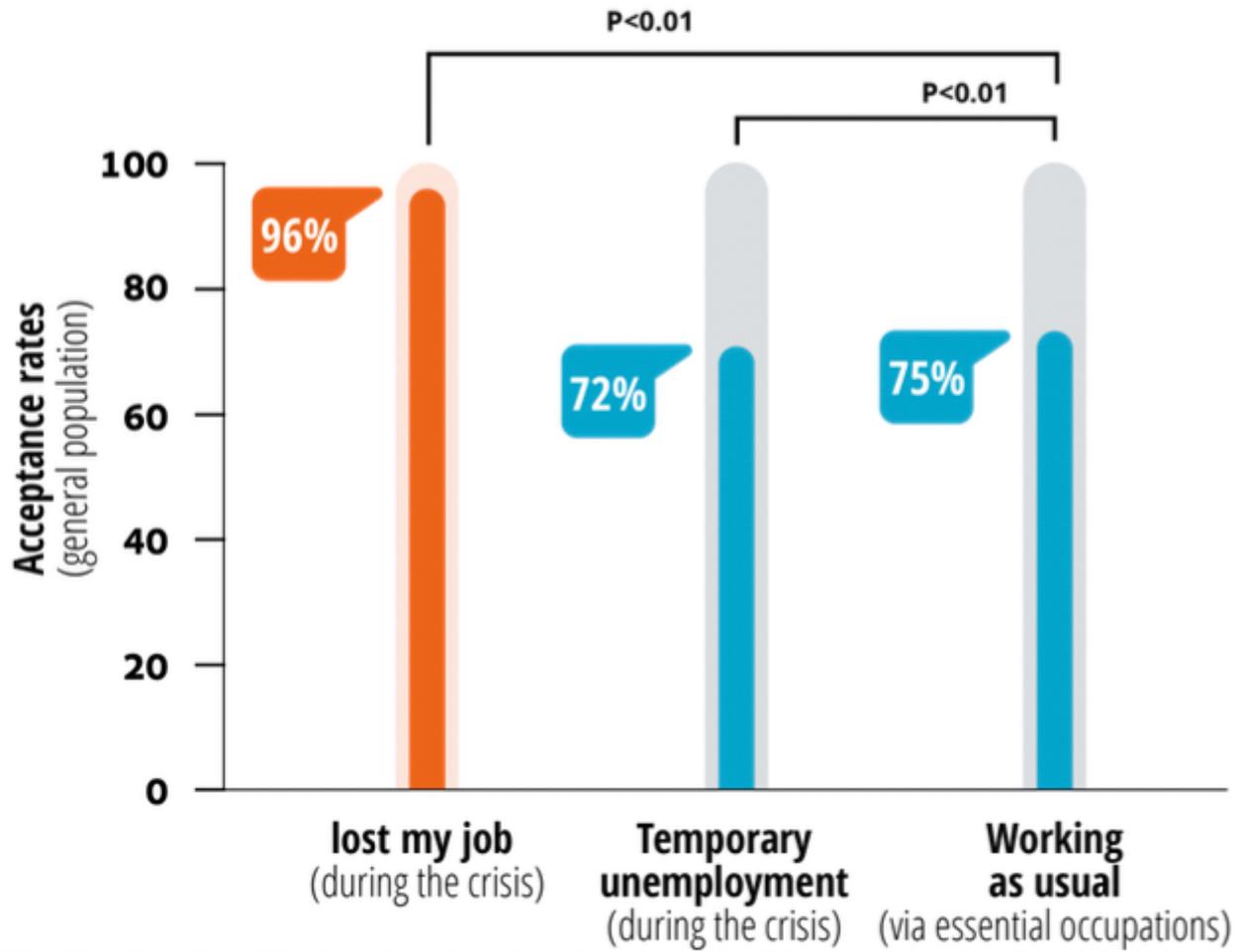


Figure 4

A significantly higher compliance for potential future vaccination among responders who lost their job during the crisis.

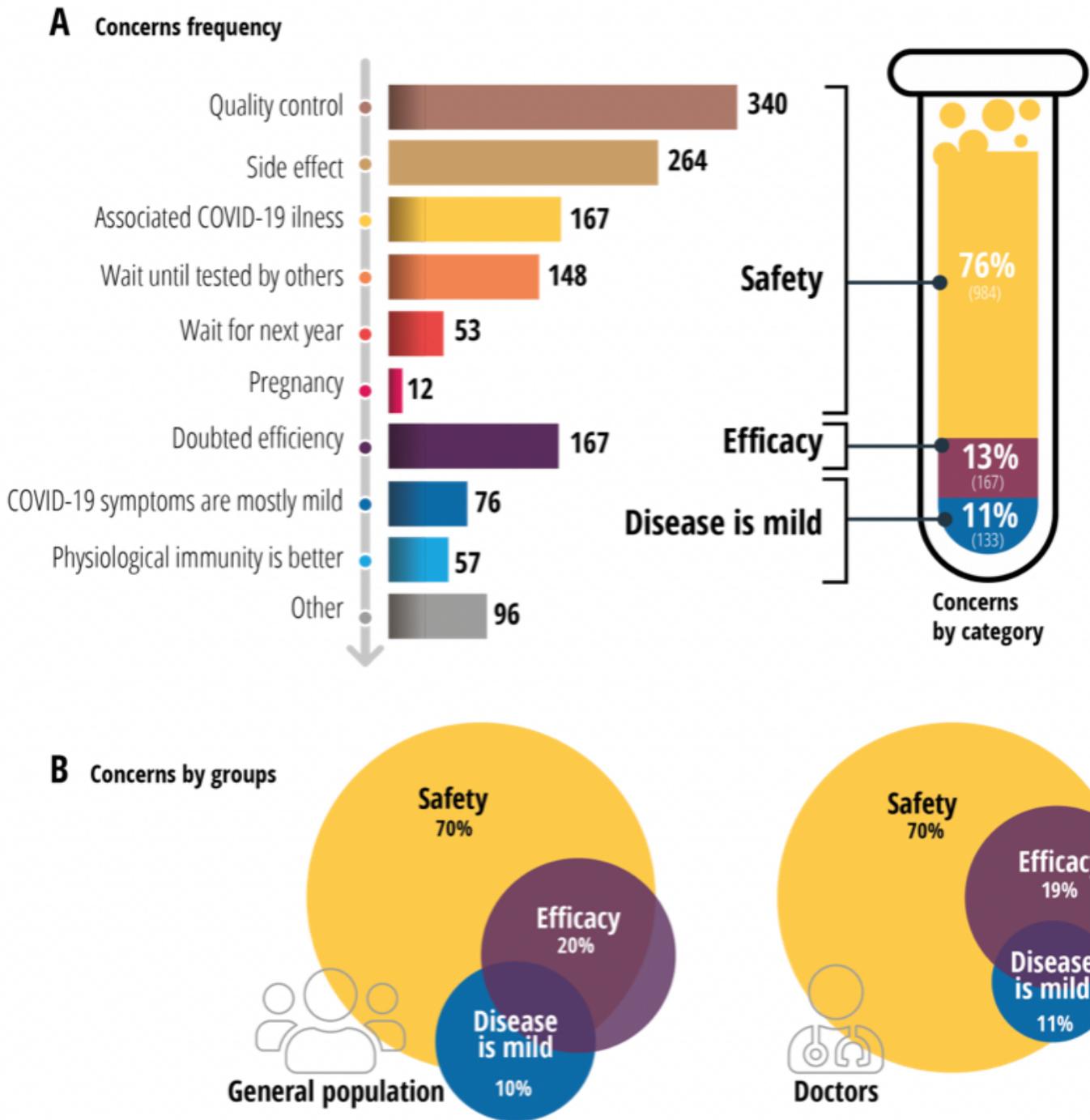


Figure 5

Concerns among responders regarding potential COVID19 vaccine. A. A list of various concerns regarding potential future COVID-19 vaccine among responders. B. Venn diagrams combining the concerns into three main categories for safety, efficacy, and mild symptoms of the disease.