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Preferences and antecedents of vaccine decision among healthcare professionals and the adult population in France

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Lucia Araujo Chaveron. Preferences and antecedents of vaccine decision among healthcare professionals and the adult population in France. Santé publique et épidémiologie. Sorbonne Université, 2024. English. NNT: 2024SORUS220 . tel-04766774

HAL Id: tel-04766774

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Sorbonne Université

École doctorale Pierre Louis de Santé Publique (ED 393)

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Preferences and antecedents of vaccine decision among healthcare professionals and the adult population in France

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Thesis submitted for the degree of Doctor in Epidemiology

Supervised by Dr. Judith Mueller (professor at EHESP)

Presented and publicly defended on October 14th, 2024 at Institut Pasteur, in front of a jury composed of:

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Réseau doctoral
en santé publique

This thesis was prepared within the framework of the Doctoral Network in Public Health, led by EHESP, and supported by a doctoral contract provided by EHESP.

Acknowledgements

I would like to express my sincere gratitude to Judith Mueller for giving me the opportunity to explore such an interesting topic over the past three years. I am deeply thankful of our fruitful discussions and all the scientific insights she has shared. Her invaluable Epidemiology lectures at EHESP prior to this thesis have been crucial in shaping my understanding and work.

My sincere thanks also go to Jonathan Sicsic for introducing me to the fascinating field of discrete choice experiments, for his statistical expertise, and for his constant availability to answer my many questions. I am also grateful to GERES for their invaluable assistance during data collection and manuscript writing.

To the members of the thesis committee, Aurélie Gauchet, Bruno Ventelou, Pierre Verger, and Sophie Vaux. I sincerely thank you for agreeing to offer your expert insight to this work.

A special thanks goes to Josée Dussault and Thomas Artiach for their thoughtful advice and support in revising this manuscript.

My sincere thanks to Arnaud Fontanet for allowing me to join the Epidemiology and Emerging Disease team, and to all the members of the team, as well as my fellow PhD colleagues at the Global Health department.

A heartfelt thank you to Mary Beth Terry and Rebecca Kehm for welcoming me to their team and for the memorable experiences in the ‘Analysis in Epidemiology’ classes at EHESP.

I also wish to thank the Réseau Doctoral en Santé Publique for financing this thesis, for offering us the opportunity to attend excellent public health courses and for organizing enriching scientific meetings.

I am forever thankful to Antoni Trilla (Hospital Clinic, Barcelona), who introduced me to the field of Epidemiology. A special thank you to Ricardo Ocaña (Escuela Andaluza de Salud Pública), whose statistics classes have always been the cornerstone of my academic foundation in statistics.

To all my family and friends, thank you for your support and encouragement. For all our adventures and for always being there throughout this journey, I am deeply grateful.

Preface

Vaccines differ from other healthcare interventions by addressing global population at large as a means to control disease spread (reducing morbidity and mortality) or to eradicate a disease, irrespective of disease status or the presence of risks factors associated with severe disease outcomes.

This inherent aspect of vaccination delves into complex ethical considerations for public health, between individual autonomy – with a trade-off between the risks of side-effects and the potential risk to suffer from a severe form of the disease - and societal well-being reducing morbidity, mortality, eradicating the disease or even reducing healthcare costs.

On one hand, for some vaccines widespread vaccination not only protects those directly immunized but also establishes a shield that protects vulnerable populations such as those unable to receive the vaccine due to contraindications. This perspective emphasizes the collective responsibility of some vaccinations to achieve “herd immunity”, thus in consequence reducing the overall disease burden and preventing outbreaks more effectively.

However, encouraging widespread vaccination can also be seen as a potential breach on personal freedom and autonomy on medical decisions. Some argue that mandating vaccination for those who are unwilling to accept it paves the way for government control over personal health choices, sparking worries about the erosion of civil liberties.

In an era where patients are fully involved in the decision-making process, their preferences are at the core of health care practices and questions such as balancing the risks of side-effects of vaccination against the risks of the disease itself are at the center of individual’s vaccine decision.

As science advances and societal perspective evolves, finding a balance between respecting individual rights and promoting public health remains a central challenge in this ongoing ethical debate.

This ethical debate was reopened during the COVID-19 pandemic, when European countries implemented various measures to increase vaccine uptake with the aim to flatter the epidemic curve, raising questions whether vaccines should remain public health recommendations or become mandatory.

At the beginning of the COVID-19 vaccine campaign, vaccination effectiveness and the extent of indirect protection were uncertain. Emerging evidence of severe side-effects in young adults, such as thrombocytopenic thrombosis and myocarditis, with a previous rapid development of clinical trials raised public concerns about COVID-19 vaccine safety. Individuals started to weight their personal benefits against their potential vaccination risks depending on their specific circumstances and relatives' comorbidities, meanwhile, public health practitioners started to raise questions on the effectiveness threshold at which vaccines should become mandatory for the population. Thus, the COVID-19 pandemic offered an opportunity to examine population preferences to vaccination and refine vaccine communication.

Résumé

La littérature sur l'hésitation vaccinale souligne l'importance de la perception de la balance bénéfice-risque (BBR) des vaccins dans l'acceptation vaccinale. La pandémie de COVID-19 et les politiques de vaccination mises en œuvre par le gouvernement français offre l'occasion a) d'évaluer l'impact du passe sanitaire et de l'obligation vaccinale sur l'intention vaccinale future contre la COVID-19 en tenant compte de la perception BBR, b) d'évaluer les antécédents psychologiques 7C de la vaccination au cours de la nouvelle campagne vaccinale contre la COVID-19, c) d'explorer les préférences autour du concept BBR parmi la population générale et parmi les professionnels de la santé, d) de définir et de caractériser les individus qui ont constamment refusé la vaccination indépendamment des attributs BBR.

Quatre études différentes ont été menées en France métropolitaine au cours de cette thèse : a) une étude transversale pour explorer l'impact du passe sanitaire et de l'obligation vaccinale ainsi que la perception BBR sur la future intention vaccinale parmi la population générale, b) une enquête transversale répétée parmi les professionnels de la santé pour suivre leurs antécédents psychologiques d'acceptation vaccinale à différents stades de la campagne de vaccination contre la COVID-19, c) une expérience de choix discrets (DCE) pour enquêter sur les préférences en matière de BBR vaccinal parmi la population général et les professionnels de la santé, et d) une échelle de certitude sur la décision vaccinal intégrée au DCE pour définir différents profils de comportement vaccinal autour du concept BBR.

Nos résultats suggèrent que la mise en œuvre du passe sanitaire n'a pas efficacement convaincu les personnes âgées, qui auraient été celles bénéficiant le plus de la vaccination, mais que céder à la forte incitation/obligation vaccinale n'était pas associé à une diminution, mais plutôt à une augmentation de l'intention de se faire vacciner à l'avenir contre la COVID-19. Parmi les professionnels de la santé, la décision d'accepter la vaccination sous l'obligation dépendait uniquement de la perception de la vaccination comme une action collective, et non de la perception BBR du vaccin contre la COVID-19. Cependant, à mesure que la pandémie et les recommandations de rappel vaccinal évoluaient et que les professionnels de la santé acquéraient plus d'expérience avec le vaccin contre la COVID-19, ils ont recommencé à prendre en compte la BBR du vaccin dans leurs décisions vaccinales. Notre étude de préférences a suggéré que tant le grand public que les professionnels de santé n'ayant pas un titre universitaire ne prenaient pas en compte l'aspect numérique des bénéfices par rapport aux risques dans des scénarios

vaccinaux hypothétiques, mais qu'ils considèrent plutôt des attributs qualitatifs entourant le concept BBR tels que la fréquence et la gravité de la maladie, et les effets de protection indirecte. En revanche, nous avons estimé que l'acceptation hypothétique du vaccin parmi les professionnels de la santé ayant un titre universitaire augmentait significativement de 40% lorsque le ratio bénéfice-risque de la vaccination passait de 10:1 à 100:1. Enfin, nous avons constaté que par rapport aux répondants qui acceptaient certains mais pas tous les scénarios du DCE, ceux qui acceptaient tous les scénarios étaient plus susceptibles d'avoir une perception positive de la BBR et d'être motivés par l'incitation de l'employeur ou des autorités à se faire vacciner, tandis que ceux qui refusaient tous les scénarios étaient plus susceptibles d'avoir une faible confiance dans les autorités pour gérer la pandémie, une faible confiance dans la sécurité des vaccins, et ne percevait pas le vaccin comme une action collective pour arrêter la pandémie. Ils ont de même montré une réactance à l'incitation de l'employeur ou des autorités à se faire vacciner.

Nos recherches suggèrent que les campagnes vaccinales visant les individus réticents à la vaccination devraient se concentrer sur l'amélioration de la confiance dans les autorités et la confiance dans le vaccin (sécurité du vaccin). De plus, les campagnes vaccinales devraient fournir des informations sur la vaccination en tant qu'action collective, en mettant l'accent sur les bénéfices de protection indirecte et les risques de développer la maladie.

Mots clés : vaccination ; pandémie COVID-19 ; balance bénéfice-risque du vaccin ; expériences de choix discrets ; antécédents psychologiques 7C ; professionnels de la santé

Abstract

The literature on vaccine hesitancy largely reports the importance of the perception of the benefit-risk balance (BRB) in vaccine acceptance. The COVID-19 pandemic and the unprecedented vaccination policies implemented by the French government during a novel vaccine campaign provided an opportunity to assess the impact of COVID-19 certificate or vaccine mandate on future COVID-19 vaccine intention considering the perceived BRB of COVID-19 vaccination, evaluate the 7C-psychological antecedents of vaccination across the novel COVID-19 vaccine campaign, explore preferences around the concept of BRB among the general adult population and among healthcare sector-workers (HCSWs), define and characterize individuals who constantly refused vaccination regardless of BRB attributes.

Four different studies were conducted during this thesis, a) a cross-sectional study to explore the impact of the COVID-19 certificate-mandate and perceived vaccination BRB on future vaccine intention among the general population, b) a repeated cross-sectional survey among HCSWs to monitor their psychological antecedents of vaccine acceptance at different stages of the COVID-19 vaccination campaign, c) a discrete choice experiment (DCE) to investigate the vaccination BRB preferences of the general public and HCSWs and d) a vaccine eagerness scale integrated into the previous DCE to define different vaccination behavior profiles around the concept of vaccine BRB.

Our findings suggest that the COVID-19 certificate enactment did not effectively persuade elderly people, who would have been those with the greatest potential benefit from vaccination, but that ceding to the strong incentive/mandate was not associated with reduced, but rather increased intention for future COVID-19 vaccination. Among HCSWs, the decision to accept vaccination under the mandate depended solely on the perception of vaccination as a collective action, but not on the vaccination perception of benefits vs. risks. However, as the pandemic and vaccine booster recommendations evolved and as HCSWs gained more experience with the COVID-19 vaccine, they resumed considering vaccine BRB in their vaccine decisions. Our preference study suggested that both the general public and non-university-level HCSWs do not consider the numerical aspect of benefits vs. risks in hypothetical vaccine scenarios, they rather consider qualitative attributes surrounding the BRB concept such as disease frequency and severity, and indirect protection effects. By contrast, we estimated that hypothetical vaccine uptake among university-level HCSWs significantly increases by 40% when vaccination

benefit-risk ratio moves from 10:1 to 100:1. Finally, we found that compared to respondents who accepted some but not all scenarios of the single profile DCE, those accepting all scenarios were more likely to have a positive perception of the BRB and were motivated by employer's or authorities' incitation to get vaccinated, while those refusing all scenarios were more likely to have low confidence in authorities to manage the epidemic, low confidence in vaccine safety, not perceive vaccine as collective action to stop the epidemic and show reactance to employer's or authorities' incitation to get vaccinated.

The research suggests that vaccine campaigns targeting vaccine-reluctant individuals should focus on improving confidence in authorities and confidence in the vaccine (vaccine safety). Additionally, vaccination campaigns should provide information about vaccination as a collective action, emphasizing its indirect protection benefits and the risks of developing the disease.

Key words: vaccination ; COVID-19 pandemic ; vaccine benefit-risk balance ; discrete choice experiments ; 7C-psychological antecedents ; healthcare workers

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Introduction

Chapter I. History of Vaccine Policies in France: Incentive and Certificate requirement for social participation

Since the first antigen inoculations, some subgroups of the population have remained skeptical about vaccines, often perceiving more risks than benefits and referring to vaccination sites as “infection sources”(1). In France, in 1902, smallpox vaccination became mandatory. Then, the list of mandatory vaccines was progressively extended to diphtheria (introduced in 1938), tetanus (1940), tuberculosis (BCG, 1950), poliomyelitis (1964) and in French Guiana, yellow fever (1967)(2). Consequently, vaccine coverage of vaccines in the official schedule were high for several decades(2).

After the elimination and subsequent cessation of smallpox vaccination, in the early 21st century, the French government shifted towards more flexible vaccination recommendations for new vaccines, thus promoting individual decision-making. In addition, recommendations shifted to specific populations. The best example is BCG vaccination, no longer mandatory for infants from 2007 on, but recommended in high-risk areas and groups(2). Another example is vaccination against Human Papillomavirus (HPV), initially recommended in 2007 exclusively for girls and extended to boys in 2019(3).

In France, healthcare-sector workers (HCSWs) are not only required to adhere to the standard vaccination schedule but also have additional vaccination responsibilities due to their regular contact with vulnerable individuals. The public health code mandates that HCSWs receive vaccination against Hepatitis B, diphtheria, tetanus and poliomyelitis(4). Despite these obligations, among HCSWs, the coverage for the seasonal influenza vaccine barely reaches 25% every year(5,6).

1.1 SARS-CoV-2 pandemic: vaccination policies and strategies

In December 2019, a novel coronavirus was identified in Wuhan, China, rapidly evolving into a global health crisis. On March 11, 2020, the World Health Organization (WHO) officially declared a pandemic(7). A survey conducted in November 2020 showed that only 54% of the French population were willing to receive the upcoming vaccine against SARS-

CoV-2 and 21% were strongly opposed to it(8). Among those not willing to accept the upcoming vaccine, 32% cited concerns about potential vaccine side effects as their main reason, indicating they were more worried about the risks of vaccination than its potential benefits, and 35% cited that the vaccine was moving through clinical trials too fast as a main reason(8).

In order to increase the number of people willing to accept COVID-19 vaccination while avoiding the outright restriction of citizens' liberty that a vaccine mandate would represent, the French government, as in other countries, adopted policies requiring COVID-19 vaccination or negative testing for accessing certain public places and services. However, among HCSWs, vaccination was mandatory to practice(9–11). French society responded with significant negativity to these requirements.

1.2 Healthcare professionals' position on vaccination

During the COVID-19 pandemic, in August 2021, COVID-19 vaccination became mandatory for HCSWs(9). The French government justified this mandate as a means to protect HCSWs who were frequently in contact with infected patients. However, another question arises concerning the moral obligation of HCSWs to be vaccinated as they are constantly in contact with vulnerable populations who might not be infected. This justification aligns with the principles underlying the Nightingale pledge for nurses and the Hippocratic oath for doctors, particularly the principle of non-maleficence ("to do no harm") and the commitment to service, highlighting the ethical responsibility of HCSWs to protect their patients. Thus, when individuals choose to pursue careers as HCSWs, they automatically decide to make certain sacrifices and assume some personal risks that are inherent to their line of work; as firefighters are not free to choose whether they will attend at a very dangerous fire or police officers have to patrol dangerous areas(12). Also, according to some authors, hospitals with very low vaccines coverage among HCSWs feed public distrust and fear of vaccines(12).

Several authors have indicated that a significant proportion of HCSWs are not always willing to accept vaccines in their personal life(13,14). HCSWs are considered trusted information sources, being key interlocutors when answering concerns related to health prevention and promotion. Thus, they are expected to set a good example of disease prevention practices, setting a positive model for the general public(15). A recent review of vaccine acceptance among HCSWs has highlighted that their behaviour towards vaccines is influenced by determinants such as vaccine risk perception. Emerging doubts about potential vaccine risks might come from a certain level of sensitivity to public controversies and media coverage as well as from interactions with hesitant patients(16).

However, setting a vaccine mandate among HCSWs violates the French law from 2002 that recognises individual right to refuse unwanted treatment and right to make decisions about their own health and well-being(17). The mandate of COVID-19 vaccination, including booster vaccination among HCSWs remained valid until 13 May 2023(18). In cases where HCSWs refused the vaccine, they were required to change their job.

Chapter II. Vaccination and Public Health Policies: An alternative to vaccine mandates

Vaccine policies can range from a simple recommendation without other actions, to “offering”, “providing” or “ensuring” vaccines to the public, to complete mandates that impose consequences for non-compliant individuals. And while vaccine mandates achieve high vaccination rates(19), they also raise questions in medical ethics, as they limit individual choice.

It is key to understand that impromptu decisions are difficult to make when considerations are complex (e.g., “*does the vaccine have more risks or benefits for me?*”) and the long-term benefits of vaccination can be difficult to perceive, especially since the primary benefit is often the absence of disease. In this situation, incentive policies can play an important role in order to guide individuals in the decision-making process(20). Also, incentive policies allow policymakers to guide individual behavior in the interest of the individual and the society while still allowing individuals to choose(20). One assumption underpinning the theory of decision-making is that individuals make suboptimal decisions not due to a lack of information, but rather because of predictably irrational biases and cognitive errors(20). One such error is omission bias, a cognitive bias where individuals tend to rate worse negative consequences from action rather than from inaction(12,21–24). This bias can influence medical decision-making as it often leads to avoiding taking a vaccine due to fear of potential side effects, even if the inaction (declining vaccination) could lead to a severe outcome due to the disease itself(25). Incentive policies can counteract omission bias, as evidence suggest that after a first positive experience, individuals are likely to repeat the choice(20). Thus, this can potentially change attitudes positively towards vaccination in general.

Vaccine incentive policies should, on the one hand, provide useful information and guidance to help individuals make informed choices(26), such as understanding benefits and risks of vaccination, and on the other hand, these policies must be applied ethically(27,28), as there is a thin line between nudging and forcefully pushing a decision(29–31). Therefore, the next question is determining the benefit-risk threshold at which individuals accept vaccination incentive policies to ensure that these policies are ethically applied to counteract omission bias.

Chapter III. Vaccine Acceptance

An important aspect of vaccine campaigns is that they sometimes include individuals with a low risk of severe disease outcomes to achieve herd immunity and protect the most vulnerable populations. However, this raises concerns among the general population about the perceived risks versus benefits associated with vaccines, particularly for those who feel they are at lower risk of severe disease(1,32,33).

Since the beginning of the first vaccinations against smallpox, confidence in vaccines has frequently wavered. At that time, concerns were primarily about the apprehension of contracting the disease as a consequence of vaccination(1). Subsequently, a sequence of global incidents raised concerns about the association of vaccination with some severe outcomes(34). The following section will quickly review historical incidents that have increased fear of vaccination risks.

In 1976, a large-scale vaccination campaign against swine flu started in the United States. Following the campaign, cases of Guillain-Barré syndrome were reported among vaccinated individuals. Although some authors at the time suggested a causal relationship between the vaccine and Guillain-Barré syndrome, these claims were not supported by scientific evidence(35). In 1993, the World Health organization (WHO) recommended the vaccine against Hepatitis B, leading to its implementation among infants in France, with an additional catch-up program for adolescents aged 11 to 17. In schools, the vaccination campaign started in 1994. In 1998, cases of multiple sclerosis emerged among recently vaccinated adults, leading the government to stop the school-based vaccine campaigns (causal relationship between vaccination and multiple sclerosis was not supported by scientific evidence)(34). In 2008, the introduction of the human papillomavirus vaccine raised concerns regarding the potential development of autoimmune disorders(36), which have never been scientifically confirmed(37). In 2009, cases of narcolepsy were declared following the vaccination against swine flu, leading to the withdrawal of the Pandemrix vaccine(38). Since then, numerous studies have confirmed a causal relationship between the AS03-adjuvanted pandemic H1N1 vaccine Pandemrix and narcolepsy(38–41). Since 2011, increased but limited risk of intussusception subsequent to the rotavirus vaccination in infants has been observed(42). However, given the morbidity and mortality of the rotavirus in young children, vaccination benefits outweigh risks, and vaccination is again recommended since(43).

Table 1. Side-effects of vaccines.

✓ Mild side effects	- Local pain - Swelling - Erythema - Fever	Frequent
✓ Major side effects	- Anaphylactic shock - Febrile convulsions - A form of the disease itself (for live attenuated vaccines) - Intussusception (from rotavirus vaccines but also from gastro-enteritis) - Myo(per)carditis (from ARNm vaccines but also from COVID-19 disease)	Extremely rare
✓ Severe side effects	- Narcolepsy (from flu H1N1 vaccine) - Thrombocytopenic thrombosis (from viral vector COVID-19 vaccines)	Vaccines no longer used or only given specific indication
✗ NOT CONFIRMED SUSPICIONS	- Guillain-Barré-syndrome - Multiple sclerosis	
✗✗ NOT SUPPORTED CLAIMS	- Autism - Sudden infant death syndrome	

Confidence in vaccines has also been jeopardized by misleading publications. In 1998, Dr. Andrew Wakefield published a study in *The Lancet*, a preeminent medical journal. The study claimed a potential link between the measles, mumps, and rubella (MMR) vaccine and the development of autism. Twelve years later, *The Lancet* retracted the paper due to the identification of several inaccuracies within the analysis. But, by that time, a significant number of parents worldwide had developed concerns about the MMR vaccine(44). This low level of confidence in vaccines is also fed by social networks, where various doctors who oppose vaccination share their perspectives.

Even though this low level of vaccine confidence has been observed globally with significant differences across social groups and countries(45,46), in France this crisis is unique(47). This is explained by numerous health emergencies that the country has gone through recently: a tainted blood scandal in 1991, a mad cow disease outbreak in 1996, the heat wave of 2009 and Médiator® in 2010(47).

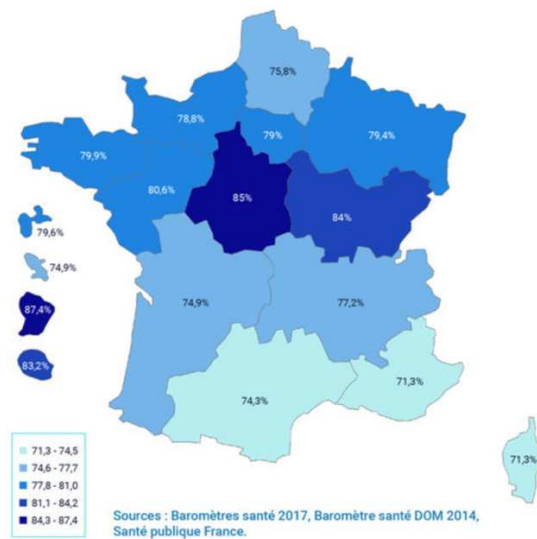
In 2016, the Health Barometer survey, which examines vaccine hesitancy, showed that 26% of parents reported having refused a recommended vaccine for their child because they considered the vaccine to be dangerous or unnecessary, 17% stated that they had delayed a vaccine recommended by a doctor due to uncertainty about vaccinating their child, and more than a quarter (27%) indicated having accepted a vaccine while having doubts about its efficacy. In 2017, seasonal influenza vaccination received the highest proportion of unfavorable opinions (14.1% of all surveyed individuals aged 18 to 75 years), surpassing hepatitis B vaccination (11.2%) and human papillomavirus vaccinations (4.9%)(48).

The demographic profile of those expressing unfavorable views towards vaccination varies depending on the type of vaccination, reflecting variation in risk perception of vaccination.

Hesitancy towards seasonal influenza vaccination is higher among adults aged 25-49 years, while hesitancy towards hepatitis B vaccination is more prevalent among individuals aged 35 to 64 years and those with higher income. On the other hand, individuals expressing unfavorable opinions about HPV vaccinations are primarily women and individuals with higher education studies. Notably, men are more likely to declare being opposed to all vaccinations(48).

France has regional disparities. In 2017, individuals residing in southern regions declared higher levels of unfavorable opinions compared to other areas (**Figure 1**).

Figure 1. Adherence to vaccination (in %) among 18–75-year-olds sorted by region of residency, in France, in 2017 (data of 2014 for French overseas territories).



3.1 Vaccination risks perception

Risk perception is the personal evaluation of characteristics and severity of a risk(49). As describe by Myhre et al.(2020), some individuals might perceive a potentially avoidable 5% risk of contracting HPV, which could lead to cervical cancer, as a significant risk, whereas others may consider this risk level low enough to not accept vaccination(49).

Risk perception about vaccines (side effects and safety) is one of the key factors influencing vaccine acceptance(50).Prior to the COVID-19 vaccine campaign, a study conducted across 15 countries showed that in case a vaccine against COVID-19 was available, among those who refused hypothetical vaccination, 34% mentioned fear of vaccination side-effects and 33% fear of vaccine safety because the vaccine was moving through clinical trials too fast(8).

HPV vaccination provides another example of how risk perception influences vaccine acceptance. The vaccine is recommended for adolescents aged 11–12, with a goal of completing the vaccine series before the initiation of sexual activity. One of the reason for parents to refuse

HPV vaccination among their child is low perceived susceptibility to HPV infection(51,52). Thus, some authors suggest that parents with strong religious or cultural beliefs in abstinence as a method to prevent their adolescent's lifetime risk of HPV infection may need alternative arguments to improve HPV vaccination rates(49). Moreover, parents who chose not to vaccinate their adolescents against HPV perceived a lower risk of HPV-related cancer and a higher risk of side-effects from the vaccine compare to those who vaccinated or intended to vaccinate their adolescent(49). Similarly, research on flu vaccination showed that people were more likely to decline vaccination if they perceived influenza as a minor illness.(53). As previously discussed in this thesis, the tendency to avoid vaccination due to fear of potential side-effects, even if the inaction (refusing the vaccine) could result in severe consequences from the disease itself, is referred to as omission bias(25). Some authors have explored the relationship between increased risk tolerance and vaccine acceptance. However, this has proven challenging because vaccination involves a trade-off between two risks: the risk of contracting the disease and the risk of potential side effects from the vaccine(54).

3.2 Public health implications

This fear of vaccination risks leads to several public health implications at a population level. According to a report from the French Public Health Agency(55), the morbidity and mortality of diseases such as tetanus and measles could have been decreased and avoided if vaccine coverage objectives had been reached. Moreover, diseases like HPV and meningitis could be eliminated if vaccine coverage were sufficiently high(55–59). However, the current HPV vaccination rates are not high enough to have a meaningful impact on morbidity and mortality, with the objective being to vaccinate 90% of girls worldwide by age 15(60,61).

3.3 Vaccine Hesitancy

Fear of vaccination risks is one aspect of what has largely been addressed in the scientific literature using the term “vaccine hesitancy”. In 2014, the SAGE group of the WHO defined vaccine hesitancy as “the delay in acceptance or refusal of vaccines despite availability of vaccine services”. Vaccine hesitancy is complex and context specific, varying across time, place, and vaccines. It is influenced by factors such as complacency, convenience, and confidence(62). Some authors have criticized this definition(63), arguing that it rather encompasses all vaccine attitudes and behaviors that do not involve either complete acceptance or complete refusal of all vaccines, irrespective of the individual vaccine's characteristics. Numerous studies have suggested that individual vaccine decisions vary depending on the characteristics of the vaccine(64,65). Thus, there is a need to delve into the complexity of

population preferences and attitudes towards vaccination. To achieve this, we choose two different but complementary approaches: preferences studies and the 7C-psychological antecedents of vaccination framework.

3.3.1 Justifying preference studies to identify approaches to increase vaccine acceptance

It has been suggested that vaccine hesitancy involves multiple factors beyond mere availability of vaccines. Preference studies start from the hypothesis that a large part of the population varies their vaccine intention based on the specific attributes of the proposed vaccination and the way in which HCSWs present it(64,66). Vaccine hesitancy encompasses an individual’s knowledge and attitude towards the context of vaccination(64–67). In this sense, it is the vaccination context that is put in doubt rather than the vaccine itself. Thus, vaccine hesitancy should not be seen as an immutable state.

An example of how vaccination behavior and preferences change with context: in France the National Institute for Health Education and Illness prevention (INPES), held a series of surveys to assess the adherence of the general population to vaccination. In 2010, following the H1N1 outbreak and Pandemrix vaccine withdrawal, there was a significant drop in the positive perception of vaccination among the general population. Since then, the positive perception of vaccination has increased, even though we have not returned to pre-2010 levels(48).

Figure 2. Evolution of adherence to vaccination (in %) among 18–75-year-olds in France, from 2000 to 2017.

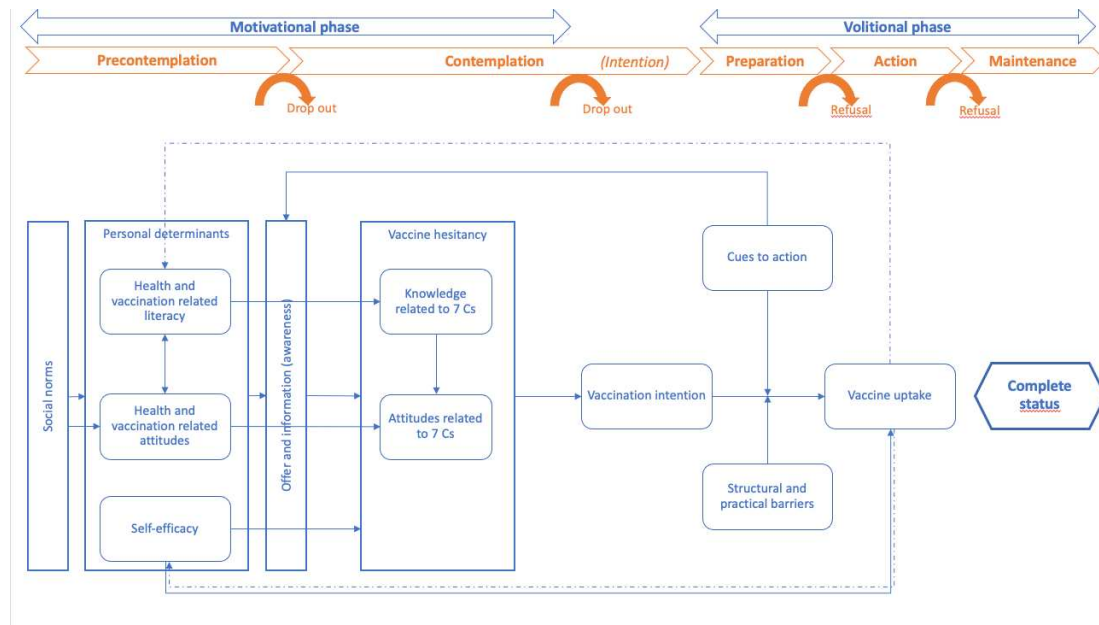


Sources : Baromètres santé 2000, 2005, 2010, 2014, 2016, 2017, Santé publique France.

Thus, preference studies are key to explore vaccine preferences among subgroups of the population in order to target vaccine campaigns and adapt vaccine risk communication to their preferences and concerns(48).

3.3.2 Psychological antecedents of vaccination: the 7C model

To better understand vaccine hesitancy and to evaluate interventions to mitigate, Oudin Doglioni & Mueller depicted the vaccine decision-making process with the integration of vaccine hesitancy through the application of Prochaska and Di Clemente transtheoretical model of behavioral change (2023). The following illustration aims to highlight the role of psychological factors in the vaccination decision-making process.

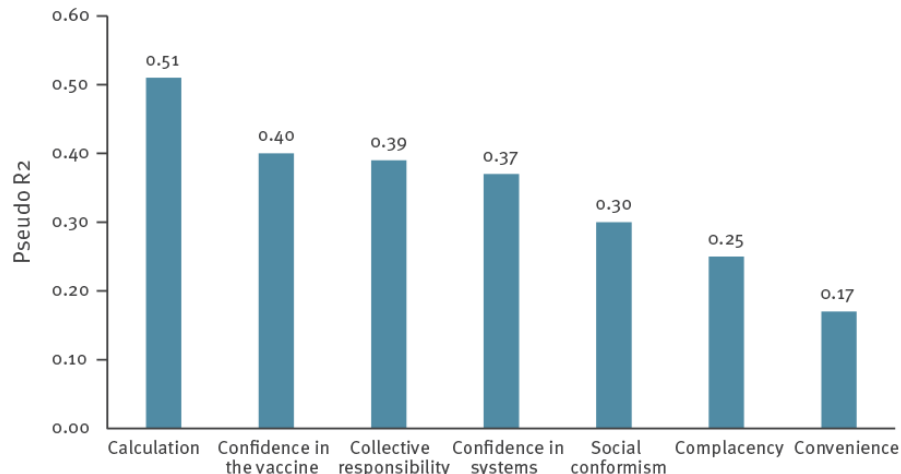


Psychological factors are placed in the contemplation phase. In the contemplation phase of vaccination, individuals start to recognize the potential importance of getting vaccinated and begin to seriously consider their intention to do so but have not yet committed to take action. They weigh the pros and cons of accepting or refusing vaccination.

The 7C-psychological antecedents of vaccine acceptance is an expansion of the original 3C model proposed by Macdonald et al. in 2015(62). The 3C model encompasses (i) confidence i.e. confidence in vaccines, the system that delivers them and motivations of policy makers who decide on needed vaccines; (ii) complacency i.e. need of the vaccine given its effectiveness and severity of the disease; and (iii) convenience i.e. accessibility. In 2018, Betsch et al.(68) proposed an expanded 5C-scale including two additional antecedents: (i) calculation (deliberation on risks and benefits of vaccination); and (ii) collective responsibility (sense of altruism towards getting vaccinated). With the emergence of the SARS-CoV-2 pandemic, two 7C-models were published nearly simultaneously. The Geiger et al. (2022)(69) 7C-model, applied to the Danish general population, introduced two additional components: conspiracy i.e. tendency to endorse conspiratorial beliefs about vaccination and compliance with

vaccination policies i.e. tendency to support monitoring to control adherence to regulations. In contrast, the Moirangthem et al. (2022)(70) 7C-model, focused on HCSWs in France, included social conformism i.e. taking decisions by imitating peers, and differentiated between confidence in the vaccine and confidence in the wider circle of systems, including authorities and employers. The results of Moirangthem et al. (2022) suggest that both antecedents are distinct and should be explored separately in future vaccine hesitancy research(71). Other studies have also explored the role of confidence in systems and provide insights on the association between vaccine acceptance, confidence in authorities, and employer reactance (*not published*).

Figure 3. Fit of regression models explaining vaccination intention among healthcare and welfare sector workers at the start of the COVID-19 vaccination campaign, contribution by each 7C-item group, France, 18 December 2020–1 February, 2021 (n = 5,234).



Moirangthem Simi, Olivier Cyril, Gagneux-Brunon Amandine, Pélissier Gérard, Abiteboul Dominique, Bonmarin Isabelle, Rouveix Elisabeth, Botelho-Nevers Elisabeth, Mueller Judith E. Social conformism and confidence in systems as additional psychological antecedents of vaccination: a survey to explain intention for COVID-19 vaccination among healthcare and welfare sector workers, France, December 2020 to February 2021. *Euro Surveill.* 2022;27(17):pii=2100617. <https://doi.org/10.2807/1560-7917.ES.2022.27.17.2100617> Received: 17 Jun 2021; Accepted: 21 Jan 2022

Several authors have highlighted that the factor that stood out as one of the most important domains on vaccine intention is "Calculation" (**Figure 3**)(70,71). Calculation stands separately from perceived usefulness and perceived safety of the vaccine. The next question raised is whether those 7C-psychological constructs vary with time and vaccination context. Some argue(68) that the pattern of psychological antecedents varies depending on the vaccination, target group, and country.

Chapter IV. Benefit-Risk Ratio (BRR)

Calculation refers to the deliberation on the balance between risks and benefits of vaccination. In the 7C-model, this calculation is based on individual perception and, according to Moirangthem et al., 2020 and to Oudin Doglioni et al., 2023(70,71), it is possibly the most important domain for vaccine decision-making.

Scientifically, the benefit-risk balance (BRB) is a ratio between vaccination benefits over vaccination risks, named benefit-risk ratio (BRR). This ratio is a key indicator used for regulatory evaluation of vaccines and considerations around vaccine strategies. It is frequently referenced in vaccine communication by health and public health professionals, often expressed as 'the benefits outweigh the risks'.

Risks are assessed during clinical trials and usually remain consistent regardless of the context. However, the extent of benefits varies depending on the context, on the epidemic situation, with higher incidences leading to higher BRR. BRR can be estimated through combining estimates of incident risk, but in epidemic situations, modeling studies provide more precise estimates(43), as they can better consider indirect protection effects. For example, BRR have been estimated for mRNA vaccination against COVID-19 in the US in 2021. Among male adolescents, the BRR of 1:1 indicated that COVID-19 vaccination avoided as many hospitalizations for COVID-related myo(pero-)carditis as it caused in vaccine-related myo(pero-)carditis. The BRR was 7:1 among young male adults(72), indicating a seven-times higher probability of benefit than risk from vaccination.. By contrast, the BRR regarding hospitalization and death related to infant rotavirus infection and intestinal intussusception related to vaccination were estimated as >200:1, meaning that the benefits strongly outweigh the risks in this case(43).

Rationale and hypothesis

As described in the introduction of this thesis, the literature shows the importance of the perception of benefits compared to risks in the vaccine decision-making process. In the context of vaccine hesitancy in France and in the aftermath of the COVID-19 crisis, we considered essential to better understand how the general population and HCSWs perceived the benefits vs. the risks of vaccination and how this perception influences their vaccine experiences.

Given the historical trajectory of vaccine acceptance and its associated aspects discussed through the previous chapters, this thesis is based on 4 personal insights.

A) The different policies implemented to increase COVID-19 vaccine coverage might have been felt as oppressive by individuals with strong certainty positions on their vaccine decision. This could impact future vaccination campaigns by backfiring those who felt oppressed from future vaccinations. As BRB perception is key in vaccination decision-making process, BRB perception could have also played a role in their vaccine experience and future vaccine intentions. Thus, it appears essential to assess future vaccine intention of the population according to their vaccine experience and perception of COVID-19 vaccine BRB.

B) If the perception of a vaccine's BRB was entirely rational, it would likely vary significantly depending on the vaccine and the context in which it is used. However, it is also possible that BRB perception is a more stable attitude that an individual maintains across different vaccines and over time, acting as an *a priori* opinion on vaccination. Additionally, the importance of BRB perception may fluctuate in influencing vaccine decisions over time. The COVID-19 vaccination campaign provided a unique opportunity to evaluate the evolving perceptions of vaccine BRB throughout various stages of the epidemic context and evolving knowledge about the vaccines, and their association with vaccine intention and uptake.

C) According to the concept of vaccine hesitancy, individual's vaccine decisions stand on a spectrum between accepting all and refusing all recommended vaccines. Vaccine promotion should therefore particularly target those who stand in-between the extremes, as their decisions vary based on the characteristics of the proposed vaccine and specific circumstances. However, there is a lack of evidence regarding the effectiveness of approaches to overcome vaccine hesitancy(45). As perceived vaccination BRB is a key determinant of vaccine acceptance, it

appears indispensable to study the effectiveness of communicating the benefits and risks of vaccination to improve vaccine acceptance. Taking a purely rational approach, individuals are expected to accept vaccination at benefit-risk ratio of 2:1, indicating that they would find it acceptable if the potential benefits in avoiding disease cases are twice as much as the potential side effects. However, individuals might demand a higher benefit-risk ratio for vaccination to be acceptable. Currently, there is no quantitative evidence available to determine the specific range of benefit-risk ratio within which individuals can prefer not to get vaccinated. In other words, we lack information about the minimum benefit-risk ratio required for the general population and HCSWs to accept vaccination.

C) Finally, we know that decision-making is a nuanced process, each choice has a spectrum of certainty level regarding the chosen course of action, thus, to implement targeting vaccine campaigns, it is crucial to understand different vaccination profiles according to BRB vaccination attributes. In this sense, it appears essential to discern among vaccine-reluctant individuals the proportion who express varying certainty about their refusal and may be compliant to persuasion through targeted vaccine communication on vaccination benefits-risks.

Thesis objectives

The work of this thesis focuses on fourth main objectives:

Aim 1. Assess the impact of COVID-19 certificate or vaccine mandate on future COVID-19 vaccine intention considering the perceived BRB of COVID-19 vaccination.

Objective 1a. To explore determinants of those who cede to the requirement and their BRB perception of the COVID-19 vaccination.

Objective 1b. To assess the impact of the requirement on future COVID-19 vaccination intention and the role of the vaccination BRB perception in these future intentions.

Objective 1c. To evaluate if the requirement had increased inequalities in vaccine uptake.

Aim 2. Evaluate the 7C-psychological antecedents of vaccination across the novel COVID-19 vaccine campaign.

Objective 2a. To assess the association between the 7C-psychological antecedents of vaccination and COVID-19 vaccine intentions, particularly the perceived BRB of COVID-19 vaccination, across various stages of the pandemic.

Aim 3. Explore preferences around the concept of benefit-risk ratio among the general adult population and among HCSWs.

Objective 3a. To identify a specific benefit-risk ratio threshold for vaccine acceptance.

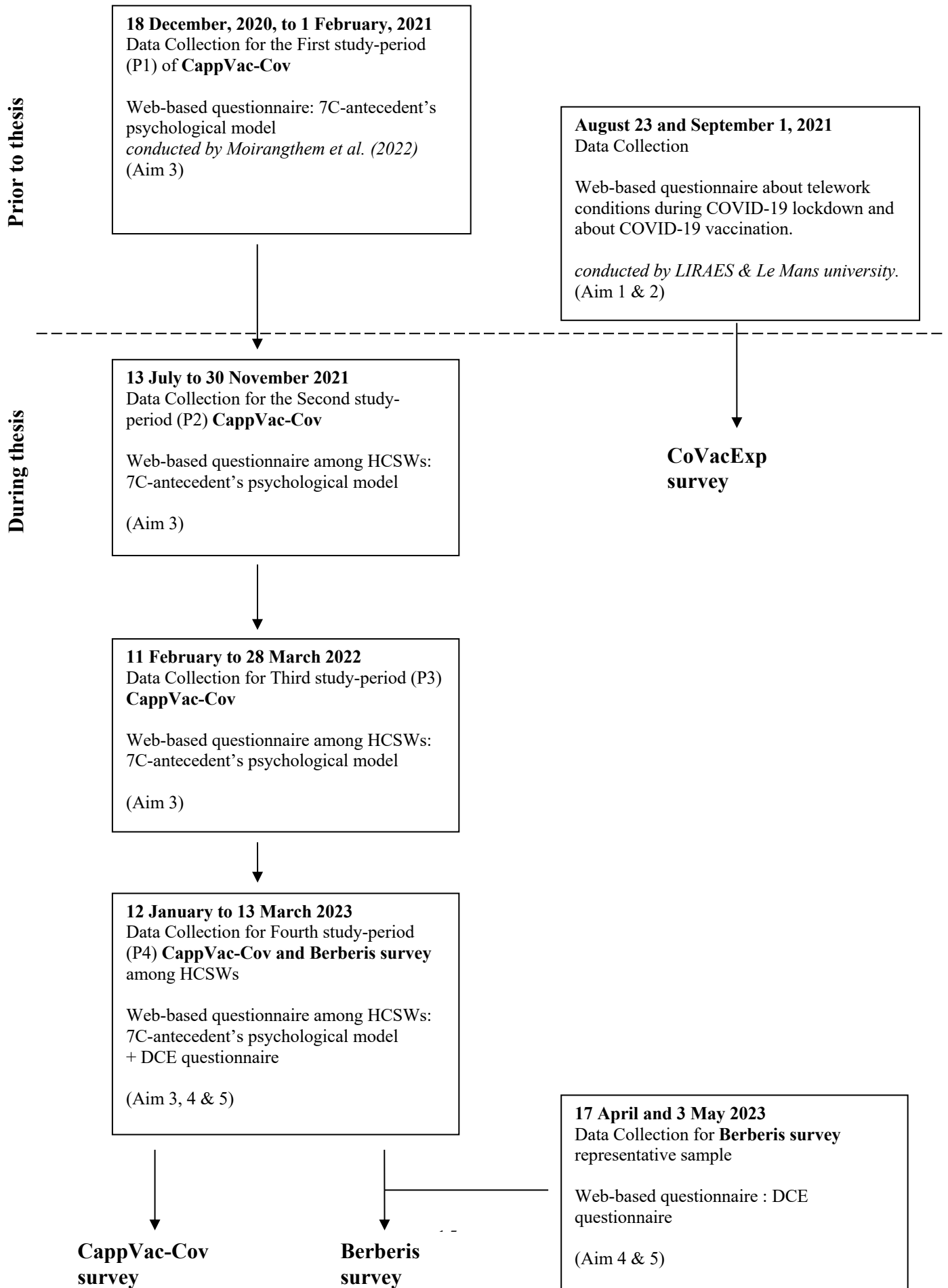
Objective 3b. To assess benefit-risk preferences among respondents who consistently refused vaccination.

Aim 4. Define and characterize serial vaccine non-demanders regardless to BRB attributes.

Objective 4a. To identify proportion of those that while initially hesitant towards vaccination, may be compliant to persuasion through targeted vaccine communication.

Objective 4b. To identify socio-demographic characteristics of serial demanding behaviors and reasons for refusing vaccination.

Methodology



Prior to this thesis, two surveys were conducted. The first by S. Moirangthem et al.(2022) studied the 7C model among HCSWs in the early stages of the COVID-19 vaccine campaign, with published in *Eurosurveillance* journal (70)). This survey represents the first study period of CappVac-Cov study (**Aim 3**). The second survey was conducted by LIRAES and Le Mans University to assess telework conditions during the lockdown. Dr. Judith E. Mueller included questions on vaccine behaviors in this survey, which constitutes the CoVacExp study, the first paper of this thesis (**Aim 1 & 2**).

Since the start of my thesis, three additional surveys have been launched to complement the CappVac-Cov study (**Aim 3**). The last questionnaire period (P4), collected data for both the final study period of CappVac-Cov and the Berberis study among HCSWs (**Aim 4 & 5**). Finally, a survey conducted between April 17 and May 3, in collaboration with the survey institute Panelia, utilized the same questionnaire previously administered among HCSWs (Berberis section of the questionnaire conducted between January 12 and March 13) to gather data among a representative sample of the adult French population (**Aim 4 & 5**).

Chapter I. Survey Research (Aims 1-5)

Surveys serve as a methodology to collect data about socio-demographic characteristics, preferences, or opinions within a group of participants. They can employ quantitative research strategies, such as utilizing numerically rated items, qualitative research strategies involving open-ended questions, or a combination of both. One of their major strengths is their efficiency in data collection, often administered via mail. These methodologies are typically conducted by survey institutes that adhere to rigorous research protocols, including quotas sampling to ensure representative samples based on the latest census data from organizations such as INSEE. They also establish protocols for initiating surveys and follow-up to reduce non-response error.

Despite the use of quota sampling, surveys may not capture fully representative samples of the overall population. One of its major limitations is the necessity for study participants to have access to an electronic device, thus, possibly excluding the most deprived population groups. Moreover, the self-administered questionnaire may introduce some misunderstandings, but can mitigate social-desirability bias.

Chapter II. Questionnaire based on a 5-point Likert-scale 7C model (Aim 3)

The perceived benefit-risk balance of vaccination is part of the 7C-model, which investigates psychological factors influencing vaccine acceptance (Calculation item). This model explores perceived vaccination BRB through responses to the statement “*I think ___*

vaccination has more benefits than risks for me". The statement is adapted to each vaccination campaign, and respondents indicate their agreement using a 5-point Likert scale: (1) strongly disagree; (2) disagree, (3) neither agree nor disagree, (4) agree, (5) strongly agree. For multivariable analyses, 7C items were grouped into categories of (strongly) disagree, undecided and (strongly) agree with the statement.

Similar statements are developed and answered by participants with this psychometric method to explore the remaining Cs of the 7C-model: complacency (not perceiving diseases as high risk and vaccination as necessary), convenience (practical barriers), collective responsibility (willingness to protect others by one's own vaccination), social conformism (influence of peers), confidence in the vaccine (lack of trust in safety and effectiveness of vaccines), confidence in the system (lack of trust in authorities that recommend the vaccine or reactance to employer vaccine recommendation). Then, the relationship between these statements and future vaccine recommendations is examined through multivariable models. Depending on study power, 7C items are grouped into 3 categories; strongly disagree and disagree as disagree, undecided, and strongly agree and agree as agree.

The original 7C-model initially included one statement for attitudes towards vaccination and one for epidemiology or vaccine knowledge for every C-item. However, due to evolving evidence on the COVID-19 epidemiology and vaccines during the pandemic, we decided neither to explore knowledge items of the 7C-model at P4 nor to analyze the association of knowledge items from P1 to P3 with vaccine decision.

The 7C-model, proposed and validated by Moirangthem et al. (2022) and Oudin Doglioni (2023) during the COVID-19 pandemic, has been built from previous frameworks(70,73). Originally, the model encompassed 3C-psychological antecedents'; complacency, convenience and confidence in the vaccines(74). Then, Betsch et al. (2018) extended the model to a 5C-model by integrating calculation and collective responsibility(68). During the COVID-19 pandemic, Moirangthem et al. (2022) and Oudin Doglioni (2023) further extended it to the 7C-model more suitable to explain the antecedents of HCSWs vaccine acceptance during the pandemic; confidence was split into confidence in the vaccine safety and on the system that recommend them, and added an additional item - social conformism.

Chapter III. Estimation of prevalence ratios in cross-sectional studies with binary outcomes

The association between the 7C-model statements, as detailed in the previous section, and future vaccine acceptance is explored through multivariable models. These models assess the contribution of each C-item to the vaccine decision. The outcome is binary as participants either indicate acceptance or non-acceptance of hypothetical future vaccination.

Binary outcomes in multivariable analyses are typically evaluated using logistic regressions, which calculates odds ratios to quantify the strength of associations with the covariates. However, it is recognized that odds ratios can overestimate risk ratios, when the outcome is frequent (>10%). Additionally, communicating results in terms of odds ratios can be challenging for audiences unfamiliar with their interpretation. Consequently, some researchers suggest reporting prevalence ratios, which closely approximate risk ratios even in scenarios of frequent outcomes. Thus, in order to report prevalence ratios, log-binomial models or Poisson regressions with robust variance estimation have been proposed as suitable methods(75). Poisson regressions are typically used for count data, they can be adapted for binary outcomes, for instance, by treating the absence of disease as 0 and the presence of disease as a count of 1.

At the beginning of this thesis, our aim was to develop log-binomial models for assessing future vaccine intentions. However, during the development of the multivariable model detailed in table 4 (article 1 of this thesis), we faced challenges. Upon incorporating the sixth variable into the model, regardless of which variable it was, we observed an increased in adjusted prevalence ratios (aPR) after adjusting the model for BRB (Calculation item of the 7C-model). Interestingly, up to the addition of the sixth variable, the aPR tended to decrease following adjustment for BRB indicating partial BRB mediation in the association between Cs-items and vaccine decision. Additionally, an error message indicated that the logarithm failed to converge. Barros et al. (2003) showed that log-binomial models are as performant as robust variance poisson regression models when the logarithm converges. Thus, we conducted a comparative analysis of both approaches (**Supplementary Table 1**). Our findings indicated that log-binomial models reached saturation earlier than Poisson regression models with robust variance. Consequently, we decided to report aPR using the Poisson regression model with robust variance.

Chapter IV. DCE (Aim 4 & 5)

Surveys use to explore vaccine behaviours with standard questions such as “Do you think that vaccination has more benefits than risks for you?”, which can be very hard to answer without defining the vaccination scenario. In this sense, DCEs are an innovative solution to explore vaccine preferences in a more realistic way. Moreover, the results of Betsch et al. using the 5C model showed that the pattern of significant predictors varies depending on the vaccination context and target or risk group, as well as country. Indeed, from the definition of vaccine hesitancy, we know that vaccine acceptance its context specific, thus DCEs are a methodological tool to explore vaccine behaviors across different vaccination contexts.

DCEs enable to establish the context in which the question is posed through a series of attributes with different levels. Attributes and their respective levels are defined by the investigator through literature review and focus groups. Then, a set of scenarios are constructed by combining the levels of the selected attributes.

The statistical analysis enables the assignment of weights to each attribute level in the vaccine decision-making process, in other words, it allows to quantify the deliberation among various characteristics of vaccination. In our case, it will allow to define the deliberation between benefits and risks of vaccination.

$$\text{Predicted Vaccine Coverage} = ([1 / (1 + e^{-\text{utility}_j})] * R + D) / (R + D + N)$$

j: vaccine scenarios

R: number of non-uniform respondents

D: number of serial demanders

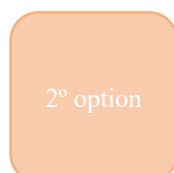
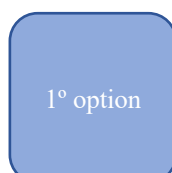
N: number of serial non-demanders

utility = sum of products (coeff_i * l)

l: attribute i level 0 (reference) or 1

In the context of vaccination, single-profile DCEs are an adaptation of the methodology that reproduces more realistically the situation of the vaccine decision as a binary choice, rather than a comparison between options(66).

- Multi-profile DCEs: the participant has to select between two options or to opt-out



○ Opt-out

- Single profile DCEs: the participant has to either accept the proposed option or to opt-out



- Opt-out

Article presentation

Aim 1. Impact of the COVID-19 certificate and role of perceiving more vaccination benefits than risks on vaccine motivation during the pandemic and on future COVID-19 vaccine intention.

The first article of this PhD thesis investigates the impact of perceived benefit-risk balance of vaccination on vaccine acceptance within the context of stringent vaccine regulations implemented by the French government during the COVID-19 pandemic. Furthermore, this study provides an analysis of potential inequalities caused by the introduction of the vaccination pass.

Article 1: Impact of a COVID-19 certificate requirement on vaccine uptake pattern and intention for future vaccination. A cross-sectional study among French adults.

Reference: Araujo-Chaveron L, Sicsic J, Moffroid H, Díaz Luévano C, Blondel S, Langot F, Mueller JE. Impact of a COVID-19 certificate requirement on vaccine uptake pattern and intention for future vaccination. A cross-sectional study among French adults. *Vaccine*. 2023 Aug 23;41(37):5412-5423. doi: 10.1016/j.vaccine.2023.07.002. Epub 2023 Jul 20. PMID: 37481404.

Journal: *Vaccine* (Impact Factor 5.5).

Background

To avoid the outright restriction of citizens' liberty that a vaccine mandate would represent, several countries adopted policies requiring COVID-19 vaccination or negative testing for accessing certain public places and services(9,11). In France, COVID-19 vaccination became accessible to the general adult population in May 2021. Given stagnating uptake, the French government announced mid-July a COVID-19 certificate (which included vaccination, recovery, or recent negative test) was required to attend specific services and gatherings (e.g., trains, restaurants, hospitals) and was enacted for adults on August 9(11). In addition, vaccination became mandatory for healthcare and welfare workers(11).

Vaccine mandates and requirements can be perceived as paternalistic policies with the risk to backfire from future vaccination campaigns (or other governmental actions) those who already

had strong vaccine positions(19,20,76,77). We hypothesized that the perception of the vaccination BRB can modify this vaccine experience.

Moreover, vaccine mandates and requirements can also be perceived as incentive policies(78,79); on a gradient of incentivization according to the degree of consequence for non-compliance. An important criterion for evaluating public health policies is whether they foster equal uptake of interventions(80). For instance, a vaccine requirement for accessing employment acts only on professionally active persons, thus, strengthening the healthy worker effect(81).

The objectives of this article are thus to assess, first, socio-economic determinants of observed and expected vaccine status if the COVID-19 certificate mandate was not enacted, second, socio-economic determinants of having ceded to vaccination despite no genuine motivation for it, and, third, the association of vaccine experience with intention for further COVID-19 vaccination.

Methods

In late August 2021, a representative sample of adults (18–75 years) completed an internet-based questionnaire. We classified vaccinated participants by stated reasons for vaccination, thus by vaccine experience.

We created a variable called Vaccine experience combining vaccine status with motivations for observed or intended COVID-19 vaccination to identify different profiles to the reaction of the implementation of the COVID-19 certificate or mandate vaccination among HCSWs.

Vaccination status was evaluated as “Today, what is your situation regarding vaccination against COVID-19?” with following modalities: vaccinated with at least one-dose/with appointment for first injection/ history of SARS-CoV-2 infection and have to wait to get the vaccine/ vaccination planned/ unsure if concerned/ do not want to be vaccinated/ do not want to answer. The motivations for observed or intended COVID-19 vaccination were explored through seven proposed personal reasons that participants placed in decreasing order of relevance: “to protect me”, “to help control the epidemic”, “to avoid transmitting the virus to my relatives”, “to follow recommendations”, “to obtain the health certificate”, “because of professional obligation”, “because the emergence of viral variants makes vaccination necessary”. Reasons for remaining unvaccinated were also explored through eleven proposed personal reasons. Participants were able to select one out of eleven reasons: “unknown serious side effects”, “not having enough perspective”, “usefulness of vaccines”, “recommendations

are influenced by pharmaceutical companies”, “afraid of injections”, “state of health does not allow vaccination”, “not a disease serious enough”, “not exposed to the risk of contamination”, “already immunised”, “feeling of indirect protection by vaccinated people”, “relatives advise against it”.

We excluded participants who reported to “have been infected with SARS-CoV-2, therefore not being concerned by vaccination”, according to the vaccine recommendation at the time of the survey (N = 13, 1.3%).

Then, 5 vaccine experience profiles were identified:

- CM-only: those vaccinated solely because the COVID-19 certificate or mandate.
- CM+others: those vaccinated because the COVID-19 certificate or mandate but also for other reasons.
- CM-not main: those vaccinated but not indicating the COVID-19 certificate or mandate as one of the three first reasons or not at all.
- Unvaccinated.
- Not Applicable (NS): We excluded participants who reported to “have been infected with SARS-CoV-2, therefore not being concerned by vaccination”, according to the vaccine recommendation at the time of the survey.

This variable enabled to address the objectives of Aim 1 of this PhD thesis:

- Aim 1, objectives 1a by identifying those who ceded to vaccination despite no genuine motivation for it (vaccine experience profile: CM-only and CM+others), it allows us to be able to identify their determinants. Additionally, we will explore whether perceived vaccination BRB significantly differentiate these groups.
- Aim 1, objectives 1b by defining 5 profiles with different vaccine experience it allows to assess the association between these profiles and future COVID-19 vaccine intention (intention for future COVID-19 vaccination: yes vs. no/do not know). We hypothesized that perceived vaccination BRB might mitigate the influence of past vaccine experience on future vaccination intentions or reduce the differences between the 5 vaccine experience profiles; individuals having ceded to the certificate constraint (getting vaccinated only to obtain the certificate, CM-only) might show lower future vaccination acceptance, even if recommended by their physician, compare to other groups. This was explored through mediation analysis.

- Aim 1, objective 1c. To be able to identify if the requirement had increase existing inequalities, we should identify what would have occurred in the absence of the requirement. This is called a counterfactual analysis. A counterfactual analysis explores outcomes that did not actually occur, but which could have occurred under different conditions. Then, we hypothesized that those vaccinated solely because the mandate or COVID-19 certificate would not have been vaccinated in the absence of the COVID-19 certificate or mandate (vaccine experience profile: CM-only and CM+others). We then compare determinants of the counterfactual analysis with those of the observed vaccine status.

Mediation analyses are employed to understand a known relationship by exploring the underlying mechanism or process by which one variable influences another variable through a mediator variable. Since, balancing benefits and risks of vaccination appears to be one the strongest determinants of vaccine intention, we hypothesized that this could be the underlying mechanism in the relation between socio-economic determinants of vaccine intention. A mediator can fully mediate the association between two variables (full mediator) leading to not significant association between the two variables in its presence in the statistical model or partially mediate the association.

Outcome and Statistical Analysis

Future vaccination intention was classified as Yes vs. No/Do Not Know. We used robust-variance Poisson regression models to estimate the unadjusted and adjusted prevalence ratios (aPR) for the different outcomes.

Results

After excluding 13 participants who reported previous SARS-CoV-2 infection and thus were not eligible for vaccination, we included 972 participants (**Figure 4**), 51.5% of which were women (**Table 2**). Age groups 18–39 years, 40–59 years and 60–75 years contributed 36.7%, 36.9% and 26.4%, respectively, of participants. One-third (30.6%) were occupationally inactive and 14.3% declared having poor financial income. Overall, 9.4% participants worked in the health or welfare sector and thus were subject to the vaccine mandate.

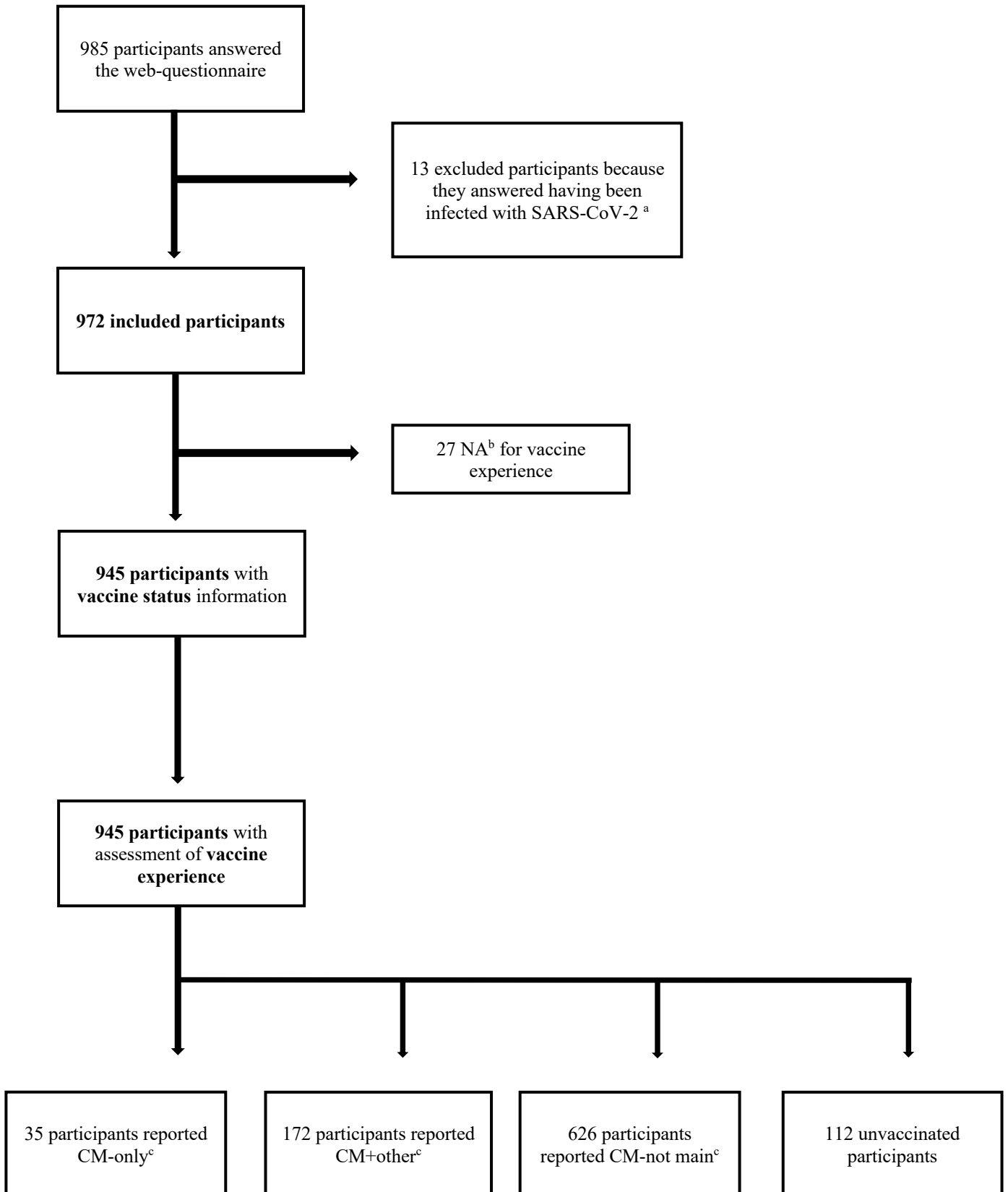


Figure 4. Flow chart of inclusion participants. ^a We excluded participants who reported to “have been infected with SARS-CoV-2, therefore not being concerned by vaccination”, according to the vaccine recommendation at the time of the survey. ^b NA not applicable to vaccine experience, participant was not sure whether concerned by vaccination or does not want to answer. ^c CM, Requirement of COVID-19 certificate or professional mandate

(CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM+other); CM not mentioned as first reason (CM-not-main).

COVID-19 vaccination was reported by 778 participants (80.0%), 55 (5.7%) had intention to do so, (subsequently combined into “vaccinated”), while 11.5% remained unvaccinated and 1.4% declared not knowing if they were concerned by vaccination. Overall, 714 (73.5%) declared they would accept COVID-19 vaccination in the future if recommended by their referring physician. Two-thirds (607, 62.4%) of participants had a favourable perception of their individual BRB with COVID-19 vaccine and one fourth (231, 23.8%) contributed a free-text testimonial with a maximum of 377 letters.

Among 972 participants, 85.7% were vaccinated or intended vaccination: 3.6% only for certificate/mandate, 17.7% mainly for certificate/mandate plus other reasons, and 64.4% mainly for other reasons.

		without genuine motivation for vaccination			
CM-not main (64.4%)	CM+others (17.7%)	CM-only (3.6%)	Unvaccinated (11.5%)	NA (2.8%)	
Vaccinated indicating CM not as first reason or not at all	Vaccinated indicating Covid-19 certificate as first reason among others	Vaccinated indicating Covid-19 certificate as sole reason			
		CM-main (21.3%)			
		CM-only and CM+others were combined into CM-main			

Table 2. Description of the study population according to the importance given to COVID-19 certificate or mandate (CM) (Vaccine experience) (N=972). Adults in France, August 2021. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

	Total	Unvaccinated			Vaccinated			NA**
	N (%)	(N=112, 11.5%)	CM-only (exclusively for requirement or professional mandate) (N=35, 3.6%)	CM+other (first reason among others) (N=172, 17.7%)	CM-not-main (not mentioned as first reason) (N=626, 64.4%)	(N=27, 2.8%)		
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Demographic and socio-economic characteristics								
Gender								
Man	471 (48.5)	49 (10.4)	13 (2.8)	78 (16.6)	320 (67.9)	11 (2.3)		
Woman	501 (51.5)	63 (12.6)	22 (4.4)	94 (18.8)	306 (61.1)	16 (3.2)		
Age (in years)								
Between 18 and 39	357 (36.7)	44 (12.3)	14 (3.9)	99 (27.7)	180 (50.4)	20 (5.6)		
Between 40 and 59	359 (36.9)	42 (11.7)	14 (3.9)	53 (14.8)	245 (68.2)	5 (1.4)		
Between 60 and 75	256 (26.4)	26 (10.2)	7 (2.7)	20 (7.8)	201 (78.5)	2 (0.8)		
Region of residence								
Paris Region	184 (18.9)	19 (10.3)	4 (2.2)	36 (19.6)	116 (63.0)	9 (4.9)		
North East	212 (21.8)	24 (11.3)	6 (2.8)	30 (14.2)	148 (69.8)	4 (1.9)		
North West	222 (22.8)	23 (10.4)	8 (3.6)	41 (18.5)	143 (64.4)	7 (3.2)		
South East	245 (25.2)	36 (14.7)	12 (4.9)	46 (18.8)	147 (60.0)	4 (1.6)		
South West	109 (11.2)	10 (9.2)	5 (4.6)	19 (17.4)	72 (66.1)	3 (2.8)		
Type of locality								
Big town (more than 100.000 inhabitants)	199 (20.5)	22 (11.1)	6 (3.0)	35 (17.6)	129 (64.8)	7 (3.5)		
Medium-size town (between 20.000 and 100.000 inhabitants)	254 (26.1)	29 (11.4)	5 (2.0)	50 (19.7)	163 (64.2)	7 (2.8)		
Small town (between 2.000 and 20.000 inhabitants)	292 (30.0)	34 (11.6)	13 (4.5)	52 (17.8)	188 (64.4)	5 (1.7)		
Village (less than 2.000 inhabitants)	227 (23.4)	27 (11.9)	11 (4.8)	35 (15.4)	146 (64.3)	8 (3.5)		
Educational level								
Lower than secondary school diploma	209 (21.5)	23 (11.0)	5 (2.4)	33 (15.8)	141 (67.5)	7 (3.3)		
Equal to secondary school diploma	240 (24.7)	34 (14.2)	7 (2.9)	41 (17.1)	154 (64.2)	4 (1.7)		

ARTICLE PRESENTATION – ARTICLE 1

	2-5 years beyond secondary school diploma	383 (39.4)	42 (11.0)	19 (5.0)	68 (17.8)	244 (63.7)	10 (2.6)
	5-7 years beyond secondary school diploma	140 (14.4)	13 (9.3)	4 (2.9)	30 (21.4)	87 (62.1)	6 (4.3)
Professional training							
	Outside health care	881 (90.6)	102 (11.6)	29 (3.3)	151 (17.1)	574 (65.2)	25 (2.8)
	Health care	91 (9.4)	10 (11.0)	6 (6.6)	21 (23.1)	52 (57.1)	2 (2.2)
Occupational status							
	Active	675 (69.4)	67 (10.5)	29 (4.3)	136 (20.1)	390 (57.8)	18 (2.7)
	Inactive	297 (30.6)	38 (12.8)	4 (1.3)	29 (9.8)	218 (73.4)	8 (2.7)
Annual income							
	> 26.700 euros	257 (26.4)	24 (9.3)	10 (3.9)	36 (14.0)	184 (71.6)	3 (1.2)
	Between 9.300 and 26.700 euros	461 (47.4)	48 (10.4)	19 (4.1)	86 (18.7)	302 (65.5)	6 (1.3)
	Between 0 and 9.300 euros	139 (14.3)	20 (14.4)	3 (2.2)	30 (21.6)	82 (59.0)	4 (2.9)
	Does not want to answer	115 (11.8)	20 (17.4)	3 (2.6)	20 (17.4)	58 (50.4)	14 (12.2)
Minor or dependent child(ren)							
	No	632 (65.0)	66 (10.4)	23 (3.6)	110 (17.4)	412 (65.2)	21 (3.3)
	Yes	340 (35.0)	46 (13.5)	12 (3.5)	62 (18.2)	214 (62.9)	6 (1.8)
Speaking other language than French							
	No	802 (82.5)	88 (11.0)	32 (4.0)	142 (17.7)	519 (64.7)	21 (2.6)
	Yes	170 (17.5)	24 (14.1)	3 (1.8)	30 (17.6)	107 (62.9)	6 (3.5)
COVID-19-related characteristics							
Previously infected by SARS-CoV-2							
	No	885 (91.0)	103 (11.6)	32 (3.6)	151 (17.1)	575 (65.0)	24 (2.7)
	Yes	87 (9.0)	9 (10.3)	3 (3.4)	21 (24.1)	51 (58.6)	3 (3.4)
Relatives previously ill with COVID-19							
	No	585 (60.2)	79 (13.5)	25 (4.3)	99 (16.9)	366 (62.6)	16 (2.7)
	Yes	387 (39.8)	33 (8.5)	10 (2.6)	73 (18.9)	260 (67.2)	11 (2.8)
Self-reported risk factor for severe COVID-19							
	No	727 (74.8)	88 (12.1)	28 (3.9)	149 (20.5)	439 (60.4)	23 (3.2)
	Yes	245 (25.2)	24 (9.8)	7 (2.9)	23 (9.4)	187 (76.3)	4 (1.6)
Level of confidence in authorities in the management of the COVID-19 crisis							
	Low	231 (23.8)	72 (31.2)	26 (11.3)	40 (17.3)	85 (36.8)	8 (3.5)
	Moderate/High	741 (76.2)	40 (5.4)	9 (1.2)	132 (17.8)	541 (73.0)	19 (2.6)
Perception of Benefit-Risk Balance (BRB)							

ARTICLE PRESENTATION – ARTICLE 1

	More risks than benefits	193 (19.9)	79 (40.9)	18 (9.3)	45 (23.3)	43 (22.3)	8 (4.1)
	More benefits than risks	607 (62.4)	9 (1.5)	4 (0.7)	75 (12.4)	510 (84.0)	9 (1.5)
	Does not know	172 (17.7)	24 (14.0)	13 (7.6)	52 (30.2)	73 (42.4)	10 (5.8)
Free-text testimonial							
	No	741 (76.2)	77 (10.4)	25 (3.4)	133 (17.9)	485 (65.5)	21 (2.8)
	Yes	231 (23.8)	35 (15.2)	10 (4.3)	39 (16.9)	141 (61.0)	6 (2.6)
Vaccine Status							
	Vaccinated	778 (80.0)	-	30 (3.9)	151 (19.4)	597 (76.7)	-
	Booked an appointment for 1st injection or with Intention to get appointment	55 (5.7)	-	5 (9.1)	21 (38.2)	29 (52.7)	-
	Unvaccinated without intention	112 (11.5)	112 (100.0)	-	-	-	-
	Not sure whether concerned	14 (1.4)	-	-	-	-	14 (100.0)
	Does not want to answer	13 (1.3)	-	-	-	-	13 (100.0)
Future intention to accept COVID-19 vaccine given medical recommendation							
	No	170 (17.5)	104 (61.2)	21 (12.4)	27 (15.9)	11 (6.5)	7 (4.1)
	Yes	714 (73.5)	4 (0.6)	8 (1.1)	112 (15.7)	586 (82.1)	4 (0.6)
	Does not know	88 (9.1)	4 (4.5)	6 (6.8)	33 (37.5)	29 (33.0)	16 (18.2)

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM+other); CM not mentioned as first reason (CM-not-main).

** “Not sure whether concerned or does not want to answer”. NA, not applicable to vaccine experience (recently infected)

In the counterfactual situation, vaccine uptake would have been significantly more likely among older vs. younger participants (aPR = 1.35) and among those with moderate-high vs. low levels of confidence in authorities for COVID-19 crisis management (aPR = 2.04). In the observed situation, confidence was the only significant determinant of vaccine status (moderate-high vs. low, aPR = 1.39) (**Table 3**).

Table 3. Determinants of counterfactual and observed COVID-19 vaccination status among adults in France (N=945), August 2021. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

	Counterfactual vaccine status: Vaccinated (N=626) vs. Unvaccinated, CM-only or CM+other* (N=319)		Observed vaccine status: Vaccinated (N=833) vs. Unvaccinated (N=112)		
	aPR	<i>p</i> -value	aPR	<i>p</i> -value	
Demographic and socio-economic characteristics					
Gender					
	Man	1.09	0.277	1.02	0.317
	Woman	1		1	
Age (in years)					
	Between 18 and 39	1		1	
	Between 40 and 59	1.28	0.014	1.03	0.358
	Between 60 and 75	1.35	0.032	1.03	0.364
Annual income					
	> 26.700 euros	1.08	0.576	1.05	0.178
	Between 9.300 and 26.700 euros	1.03	0.838	1.04	0.352
	Between 0 and 9.300 euros	1		1	
	Does not want to answer	0.96	0.793	0.95	0.364
Professional training					
	Outside health care	1			
	Health care	0.89	0.449		
Occupational status					
	Active	1			
	Inactive	1.07	0.557		
Minor or dependent child(ren)					
	No			1	
	Yes			0.96	0.107
COVID-19 related characteristics					
Relatives previously ill with COVID-19					
	No	1		1	
	Yes	1.02	0.806	1.04	0.098
Self-reported risk factor for severe COVID-19					
	No	1			
	Yes	1.17	0.088		
Level of confidence in authorities in the management of the COVID-19 crisis					

Low	1		1	
Moderate/High	2.04	<0.001	1.39	<0.001

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); requirement of certificate or professional mandate as first reason among others (CM+other).

Among those without genuine motivation for vaccination, professionally active persons were more likely to have ceded to the certificate requirement (aPR = 3.76). Those vaccinated only for the certificate were more likely to express future COVID-19 vaccine intention than unvaccinated persons (aPR = 6.41). Themes significantly associated with lower confidence were criticism of morality (aPR = 1.76) and poor communication by the authorities (aPR = 1.66) (Table 4).

Table 4. Determinants of vaccine experience (vaccine uptake and motivation) among participants without genuine motivation for vaccination (N=147) and among vaccinated participants (N=833). Adults in France, August 2021. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

		Among persons without genuine motivation for vaccination; CM-only (N=35) vs. Unvaccinated (N=112)			
		aPR	<i>p</i> -value	aPR with BRB	<i>p</i> -value
Demographic and socio-economic characteristics					
Gender					
	Man	1		1	
	Woman	1.22	0.528	1.23	0.515
Age (in years)					
	Between 18 and 39	0.58	0.188	0.72	0.458
	Between 40 and 59	0.56	0.181	0.67	0.382
	Between 60 and 75	1		1	
Professional training					
	Outside health care	1		1	
	Health care	1.38	0.382	1.45	0.345
Occupational status					
	Active	3.76	0.013	3.46	0.020
	Inactive	1		1	
Annual income					
	> 26.700 euros	1		1	
	Between 9.300 and 26.700 euros	0.84	0.648	0.78	0.504
	Between 0 and 9.300 euros	0.60	0.376	0.58	0.321
	Does not want to answer	0.44	0.136	0.41	0.113
Speaking other language than French					
	No	1		1	
	Yes	0.45	0.157	0.46	0.167
Perception of vaccination Benefit-Risk Balance (BRB)					
	More risks than benefits			0.70	0.449
	More benefits than risks			1	
	Does not know			1.42	0.487

Vaccinated persons in all vaccine experience groups, including those vaccinated only due to the requirement, were more likely to express intention of future COVID-19 vaccination than unvaccinated persons: CM-only (aPR=6.00), CM+others (aPR=13.71) and CM-not-main groups (aPR=16.50) (**Table 5**). Negative individual BRB perception significantly decreased intention for future COVID-19 vaccination (negative vs. positive, aPR=0.55), but did not substantially mediate the effect of vaccine experience on this intention.

Table 5. Association of vaccine experience with intention for future vaccine among adults in France (N=972), August 2021. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

		Intention (N=714) vs. No intention /do not know (N=258)			
		aPR	<i>p</i> -value	aPR with BRB	<i>p</i> -value
Demographic and socio-economic characteristics					
Gender					
	Man	1.05	0.054	1.03	0.209
	Woman	1		1	
Age (in years)					
	Between 18 and 39	1		1	
	Between 40 and 59	1.02	0.505	0.99	0.781
	Between 60 and 75	1.04	0.487	1.00	0.965
Occupational status					
	Active	1		1	
	Inactive	1.01	0.752	1.00	0.907
Annual income					
	> 26.700 euros	1		1	
	Between 9.300 and 26.700 euros	0.99	0.714	0.98	0.502
	Between 0 and 9.300 euros	0.91	0.066	0.93	0.170
	Does not want to answer	0.92	0.114	0.92	0.084
Speaking other language than French					
	No	1		1	
	Yes	0.96	0.318	0.98	0.673
COVID-19 related characteristics					
Relatives previously ill with COVID-19					
	No	1		1	
	Yes	0.99	0.725	1.00	0.886
Self-reported risk factor for severe COVID-19					
	No	1		1	
	Yes	1.04	0.174	1.02	0.532
Level of confidence in the authorities' management of the COVID-19 crisis					
	Low	1		1	
	Moderate/High	1.17	0.002	1.08	0.093
Vaccine experience					

	Unvaccinated	1		1	
	CM-only	6.41	0.001	6.00	0.002
	CM+others	17.20	<0.001	13.71	<0.001
	CM-not-main	23.72	<0.001	16.50	<0.001
	NA	4.10	0.037	3.38	0.068
Perception of vaccination Benefit-Risk Balance (BRB)					
	More risks than benefits			0.55	<0.001
	More benefits than risks			1	
	Does not know			0.71	<0.001

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM+other); CM not mentioned as first reason (CM-not-main).NA, not applicable to vaccine experience (recently infected).

Discussion

In this cross-sectional study including a representative sample of adults living in France in August 2021, we estimated that the COVID-19 certificate requirement increased vaccine uptake among younger persons and persons with low levels of confidence in authorities, without creating substantial social inequalities. Compared to unvaccinated persons, declaring vaccination only to obtain the certificate was associated with active occupational status, but also with higher intention for future vaccination. Perceiving vaccination as having more benefits than risks was not a determinant of having cede to the vaccine requirement, indicating that both groups shared similar perceptions of the vaccination BRB. However, BRB perception was a partial mediator between vaccine experience and future vaccine intention, reducing the strength of this association. Perceiving the vaccine as having more benefits than risks increased vaccine acceptance and reduce the impact of vaccine experience on future vaccine intention. Additionally, BRB vaccine perception acted as a full mediator between level of confidence in authorities and future vaccine uptake with those perceiving the vaccine as having more benefits than risks with higher vaccine intentions compared to those perceiving vaccination as having more risks than benefits.

Beyond individual protection against COVID-19, increasing COVID-19 vaccine uptake among the younger population can be considered a public health achievement under the assumption that this reduced the viral transmission and thus slowed the epidemic progress in 2021. In contrast, in France, the age group >80 years has remained the group with the lowest vaccine coverage (89.20% as of April 1, 2022)(82). A stronger incentive for vaccination or even a mandate in this group could have further reduced COVID-19 mortality.

The COVID-19 certificate requirement was tailored to a young active population and counter-intuitively less targeted to those with the greatest potential benefit from vaccination. This increases health inequalities between professionally active and inactive population. Several studies have reported that isolated or professionally inactive persons remained unvaccinated during the COVID-19 pandemic(83–85), as they perceived to be at lower risk of infection due to low social interactions(83). The requirement did not motivate them to perceive the benefits of vaccination, as their need to attend services and public places was lower, and at that time, the government emphasized the vaccine's benefits for indirect protection. Substantial evidence now suggests that the indirect protection effect from COVID-19 vaccination is short-lived and the impact beyond three months primarily consists of protection against severe disease(86,87).

In our study, ceding to the constraint does not appear to have decreased future COVID-19 vaccine intention, rather, it was associated with higher intention compared to those remaining

unvaccinated. We cannot conclude whether this was a specific positive psychological effect or whether those ceding had weaker initial opposition. However, the fact that the perception of benefits and risks did not explain the association suggests that no rationalised consideration was involved in this difference in intention for future vaccination. Interestingly, as the certificate requirement or professional mandate was the only vaccination motivation for just 4% of the population, suggesting that the policy in France acted as an incentive rather than a coercion. A large body of literature has documented the association between the level of confidence in authorities and vaccine intention, prior(88,89) and during the COVID-19 pandemic(70,90). Our findings suggest that increasing the positive perception of vaccination benefits might counteract the negative effect of low confidence in authorities on vaccination uptake.

Limitations

Our study has several limitations. The self-administered questionnaire may have led to misunderstanding, while reducing social-desirability bias. Reporting constraint as the sole motivation for vaccination might have been a way to express criticism with such decisions, while other persons may have given post-hoc sense to “forced” vaccination. The generalizability of our results is naturally limited by several factors: our results apply specifically to the initial vaccination campaign against COVID-19 in France: a passive campaign with large sub-regional vaccine centres and little vaccine promotion apart from governmental announcements. Participants were members of an online-panel, therefore - despite quota sampling - people living in poverty, low health literacy and possibly high-risk behaviour were likely underrepresented. We also cannot infer our results to persons aged ≥ 76 , who had relatively low coverage in France despite being at highest risk of severe COVID-19 infections, and French citizens from overseas departments where inequalities tend to be higher than in mainland France(90,91).

Conclusion

Vaccination BRB perception was not different among those having ceded to the requirement and those remaining unvaccinated. However, regardless of vaccine experience under the requirement, perceived BRB was strongly associated with the intention to accept hypothetical future COVID-19 vaccination (booster doses). Moreover, the requirement did not negatively impact future COVID-19 vaccine intention. It reduced the negative association of vaccine status with younger age and low confidence in authorities but may have reinforced isolation of professionally inactive persons who did not perceived the vaccination indirect protection benefits highlighted by the government. Future vaccine-incentive policies should tailor communication on vaccination benefits according to the preferences of different sub-groups.

Aim 2. Studying the 7C psychological antecedents of vaccine acceptance throughout the novel COVID-19 vaccine campaign among HCSWs in metropolitan France.

The COVID-19 pandemic provided an unprecedented opportunity to explore the perceived benefit-risk balance of vaccination through the vaccine campaign of a novel vaccine. The second article of this thesis assess the 7C-psychological antecedents of vaccine acceptance, including the perception of vaccination benefit-risk balance (Calculation), at various stages throughout the COVID-19 pandemic.

Article 2: Analyzing the 7C psychological antecedents of vaccine acceptance throughout the COVID-19 pandemic among healthcare sector workers in France.

Reference: Araujo-Chaveron L, Olivier C, Pellissier G, Bouvet E, Mueller JE. Analyzing the 7C psychological antecedents of vaccine acceptance throughout the COVID-19 pandemic among healthcare sector workers in France: A repeated cross-sectional study (CappVac-Cov). *Vaccine*. 2024 Jul 6:S0264-410X(24)00744-8. doi: 10.1016/j.vaccine.2024.07.004. Epub ahead of print. PMID: 38972764.

Journal: *Vaccine* (Impact Factor 5.5).

Background

The World Health Organization asks countries to monitor vaccine hesitancy in their annual joint reporting form to identify changes and trends over time and detect vaccine concerns at the early stages(92,93). Vaccine hesitancy has been repeatedly reported in HCSWs(94–97). Thus, to better understand vaccine acceptance among HCSWs, a 7C-model was developed which encompassed the main drivers of vaccine acceptance, referred to as the psychological antecedents of vaccination(70,71).

The COVID-19 vaccine campaign was characterized by an initial low uptake in HCSWs, until COVID-19 vaccine mandates were implemented(11,82). The enactment of this mandate raised important ethical concerns between professional obligation of HCSWs to protect others and the individual autonomy of HCSWs on its own medical decision(98). Moreover, given the novel nature of the COVID-19 vaccine and the rapid timeline for its clinical trials, some individuals remained skeptical about its safety and efficacy(8). Over time, as more data and experience

with the vaccine were gathered, HCSWs' perceptions of risks and benefits of vaccination may have evolved.

Due to these evolutions over the course of the COVID-19 vaccine campaign in HCSWs, understanding the drivers of COVID-19 vaccine acceptance among HCSWs requires repeated assessment over time.

To our knowledge, no study has monitored HCSWs' psychological antecedents of vaccination over time. This lack of evidence makes it difficult to anticipate vaccine uptake during crises such as COVID-19 pandemic. In addition, it remains unclear in how far individual attitudes, particularly benefit-risks perception, about vaccination vary or can be influenced.

This study aimed to evaluate, among HCSWs in France and across evolving vaccine recommendations made by the French government at different stages of the COVID-19 pandemic, i) the association between the 7C-psychological antecedents of vaccination and vaccine intentions, and ii) changes of 7C-psychological antecedents' overtime.

Methodology

Study design and participant inclusion

We conducted a series of three repeated cross-sectional studies. The Research Group for the Prevention of Occupational Infections in Healthcare Workers (GERES) implemented repeated online surveys via the Sphinx (two first surveys) and RedCap (third survey) survey platforms. Study invitations were disseminated by email to a group of HCSWs throughout France who previously had signaled interest to participate in a longitudinal study. Participants were encouraged to chain-refer the invitation email for the first, but not the following surveys. The questionnaire waves took place between 13 July to 30 November 2021 (study period P2), 11 February and 28 March 2022 (study period P3) and 12 January to 13 March 2023 (study period P4). Any ≥ 18 -year-old health professional working in mainland France was eligible for participation. We also used data from a prior study conducted between December 18 2020, and February 1 2021(70). In this study, the GERES also published an online questionnaire on the Sphinx online survey platform, which was disseminated throughout France through chain referral. Several formal and informal networks of hospital-based and private practice HCSWs and of nursing home directors contributed to its dissemination. This study had comprised any ≥ 18 -year-old professional in healthcare- or welfare-related careers, including physicians, nurses, nurse assistants, other paramedical professionals and social workers, administrative and logistic staff. We labelled the Moirangthem et al. (2022)(70) study as the “first study-period” and subsequent studies as the “second”, “third” and “fourth” study periods. For all study periods, since each participant could forward the survey across its own networks, we did not estimate a response rate. We did not count visits to the survey website, neither. The planning, conduct and reporting of the study were in line with the Declaration of Helsinki (2013) and the GDPR regulation. The study protocol was approved by the Institut Pasteur IRB on 8 July 2021. Because the data collection was anonymous without risk of indirect identification and did not collect any sensitive information, only self-declared biomedical information, no informed consent or full ethical review was required according to French regulation.

Data collection

Each survey questionnaire, P1-P4, contained three parts: (1) sociodemographic characteristics, (2) perceived health status, perceptions related to the COVID-19 epidemic and information on the intention to accept COVID-19 vaccination, (3) attitudes and knowledge related to COVID-19 vaccination, based on a short list of 7C psychological antecedents of vaccination, which has been previously published(70). As the evidence of COVID-19 epidemiology and COVID-19 vaccines evolved during the pandemic, we decided not to explore knowledge items of the 7C-model at P4. Each 7C-dimension was evaluated by at least one attitude and one knowledge, in total, the short version of the 7C questionnaire included 10 questions associated with attitudes towards vaccination and 9 associated with knowledge about the vaccine. The 7C-knowledge items were presented either as a statement to which participants could answer ‘True’, ‘Do not know’ or ‘False’ or requested a single choice answer to a question from several options which included ‘Do not know’ (**Supplementary Table 2**). The 7C-attitudes were explored through 5-point Likert-scale which is a psychometric response method where respondents can state their level of agreement in five points: (1) strongly disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) strongly agree. For analyses, 7C-items were grouped into 3 categories: i) strongly disagree and disagree, ii) undecided, iii) strongly agree and agree.

Monitoring of COVID-19 vaccine intentions and uptake

P1 explored vaccine intention through the question “If a vaccine was available now against Coronavirus (COVID-19), would you get vaccinated?” (Current Vaccine Intention December 2020-February 2021).

P2 occurred between July and November 2021, when daily COVID19 incidence rate ranged between 43 and 370 per 100,000 persons(99) and COVID-19 vaccination was mandatory for HCSWs. During P2, participants’ vaccine intentions were explored through the question “currently, what is your vaccination intention (summer-fall 2021)? “(Current Vaccine Uptake summer-fall 2021), and on hypothetical booster intention to get COVID-19 vaccine “Would you accept a booster of this vaccine (outside of any obligation)?” (Hypothetical booster vaccine intention).

P3 occurred between February and March 2022, when daily COVID19 incidence ranged between 540 and 1 500 per 100 000 persons(99) and booster vaccination was mandatory for HCSWs. P3 explored booster vaccine uptake (Current booster vaccine uptake) and among those vaccinated with it, we explored hypothetical vaccine intention for a second booster “Currently, what is your vaccination intention regarding a booster in the fall of 2022, if it was recommended (outside of any obligation)?” (Hypothetical 2nd booster vaccine intention).

P4 occurred between January and March 2023, when daily COVID19 incidence ranged between 33 and 70 per 100 000 persons(99). Booster was still mandatory for HCSWs during the survey, but the mandate was lifted soon after, on 13 May 2023(18). At P4 the question “Today, would you accept vaccination against COVID-19, if it was recommended to you by your general practitioner (GP) (outside of any obligation)?” was asked to the full sample (Hypothetical 3rd booster vaccine intention). The last study-period focused on further booster vaccine intention and did not explore any vaccine uptake, in the context of the COVID-19 vaccination mandate enacted by the French government in July 2021(10,100).

Covariables: Examining Socio-demographic, and psychological factors in COVID-19 vaccination Intention and Uptake

Socio-demographic information comprised gender, age, region of residence, professional category. 7C antecedents of vaccination (7C-model): Confidence in the vaccine was evaluated as perceived vaccination safety, Confidence in systems as reliability on entities that give vaccine recommendations, Complacency referred to the perceived risks of vaccine-preventable diseases, Calculation referred to the perception of the benefit-risk balance (BRB) of vaccination; Collective responsibility, referred to perceiving vaccination as a collective action to stop the pandemic; Social conformism, to the majority opinion on COVID-19 vaccination in the social environment, and Convenience the perceived accessibility of vaccination. 7C-items were adapted during each study period to the current vaccine recommendation: questions in P1 related to hypothetical primo-vaccination, P2 to hypothetical first booster vaccine, P3 to a hypothetical second booster, P4 to a hypothetical third booster dose.

Statistical analyses

Due to the evolution of biomedical evidence on COVID-19 vaccines during the pandemic, we opted not to explore the association between 7C-knowledge items and vaccine acceptance, and only described frequencies of knowledge items. We used robust variance Poisson regression models to estimate the unadjusted and adjusted prevalence ratios (aPR) and 95%-confidence intervals (95%-CI) to explore the association of participant characteristics and individual 7C-items with vaccine status and future vaccine intention at each period. To identify socio-demographic and health related determinants of vaccine intention, we included independent variables that had a p-value < 0.20 in bivariable models. Essential potential confounders (age, gender and profession category) were forced into the full multivariable models. In France, most professional categories in the healthcare and welfare sector correspond to educational trajectories(101,102), we therefore did not add educational level to

the models. In the multivariable analysis, the 5-point Likert-scale of the 7C-attitudes were grouped; categories 1 and 2 as disagree, and 4 and 5 as agree. Also, to assess the impact of 7C-items on vaccine intention at the population level, we estimated the loss in vaccine intention attributable to each 7C-attitude (population attributable risk):

$$\Delta CV_{\text{pop}} = CV_{\text{RF}^+} * (aPR_{\text{RF}} - 1) * Pr_{\text{RF}^+}$$

CV_{RF^+} : frequency of no vaccine intention among those having a negative attitude towards the C-item.

aPR_{RF} = adjusted prevalence ratio of C-item with vaccine intention/ uptake.

Pr_{RF^+} = frequency of the negative C-attitude in the sample.

Results

P1 encompassed the largest sample with 5 234 participants; mainly females (78.4 %). Participants were aged 18–34 years (23.2 %), 35–49 years (40.0 %) and 50 years or older (36.8 %). Nurses (22.9 %), nurse assistants (9.4 %) and biomedical professionals (including physicians, midwives, pharmacists and biologists) (27.7 %), were among the largest groups (**Table 6**). Subsequent surveys (P2, P3 and P4) included 339, 351, and 437 participants, respectively. Participants characteristics remained similar to those in P1, with predominantly female participants (76.1 %, 74.6 % and 76.1 %, respectively) and balanced age representation (**Table 6**).

Contribution by nurses increased from 22.9 % at P1 to 34.7 % at P4 and by biomedical professions from 27.7 % (P1) to 30.3 % (P4). Nurse assistants' contribution decreased from 9.4 % to 1.9 %, and contribution by administrative and technical staff from 24.4 % to 21.1 %. The proportion of hospital workers remained stable (around 65%).

Table 6. Description of the study population. Healthcare sector workers in France. CappVac-Cov study.

		P1 December 2020 - February 2021 N=5 234	P2 July - November 2021 N=339	P3 February - March 2022 N=351	P4 January-February 2023 N=360
Demographic and socio-economic characteristic					
Gender					
	Male	1 131 (21.6%)	81 (23.9%)	89 (25.4%)	86 (23.9%)
	Female	4 103 (78.4%)	258 (76.1%)	262 (74.6%)	274 (76.1%)
Age (in years)					
	18-34	1 215 (23.2%)	58 (17.1%)	55 (15.7%)	45 (12.5%)
	35-49	2 092 (40.0%)	137 (40.4%)	146 (41.6%)	152 (42.2%)
	>=50	1 927 (36.8%)	144 (42.5%)	150 (42.7%)	163 (45.3%)
Region of work					
	DROMs and Corsica	23 (0.4%)	4 (1.2%)	3 (0.9%)	2 (0.6%)
	North-Est	1 183 (22.6%)	83 (24.5%)	96 (27.4%)	77 (21.5%)
	North-West	1 301 (24.9%)	67 (19.8%)	61 (17.4%)	65 (18.1%)
	South-Est	1 683 (32.2%)	65 (19.2%)	77 (21.9%)	100 (27.9%)
	South-West	446 (8.5%)	38 (11.2%)	53 (15.1%)	47 (13.1%)
	Paris Region	598 (11.4%)	82 (24.2%)	61 (17.4%)	68 (18.9%)
Profession					
	Biomedical profession	1 449 (27.7%)	107 (31.6%)	122 (34.8%)	109 (30.3%)
	Paramedical professions	818 (15.6%)	42 (12.4%)	47 (13.4%)	43 (11.9%)
	Nurse	1 197 (22.9%)	104 (30.7%)	115 (32.8%)	125 (34.7%)
	Nurse Assistants / Other assistants	491 (9.4%)	22 (6.5%)	17 (4.8%)	7 (1.9%)
	Administrative / Technical staff	1 279 (24.4%)	64 (18.9%)	50 (14.3%)	76 (21.1%)
Direct contact with patients					
	No		94 (27.7%)	78 (22.2%)	101 (28.1%)
	Yes		245 (72.3%)	273 (77.8%)	259 (71.9%)
Work in Hospitals					
	No	1 971 (37.7%)	103 (30.4%)	117 (33.3%)	112 (31.1%)
	Yes	3 263 (62.3%)	236 (69.6%)	234 (66.7%)	248 (68.9%)
Work in Nursing Home					
	No	4 429 (84.6%)	294 (86.7%)	319 (90.9%)	317 (88.1%)
	Yes	805 (15.4%)	45 (13.3%)	32 (9.1%)	43 (11.9%)
Off-site					
	No	4 502 (86.0%)	277 (81.7%)	268 (76.4%)	284 (78.9%)
	Yes	732 (14.0%)	62 (18.3%)	83 (23.7%)	76 (21.1%)

Behavioral characteristics

Level of confidence in authorities *

(N= 6 217)

Low	956 (18.5%)	111 (32.7%)	84 (23.9%)	74 (20.6%)
Moderate	1 954 (37.8%)	106 (31.3%)	127 (36.2%)	124 (34.4%)
High	2 255 (43.7%)	122 (36.0%)	140 (40.0%)	162 (45.0%)

Vaccinated because the mandate (as one of the 3 main raisons) (N=690)

No		330 (97.4%)	326 (92.9%)	<i>Question not included in questionnaire</i>
Yes	<i>Mandate not enacted yet</i>	9 (2.7%)	25 (7.1%)	

Opinion on vaccination in general

Very Favourable / Favourable

310 (91.5%) 338 (96.3%) 343 (95.3%)

Undecided

14 (4.1%) 3 (0.9%) 8 (2.2%)

Very Skeptical / Skeptical

15 (4.4%) 10 (2.9%) 9 (2.5%)

Current vaccine intention Winter 2020-2021

With intention 3 043 (58.1%)

Do not know 1 038 (19.8%)

With no intention 1 153 (22.0%)

Current vaccine uptake

Summer - Fall 2021

Vaccinated

309 (91.2%)

Unvaccinated

30 (8.8%)

Hypothetical booster vaccine intention

Winter - Spring 2022

With intention

239 (78.1%)

Do not know

35 (11.4%)

With no intention

32 (10.5%)

Current booster vaccine uptake

Winter - Spring 2022

Vaccinated with booster

329 (93.7%)

Vaccinated without booster

8 (2.3%)

Unvaccinated

14 (4.0%)

Hypothetical 2nd booster vaccine

intention Fall 2022

With intention

253 (76.9%)

Do not know

37 (11.2%)

With no intention

39 (11.9%)

Hypothetical 3rd booster vaccine
intention Fall 2022

With intention	263 (73.1%)
Do not know	34 (9.4%)
With no intention	63 (17.5%)

7C-dimensions

Calculation

'I think that vaccination against COVID-19 will have more benefits than risks for me.'

Agree	2 932 (56.0%)	246 (72.6%)	242 (69.0%)	230 (64.0%)
Undecided	1 136 (21.7%)	37 (10.9%)	57 (16.2%)	46 (12.7%)
Disagree	1 166 (22.3%)	56 (16.5%)	52 (14.8%)	84 (23.3%)

Convenience

'In practice, it will be difficult for me to get vaccinated.'

Agree	654 (12.5%)	14 (4.1%)	15 (4.3%)	22 (6.1%)
Undecided	765 (14.6%)	24 (7.1%)	18 (5.1%)	26 (7.2%)
Disagree	3 815 (72.9%)	301 (88.8%)	318 (90.6%)	312 (86.7%)

Collective Responsibility

'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'

Agree	3 977 (76.0%)	276 (81.4%)	268 (76.4%)	272 (75.6%)
Undecided	686 (13.1%)	19 (5.6%)	36 (10.3%)	27 (7.5%)
Disagree	571 (11.0%)	44 (13.0%)	47 (13.4%)	61 (16.9%)

Social Conformism

'Among your family and friends, how would you describe the majority opinion towards COVID-19 vaccination?'

Favorable	1 808 (34.5%)	230 (67.9%)	240 (68.4%)	206 (57.2%)
Both skeptical and favorable	1 653 (31.6%)	62 (18.3%)	68 (19.4%)	97 (26.9%)
Skeptical	1 773 (33.9%)	47 (13.9%)	43 (12.3%)	57 (15.8%)

Complacency

'I am afraid of getting a severe form of COVID-19.'

Agree	1 379 (26.4%)	95 (28.0%)	104 (29.6%)	120 (33.3%)
Undecided	1 222 (23.4%)	69 (20.4%)	84 (23.9%)	40 (11.1%)
Disagree	2 633 (50.3%)	175 (51.6%)	163 (46.4%)	200 (55.6%)

Confidence in COVID-19 vaccine

'I am afraid of having a severe side effect of vaccination.'

Agree	1731 (33.1%)	67 (19.8%)	54 (15.4%)	63 (17.5%)
Undecided	959 (18.3%)	50 (14.8%)	55 (15.7%)	36 (10.0%)
Disagree	2 544 (48.6%)	222 (65.5%)	242 (69.0%)	261 (72.5%)

Confidence in systems

'If my employer encourages me to get vaccinated, this...'

ARTICLE PRESENTATION – ARTICLE 2

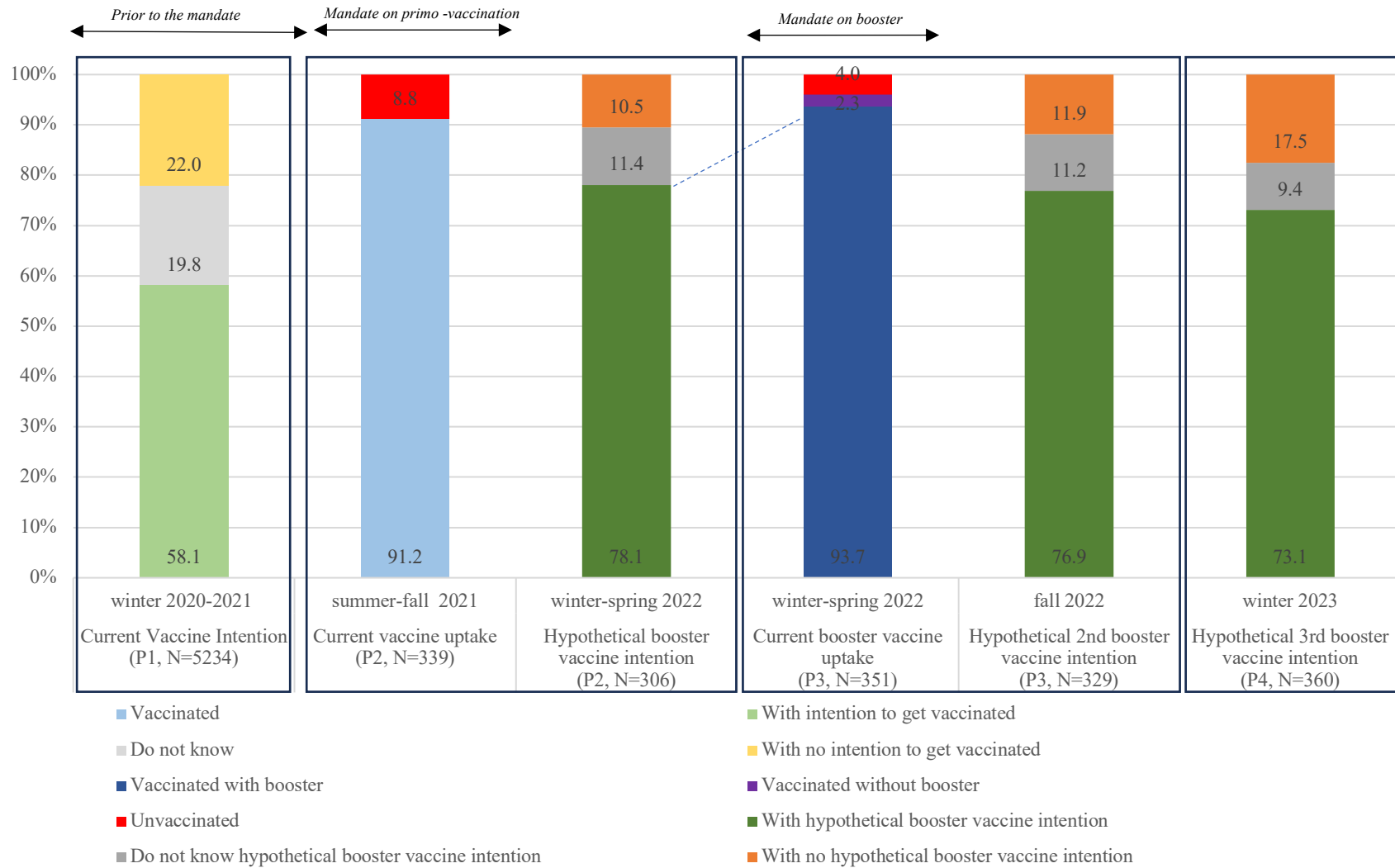
Dissuades-me	274 (5.2%)	28 (8.3%)	22 (6.3%)	18 (5.0%)
Has no effect	3 409 (65.1%)	209 (61.7%)	212 (60.4%)	222 (61.7%)
Motivates-me	1 551 (29.6%)	102 (30.1%)	117 (33.3%)	120 (33.3%)

* Level of confidence in authorities to manage the health and economic crisis related to the COVID-19 epidemic

Evolution of self-reported vaccine intentions/ uptake among participants (Figure 5)

Primary intended vaccination (uptake or intention) increased from 58.1 % (winter 2020–2021) to 91.2 % (summer-fall 2021) (P2), and vaccine refusal decreased from 22.0 % to 8.8 %. At P2, only 8.8 % of 339 remained unvaccinated and 9 of 339 (2.7 %) participants cited vaccination mandate as a main reason for getting vaccinated against COVID-19. Hypothetical future booster vaccine intentions were assessed at P2 and P3 vaccinated participants or those with intention to do so. In summer-fall 2021 (P2), while 91.2 % of the 339 participants were vaccinated in the context of the mandate, only 78.1 % were willing to accept a hypothetical booster vaccine if recommended by their General Practitioner (GP), and 11.4 % were undecided. Similarly, in winter-spring 2022 (P3), while 93.7 % of the 351 participants were vaccinated in the context of the mandate, only 76.9 % were willing to accept a hypothetical second booster dose, and 11.2 % were undecided. Similarly, in winter 2023 (P4), 73.1 % of participants were willing to accept a hypothetical third dose of booster if recommended by their GP.

Figure 5. Vaccine intentions during the COVID-19 pandemic among health care sector workers in France. CappVac-Cov study.



1st period of study (P1), 18 December 2020 to 1 February 2021; 2nd period of study (P2), 13 July to 30 November 2021

3rd period of study (P3), 11 February and 28 March 2022; 4th period of study (P4), 12 January to 13 March 2023

Hypothetical booster vaccine intention was explored among those vaccinated through the question “Would you accept a booster of this vaccine (outside of any obligation)”

Associations between 7C-attitudes dimensions and vaccine intention during the COVID-19 pandemic (Table 7 & Figure 6)

Calculation (perceived BRB) was the principal antecedent of primary vaccination intention in winter 2020–21 (P1) (favourable vs. unfavourable, aPR: 2.92; p-value < 0.001). Under the vaccine mandate for HCSWs, its association with vaccine uptake was dissipated, but regained importance for the intention of a hypothetical first (P2), second (P3), and third (P4) booster dose (aPR: 2.29, 2.04, and 2.07, respectively). Perceiving vaccination as a collective action was the second strongest antecedent of primary vaccination intention in winter 2020–21 (P1) (agree vs. disagree, aPR: 2.84; p-value < 0.001). In summer-fall 2021 (P2), it remained the only psychological antecedent associated with vaccine status (agree vs. disagree, aPR: 2.19; p-value < 0.001) and persisted, albeit more weakly, under the mandate for booster vaccination at P3 (aPR: 1.20). Additionally, it was strongly associated with third and fourth hypothetical booster dose intentions (agree vs. disagree, aPR: 2.18 and 1.69, respectively). Confidence in the vaccine was positively associated with primary vaccination intention in winter 2020–21 (P1) (agree vs. disagree, aPR: 1.84; p-value < 0.001), its association with vaccine uptake was dissipated in summer-fall 2021 (P2), but regained importance on booster vaccine uptake (agree vs. disagree, aPR: 1.14; p-value = 0.04). Its association increased for hypothetical booster vaccine intention (agree vs. disagree, aPR: 1.45, 1.67, and 1.43 for the first (P2), second (P3), and third hypothetical booster dose (P4)). Reactance to employer's encouragement to get vaccinated (Confidence in systems) (motivates vs. dissuades, aPR: 2.15; p-value < 0.001), and Social conformism (favourable vs. skeptical opinion, aPR: 1.33; pvalue < 0.001) were significantly associated with primary vaccination intention in winter 2020–21 (P1) but these associations disappeared during the rest of the study periods. Both antecedents were not significantly associated with hypothetical booster dose intention at any survey periods. When assessing the absolute impact of negative attitudes on vaccine behavior across the observed periods, low confidence in the vaccine (fear of severe side effects from vaccination) was related to the highest population attributable loss in vaccine uptake or intention during any survey (e.g., -26.2 % loss in hypothetical 2nd booster vaccine intention at P3), with exception to P2 (early mandate) (**Table 8**). Calculation showed lower, but similarly constant importance. In longitudinal follow-up of seven participants, relatively stable attitudes were observed only for perceiving vaccination as collective action, and capacity for reactance (**Supplementary File 2**).

Table 7. Association of sociodemographic characteristics and of 7C-attitude items with vaccine intention, vaccine uptake or future vaccine intention (vs. undecided/no intention) during the COVID-19 pandemic among health care sector workers in France. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model. CappVac-Cov study. France.

	Current vaccine intention winter 2020- 2021 (N=5234) P1			Current vaccine uptake summer - fall 2021 (N=339) P2			Hypothetical booster vaccine intention winter - spring 2022 (N=306) P2			Current booster vaccine uptake winter - spring 2022 (N=351) P3			Hypothetical 2 nd booster vaccine intention fall 2022 (N=329) P3			Hypothetical 3 rd booster vaccine intention winter 2023 (N=360) P4								
	With intention (n=3043, 58.1%)			Vaccinated (n=309, 91.2%)			With intention (n=239, 78.1%)			Vaccinated (n=329, 93.7%)			With intention (n=253, 76.9%)			With intention (n=263, 73.1%)								
	n(%)	aPR	P-value	n(%)	aPR	P-value	n(%)	aPR	P-value	n(%)	aPR	P-value	n(%)	aPR	P-value	n(%)	aPR	P-value						
Gender																								
Male	302	(13.8)	1	76	(24.6)	1	64	(26.8)	1	87	(26.4)	1	75	(29.6)	1	71	(27.0)	1						
Female	1889	(86.2)	0.98	0.182	233	(75.4)	0.98	0.495	175	(73.2)	0.95	0.256	242	(73.6)	0.99	0.684	178	(70.4)	1.01	0.81	192	(73.0)	0.99	0.873
Age (years)																								
18-34	534	(17.6)	1	48	(15.5)	1	33	(13.8)	1	49	(14.9)	1	35	(13.8)	1	31	(11.8)	1						
35-49	1160	(38.1)	1.04	0.113	126	(40.8)	1.04	0.422	95	(39.8)	1.02	0.761	137	(41.6)	1.01	0.824	108	(42.7)	1.01	0.919	104	(39.5)	0.96	0.565
>=50	1349	(44.3)	1.08	0.001	135	(43.7)	1.03	0.451	111	(46.4)	1.01	0.847	143	(43.5)	1.01	0.793	110	(43.5)	0.95	0.521	128	(48.7)	0.97	0.625
Profession																								
Admin/ technical staff	725	(23.8)	0.97	0.064	62	(20.1)	1.01	0.705	51	(21.3)	0.99	0.912	46	(14.0)	0.99	0.761	36	(14.2)	0.98	0.772	51	(19.4)	0.88	0.026
Biomedical profession	1162	(38.2)	1	104	(33.7)	1	89	(37.2)	1	117	(35.6)	1	105	(41.5)	1	93	(35.4)	1						
Nurse Assistants	150	(4.9)	0.87	0.001	19	(6.2)	0.97	0.594	9	(3.8)	0.74	0.158	15	(4.6)	1.05	0.544	8	(3.2)	0.90	0.604	3	(1.1)	0.76	0.465
Nurses	594	(19.5)	0.96	0.055	91	(29.5)	0.96	0.235	67	(28.0)	1.02	0.740	110	(33.4)	1.06	0.048	73	(28.9)	0.88	0.048	85	(32.3)	0.90	0.101
Other paramedical staff	412	(13.5)	0.92	0.001	33	(10.7)	0.94	0.267	23	(9.6)	0.97	0.747	41	(12.5)	0.99	0.892	31	(12.3)	1.01	0.856	31	(11.8)	0.95	0.410
Calculation																								
<i>'I think that vaccination against COVID-19 will have more benefits than risks for me.'</i>																								
Agree	2622	(86.2)	2.92	<0.001	244	(79.0)	1.13	0.208	216	(90.4)	2.29	0.008	238	(72.3)	1.18	0.053	218	(86.2)	2.04	0.012	218	(82.9)	2.07	<0.001
Undecided	295	(9.7)	1.50	<0.001	34	(11.0)	1.14	0.197	16	(6.7)	1.68	0.128	56	(17.0)	1.23	0.015	26	(10.3)	1.37	0.296	25	(9.5)	1.56	0.041
Disagree	126	(4.1)	1	31	(10.0)	1	7	(2.9)	1	35	(10.6)	1	9	(3.6)	1	20	(7.6)	1						

Convenience

'In practice, it will be difficult for me to get vaccinated.'

ARTICLE PRESENTATION – ARTICLE 2

Agree	281 (9.2)	1		12 (3.9)	1		10 (4.2)	1		15 (4.6)	1		10 (4.0)	1		19 (7.2)	1	
Undecided	329 (10.8)	0.95	0.200	20 (6.5)	0.99	0.949	15 (6.3)	0.86	0.309	18 (5.5)	0.92	0.118	14 (5.5)	0.95	0.801	11 (4.2)	0.65	0.004
Disagree	2433 (80.0)	1.02	0.464	277 (89.6)	1.11	0.282	214 (89.5)	0.89	0.312	296 (90.0)	0.90	0.020	229 (90.5)	0.97	0.849	233 (88.6)	0.93	0.218

Collective Responsibility

'Avoiding transmission to others is an important reason for getting vaccinated'

Agree	0.0		268 (86.7)		231 (96.7)		264 (80.2)		220 (87.0)		238 (90.5)
Undecided	0.0		22 (7.1)		1 (0.4)		38 (11.6)		23 (9.1)		10 (3.8)
Disagree	0.0		19 (6.2)		7 (2.9)		27 (8.2)		10 (4.0)		15 (5.7)

'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'

Agree	2934 (96.4)	2.84	<0.001	275 (89.0)	2.19	<0.001	232 (97.1)	1.56	0.278	262 (79.7)	1.20	0.048	230 (90.9)	2.18	0.034	242 (92.0)	1.69	0.039
Undecided	66 (2.2)	0.99	0.950	17 (5.5)	2.21	<0.001	3 (1.3)	0.68	0.537	36 (10.9)	1.29	0.004	17 (6.7)	1.73	0.146	8 (3.0)	0.96	0.907
Disagree	43 (1.4)	1		17 (5.5)	1		4 (1.7)	1		31 (9.4)	1		6 (2.4)	1		13 (4.9)	1	

Social Conformism

'Among your family and friends, how would you describe the majority opinion towards COVID-19 vaccination?'

Favourable	1601 (52.6)	1.33	<0.001	226 (73.1)	1.08	0.385	193 (80.8)	1.20	0.293	235 (71.4)	1.11	0.156	198 (78.3)	1.25	0.272	175 (66.5)	1.07	0.551
Both skeptical and favourable	952 (31.3)	1.24	<0.001	53 (17.2)	1.06	0.564	35 (14.6)	1.15	0.453	62 (18.8)	1.06	0.516	44 (17.4)	1.23	0.316	66 (25.1)	1.10	0.426
Skeptical	490 (16.1)	1		30 (9.7)	1		11 (4.6)	1		32 (9.7)	1		11 (4.4)	1		22 (8.4)	1	

Complacency

'I am afraid of getting a severe form of COVID-19.'

Agree	877 (28.8)	1.08	<0.001	94 (30.4)	1.04	0.103	79 (33.1)	1.00	0.943	101 (30.7)	0.99	0.843	83 (32.8)	1.09	0.095	103 (39.2)	1.18	<0.001
Undecided	734 (24.1)	0.99	0.677	67 (21.7)	1.06	0.112	49 (20.5)	0.95	0.378	81 (24.6)	0.99	0.783	63 (24.9)	1.01	0.873	30 (11.4)	1.04	0.516
Disagree	1432 (47.1)	1		148 (47.9)	1		111 (46.4)	1		147 (44.7)	1		107 (42.3)	1		130 (49.2)	1	

Confidence in COVID-19 vaccine

'I am afraid of having a severe side effect of vaccination.'

Agree	330 (10.8)	1		46 (14.9)	1		17 (7.1)	1		40 (12.2)	1		14 (5.5)	1		18 (6.8)	1	
Undecided	541 (17.8)	1.62	<0.001	45 (14.6)	1.02	0.773	33 (13.8)	1.49	0.019	54 (16.4)	1.14	0.039	35 (13.8)	1.53	0.045	23 (8.8)	1.41	0.058
Disagree	2172 (71.4)	1.84	<0.001	218 (70.6)	1.03	0.564	189 (79.1)	1.45	0.019	235 (71.4)	1.14	0.040	204 (80.6)	1.67	0.009	223 (84.4)	1.43	0.023

Confidence in systems

'If my employer encourages me to get vaccinated, this...'

ARTICLE PRESENTATION – ARTICLE 2

Dissuades-me	1302	(42.8)	1		19	(6.2)	1		3	(1.3)	1		15	(4.6)	1		3	(1.2)	1		1	(0.4)	1	
Has no effect	27	(0.9)	1.90	<0.001	101	(32.7)	0.91	0.398	91	(38.1)	2.33	0.092	117	(35.6)	0.99	0.953	100	(39.5)	1.20	0.687	154	(58.6)	5.68	0.052
Motivates-me	1714	(56.3)	2.15	<0.001	189	(61.2)	0.96	0.724	145	(60.7)	2.65	0.051	197	(59.9)	1.04	0.787	150	(59.3)	1.23	0.639	108	(41.1)	5.80	0.050

Hypothetical booster vaccine intention was explored among those vaccinated through the question “Would you accept a booster of this vaccine (outside of any obligation)?”

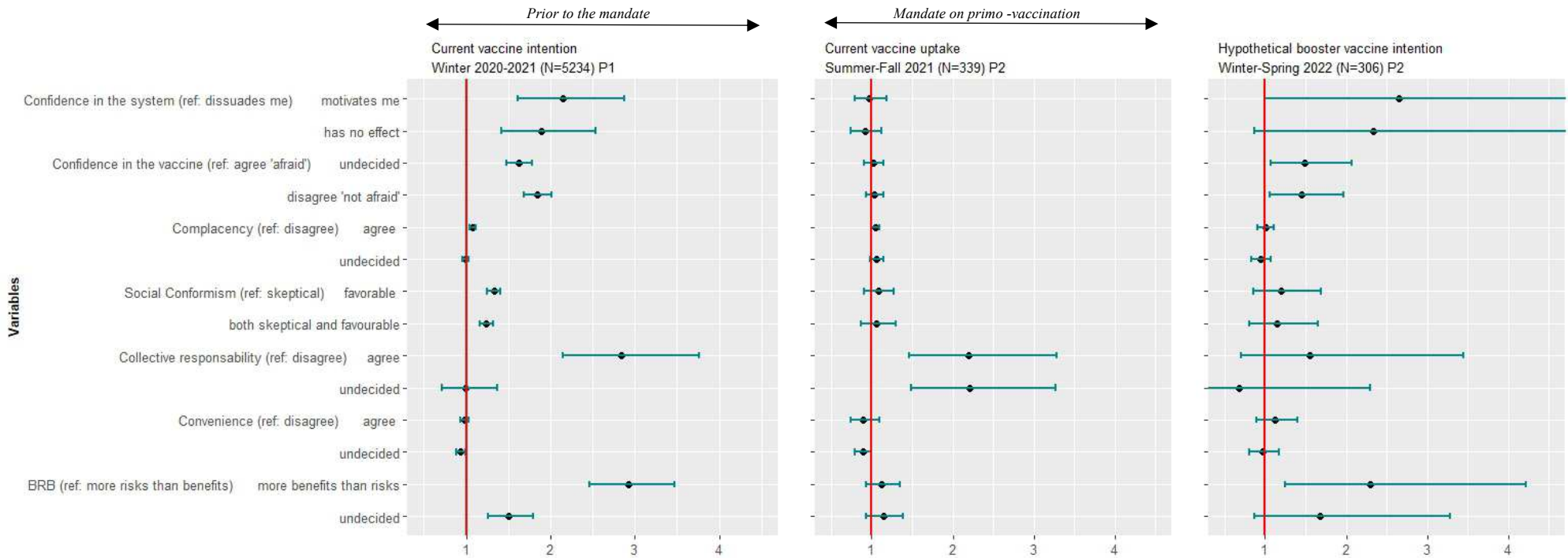
1st period of study (P1): 18 December 2020 to 1 February 2021

2nd period of study (P2): 13 July to 30 November 2021

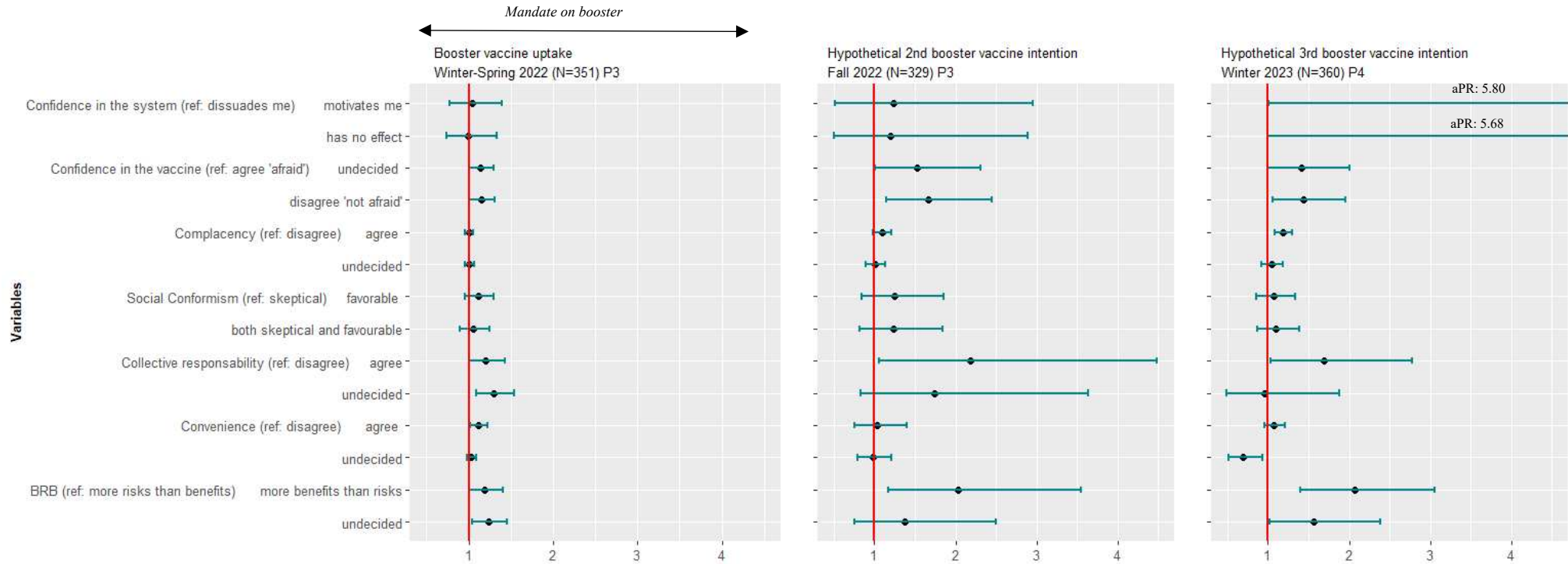
3rd period of study (P3): 1 February and 28 March 2022

4th period of study (P4): 12 January to 13 March 2023

Figure 6. Association of 7C-attitude items with vaccine intention, vaccine uptake or future vaccine intention (vs. undecided/no intention) during the COVID-19 pandemic among health care sector workers in France. Adjusted Prevalence Ratio (aPR) obtained with multivariable robust-variance Poisson regression model. CappVac-Cov study.



(Continuation Figure 6). Association of 7C-attitude items with vaccine intention, vaccine uptake or future vaccine intention (vs. undecided/no intention) during the COVID-19 pandemic among health care sector workers in France. Adjusted Prevalence Ratio (aPR) obtained with multivariable robust-variance Poisson regression model. CappVac-Cov study.



*Detailed results for confidence in the system in the hypothetical 3rd booster vaccine intention (ref: dissuades me):

- “motivates me”: aPR 5.80, 95%CI 1.00-33.55
- “has no effect”: aPR 5.68, 95%CI 0.99-32.65

1st period of study (P1): 18 December 2020 to 1 February 2021

2nd period of study (P2): 13 July to 30 November 2021

3rd period of study (P3): 1 February and 28 March 2022


4th period of study (P4): 12 January to 13 March 2023


Hypothetical Future Vaccine Intention was explored among those vaccinated through the question “Would you accept a booster of this vaccine (outside of any obligation)”


Table 8. Reduction in vaccination prevalence/intention (%) attributable to 7C-attitude items.

	Current vaccine intention winter 2020-21 (N=5234) P1	Current vaccine uptake summer - fall 2021 (N=339) P2	Hypothetical booster Vaccine intention winter - spring 2022 (N=306) P2	Current booster vaccine uptake winter - spring 2022 (N=351) P3	Hypothetical 2 nd booster Vaccine intention fall 2022 (N=329) P3	Hypothetical 3 rd booster Vaccine intention winter 2023 (N=360) P4
<i>Calculation: 'I think that vaccination against COVID-19 will have more benefits than risks for me.'</i>						
Disagree	-14.07	NA	-9.02	NA	-7.28	-11.13
<i>Convenience: 'In practice, it will be difficult for me to get vaccinated'</i>						
Agree	-0.22	NA	NA	0.46	NA	NA
<i>Collective Responsibility: 'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>						
Disagree	-7.03	-6.68	NA	-2.02	-7.08	-6.56
<i>Social Conformism: 'Among your family and friends, how would you describe the majority opinion towards COVID-19 vaccination?'</i>						
Skeptical	-7.06	NA	NA	NA	NA	NA
<i>Complacency: 'I am afraid of getting a severe form of COVID-19.'</i>						
Disagree	-1.97	NA	NA	NA	NA	-4.31
<i>Confidence in COVID-19 vaccine: 'I am afraid of having a severe side effect of vaccination.'</i>						
Agree	-19.79	NA	-18.88	-7.44	-26.16	-2.44
<i>Confidence in system : 'If my employer encourages me to get vaccinated, this...'</i>						
Dissuades-me	-1.59	NA	NA	NA	NA	NA

NA Not Applicable because C-item not significant in multivariable model

 >10% point reduction in vaccine intention

 10% to 5% point reduction in vaccine intention

 <5% point reduction in vaccine intention

Discussion

In this series of surveys during the COVID-19 vaccine campaign among HCSWs in France, we found that the associations between 7C-psychological antecedents and vaccine behaviour changed over time, in particular during the initial phase of the epidemic with a novel vaccine campaign. Furthermore, we found substantial variability of 7C-attitudes over time, specifically description of the majority opinion about the vaccine in the social environment (Social conformism), perception of benefits vs. risks (Calculation), and fear of side effects from vaccination (Confidence in the vaccine). Relatively stable 7C-attitudes were Collective responsibility and capacity for reactance (Confidence in the system). Overall, Calculation and Collective responsibility appeared as strongest determinants in most behaviour contexts during this study, while Confidence in the vaccine was related to the strongest attributable loss in vaccine intention in this HCSWs sample.

In the first survey at the start of the vaccine campaign, Calculation was one of the principal determinants of vaccine intention, and it was in following surveys a determinant for booster intention and uptake outside mandates. By contrast, under the mandate for primary vaccination for HCSWs (issued in July 2021(10,100)) when 91.2 % of participants were vaccinated, and for booster vaccination, Calculation was no determinant. In coherence with previous studies conducted among 3870 HCSWs during the beginning of the COVID-19 vaccine campaign(71), these results underpin the importance of the benefit-risk consideration in vaccine decisions and that this prominent role is modified by mandates, albeit only temporally. The perception of vaccination benefits-risks did not drastically change across surveys in our study, but some changes could indicate that participants perceived loss risks after the first year of vaccination, while consequently, benefits were estimated lower, as well. The question arises whether individuals changed from poor to favourable benefit-risk perception following the vaccination under the mandate, which requires a longitudinal study in a larger sample. The first article of this thesis, among the general population in France in summer 2021, found that intention for future vaccination among persons vaccinated only to obtain a vaccine pass or to satisfy a professional mandate compare to unvaccinated, did not depend on a favourable benefit-risk perception(103). One of the Cs from the 7C-model closely related to Calculation (perceived benefit-risk balance of vaccination) is confidence in the vaccine (fear of vaccination side-effects). As Calculation, confidence in the vaccine showed no absolute impact on hypothetical vaccine intention under the mandate for primary vaccination for HCSWs (P2) but it was the antecedent with the strongest absolute impact on hypothetical future vaccine intention in most surveys.

Despite an only moderate association with vaccine intention, the moderate prevalence of fear of side effects makes a substantial impact on vaccine coverage plausible. The high prevalence of low confidence in winter 2020–21 (33 %) can be partly explained by the novelty of the vaccine in 2021, with limited safety data and minimal personal experience. In our survey, low confidence in the vaccine among those with no intention to get vaccinated HCSWs was 26.8 % in winter 2020 (P1), and 22.0 % among the general population in spring 2020(104). By 2022, this increased to 74.1 % in our survey (P3 fall 2022) and 63.0 % among the general population in summer-fall 2022(105). The lower prevalences thereafter (15–20 %), despite emerging evidence on severe side effects such as thrombocytopenic thrombosis and myocarditis, could reflect reassuring personal experience. Studies among mothers suggest that primiparous mothers show more reluctance toward childhood vaccinations than multiparous mothers(106). This highlights that even during epidemic response vaccination, vaccine delivery needs to yield positive experience with regard to mild and severe side effects, and the way they are handled. The associations of Collective responsibility (seeing vaccination as a collective action to stop the crisis related to the epidemic) with vaccine uptake and hypothetical intention remained constant during the study period, and the prevalence of agreement with this statement was high across all surveys. Collective responsibility was the only significant determinant of vaccine uptake under the mandate, which means that HCSWs refusing vaccination despite the mandate (with the consequence of job exclusion) refused to see the collective potential in vaccination. Knowledge about Sars-Cov-2 transmission mechanisms have been found to be associated with the sustained or increased adoption of preventive measures(107). However, detailed (and variable) evidence on the vaccines' effectiveness against infection and transmission became available only later during 2021. We therefore suggest that disagreement with vaccination as a collective action in summer 2021 was rather grounded on ideological attitudes and beliefs. Interestingly, only 9 of the 339 participants in summer 2021 cited the mandate as the reason for vaccination, which suggests that Collective responsibility substantially contributed to the high vaccine uptake observed among our participants. Previous studies have found that compliance with regulations and recommendations is driven by social norms(107). Surprisingly, even though there was a trend towards an increase of favourable opinion among family and friends (Social conformism) across surveys, it did not significantly influence vaccine intention at later stages. Social conformism to the private environment appears to have played a role during the initial phase of the vaccine campaign only, when the heuristic of following other people's example had the highest facilitating effect on decision-making. Similarly, reactance to employer vaccine encouragement (Confidence in the system) was associated to absence of vaccine intention/ uptake only during the initial phase of the vaccine campaign, before the

mandate enactment. Social conformism and Confidence in the system are the only 7C-antecedents that are strictly interpersonal and without direct relation to the perception of the vaccine or vaccination. At later stages of the pandemic, a first experience with the COVID-19 vaccine seems to have mitigated the role of these interpersonal antecedents. Despite previous studies that have shown how compliance with prevention behaviours rely on high perceived vulnerability and fear of severe COVID-19(107,108), we found that fear of a severe form of COVID-19 (Complacency) was not a substantial determinant of vaccine intention or uptake at any time, while one quarter to one third of participants did express this fear across surveys. This could be related to the fact that other more important reasons for COVID-19 vaccination existed for HCSWs in this study, including Collective responsibility and vaccination against any form of COVID-19 infection. Convenience was never associated with vaccine uptake or hypothetical vaccine intention, likely due to the high accessibility of COVID-19 vaccination for HCSWs during the pandemic.

Limitations

Our study has several limitations. The generalizability of our results is limited because our samples are not representative of the HCSWs French population. Some professions such as nurse assistants were under represented across the survey periods and thus, we cannot conclude whether there were vaccine disparities between professions. Another main limitation is that we cannot assume that the same persons participated at each step. Also, our study uses a limited number of cross-sectional surveys, which affects the description of 7C-psychological antecedents over time, but has less impact on measuring their associations with vaccine behavior. Thus, it does not accurately capture the variability within the population. Our original plan was to obtain a longitudinal follow up of participants, but our ID creation system proved not adapted to real life, with many participants opting for simpler, instantaneous participations or losing their ID. Nevertheless, we have included the results of the small sample obtained in the Supplementary File 1, as inspiration for future work. Given the difficulty in obtaining longitudinal data, we have to rely on careful interpretation of 7C-attitude frequencies across the surveys. The characteristics of the participant groups remained relatively stable, based on which we attempt an interpretation of the 7Cs evolution over time. In particular, the interpretation of associations between 7C and vaccine behaviour maintains reasonable validity, as selection bias impacts less these estimates(109). Our study is, to the best of our knowledge, the first to assess the association of the 7C-model with vaccine acceptance throughout time and during a pandemic. It is also the first, to evidence that psychological antecedents of vaccination vary through time and context at an individual level. Despite the limitations mentioned above, given

the absence of previous data, this study could serve as a starting point for future longitudinal research regarding vaccine acceptance and its promotion in epidemic contexts.

Conclusion

Our study provides evidence that among HCSWs, the perception of the vaccine's BRB, is context-specific and changes over time, as does the significance of BRB perception in influencing vaccination intention and uptake. However, among all psychological antecedents, the perceived BRB remained a relatively stable determinant of behaviour.

More generally, our study suggests that, among HCSWs, several 7C-psychological antecedent's attitudes of vaccination are context-specific and thus change over time, while others, in particular the perception of vaccination as a collective action and the capacity for reactance, remain relatively stable. Also, our finding provides some evidence on the importance of Confidence in the vaccine to improve vaccine intention at a population level. As important determinants on the long-term, including given coercive policies, the perception of the vaccine's BRB and of the collective dimension of a vaccine recommendation stand out. By contrast, during the initial stage of a novel vaccine campaign in an epidemic context, the influence from the social environment, reactance against a recommendation source (the employer) and fear of vaccine side effects also play an important role. If 7C-attitudes evolve over time and are influenced by context, and are strongly associated to vaccine behaviour, the question arises if they can be influenced. Our finding calls for longitudinal studies to track changes of 7C-psychological antecedents of vaccination and their association with vaccine decision. A better understanding of the dynamic nature of 7C-psychological antecedents would help tailoring vaccine promotion strategies to profiles of vaccine hesitancy and readiness.

Aim 3. Preferences around the concept of benefit-risk ratio among the general adult population and among HCSWs in metropolitan France.

The second article of this thesis showed that 7C-attitudes evolve over time and are influenced by context, particularly the perceived benefit-risk balance of vaccination. It emphasized the need for longitudinal studies to track changes in the perception of vaccination BRB. Thus, the third article of this thesis focuses on identifying the contextual factors that shift the perceived vaccination BRB from favorable to unfavorable.

In this study, we will explore the existence of a BRB threshold for vaccine acceptance, thus, we will refer to the benefit-risk balance (BRB) as a ratio, benefit-risk ratio (BRR).

Article 3: Communicating on the Vaccine Benefit-Risk Ratios: A Discrete-Choice Experiment Among Healthcare Professionals and the General Population in France.

Journal: Article under revision at *Medical Decision Making* journal.

Background

Public discussions around vaccination often focus on vaccine benefits - overrated by some or not sufficiently recognized by others -, and side-effects – which can be well described, suspected or vaguely feared. The opposition of the two aspects leads, under which circumstances a vaccine would be considered “worth it” by individuals.

The concept of vaccine readiness(69) places vaccine decisions on a spectrum between complete acceptance and refusal(110,111) that depend on the characteristics of the proposed vaccination and specific individual and social circumstances.

As seen in previous chapters of this thesis, the tendency to weight perceived vaccine benefits against potential side-effects of vaccination (Calculation) has been identified as an important independent determinant of vaccine acceptance(68,70). For example in France, among healthcare sector workers (HCSWs) regarding COVID-19 vaccination, and among adolescents and parents of adolescents regarding human papillomavirus (HPV) vaccination, the positive perception of the vaccine benefit-risk ratio (BRR) stood out as one of, or even the most important determinant of vaccine intention or uptake(70,71), independently from fear of the disease or fear of vaccine side-effects.

By contrast, preference studies exploring optimized vaccine communication found that the statement “the benefits from this vaccine outweigh its risks” substantially decreased hypothetical vaccine acceptance and choice certainty compared to stating that “no suspected severe side-effect has been scientifically confirmed”(65,112). Despite methodological differences between the studies, this preference seems to be in contrast with the theoretical and observed importance that a positive BRR perception has in vaccine intention. This calls for further exploration on both, what people understand when they receive BRR information and on which factors shift the balance from unfavourable to favourable towards accepting vaccination.

Thus, during the COVID-19 and HPV vaccine campaigns, Public Health agencies have used the concept of benefit-risk ratio(113) assuming that avoided disease events and potentially induced side-effect events are of similar gravity. Clinicians have questioned its effectiveness(66). There is a long history in risk communication literature showing that communications that "equate" different outcomes simply because they have similar severity profiles evoke strong negative reactions from the public(114–116). This has been shown in the psychology literature as “omission bias” and in the economy literature as “loss aversion”(25,117); individuals tend to rate worse negative consequences from action than from inaction(12,21–24,118). Despite this evidence there is a gap in the literature assessing whether and up to which threshold this attitude prevails.

In the present study, we used DCE methodology to explore if there is a BRR threshold where rationality prevails omission bias. The objectives of this study, named Berberis, were to examine the existence of a BRR threshold among the general adult population and HCSWs. We estimated preference weights and expected vaccine uptake for different levels of BRR for a vaccine recommended during an infectious disease emergence. We also explored in how far qualitative information about disease severity, epidemiological context and indirect protection effects interacts with these preferences.

Methodology

Study design and participant enrolment.

We conducted two cross-sectional surveys using self-administered online questionnaires with a DCE: one with a representative sample of the general population of adults in France and the other with a convenience sample of French healthcare sector workers (HCSWs).

The representative sample of French adults was established by a survey institute (Panelia), using quota sampling based on age group, socio-professional category, region of residence and urban area size per the 2016 census(119). Participants accessed the online questionnaire between 17 April and 3 May 2023.

According to guidelines(120) and previous DCEs(64,65,67), at least 200 participants were required per stratum to estimate preference weights with sufficient power. We aimed to include 1500 participants for stratified analysis by age (three groups) and gender (two groups).

For the HCSWs convenience sample, participants were recruited via snowball sampling through the Group for the Prevention of Occupational Infections in Healthcare Workers (GERES) network. On 12 January 2023, members who previously had expressed their interest in participating in research on COVID-19 received an email invitation containing a questionnaire link on the RedCap platform. Participants could forward the invitation among their professional environment. Eligibility criteria included being ≥ 18 years old and working as an HCSW in mainland France the questionnaire was accessible until 13 March 2023. We aimed to include 400 HCSWs for subgroup analyses by professional category (biomedical vs. care profession), known to be a determinant of vaccine acceptance(70).

Participants read study information on data confidentiality and autonomy before the questionnaire and actively agreed to participate. The study protocol received clearance by the Pasteur Institute IRB on 9 December 2022.

Questionnaire

The questionnaires for both study samples were identical, except for specific socio-professional information in the general population representative sample. They included three parts: 1) socio-demographic and professional details, including age, gender, region of residence/work, educational level, chronic disease diagnosis, general vaccination favorability and influenza vaccination status in the past three years; 2) the DCE tool and 3) attitudes towards COVID-19 vaccination, which will be reported elsewhere.

The DCE tool

We designed the DCE tool based on available literature, expert opinions and iterative pilot testing. A single-profile DCE was used to simulate a binary vaccine decision-choice, which reproduces more realistically the situation than comparison between vaccinations(66). Participants chose to accept or refuse immediate, free vaccination against an unnamed,

emerging disease to avoid preconceived idea of disease. Each participant completed 10 choice tasks and rated their decision certainty on a scale from 1 to 10(112).

Attributes and levels

Previous DCEs have explored preferences around expectable vaccine benefits and risks as separate attributes(64,67,121). In our study, to quantify preferences around the BRR, we included one attribute with varying levels of BRR. Based on literature and expert opinions, the BRR levels were set at 10:1, 50:1, 100:1 and 500:1. Other attributes included syndrome type (neurological or respiratory); and severity (duration of one week to 30 days, with immobilization at home or hospitalization, with and without sequelae).

During think-aloud pilot testing, participants reported that their decision would depend on protection to others, vaccine coverage and disease frequency. We thus added qualitative attributes on disease frequency and the potential to protect others.

The DCE tool contained five attributes with the following hypothesis (**Table 9, Figure 7**):

- DISEASE (2 levels): type of vaccine-preventable disease or side effect (respiratory or neurological) independently impacts vaccine acceptance.
- EPI (epidemic situation) (2 levels): disease risk perception is an independent factor in vaccine decision (frequent, 10% to develop the disease during the coming year or rare, <1%).
- UNIT OF BRR (3 levels), stake of vaccination, i.e., event severity that vaccination could either avoid or induce: higher severity of avoided or induced events would not decrease vaccine acceptance.
- BRR (4 levels), number of avoided events for one induced, in a population with the size of Paris (2.2 million people) and for the participant's age group: higher BRR favourably impact vaccine acceptance.
- INDIRECT PROTECTION (2 levels): Based on previous findings among French university students(67): vaccine acceptance is higher with potential for indirect protection (reduced risk of infection and transmission to close contacts).

Table 9. Attributes and levels in the discrete choice experiment. Berberis study, France, 2023.

Attributes	Levels	Hypothesis
Type of disease (DISEASE)	The vaccine protects against a neurological disease. The vaccine protects against a respiratory disease.	The type of vaccine-preventable disease or side effect independently impacts vaccine acceptance.
Epidemic situation (EPI)	The risk of getting the disease, the next year for your age group is low (less than one person in a thousand). The risk of getting the disease, the next year for your age group is high (one in ten people).	Disease risk perception is an independent factor in vaccine decision.
Stake of vaccination (UNIT BRR)	The stake of vaccination is an immobilization at home with a work sick leave for one week without sequelae. The stake of vaccination is a one week of hospitalization without any risk of sequelae. The stake of vaccination is 30 days of hospitalization with sequelae risk.	Higher severity of avoided or induced events would not decrease vaccine acceptance.
Vaccination Benefit-risk ratio (BRR)	In a population with the size of Paris (2.2 million of people) for a given period of time, and for your age group, it is estimated that vaccination avoids: <ul style="list-style-type: none"> - 500 events caused by the disease for one induced event related to the side-effect. - 100 events caused by the disease for one induced event related to the side-effect. - 50 events caused by the disease for one induced event related to the side-effect. - 10 events caused by the disease for one induced event related to the side-effect. 	Levels of vaccination BRR influence vaccine decision.
Potential for indirect protection (INDIRECT PROTECTION)	The vaccine confers only individual protection . The vaccine confers indirect protection to relatives .	Vaccine acceptance is higher with potential for indirect protection (reduced risk of infection and transmission to close contacts).

The final pilot study included one nurse, one veterinary doctor, one speech therapist, two engineers, one physician, one pharmacist, one marketing content manager, who self-administered the questionnaire. Their feedback helped simplify the DCE tool's introduction and clarify attributes and levels.

Figure 7. Example choice task

You are in consultation with your doctor who offers you an immediate and free vaccination. The proposed vaccination protects against a new disease. Vaccination coverage in the adult population is about 50%. The vaccine helps prevent episodes due to the disease, but it can also cause a rare adverse side effect.

Here is the information about the vaccine:

The vaccine protects against a respiratory disease .
The risk of developing this disease in the next year, for your age group, is high (about one in ten people).
The stake of vaccination is to avoid a 30-day long hospitalization with sequelae risk .
In a population with the size of Paris, for a given period of time, and for your age group, it is estimated that vaccination:	- avoids 10 long hospitalizations caused by the disease - induces 1 long hospitalization related to the side effect.
The vaccine confers indirect protection to your relatives.

In this situation, do you agree to be vaccinated?

Yes

No

How sure are you about the choice you just made? (0: not at all certain; 10: perfectly certain)

0

1

2

3

4

5

6

7

8

9

10

Not certain at all

Neutral

Perfectly certain

Experimental design

The choice task used a fractional single-profile format with an opt-out. From 96 combinations in a full-factorial design; STATA generated 16 scenarios in two blocks of 8, allowing estimation of all main effects. Participants were randomly assigned to a block and task ordering within it was randomized. After each task, participants reported their certainty level on a scale from 0 (not at all certain) to 10 (absolutely certain).

To test preference monotonicity (“more is preferred to less”, a core assumption of revealed preference theory), we repeated two scenarios with modified BRR levels, keeping other attributes constant. One scenario modified BRR from 10:1 to 2:1 and another from BRR 500:1 to 1000:1 (**Supplementary Table 3**). We compared responses between these repeated scenarios. Based on monotonicity, we expected decreased vaccine acceptance for the 2:1 BRR (less favorable), and increased acceptance for 1000:1 BRR (more favorable).

We explored serial choice behaviors (participants accepting or refusing all scenarios) across the 8 DCE tasks. Individuals who declined all 8 scenarios and the extreme 1000:1 BRR scenario were asked to select the minimum number of preventable events per one adverse event that would justify vaccination, from a list ranging from 1000 to 1 million, including an option “no number justifies”.

Statistical analyses

We distinguished HCSWs by education level: university-degree, and non-university-degree. In France, university-degree HCSWs include physicians, nurses and mid-wives. Non-university-degree HCSWs have vaccination attitudes similar to the general public(70), and different from university-degree HCSWs(15). Thus, we conducted the analysis in four groups: the representative general population sample, general population excluding HCSWs (non-HCSW), combining the non-university-degree HCSWs from the representative sample and HCSW convenience sample (non-university-degree HCSWs), and combining university-degree HCSWs from the representative sample and HCSW convenience sample (university-degree HCSWs).

All analyses were performed in STATA statistical software (version 16.0; StataCorp LP, College Station, Texas) with statistical significance set at $p < 0.05$.

Objective 1: Preference weights on binary vaccine acceptance

We evaluated the effect of attributes on hypothetical vaccine acceptance (yes vs. no) using random effects linear regressions in a panel logit model (xtlogit command in STATA).

Preference weights were expressed as odds ratios (ORs) and 95%-confidence intervals (95%CI). To align fixed and random effects models, we estimated random effects model including only participants making variable decisions (non-uniform respondents). Participants were randomly assigned to choice sets blocks, independent of socio-demographic characteristics, ensuring no confounding. We verified correct randomization by adding individual characteristics to the model and checking for changes in preference weights. The effect of attributes was evaluated using marginal effects from a random effects linear regression. Focusing on BRR attribute, we examined its interaction with individual characteristics, including gender, age and educational attainment (high school diploma or lower vs. higher). Subsequently, we conducted latent class analysis to identify latent classes (**Supplementary File 1**).

Objective 2: Preference weights on vaccine eagerness

Vaccine decision-making is a nuanced process involving varying levels of certainty(122). Chyderiotis et al. (2022)(112) introduced a vaccine eagerness scale to quantify certainty in binary vaccine decisions from 0 to 10. Negative values indicate refusal (certainty 0 to 10 becomes 0 to -10, -10 strong refusal) while positive values indicate acceptance (certainty 0 to 10 becomes 0 to +10, +10 strong acceptance), 0 reflect relative indecision. Using this scale in single-profile DCE allows for preference elicitation, even among respondents who consistently accept (serial demanders) or refuse (serial non-demanders) all scenarios. We evaluated attribute effects on vaccine eagerness using random-effects linear regression, estimating marginal and subgroup effects similar to those for binary acceptance decisions.

Objective 3: Predict hypothetical vaccine coverage across different vaccine scenarios.

Predicted vaccine coverage was estimated based on each attribute weights and prevalence of serial demanders and non-demanders. Predicted acceptance was estimated based on the simulation of the utility (assuming linear-in-parameters underlying utility functions) of the respective combination of attribute levels for scenarios j using the standard formulae for predictions in logit models:

$$\text{Predicted Vaccine Coverage} = ([1 / (1 + e^{-\text{utility}_j})] * R + D) / (R + D + N)$$

j: vaccine scenarios

R: number of non-uniform respondents

D: number of serial demanders

N: number of serial non-demanders

utility = sum of products (coeff_i * *l*)

l: attribute i level 0 (reference) or 1

All scenarios assumed a respiratory disease, stake of vaccination being one week of hospitalization and no potential for indirect protection. Scenarios varied for levels of BRR and risk of developing the disease.

Results

The representative sample of the French adult population included 1505 participants in age groups 18-34 years (25.2%), 35-49 years (27.2%) and ≥50 years (47.5%), of whom 730 (48.5%) were women and 121(8.1%) persons declared being HCSWs. The convenience sample of HCSW included 364 participants in age groups 18-34 years (12.6%), 35-49 years (41.8%) and ≥50 years (45.6%) of whom 277 (76.1%) were women and 281(77.2%) university-degree HCSWs (**Supplementary Table 4**).

After combination of the two study samples (total of 1869 participants), the non-HCSW, non-university-degree HCSW and university-degree HCSW subgroups included 1384, 146 and 399 participants respectively (**Table 10**). University-degree HCSW differed by being predominantly female (72.3% vs. 49.0% in non-HCSW subgroup), younger (37.8% ≥50 years vs. 49.3%), more favorable towards vaccines in general (93.5% vs. 76.4%) and with a more positive perception of COVID-19 vaccination's BRR (63.4% vs. 47.4%) (**Table 10**).

Overall, 60.4% of participants found the DCE exercise not complicated, while 10.5% found it very complicated: non-HCSWs were significantly more likely to find the exercise complicated (Chi2 test, p-value<0.001).

Hypothetical vaccination was accepted on average by 62.6% of participants, ranging from 43.0% in the least favourable to 72.0% in the most favourable scenario among the representative sample (**Supplementary Table 3**). Serial demanders comprised 30.6% of the representative sample, 30.7% of non-HCSWs, 30.1% of non-university-degree HCSWs and 41.0% of university-degree HCSWs. Serial non-demanders accounted for 14.0%, 14.7%, 4.8% and 3.8%, respectively. This left 1038 non-uniform respondents, 756 non-HCSWs, 95 non-university-degree HCSWs and 187 university-degree HCSWs (**Table 10**).

Table 10. Description of the study participants, in the representative population sample (N=1505) and in the Healthcare Sector Workers (HCSWs) sample by HCSW status. Berberis study, France, 2023.

	Representative population sample N=1505	Non-HCSWs N=1384	Non-university-degree HCSWs N=146	University-degree HCSWs N=339
Gender				
Male	775 (51.5%)	706 (51.0%)	62 (42.5%)	94 (27.7%)
Female	730 (48.5%)	678 (49.0%)	84 (57.5%)	245 (72.3%)
Age (in years)				
18-34	380 (25.2%)	334 (24.1%)	25 (17.1%)	67 (19.8%)
35-49	410 (27.2%)	368 (26.6%)	50 (34.2%)	144 (42.5%)
≥50	715 (47.5%)	682 (49.3%)	71 (48.6%)	128 (37.8%)
Region of residence/work (N=1865)				
Paris Region	282 (18.7%)	255 (18.4%)	35 (24.1%)	60 (17.9%)
North East	330 (21.9%)	305 (22.0%)	34 (23.4%)	68 (20.2%)
North West	343 (22.8%)	322 (23.3%)	21 (14.5%)	67 (19.9%)
South East	377 (25.0%)	342 (24.7%)	26 (17.9%)	110 (32.7%)
South West	173 (11.5%)	160 (11.6%)	29 (20.0%)	31 (9.2%)
DROMs	0 (0.0%)	0 (0.0%)	1 (0.7%)	3 (0.9%)
Speaking other language than French (N=1867)				
No	1193 (79.3%)	1118 (80.8%)	120 (82.2%)	266 (78.9%)
Yes	312 (20.7%)	266 (19.2%)	26 (17.8%)	71 (21.1%)
Educational level (N=1505)				
Lower than secondary school diploma	355 (23.6%)	343 (24.8%)	12 (19.0%)	0 (0.0%)
Equal to secondary school diploma	377 (25.0%)	361 (26.1%)	16 (25.4%)	0 (0.0%)
Higher than secondary school diploma	773 (51.4%)	680 (49.1%)	35 (55.6%)	58 (100.0%)
General opinion about vaccines				
Very Favorable	453 (30.1%)	403 (29.1%)	66 (45.2%)	207 (61.1%)
Favorable	710 (47.2%)	654 (47.3%)	69 (47.3%)	110 (32.4%)
Undecided	208 (13.8%)	202 (14.6%)	3 (2.1%)	11 (3.2%)
Skeptical	95 (6.3%)	89 (6.4%)	6 (4.1%)	9 (2.7%)
Very Skeptical	39 (2.6%)	36 (2.6%)	2 (1.4%)	2 (0.6%)
Seasonal Flu Vaccine Status (N=362)				
Unvaccinated			17 (20.5%)	43 (15.4%)
Vaccinated (every year)			45 (54.2%)	182 (65.2%)
Vaccinated (twice)			12 (14.5%)	29 (10.4%)
Vaccinated (once)			9 (10.8%)	25 (9.0%)
COVID-19 Vaccine Status (N=1384)				

ARTICLE PRESENTATION – ARTICLE 3

Unvaccinated	196 (14.2%)	196 (14.2%)		
Vaccinated (more than 6 months ago)	978 (70.7%)	978 (70.7%)		
Vaccinated (less than 6 months ago)	210 (15.2%)	210 (15.2%)		
Perception of Benefit-Risk Ratio of Covid-19 vaccination (N=1866)				
More risks than benefits	408 (27.1%)	371 (26.8%)	44 (30.1%)	77 (22.9%)
Do not know	382 (25.4%)	357 (25.8%)	25 (17.1%)	46 (13.7%)
More benefits than risks	715 (47.5%)	656 (47.4%)	77 (52.7%)	213 (63.4%)
Level of confidence in authorities in the management of the COVID-19 crisis (N=1867)				
Low	328 (21.8%)	307 (22.2%)	34 (23.3%)	62 (18.4%)
Moderate	496 (33.0%)	456 (32.9%)	52 (35.6%)	113 (33.5%)
High	681 (45.2%)	621 (44.9%)	60 (41.1%)	162 (48.1%)
Vaccination Behavior Type				
Serial non-demanders	211 (14.0%)	203 (14.7%)	7 (4.8%)	13 (3.8%)
Non-uniform vaccine responder	833 (55.4%)	756 (54.6%)	95 (65.1%)	187 (55.2%)
Serial demanders	461 (30.6%)	425 (30.7%)	44 (30.1%)	139 (41.0%)

HCSW: Healthcare sector worker

Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8.1%) were further categorized based on their professional education into their respective HCSW occupational groups.

In the HCSW sample, some socio-demographic questions were asked at the end of the questionnaire, some participants did not answer those questions (n=3).

Benefit-risk ratio across different vaccine scenarios.

Among university-degree HCSWs, BRR levels 100:1 and 500:1, significantly increased vaccine acceptance compared to level 10:1 (OR=1.99 and 2.30, respectively), but not BRR level 50:1 (**Table 11**). No significant effect of BRR on decisions was observed in the representative sample, non-HCSWs or non-university-degree HCSWs. Other attributes (type of disease, epidemic situation, stake of vaccination and potential for indirect protection) significantly influenced vaccine decisions among non-uniform respondents regardless of professional category.

Among serial non-demanders who refused vaccination of 1000:1 BRR, 85.7% considered that “no BRR justifies vaccination” (**Table 12**).

In the repeated scenarios hypothetical vaccine acceptance did not change substantially with extreme BRR values. Among university-degree HCSWs with non-uniform responses, acceptance rates were 67.8% for BRR 10:1 vs. 54.3% for BRR 2:1 ($p=0.488$), and 84.9% for BRR 500:1 vs. 88.2% for BRR 1000:1 ($p=0.447$). Among 211 serial non-demanders of the representative sample, 205 refused a vaccine with BRR 1000:1; 6.3% chose 1 million avoided diseases cases per adverse event to justify vaccination, and 88.8% believed that no BRR justify vaccination (**Table 12**).

Qualitative attributes had notable effects (**Table 11**). High disease risk (in the representative sample, vs. low risk, OR=6.87) and “30 days of hospitalization with sequelae risk” (vs. 1 week of sick leave, OR=2.11) had strongest impact on vaccine acceptance. All effects increased among university-degree HCSWs.

Table 11. Preference weights for attributes of hypothetical vaccination acceptance (binary outcome) and β -coefficient for vaccine eagerness by Healthcare Worker (HCSW) status. Berberis study, France, 2023.

	Hypothetical Vaccine Acceptance (non-uniform respondents)								Vaccine Eagerness (all respondents)							
	Representative sample (N=833)		Non-HCSWs (n=756)		Non-university-degree HCSWs (n=95)		University-degree HCSWs (n=187)		Representative sample (N=1505)		Non-HCSWs (n=1384)		Non-university-degree HCSWs (n=146)		University-degree HCSWs (n=339)	
	OR	<i>p</i> -value	OR	<i>p</i> -value	OR	<i>p</i> -value	OR	<i>p</i> -value	β -coefficient	<i>p</i> -value	β -coefficient	<i>p</i> -value	β -coefficient	<i>p</i> -value	β -coefficient	<i>p</i> -value
Type of disease																
respiratory disease	1		1		1		1		0		0		0		0	
neurological disease	1.43	<0.001	1.42	<0.001	1.80	0.001	2.58	<0.001	0.685	<0.001	0.649	<0.001	1.166	<0.001	1.593	<0.001
Epidemiologic situation																
low risk of developing the disease	1		1		1		1		0		0		0		0	
high risk of developing the disease	6.87	<0.001	7.19	<0.001	5.83	<0.001	8.68	<0.001	3.227	<0.001	3.242	<0.001	3.515	<0.001	3.139	<0.001
Stake of vaccination																
immobilization at home	1		1		1		1		0		0		0		0	
one week of hospitalization without any sequelae	0.98	0.775	1.00	0.958	0.71	0.120	1.12	0.507	-0.006	0.958	0.004	0.971	-0.488	0.218	0.203	0.391
30 days of hospitalization with sequelae risk	2.11	<0.001	2.12	<0.001	3.12	<0.001	6.03	<0.001	1.236	<0.001	1.216	<0.001	2.056	<0.001	2.651	<0.001
Benefit-Risk Ratio of vaccination																
avoid 10 events for 1 induced event	1		1		1		1		0		0		0		0	
avoid 50 events for 1 induced event	0.93	0.374	0.93	0.387	0.89	0.644	1.22	0.307	-0.024	0.848	-0.029	0.823	-0.148	0.738	0.465	0.078
avoid 100 events for 1 induced event	1.05	0.526	1.07	0.425	1.45	0.127	1.99	<0.001	0.158	0.203	0.194	0.130	0.706	0.110	1.219	<0.001
avoid 500 events for 1 induced event	1.03	0.693	1.06	0.554	0.95	0.859	2.30	<0.001	0.064	0.616	0.082	0.532	-0.157	0.726	1.059	<0.001
Protection of the vaccine																
no indirect protection	1		1		1		1		0		0		0		0	
indirect protection	1.58	<0.001	1.63	<0.001	2.13	<0.001	2.52	<0.001	0.702	<0.001	0.720	<0.001	1.420	<0.001	1.520	<0.001

Hypothetical vaccine acceptance: Odds Ratio (OR) and *p*-value from random effect generalized multinomial logit model.

Vaccine eagerness: β -coefficient and *p*-value from generalized linear model.

HCSW: Healthcare sector worker

Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8%) were further categorized based on their professional education into their respective HCSW occupational groups.

Table 12. Minimal number of avoidable disease events per one adverse event that is required for vaccination acceptance. Serial vaccine non-demanders (N=223). Berberis study, France, 2023.

Number of avoidable events per one adverse event required for vaccination acceptance	Representative sample (n=211)	Non-HCSWs (n=203)	Non-university-degree HCSWs (n=7)	University-level HCSWs (n=13)
Hypothetical vaccine acceptance of BRR 1000:1 among serial non-demanders				
1 000 : 1	6 (14.0%)	6 (12.2%)	0 (0.0%)	0 (0.0%)
Number of avoidable events per one adverse event required for vaccination acceptance				
	Representative sample (n=205)	Non-HCSWs (n=197)	Non-university-degree HCSWs (n=7)	University-degree HCSWs (n=13)
Among those who refused a BRR of 1000:1, "How many avoided sick leave episodes would be required for you to accept vaccination?"				
5 000 : 1	2 (1.0%)	2 (1.0%)	0 (0.0%)	0 (0.0%)
10 000 : 1	3 (1.5%)	3 (1.5%)	0 (0.0%)	0 (0.0%)
20 000 : 1	2 (1.0%)	2 (1.0%)	0 (0.0%)	0 (0.0%)
50 000 : 1	2 (1.0%)	2 (1.0%)	0 (0.0%)	0 (0.0%)
100 000 : 1	1 (0.5%)	1 (0.5%)	0 (0.0%)	1 (4.5%)
1 000 000 : 1	13 (6.3%)	13 (6.6%)	1 (12.5%)	1 (4.5%)
No number justifies	182 (88.8%)	174 (88.3%)	6 (75.0%)	11 (50.0%)

BRR: Benefit-Risk Ratio

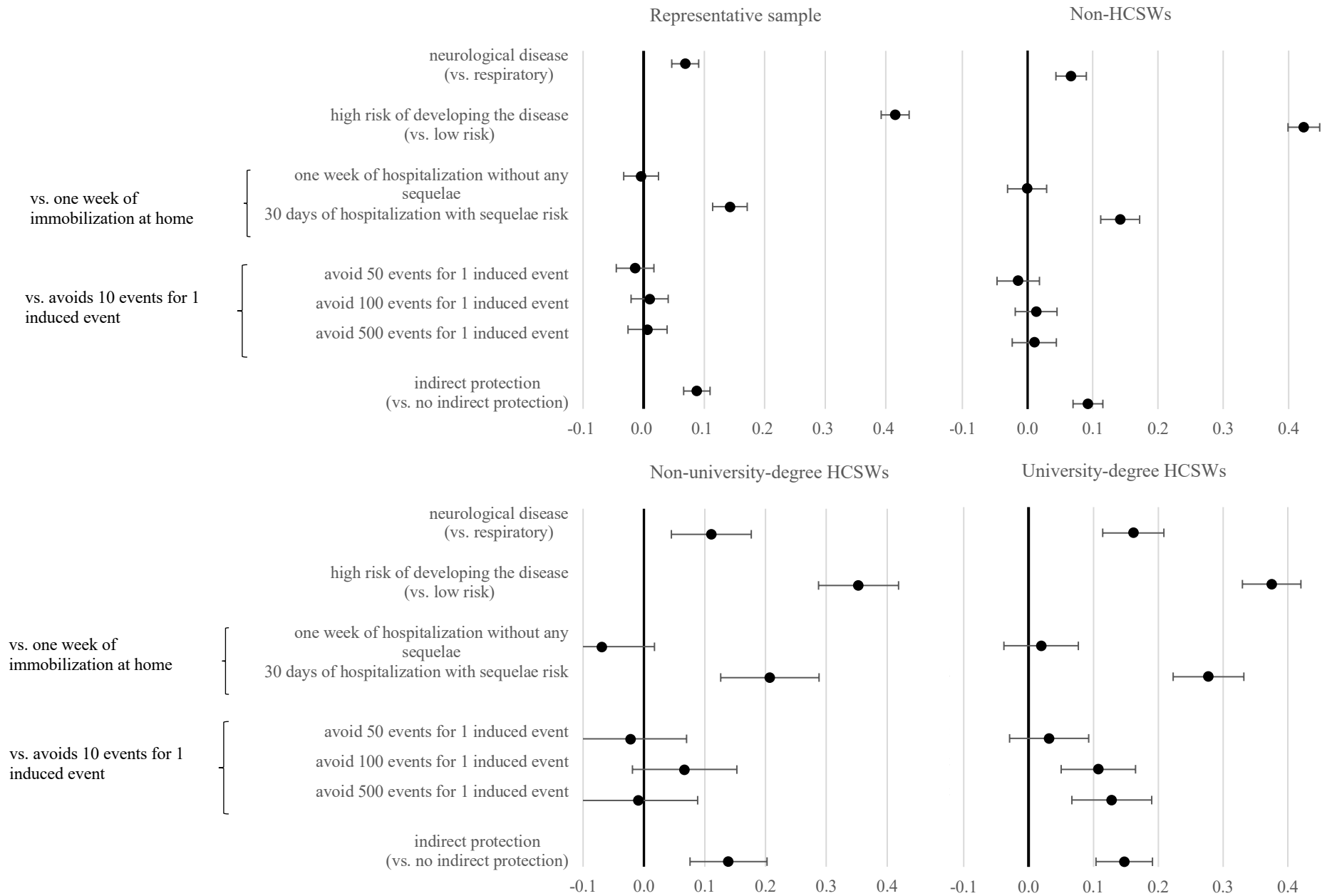
Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8%) were further categorized based on their professional education into their respective HCSW occupational groups.

No interaction was observed between BRR levels and individual characteristics (age, gender, educational level, vaccine opinion of COVID-19 and vaccine BRR perception), among the representative sample and all professional subgroups. Inclusion of individual characteristics in the models did not change preference weights (**Supplementary Table 5**).

Among non-uniform respondents of the representative sample, moving from low to high disease risk increased the probability of acceptance by 41% (marginal effects, **Figure 8**), consistent across subgroups.

Among university-degree HCSWs, a vaccine with BRR 100:1 increased average vaccine acceptance by +10%, compared to BRR 10:1.

Figure 8. Average marginal effects (change in probability of vaccine acceptance) of attribute levels on hypothetical acceptance of vaccination among non-uniform respondents. Among the representative population sample (N=833), non-Healthcare Sector Workers (non-HCSWs) (N=756), non-university-degree Healthcare Sector Workers (HCSWs) (n=95) and university-degree HCSWs (N=187). Berberis studv. France. 2023.



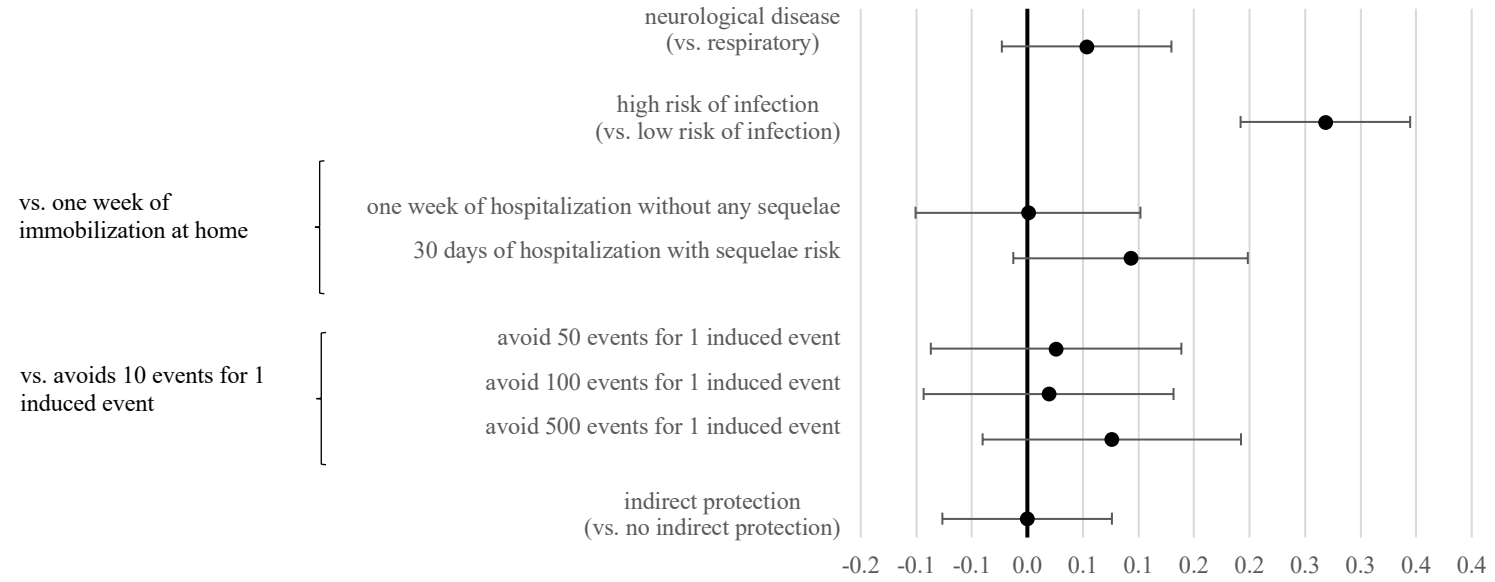
Vaccine eagerness scale

Among the representative sample, the average level of vaccine eagerness (on a –10 to 10 scale) in the 8 scenarios ranged from -0.64 to 4.60 (**Supplementary Table 3**). University-degree HCSWs had constantly higher vaccine eagerness than other subgroups, except in bloc 1 extreme scenario with BRR 2:1, where their eagerness was the lowest (0.99 vs >3.0).

Attribute effects on vaccine eagerness, combining uniform and non-uniform respondents, showed similar preference weights pattern seen in vaccine acceptance among non-uniform respondents. The strongest impact was observed with high disease risk ($\beta=3.227$ in the representative sample) (**Table 11**). Among 223 serial non-demanders, disease risk was the only attribute significantly affecting the vaccine eagerness scale (high vs. low, $\beta=0.268$) (**Figure 9**).

In repeated scenarios among the representative sample, vaccine eagerness showed no significant change with extreme BRR values.

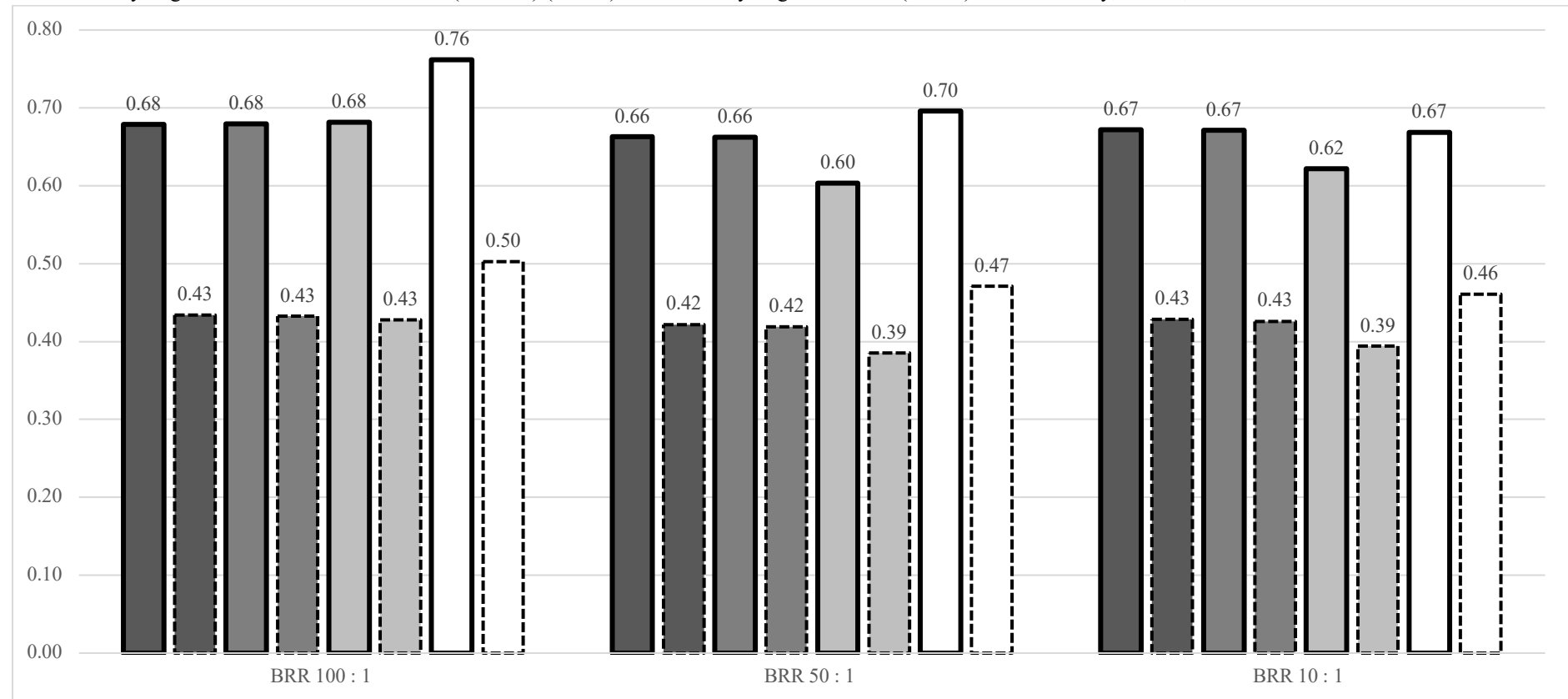
Figure 9. Average marginal effects of attribute levels on vaccine eagerness of vaccination among vaccine serial non-demanders (n=223). Berberis study, France, 2023.



Predicted Vaccine Coverage

Overall, predicted vaccine coverage varied substantially by disease risk, but not by professional groups or BRR. The highest predicted coverage was 76.0% among university-degree HCSWs with 100:1 BRR. In scenarios with low disease risk, predicted coverage across all professional categories did not exceed 50% (**Figure 10**).

Figure 10. Predicted vaccine coverage according to benefit-risk ratio and disease frequency, among representative sample(n=1505), non-Healthcare Sector Workers (non-HCSWs) (n=1384), non-university-degree Healthcare Sector Worker (HCSWs) (n=146) and university-degree HCSWs (n=339). Berberis study, France, 2023.



- ▬ high risk of developing the disease
- ▬ low risk of developing the disease
- Representative sample
- Non-HCSWs
- Non-university-degree HCSWs
- University-degree HCSWs

*Stable assumptions for other attributes: respiratory disease, stake of vaccination being one week of hospitalization, no potential for indirect protection.
 BRR: Benefit-Risk Ratio

Discussion

In this DCE study among adults in France, we found that university-degree HCSWs, unlike other population subgroups, considered the BRR during hypothetical vaccine decisions. In contrast, qualitative attributes surrounding disease frequency and severity, and indirect protection significantly influenced vaccine decisions across all participants, irrespective of professional categories.

Several interpretations are possible for these results. The concept of individual BRR might be too complex and understood primarily by individuals with high health literacy levels. Non-university-degree HCSWs showed preferences similar to those of the general population, reflecting their distinct training duration and level of education. The BRR attribute possibly required good numeracy and rational reasoning, which are more frequent among university-degree HCSWs. However, individuals with higher education diplomas in the general population, who may have similar health literacy and numeric reasoning abilities as university-degree HCSWs, did not show sensitivity to BRR. This suggests that general health literacy or numeric reasoning are insufficient to consider BRR in vaccine decisions. We hypothesize that routine practice of benefit-risk considerations in medical healthcare enables university-degree HCSWs to consider BRR into vaccine decisions. Therefore, discussing vaccine's BRR, a term that healthcare professionals may find informative and appropriate to motivate vaccine acceptance, does not provide useful information to the general public and rather create a communication gap between provider and patient.

A substantial proportion of the representative sample (50% and 25%, depending on epidemic situation) refused vaccines despite clear benefits outweighing risks, including for short-term consequences and irrespective of indirect protection effects, indicating high prevalence of omission bias. All DCE scenarios involved a vaccine with a confirmed severe side-effect which likely led participants to perceive the vaccine as unsafe, even with favourable BRR. This aligns with previous studies, including among HCSWs, showing that mentioning a favourable BRR decreased vaccine acceptance, compared to stating no confirmed severe side-effect(65,66). Surprisingly, even among university-degree HCSWs, a substantial proportion refused vaccination despite 50:1 BRR, while favourable qualitative levels strongly motivated acceptance. This suggests that BRR is ineffective for communicating with the general public and non-university-degree HCSWs, possibly implying risks and leading participants to become insensitive to BRR. This aligns with previous studies showing that equating similar outcomes is poorly understood and can increase the perceived effect of treatment(123), thus increasing omission bias.

Personalised recommendation based on specific individual benefits, including protection to others, may be more effective in promoting vaccines with potential rare severe side-effect.

Participants in pilot testing requested information on qualitative attributes, specifically disease frequency (high or low-risk in the next year). Although disease frequency is included in the BRR concept, our initial DCE format did not include this qualitative information which had the strongest impact on vaccine decisions. Severity of disease/vaccine consequences (mild or severe) is also part of the BRR (neutralized within the ratio) but it strongly impacted vaccine decisions: more severe outcome at stake led more participants to accept vaccination. These results suggest that BRR is too complex, and not well understood by participants, making seem irrelevant.

Pilot testing also required the inclusion of indirect protection (vs. no indirect protection) as a qualitative attribute, significantly impacting vaccine acceptance. This aligns with previous studies(65) showing higher acceptance when indirect protection is included. Concepts like disease risk, severity and indirect protection are more comprehensible, and could have dominated vaccine decision across scenarios. Traditional communication methods made difficult to extract qualitative information and solely discuss BRR, thus, participants requested this information during pilot testing.

Marginal effects and predicted coverage in different vaccine scenarios highlighted the importance of disease frequency. Acceptance increased by 40% among the representative sample when disease risk was high compare to low risk, and vaccine coverage exceeded 50% only in high disease risk scenarios.

The concept of vaccine eagerness showed that disease frequency was the only attribute significantly impacting serial non-demanders in their vaccine decision, highlighting the importance of disease risk perception on vaccine decision-making(117), including among those initially unlikely to accept vaccination.

A significant amount of literature suggests that instant healthcare decisions are challenging, often requiring guidance to choose the most suitable option(20). Without trusted guidance, choices may be influenced by heuristics(124) and irrational motivations(20). Our data suggest that BRR should not be used in vaccine promotion. Instead, communication should highlight wider vaccine benefits and risks, allowing individuals to judge whether the vaccine “is worth it”.

Limitations

Our study has several limitations. We cannot exclude that except for university-degree HCSWs, most participants had difficulties in understanding the exercise, possibly explaining why BRR did not influence hypothetical decisions. However, most participants reported finding the exercise uncomplicated. Also, the generalizability of this BRR weightings is limited as weightings would likely change significantly in DCEs using alternate methods of communicating vaccine risks and benefits.

As in all stated preferences studies, interpretation of results must consider the hypothetical nature of decisions.

The lowest BRR in the DCE was 10:1, with 2:1 used to explore monotonicity. Monotonicity was confirmed by slightly lower acceptance (67.8% with 10:1 vs. 54.3% with 2:1, among university-degree HCSWs, non-uniform respondents). This design did not identify the lower limit of acceptable BRR but showed that outside an epidemic, about 50% of university-degree HCSWs accept vaccines with a relatively low BRR of 10:1, and higher BRRs increased acceptance.

In the DCE, “high disease risk” was defined as a 1 in 10 probability for the coming year, which could appear as an unrealistically high level that dominated any decision. However, this aligns with the seasonal risk of healthcare consultation for influenza in adults, as reported in New Zealand during a non-epidemic season(125).

Internet panel participants are not completely representative of the French population due to selection on internet access and use. Despite the quota sampling, people in poverty, with low health literacy and possibly high-risk behaviour may be underrepresented. However, 85.8% of participants declared receiving at least one COVID-19 vaccine dose, aligning with estimations from the French Ministry of Health(81%)(126). The internet panel of adults is not representative in subgroup analyses, which should be considered during data interpretation.

HCSWs in the snowballing sample were self-selected on favourable vaccination attitudes. Given their involvement in the GERES, they likely prioritize health recommendations : 78.2% of physicians and 59.5% of nurses reported influenza vaccination for the current season, compared to 51% and 29% estimated for physicians and nurses working in hospitals in France 2022(127) during the preceding season. This suggest that BRR effects on vaccine decision may vary among HCSWs less vaccine-favourable.

To identify potential heterogeneity in our data, we performed a latent class analysis (Supplementary File 1), which confirmed our results. The analysis identified one cluster

characterized by lower vaccine acceptance for neurological diseases compared to respiratory diseases, particularly in an epidemic situation, and reacted little to severity of consequences.

To further assess data quality, the HCSWs convenience sample gathered information on the time taken to complete the questionnaire, but this information was not collected from the representative sample of French adults. In the convenience sample of HCSWs, we performed a sensitivity analysis by excluding respondents who completed the questionnaire in less than 9 minutes and did not vary their certainty levels. The results remained consistent after these exclusions. Additionally, we performed sensitivity analyses on both samples, excluding participants whose choice certainty did not vary across different scenarios, and found that the results remained consistent.

Conclusion

Our results reflect the need for tailored communication strategies to effectively promote vaccination. Specifically, BRR considerations should be targeted at university-degree HCSWs, as the general public appears indifferent to this information. In our example, effective vaccine promotion for a highly effective vaccination against an emerging disease in France, focused on disease frequency, severity, and indirect protection effects. For vaccines with confirmed severe side-effect beyond allergic reactions, personalised recommendation considering individual benefits may be necessary.

The perception that a vaccine “has more benefits than risks for me” is crucial for vaccine acceptance, but strategies to foster this attitude remain unclear. However, promoting favourable BRR should not be part of communication strategies.

Aim 4. Proportion of individuals that while initially hesitant towards vaccination, may be compliant to persuasion through targeted vaccine communication on vaccination benefit-risk balance.

The fourth article of this thesis define different vaccination behaviour profiles and assess the proportion of individuals that communicating on the benefit-risk balance of vaccination might engage them towards vaccine acceptance.

Article 4: Understanding Vaccine Non-Demanders: Determinants and Motivations in Vaccine Decision Profiles.

Journal: Submission pending

Background

Vaccine hesitancy poses a significant challenge in public health, with a persistent subset of the target population, often estimated at around 30%, refusing vaccination(128,129). Understanding behaviors and motivations of this vaccine-hesitant group is crucial for developing effective strategies to address their concerns. However, engaging individuals who are not favorable of vaccines in research has proven to be very difficult. Discrete Choice Experiments (DCEs) are a tool that enables to counteract this issue, by repeatedly asking participants their vaccine decision over different hypothetical vaccine scenarios(64,65,67,112,121).

Decision-making is a nuanced process, each choice has a spectrum of certainty levels regarding the chosen course of action(130), this spectrum applies also when it comes to vaccine decisions. In single profile DCE, which imitate the binary vaccine decision “accept or refuse”, participants not only make decisions regarding individual scenarios, but individual decisions can be further examined with regard to their choice certainty. Chyderiotis et al., evaluated post-choice certainty information to elicit preferences even among respondents who consistently accepted (vaccine serial demanders) or refused (vaccine serial non-demanders) hypothetical vaccination scenarios(131). They provided a concept of “vaccine eagerness”, where all decisions can be ranked on a scale between certainly refuse to certainly accept, going through uncertain refusal and uncertain acceptance.

In single-profile DCE, participants can be categorized based on their decision-making patterns: those who make variable accept-refuse decisions (non-uniform respondents), and those who

consistently accept or refuse all scenarios (serial demanders and serial non-demanders, respectively). Serial choice behavior can be further analyzed using choice certainty: serial demanders and non-demanders may exhibit consistent choice certainty, which could indicate a fundamental acceptance or opposition to vaccination—or, in some cases, it may reflect poor response quality. On the other side, serial demanders and non-demanders may display varying levels of choice certainty, suggesting some sensitivity to arguments either for or against vaccination.

This framework using hypothetical vaccine choices could thus facilitates a more precise identification and characterization of individuals who, while initially hesitant towards vaccination, may be sensitive to targeted vaccine communication. To delve deeper in this reflection, we suggest to distinguish, among vaccine-reluctant individuals (i.e., who refuse vaccination under any scenario), those who express a constant level of certainty in their refusal regardless of the scenario (strong vaccine position) from those who express varying levels of certainty depending on the scenario. For this, we included a vaccine certainty tool into a DCE that explored individuals' preferences around the concept of the benefit-risk balance of vaccination (the third article of this thesis present the DCE results). To our knowledge, no prior study has aimed to discern among vaccine-reluctant individuals the proportion who express varying certainty about their refusal.

In the present study, we aim i) to investigate the determinants of individuals who consistently refuse vaccination across all scenarios, categorizing them as vaccine non-serial demanders, ii) to explore the reasons that could potentially motivate serial non-demanders to accept hypothetical vaccination, iii) to identify the proportion of individuals who are not entirely certain to refuse vaccination.

Methodology

In this study, we used the same data that was collected for the third article of this thesis, titled “Communicating on the Vaccine Benefit-Risk Ratios: A Discrete-Choice Experiment Among Healthcare Professionals and the General Population in France”. Consequently, the study design, participant enrollment, questionnaire, and DCE tool are detailed in the methodology section of Aim 3 of this thesis.

We also maintained the HCSWs sub-groups detailed in article 3: representative sample, non-HCSWs, non-university-degree HCSWs and university-degree HCSWs.

*Statistical Analysis*Vaccine-decision certainty scale

Chyderiotis et al. (2022) developed a vaccine certainty scale by reverse coding certainty of refusal (– 10 to 0) and positive values for certainty of acceptance (0 to +10), meaning that a -10 vaccine certainty represent a strong and certain vaccine refusal and +10 represent a strong and certain vaccine acceptance. When the participant has a vaccine certainty of 0, it means a high level of hesitancy or uncertainty depending on its vaccine decision (accepted or opted-out). Participants whose certainty did not vary across DCE scenarios were not influenced by benefit-risks vaccination attributes, suggesting that their vaccine decisions were based on a strong, pre-existing stance either in favour of or against vaccination in general.

We created a variable called “vaccine behaviour profile”, which combines the information on the hypothetical choices with their choice certainty and resumes the participant’s choice behaviour across all scenarios. Thus, 5 vaccine behaviour profiles were defined:

- Serial vaccine non-demanders with no certainty variation: individuals who refused all hypothetical vaccination scenarios, with no variation in their certainty level for each hypothetical vaccine decision.
- Serial vaccine non-demanders with certainty variations: individuals who refused all hypothetical vaccination scenarios, with variations in their certainty level for each hypothetical vaccine decision depending on DCE attributes.
- Non-uniform vaccine demanders: individuals whose hypothetical vaccine acceptance varied across DCE scenarios.
- Serial vaccine demanders with certainty variations: individuals who accepted all hypothetical vaccination scenarios, with variations in their certainty level for each hypothetical vaccine decision depending on DCE attributes.
- Serial vaccine demanders with no certainty variation: individuals who accepted all hypothetical vaccination scenarios, with no variation in their certainty level for each hypothetical vaccine decision.

This variable enabled to address the objectives of Aim 4 of this PhD thesis.

Objective 4a: to identify socio-demographic characteristics of serial demanding behaviors and reasons for refusing vaccination

We used robust-variance Poisson regression models to estimate adjusted prevalence ratios (aPR) for the determinants of serial vaccine non-demanders with no certainty and with certainty

variation separately(75). Independent variables that had a p-value<0.20 in bivariable models or essential potential confounders (i.e., age) were introduced into a full multivariable model.

Then, to explore the reasons that might motivate serial vaccine non-demanders (with and without certainty variation) to accept hypothetical vaccination, they answered a question “What might motivate you to accept vaccination through scenarios?”.

Objective 4b. To identify proportion of those that while initially hesitant towards vaccination, may be compliant to persuasion through targeted vaccine communication on vaccination benefits-risks.

We utilize descriptive analysis to determine the proportion within each vaccine behavior profile. The vaccine behaviour profile variable allows us to understand vaccine decision-making with a deeper insight into vaccination behaviour that mere accept vs. refuse vaccination. The vaccine behavior profile differentiates between individuals with strong vaccine positions (i.e., those who refuse all vaccine scenarios and are not influenced by benefit-risks vaccination attributes) and those who, despite initially refusing all vaccine scenarios, show sensitivity to vaccination attributes on vaccination benefits and risks and may be persuaded by targeted strategies.

We conducted analysis to check the quality of our data which are detailed in Supplementary File 1.

Results

The data set used in this study is the same as the one described in the third article of this thesis. Briefly, after combination of the representative sample of the French adult population and the convenience sample of HCSWs (yielding a total of 1869 participants), the non-HCSW, non-university-degree HCSW and university-degree HCSW subgroups included 1384, 146 and 399 participants respectively (**Table 10**). University-degree HCSW differed from the other two subgroups by being predominantly female (72.3% vs. 49.0% in non-HCSW subgroup), younger (37.8% \geq 50 years vs. 49.3%), more frequently favorable towards vaccines in general (93.5% vs. 76.4%) and more frequently with a positive perception of COVID-19 vaccination’s BRR (63.4% vs. 47.4%) (**Table 10**). For a detailed description of the two samples, please refer to the third article of this thesis.

Serial vaccine demanders with and with no certainty variation were more likely females (60.0%), aged \geq 50 years (55.0%), with higher than secondary school diploma (50.0%) and with a high level of confidence in authorities towards the COVID-19 crisis management (65.0%). Serial vaccine non-demanders with and with no certainty variation were more likely males

(60.0%), aged between 35-49 years (30.0%) and with secondary school diploma (30.0%) and with low level of confidence in authorities (60.0%) (**Table 14**).

Non-uniform vaccine demanders with certainty variation accounted for more than half of each sub-group, 52.4%, 51.6%, 59.6% and 51.9% among the representative sample, non-HCSWs, non-university-degree HCSWs and university-degree HCSWs, respectively. Serial vaccine non-demanders who show sensitivity to benefits-risks vaccination attribute accounted for 113 (7.5%) participants in the representative sample and 7.9%, 2.7% and 1.2% among non-HCSWs, non-university-degree HCSWs and university-degree HCSWs (**Figure 11**).

If the vaccine had no side effects at all 57.1% non-university-level HCSWs, 53.8% university-level HCSWs and 37.4% of non-HCSWs serial vaccine non-demanders would accept vaccination. Also, 46.1% of university-level HCSWs serial vaccine non-demanders refuse vaccination because previous bad experiences and 23.1% refuse vaccination because it goes against their principles (**Figure 12**).

Table 13. Description of study participants by vaccine behaviour profile, in the representative population sample of the French adult population (N=1505). Berberis study, France, 2023.

	Total N=1.505	Serial non demanders with no varied N=98	Serial non- demanders with varied certainty N=113	Non-uniform respondents N=833	Serial demanders with varied certainty N=333	Serial demanders with no varied certainty N=128	<i>p-value</i>
Socio-demographic characteristics							
Gender							<0.001
Male	775 (51.5%)	59 (60.2%)	74 (65.5%)	452 (54.3%)	139 (41.7%)	51 (39.8%)	
Female	730 (48.5%)	39 (39.8%)	39 (34.5%)	381 (45.7%)	194 (58.3%)	77 (60.2%)	
Age (in years)							<0.001
18-34	380 (25.2%)	28 (28.6%)	24 (21.2%)	233 (28.0%)	80 (24.0%)	15 (11.7%)	
35-49	410 (27.2%)	22 (22.4%)	38 (33.6%)	245 (29.4%)	78 (23.4%)	27 (21.1%)	
>=50	715 (47.5%)	48 (49.0%)	51 (45.1%)	355 (42.6%)	175 (52.6%)	86 (67.2%)	
Region of residence/work							0.27
North East	330 (21.9%)	23 (23.5%)	19 (16.8%)	172 (20.6%)	87 (26.1%)	29 (22.7%)	
North West	343 (22.8%)	19 (19.4%)	29 (25.7%)	197 (23.6%)	66 (19.8%)	32 (25.0%)	
South East	377 (25.0%)	26 (26.5%)	32 (28.3%)	213 (25.6%)	71 (21.3%)	35 (27.3%)	
South West	173 (11.5%)	12 (12.2%)	6 (5.3%)	97 (11.6%)	47 (14.1%)	11 (8.6%)	
Paris Region	282 (18.7%)	18 (18.4%)	27 (23.9%)	154 (18.5%)	62 (18.6%)	21 (16.4%)	
Educational level							0.015
Lower than secondary school diploma	355 (23.6%)	29 (29.6%)	27 (23.9%)	176 (21.1%)	85 (25.5%)	38 (29.7%)	
Equal to secondary school diploma	377 (25.0%)	30 (30.6%)	38 (33.6%)	207 (24.8%)	71 (21.3%)	31 (24.2%)	
Higher than secondary school diploma	773 (51.4%)	39 (39.8%)	48 (42.5%)	450 (54.0%)	177 (53.2%)	59 (46.1%)	
Minor or dependent child(ren)							0.24
No	1.035 (68.8%)	74 (75.5%)	82 (72.6%)	564 (67.7%)	221 (66.4%)	94 (73.4%)	
Yes	470 (31.2%)	24 (24.5%)	31 (27.4%)	269 (32.3%)	112 (33.6%)	34 (26.6%)	
Work in contact with the public							0.26
No	912 (60.6%)	63 (64.3%)	74 (65.5%)	484 (58.1%)	212 (63.7%)	79 (61.7%)	
Yes	593 (39.4%)	35 (35.7%)	39 (34.5%)	349 (41.9%)	121 (36.3%)	49 (38.3%)	
Previous hospitalisation (>10 days)							<0.001
No	1,235 (82.1%)	91 (92.9%)	101 (89.4%)	688 (82.6%)	260 (78.1%)	95 (74.2%)	
Yes	270 (17.9%)	7 (7.1%)	12 (10.6%)	145 (17.4%)	73 (21.9%)	33 (25.8%)	

General opinion about vaccines							<0.001
Very Favorable	453 (30.1%)	3 (3.1%)	6 (5.3%)	210 (25.2%)	166 (49.8%)	68 (53.1%)	
Favorable	710 (47.2%)	18 (18.4%)	39 (34.5%)	454 (54.5%)	152 (45.6%)	47 (36.7%)	
Undecided	208 (13.8%)	36 (36.7%)	35 (31.0%)	114 (13.7%)	12 (3.6%)	11 (8.6%)	
Skeptical	95 (6.3%)	16 (16.3%)	25 (22.1%)	49 (5.9%)	3 (0.9%)	2 (1.6%)	
Very Skeptical	39 (2.6%)	25 (25.5%)	8 (7.1%)	6 (0.7%)	0 (0.0%)	0 (0.0%)	
COVID-19 Vaccine Status							<0.001
Unvaccinated	196 (14.2%)	56 (59.6%)	41 (37.6%)	85 (11.2%)	9 (2.9%)	5 (4.3%)	
Vaccinated (more than 6 months ago)	978 (70.7%)	32 (34.0%)	61 (56.0%)	566 (74.9%)	235 (76.3%)	84 (71.8%)	
Vaccinated (less than 6 months ago)	210 (15.2%)	6 (6.4%)	7 (6.4%)	105 (13.9%)	64 (20.8%)	28 (23.9%)	
Level of confidence in authorities in the management of the COVID-19 crisis							<0.001
Low	328 (21.8%)	70 (71.4%)	53 (46.9%)	175 (21.0%)	22 (6.6%)	8 (6.2%)	
Moderate	496 (33.0%)	23 (23.5%)	44 (38.9%)	311 (37.3%)	82 (24.6%)	36 (28.1%)	
High	681 (45.2%)	5 (5.1%)	16 (14.2%)	347 (41.7%)	229 (68.8%)	84 (65.6%)	
Mean certainty in vaccine decision (sd)	7.18 (0.04)	7.9 (0.28)	6.5 (0.21)	6.8 (0.05)	7.7 (0.07)	8.2 (0.17)	
7C psychological antecedents							
Calculation							
<i>'I think that vaccination against COVID-19 will have more benefits than risks for me'</i>							<0.001
Agree	408 (27.1%)	71 (72.4%)	59 (52.2%)	242 (29.1%)	29 (8.7%)	7 (5.5%)	
Undecided	382 (25.4%)	19 (19.4%)	38 (33.6%)	236 (28.3%)	61 (18.3%)	28 (21.9%)	
Disagree	715 (47.5%)	8 (8.2%)	16 (14.2%)	355 (42.6%)	243 (73.0%)	93 (72.7%)	
Convenience							
<i>'In practice, it will be difficult for me to get vaccinated'</i>							<0.001
Agree	950 (63.1%)	61 (62.2%)	60 (53.1%)	534 (64.1%)	220 (66.1%)	75 (58.6%)	
Undecided	309 (20.5%)	27 (27.6%)	39 (34.5%)	165 (19.8%)	49 (14.7%)	29 (22.7%)	
Disagree	246 (16.3%)	10 (10.2%)	14 (12.4%)	134 (16.1%)	64 (19.2%)	24 (18.8%)	
Collective responsibility							<0.001

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<i>'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>							
Agree	294 (19.5%)	65 (66.3%)	51 (45.1%)	150 (18.0%)	21 (6.3%)	7 (5.5%)	
Undecided	317 (21.1%)	21 (21.4%)	39 (34.5%)	201 (24.1%)	34 (10.2%)	22 (17.2%)	
Disagree	894 (59.4%)	12 (12.2%)	23 (20.4%)	482 (57.9%)	278 (83.5%)	99 (77.3%)	
Social conformism							
<i>'Among your family and friends. How would you describe the majority opinion towards COVID-19 vaccination.'</i>							<0.001
Favourable	582 (38.7%)	10 (10.2%)	11 (9.7%)	296 (35.5%)	196 (58.9%)	69 (53.9%)	
Both skeptical and favourable	465 (30.9%)	35 (35.7%)	44 (38.9%)	262 (31.5%)	88 (26.4%)	36 (28.1%)	
Skeptical	458 (30.4%)	53 (54.1%)	58 (51.3%)	275 (33.0%)	49 (14.7%)	23 (18.0%)	
Complacency							
<i>'I am afraid of getting a severe form of COVID-19.'</i>							<0.001
Agree	624 (41.5%)	59 (60.2%)	56 (49.6%)	357 (42.9%)	114 (34.2%)	38 (29.7%)	
Undecided	345 (22.9%)	19 (19.4%)	35 (31.0%)	187 (22.4%)	71 (21.3%)	33 (25.8%)	
Disagree	536 (35.6%)	20 (20.4%)	22 (19.5%)	289 (34.7%)	148 (44.4%)	57 (44.5%)	
Confidence in COVID-19 vaccine							
<i>'I am afraid of having a severe side effect of vaccination.'</i>							<0.001
Agree	544 (36.1%)	21 (21.4%)	19 (16.8%)	291 (34.9%)	154 (46.2%)	59 (46.1%)	
Undecided	349 (23.2%)	19 (19.4%)	36 (31.9%)	186 (22.3%)	72 (21.6%)	36 (28.1%)	
Disagree	612 (40.7%)	58 (59.2%)	58 (51.3%)	356 (42.7%)	107 (32.1%)	33 (25.8%)	
Confidence in systems							
<i>'If my employer encourages me to get vaccinated. this...</i>							<0.001
Motivates me	219 (14.6%)	48 (49.0%)	43 (38.1%)	107 (12.8%)	18 (5.4%)	3 (2.3%)	
Has no effect	588 (39.1%)	3 (3.1%)	6 (5.3%)	287 (34.5%)	209 (62.8%)	83 (64.8%)	
Dissuade-me	698 (46.4%)	47 (48.0%)	64 (56.6%)	439 (52.7%)	106 (31.8%)	42 (32.8%)	

Figure 11. Vaccine behaviors (%) according to participants healthcare-sector workers (HCSWs) status. France, 2023. Berberis survey.

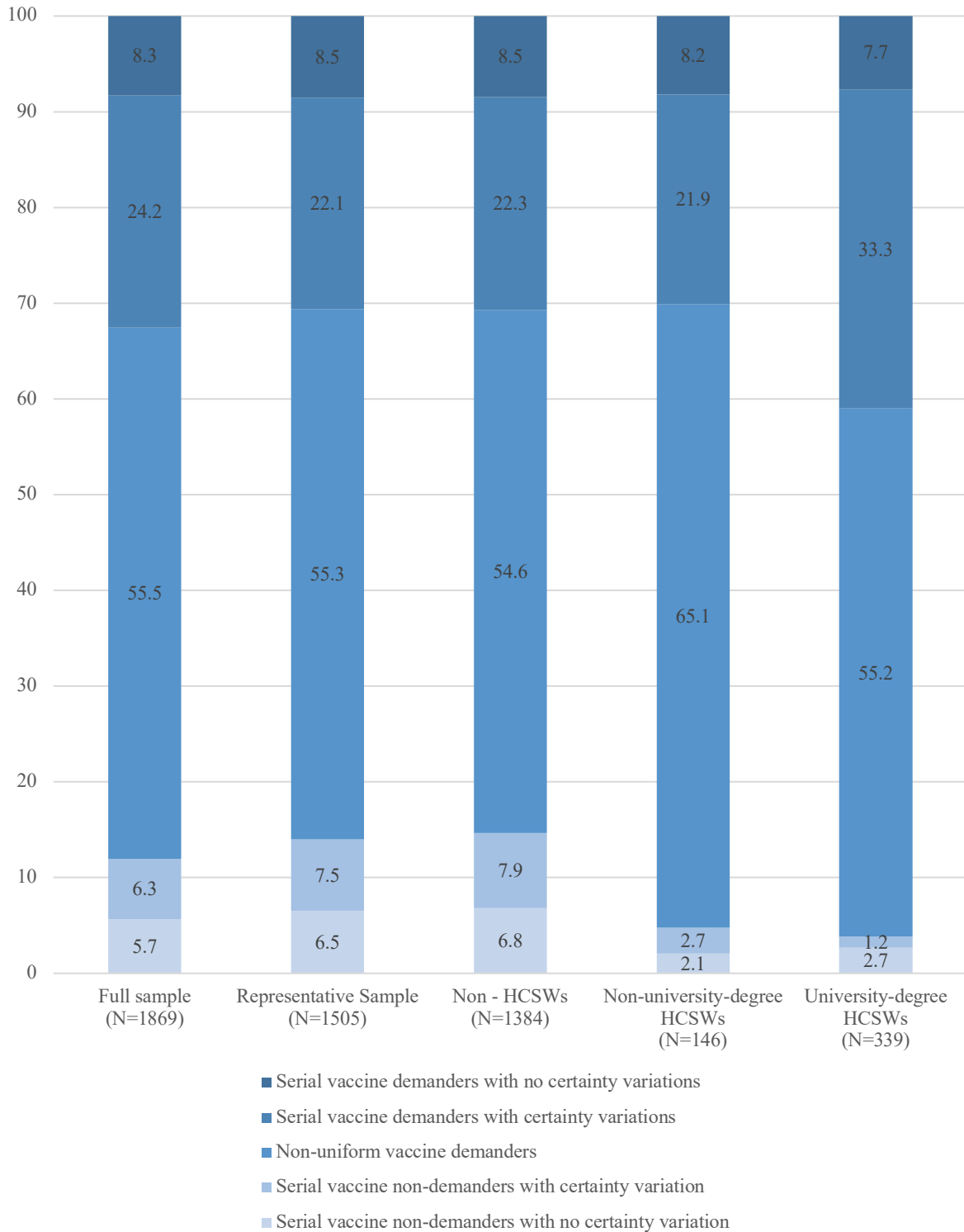
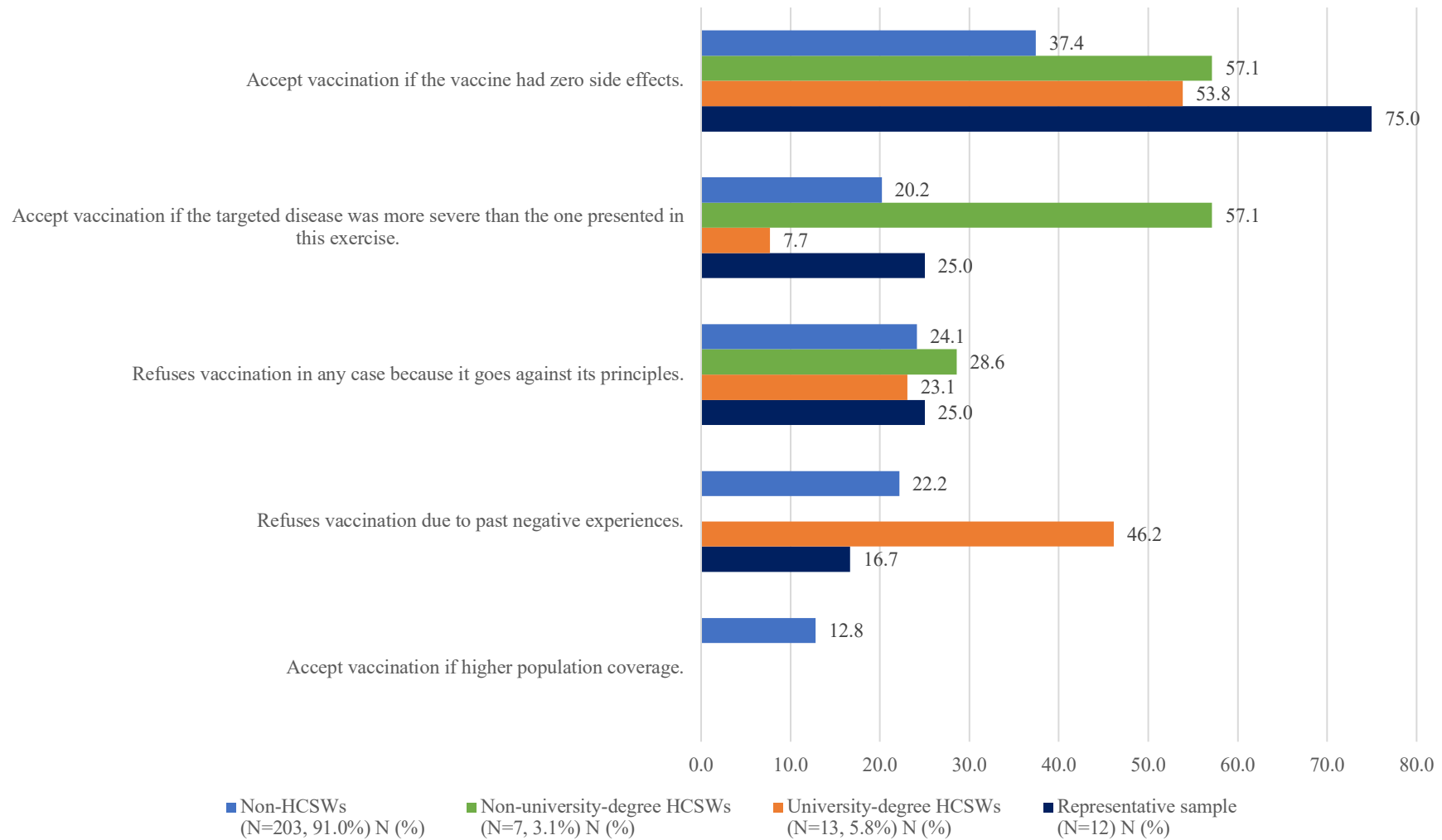


Figure 12. Reasons for not accepting hypothetical vaccination among serial vaccine non-demanders (N=223), Adults in France, 2023. (%; Multiple Choices).



Determinants of serial demanding behaviors (Table 14).

Among the representative sample of the French adult population, non-uniform respondents, serial vaccine non-demanders and serial vaccine demanders represented 55.4%, 14.0% and 30.6% of the sample. In multivariate analyses adjusting for the 7C-model, serial vaccine non-demanders compared to non-uniform respondents were more likely to be aged ≥ 50 years (vs. 18-34 years; aPR=1.55, p -value=0.003), employed (vs. executive liberal profession; aPR=1.60, p -value=0.025), not working in contact with the public (vs. yes; aPR=1.49, p -value=0.003), having not been hospitalised for more than 10 days (vs. yes; aPR=1.57, p -value=0.032) and with a low level of confidence towards authorities in the management of the COVID-19 crisis (vs. high level; aPR=2.39, p -value=0.001). The difference in the 7Cs included Collective responsibility (not considering vaccination as a public action vs. considering vaccination as a public action; aPR=2.38, p -value<0.001), Confidence in COVID-19 vaccination (undecided about confidence in COVID-19 vaccination vs. not being confident in COVID-19 vaccination; aPR=1.72, p -value=0.003), Confidence in systems - reactance to employer vaccine encouragement (dissuades-me vs. motivates-me; aPR=3.98, p -value<0.001).

Serial vaccine demanders differentiate non-uniform respondents on being less likely to; be male (aPR=0.82, p -value=0.007), having been hospitalised for more than 10 days (yes vs. no; aPR=0.84, p -value=0.029) and with a higher level of confidence towards authorities in the management of the COVID-19 crisis (low vs. high level; aPR=0.60, p -value=0.007). The difference in the 7Cs included Calculation (perceiving vaccination as having more risks than benefits vs. more benefits than risks; aPR=48, p -value<0.001) and Confidence in systems - reactance to employer vaccine encouragement (has no effect vs. motivates-me; aPR=0.76, p -value=0.003).

Table 14. Determinants of being a serial non-demander or a serial demander compared to non-uniform respondents among a representative sample of adults in France 2023 (N=1505). Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

		Serial non-demanders (N= 211) vs. Non-uniform respondents (N= 833)				Serial demanders (N= 461) vs. Non-uniform respondents (N= 833)		
		N (%)	Serial non-demanders N (%)	aPR	<i>p</i> -value	Serial demanders N (%)	aPR with level of confidence	<i>p</i> -value
Socio-demographic characteristics								
Gender								
	Female	730 (48.5)	78 (37.0)	1		271 (58.8)	1	
	Male	775 (51.5)	133 (63.0)	1.06	0.603	190 (41.2)	0.82	0.007
Age (years)								
	18 - 34	380 (25.3)	52 (24.7)	1		95 (20.6)	1	
	35-49	410 (27.2)	60 (28.4)	1.14	0.415	105 (22.8)	0.97	0.818
	>=50	715 (47.5)	99 (46.9)	1.55	0.003	261 (56.6)	1.16	0.130
Region of residence								
	North-Est	330 (21.9)	42 (19.9)	1		116 (25.2)	1	
	North-West	343 (22.8)	48 (22.8)	1.12	0.503	98 (21.3)	0.88	0.208
	South-Est	377 (25.1)	58 (27.5)	1.25	0.179	106 (23.0)	0.84	0.095
	South-West	173 (11.5)	18 (8.5)	0.95	0.827	58 (12.6)	0.96	0.713
	Paris region	282 (18.7)	45 (21.3)	1.32	0.094	83 (18.0)	0.89	0.276
Profession								
	Executive or Liberal Profession	197 (13.1)	19 (9.0)	1				
	Farmer	6 (0.4)	0 (0.0)	-				
	Craftsman, Entrepreneur	49 (3.3)	6 (2.8)	0.79	0.563			
	Employee	306 (20.3)	69 (32.7)	1.60	0.025			
	Student	94 (6.3)	5 (2.4)	0.51	0.144			
	Worker	111 (7.4)	21 (10.0)	1.33	0.264			
	Intermediary Occupations	215 (14.3)	20 (9.5)	0.89	0.680			
	Retired	386 (25.7)	43 (20.4)	0.71	0.174			

Without Professional Activity	141 (9.4)	28 (13.3)	1.19	0.476				
Work in direct contact with the public								
No	912 (60.6)	137 (64.9)	1.49	0.003	291 (63.1)			
Yes	593 (39.4)	74 (35.1)	1		170 (36.9)			
Previous hospitalisation (>10 days)								
No	1235 (82.1)	192 (91.0)	1.57	0.032	355 (77.0)	1		
Yes	270 (17.9)	19 (9.0)	1		106 (23.0)	0.84	0.029	
Minor children								
No	1035 (68.7)	156 (73.9)	1.32	0.046	315 (68.3)			
Yes	470 (31.2)	55 (26.1)	1		146 (31.7)			
Level of confidence in authorities in the management of the COVID-19 crisis								
Low	328 (21.8)	123 (58.3)	2.39	0.001	30 (6.5)	0.60	0.007	
Moderate	496 (33.0)	67 (31.8)	1.46	0.122	118 (25.6)	0.85	0.088	
High	681 (45.3)	21 (10.0)	1		313 (67.9)	1		
7C-Psychological Antecedents								
Calculation								
<i>'I think that vaccination against COVID-19 will have more benefits than risks for me'</i>								
Agree	715 (47.5)	24 (11.4)	1		336 (72.9)	1		
Undecided	382 (25.4)	57 (27.0)	1.17	0.514	89 (19.3)	0.76	0.014	
Disagree	408 (27.1)	130 (61.6)	1.31	0.223	36 (7.8)	0.48	<0.001	
Convenience								
<i>'In practice, it will be difficult for me to get vaccinated'</i>								
Agree	246 (16.4)	24 (11.4)	1.20	0.331	88 (19.1)	1.14	0.192	
Undecided	309 (20.5)	66 (31.3)	1.13	0.331	78 (16.9)	1.11	0.293	
Disagree	950 (63.1)	121 (57.4)	1		295 (64.0)	1		
Collective responsibility								
<i>'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>								

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	Agree	894 (59.4)	35 (16.6)	1		377 (81.8)	1	
	Undecided	317 (21.1)	60 (28.4)	1.30	0.244	56 (12.2)	0.90	0.442
	Disagree	294 (19.5)	116 (55.0)	2.38	<0.001	28 (6.1)	1.00	0.995
Social conformism								
<i>'Among your family and friends. How would you describe the majority opinion towards COVID-19 vaccination.'</i>								
	Favourable	458 (30.4)	111 (52.6)	1.17	0.490	72 (15.6)	0.78	0.715
	Both skeptical and favourable	465 (30.9)	79 (37.4)	1.24	0.366	124 (26.9)	0.97	0.045
	Skeptical	582 (38.7)	21 (10.0)	1		265 (57.5)	1	
Complacency								
<i>'I am afraid of getting a severe form of COVID-19.'</i>								
	Agree	536 (35.6)	42 (19.9)	1.10	0.573	205 (44.5)	1.06	0.574
	Undecided	345 (22.9)	54 (25.6)	1.22	0.169	104 (22.6)	1.11	0.318
	Disagree	624 (41.5)	115 (54.5)	1		152 (33.0)	1	
Confidence in COVID-19 vaccine								
<i>'I am afraid of having a severe side effect of vaccination.'</i>								
	Agree	612 (40.7)	116 (55.0)	0.99	0.964	140 (30.4)	0.99	0.939
	Undecided	349 (23.2)	55 (26.1)	1.72	0.003	108 (23.4)	0.99	0.942
	Disagree	544 (36.2)	40 (19.0)	1		213 (46.2)	1	
Confidence in systems								
<i>'If my employer encourages me to get vaccinated. this...</i>								
	Motivates me	588 (39.1)	9 (4.3)	1		292 (63.3)	1	
	Has no effect	698 (46.4)	111 (52.6)	2.62	0.008	148 (32.1)	0.76	0.003
	Dissuade-me	219 (14.6)	91 (43.1)	3.98	<0.001	21 (4.6)	0.75	0.176

Relative risk Ratio of serial demanders with certainty variation compared to uniform respondents (Table 15).

After adjusting for the 7C-model, socio-demographic characteristics that differentiate serial vaccine non-demanders with certainty variation and non-uniform respondents were to be aged ≥ 50 years (vs. 18-34 years; aPR=2.06, p -value=0.003), employed (vs. executive liberal profession; aPR=1.72, p -value=0.035), work in contact with the public (yes vs. no; aPR=1.67, p -value=0.010). The difference in the 7Cs included Collective responsibility (not considering vaccination as a public action vs. considering vaccination as a public action; aPR=2.45, p -value=0.002), Confidence in COVID-19 vaccination (undecided about confidence in COVID-19 vaccination vs. not being confident in COVID-19 vaccination; aPR=1.72, p -value=0.037) and Confidence in systems, reactance to employer vaccine encouragement (dissuades-me vs. motivates-me; aPR=4.76, p -value<0.001).

Table 15. Determinants of being vaccine serial non-demanders with no constant certainty level compared to non-uniform respondents among a representative sample of adults in France 2023. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

		Serial non-demanders with no constant certainty (N=113) vs. Non-uniform respondents (N=833)							
		N (%)	Serial non-demanders with no constant certainty N (%)	PR	<i>p</i> -value	aPR	<i>p</i> -value	aPR with 7C-antecedents	<i>p</i> -value
Gender									
	Female	420 (44.4)	74 (65.5)	1					
	Male	526 (55.6)	39 (34.5)	1.51	0.026				
Age (years)									
	18 - 34	257 (27.2)	24 (21.2)	1		1		1	
	35-49	283 (29.9)	38 (33.6)	1.44	0.140	1.21	0.429	1.33	0.227
	>=50	406 (42.9)	51 (45.1)	1.35	0.206	1.69	0.031	2.06	0.003
Region of residence									
	North-Est	191 (20.2)	19 (16.8)	1					
	North-West	226 (23.9)	29 (25.7)	1.29	0.361				
	South-Est	245 (25.9)	32 (28.3)	1.31	0.319				
	South-West	103 (10.9)	6 (5.3)	0.59	0.237				
	Paris region	181 (19.1)	27 (23.9)	1.50	0.149				
Profession									
	Executive or Liberal Profession	128 (13.5)	12 (10.6)	1		1		1	
	Farmer	5 (0.5)	0 (0.0)	-		-		-	
	Craftsman, Entrepreneur	32 (3.4)	3 (2.7)	1.0	1.000	0.96	0.939	0.76	0.645
	Employee	198 (20.9)	44 (38.9)	2.37	0.005	2.21	0.006	1.76	0.035
	Student	66 (7.0)	3 (2.7)	0.49	0.249	0.59	0.412	0.55	0.350
	Worker	77 (8.1)	12 (10.6)	1.66	0.184	1.38	0.376	1.32	0.413
	Intermediary Occupations	130 (13.7)	7 (6.2)	0.57	0.227	0.52	0.157	0.51	0.133
	Retired	219 (23.2)	21 (18.6)	1.02	0.948	0.58	0.129	0.55	0.067

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Without Professional Activity	91 (9.6)	11 (9.7)	1.29	0.519	0.84	0.658	0.89	0.738
Work in direct contact with the public								
No	558 (59.0)	74 (65.5)	1.32	0.137	1.88	0.001	1.67	0.010
Yes	388 (41.0)	39 (34.5)	1		1		1	
Previous hospitalisation (>10 days)								
No	789 (83.4)	101 (89.4)	1.67	0.078				
Yes	157 (16.6)	12 (10.6)	1					
Chronic disease								
No			1.89	0.038				
Yes			1					
Minor children								
No	646 (68.3)	82 (72.6)	1.23	0.301				
Yes	300 (31.7)	31 (27.4)	1					
Level of confidence in authorities in the management of the COVID-19 crisis								
Low	228 (24.1)	53 (46.9)	5.27	<0.001	5.17	<0.001	1.69	0.101
Moderate	355 (37.5)	44 (38.9)	2.81	<0.001	2.61	0.001	1.23	0.491
High	363 (38.4)	16 (14.2)	1		1		1	
<i>7C-Psychological Antécédents</i>								
Calculation								
<i>'I think that vaccination against COVID-19 will have more benefits than risks for me'</i>								
Agree	301 (31.8)	59 (52.2)	1				1	
Undecided	371 (39.2)	16 (14.2)	3.22	<0.001			1.29	0.702
Disagree	274 (29.0)	38 (33.6)	4.55	<0.001			1.19	0.563
Convenience								
<i>'In practice, it will be difficult for me to get vaccinated'</i>								
Agree	148 (15.6)	14 (12.4)	1				1	
Undecided	204 (21.6)	39 (34.5)	2.02	0.016			0.98	0.933
Disagree	594 (62.8)	60 (53.1)	1.07	0.816			0.79	0.356
Collective responsibility								

<i>'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>								
	Agree	505 (53.4)	23 (20.4)	1			1	
	Undecided	240 (25.4)	39 (34.5)	3.57	<0.001		1.38	0.269
	Disagree	201 (21.3)	51 (45.1)	5.57	<0.001		2.45	0.002
Social conformism								
<i>'Among your family and friends. How would you describe the majority opinion towards COVID-19 vaccination.'</i>								
	Favourable	333 (35.2)	58 (51.3)	1			1	
	Both skeptical and favourable	306 (32.4)	44 (38.9)	0.83	0.297		1.09	0.639
	Skeptical	307 (32.5)	11 (9.7)	0.21	<0.001		0.79	0.430
Complacency								
<i>'I am afraid of getting a severe form of COVID-19.'</i>								
	Agree	311 (32.9)	22 (19.5)	1			1	
	Undecided	222 (23.5)	35 (31.0)	2.23	0.002		1.41	0.182
	Disagree	413 (43.7)	56 (49.6)	1.92	0.007		1.08	0.763
Confidence in COVID-19 vaccine								
<i>'I am afraid of having a severe side effect of vaccination.'</i>								
	Agree	414 (43.8)	58 (51.3)	2.29	0.001		1.03	0.907
	Undecided	222 (23.5)	36 (31.9)	2.65	<0.001		1.72	0.037
	Disagree	310 (32.8)	19 (16.8)	1			1	
Confidence in systems								
<i>'If my employer encourages me to get vaccinated. this...</i>								
	Motivates me	293 (31.0)	6 (5.3)	1			1	
	Has no effect	503 (53.2)	64 (56.6)	6.21	<0.001		2.71	0.019
	Dissuade-me	150 (15.9)	43 (38.1)	14.0	<0.001		4.76	<0.001

Relative risk Ratio of serial vaccine non-demander with certainty variation vs. with no certainty variation (Table 16).

Among the representative sample of the French adult population, serial vaccine non-demanders with no certainty variation accounted for 6.5% and those with certainty variation for 7.5%. No socio-demographic determinants differentiated these two groups. The only significant difference was in confidence in COVID-19 vaccination. Serial vaccine non-demanders sensitive to benefit-risk vaccination attributes (with certainty variation) were 1.36 times more likely to have high confidence in vaccination compared to those with no certainty variation.

Table 16. Determinants of vaccine serial non-demanders with no certainty variation compared to serial non-demanders with certainty variation among a representative sample of adults in France 2023. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

		Serial non-demanders with varied certainty (N=113) vs. Serial non-demanders with no varied certainty (N=106)							
		N (%)	Serial non-demanders with varied certainty N (%)	PR	<i>p</i> -value	aPR	<i>p</i> -value	aPR including 7C-antecedents	<i>p</i> -value
Gender									
	Female	113 (63.0)	74 (65.5)	1					
	Male	78 (37.0)	39 (34.5)	1.11	0.437				
Age (years)									
	18 - 34	52 (24.6)	24 (21.2)	1		1		1	
	35-49	60 (28.4)	38 (33.6)	1.37	0.078	1.37	0.069	1.40	0.066
	>=50	99 (46.9)	51 (45.1)	1.12	0.540	1.17	0.391	1.20	0.361
Region of residence									
	North-Est	42 (19.9)	19 (16.8)	1					
	North-West	48 (22.8)	29 (25.7)	1.36	0.161				
	South-Est	58 (27.5)	32 (28.3)	1.22	0.339				
	South-West	18 (8.5)	6 (5.3)	0.74	0.415				
	Paris region	45 (21.3)	27 (23.9)	1.33	0.177				
Profession									
	Executive or Liberal Profession	19 (9.0)	12 (10.6)	1					
	Farmer	0 (0.0)	0 (0.0)	-					
	Craftsman, Entrepreneur	6 (2.8)	3 (2.7)	0.79	0.600				
	Employee	69 (32.7)	44 (38.9)	1.01	0.961				
	Student	5 (2.4)	3 (2.7)	0.95	0.899				
	Worker	21 (10.0)	12 (10.6)	0.90	0.698				
	Intermediary Occupations	20 (9.5)	7 (6.2)	0.55	0.094				
	Retired	43 (20.4)	21 (18.6)	0.77	0.274				

Without Professional Activity	28 (13.3)	11 (9.7)	0.62	0.106				
Work in direct contact with the public								
No	137 (64.9)	74 (65.5)	1.02	0.856				
Yes	74 (35.1)	39 (34.5)	1					
Previous hospitalisation (>10 days)								
No	192 (91.0)	101 (89.4)	0.83	0.332				
Yes	19 (9.0)	12 (10.6)	1					
Minor children								
No	156 (73.9)	82 (72.6)	0.93	0.621				
Yes	55 (26.1)	31 (27.4)	1					
Level of confidence in authorities in the management of the COVID-19 crisis								
Low	123 (58.3)	53 (46.9)	1		1		1	
Moderate	67 (31.8)	44 (38.9)	1.52	0.002	1.53	0.002	1.79	0.145
High	21 (10.0)	16 (14.2)	1.77	<0.001	1.76	<0.001	1.36	0.011
<i>7C-Psychological Antécédents</i>								
Calculation								
<i>'I think that vaccination against COVID-19 will have more benefits than risks for me'</i>								
Agree	24 (25.4)	16 (14.2)	1.47	0.027			1.31	0.357
Undecided	57 (47.5)	38 (33.6)	1.47	0.004			1.24	0.352
Disagree	130 (27.1)	59 (52.2)	1				1	
Convenience								
<i>'In practice, it will be difficult for me to get vaccinated'</i>								
Agree	24 (11.4)	14 (12.4)	1.18	0.407			0.94	0.703
Undecided	66 (31.3)	39 (34.5)	1.19	0.203			1.01	0.973
Disagree	121 (57.4)	60 (53.1)	1				1	
Collective responsibility								
<i>'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>								
Agree	35 (16.6)	23 (20.4)	1.49	0.013			1.06	0.834
Undecided	60 (28.4)	39 (34.5)	1.48	0.006			1.11	0.614

ARTICLE PRESENTATION – ARTICLE 4

	Disagree	116 (55.0)	51 (45.1)	1			1	
Social conformism								
<i>'Among your family and friends. How would you describe the majority opinion towards COVID-19 vaccination.'</i>								
	Favourable	111 (52.6)	58 (51.3)	1.00	0.991		1.40	0.266
	Both skeptical and favourable	79 (37.4)	44 (38.9)	1.06	0.791		1.24	0.442
	Skeptical	21 (10.0)	11 (9.7)	1			1	
Complacency								
<i>'I am afraid of getting a severe form of COVID-19.'</i>								
	Agree	42 (19.9)	22 (19.5)	1.08	0.678		0.77	0.210
	Undecided	54 (25.6)	35 (31.0)	1.33	0.040		1.04	0.856
	Disagree	115 (54.5)	56 (49.6)	1			1	
Confidence in COVID-19 vaccine								
<i>'I am afraid of having a severe side effect of vaccination.'</i>								
	Agree	116 (55.0)	58 (51.3)	1.05	0.788		1.20	0.385
	Undecided	55 (26.1)	36 (31.9)	1.38	0.097		1.07	0.668
	Disagree	40 (19.0)	19 (16.8)	1			1	
Confidence in systems								
<i>'If my employer encourages me to get vaccinated. this...</i>								
	Motivates me	9 (4.3)	6 (5.3)	1.41	0.187		1.13	0.733
	Has no effect	111 (52.6)	64 (56.6)	1.22	0.149		0.98	0.923
	Dissuade-me	91 (43.1)	43 (38.1)	1			1	

Discussion

In this secondary analysis of a single-profile discrete choice experiment with an opt-out option, we found that incorporating a certainty scale provides valuable insights into respondents consistently choosing the same option (in this case, acceptance or refusal of theoretical vaccination). Adding the choice certainty scale to the single-profile DCE allowed to identify different vaccination behaviour profiles based on sensitivities to vaccination attributes.

Our findings reveal that about one-sixth of the population maintains a strong vaccine position (for or against vaccination), with their decision-making unaffected by the vaccination context. One-third display invariable vaccine decisions (consistently refusing or accepting all vaccination scenarios), but with fluctuating certainty depending on the vaccination benefit-risk context. More than half of the population varies their vaccine decision based on the context. Among HCSWs, 10% showed consistent vaccine decisions with constant certainty across different contexts. The majority of HCSWs consider vaccination characteristics before making a decision.

Our results suggest that the commonly reported 30% vaccine refusal during vaccination campaigns actually comprises different subgroups: 6.5% refuse vaccination regardless of context, 7.5% assess the benefits and risks of vaccination but ultimately tend to refuse vaccination, and the remainder vary their decision based on the context, choosing to accept or refuse vaccination in different scenarios. These results suggest that effective communication about the benefits of vaccination could engage a significant number of the population. In fact, compared to non-uniform respondents, serial vaccine demanders consider the benefit-risk of vaccination, while serial non-demanders focus solely on the perceived risks of vaccination.

Working in contact with the public or having been hospitalized significantly motivates individuals towards vaccination probably due to a heightened awareness of health risks and benefits. This aligns with previous studies showing that primary motivators for vaccination include the desire to protect those around them in both family and professional environments, as well as the aim to control the spread of disease within one's profession(132).

One of the strongest psychological antecedents differentiating serial vaccine non-demanders from non-uniform respondents was confidence in the system. Serial vaccine non-demanders were highly dissuaded by employer encouragement towards vaccination, aligning with previous literature indicating the counterproductive effects of incentive policies when not targeted to the appropriate population(19,20,76,77). Our results indicate that employer encouragement does not promote vaccination among vaccine-reluctant individuals.

Regarding serial vaccine behaviors, the strongest determinant was confidence in authorities managing the COVID-19 crisis. Individuals with low confidence in authorities were more likely to be serial vaccine non-demanders, while those with high confidence were more likely to be serial vaccine demanders compared to non-uniform respondents. Previous studies have emphasized the importance of confidence in authorities for vaccination acceptance, identifying it as one of the strongest determinants, even more than socio-demographic variables(103,133).

In the 7C-model, surprisingly, serial vaccine non-demanders did not differ from non-uniform respondents in terms of Calculation. This indicates that despite refusing vaccines, they did not perceive more risks from vaccination than those who vary their decisions across vaccination scenarios. In contrast, one of the strongest Cs for serial vaccine demanders was Calculation; they were more likely to perceive the benefits of vaccination compared to those who vary their vaccine decisions. This suggests that non-uniform respondents primarily base their vaccine decisions on weighing the benefits against the risks. Moreover, confidence in vaccines did not significantly differ between serial vaccine demanders and non-uniform respondents. However, serial vaccine non-demanders were significantly more afraid of vaccine side-effects (Confidence in vaccine) than non-uniform respondents. Additionally, neither group expressed fear of the consequences of developing the disease (Complacency). This reflects their tendency to prioritize the risks of action (vaccination) over the risks of inaction (disease), reported in the literature as “omission bias”. Indeed, the DCEs results (article under review) among vaccine serial non-demanders showed that the only attribute that decreases their certainty of refusal is a high risk of contracting the disease, suggesting that there might be a threshold of disease risk that could potentially engage them to consider vaccination.

In fact, in the representative sample, the most cited reasons to accept vaccination among serial vaccine non-demanders were the absence of side-effects and previous negative experiences with vaccination. Surprisingly, among HCSWs with serial vaccine non-demanding behaviour, the most cited reason to accept vaccination was also the absence of side-effects. The second most cited reason among university-level HCSWs was negative past experiences, likely influenced by their frequent interactions with hesitant patients and individuals affected by vaccine side-effects. This aligns with previous studies highlighting the emerging doubts among HCSWs regarding vaccine risks which come from interactions with hesitant patients and their experiences(16).

Finally, the only difference observed among serial vaccine non-demanders with and without certainty variation was their level of confidence in authorities; serial vaccine non-demanders

with varying certainty levels exhibited significantly higher confidence in authorities. The deliberation between the benefits and risks of vaccination did not differ between the two groups.

Limitations

Our study has several limitations. As in all stated preferences studies, interpretation of results must consider the hypothetical nature of decisions: the vaccine certainty scale is based on the certainty level of the decision and not the decision itself. The choice certainty could thus be less accurate than the decision in predicting real life for people with nonuniform decisions.

The scenarios did not focus on one specific, well characterized vaccine, but instead described a hypothetical vaccination against an emerging disease. This approach may have allowed for significant individual interpretation, leading to considerable heterogeneity in the individual participants' decision frames.

Internet panel participants are not completely representative of the French population due to selection on internet access and use. Despite the quota sampling, people in poverty, with low health literacy and possibly high-risk behaviour may be underrepresented. However, 85.8% of participants declared receiving at least one COVID-19 vaccine dose, aligning with estimations from the French Ministry of Health(81%)(126). The internet panel of adults is not representative in subgroup analyses, which should be considered during data interpretation.

HCSWs in the snowballing sample were self-selected on favourable vaccination attitudes. Given their involvement in the GERES, they likely prioritize health recommendations : 78.2% of physicians and 59.5% of nurses reported influenza vaccination for the current season, compared to 51% and 29% estimated for physicians and nurses working in hospitals in France 2022(127) during the preceding season. This suggest that BRR effects on vaccine decision may vary among HCSWs less vaccine-favourable.

Conclusion

A favourable perception of vaccine BRB was the key determinant of participant's serial demanding behaviour in this single profile DCE, meaning they consistently accepted all scenarios with little or no sensitivity to other attributes. By contrast, serial non-demanding behaviour was not associated to an unfavourable perception of the vaccine BRB.

The vaccine certainty scale enables to build different vaccination behaviour profiles to elucidate how individuals consider benefit-risk balance of vaccination in their vaccine decisions. Serial vaccine non-demanders' decisions are predominantly influenced by omission bias, driven by a strong fear of vaccine side-effects rather than the perceived risks associated with contracting

the disease. Also, employer encouragement does not promote vaccination among vaccine-reluctant individuals.

Our study highlights the need for further research into vaccine-reluctant individuals' confidence in authorities.

Discussion

The role of benefit-risk balance in vaccine decision-making

The four studies presented above delve into the complexities of deliberation between the benefits and risks of vaccination in vaccine decision-making. The perception of vaccine BRB among HCSWs, particularly those with a university-level education, tends to be rational and quantitative, evolving with increased knowledge about the vaccine and the context of its use. However, the general population and HCSWs without university-level education their vaccine decisions were primarily influenced by qualitative attributes such as disease risk, indirect protection, type of disease, or the importance of vaccination. Within the HCSWs population, perceived vaccination BRB is associated with vaccination intention in most contexts and situations. For unconditional vaccine acceptance (serial vaccine demanders), a favorable perception of vaccination BRB is crucial. While we did not investigate the perceived vaccination BRB over time among the general population, evidence suggests that it also plays a significant role in influencing vaccine intention within this group(71).

It is essential to raise awareness among university-level HCSWs that the general population may not engage in the same detailed BRB considerations, and under certain conditions, this perception could have a discouraging effect on vaccine uptake as serial vaccine non-demanders focused on vaccination risks. Indeed, several authors have emphasized that public reactions tend to be strongly negative when communications equate different outcomes based only on their similar severity levels(114–116). Research on cancer has highlighted the challenges patients face in understanding their survival chances or side-effect risks when these are presented as numerical values(134). The same study found that the Number Needed to Treat (NNT) format was particularly difficult for patients to understand, and the authors recommended against using it as the sole method of presenting information. Other studies have shown how low numeracy participants present difficulties understanding percentages of risk information(135), however in our studies no interaction was found between benefit-risk ratio attribute and education level.

Thus, even though public health authorities use the benefit-risk ratio as an indicator for healthcare practitioners(113), our findings emphasize the importance of simplifying this communication for the general population, avoiding technical or numeric ratios. Based on the literature, health communicators need to be aware that different formats can lead to varying risk

perceptions among patients(115,135). Authors suggest that probabilistic information should be presented not only in numerical format but also graphically(136). They also advise against presenting too much information since it can be distracting and prevent people to focus on the key details necessary for informed decision-making(137–139).

Applying the 7C-model to analyze benefit-risk balance in vaccine decision-making

Throughout this thesis, we have employed a psychological antecedent framework of vaccine acceptance known as the 7C-model, which integrates various psychological factors into vaccine decision processes. This model was used as a foundation for developing the DCE questionnaire (statement and attributes), ensuring that all critical aspects of vaccine decision-making were addressed. Additionally, by completing the DCE study with repeated cross-sectional studies using the 7C-model, we were able to identify whether some individuals omitted vaccination BRB and based their vaccine decisions on other psychological factors.

In previous research, Calculation (representing the deliberation between the benefits and risks of vaccination) emerged as one of the strongest psychological antecedents. However, our results showed that, among HCSWs, the introduction of a novel vaccine and the implementation of health certificates during the COVID-19 pandemic resulted in a diminished influence of Calculation, while Collective responsibility became the primary antecedent affecting vaccine acceptance.

Similarly, among the general population, individuals who complied with vaccination requirements due to COVID-19 certificates did so not necessarily because they perceived greater benefits than risks or had high confidence in the vaccine, but rather due to their occupational obligations. Their active social lives obligate them to have the certificate to maintain their social interactions. Then, over time and with experience, HCSWs began to weigh the benefits and risks of vaccination as much as prior to the COVID-19 certificate.

Taking non-uniform respondents as a basis for comparison, we found that serial vaccine demanders made decisions by weighing the benefits and risks of vaccination. In contrast, serial non-demanders focused exclusively on the risks associated with vaccination. Surprisingly, serial vaccine non-demanders did not differ from non-uniform respondents in terms of vaccination benefit-risk balance perception (Calculation) or fear of the consequences of developing the disease (Complacency). This suggest that non-uniform responders, despite accepting some vaccines, did not perceive greater benefits from vaccination than those who refused vaccination across all scenarios, suggesting that their decision was mainly based on vaccination risk perception without deliberating on its benefits.

Those who refused all vaccination scenarios primarily cited fear of side effects and past negative experiences as key reasons for their refusal, indicating a significant omission bias among serial vaccine non-demanders. However, our results are encouraging: when presented with scenarios involving high risks of contracting a disease, the certainty of serial non-demanders to refuse vaccination decreased. This opens an opportunity to address and potentially mitigate omission bias. Future research on vaccination should explore strategies to reduce omission bias among serial vaccine non-demanders.

Impact of COVID-19 certificate or vaccine mandate

The implementation of a COVID-19 certificate to access social and public venues has notably increased vaccination coverage among the French population. Moreover, mandates reduce inequalities by ensuring that everyone is on an equal footing. Through our surveys (VaxExp & CappVac-Cov), we observed that social inequalities related to vaccination decreased with the COVID-19 certificate enactment among the general public.

We also observed a change in how the influence of the 7C-psychological antecedents to vaccination varied in light of mandatory vaccination among HCSWs. For example, at early stages of the vaccination campaign, the influence of Calculation was diminished and Collective Responsibility appeared as the only “C” influencing vaccine decisions, likely due to the consistent messaging from the French government on the importance of the indirect protection the COVID-19 vaccine offered. Substantial evidence now suggests that the indirect protection from COVID-19 vaccination is short-lived and the impact beyond three months primarily consists of protection against severe disease(86,87). Among the general population, we observed that the groups showing the least motivation towards vaccination in response to the COVID-19 certificate or mandate were those aged over 80 and individuals with no professional activity, who may experience social isolation and therefore were not motivated by being able to engage in social activities with the vaccine certificate. Thus, the incentive policy implemented by the French government did not effectively persuade individuals with the greatest potential benefit from vaccination. Indeed, a stronger incentive for vaccination or even a mandate in the older population group could have further reduced COVID-19 mortality. Moreover, the COVID-19 certificate has increased health inequalities between the professionally active and inactive population, increasing the healthy worker effect.

One of our primary concerns was the impact of the COVID-19 certificate or mandate on future vaccine campaigns, specifically whether it would backfire such that those who concede to getting vaccinated due to the certificate-mandate may resist accepting future vaccinations. By

contrast, our results suggested that, among the general public, the COVID-19 vaccine requirement had no negative impact on future vaccine intention. Indeed, those who agreed to get vaccinated due to the certificate-mandate were significantly more likely to accept future vaccinations compared to those who did not comply with the mandate.

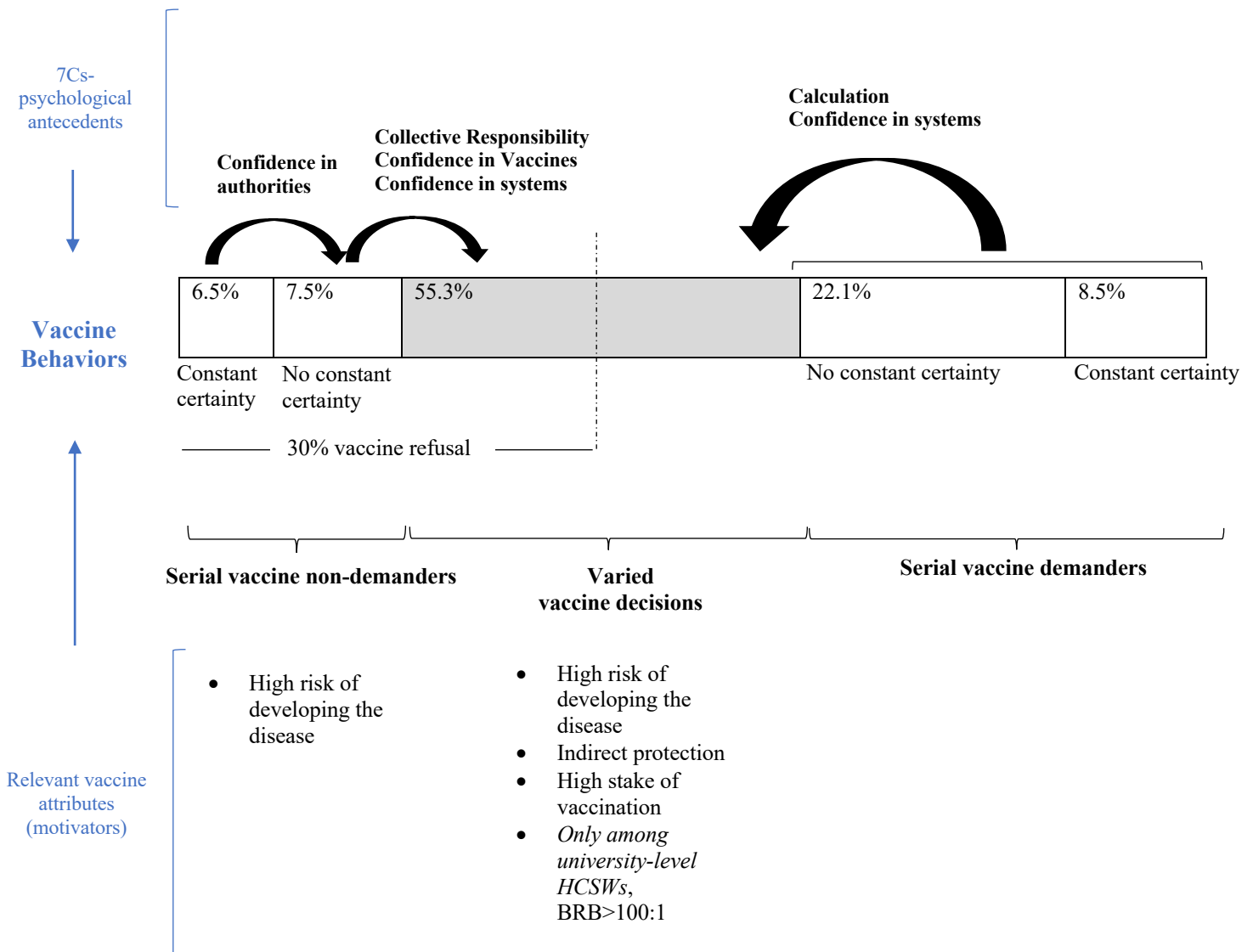
Vaccination behaviour profiles

In vaccine campaigns, it is observed that approximately 30% of the population consistently refuse vaccination. However, the third article of this thesis suggests that this 30% may involve individuals with varying vaccine behavior profiles at each vaccine campaign. Figure 13 summarizes the findings from articles 2 and 4, illustrating the key differences in vaccine preferences and psychological antecedents across different vaccination behaviour profiles. We noted that the only difference between those who constantly refuse vaccination with a constant level of certainty and those who constantly refuse vaccination with varying levels of certainty is their confidence in authorities. Those who vary their certainty level while refusing had higher confidence in authorities than those who had constant levels of certainty when refusing. When compared to serial vaccine non-demanders, non-uniform respondents were more likely to perceive vaccination as a collective action (Collective responsibility), without fear of vaccine side-effects (Confidence in vaccine) and motivated by employer vaccine encouragement (Confidence in systems). Among the 7C-psychological antecedents, Calculation did not significantly differentiate serial vaccine non-demanders from non-uniform respondents.

Of note, the attribute with the strongest impact on vaccine acceptance was having a high-risk of developing the disease. This was also the only attribute which decreased the certainty with which serial vaccine non-demanders refused vaccination. These findings suggest that there might be a threshold of disease risk perception (rather than direct vaccine benefits) that could encourage serial non-demanders to consider vaccination.

Taken together, results from this thesis provide insights for future vaccine campaigns. Our results highlight the importance of improving confidence in authorities among the general population and the need to communicate disease risk to alter perceptions of risk rather than focusing on vaccine benefits among persons who are unlikely to accept vaccination *a priori*.

Figure 13. Vaccination Behaviour profile in a representative sample of the French adult population. Berberis study, 2024.



Public Health Recommendations

Based on the findings of this thesis, targeted vaccine campaigns should address each subgroup of the population differently:

- For university-level HCSWs who vary their vaccine decision, campaigns should emphasize both quantitative Benefit-Risk Balance (BRB) metrics and relevant qualitative information.
- For the general population who vary their vaccine decision, messaging should emphasize qualitative information related to BRB considerations.

- Among people expected to be reluctant to vaccinating, effective communication should prioritize highlighting the risks associated with contracting the disease rather than benefits of the vaccine. It should also emphasize the absence of vaccine side-effects, when applicable, and focus on building confidence in authorities.

Our findings indicate that communicating specific BRB metrics could potentially convince 10% (serial vaccine demanders) of the population to accept vaccination under any circumstance involving vaccination attributes.

To better prepare for future pandemics, further research should focus on enhancing confidence in authorities and addressing omission bias to improve vaccination coverage.

Importance of Discrete Choice Experience in vaccine acceptance studies

Understanding behaviors and motivations of vaccine-hesitant individuals is crucial for developing effective strategies to address their concerns. However, including these groups of individuals who are not favorable of vaccines in research has proven to be a very difficult task, often resulting in studies with limited statistical power concerning this subgroup. Discrete Choice Experiments (DCEs) offer a potential solution to counteract this issue. By repeatedly asking participants about their vaccine decision across diverse hypothetical vaccine scenarios, creating a longitudinal database with multiple observations per individual. Moreover, the development of the vaccine eagerness tool enables us to explore vaccination preferences among recurrent patterns of vaccine refusal, varying in certainty based on vaccine attributes.

One of the primary limitations associated with conventional questionnaires concerning vaccine acceptance is the potential disparity between participants' stated intention to accept a future vaccine and their actual acceptance when presented the opportunity. This limitation is also present in DCEs questionnaires. However, their design engages participants to make trade-offs between various attributes, providing a more comprehensive insight into population preferences with more accurate predicting factors than conventional questionnaires(140,141).

Limitations

This thesis has several limitations. Firstly, our studies utilized cross-sectional surveys rather than longitudinal follow-up surveys, which limits our ability to observe the evolution of the 7C-psychological antecedents and changes in vaccine perception over time. Secondly, the use of a self-administered questionnaire may have led to misunderstandings, although it helped reduce social desirability bias.

The generalizability of our results is naturally limited by several factors: our results apply specifically to a vaccination campaign against COVID-19 in France: a passive campaign with large sub-regional vaccine centers and little vaccine promotion apart from government announcements. Additionally, the use of web-based questionnaires means that our sample may not completely represent the French population due to selection on internet access and use. Despite the quota sampling, people in poverty, with low health literacy and possibly high-risk behaviour, may be underrepresented.

The HCSWs snowballing sampling technique produced a self-selected sample of HCSWs based, likely based on favourable vaccination attitudes. Given their involvement in the GERES, these participants likely prioritized health recommendation. Our different HCSW samples also had a low proportion of nurse assistants, who are the healthcare professionals spending the most time in direct contact with patients. Finally, our study did not take into account French citizens from overseas departments where inequalities tend to be higher than in mainland France(90,91).

Conclusion

During this thesis we have used two different but complementary methodologies, one focusing on psychological factors influencing vaccine acceptance to characterize HCSWs attitudes towards vaccination, the second method focused on discerning preferences in vaccination, trying to identify factors that might motivate HCSWs and the general population for future vaccination campaigns. These two methodologies together have facilitated a better insight of the motivators behind vaccine acceptance.

Our findings have largely reported the significant role of a favourable perception of the BRB in vaccine acceptance, however, it is crucial to adopt tailored strategies when addressing BRB among different subgroups. Within the general public, vaccine campaigns should avoid to explicitly mention the term vaccination BRB and instead emphasize qualitative information such as disease risk, indirect protection and stake (implications) of vaccination. In doing so, campaigns will be simplifying the concept of BRB for better comprehension among the general public. By contrast, for university-level HCSWs, communication can focus explicitly on the vaccination BRB, in particular when its value is higher than 100:1.

Concerning those who might not be willing to accept vaccination, vaccine campaigns should focus on improving confidence in authorities and confidence in the vaccine (vaccine safety), on information about vaccination as a collective action, such as its indirect protection, and the risk of developing the disease. Such communication strategies should better motivate serial vaccine non-demanders and other individuals that may accept vaccination depending on vaccine characteristics. However, we acknowledge that certain circumstances may need communication targeting the entire population. In such cases, our results showed that a better vaccine coverage could be achieved when communication focused on risk of developing the disease.

Overall, our findings illustrate that building and maintaining trustful relations between the public and decision makers is an essential component of pandemic preparedness. The next point would be to explore if we can modify confidence in systems in order to increase vaccine coverage.

Perspectives

Preferences studies facilitate investigation into vaccine acceptance by identifying motivators for vaccination. This enables practitioners to prioritize patient preferences during individual patient-practitioner interviews. The benefits of personalized medicine, together with motivational interviewing techniques that foster patient autonomy in care decision-making, have been extensively documented. They have the potential to tailor therapy for optimal response and safety, thus enhancing patient care outcomes(142,143).

As mentioned in the preface of this thesis, vaccination differs from other health interventions by addressing the population irrespective of disease status or presence of risks factors. This aspect of vaccination can involve complex considerations, with an individual trade-off between risks of side-effects, the potential risk of suffering from a severe form of disease, and the risk of disease transmission to friends and relatives. These complexities may lead individuals to need further information about the benefits of vaccination before deciding to get vaccinated. Therefore, having patient-centered conversations that align with patient preferences may be crucial in raising awareness about the importance of vaccination on an individual level.

Additionally, future research should explore vaccine acceptance longitudinally in order to identify changes over time, providing insights into how and why attitudes towards vaccination shift over time. Also, it will enable to track if public health interventions or new scientific findings have significantly impact public perception of vaccination BRB.

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Appendices

Supplementary Table 1. Comparative analysis of log-binomial regressions and poisson regressions with robust variance (n= 833). Association between future intention to accept COVID-19 vaccine given medical recommendation and COVID-19 vaccine experience. CoVacExp study

LOG-BINOMIAL

POISSON

ADJUSTED FOR BRB

NON ADJUSTED FOR BRB

ADJUSTED FOR BRB

NON ADJUSTED FOR BRB

Future vaccine intention ~ Vaccine
Experience + BRB

Future vaccine intention ~ Vaccine
Experience

Future vaccine intention ~ Vaccine
Experience + BRB

Future vaccine intention ~ Vaccine
Experience

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		AIC 503.66
CM-only	5.90	0.002	
CM+others	14.91	<0,001	
CM_not main	16.97	<0,001	
NA	3.43	0.064	

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		AIC 624.69
CM-only	6.40	0.001	
CM+others	18.23	<0,001	
CM_not main	26.21	<0,001	
NA	4.15	0.035	

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		
CM-only	6.00	0.002	
CM+others	14.1 1	<0,001	
CM_not main	17.1 5	<0,001	
NA	3.37	0.069	

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		
CM-only	6.40	0.001	
CM+others	18.2 3	<0,001	
CM_not main	26.2 1	<0,001	
NA	4.15	0.035	

Future vaccine intention ~ Vaccine
Experience + BRB + confidence

Future vaccine intention ~ Vaccine
Experience + confidence

Future vaccine intention ~ Vaccine
Experience + BRB + confidence

Future vaccine intention ~ Vaccine
Experience + confidence

SUPPLEMENTARY TABLE 1

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	5.89	0.002
CM+others	14.95	<0,001
CM_not main	17.09	<0,001
NA	3.45	0.063

AIC 504.67

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.46	0.001
CM+others	17.71	<0,001
CM_not main	25.09	<0,001
NA	4.02	0.039

AIC 621.82

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.05	0.002
CM+others	13.76	<0,001
CM_not main	16.67	<0,001
NA	3.30	0.075

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.49	0.001
CM+others	17.22	<0,001
CM_not main	24.44	<0,001
NA	3.95	0.043

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	5.89	0.002
CM+others	14.95	<0,001
CM_not main	17.09	<0,001
NA	3.45	0.063

AIC 506.67

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.45	0.001
CM+others	17.81	<0,001
CM_not main	25.01	<0,001
NA	4.03	0.039

AIC 619.95

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.06	0.002
CM+others	13.78	<0,001
CM_not main	16.63	<0,001
NA	3.30	0.074

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.50	0.001
CM+others	17.24	<0,001
CM_not main	24.25	<0,001
NA	3.96	0.043

SUPPLEMENTARY TABLE 1

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		510.51
CM-only	5.88	0.002	
CM+others	14.94	<0,001	
CM_not main	17.05	<0,001	
NA	3.44	0.063	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		621.11
CM-only	6.46	0.001	
CM+others	17.92	<0,001	
CM_not main	24.99	<0,001	
NA	4.07	0.037	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		621.11
CM-only	6.06	0.002	
CM+others	13.79	<0,001	
CM_not main	16.62	<0,001	
NA	3.31	0.074	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		621.11
CM-only	6.51	0.001	
CM+others	17.36	<0,001	
CM_not main	24.08	<0,001	
NA	4.01	0.041	

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		512.61
CM-only	5.83	0.002	
CM+others	14.82	<0,001	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		617.96
CM-only	6.47	0.001	
CM+others	18.02	<0,001	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		617.96
CM-only	6.08	0.002	
CM+others	13.78	<0,001	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		617.96
CM-only	6.54	0.001	
CM+others	17.32	<0,001	

SUPPLEMENTARY TABLE 1

CM_not main	16.90	<0,001
NA	3.42	0.064

CM_not main	24.94	<0,001
NA	4.10	0.037

CM_not main	16.59	<0,001
NA	3.31	0.074

CM_not main	23.92	<0,001
NA	4.02	0.040

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		
CM-only	5.21	0.003	
CM+others	13.17	<0,001	
CM_not main	14.92	<0,001	
NA	3.06	0.08	

	Future vaccine intention		AIC
Vaccine Experience			
Unvaccinated	1		
CM-only	6.39	0.001	
CM+others	17.82	<0,001	
CM_not main	24.65	<0,001	
NA	4.08	0.036	

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.00	0.002
CM+others	13.71	<0,001
CM_not main	16.50	<0,001
NA	3.38	0.068

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.43	0.001
CM+others	17.21	<0,001
CM_not main	23.72	<0,001
NA	4.11	0.037

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. status

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. status

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. status

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. status

	Future vaccine intention
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	Future vaccine intention
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	Future vaccine intention
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	Future vaccine intention
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SUPPLEMENTARY TABLE 1

Vaccine Experience		
Unvaccinated	1	
CM-only	4.61	0.004
CM+others	11.60	<0,001
CM_not main	13.15	<0,001
NA	2.74	0.10

AIC 512.52

Vaccine Experience		
Unvaccinated	1	
CM-only	5.60	0.002
CM+others	15.41	<0,001
CM_not main	21.26	<0,001
NA	3.62	0.044

AIC 621.86

Vaccine Experience		
Unvaccinated	1	
CM-only	6.01	0.002
CM+others	13.72	<0,001
CM_not main	16.50	<0,001
NA	3.38	0.068

Vaccine Experience		
Unvaccinated	1	
CM-only	6.45	0.001
CM+others	17.22	<0,001
CM_not main	23.73	<0,001
NA	4.10	0.037

Incorporation of the sixth variable

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf.

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf.

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf.

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf.

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	4.62	0.003
CM+others	11.48	<0,001
CM_not main	13.03	<0,001
NA	2.76	0.10

AIC 512.04

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	3.62	0.004
CM+others	9.31	<0,001
CM_not main	12.75	<0,001
NA	2.48	0.09

AIC 626.15

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.01	0.002
CM+others	13.71	<0,001
CM_not main	16.50	<0,001
NA	3.38	0.068

	Future vaccine intention	
Vaccine Experience		
Unvaccinated	1	
CM-only	6.45	0.001
CM+others	17.24	<0,001
CM_not main	23.75	<0,001
NA	4.11	0.037

SUPPLEMENTARY TABLE 1

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf. + speaking other languages

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		AIC 514.32
CM-only	4.52	0.004	
CM+others	11.22	<0,001	
CM_not main	12.74	<0,001	
NA	2.71	0.10	

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf. + speaking other languages

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		AIC 628.67
CM-only	2.80	0.009	
CM+others	6.78	<0,001	
CM_not main	9.25	<0,001	
NA	2.03	0.14	

Future vaccine intention ~ Vaccine Experience + BRB + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf. + speaking other languages

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		
CM-only	6.00	0.002	
CM+others	13.71	<0,001	
CM_not main	16.50	<0,001	
NA	3.38	0.068	

Future vaccine intention ~ Vaccine Experience + confidence + self-reported risk factor + age + gender + income + occupat. Status + relative inf. + speaking other languages

	Future vaccine intention		
Vaccine Experience			
Unvaccinated	1		
CM-only	6.41	0.001	
CM+others	17.20	<0,001	
CM_not main	23.72	<0,001	
NA	4.10	0.037	

SUPPLEMENTARY TABLE 2

Supplementary Table 2. Questionnaire items evaluating knowledge according to the 7C-model . CappVac-Cov study.

7C-Knowledge item	Question	Answers
Confidence in systems	<i>'Some stages of vaccine development (testing) have been skipped because of the epidemic emergency.'</i>	<ul style="list-style-type: none"> • False • Do not know • True
Confidence in COVID-19 vaccines	<i>'Serious side effects may occur >6 months after vaccination.'</i>	<ul style="list-style-type: none"> • False • Do not know • True
Social Conformism	<i>'Do you know the approximate percentage of healthcare workers who intend to get the COVID-19 vaccine?'</i>	<ul style="list-style-type: none"> • 30% • 60% • 90% • Do not know
Complacency	<i>'The main risk factor for severe disease is age.'</i>	<ul style="list-style-type: none"> • False • Do not know • True
Calculation	<i>'For a person with risk factors, these vaccines have more benefits than risks in the current epidemic situation.'</i>	<ul style="list-style-type: none"> • False • Do not know • True
Collective Responsibility	<i>'The vaccine blocks transmission of the virus to those around you in case of infection.'</i>	<ul style="list-style-type: none"> • False • Do not know • True
Convenience	<i>Convenience was not evaluated because was not relevant anymore due to the COVID-19 vaccine mandate among healthcare workers</i>	

SUPPLEMENTARY TABLE 3

Supplementary Table 3. Hypothetical vaccine acceptance and average vaccine eagerness by scenario. Berberis study among 1869 Adults in France, March 2023.

		Hypothetical Vaccine Acceptance. N (%) (all respondents)				Average Vaccine Eagerness: certainty (-10 to 10) (all respondents)			
		Representative sample	Non-HCSWs	Non-university-degree HCSWs	University-degree HCSWs	Representative sample	Non-HCSWs	Non-university-degree HCSWs	University-degree HCSWs
BLOC 1		N=740	N=686	N=72	N=149	N= 740	N=686	N=72	N=149
1	Neurological disease with paralysis High risk (about one in ten people) Immobilization at home with a work sick leave for one week without sequelae 10 avoided events for one induced side-effect Provides only individual protection	510 (68.9)	470 (68.5)	51 (70.8)	114 (76.5)	3.23	3.16	3.75	4.15
2	Neurological disease with paralysis Low risk (less than one person in a thousand) One week of hospitalization without any risk of sequelae 10 avoided events for one induced side-effect Provides indirect protection to your relatives	393 (53.1)	361 (52.6)	40 (55.6)	95 (63.8)	0.78	0.70	1.46	2.20
3	Respiratory disease High risk (about one in ten people) One week of hospitalization without any risk of sequelae 100 avoided events for one induced side-effect Provides indirect protection to your relatives	528 (71.4)	490 (71.4)	55 (76.4)	123 (82.6)	3.55	3.58	4.68	5.28
4	Neurological disease with paralysis Low risk (less than one person in a thousand) Immobilization at home with a work sick leave for one week without sequelae 500 avoided events for one induced side-effect	413 (55.8)	381 (55.5)	44 (61.1)	108 (72.5)	1.18	1.14	1.78	3.79

SUPPLEMENTARY TABLE 3

	Provides indirect protection to your relatives								
5	Respiratory disease High risk (about one in ten people) Immobilization at home with a work sick leave for one week without sequelae 50 avoided events for one induced side-effect Provides only individual protection	491 (66.4)	451 (65.7)	49 (68.1)	100 (67.1)	2.76	2.70	2.66	3.07
6	Respiratory disease High risk (about one in ten people) 30 days of hospitalization with sequelae risk 10 avoided events for one induced side-effect Provides indirect protection to your relatives	570 (77.0)	526 (76.7)	63 (87.5)	135 (90.6)	4.57	4.55	6.22	6.83
7	Neurological disease with paralysis Low risk (less than one person in a thousand) 30 days of hospitalization with sequelae risk 100 avoided events for one induced side-effect Provides only individual protection	434 (58.7)	399 (58.2)	50 (69.4)	119 (79.9)	1.62	1.58	6.97	4.76
8	Respiratory disease Low risk (less than one person in a thousand) One week of hospitalization without any risk of sequelae 50 avoided events for one induced side-effect Provides only individual protection	326 (44.1)	300 (43.7)	25 (34.7)	76 (51.0)	-0.64	-0.69	-1.93	0.12
9	Neurological disease with paralysis High risk (about one in ten people) Immobilization at home with a work sick leave for one week without sequelae 2 avoided events for one induced side-effect Provides only individual protection	507 (68.5)	467 (68.1)	52 (72.2)	84 (56.4)	3.07	3.01	3.45	0.99
10	Neurological disease with paralysis Low risk (less than one person in a thousand)	403 (54.5)	366 (53.4)	46 (63.4)	122 (81.9)	0.97	0.82	2.49	5.16

SUPPLEMENTARY TABLE 3

	Immobilization at home with a work sick leave for one week without sequelae 1000 avoided events for one induced side-effect Provides indirect protection to your relatives								
BLOC 2		N=765	N=698	N=74	N=190	N=765	N=698	N=74	N=190
1	Respiratory disease Low risk (less than one person in a thousand) 30 days of hospitalization with sequelae risk 10 avoided events for one induced side-effect Provides only individual protection	409 (53.5)	372 (53.3)	45 (60.8)	116 (61.1)	0.79	0.76	1.58	1.98
2	Respiratory disease Low risk (less than one person in a thousand) Immobilization at home with a work sick leave for one week without sequelae 100 avoided events for one induced side-effect Provides indirect protection to your relatives	367 (48.0)	338 (48.4)	42 (56.8)	114 (60.0)	-0.04	-0.01	1.20	1.86
3	Neurological disease with paralysis Low risk (less than one person in a thousand) 30 days of hospitalization with sequelae risk 50 avoided events for one induced side-effect Provides indirect protection to your relatives	456 (60.0)	411 (58.8)	58 (78.4)	159 (83.7)	1.75	1.64	4.22	5.53
4	Neurological disease with paralysis High risk (about one in ten people) 30 days of hospitalization with sequelae risk 500 avoided events for one induced side-effect Provides only individual protection	583 (76.2)	530 (75.7)	63 (85.1)	179 (94.2)	4.30	4.24	5.81	7.39
5	Neurological disease with paralysis High risk (about one in ten people) One week of hospitalization without any risk of sequelae	543 (71.0)	495 (70.6)	59 (79.7)	162 (85.3)	3.47	3.43	4.42	5.66

SUPPLEMENTARY TABLE 3

	100 avoided events for one induced side-effect Provides only individual protection								
6	Neurological disease with paralysis High risk (about one in ten people) One week of hospitalization without any risk of sequelae 50 avoided events for one induced side-effect Provides indirect protection to your relatives	574 (75.0)	526 (75.3)	58 (78.4)	167 (87.9)	4.01	4.04	4.62	6.23
7	Respiratory disease High risk (about one in ten people) 30 days of hospitalization with sequelae risk 500 avoided events for one induced side-effect Provides indirect protection to your relatives	600 (78.4)	546 (78.1)	64 (86.5)	180 (94.7)	4.60	4.59	5.99	7.68
8	Respiratory disease Low risk (less than one person in a thousand) One week of hospitalization without any risk of sequelae 500 avoided events for one induced side-effect Provides only individual protection	329 (43.0)	302 (43.2)	32 (43.2)	99 (52.1)	-0.52	-0.76	-0.99	0.55
9	Respiratory disease Low risk (less than one person in a thousand) 30 days of hospitalization with sequelae risk 2 avoided events for one induced side-effect Provides only individual protection	384 (50.2)	346 (49.6)	44 (59.5)	100 (52.6)	0.43	0.33	1.74	0.55
10	Respiratory disease High risk (about one in ten people) 30 days of hospitalization with sequelae risk 1000 avoided events for one induced side-effect	601 (78.6)	544 (77.9)	67 (90.5)	177 (93.2)	5.29	4.62	6.64	7.46

SUPPLEMENTARY TABLE 3

Provides indirect protection to your relatives								
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* Colors and frame correspond to repeated scenarios

HCSW: Healthcare sector worker

Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8.1%) were further categorized based on their professional education into their respective HCSW occupational groups.

SUPPLEMENTARY TABLE 4

Supplementary Table 4. Description of the study participants, in the representative population sample (N=1505) and in the Healthcare Sector Worker (HCSW) sample (N=369). Berberis study, France, 2023.

	Total N=1869	Representative population sample N=1505	HCSW sample N=364
Gender			
Male	862 (46.1%)	775 (51.5%)	87 (23.9%)
Female	1,007 (53.9%)	730 (48.5%)	277 (76.1%)
Age (in years)			
18-34	426 (22.8%)	380 (25.2%)	46 (12.6%)
35-49	562 (30.1%)	410 (27.2%)	152 (41.8%)
≥50	881 (47.1%)	715 (47.5%)	166 (45.6%)
Region of residence/work (N=1868)			
Paris Region	350 (18.8%)	282 (18.7%)	68 (18.9%)
North East	410 (22.0%)	330 (21.9%)	77 (21.4%)
North West	410 (22.0%)	343 (22.8%)	67 (18.6%)
South East	478 (25.6%)	377 (25.0%)	101 (28.1%)
South West	220 (11.8%)	173 (11.5%)	47 (13.1%)
DROMs	4(0.2%)	0 (0.0%)	4 (1.1%)
Speaking other language than French (N=1867)			
No	1,504 (80.6%)	1,193 (79.3%)	311 (85.9%)
Yes	363 (19.4%)	312 (20.7%)	51 (14.1%)
Educational level (N=1505)			
Lower than secondary school diploma	355 (23.6%)	355 (23.6%)	
Equal to secondary school diploma	377 (25.0%)	377 (25.0%)	
Higher than secondary school diploma	773 (51.4%)	773 (51.4%)	
Occupational HCSW status			
Non-HCSW	1384 (74.1%)	1384 (92.0%)	0 (0.0%)
Healthcare support professions	146 (7.8%)	63 (4.2%)	83 (22.8%)
University-level HCW	339 (18.1%)	58 (3.9%)	281 (77.2%)
General opinion about vaccines			
Very Favorable	676 (36.2%)	453 (30.1%)	223 (61.3%)
Favorable	833 (44.6%)	710 (47.2%)	123 (33.8%)
Undecided	216 (11.6%)	208 (13.8%)	8 (2.2%)
Skeptical	104 (5.6%)	95 (6.3%)	9 (2.5%)
Very Skeptical	40 (2.1%)	39 (2.6%)	1 (0.3%)
Seasonal Flu Vaccine Status (N=362)			
Unvaccinated	60 (16.6%)		60 (16.6%)
Vaccinated (every year)	227 (62.7%)		227 (62.7%)
Vaccinated (twice)	41 (11.3%)		41 (11.3%)
Vaccinated (once)	34 (9.4%)		34 (9.4%)

SUPPLEMENTARY TABLE 4

COVID-19 Vaccine Status (N=1384)			
Unvaccinated	196 (14.2%)	196 (14.2%)	
Vaccinated (more than 6 months ago)	978 (70.7%)	978 (70.7%)	
Vaccinated (less than 6 months ago)	210 (15.2%)	210 (15.2%)	
Perception of Benefit-Risk Ratio of Covid-19 vaccination (N=1866)			
More risks than benefits	492 (26.4%)	408 (27.1%)	84 (23.3%)
Do not know	428 (22.9%)	382 (25.4%)	46 (12.7%)
More benefits than risks	946 (50.7%)	715 (47.5%)	231 (64.0%)
Level of confidence in authorities in the management of the COVID-19 crisis (N=1867)			
Low	403 (21.6%)	328 (21.8%)	75 (20.7%)
Moderate	621 (33.3%)	496 (33.0%)	125 (34.5%)
High	843 (45.2%)	681 (45.2%)	162 (44.8%)

HCSW: Healthcare sector worker

Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8.1%) were further categorized based on their professional education into their respective HCSW occupational groups.

In the HCSW sample, some socio-demographic questions were asked at the end of the questionnaire, some participants did not answer those questions (n=3).

SUPPLEMENTARY TABLE 5

Supplementary Table 5. Preference weights for attributes of hypothetical vaccination acceptance (binary outcome) with and without individual characteristics by Healthcare Sector Worker (HCSW) status. Berberis study, France, 2023.

Hypothetical Vaccine Acceptance (non-uniform respondents)

		Representative sample (N=833)				Non-HCSWs (n=756)				Non-university-degree HCSWs (n=95)				University-degree HCSWs (n=187)			
		With individual characteristics		Without individual characteristics		With individual characteristics		Without individual characteristics		With individual characteristics		Without individual characteristics		With individual characteristics		Without individual characteristics	
		OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value
Gender	Male	1				1				1				1			
	Female	1.31	0.001			1.36	<0.001			0.97	0.904			0.88	0.538		
Age (in years)	18-34	1				1				1				1			
	35-49	0.87	0.186			0.91	0.399			0.59	0.104			0.89	0.644		
	≥50	1.02	0.875			1.02	0.625			0.92	0.789			0.88	0.607		
Educational level	Lower than secondary school diploma	1				1											
	Equal to secondary school diploma	0.93	0.545			0.91	0.446										
	Higher than secondary school diploma	0.99	0.951			1.02	0.844										
Type of disease	respiratory disease	1		1		1		1		1		1		1		1	
	neurological disease	1.43	<0.001	1.43	<0.001	1.42	<0.001	1.42	<0.001	1.80	0.001	1.80	0.001	2.58	<0.001	2.58	<0.001
Epidemiologic situation	low risk of developing the disease	1		1		1		1		1		1		1		1	
	high risk of developing the disease	6.87	<0.001	6.87	<0.001	7.19	<0.001	7.19	<0.001	5.83	<0.001	5.83	<0.001	8.68	<0.001	8.68	<0.001
Stake of vaccination	immobilization at home	1		1		1		1		1		1		1		1	
	one week of hospitalization without any sequelae	0.98	0.785	0.98	0.775	1.00	0.972	1.00	0.958	0.70	0.109	0.71	0.120	1.12	0.504	1.12	0.507
	30 days of hospitalization with sequelae risk	2.12	<0.001	2.11	<0.001	2.13	<0.001	2.12	<0.001	3.06	<0.001	3.12	<0.001	6.03	<0.001	6.03	<0.001

SUPPLEMENTARY TABLE 5

Benefit-Risk Ratio of vaccination																
avoid 10 events for 1 induced event	1		1		1		1		1		1		1		1	
avoid 50 events for 1 induced event	0.93	0.380	0.93	0.374	0.93	0.395	0.93	0.387	0.88	0.606	0.89	0.644	1.22	0.306	1.22	0.307
avoid 100 events for 1 induced event	1.05	0.520	1.05	0.526	1.07	0.418	1.07	0.425	1.43	0.137	1.45	0.127	1.99	<0.001	1.99	<0.001
avoid 500 events for 1 induced event	1.03	0.682	1.03	0.693	1.06	0.539	1.06	0.554	0.94	0.812	0.95	0.859	2.30	<0.001	2.30	<0.001
Protection of the vaccine																
no indirect protection	1		1		1		1		1		1		1		1	
indirect protection	1.58	<0.001	1.58	<0.001	1.63	<0.001	1.63	<0.001	2.12	<0.001	2.13	<0.001	2.52	<0.001	2.52	<0.001

Hypothetical vaccine acceptance: Odds Ratio (OR) and *p*-value from random effect generalized multinomial logit model.

HCSW: Healthcare sector worker

Two sampling methods were used in this study: a snowball sampling for healthcare sector workers (HCSWs) and quotas sampling until completion of a representative sample of the French adult population. The quotas were defined based on demographic variables, including age group, socio-professional category (SPC), region of residence, and size of the urban area. These demographic categories were established in accordance with the National Institute of Statistics and Economic Studies' 2016 census. Then, HCSWs who participated in the representative sample (n=121, 8.1%) were further categorized based on their professional education into their respective HCSW occupational groups.

Supplementary File 1. Data quality check and heterogeneity analysis.

A. Data quality check

To test the quality of our data, we used the certainty scale among the representative sample and HCSWs sample, excluding those whose vaccine certainty did not change across the different scenarios from the main analysis and preference weights remained stable.

Then, we explored monotonicity by the inclusion of extreme scenarios (repetition of a scenario replacing the levels of BRB with extreme values of BRB) at the end of the exercise to compare them with their original scenario. We included two extreme scenarios: one with a more favourable BRB, positive extreme scenario and one with a worst BRB, negative extreme scenario.

The representative sample (where attribute BRB did not play a role in vaccine decision), vaccine acceptance for repeated scenarios were not different that for their respective extreme scenarios (**Supplementary Table 3**). Among university-level HCSWs (where attribute BRB did play a role in vaccine decision), vaccine acceptance for repeated negative extreme scenarios was not higher that for its corresponding scenario. Similarly, vaccine acceptance for positive extreme scenarios was not lower than for its corresponding scenario.

B. Heterogeneity analysis - latent class analysis

We performed latent class analysis (**Supplementary Tables 6 and 7**) to examine the BRB attribute across different groups: the representative sample, non-HCSWs, and university-level HCSWs. The results of the latent class analysis were consistent with our findings. Some factors explaining membership in the different clusters may reflect differences in "quality" and by excluding the unusual classes (which never exceed 20% of the sample), the results appear more robust, sensible, and significant: among the representative sample it appears that cluster 2 (16.2%) has very different preferences, as the coefficient signs for "neurological disease" and "high risk disease" are opposite to the expected signs and those of other clusters. Similarly, Cluster 1 of non-HCWs and non-University-level HCWs, respectively, showed also unusual preferences for "neurological disease" and "high risk disease". Regarding university-level-HCSWs, Cluster 2 (78%) seems to be the most "rational," especially considering indirect protection and the lower weight for "high risk neurological disease".

SUPPLEMENTARY FILE 1

Supplementary Table 5. Latent Class Analysis of preference weights for attributes of hypothetical vaccination acceptance (binary outcome) among representative sample of French adult population (N=1505) (% cluster size). Berberis Study, France 2023.

		Cluster 1 (26.0%)		Cluster 2 (16.2%)		Cluster 3 (19.9%)		Cluster 4 (38.0%)	
		Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value
Type of disease									
	respiratory disease	0		0		0		0	
	neurological disease	0.38	0.270	-0.73	<0.001	0.51	0.041	1.04	<0.001
Epidemiologic situation									
	low risk of developing the disease	0		0		0		0	
	high risk of developing the disease	5.52	<0.001	-0.63	0.017	1.69	<0.001	2.11	<0.001
Stake of vaccination									
	immobilization at home	0		0		0		0	
	one week of hospitalization without any sequelae	0.58	0.366	-0.14	0.619	0.36	0.327	-0.34	0.034
	30 days of hospitalization with sequelae risk	1.23	0.040	1.04	<0.001	1.97	<0.001	1.45	<0.001
Benefit-Risk Ratio of vaccination									
	avoid 10 events for 1 induced event	0		0		0		0	
	avoid 50 events for 1 induced event	0.84	0.045	-0.05	0.830	-0.24	0.433	-0.37	0.113
	avoid 100 events for 1 induced event	0.26	0.531	0.05	0.847	0.04	0.878	-0.12	0.543
	avoid 500 events for 1 induced event	0.09	0.859	0.26	0.269	-0.11	0.695	-0.01	0.953
Protection of the vaccine									
	no indirect protection	0		0		0		0	
	indirect protection	0.10	0.789	0.20	0.306	0.58	0.027	0.78	<0.001

Determinants for: cluster 2, being aged 35-49 (coefficient=-1.80, p-value <0.001) and over 50years (coefficient=-1.05, p-value =0.002) ; cluster 3, being aged over 50years (coefficient=-0.88, p-value =0.014); cluster 4, being aged 35-49 (coefficient=-0.80, p-value =0.016) and over 50years (coefficient=-0.78, p-value =0.012) and being university-level-HCSWs (coefficient=-2.19, p-value =0.048).

SUPPLEMENTARY FILE 1

Supplementary Table 6. Latent Class Analysis of preference weights for attributes of hypothetical vaccination acceptance (binary outcome) by Healthcare Sector Worker (HCSW) status (% cluster size). Berberis Study, France 2023.

		Non-HCSWs								Non-university-level-HCSWs			
		Cluster 1 (17.2%)		Cluster 2 (38.4%)		Cluster 3 (20.5%)		Cluster 4 (23.8%)		Cluster 1 (19.4%)		Cluster 2 (80.6%)	
		Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value
Type of disease													
	respiratory disease	0		0		0		0		0		0	
	neurological disease	-0.69	<0.001	1.13	<0.001	0.56	0.044	0.02	0.976	-0.56	0.315	0.76	<0.001
Epidemiologic situation													
	low risk of developing the disease	0		0		0		0		0		0	
	high risk of developing the disease	-0.38	0.115	2.14	<0.001	2.00	<0.001	6.04	<0.001	-0.75	0.151	2.29	<0.001
Stake of vaccination													
	immobilization at home	0		0		0		0		0		0	
	one week of hospitalization without any sequelae	-0.19	0.497	-0.30	0.071	0.50	0.224	0.63	0.351	-1.74	0.021	-0.19	0.455
	30 days of hospitalization with sequelae risk	-1.07	<0.001	1.80	<0.001	1.96	<0.001	1.26	0.035	-1.79	0.020	1.76	<0.001
Benefit-Risk Ratio of vaccination													
	avoid 10 events for 1 induced event	0		0		0		0		0		0	
	avoid 50 events for 1 induced event	0.15	0.523	-0.23	0.413	-0.30	0.350	0.44	0.403	-2.87	0.006	0.36	0.283
	avoid 100 events for 1 induced event	0.19	0.405	-0.06	0.800	-0.01	0.959	0.29	0.622	-0.94	0.417	0.67	0.024
	avoid 500 events for 1 induced event	0.41	0.088	0.10	0.696	-0.25	0.385	0.37	0.495	-2.82	0.008	0.70	0.043
Protection of the vaccine													
	no indirect protection	0		0		0		0		0		0	
	indirect protection	0.22	0.251	0.86	<0.001	0.59	0.049	0.39	0.417	1.03	0.075	0.74	0.001

For non-HCSW : no determinants for cluster 2 ; determinants for cluster 3, being female (coefficient=-1.11, p-value <0.001) ; for cluster 4, being aged 35-49 (coefficient=1.44, p-value <0.001 and over 50years (coefficient=0.78, p-value =0.027).

For non-university-level-HCSWs: no determinants for any cluster.

SUPPLEMENTARY FILE 1

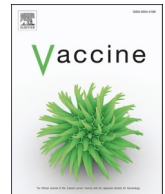
(continuation) **Supplementary Table 6.** Latent Class Analysis of preference weights for attributes of hypothetical vaccination acceptance (binary outcome) by Healthcare Sector Worker (HCSW) status (% cluster size). Berberis Study, France 2023.

University -level-HCSWs					
		Cluster 1 (22.2%)		Cluster 2 (77.8%)	
		Coefficients	<i>p</i> -value	Coefficients	<i>p</i> -value
Type of disease					
	respiratory disease	0		0	
	neurological disease	1.20	0.097	0.95	<0.001
Epidemiologic situation					
	low risk of developing the disease	0		0	
	high risk of developing the disease	4.54	<0.001	1.73	<0.001
Stake of vaccination					
	immobilization at home	0		0	
	one week of hospitalization without any sequelae	0.61	0.634	0.09	0.637
	30 days of hospitalization with sequelae risk	2.86	<0.001	1.89	<0.001
Benefit-Risk Ratio of vaccination					
	avoid 10 events for 1 induced event	0		0	
	avoid 50 events for 1 induced event	0.62	0.387	0.36	0.149
	avoid 100 events for 1 induced event	0.41	0.714	0.74	<0.001
	avoid 500 events for 1 induced event	0.09	0.917	0.93	<0.001
Protection of the vaccine					
	no indirect protection	0		0	
	indirect protection	-0.28	0.729	1.12	<0.001

For university-level-HCSWs: no determinants for any cluster.

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Impact of a COVID-19 certificate requirement on vaccine uptake pattern and intention for future vaccination. A cross-sectional study among French adults

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ARTICLE INFO

Keywords:

Vaccine hesitancy
Benefit-risk balance
COVID-19 certificate
Level of confidence
Health inequalities

ABSTRACT

Background: In August 2021, France enacted a COVID-19 certificate requirement (vaccination/recovery/test) to access specific services, with mandates for professional groups. We evaluated the impact of this incentive-coercive policy in terms of vaccine uptake equality, future vaccine intention and confidence in authorities' crisis management.

Methods: In late August 2021, a representative sample of adults (18–75 years) completed an internet-based questionnaire. We classified vaccinated participants by stated reasons for vaccination and estimated adjusted prevalence ratios (aPR) using multivariable Poisson regression. Counterfactual vaccine status assumed non-vaccination of those vaccinated for the certificate. We analysed the association of free-text testimonial themes with level of confidence in authorities.

Results: Among 972 participants, 85.7% were vaccinated or intended vaccination: 3.6% only for certificate/mandate, 17.7% mainly for certificate/mandate plus other reasons, and 64.4% mainly for other reasons. In the counterfactual situation, vaccine uptake would have been significantly more likely among older vs. younger participants (aPR = 1.35) and among those with moderate-high vs. low levels of confidence in authorities for COVID-19 crisis management (aPR = 2.04). In the observed situation, confidence was the only significant determinant of vaccine status (moderate-high vs. low, aPR = 1.39). Among those without genuine motivation for vaccination, professionally active persons were more likely to have ceded to the certificate requirement (aPR = 3.76). Those vaccinated only for the certificate were more likely to express future COVID-19 vaccine intention than unvaccinated persons (aPR = 6.41). Themes significantly associated with lower confidence were criticism of morality (aPR = 1.76) and poor communication by the authorities (aPR = 1.66).

Conclusion: The incentive-coercive policy has reduced the negative association of vaccine status with younger age and low confidence in authorities, but may have reinforced isolation of professionally inactive persons. The requirement did not negatively impact future COVID-19 vaccine intention. Future vaccine-incentive policies should pay special attention to populations with low levels of confidence in authorities.

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<https://doi.org/10.1016/j.vaccine.2023.07.002>

Received 21 March 2023; Received in revised form 22 May 2023; Accepted 2 July 2023

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1. Introduction

The rapid roll-out of COVID-19 vaccination in Europe during 2021 has substantially reduced COVID-19-related morbidity and mortality [1,2]. To avoid the outright restriction of citizens' liberty that a vaccine mandate would represent, several countries adopted policies requiring COVID-19 vaccination or negative testing for accessing certain public places and services [3,4]. These policies in general lead to increased, albeit not complete vaccine uptake [5–7].

Vaccine mandates and requirements are referred to as incentive policies [8,9]. These can be placed on a gradient of incentivisation according to the degree of consequence for non-compliance. This ranges from punctual non-access to services, to permanent exclusion and isolation, financial fines, and even punishment [10]. Such measures can be perceived as more or less coercive by the individual. Incentive-coercive policies can have a positive impact on preventative interventions, especially when individual decisions are difficult to make, e.g., when facing complex and uncertain long-term consequences [11–14]. However, ethical concerns are raised [13,15] about the thin line between encouragement and coercion [11,16,17]. An important criterion for evaluating public health policies is whether they foster equal uptake of interventions [18]. For example, a vaccine requirement for accessing employment acts only on professionally active persons, thus, strengthening the healthy worker effect [19]. Paternalistic policies may reduce confidence in authorities and disengage the population from future governmental actions [20–22].

Policies for vaccine requirements therefore should be evaluated for effects on inequalities of vaccine uptake, long-term effects on vaccine intention and trust in the wider system. These elements can inform decision making in future vaccination campaigns in public-health emergencies.

In France, COVID-19 vaccination became accessible to the general adult population starting May 2021. Given stagnating uptake, the French government announced mid-July a COVID-19 certificate - which included vaccination, recovery or recent negative test - were required to attend specific services and gatherings (e.g., trains, restaurants, hospitals) and was enacted for adults on August 9(3). In addition, vaccination became mandatory for healthcare and welfare workers [4]. Age-specific one-dose vaccine coverage increased between July 16 and August 27, 2021 from 54.6% to 84.6% (18–24 years) 59.1% to 82.3% (25–49 years), 74.6% to 88.7% (50–59 years), 81.1% to 89.0% (60–69 years), 91.8% to 96.6% (70–79 years) and from 81.6% to 85.4% (80+ years) [23]. In a series of population-based surveys in France during the implementation of the COVID-19 certificate [24], vaccination steadily increased among those reluctant to get vaccinated.

This context in France provided the opportunity to evaluate, by the end of August 2021, how the COVID-19 certificate requirement impacted individual vaccine motivations and the equity of vaccine experience (defined as a combination of vaccine status and stated motivations for vaccination). Our objectives are thus to assess, first, socio-economic determinants of observed and expected vaccine status, second, socio-economic determinants of having ceded to vaccination despite no genuine motivation for it; third, the association of vaccine experience with intention for further COVID-19 vaccination, and fourth, the association of vaccine experience with confidence in authorities for managing the COVID-19 crisis. As a complement to the latter objective, we used free-text testimonials left by participants to explore themes that were associated with low confidence in authorities.

2. Methods

2.1. Study design and participant inclusion

Any 18- to 75-year-old resident of mainland France (excluding Corsica and overseas territories) was eligible for participation. We recruited participants through a representative online-panel using quotas

according to age, gender, geographical location, and socio-economic groups. Study invitations were sent until completion of the expected sample size. Invited respondents completed the anonymous online questionnaire between August 23 and September 1, 2021. The differences in representation of gender, age group, region of residence and socio-professional category between our sample and quotas reported by the National Institute of Statistics and Economic Studies 2016 census [25] were at maximum 0.3%.

The planning, conduct and reporting of the study was in line with the Declaration of Helsinki (2013) and the GDPR regulation. Because the data collection was anonymous (without risk of indirect identification), observational and collected no sensitive and only self-declared biomedical information, no informed consent or ethical approval was required according to French regulation. Participants visiting the study website saw the complete study information and had to consent to accept participation before starting the questionnaire.

2.2. Data collection

The questionnaire contained four parts: part 1 collected socio-demographic characteristics and part 2 investigated perceived health status, preventive behaviour and perceptions related to the COVID-19 epidemic. Participants were also invited to leave an anonymous free-text testimonial commenting the measures taken against the COVID-19 epidemic since March 2020 – which consisted of three periods of lock-down with and without school closure, without and with curfews. Parts 3–4 explored teleworking habits and decisions involving financial amounts, which will be reported elsewhere.

Socio-demographic and economic information comprised gender, age, annual income, region of residence, locality size, educational level, area of professional training, occupational status (active: self-employed, employed/student; inactive: retired, unemployed, housekeeper), taking care of children, multilingualism (speaking another language other than French in the household).

Characteristics related to the COVID-19 pandemic included COVID-19 diagnosis for oneself or relatives, and declaration of risk factors for severe COVID-19. A scale-based score was recorded for the level of confidence in authorities to manage the health and economic crisis caused by COVID-19 (0–3, low confidence; 4–10, moderate-high confidence).

Perception of the individual vaccine benefit-risk balance (BRB) was assessed as “Do you think that vaccination against COVID-19 has more benefits than risks for you?” (Yes/No/Do-not-know (DNK)).

Vaccination status was evaluated as “Today, what is your situation regarding vaccination against COVID-19?” with following modalities: vaccinated with at least one-dose/with appointment for first injection/history of SARS-CoV-2 infection and have to wait to get the vaccine/vaccination planned/ unsure if concerned/ do not want to be vaccinated/ do not want to answer.

The motivations for observed or intended COVID-19 vaccination were explored through seven proposed personal reasons that participants placed in decreasing order of relevance: “to protect me”, “to help control the epidemic”, “to avoid transmitting the virus to my relatives”, “to follow recommendations”, “to obtain the health certificate”, “because of professional obligation”, “because the emergence of viral variants makes vaccination necessary”. Reasons for remaining unvaccinated were also explored through eleven proposed personal reasons. Participants were able to select one out of eleven reasons: “unknown serious side effects”, “not having enough perspective”, “usefulness of vaccines”, “recommendations are influenced by pharmaceutical companies”, “afraid of injections”, “state of health does not allow vaccination”, “not a disease serious enough”, “not exposed to the risk of contamination”, “already immunised”, “feeling of indirect protection by vaccinated people”, “relatives advise against it”.

An additional question explored future intention to get COVID-19 vaccine “Would you accept COVID-19 vaccination today, if recommended by your referring physician (regardless of whether you already

are vaccinated)?”.

Testimonials were evaluated by three researchers who identified recurrent themes (e.g., poor communication by authorities, decisions focussing too much on biomedical arguments). Then, two reviewers coded individual observations with regarding the presence or absence of themes in the testimonial. The database subsequently created was merged into the survey database.

2.3. Statistical analyses

We defined the vaccine experience as a combination of vaccine status (unvaccinated; vaccinated or with appointment) and motivation for vaccination (COVID-19 certificate or mandate because of professional obligation (CM) as sole, primary or additional reasons). Participants were classified as unvaccinated; vaccinated indicating CM as sole reason (CM-only); vaccinated indicating CM as first reason among others (CM + other); and vaccinated indicating CM not as first reason or not at all (CM-not-main). We excluded participants who reported to “have been infected with SARS-CoV-2, therefore not being concerned by vaccination”, according to the vaccine recommendation at the time of the survey (N = 13, 1.3%). Future vaccination intention was classified as Yes vs. No/DNK.

We used robust-variance Poisson regression models to estimate the unadjusted and adjusted prevalence ratios (aPR) for the different outcomes [26]. Independent variables that had a p-value < 0.20 in bivariable models or essential potential confounders (age, gender) were introduced into a full multivariable model. The resulting narrative assumes statistical significance at $p < 0.05$. Models were analysed with and without the perception of the individual BRB, to explore and control for the specific contribution of vaccine perception. Statistical analyses were performed using RStudio software version 4.1.1(2021-08-10).

Main analyses had four objectives (supplementary Table 1). First, we explored if the constraint of the certificate requirement had increased inequalities in vaccine uptake. Equality of vaccine status was explored, first, by comparing the determinants of observed vs. counterfactual vaccine status using a Z-test. “Counterfactual vaccine status” assumed that those who indicated CM as main reason for vaccination would not have been vaccinated in the absence of the COVID-19 certificate or mandate. The second approach consisted in evaluating the determinants of those who got vaccinated only to obtain the certificate among all persons without genuine motivation for vaccination (CM-only vs. unvaccinated). In addition, we evaluated the determinants of indicating the certificate as main motivation vs. declaring other primary motivations. We also analysed the frequency of reasons (among three mentioned) for remaining unvaccinated.

The third objective was to analyse the association of reported vaccine experience with intention of future COVID-19 vaccination (intention for future COVID-19 vaccination: yes vs. no/do not know). We hypothesized that having ceded to the certificate constraint (getting vaccinated only to obtain the certificate, CM-only) could have reduced the acceptance of future vaccination if recommended by the referring physician.

The fourth objective was to evaluate the association of reported vaccine experience with low confidence in authorities to manage the health and economic crisis caused by COVID-19 (low confidence in authorities vs. moderate-high confidence in authorities), hypothesising that having ceded to the certificate constraint could be associated with lower confidence.

In addition, we analysed the association of themes expressed in testimonials with confidence in authorities and vaccine experience levels. Finally, to explore potential mediation, the perception of the individual benefit-risk balance (BRB) and the testimonial theme of emotion was included in specific models.

3. Results

After excluding 13 participants who reported previous SARS-CoV-2 infection and thus were not eligible for vaccination, we included 972 participants (Fig. 1), 51.5% of which were women (Table 1). Age groups 18–39 years, 40–59 years and 60–75 years contributed 36.7%, 36.9% and 26.4%, respectively, of participants. One-third (30.6%) were occupationally inactive and 14.3% declared having poor financial income. Overall, 9.4% participants worked in the health or welfare sector and thus were subject to the vaccine mandate.

COVID-19 vaccination was reported by 778 participants (80.0%), 55 (5.7%) had intention to do so, (subsequently combined into “vaccinated”), while 11.5% remained unvaccinated and 1.4% declared not knowing if they were concerned by vaccination. Overall, 714 (73.5%) declared they would accept COVID-19 vaccination in the future if recommended by their referring physician. Two-thirds (607, 62.4%) of participants had a favourable perception of their individual BRB with COVID-19 vaccine and one fourth (231, 23.8%) contributed a free-text testimonial with a maximum of 377 letters.

3.1. Socio-economic determinants of observed and expected vaccine status

In the absence of certificate (“counterfactual” vaccine status), vaccine uptake would have been more likely among participants aged 60–75 years compared to younger groups (vs. 18–39 years, aPR = 1.35, p -value = 0.032), while this effect did not appear in the “observed” vaccine status (aPR = 1.03, p -value = 0.364) (Table 2). Furthermore, in the absence of certificate, vaccine uptake would have been more likely among those with moderate-high compared to low level of confidence in authorities in the management of the COVID-19 crisis (aPR = 2.04, p -value < 0.001). This effect of confidence was significantly weaker (p -value < 0.001) for the “observed” vaccine status (aPR = 1.39, p -value < 0.001). Excluding confidence from the model did not change the contribution of socio-demographic and economic variables to the explanation of any vaccine status.

3.2. Socio-economic determinants of having ceded to vaccination despite no genuine motivation for it

Among persons without genuine motivation for vaccination (CM-only and unvaccinated), professionally active participants were significantly more likely to have ceded to the certificate requirement in comparison to those professionally inactive (aPR = 3.46), without any contribution or mediation by the individual BRB perception (Table 3). Among 112 unvaccinated participants, the most frequently cited reasons for not getting vaccinated (first three items) were fear of unknown serious side effects (26.6%), belief that there was not yet enough experience with the new vaccines (25.2%) and that the usefulness of the vaccines was not yet sufficiently documented (17.0%) (supplementary Figure 1).

3.3. Association of vaccine experience with intention for further COVID-19 vaccination

Vaccinated persons in all vaccine experience groups, including those vaccinated only due to the requirement, were more likely to express intention of future COVID-19 vaccination than unvaccinated persons: CM-only (aPR = 6.00), CM + others (aPR = 13.71) and CM-not-main groups (aPR = 16.50) (Table 4). Negative individual BRB perception significantly decreased intention for future COVID-19 vaccination (negative vs. positive, aPR = 0.55), but did not substantially mediate the

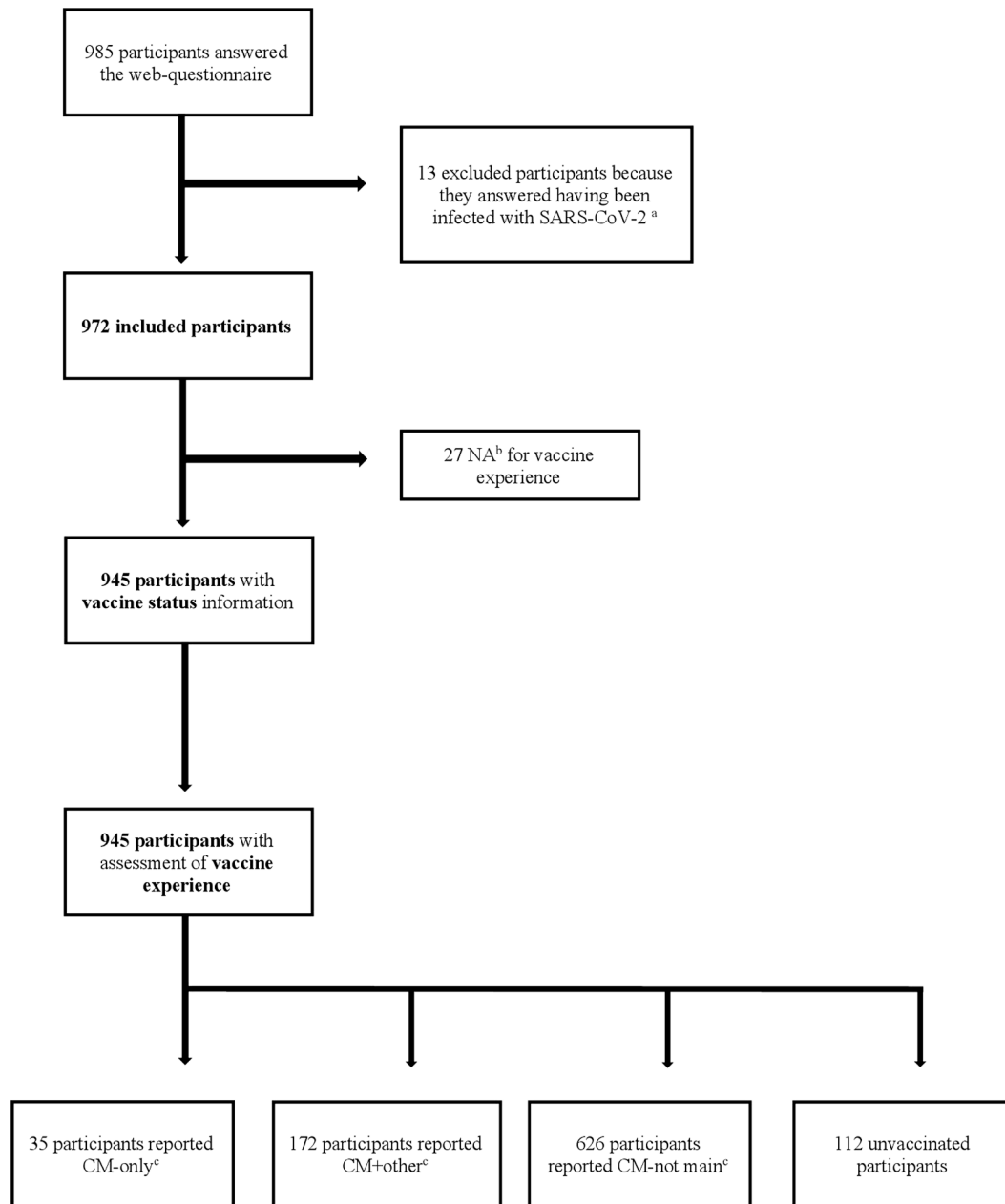


Fig. 1. Flow chart of inclusion participants. ^a We excluded participants who reported to “have been infected with SARS-CoV-2, therefore not being concerned by vaccination”, according to the vaccine recommendation at the time of the survey. ^b NA not applicable to vaccine status, participant was not sure whether concerned by vaccination or does not want to answer. ^c CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM + other); CM not mentioned as first reason (CM-not-main).

Table 1

Description of the study population according to the importance given to COVID-19 certificate or mandate (vaccine experience) (N = 972). Adults in France, Auguste 2021.

	N (%)	Unvaccinated (N = 112, 11.5%)		Vaccinated				NA*	
		N (%)	N (%)	CM-only (exclusively for requirement or professional mandate) (N = 35, 3.6%)	CM + other (first reason among others) (N = 172, 17.7%)	CM-not-main (not mentioned as first reason) (N = 626, 64.4%)	(N = 27, 2.8%)		
Demographic and socio-economic characteristics									
Gender									
Man	471 (48.5)	49 (10.4)	13 (2.8)	78 (16.6)	320 (67.9)	11 (2.3)			
Woman	501 (51.5)	63 (12.6)	22 (4.4)	94 (18.8)	306 (61.1)	16 (3.2)			
Age (in years)									
Between 18 and 39	357 (36.7)	44 (12.3)	14 (3.9)	99 (27.7)	180 (50.4)	20 (5.6)			
Between 40 and 59	359 (36.9)	42 (11.7)	14 (3.9)	53 (14.8)	245 (68.2)	5 (1.4)			
Between 60 and 75	256 (26.4)	26 (10.2)	7 (2.7)	20 (7.8)	201 (78.5)	2 (0.8)			
Region of residence									
Paris Region	184 (18.9)	19 (10.3)	4 (2.2)	36 (19.6)	116 (63.0)	9 (4.9)			
North East	212 (21.8)	24 (11.3)	6 (2.8)	30 (14.2)	148 (69.8)	4 (1.9)			
North West	222 (22.8)	23 (10.4)	8 (3.6)	41 (18.5)	143 (64.4)	7 (3.2)			
South East	245 (25.2)	36 (14.7)	12 (4.9)	46 (18.8)	147 (60.0)	4 (1.6)			
South West	109 (11.2)	10 (9.2)	5 (4.6)	19 (17.4)	72 (66.1)	3 (2.8)			
Type of locality									
Big town (> 100.000 inhabitants)	199 (20.5)	22 (11.1)	6 (3.0)	35 (17.6)	129 (64.8)	7 (3.5)			
Medium-size town (between 20.000 and 100.000 inhabitants)	254 (26.1)	29 (11.4)	5 (2.0)	50 (19.7)	163 (64.2)	7 (2.8)			
Small town (between 2.000 and 20.000 inhabitants)	292 (30.0)	34 (11.6)	13 (4.5)	52 (17.8)	188 (64.4)	5 (1.7)			
Village (<2.000 inhabitants)	227 (23.4)	27 (11.9)	11 (4.8)	35 (15.4)	146 (64.3)	8 (3.5)			
Educational level									
Lower than secondary school diploma	209 (21.5)	23 (11.0)	5 (2.4)	33 (15.8)	141 (67.5)	7 (3.3)			
Equal to secondary school diploma	240 (24.7)	34 (14.2)	7 (2.9)	41 (17.1)	154 (64.2)	4 (1.7)			
2-5 years beyond secondary school diploma	383 (39.4)	42 (11.0)	19 (5.0)	68 (17.8)	244 (63.7)	10 (2.6)			
5-7 years beyond secondary school diploma	140 (14.4)	13 (9.3)	4 (2.9)	30 (21.4)	87 (62.1)	6 (4.3)			
Professional training									
Outside health care	881 (90.6)	102 (11.6)	29 (3.3)	151 (17.1)	574 (65.2)	25 (2.8)			
Health care	91 (9.4)	10 (11.0)	6 (6.6)	21 (23.1)	52 (57.1)	2 (2.2)			
Occupational status									
Active	675 (69.4)	67 (10.5)	29 (4.3)	136 (20.1)	390 (57.8)	18 (2.7)			
Inactive	297 (30.6)	38 (12.8)	4 (1.3)	29 (9.8)	218 (73.4)	8 (2.7)			
Annual income									
> 26.700 euros	257 (26.4)	24 (9.3)	10 (3.9)	36 (14.0)	184 (71.6)	3 (1.2)			
Between 9.300 and 26.700 euros	461 (47.4)	48 (10.4)	19 (4.1)	86 (18.7)	302 (65.5)	6 (1.3)			
Between 0 and 9.300 euros	139 (14.3)	20 (14.4)	3 (2.2)	30 (21.6)	82 (59.0)	4 (2.9)			
Does not want to answer	115 (11.8)	20 (17.4)	3 (2.6)	20 (17.4)	58 (50.4)	14 (12.2)			
Minor or dependent child(ren)									
No	632 (65.0)	66 (10.4)	23 (3.6)	110 (17.4)	412 (65.2)	21 (3.3)			
Yes	340 (35.0)	46 (13.5)	12 (3.5)	62 (18.2)	214 (62.9)	6 (1.8)			
Speaking other language than French									
No	802 (82.5)	88 (11.0)	32 (4.0)	142 (17.7)	519 (64.7)	21 (2.6)			
Yes	170 (17.5)	24 (14.1)	3 (1.8)	30 (17.6)	107 (62.9)	6 (3.5)			
COVID-19-related characteristics									
Previously infected by SARS-CoV-2									
No	885 (91.0)	103 (11.6)	32 (3.6)	151 (17.1)	575 (65.0)	24 (2.7)			
Yes	87 (9.0)	9 (10.3)	3 (3.4)	21 (24.1)	51 (58.6)	3 (3.4)			
Relatives previously ill with COVID-19									
No	585 (60.2)	79 (13.5)	25 (4.3)	99 (16.9)	366 (62.6)	16 (2.7)			
Yes	387 (39.8)	33 (8.5)	10 (2.6)	73 (18.9)	260 (67.2)	11 (2.8)			
Self-reported risk factor for severe COVID-19									
No	727 (74.8)	88 (12.1)	28 (3.9)	149 (20.5)	439 (60.4)	23 (3.2)			
Yes	245 (25.2)	24 (9.8)	7 (2.9)	23 (9.4)	187 (76.3)	4 (1.6)			
Level of confidence in authorities in the management of the COVID-19 crisis									
Low	231 (23.8)	72 (31.2)	26 (11.3)	40 (17.3)	85 (36.8)	8 (3.5)			
Moderate/High	741 (76.2)	40 (5.4)	9 (1.2)	132 (17.8)	541 (73.0)	19 (2.6)			
Perception of vaccine benefit-risk balance (BRB)									
More risks than benefits	193 (19.9)	79 (40.9)	18 (9.3)	45 (23.3)	43 (22.3)	8 (4.1)			
More benefits than risks	607 (62.4)	9 (1.5)	4 (0.7)	75 (12.4)	510 (84.0)	9 (1.5)			
Does not know	172 (17.7)	24 (14.0)	13 (7.6)	52 (30.2)	73 (42.4)	10 (5.8)			
Left a free-text testimonial									
No	741 (76.2)	77 (10.4)	25 (3.4)	133 (17.9)	485 (65.5)	21 (2.8)			
Yes	231 (23.8)	35 (15.2)	10 (4.3)	39 (16.9)	141 (61.0)	6 (2.6)			
Vaccine Status									

(continued on next page)

Table 1 (continued)

	N (%)	Unvaccinated		Vaccinated			NA*	
		(N = 112, 11.5%)		CM-only (exclusively for requirement or professional mandate) (N = 35, 3.6%)	CM + other (first reason among others) (N = 172, 17.7%)	CM-not-main (not mentioned as first reason) (N = 626, 64.4%)	(N = 27, 2.8%)	
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Vaccinated	778 (80.0)	–	30 (3.9)	151 (19.4)	597 (76.7)	–	–	–
Booked an appointment for 1st injection or with intention to get appointment	55 (5.7)	–	5 (9.1)	21 (38.2)	29 (52.7)	–	–	–
Unvaccinated without intention	112 (11.5)	112 (100.0)	–	–	–	–	–	–
Not sure whether concerned	14 (1.4)	–	–	–	–	–	14 (100.0)	–
Does not want to answer	13 (1.3)	–	–	–	–	–	13 (100.0)	–
Future intention to accept COVID-19 vaccine given medical recommendation								
No	170 (17.5)	104 (61.2)	21 (12.4)	27 (15.9)	11 (6.5)	7 (4.1)	–	–
Yes	714 (73.5)	4 (0.6)	8 (1.1)	112 (15.7)	586 (82.1)	4 (0.6)	–	–
Does not know	88 (9.1)	4 (4.5)	6 (6.8)	33 (37.5)	29 (33.0)	16 (18.2)	–	–

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM + other); CM not mentioned as first reason (CM-not-main).

* NA, not applicable to vaccine experience, “Not sure whether concerned by vaccination or does not want to answer”.

Table 2

Determinants of counterfactual and observed COVID-19 vaccination status among adults in France (N = 945), August 2021. Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

	Counterfactual vaccine status: Vaccinated (N = 626) vs. Unvaccinated, CM-only or CM + other* (N = 319)		Observed vaccine status: Vaccinated (N = 833) vs. Unvaccinated (N = 112)	
	aPR	<i>p</i> -value	aPR	<i>p</i> -value
Demographic and socio-economic characteristics				
Gender				
Man	1.09	0.277	1.02	0.317
Woman	1		1	
Age (in years)				
Between 18 and 39	1		1	
Between 40 and 59	1.28	0.014	1.03	0.358
Between 60 and 75	1.35	0.032	1.03	0.364
Annual income				
> 26.700 euros	1.08	0.576	1.05	0.178
Between 9.300 and 26.700 euros	1.03	0.838	1.04	0.352
Between 0 and 9.300 euros	1		1	
Does not want to answer	0.96	0.793	0.95	0.364
Professional training				
Outside health care	1			
Health care	0.89	0.449		
Occupational status				
Active	1			
Inactive	1.07	0.557		
Minor or dependent child(ren)				
No			1	
Yes			0.96	0.107
COVID-19 related characteristics				
Relatives previously ill with COVID-19				
No	1		1	
Yes	1.02	0.806	1.04	0.098
Self-reported risk factor for severe COVID-19				
No	1			
Yes	1.17	0.088		
Level of confidence in authorities in the management of the COVID-19 crisis				
Low	1		1	
Moderate/High	2.04	<0.001	1.39	<0.001

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); requirement of certificate or professional mandate as first reason among others (CM + other).

Table 3

Determinants of vaccine experience (vaccine uptake and motivation) among participants without genuine motivation for vaccination (N = 147) and among vaccinated participants (N = 112). Adjusted Prevalence Ratio (aPR), *p*-value obtained with multivariable robust-variance Poisson regression model.

	Among persons without genuine motivation for vaccination; CM-only (N = 35) vs. Unvaccinated (N = 112)			
	aPR	<i>p</i> -value	aPR with BRB	<i>p</i> -value
Gender				
Man	1		1	
Woman	1.22	0.528	1.23	0.515
Age (in years)				
Between 18 and 39	0.58	0.188	0.72	0.458
Between 40 and 59	0.56	0.181	0.67	0.382
Between 60 and 75	1		1	
Professional training				
Outside health care	1		1	
Health care	1.38	0.382	1.45	0.345
Occupational status				
Active	3.76	0.013	3.46	0.020
Inactive	1		1	
Annual income				
> 26,700 euros	1		1	
Between 9,300 and 26,700 euros	0.84	0.648	0.78	0.504
Between 0 and 9,300 euros	0.60	0.376	0.58	0.321
Does not want to answer	0.44	0.136	0.41	0.113
Speaking other language than French				
No	1		1	
Yes	0.45	0.157	0.46	0.167
Perception of vaccine benefit-risk balance (BRB)				
More risks than benefits			0.70	0.449
More benefits than risks			1	
Does not know			1.42	0.487

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requir

Table 4

Association of vaccine experience with intention for future vaccine, and with and level of confidence in the authorities' management of the COVID-19 crisis among adults in France (N = 972), August 2021. Adjusted Prevalence Ratio (aPR), p-value obtained with multivariable robust-variance Poisson regression model.

	Intention (N = 714) vs. No intention /do not know (N = 258)				Low (N = 231) vs. Moderate-high level of confidence (N = 741)			
	aPR	p-value	aPR with BRB	p-value	aPR	p-value	aPR with BRB	p-value
Demographic and socio-economic characteristics								
Gender								
Man	1.05	0.054	1.03	0.209	1.22	0.058	1.26	0.028
Woman	1		1		1		1	
Age (in years)								
Between 18 and 39	1		1		0.85	0.371	0.85	0.350
Between 40 and 59	1.02	0.505	0.99	0.781	1.09	0.617	1.10	0.565
Between 60 and 75	1.04	0.487	1.00	0.965	1		1	
Type of locality								
Big town (more than 100.000 inhabitants)					1		1	
Medium-size town (between 20.000 and 100.000 inhabitants)					0.99	0.937	0.99	0.972
Small town (between 2.000 and 20.000 inhabitants)					1.06	0.719	1.07	0.647
Village (<2.000 inhabitants)					1.23	0.206	1.22	0.214
Educational level								
Lower than secondary school diploma					1		1	
Equal to secondary school diploma					0.71	0.037	0.72	0.053
2-5 years beyond secondary school diploma					0.98	0.874	1.00	0.988
5-7 years beyond secondary school diploma					0.88	0.513	0.90	0.571
Professional training								
Outside health care					1		1	
Health care					0.70	0.107	0.69	0.079
Occupational status								
Active	1		1		1		1	
Inactive	1.01	0.752	1.00	0.907	1.12	0.475	1.13	0.440
Annual income								
> 26.700 euros	1		1					
Between 9.300 and 26.700 euros	0.99	0.714	0.98	0.502				
Between 0 and 9.300 euros	0.91	0.066	0.93	0.170				
Does not want to answer	0.92	0.114	0.92	0.084				
Speaking other language than French								
No	1		1					
Yes	0.96	0.318	0.98	0.673				
COVID-19 related characteristics								
Relatives previously ill with COVID-19								
No	1		1		1		1	
Yes	0.99	0.725	1.00	0.886	0.87	0.226	0.87	0.199
Self-reported risk factor for severe COVID-19								
No	1		1		1		1	
Yes	1.04	0.174	1.02	0.532	1.44	0.003	1.45	0.002
Level of confidence in the authorities' management of the COVID-19 crisis								
Low	1		1					
Moderate/High	1.17	0.002	1.08	0.093				
Vaccine experience								
Unvaccinated	1		1		5.02	<0.001	3.08	<0.001
CM-only	6.41	0.001	6.00	0.002	5.94	<0.001	3.81	<0.001
CM + others	17.20	<0.001	13.71	<0.001	2.04	<0.001	1.63	0.021
CM-not-main	23.72	<0.001	16.50	<0.001	1		1	
NA	4.10	0.037	3.38	0.068	2.53	0.014	2.01	0.072
Perception of vaccine benefit-risk balance (BRB)								
More risks than benefits			0.55	<0.001			2.02	<0.001
More benefits than risks			1				1	
Does not know			0.71	<0.001			1.58	0.010

CM, Requirement of COVID-19 certificate or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement or professional mandate (CM-only); CM as first reason among others (CM + other); CM not mentioned as first reason (CM-not-main). NA, not applicable to vaccine experience, "Not sure whether concerned by vaccination or does not want to answer".

effect of vaccine experience on this intention.

3.4. Association of vaccine experience with confidence in authorities for managing the COVID-19 crisis

Levels of confidence were comparable between unvaccinated persons and those vaccinated only due to constraint (CM-only vs. unvaccinated, aPR = 1.18, non-significant) (Table 4). Negative individual BRB perception was significantly associated with low confidence (aPR = 2.02) but did not substantially mediate the association between vaccine experience and low confidence.

Testimonials were represented through eleven themes: emotional

expression, criticism about amorality, infantilisation, contradiction in decisions or poor communication; positive or negative comments on epidemic response strategy, scientific reasoning, biomedical vs. societal trade-offs, rigor vs. authoritarianism, organisation of pandemic management and hidden vaccine requirement. Testimonials were left by 31.3% of unvaccinated and 22.8% of vaccinated participants. Participants with low level of confidence in the authorities (231, 23.8%) were significantly more likely to leave a testimonial (PR 2.09) compared to those with moderate-high level of confidence (Table 5). Themes significantly associated with lower confidence were criticism of morality (PR = 1.76; an association that was fully mediated by expression of emotion) and poor communication (PR = 1.66; an association that was fully

Table 5

Association of testimonial themes with the level of confidence in authorities in the management of the COVID-19 pandemic (N = 231) and with vaccine experience among participants without genuine motivation for vaccination (N = 45). Crude Prevalence Ratio (PR) with having reported a negative emotional expression, *p*-value obtained with bivariable robust-variance Poisson regression model.

		Low (N=231) vs. Moderate-high level of confidence (N=741)		Among participants without genuine motivation for vaccination; CM-only (N=35) vs. Unvaccinated (N=112)			
		Low level of confidence	Crude PR	<i>p</i> -value	CM-only	Crude PR	<i>p</i> -value
		N (%)		N (%)			
Having reported a free-text testimonial							
No		741 (76.2)	140 (60.6)	1	25 (71.4)	1	
Yes		231 (23.8)	91 (39.4)	2.09	10 (28.6)	0.91	0.793
				< 0.001			
Testimonial theme	Example	Low (N=91) vs. Moderate-high level of confidence (N=140)					
		Low level of confidence	Crude PR	<i>p</i> -value	aPR with Negative emotional expression	<i>p</i> -value	
		N (%)					
Criticism about amorality							
Not mentioned		192 (83.1)	67 (73.6)	1			
Mentioned	<i>"A series of lies"</i>	39 (16.9)	24 (26.4)	1.76	0.017	1.24	
Emotional expression*							
Not reported		157 (68.0)	44 (48.4)	1			
Negative	<i>"I'm furious because of liberticide measures"</i>	68 (29.4)	46 (50.6)	2.41	<0.001		
Mixed	<i>"Exhausting but necessary"</i>	2 (0.9)	1 (1.1)				
Positive	<i>"They are proportionate to this very serious situation"</i>	4 (1.7)	0 (0.0)				
Authoritarianism perception							
Not mentioned		204 (88.3)	80 (87.9)	1			
Not enough authoritarianism	<i>"Not strict enough to enforce the laws"</i>	15 (6.5)	3 (3.3)	0.51	0.252		
Too much authoritarianism	<i>"Dictatorship, rule by terror"</i>	12 (5.2)	8 (8.8)	1.70	0.152		
Obligation							
Not mentioned		210 (90.9)	85 (93.4)	1			
Not restrictive enough	<i>"I don't understand why vaccination it is not mandatory"</i>	10 (4.3)	2 (2.2)	0.45	0.263		
Too restrictive	<i>"Make vaccination compulsory with a pass it's inhuman"</i>	11 (4.8)	4 (4.4)	0.99	0.982		
Organisation of pandemic management							
Not mentioned		84 (36.4)	22 (24.2)				
Negative perception	<i>"Everything is done too slowly"</i>	131 (56.7)	69 (75.8)				
Positive perception	<i>"Government did what should be done"</i>	16 (6.9)	0 (0.0)				
Epidemic response strategy							
Not mentioned		167 (72.3)	74 (81.3)				
Negative comment	<i>"Not useful to close so-called non-essential businesses"</i>	56 (24.3)	17 (18.7)				
Positive comment	<i>"Tenacity about vaccination has paid off"</i>	8 (3.5)	0 (0.0)				
Scientific reasoning							
Absent		224 (97.0)	89 (97.8)	1			
Present	<i>"The so-called scientific opinions are far from being consistent and sow doubt"</i>	7 (3.0)	2 (2.2)	0.72	0.645		
Biomedical vs. societal trade-off							
Absent		226 (97.8)	88 (96.7)	1			
Present	<i>"The economic and the health crisis are not easy to manage"</i>	5 (2.2)	3 (3.3)	1.54	0.461		
Contradiction in decisions							
Not mentioned		185 (80.1)	73 (80.2)	1			
Mentioned	<i>"It's a nonsense, one day no mask the next day it's mandatory"</i>	46 (19.9)	18 (19.8)	0.99	0.975		
Poor communication							
Not mentioned		172 (74.5)	58 (63.7)	1			
Mentioned	<i>"Confusion and lack of transparency..."</i>	59 (25.5)	33 (36.3)	1.66	0.020	1.41	
Hidden vaccine requirement							
Not mentioned		219 (94.8)	89 (97.8)				
Negative	<i>"I don't like the hidden obligation at all"</i>	5 (2.2)	2 (2.2)				

(continued on next page)

Table 5 (continued)

		Low (N=231) vs. Moderate-high level of confidence (N=741)			Among participants without genuine motivation for vaccination; CM-only (N=35) vs. Unvaccinated (N=112)		
		Low level of confidence	Crude PR	p-value	CM-only	Crude PR	p-value
N (%)		N (%)			N (%)		
Positive	<i>"Vaccination is finally accelerating"</i>	7 (3.0)	0 (0.0)				
Infantilisation							
Not mentioned		227 (98.3)	87 (95.6)	1			
Mentioned	<i>"They imagine that the population is incapable of acting correctly on its own"</i>	4 (1.7)	4 (4.4)	2.61	0.061		

ΔCOVID-19 Certificate for requirement or professional mandate (CM). We classified vaccinated participants by reasons for COVID-19 vaccination: exclusively for requirement and professional mandate (CM-only); CM as first reason among others (CM + other); and no CM as first reason (CM-not-main).

*Positive and mixed emotional expressions not included in analysis (N = 225).

PR is only calculated if ≥ 2 observations per group.

mediated by expression of emotion). Because of negativity bias [27], expression of emotion was analysed as negative vs. no emotion reported. No association between vaccine experience and testimonial themes were found (Table 5).

4. Discussion

In this cross-sectional study including a representative sample of adults living in France in August 2021, we estimated that the COVID-19 certificate requirement increased vaccine uptake among younger persons and persons with low levels of confidence in authorities, without creating substantial social inequalities. Compared to unvaccinated persons, declaring vaccination only to obtain the certificate was associated with active occupational status, but also with higher intention for future vaccination. Confidence in authorities for managing the health and economic crisis caused by COVID-19 was strongly associated with vaccine uptake. However, adjusted confidence levels were similar between unvaccinated persons and those reporting vaccination only to obtain the certificate, although this finding is limited by small sample size.

Beyond individual protection against COVID-19, increasing COVID-19 vaccine uptake among the younger population can be considered a public health achievement under the assumption that this reduced the viral transmission and thus slowed the epidemic progress in 2021. On the other hand, substantial evidence now suggests that the indirect protection effect from COVID-19 vaccination is short-lived and the impact beyond three months primarily consists of protection against severe disease [28,29]. In contrast, in France, the age group >80 years has remained the group with the lowest vaccine coverage (89.20% as of April 1, 2022) [23]. A stronger incentive for vaccination or even a mandate in this group may have further reduced COVID-19 mortality. The COVID-19 certificate requirement was tailored to a young active population and counter-intuitively less targeted to those with the greatest potential benefit from vaccination. This increases health inequalities between professionally active and inactive population. This illustrates that incentive-coercive policies should be adapted to the target population for optimal impact and such elements should be considered in future vaccine requirements and mandates.

Vaccine programs need to monitor for any inadvertent creation of inequalities in uptake and counteract them. An important inconvenience of soft requirements compared to mandates is that they may increase social inequalities of vaccine uptake, as specific groups may refrain from services and social participation rather than accept vaccination. Several studies have reported that isolated or professionally inactive persons remained unvaccinated during the COVID-19 pandemic [30–32], as they perceived to be at lower risk of infection due to low social interactions [30]. In this sense, our results are reassuring, as they suggest that the COVID-19 certificate requirement for public spaces and services access did not create substantial social inequalities and reduced inequalities related to confidence in authorities. However, among persons without

genuine motivation for vaccination, the requirement acted only on professionally active persons but had no impact on unemployed and retired persons, people living with disability, and homemakers, probably as their need to attend services and public places was lower. At the population level, this effect may be negligible, but a clear vaccine mandate may have avoided such a trend and protected persons in marginalised groups from severe disease related to COVID-19. Such effects must be carefully considered during policy development, to avoid the creation of inequalities of opportunity.

One concern about incentive-coercive policies is that constraining people to vaccination could lead to a reduced acceptance of following vaccinations [6,33]. Thus, a feeling of constraint could emerge from the belief that negative outcomes occurred because they ceded to vaccination [22]. However, in our study, ceding to the constraint does not appear to have decreased future COVID-19 vaccine intention, rather, it was associated with higher intention compared to those remaining unvaccinated. We cannot conclude whether this was a specific positive psychological effect or whether those ceding had weaker initial opposition. However, the fact that the perception of benefits and risks did not explain the association suggests that no rationalised consideration was involved in this difference in intention for future vaccination. Interestingly, as the certificate requirement or professional mandate was the only vaccination motivation for just 4% of the population, suggesting that the policy in France acted as an incentive rather than a coercion.

A large body of literature has documented the association between the level of confidence in authorities and vaccine intention, prior [34,35] and during the COVID-19 pandemic [36,37]. This is reflected in our finding that even under the certificate requirement and even in multiply adjusted analyses, confidence in authorities remained an important determinant of vaccine uptake. The level of confidence in authorities appeared similar among those ceding to the requirement or remaining unvaccinated, which suggests that the low confidence pre-existed and in fact was not further impacted by the incentive-coercive policy. In France, several governmental decisions and management practices during the COVID-19 pandemic were criticized [38], such as the delayed recommendation of facial masks and the implementation of a strict lockdown during spring 2020. Such decisions in the context of scientific uncertainty could have impacted the participants' confidence in authorities. This aligns with testimonials criticising the poor communication regarding the organisation of epidemic measures, which was associated with low confidence in authorities. Low confidence in authorities was also associated with criticism about their morality (i.e., lies or corruption). However, both associations were fully explained by expression of emotion as the latter mediated the relation of these testimonials with confidence in authorities. These observations suggest that lower confidence – at least in the context of August 2021 when the pandemic thread started to resolve – depended not only on specific decisions made by authorities, but also underlying resentment. This joins reports relating COVID-19 vaccine intention and uptake to voting

behaviours at the extremes of the political spectrum [22,39]. The conclusions on pre-existing resentments would also be congruent with the finding that the level of confidence in August 2021 was similar to that observed in November 2020 using a similar survey methodology [40]. Overall, this illustrates that building and maintaining trustful relations between different population groups and decision makers is an essential component of pandemic preparedness.

5. Limitations

Our study has several limitations. The cross-sectional design of this study did not allow any conclusion on the direction of association between vaccine experience and confidence in authorities. The self-administered questionnaire may have led to misunderstanding, while reducing social-desirability bias. Reporting constraint as the sole motivation for vaccination might have been a way to express criticism with such decisions, while other persons may have given post-hoc sense to “forced” vaccination. The generalizability of our results is naturally limited by several factors: our results apply specifically to the initial vaccination campaign against COVID-19 in France: a passive campaign with large sub-regional vaccine centres and little vaccine promotion apart from governmental announcements. Participants were members of an online-panel, therefore - despite quota sampling - people living in poverty, low health literacy and possibly high-risk behaviour were likely underrepresented. Our study found that age and confidence in authorities were the only determinant of counterfactual vaccine uptake in the French adult population, while an ecological analysis [39] and a large-scale survey described economic inequalities in July 2021 [36]. Despite using a quota for socio-economic status, our study participant selection required access to an electronic device, possibly excluding the most deprived population groups with lower vaccine uptake. We also cannot infer our results to persons aged ≥ 76 , who had relatively low coverage in France despite being at highest risk of severe COVID-19 infections, and French citizens from overseas departments where inequalities tend to be higher than in mainland France [36,41].

6. Conclusions

In summary, our study provides evidence that the requirement of a COVID-19 certificate in France during the initial vaccination campaign has neutralized the impact of younger age and reduced the one of the low confidence in authorities as negative determinants of vaccine uptake. Of concern is the fact that, specifically among those genuinely refusing vaccination, the requirement could have further isolated professionally inactive persons. However, the vaccination certificate requirement was not related to lower intention for future vaccination. Our analysis helps refine our understanding of the impact that vaccine requirements can have on vaccine programmes and will guide decision-makers in tailoring vaccine mandates and requirements for vaccine response to future epidemics. Future incentive-coercive policies on vaccination should specifically address population groups with low levels of confidence in authorities.

Funding

This research is part of a PhD project funded by the French network of doctoral programmes, coordinated by EHESP French School of Public Health. This study was jointly funded by the laboratories GAINS (Le Mans University), GRANEM (University of Angers), LIRAES (University of Paris) and the faculty of Economics, Law and Management of the University of Angers.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2023.07.002>.

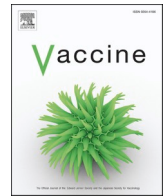
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Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Analyzing the 7C psychological antecedents of vaccine acceptance throughout the COVID-19 pandemic among healthcare sector workers in France: A repeated cross-sectional study (CappVac-Cov)

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ARTICLE INFO

Keywords:

COVID-19 vaccination
Healthcare workers
Vaccine acceptance
Vaccine hesitancy
Benefit-risk balance

ABSTRACT

Background: Across various stages of the COVID-19 pandemic and related vaccine recommendations in France, we assessed the association of the 7C-psychological antecedents with vaccine uptake/intention for booster vaccination among healthcare-sector workers (HCSWs). We also assessed whether 7C-antecedent profiles changed over time.

Methodology: The Research Group for the Prevention of Occupational Infections in Healthcare Workers (GERES) conducted three repeated web-surveys which were disseminated by email chain-referral among HCSWs throughout France. The questionnaires waves took place: July-November 2021, February-March 2022 and January-March 2023 (P2, P3 and P4). We also reanalysed data from a prior similar study conducted late 2020-early 2021 (Moirangthem et al. (2022)) (P1). To evaluate the association of 7C-items with vaccine uptake-intention for future vaccination, we estimated adjusted prevalence ratios (aPR) using robust variance Poisson regression. We report the 7C-item population attributable loss in vaccine intention.

Results: The four surveys (P1-P4) encompassed 5234, 339, 351 and 437 participants. At earlier stages of the vaccine campaign, the principal antecedents of vaccine intention were favorable perception of vaccination benefit-risk-balance (BRB) (vs. unfavorable, aPR: 2.32), reactance to employer encouragement for vaccination (motivates vs. dissuades-me, aPR:2.23), vaccine confidence (vs. not-being-confident, aPR: 1.71) and social conformism towards vaccination (favorable vs. skeptical opinion in private environment, aPR: 1.33). Under a vaccine mandate for HCSWs, only perceiving vaccination as a collective action was associated with current vaccine status (agree vs. disagree, aPR: 2.19). At later stages of the epidemic, hypothetical booster vaccine intentions were strongly associated with BRB perception (favorable vs. unfavorable, aPR: 2.07) and perceiving vaccination as a collective action (agree vs. disagree, aPR: 1.69). Fearing a severe side effect from vaccination decreased population vaccine intention by 26.2 %.

Conclusion: Our results suggest that both 7C-antecedents and their association with vaccine behaviour can change over time, and underscore the importance of assuring confidence in vaccine safety.

1. Introduction

Vaccine acceptance appears as a variable state that depends on the specific vaccine [1,2]. The World Health Organization asks countries to monitor vaccine hesitancy in their annual joint reporting form to identify changes and trends over time and detect vaccine concerns at the

early stages [3,4]. To better understand vaccine acceptance, a 3C-model was developed which encompassed the main drivers of vaccine acceptance, referred to as the psychological antecedents of vaccination [5]. This model comprises Complacency (not perceiving diseases as high risk and vaccination as necessary), Convenience (perception of access barriers) and Confidence (lack of trust in safety and effectiveness of

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<https://doi.org/10.1016/j.vaccine.2024.07.004>

Received 6 April 2024; Received in revised form 1 July 2024; Accepted 2 July 2024

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vaccines). Betsch et al. (2018) [6] extended the original model to a 5C-model integrating Calculation (deliberation between benefits and risks of the vaccine) and Collective responsibility (willingness to protect others by one's own vaccination). During the COVID-19 pandemic, Moirangthem et al. (2022) [7] and Oudin Doglioni et al. (2023) [8] proposed and validated an extended version of the psychological antecedents' model including 7 dimensions, which explained well Health Care Sector Workers' (HCSWs) vaccine acceptance during the pandemic. Confidence was split into *Confidence in the vaccine safety* and *Confidence in systems (capacity for reactance)*, and *Social conformism* (influence of the social environment) added as an additional item.

HCSWs have a strong influence in vaccine decisions of the general population [9–12] and the COVID-19 crisis has illustrated the importance of their commitment to health recommendations, through care practice and own health protection. However, vaccine hesitancy repeatedly has been reported in HCSWs [10,13–15] and uptake of the influenza vaccine remains low in France among HCSWs [16]. The COVID-19 vaccine campaign was characterized by an initial low uptake in HCSWs, until vaccine mandates were implemented [17]. The enactment of this mandate raised important ethical concerns between professional obligation of HCSWs to protect others and the individual autonomy of the HCSW on its own medical decision [18]. Due to these evolutions over the course of the COVID-19 vaccine campaign in HCSWs, understanding the drivers of vaccine acceptance among HCSWs requires repeated assessment over time.

To our knowledge, no study has monitored HCSWs' psychological antecedents of vaccination over time. This lack of evidence makes it difficult to anticipate vaccine uptake during crises such as COVID-19 pandemic. In addition, it remains unclear in how far individual attitudes about vaccination vary or can be influenced.

This study aimed to evaluate, among HCSWs in France and across evolving vaccine recommendations made by the French government at different stages of the COVID-19 pandemic, i) the association between the 7C-psychological antecedents of vaccination and vaccine intentions, and ii) changes of 7C-psychological antecedents overtime.

2. Methodology

2.1. Study design and participant inclusion

We conducted a series of three repeated cross-sectional studies. The Research Group for the Prevention of Occupational Infections in Healthcare Workers (GERES) implemented repeated online surveys via the Sphinx (two first surveys) and RedCap (third survey) survey platforms. Study invitations were disseminated by email to a group of HCSWs throughout France who previously had signalled interest to participate in a longitudinal study. Participants were encouraged to chain-refer the invitation email for the first, but not the following surveys. The questionnaire waves took place between 13 July to 30 November 2021 (study period P2), 11 February and 28 March 2022 (study period P3) and 12 January to 13 March 2023 (study period P4). Any ≥ 18 -year-old health professional working in mainland France was eligible for participation.

We also used data from a prior study conducted between December 18 2020, and February 1 2021 [7]. In this study, the GERES also published an online questionnaire on the Sphinx online survey platform, which was disseminated throughout France through chain referral. Several formal and informal networks of hospital-based and private practice HCSWs and of nursing home directors contributed to its dissemination. This study had comprised any ≥ 18 -year-old professional in healthcare- or welfare-related careers, including physicians, nurses, nurse assistants, other paramedical professionals and social workers, administrative and logistic staff.

We labelled the Moirangthem et al. (2022) [7] study as the "first study-period" and subsequent studies as the "second", "third" and "fourth" study periods.

For all study periods, since each participant could forward the survey across its own networks, we did not estimate a response rate. We did not count visits to the survey website, neither.

The planning, conduct and reporting of the study were in line with the Declaration of Helsinki (2013) and the GDPR regulation. The study protocol was approved by the Institut Pasteur IRB on 8 July 2021. Because the data collection was anonymous without risk of indirect identification and did not collect any sensitive information, only self-declared biomedical information, no informed consent or full ethical review was required according to French regulation.

2.2. Data collection

Each survey questionnaire, P1-P4, contained three parts: (1) socio-demographic characteristics, (2) perceived health status, perceptions related to the COVID-19 epidemic and information on the intention to accept COVID-19 vaccination, (3) attitudes and knowledge related to COVID-19 vaccination, based on a short list of 7C psychological antecedents of vaccination, which has been previously published [7]. As the evidence of COVID-19 epidemiology and COVID-19 vaccines evolved during the pandemic, we decided not to explore knowledge items of the 7C-model at P4. Each 7C-dimension was evaluated by at least one attitude and one knowledge, in total, the short version of the 7C questionnaire included 10 questions associated with attitudes towards vaccination and 9 associated with knowledge about the vaccine. The 7C-knowledge items were presented either as a statement to which participants could answer 'True', 'Do not know' or 'False' or requested a single choice answer to a question from several options which included 'Do not know' (Supplementary Table 1). The 7C-attitudes were explored through 5-point Likert-scale which is a psychometric response method where respondents can state their level of agreement in five points: (1) strongly disagree, (2) disagree, (3) neither agree nor disagree, (4) agree, (5) strongly agree. For analyses, 7C-items were grouped into 3 categories: i) strongly disagree and disagree, ii) undecided, iii) strongly agree and agree.

2.2.1. Monitoring of COVID-19 vaccine intentions and uptake

P1 explored vaccine intention through the question "If a vaccine was available now against Coronavirus (COVID-19), would you get vaccinated?" (**Current Vaccine Intention December 2020-February 2021**).

P2 occurred between July and November 2021, when daily COVID-19 incidence rate ranged between 43 and 370 per 100,000 persons [19] and COVID-19 vaccination was mandatory for HCSWs. During P2, participants' vaccine intentions were explored through the question "currently, what is your vaccination intention (summer-fall 2021)?" (**Current Vaccine Uptake summer-fall 2021**), and on hypothetical booster intention to get COVID-19 vaccine "Would you accept a booster of this vaccine (outside of any obligation)?" (**Hypothetical booster vaccine intention**).

P3 occurred between February and March 2022, when daily COVID-19 incidence ranged between 540 and 1 500 per 100 000 persons [19] and booster vaccination was mandatory for HCSWs. P3 explored booster vaccine uptake (**Current booster vaccine uptake**) and among those vaccinated with it, we explored hypothetical vaccine intention for a second booster "Currently, what is your vaccination intention regarding a booster in the fall of 2022, if it was recommended (outside of any obligation)?" (**Hypothetical 2nd booster vaccine intention**).

P4 occurred between January and March 2023, when daily COVID-19 incidence ranged between 33 and 70 per 100 000 persons [19]. Booster was still mandatory for HCSWs during the survey, but the mandate was lifted soon after, on 13 May 2023 [20]. At P4 the question "Today, would you accept vaccination against COVID-19, if it was recommended to you by your general practitioner (GP) (outside of any obligation)?" was asked to the full sample (**Hypothetical 3rd booster vaccine intention**). The last study-period focused on further booster

vaccine intention and did not explore any vaccine uptake, in the context of the COVID-19 vaccination mandate enacted by the French government in July 2021 [21,22].

2.2.2. Covariables: Examining Socio-demographic, and psychological factors in COVID-19 vaccination Intention and Uptake

Socio-demographic information comprised gender, age, region of residence, professional category.

7C antecedents of vaccination (7C-model): Confidence in the vaccine was evaluated as perceived vaccination safety, Confidence in systems as reliability on entities that give vaccine recommendations, Complacency referred to the perceived risks of vaccine-preventable diseases, Calculation referred to the perception of the benefit-risk balance (BRB) of vaccination; Collective responsibility, referred to perceiving vaccination as a collective action to stop the pandemic; Social conformism, to the majority opinion on COVID-19 vaccination in the social environment, and Convenience the perceived accessibility of vaccination. 7C-items were adapted during each study period to the current vaccine recommendation: questions in P1 related to hypothetical primo-vaccination, P2 to hypothetical first booster vaccine, P3 to a hypothetical second booster, P4 to a hypothetical third booster dose.

2.3. Statistical analyses

Due to the evolution of biomedical evidence on COVID-19 vaccines during the pandemic, we opted not to explore the association between 7C-knowledge items and vaccine acceptance, and only described frequencies of knowledge items.

We used robust variance Poisson regression models to estimate the unadjusted and adjusted prevalence ratios (aPR) and 95%-confidence intervals (95%-CI) to explore the association of participant characteristics and individual 7C-items with vaccine status and future vaccine intention at each period. To identify socio-demographic and health-related determinants of vaccine intention, we included independent variables that had a p-value < 0.20 in bivariable models. Essential potential confounders (age, gender and profession category) were forced into the full multivariable models. In France, most professional categories in the healthcare and welfare sector correspond to educational trajectories [23,24], we therefore did not add educational level to the models.

In the multivariable analysis, the 5-point Likert-scale of the 7C-attitudes were grouped; categories 1 and 2 as disagree, and 4 and 5 as agree.

Also, to assess the impact of 7C-items on vaccine intention at the population level, we estimated the loss in vaccine intention attributable to each 7C-attitude (population attributable risk):

$$\Delta CV_{\text{pop}} = CV_{\text{RF}+} * (aPR_{\text{RF}} - 1) * Pr_{\text{RF}+}$$

$CV_{\text{RF}+}$: frequency of no vaccine intention among those having a negative attitude towards the C-item.

aPR_{RF} = adjusted prevalence ratio of C-item with vaccine intention/uptake.

$Pr_{\text{RF}+}$ = frequency of the negative C-attitude in the sample.

3. Results

P1 encompassed the largest sample with 5 234 participants; mainly females (78.4 %). Participants were aged 18–34 years (23.2 %), 35–49 years (40.0 %) and 50 years or older (36.8 %). Nurses (22.9 %), nurse assistants (9.4 %) and biomedical professionals (including physicians, midwives, pharmacists and biologists) (27.7 %), were among the largest groups (Table 1).

Subsequent surveys (P2, P3 and P4) included 339, 351, and 437 participants, respectively. Participants characteristics remained similar to those in P1, with predominantly female participants (76.1 %, 74.6 % and 76.1 %, respectively) and balanced age representation (Table 1).

Contribution by nurses increased from 22.9 % at P1 to 34.7 % at P4 and by biomedical professions from 27.7 % (P1) to 30.3 % (P4). Nurse assistants' contribution decreased from 9.4 % to 1.9 %, and contribution by administrative and technical staff from 24.4 % to 21.1 %. The proportion of hospital workers remained stable (around 65%).

3.1. Evolution of self-reported vaccine intentions/ uptake among participants (Supplementary Fig. 1)

Primary intended vaccination (uptake or intention) increased from 58.1 % (winter 2020–2021) to 91.2 % (summer-fall 2021) (P2), and vaccine refusal decreased from 22.0 % to 8.8 %. At P2, only 8.8 % of 339 remained unvaccinated and 9 of 339 (2.7 %) participants cited vaccination mandate as a main reason for getting vaccinated against COVID-19.

Hypothetical future booster vaccine intentions were assessed at P2 and P3 vaccinated participants or those with intention to do so. In summer-fall 2021 (P2), while 91.2 % of the 339 participants were vaccinated in the context of the mandate, only 78.1 % were willing to accept a hypothetical booster vaccine if recommended by their General Practitioner (GP), and 11.4 % were undecided. Similarly, in winter-spring 2022 (P3), while 93.7 % of the 351 participants were vaccinated in the context of the mandate, only 76.9 % were willing to accept a hypothetical second booster dose, and 11.2 % were undecided. Similarly, in winter 2023 (P4), 73.1 % of participants were willing to accept a hypothetical third dose of booster if recommended by their GP.

3.2. Description of 7C-attitudes

Several items of 7C-antecedents of vaccination showed substantial evolution across surveys, with particularly pronounced differences between P1 and P2, i.e., between winter 2020–21 and summer-fall 2021. The percentage of participants describing a favourable majority opinion about COVID-19 vaccination among family and friends (Social conformism), increased from 34.5 % at P1 to 68.0 % at P2-P3, and remained at 57.2 % at P4. The percentage of participants perceiving more benefits than risks from COVID-19 vaccination (Calculation) increased substantially between P1 (56.0 %) and P2 (72.6 %) and then stabilized with 69.0 % at P3, and 64.0 % at P4 (Table 1). The percentage of participants not expressing fear of getting severe side effects from vaccination (Confidence in the vaccine) substantially increased from P1 (48.6 %) to P2 (65.5 %), and then to P4 (72.5 %) (Table 1). The percentage of participants expressing no difficulties in getting vaccinated (Convenience) increased from 72.9 % at P1 to around 88.0 % thereafter.

Other antecedents remained relatively constant across surveys. The percentage of participants perceiving the employer's incitation for vaccination as motivating or dissuading (Confidence in the system) remained at 30–33 % and 5–8 %, respectively, across all surveys. The percentage of participants who perceived vaccination as a collective action (Collective responsibility) remained relatively stable (around 76.0 % at P1, P3 and P4, with a peak at 81.4 % at P2). The percentage of participants afraid of getting a severe form of COVID-19 (Complacency) increased slightly from 26.4 % to 33.3 %.

Knowledge items of the 7C-model remained constant across P1 to P3, except for 'Serious side effects might occur > 6 months after vaccination' (False; 18.2 % at P1 and 67.2 % at P3) and 'The vaccine blocks transmission of the virus to those around you in case of infection.' (False; 50.2 % at P1 and 18.5 % at P3) (Supplementary Fig. 2).

3.3. Associations between 7C-attitudes dimensions and vaccine intention (Table 2 & Fig. 1)

Calculation (perceived BRB) was the principal antecedent of primary vaccination intention in winter 2020–21 (P1) (favourable vs. unfavourable, aPR: 2.92; p-value < 0.001). Under the vaccine mandate for HCSWs, its association with vaccine uptake was dissipated, but regained

Table 1
Description of the study population. Healthcare sector workers in France. CappVac-Cov study.

	P1 December 2020–February 2021 N = 5 234	P2 July–November 2021 N = 339	P3 February–March 2022 N = 351	P4 January–February 2023 N = 360
Socio-demographic characteristics				
Gender				
Male	1 131 (21.6 %)	81 (23.9 %)	89 (25.4 %)	86 (23.9 %)
Female	4 103 (78.4 %)	258 (76.1 %)	262 (74.6 %)	274 (76.1 %)
Age (in years)				
18–34	1 215 (23.2 %)	58 (17.1 %)	55 (15.7 %)	45 (12.5 %)
35–49	2 092 (40.0 %)	137 (40.4 %)	146 (41.6 %)	152 (42.2 %)
>=50	1 927 (36.8 %)	144 (42.5 %)	150 (42.7 %)	163 (45.3 %)
Region of work				
DROMs and Corsica	23 (0.4 %)	4 (1.2 %)	3 (0.9 %)	2 (0.6 %)
North-Est	1 183 (22.6 %)	83 (24.5 %)	96 (27.4 %)	77 (21.5 %)
North-West	1 301 (24.9 %)	67 (19.8 %)	61 (17.4 %)	65 (18.1 %)
South-Est	1 683 (32.2 %)	65 (19.2 %)	77 (21.9 %)	100 (27.9 %)
South-West	446 (8.5 %)	38 (11.2 %)	53 (15.1 %)	47 (13.1 %)
Paris Region	598 (11.4 %)	82 (24.2 %)	61 (17.4 %)	68 (18.9 %)
Profession				
Biomedical profession	1 449 (27.7 %)	107 (31.6 %)	122 (34.8 %)	109 (30.3 %)
Paramedical professions	818 (15.6 %)	42 (12.4 %)	47 (13.4 %)	43 (11.9 %)
Nurse	1 197 (22.9 %)	104 (30.7 %)	115 (32.8 %)	125 (34.7 %)
Nurse Assistants/Other assistants	491 (9.4 %)	22 (6.5 %)	17 (4.8 %)	7 (1.9 %)
Administrative/Technical staff	1 279 (24.4 %)	64 (18.9 %)	50 (14.3 %)	76 (21.1 %)
Direct contact with patients				
No		94 (27.7 %)	78 (22.2 %)	101 (28.1 %)
Yes		245 (72.3 %)	273 (77.8 %)	259 (71.9 %)
Work in Hospitals				
No	1 971 (37.7 %)	103 (30.4 %)	117 (33.3 %)	112 (31.1 %)
Yes	3 263 (62.3 %)	236 (69.6 %)	234 (66.7 %)	248 (68.9 %)
Work in Nursing Home				
No	4 429 (84.6 %)	294 (86.7 %)	319 (90.9 %)	317 (88.1 %)
Yes	805 (15.4 %)	45 (13.3 %)	32 (9.1 %)	43 (11.9 %)
Off-site				
No	4 502 (86.0 %)	277 (81.7 %)	268 (76.4 %)	284 (78.9 %)
Yes	732 (14.0 %)	62 (18.3 %)	83 (23.7 %)	76 (21.1 %)
Behavioral characteristics				
Level of confidence in authorities * (N = 6 217)				
Low	956 (18.5 %)	111 (32.7 %)	84 (23.9 %)	74 (20.6 %)
Moderate	1 954 (37.8 %)	106 (31.3 %)	127 (36.2 %)	124 (34.4 %)
High	2 255 (43.7 %)	122 (36.0 %)	140 (40.0 %)	162 (45.0 %)
Vaccinated because of the mandate (as one of the 3 main reasons) (N = 690)				
No	<i>Mandate not yet enacted</i>	330 (97.4 %)	326 (92.9 %)	<i>Question not included in the questionnaire</i>
Yes		9 (2.7 %)	25 (7.1 %)	
Opinion on vaccination in general				
Very favourable/Favourable		310 (91.5 %)	338 (96.3 %)	343 (95.3 %)
Undecided		14 (4.1 %)	3 (0.9 %)	8 (2.2 %)
Very skeptical/skeptical		15 (4.4 %)	10 (2.9 %)	9 (2.5 %)
Current vaccine intention, winter 2020–2021				
With intention	3 043 (58.1 %)			
Do not know	1 038 (19.8 %)			
With no intention	1 153 (22.0 %)			
Current vaccine uptake, summer–fall 2021				
Vaccinated		309 (91.2 %)		
Unvaccinated		30 (8.8 %)		
Hypothetical booster vaccine intention, winter–spring 2022				
With intention		239 (78.1 %)		
Do not know		35 (11.4 %)		
With no intention		32 (10.5 %)		
Current booster vaccine uptake, winter–spring 2022				
Vaccinated with booster			329 (93.7 %)	
Vaccinated without booster			8 (2.3 %)	
Unvaccinated			14 (4.0 %)	
Hypothetical 2nd booster vaccine intention, fall 2022				
With intention			253 (76.9 %)	
Do not know			37 (11.2 %)	
With no intention			39 (11.9 %)	

(continued on next page)

Table 1 (continued)

	P1 December 2020–February 2021 N = 5 234	P2 July–November 2021 N = 339	P3 February–March 2022 N = 351	P4 January–February 2023 N = 360
Hypothetical 3rd booster vaccine intention, winter 2023				
With intention				263 (73.1 %)
Do not know				34 (9.4 %)
With no intention				63 (17.5 %)
7C-items				
Calculation 'I think that vaccination against COVID-19 will have more benefits than risks for me.'				
Agree	2 932 (56.0 %)	246 (72.6 %)	242 (69.0 %)	230 (64.0 %)
Undecided	1 136 (21.7 %)	37 (10.9 %)	57 (16.2 %)	46 (12.7 %)
Disagree	1 166 (22.3 %)	56 (16.5 %)	52 (14.8 %)	84 (23.3 %)
Convenience				
'In practice, it will be difficult for me to get vaccinated.'				
Agree	654 (12.5 %)	14 (4.1 %)	15 (4.3 %)	22 (6.1 %)
Undecided	765 (14.6 %)	24 (7.1 %)	18 (5.1 %)	26 (7.2 %)
Disagree	3 815 (72.9 %)	301 (88.8 %)	318 (90.6 %)	312 (86.7 %)
Collective Responsibility				
'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'				
Agree	3 977 (76.0 %)	276 (81.4 %)	268 (76.4 %)	272 (75.6 %)
Undecided	686 (13.1 %)	19 (5.6 %)	36 (10.3 %)	27 (7.5 %)
Disagree	571 (11.0 %)	44 (13.0 %)	47 (13.4 %)	61 (16.9 %)
Social Conformism				
'Among your family and friends, how would you describe the majority opinion towards COVID-19 vaccination?'				
Favorable	1 808 (34.5 %)	230 (67.9 %)	240 (68.4 %)	206 (57.2 %)
Both skeptical and favorable	1 653 (31.6 %)	62 (18.3 %)	68 (19.4 %)	97 (26.9 %)
Skeptical	1 773 (33.9 %)	47 (13.9 %)	43 (12.3 %)	57 (15.8 %)
Complacency				
'I am afraid of getting a severe form of COVID-19.'				
Agree	1 379 (26.4 %)	95 (28.0 %)	104 (29.6 %)	120 (33.3 %)
Undecided	1 222 (23.4 %)	69 (20.4 %)	84 (23.9 %)	40 (11.1 %)
Disagree	2 633 (50.3 %)	175 (51.6 %)	163 (46.4 %)	200 (55.6 %)
Confidence in COVID-19 vaccine				
'I am afraid of having a severe side effect of vaccination.'				
Agree	1731 (33.1 %)	67 (19.8 %)	54 (15.4 %)	63 (17.5 %)
Undecided	959 (18.3 %)	50 (14.8 %)	55 (15.7 %)	36 (10.0 %)
Disagree	2 544 (48.6 %)	222 (65.5 %)	242 (69.0 %)	261 (72.5 %)
Confidence in systems				
'If my employer encourages me to get vaccinated, this...'				
Dissuades me	274 (5.2 %)	28 (8.3 %)	22 (6.3 %)	18 (5.0 %)
Has no effect	3 409 (65.1 %)	209 (61.7 %)	212 (60.4 %)	222 (61.7 %)
Motivates me	1 551 (29.6 %)	102 (30.1 %)	117 (33.3 %)	120 (33.3 %)

* Level of confidence in authorities to manage the health and economic crisis related to the COVID-19 pandemic.

importance for the intention of a hypothetical first (P2), second (P3), and third (P4) booster dose (aPR: 2.29, 2.04, and 2.07, respectively).

Perceiving vaccination as a collective action was the second strongest antecedent of primary vaccination intention in winter 2020–21 (P1) (agree vs. disagree, aPR: 2.84; p -value < 0.001). In summer-fall 2021 (P2), it remained the only psychological antecedent associated with vaccine status (agree vs. disagree, aPR: 2.19; p -value < 0.001) and persisted, albeit more weakly, under the mandate for booster vaccination at P3 (aPR: 1.20). Additionally, it was strongly associated with third and fourth hypothetical booster dose intentions (agree vs. disagree, aPR: 2.18 and 1.69, respectively).

Confidence in the vaccine was positively associated with primary vaccination intention in winter 2020–21 (P1) (agree vs. disagree, aPR: 1.84; p -value < 0.001), its association with vaccine uptake was dissipated in summer-fall 2021 (P2), but regained importance on booster vaccine uptake (agree vs. disagree, aPR: 1.14; p -value = 0.04). Its

association increased for hypothetical booster vaccine intention (agree vs. disagree, aPR: 1.45, 1.67, and 1.43 for the first (P2), second (P3), and third hypothetical booster dose (P4)).

Reactance to employer's encouragement to get vaccinated (Confidence in systems) (motivates vs. dissuades, aPR: 2.15; p -value < 0.001), and Social conformism (favourable vs. skeptical opinion, aPR: 1.33; p -value < 0.001) were significantly associated with primary vaccination intention in winter 2020–21 (P1) but these associations disappeared during the rest of the study periods. Both antecedents were not significantly associated with hypothetical booster dose intention at any survey periods.

When assessing the absolute impact of negative attitudes on vaccine behavior across the observed periods, low confidence in the vaccine (fear of severe side effects from vaccination) was related to the highest population attributable loss in vaccine uptake or intention during any survey (e.g., -26.2 % loss in hypothetical 2nd booster vaccine intention

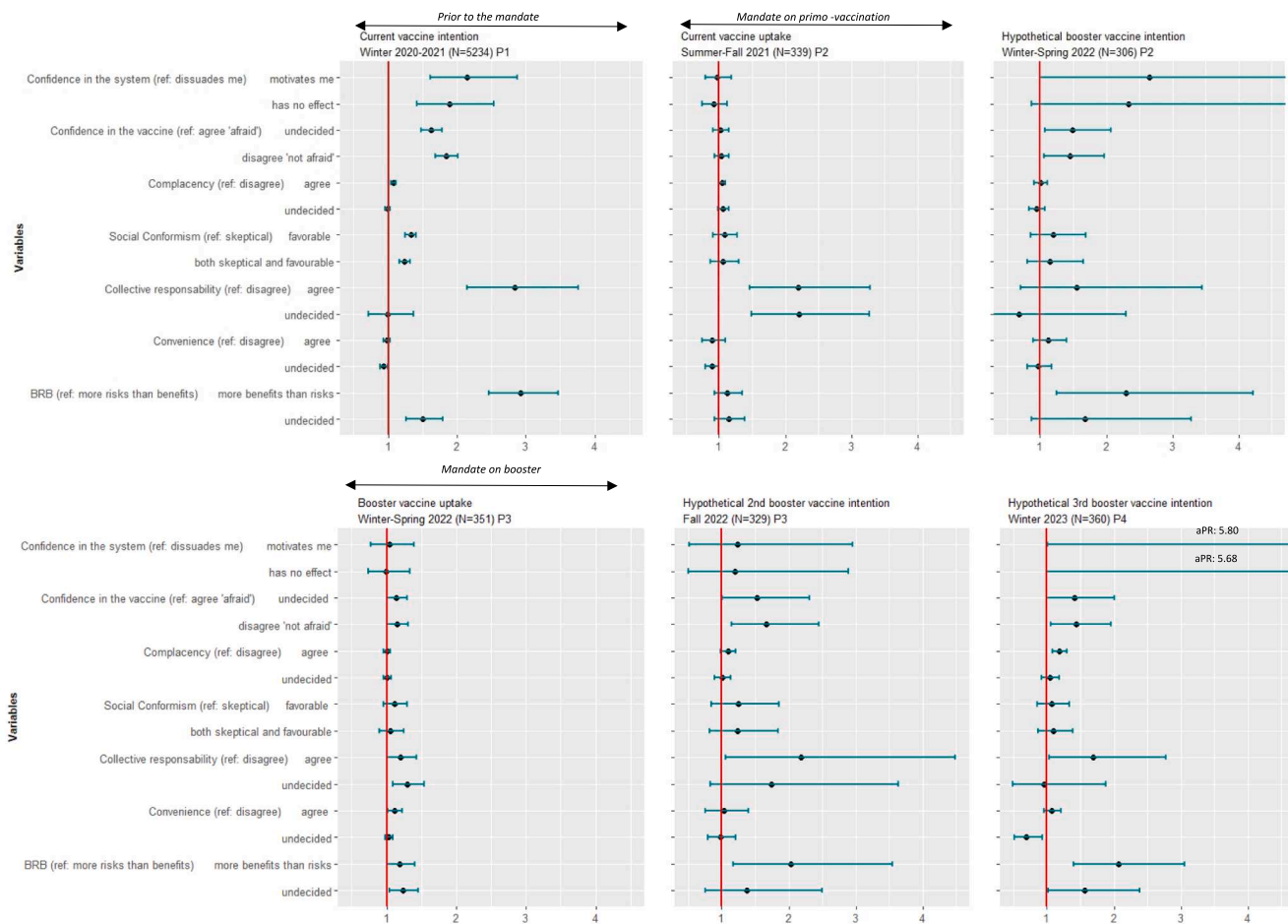


Fig. 1. Association of 7C-attitude items with vaccine intention, vaccine uptake or future vaccine intention (vs. undecided/no intention) during the COVID-19 pandemic among health care sector workers in France. Adjusted prevalence ratio (aPR) obtained from multivariable robust-variance Poisson regression models. CappVac-Cov study. *Detailed results for confidence in the system in the hypothetical 3rd booster vaccine intention (ref: dissuades me): “motivates me”: aPR 5.80, 95%-CI 1.00–33.55. “has no effect”: aPR 5.68, 95%-CI 0.99–32.65. 1st period of study (P1): 18 December 2020 to 1 February 2021. 2nd period of study (P2): 13 July to 30 November 2021. 3rd period of study (P3): 1 February and 28 March 2022. 4th period of study (P4): 12 January to 13 March 2023. Hypothetical Future Vaccine Intention was explored among those vaccinated through the question “Would you accept a booster of this vaccine (outside of any obligation)”.

at P3), with exception to P2 (early mandate) (Table 3). Calculation showed lower, but similarly constant importance.

In longitudinal follow-up of seven participants, relatively stable attitudes were observed only for perceiving vaccination as collective action, and capacity for reactance (Supplementary File 1).

4. Discussion

In this series of surveys during the COVID-19 vaccine campaign among HCSWs in France, we found that the associations between 7C-psychological antecedents and vaccine behaviour changed over time, in particular during the initial phase of the epidemic with a novel vaccine campaign. Furthermore, we found substantial variability of 7C-attitudes over time, specifically description of the majority opinion about the vaccine in the social environment (Social conformism), perception of benefits vs. risks (Calculation), and fear of side effects from vaccination (Confidence in the vaccine). Relatively stable 7C-attitudes were Collective responsibility and capacity for reactance (Confidence in the system). Overall, Calculation and Collective responsibility appeared as strongest determinants in most behaviour contexts during this study, while Confidence in the vaccine was related to the strongest attributable loss in vaccine intention in this HCSWs sample.

In the first survey at the start of the vaccine campaign, Calculation was one of the principal determinants of vaccine intention, and it was in

following surveys a determinant for booster intention and uptake outside mandates. By contrast, under the mandate for primary vaccination for HCSWs (issued in July 2021 [21,22]) when 91.2 % of participants were vaccinated, and for booster vaccination, Calculation was no determinant. In coherence with previous studies conducted among 3870 HCSWs during the beginning of the COVID-19 vaccine campaign [8], these results underpin the importance of the benefit-risk consideration in vaccine decisions and that this prominent role is modified by mandates, albeit only temporally. The perception of benefits vs. risks did not drastically change across surveys in our study, but some changes could indicate that participants perceived less risks after the first year of vaccination, while consequently, benefits were estimated lower, as well. The question arises whether individuals changed from poor to favourable benefit-risk perception following the vaccination under the mandate, which requires a longitudinal study in a larger sample. A previous study among the general population in France in summer 2021 found that intention for future vaccination among persons vaccinated only to obtain a vaccine pass or to satisfy a professional mandate did not depend on a favourable benefit-risk perception [25].

Low confidence in the vaccine (fear of vaccination side-effects) was the antecedent with the strongest absolute impact on hypothetical vaccine intention in most surveys. Despite an only moderate association with vaccine intention, the moderate prevalence of fear of side effects makes a substantial impact on vaccine coverage plausible. The high

Table 3
Reduction in vaccination prevalence/intention (%) attributable to 7C-attitude items.

	Current vaccine intention winter 2020–21 (N = 5234) P1	Current vaccine uptake summer–fall 2021 (N = 339) P2	Hypothetical booster Vaccine intention winter–spring 2022 (N = 306) P2	Current booster vaccine uptake winter–spring 2022 (N = 351) P3	Hypothetical 2nd booster Vaccine intention fall 2022 (N = 329) P3	Hypothetical 3rd booster Vaccine intention winter 2023 (N = 360) P4
<i>Calculation: 'I think that vaccination against COVID-19 will have more benefits than risks for me.'</i>						
Disagree	-14.07	NA	-9.02	NA	-7.28	-11.13
<i>Convenience: 'In practice, it will be difficult for me to get vaccinated.'</i>						
Agree	-0.22	NA	NA	0.46	NA	NA
<i>Collective Responsibility: 'Getting vaccinated will also be a collective action to stop the crisis caused by the epidemic.'</i>						
Disagree	-7.03	-6.68	NA	-2.02	-7.08	-6.56
<i>Social Conformism: 'Among your family and friends, how would you describe the majority opinion towards COVID-19 vaccination?'</i>						
Skeptical	-7.06	NA	NA	NA	NA	NA
<i>Complacency: 'I am afraid of getting a severe form of COVID-19.'</i>						
Disagree	-1.97	NA	NA	NA	NA	-4.31
<i>Confidence in COVID-19 vaccine: 'I am afraid of having a severe side effect of vaccination.'</i>						
Agree	-19.79	NA	-18.88	-7.44	-26.16	-2.44
<i>Confidence in system: 'If my employer encourages me to get vaccinated, this...'</i>						
Dissuades-me	-1.59	NA	NA	NA	NA	NA

NA: Not Applicable because C-item not significant in multivariable model.

>10 % point reduction in vaccine intention.

10% to 5% point reduction in vaccine intention.

<5% point reduction in vaccine intention.

prevalence of low confidence in winter 2020–21 (33 %) can be partly explained by the novelty of the vaccine in 2021, with limited safety data and minimal personal experience. In our survey, low confidence in the vaccine among those with no intention to get vaccinated HCSWs was 26.8 % in winter 2020 (P1), and 22.0 % among the general population in spring 2020 [26]. By 2022, this increased to 74.1 % in our survey (P3 fall 2022) and 63.0 % among the general population in summer-fall 2022 [27]. The lower prevalences thereafter (15–20 %), despite emerging evidence on severe side effects such as thrombocytopenic thrombosis and myocarditis, could reflect reassuring personal experience. Studies among mothers suggest that primiparous mothers show more reluctance toward childhood vaccinations than multiparous mothers [11]. This highlights that even during epidemic response vaccination, vaccine delivery needs to yield positive experience with regard to mild and severe side effects, and the way they are handled.

The associations of Collective responsibility (seeing vaccination as a collective action to stop the crisis related to the epidemic) with vaccine uptake and hypothetical intention remained constant during the study period, and the prevalence of agreement with this statement was high across all surveys. Collective responsibility was the only significant determinant of vaccine uptake under the mandate, which means that HCSWs refusing vaccination despite the mandate (with the consequence of job exclusion) refused to see the collective potential in vaccination. Knowledge about Sars-Cov-2 transmission mechanisms have been found to be associated with the sustained or increased adoption of preventive measures [28]. However, detailed (and variable) evidence on the vaccines' effectiveness against infection and transmission became available only later during 2021. We therefore suggest that disagreement with vaccination as a collective action in summer 2021 was rather grounded on ideological attitudes and beliefs. Interestingly, only 9 of the 339 participants in summer 2021 cited the mandate as the reason for vaccination, which suggests that Collective responsibility substantially contributed to the high vaccine uptake observed among our participants.

Previous studies have found that compliance with regulations and recommendations is driven by social norms [28]. Surprisingly, even though there was a trend towards an increase of favourable opinion among family and friends (Social conformism) across surveys, it did not significantly influence vaccine intention at later stages. Social conformism to the private environment appears to have played a role during the initial phase of the vaccine campaign only, when the heuristic of following other people's example had the highest facilitating effect on

decision-making.

Similarly, reactance to employer vaccine encouragement (Confidence in the system) was associated to absence of vaccine intention/uptake only during the initial phase of the vaccine campaign, before the mandate enactment. Social conformism and Confidence in the system are the only 7C-antecedents that are strictly interpersonal and without direct relation to the perception of the vaccine or vaccination. At later stages of the pandemic, a first experience with the COVID-19 vaccine seems to have mitigated the role of these interpersonal antecedents.

Despite previous studies that have shown how compliance with prevention behaviours rely on high perceived vulnerability and fear of severe COVID-19 [28,29], we found that fear of a severe form of COVID-19 (Complacency) was not a substantial determinant of vaccine intention or uptake at any time, while one quarter to one third of participants did express this fear across surveys. This could be related to the fact that other more important reasons for COVID-19 vaccination existed for HCSWs in this study, including Collective responsibility and vaccination against any form of COVID-19 infection.

Convenience was never associated with vaccine uptake or hypothetical vaccine intention, likely due to the high accessibility of COVID-19 vaccination for HCSWs during the pandemic.

Our study has several limitations. The generalizability of our results is limited because our samples are not representative of the HCSWs French population. Some professions such as nurse assistants were under represented across the survey periods and thus, we cannot conclude whether there were vaccine disparities between professions. Another main limitation is that we cannot assume that the same persons participated at each step. Also, our study uses a limited number of cross-sectional surveys, which affects the description of 7C-psychological antecedents over time, but has less impact on measuring their associations with vaccine behavior. Thus, it does not accurately capture the variability within the population. Our original plan was to obtain a longitudinal follow up of participants, but our ID creation system proved not adapted to real life, with many participants opting for simpler, instantaneous participations or losing their ID. Nevertheless, we have included the results of the small sample obtained in the [Supplementary File 1](#), as inspiration for future work.

Given the difficulty in obtaining longitudinal data, we have to rely on careful interpretation of 7C-attitude frequencies across the surveys. The characteristics of the participant groups remained relatively stable, based on which we attempt an interpretation of the 7Cs evolution over time. In particular, the interpretation of associations between 7C and

vaccine behaviour maintains reasonable validity, as selection bias impacts less these estimates [30]. Our study is, to the best of our knowledge, the first to assess the association of the 7C-model with vaccine acceptance throughout time and during a pandemic. It is also the first, to evidence that psychological antecedents of vaccination vary through time and context at an individual level. Despite the limitations mentioned above, given the absence of previous data, this study could serve as a starting point for future longitudinal research regarding vaccine acceptance and its promotion in epidemic contexts.

5. Conclusion

Our study provides some evidence that several 7C-psychological antecedent's attitudes of vaccination are context-specific and thus change over time, while others, in particular the perception of vaccination as a collective action and the capacity for reactance, remain relatively stable. Also, our finding provides some evidence on the importance of Confidence in the vaccine to improve vaccine intention at a population level. As important determinants on the long-term, including given coercive policies, the perception of the vaccine's BRB and of the collective dimension of a vaccine recommendation stand out. By contrast, during the initial stage of a novel vaccine campaign in an epidemic context, the influence from the social environment, reactance against a recommendation source (the employer) and fear of vaccine side effects also play an important role.

If 7C-attitudes evolve over time and are influenced by context, and are strongly associated to vaccine behavior, the question arises if they can be influenced. Our finding calls for longitudinal studies to track changes of 7C-psychological antecedents of vaccination and their association with vaccine decision. A better understanding of the dynamic nature of 7C-psychological antecedents would help tailoring vaccine promotion strategies to profiles of vaccine hesitancy and readiness.

Funding

This research is part of a PhD project funded by EHESP French School of Public Health. The study received financial support by Institut Pasteur.

CRediT authorship contribution statement

Lucia Araujo-Chaveron: Writing – review & editing, Writing – original draft, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Cyril Olivier:** Writing – review & editing, Validation, Data curation. **Gérard Pellissier:** Writing – review & editing, Validation. **Elisabeth Bouvet:** Writing – review & editing, Validation. **Judith E. Mueller:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

We would like to thank Brenda Kinloch for her valuable help in the English revision of this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2024.07.004>.

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