vaccines

MDPI

Article

Sensitivity to COVID-19 vaccine effectiveness and safety in Shanghai, China

Jia Lu [1,†], Xiaosa Wen [1], Qi Guo [1,†], Mengdi Ji [2], Felicia Zhang [2], Abram L. Wagner [2,*], and Yihan Lu [3]

[1] Department of Immunizations, Minhang Centers for Disease Control and Prevention, Shanghai, China
[2] Department of Epidemiology, University of Michigan, Ann Arbor, MI, USA
[3] Key Laboratory of Public Health Safety (Ministry of Education), Fudan University School of Public Health, Shanghai, China
* Correspondence: awag@umich.edu
† The authors have equally contributed to this work.

Abstract: Several COVID-19 vaccines are on the market or will be on the market as of early 2021. These vaccines may vary in terms of their effectiveness and safety profile. This study characterizes vaccine hesitancy towards the COVID-19 vaccine among parents in Shanghai, China, and identifies how sensitive they are to changes in the vaccine safety and effectiveness profile. Schools in each township of Minhang District, Shanghai, were sampled, and parents in the WeChat group of each school were asked to participate in this cross-sectional internet-based survey. Parents responded to questions about vaccine hesitancy, and were given information about five different COVID-19 vaccine candidates, whose effectiveness varied between 50% and 95% and whose risk of fever as a side effect varied between 5% and 20%. Overall, 3,673 parents responded to the survey. Almost 90% would accept a vaccine for themselves (89.7%), for their child (87.5%) or for an elderly parent (88.5%) with the most ideal attributes (95% effective with 5% risk of fever). But with the least ideal attributes (50% effective with a 20% risk of fever) these numbers dropped to 33.5%, 31.3%, and 31.8%, respectively. Vaccine hesitancy, age at child's birth, and stated relative income were all significantly related to sensitivity to vaccine safety and effectiveness. Parents showed a substantial shift in attitudes towards the COVID-19 vaccine based on the vaccine's safety and effectiveness profile. These findings indicate that COVID-19 vaccine uptake may be heavily influenced by how effective the vaccine actually is, and uptake could be stymied, or facilitated, based on the actual vaccines on the market.

Keywords: COVID-19 vaccination; vaccine hesitancy; China; urban health

Citation: Lastname, F.; Lastname, F.; Lastname, F. Title. *Vaccines* **2021**, *9*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Received: date
Accepted: date
Published: date

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease [1], has led to substantial morbidity and mortality globally and put considerable pressure on the public health system worldwide. Since then, the global need for the vaccine, one of the most powerful tools to prevent disease in large populations at relatively low cost, has never been more urgent [2]. Unlike previous vaccine development, which takes years or even decades for clinical trials, the development of the vaccine against COVID-19 is in a "warp speed" [3-4]. This vaccine has been produced at a much quicker speed than previous vaccines [5]. More than 50 COVID-19 vaccine candidates are currently in trials, and several vaccines have already been approved and distributed. By January 14, 2021, more than 35 million doses in 49 countries have been administered [6].

However, a vaccine is only useful if people are willing to receive it. Various countries started rolling out vaccines in late 2020, prioritizing healthcare workers and essential workers and members of the general population with high risk health conditions.

However, members of the general population may be hesitant to receive a vaccine due to concerns over the speed of vaccine development and over concerns about how safe or effective the vaccine is. Especially in an era where vaccine hesitancy is listed as one of the top ten global health threats, it may provoke a higher round of hesitancy and refusal against vaccines [7]. According to a survey conducted in 19 countries, only 71.5% of the respondents would consider taking a COVID-19 vaccine [8]. The hesitancy and refusal may intensify the pandemic and put more pressure on the health system.

A previous study has shown that respondents from China showed the highest positive response (88.6%) and lowest negative response (0.7%) when asked if they would accept a "proven, safe and effective COVID-19 vaccine" [8]. However, it is still unclear their sensitivity to different levels of effectiveness and safety of the COVID-19 vaccine. It is also not clear what factors may influence their acceptance. It is crucial to consider the public's acceptance of vaccines with different levels of safety and effectiveness and factors related to the differences. Understanding the differences is useful for adopting evidence-based interventions under varying vaccine levels in the market to counter future outbreaks. This study characterizes vaccine hesitancy towards the COVID-19 vaccine among parents in Shanghai, China, and identifies how sensitive they are to changes in the vaccine safety and effectiveness profile.

2. Materials and Methods

2.1 Study population

In this study, a stratified cluster sampling method was used to conduct a questionnaire survey in each of 13 townships in Minhang District, Shanghai. We wanted a sample size of 2,345 in order to have a margin of error of at least 2% for our outcome – the proportion who would accept a given vaccine, with alpha of 0.05. We obtained a larger sample given the ease at obtaining data within schools. Within each township, a convenience sample of one school was chosen. In each sampled school, the school's health instructor sent the questionnaire link to each class' WeChat group chat. Following this, the parents of the students filled out the questionnaire. In order to improve the controllability of the questionnaire's source, the fidelity of the sampling, and the participation of the parents, researchers answered live any questions that parents had during the survey completion; questionnaires that took less than 5 minutes (estimated time) were excluded from the data analysis. The questionnaire was developed by staff at the Minhang Centers for Disease Control and Prevention.

2.2 Derived variables

Vaccine hesitancy was assessed through a 10-item adult Vaccine Hesitancy Scale (aVHS) (Figure 1). This questionnaire has previously been validated in US and Chinese samples (ref when published), and within this sample, there was high internal reliability of this scale (Standardized Crohnbach's alpha=0.82). Briefly, each item was on a 5-point Likert scale (with a score of "1" representing lowest amounts of vaccine hesitancy and "5" the most), which was summed, for a possible range of 10-50. Scores of 10-24 were categorized as "not hesitant" and 25-50 as "hesitant" [9].

We assessed acceptance of a vaccine by first providing participants with different vaccine effectiveness and safety profiles (varying vaccine effectiveness between 95%, 60% and 50%, and varying the risk of fever between 5%, 10%, and 20%). We then asked if they would accept a vaccine with that profile for themselves, for their child, or for an elderly parent. From this information, we also assessed if someone was sensitive to vaccine effectiveness (meaning they would accept a vaccine if it were 95% but not 50% effective) or vaccine safety (meaning they would accept a vaccine with a 5% risk of fever, not a 20% risk). Across each characteristic (effectiveness and safety) individuals could fall in one of three categories: they would not accept a vaccine in any circumstance, they were sensitive to the profile, or they would accept any vaccine.

Demographic characteristics of the parents, including their age, second child, and their stated relative income in their peer group, were also collected.

2.3 Statistical analysis

After quantifying the proportion of individuals with sensitivity to vaccine safety and vaccine effectiveness, we created two multivariable models, in which the outcomes were the three-level characteristics of sensitivity to vaccine effectiveness and sensitivity to vaccine safety. The primary independent variable was vaccine hesitancy, as measured by the aVHS. We also included mother vs father, age of parent, presence of second child, age of first child, sex of first child, and stated relative income as confounders in this analysis based on an a priori consideration of these variables relationships with vaccine hesitancy and with vaccine profile sensitivity. This model output odds ratios (ORs) and 95% confidence intervals (CI). Data were analyzed in SAS version 9.5 (SAS Institute, Cary, NC, USA).

3. Results

Overall, 3,673 parents responded to the survey. Demographic characteristics of the parents are shown in Table 1. Most (69.1%) respondents were mothers, a plurality (37.1%) had their first child when 25-29 years old, most (67.2%) did not have a second child, and for a bit less than half (45.3%), their first child was elementary aged (6-11 years old).

Table 1. Demographic characteristics of a sample of Shanghai parents of school-aged children, 2020.

Characteristic	Category	Count (column %)	Vaccine hesitant (row %)	P-value
Relation to child	Mother	2538 (69.1%)	762 (30.0%)	0.3162
	Father	1093 (29.8%)	306 (28.0%)	
	Other	42 (1.1%)	15 (35.7%)	
Age at first child's birth	18-22 years	346 (9.9%)	67 (19.4%)	<0.0001
	23-25 years	837 (24.0%)	209 (25.0%)	
	26-29 years	1291 (37.1%)	418 (32.4%)	
	30-45 years	1010 (29.0%)	324 (32.1%)	
Have a second child?	No	2412 (67.2%)	758 (31.4%)	<0.0001
	Yes	1177 (32.8%)	293 (24.9%)	
Age of first child	0-5 years	35 (1.0%)	9 (25.7%)	0.0702
	6-11 years	1624 (45.3%)	468 (28.8%)	
	12-14 years	1133 (31.6%)	338 (29.8%)	
	15-17 years	555 (15.5%)	181 (32.6%)	
	≥18 years			
Gender of first child	Male	1844 (50.8%)	537 (29.1%)	0.6950
	Female	1787 (49.2%)	531 (29.7%)	
Stated relative income	Less than average	424 (11.5%)	146 (34.4%)	0.0588
	About average	2710 (73.8%)	783 (28.9%)	
	More than average	539 (14.7%)	154 (28.6%)	

Responses to vaccine hesitancy items are shown in Figure 1. Individuals expressed a great deal of concern about serious adverse effects (40.1% agreed and 30.1% strongly agreed), believed that newer vaccines carried more risks than older vaccines (22.2%

agreed and 25.2% strongly agreed), and that vaccines for diseases no longer common were not needed (23.1% agreed and 13.8% strongly agreed).

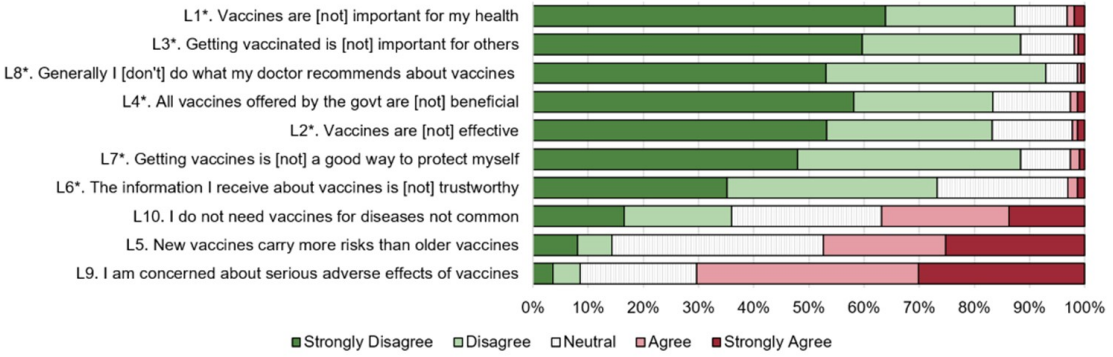

Figure 1. Responses to questions about vaccine hesitancy among parents of school-aged children in Shanghai, China, 2020. Questions with an asterisk have been reverse coded so that all questions have responses with higher values being more vaccine hesitant.

Overall, 29.5% (1083) were vaccine hesitant, with some trends by demographic group. Individuals were more vaccine hesitant at an older age when child was born (32.1% of those 30-45 years at child's birth were vaccine hesitant, compared to 19.4% who were 18-22 years at child's birth, P<0.0001). Additionally, those with a second child were less vaccine hesitant (24.9%), compared to those with only one child (31.4%), (P<0.0001).

Acceptance of a COVID-19 vaccine varied by the vaccine's safety and effectiveness profile, with the highest levels of acceptance for a vaccine 95% effective with a 5% risk of fever, and lowest among vaccines that were 50% effective with a 20% risk of fever (Table 2). Almost 90% would accept a vaccine for themselves (89.7%), for their child (87.5%) or for an elderly parent (88.5%) with the most ideal attribute. But with the least ideal attribute these numbers dropped to 33.5%, 31.3%, and 31.8%, respectively.

Table 2. Acceptance of a COVID-19 vaccine, based on the safety and effectiveness profile.

Sensitivity	**Condition**	For self	For child	For parent
Acceptance of a vaccine based on effectiveness and safety profile	95% effective, 5% risk of fever	3294 (89.7%)	3213 (87.5%)	3250 (88.5%)
	95% effective, 20% risk of fever	2330 (63.4%)	2164 (58.9%)	2154 (58.6%)
	60% effective, 10% risk of fever	1662 (45.3%)	1569 (42.7%)	1567 (42.7%)
	50% effective, 5% risk of fever	1790 (48.7%)	1708 (46.5%)	1716 (46.7%)
	50% effective, 20% risk of fever	1230 (33.5%)	1151 (31.3%)	1166 (31.8%)
Sensitivity to COVID-19 vaccine effectiveness	Would not accept any vaccine	369 (10.1%)	453 (12.4%)	413 (11.3%)
	Would accept 95% effective vaccine, not 50%	1514 (41.3%)	1512 (41.2%)	1544 (42.2%)
	Would accept any vaccine	1780 (48.6%)	1701 (46.4%)	1706 (46.6%)
Sensitivity to COVID-19 vaccine safety	Would not accept any vaccine	363 (9.9%)	445 (12.2%)	405 (11.1%)
	Would accept vaccine with 5% risk of fever, not 20% risk	980 (26.8%)	1064 (29.1%)	1114 (30.5%)
	Would accept any vaccine	2314 (63.3%)	2149 (58.8%)	2136 (58.4%)

Overall, about 10% of individuals would not accept a vaccine, regardless of its safety or effectiveness profile. Almost half (48.6%) were not sensitive to vaccine effectiveness, but 31.3% were sensitive to vaccine effectiveness, and would accept a 95% effective vaccine, but not a 50% effective one. There was less sensitivity to vaccine safety, as measured by risk of fever. Almost two-thirds, 63.3%, would accept a vaccine regardless of a change in its risk of fever, and about one-fourth, 26.8%, would only accept a vaccine with a 5% risk of fever, but not a 20% risk.

Sensitivity to vaccine safety and effectiveness was tested in Table 3. Vaccine hesitancy, age at child's birth, and stated relative income were all significantly related to sensitivity to vaccine safety and effectiveness. Having a second child was significantly related to sensitivity to vaccine effectiveness (P=0.0334), but not safety (P=0.0998). For example, those who were vaccine hesitant had 10.47 times greater odds of not accepting a vaccine, and 2.60 times greater odds of being sensitive to vaccine effectiveness, compared to those not vaccine hesitant (P<0.0001), and vaccine hesitancy was associated with greater odds of not accepting any vaccine or being sensitive to risk of fever (P<0.0001). Those who were younger at their first child's birth had reduced odds of not accepting a vaccine or being sensitive to effectiveness or safety profile (P<0.0001 for effectiveness, P=0.0055 for safety). And those stating that there income was less than average were less sensitive, both to the effectiveness profile (P=0.0035) and to the safety profile (P=0.0067).

Table 3. Sensitivity to COVID-19 vaccine effectiveness and safety in multinomial logistic regression models among Shanghai parents of school-aged children, 2020.

Characteristic	Compared to those who would accept a vaccine, regardless of effectiveness		Compared to those who would accept a vaccine, regardless of risk of fever	
	Would not accept any vaccine, OR (95% CI)	Would only accept 95% effective vaccine, OR (95% CI)	Would not accept any vaccine, OR (95% CI)	Would only accept vaccine with 5% risk of fever, OR (95% CI)
Vaccine hesitant				
No	ref	ref	ref	ref
Yes	**10.47 (8.03, 13.67)**	**2.60 (2.19, 3.09)**	**8.45 (6.54, 10.91)**	**2.48 (2.09, 2.94)**
Relation to child				
Mother	ref	ref	ref	ref
Father	1.14 (0.87, 1.51)	0.93 (0.79, 1.10)	1.09 (0.83, 1.42)	**0.84 (0.70, 1.00)**
Age at first child's birth				
18-22 years	**0.46 (0.27, 0.79)**	**0.43 (0.32, 0.58)**	**0.55 (0.32, 0.94)**	**0.53 (0.38, 0.74)**
23-25 years	**0.52 (0.36, 0.75)**	**0.54 (0.43, 0.66)**	**0.67 (0.47, 0.97)**	**0.79 (0.63, 0.99)**
26-29 years	0.78 (0.57, 1.05)	**0.82 (0.68, 0.99)**	0.81 (0.60, 1.09)	0.85 (0.70, 1.03)
30-45 years	ref	ref	ref	ref
Have a second child				
No	ref	ref	ref	ref
Yes	0.75 (0.55, 1.01)	**0.83 (0.70, 0.98)**	0.81 (0.61, 1.09)	0.84 (0.70, 1.01)
Age of first child				
0-5 years	1.37 (0.45, 4.18)	0.67 (0.31, 1.43)	1.65 (0.56, 4.85)	0.82 (0.36, 1.84)
6-11 years	ref	ref	ref	ref
12-14 years	1.16 (0.86, 1.55)	1.03 (0.87, 1.22)	1.14 (0.85, 1.51)	0.97 (0.81, 1.16)
15-17 years	1.26 (0.88, 1.79)	0.92 (0.74, 1.15)	1.26 (0.89, 1.79)	0.84 (0.66, 1.06)
≥18 years	1.44 (0.80, 2.60)	0.89 (0.63, 1.26)	1.33 (0.74, 2.39)	0.76 (0.51, 1.14)
Gender of first child				
Male	ref	ref	ref	ref

Female	0.94 (0.73, 1.21)	1.09 (0.94, 1.26)	0.87 (0.68, 1.12)	0.97 (0.83, 1.13)
Stated relative income				
Less than average	0.86 (0.59, 1.28)	**0.66 (0.52, 0.84)**	1.00 (0.69, 1.46)	**0.69 (0.53, 0.91)**
About average	ref	ref	ref	ref
More than average	1.39 (0.99, 1.96)	1.05 (0.85, 1.29)	1.50 (1.08, 2.09)	1.14 (0.92, 1.42)

Note: significant results are bolded.

4. Discussion

Safety and effectiveness are the two of the most important indicators to evaluate a new vaccine, and new vaccines undergo substantial tests of their safety and effectiveness before and after coming onto the market [10-11]. Previous studies showed that most parents expressed concerns about vaccine side effects, safety, and effectiveness [12]. Similarly, parents showed a substantial shift in attitudes towards the COVID-19 vaccine based on the safety and effectiveness. The majority of the respondents would accept a vaccine with high levels of safety and effectiveness, but only one-third of the people would accept vaccines with lower levels of safety and effectiveness. These preferences could hamper uptake of the vaccine. Interestingly, the public showed a different level of sensitivity toward safety and effectiveness, with more sensitivity towards effectiveness.

Although vaccines are currently available in some locations, safety and effectiveness may vary. For example, for two of the vaccines approved in the U.S., Pfizer-BioNTech was 95% efficacious and the Moderna vaccine 94.1% efficacious in preventing COVID-19 disease [13-14]. The AstraZeneca vaccine used in the U.K., India, and Mexico was reported to have average efficacy of 70% [15]. For the inactivated vaccines produced by Chinese pharmaceutical companies, efficacy ranges from 50% to over 90%, depending on outcome considered and study site [16]. Currently, 68 vaccines are being tested in clinical trials, and 20 have reached the final stage [17]. As more vaccines come into the market, the public may choose between vaccines with widely varying efficacy.

The study found a strong relationship between vaccine hesitancy and COVID-19 vaccination, and the respondents believe that the new vaccine carried more risk than the older vaccine. The role of vaccine hesitancy, and anti-vaccine movements, has been previously explored. For instance, Gaulano et al. found that Italian women who received information from anti-vaccination movements were less likely to accept mandatory vaccines [18]. However, it is essential to note that people might be hesitant about the COVID-19 vaccine but not for vaccines in general. The COVID-19 vaccine went through the process from development to distribution worldwide under a "warp speed." It also adopted a new approach of using mRNA, which is different from traditional vaccines that use weakened or inactive components of the pathogen [19]. Scientists and governments are still assessing the effectiveness after the COVID-19 vaccine has been authorized for emergency use [20].

COVID-19 vaccine hesitancy is present not only in the general public, but also among healthcare workers. A recent survey by Kaiser Family Foundation found that nearly a third of the healthcare workers would probably or definitely refuse the vaccine [21]. Healthcare workers expressed concerns about not having enough research, not transparent enough between pharmaceutical companies, research companies, or the government, and they were afraid to be a part of another "Tuskegee Study" [22]. Thus, how to break through the vaccine hesitant among healthcare workers, who have a higher risk of contracting the virus and play important roles in their patients' vaccine decision making, is of the utmost importance. Even in non-pandemic settings, health care workers have relatively low coverage of non-mandatory vaccines, and this differed by age, with younger personnel more likely to be vaccinated [23].

4.1 Strengths and limitations

This is a cross-sectional study and so we were unable to look at longitudinal connections. Additionally, we assessed intent to get a vaccine, but actual vaccine uptake may differ as more information is available. The vaccine effectiveness and safety profiles that we chose were based on possible ranges from existing influenza and measles vaccines, but the actual characteristics of COVID-19 vaccines may differ. We also did not evaluate uptake or hesitancy towards other vaccines routinely provided to children, for instance the measles-mumps-rubella vaccine, and did not adjust our analyses for this variable. Nonetheless, using a large sample of parents, we have been able to assess variations in vaccination intent using a validated vaccination hesitancy scale.

5. Conclusions

In this study of parents of school-aged children in a suburb of Shanghai, parents showed a substantial shift in attitudes towards the COVID-19 vaccine based on the vaccine's safety and effectiveness. The majority of respondents would accept a vaccine with the most ideal levels of safety and effectiveness, but only one-third of the people would accept vaccines with the least ideal attributes. These findings indicate that COVID-19 vaccine uptake may be substantially influenced by how effective the vaccine actually is. Controlling outbreaks of COVID-19 in the presence of these strong preferences would require substantial use of non-pharmaceutical interventions.

Local circumstances are important to consider when developing programs to promote vaccines, as thoughts about different aspects of vaccination are not uniform across countries. We did not find consistent associations about education and vaccine hesitancy, in contrast to prevailing findings about this relationship in high income countries; more work needs to be done on fully understanding socio-cultural influences on vaccine decision-making. Continued surveillance of attitudes towards vaccination in LMICs can help identify shifts in future opinions in vaccination attitudes.

Author Contributions: Conceptualization, Abram L. Wagner and Yihan Lu; Data curation, Jia Lu, Xiaosa Wen and Qi Guo; Formal analysis, Abram L. Wagner; Investigation, Jia Lu, Xiaosa Wen, Qi Guo and Yihan Lu; Writing – original draft, Mengdi Ji and Abram L. Wagner; Writing – review & editing, Jia Lu, Xiaosa Wen, Qi Guo, Felicia Zhang and Yihan Lu.

Funding: A.L.W. received salary support from the National Science Foundation, Division of Social and Economic Sciences (#2027836).

Institutional Review Board Statement: This study has passed the ethical review of the Minhang District Center for Disease Control and Prevention. EC-P-2020-009

Informed Consent Statement: "Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: In this section, please provide details regarding where data supporting reported results can be found, including links to publicly archived datasets analyzed or generated during the study. Please refer to suggested Data Availability Statements in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics. You might choose to exclude this statement if the study did not report any data.

Acknowledgments: We appreciate the openness of Minhang schools to participate in this project.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results".

References

1. Harapan, H.; Mudatsir, M.; Yufika, A.; Nawawi, Y.; Wahyuniati, N.; Anwar, S.; Yusri, F.; Haryanti, N.; Wijayanti, N. P.; Rizal, R.; Fitriani, D.; Maulida, N. F.; Syahriza, M.; Ikram, I.; Fandoko, T. P.; Syahadah, M.; Asrizal, F. W.; Aletta, A.; Jamil, K. F.; Rajamoorthy, Y.; Hadisoemarto, P. F.; Wagner, A. L.; Groneberg, D. A.; Kuch, U.; Sasmono, R. T.; Müller, R.; Imrie, A. Community acceptance and willingness-to-pay for a hypothetical Zika vaccine: A cross-sectional study in Indonesia. *Vaccine* **2019**, *37*, 1398–1406, doi:10.1016/j.vaccine.2019.01.062.
2. Su, S.; Du, L.; Jiang, S. Learning from the past: development of safe and effective COVID-19 vaccines. *Nat. Rev. Microbiol.* 2020.
3. Zhu, F. C.; Guan, X. H.; Li, Y. H.; Huang, J. Y.; Jiang, T.; Hou, L. H.; Li, J. X.; Yang, B. F.; Wang, L.; Wang, W. J.; Wu, S. P.; Wang, Z.; Wu, X. H.; Xu, J. J.; Zhang, Z.; Jia, S. Y.; Wang, B. Sen; Hu, Y.; Liu, J. J.; Zhang, J.; Qian, X. A.; Li, Q.; Pan, H. X.; Jiang, H. D.; Deng, P.; Gou, J. B.; Wang, X. W.; Wang, X. H.; Chen, W. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet* **2020**, *396*, 479–488, doi:10.1016/S0140-6736(20)31605-6.
4. Trogen, B.; Oshinsky, D.; Caplan, A. Adverse Consequences of Rushing a SARS-CoV-2 VaccineImplications for Public Trust. *JAMA Netw.* **2020**, doi:10.1001/jama.2020.8917.
5. Brothers, W. *BioSpace*. December 3, 2020,.
6. Randall, T.; Sam, C.; Tartar, A.; Murray Paul; Cannon Christopher More Than 108 Million Shots Given: Covid-19 Tracker Available online: https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/ (accessed on Jan 28, 2021).
7. Ten threats to global health in 2019 Available online: https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019 (accessed on Jan 28, 2021).
8. Lazarus, J. V; Ratzan, S. C.; Palayew, A.; Gostin, L. O.; Larson, H. J.; Rabin, K.; Kimball, S.; El-Mohandes, A. A global survey of potential acceptance of a COVID-19 vaccine. *Nat. Med.*, doi:10.1038/s41591-020-1124-9.
9. Akel, K. B.; Masters, N. B.; Shih, S.-F.; Lu, Y.; Wagner, A. L. Modification of a Vaccine Hesitancy Scale for use in adult vaccinations in the United States and China. *Hum. Vaccin. Immunother.* **2021**, ahead of print, doi:10.1080/21645515.2021.1884476.
10. World Health Organization *Guidelines on clinical evaluation of vaccines: regulation expectations*; 2004;
11. Vaccine Development, Testing, and Regulation | History of Vaccines Available online: https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation%0Ahttps://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation%0Ahttps://www.historyofvaccines.org/content/articles/vaccine-deve.
12. Wagner, A. L.; Huang, Z.; Ren, J.; Laffoon, M.; Ji, M.; Pinckney, L. C.; Sun, X.; Prosser, L. A.; Boulton, M. L.; Zikmund-Fisher, B. J. Vaccine Hesitancy and Concerns About Vaccine Safety and Effectiveness in Shanghai, China. *Am. J. Prev. Med.* **2021**, *60*, S77–S86, doi:10.1016/j.amepre.2020.09.003.
13. Pfizer-BioNTech COVID-19 Vaccine Frequently Asked Questions Available online: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/pfizer-biontech-covid-19-vaccine-frequently-asked-questions.
14. Vaccine information-Moderna Available online: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Moderna.html.
15. Smith, J. How Does the AstraZeneca COVID-19 Vaccine Compare to Pfizer's and Moderna's? Available online: https://www.prevention.com/health/a35118263/astrazeneca-vs-pfizer-vs-moderna-covid-19-vaccine/.
16. Creech, C. B.; Walker, S. C.; Samuels, R. J. SARS-CoV-2 Vaccines. *JAMA* **2021**, doi:10.1001/jama.2021.3199.
17. Zimmer Cari; Corum Jonathan; Wee Sul Lee Coronavirus Vaccine Tracker. *New York Time* 2021.

18. Gualano, M. R.; Bert, F.; Voglino, G.; Buttinelli, E.; D'Errico, M. M.; De Waure, C.; Di Giovanni, P.; Fantini, M. P.; Giuliani, A. R.; Marranzano, M.; Masanotti, G.; Massimi, A.; Nante, N.; Pennino, F.; Squeri, R.; Stefanati, A.; Signorelli, C.; Siliquini, R.; Castaldi, S.; Di Donna, F.; Di Martino, G.; Genovese, C.; Golfera, M.; Gori, D.; Greco, P.; Loperto, I.; Miduri, A.; Olivero, E.; Prospero, E.; Quattrocolo, F.; Rossello, P.; Rosso, A.; Sisti, L. G.; Stracci, F.; Zappalà, G. Attitudes towards compulsory vaccination in Italy: Results from the NAVIDAD multicentre study. *Vaccine* **2018**, *36*, 3368–3374, doi:10.1016/j.vaccine.2018.04.029.
19. Understanding and Explaining mRNA COVID-19 Vaccines Available online: https://www.cdc.gov/vaccines/covid-19/hcp/mrna-vaccine-basics.html#:~:text=Like all vaccines%2C COVID,more than a decade.
20. Centers for Disease Control and Prevention (CDC) Ensuring COVID-19 Vaccines Work CDC Available online: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness.html.
21. Hamel Liz; Kirzinger Ashley; Munana Ca; Brodie Mollyann *KFF COVID-19 Vaccine Monitor: December 2020*; 2020;
22. Hopkins Dean Christopher; Valentine Ashish Some Health Care Workers Are Hesitant About Getting COVID-19 Vaccines. *Natl. Public Radio* 2021.
23. Guthmann, J. P.; Fonteneau, L.; Ciotti, C.; Bouvet, E.; Pellissier, G.; Lévy-Bruhl, D.; Abiteboul, D. Vaccination coverage of health care personnel working in health care facilities in France: Results of a national survey, 2009. *Vaccine* **2012**, *30*, 4648–4654, doi:10.1016/j.vaccine.2012.04.098.