

# Exploring perceptions of vaccine safety: an Italian national survey on different COVID-19 vaccine formulations

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## Abstract

**Objectives.** COVID-19 vaccines have proven effective and safe, enabling the resumption of normal life. However, misinformation has hindered vaccination efforts. This study aimed to investigate perceptions of vaccine safety among Italians through an anonymous online survey.

**Study design.** An anonymous online survey was conducted from April to July 2022 and disseminated through social platforms, among adult individuals living in Italy.

**Results.** A total of 1,329 individuals participated. Younger individuals and healthcare professionals showed greater trust in vaccines. Education level was significantly associated with perceived vaccine safety. Most respondents, including many healthcare workers and highly educated individuals, believed vaccines to be safe, with confidence levels of 39.5% for mRNA, 32.9% for viral vector, and 39% for protein subunit vaccines. Younger age and trust in institutions were linked to higher confidence in all vaccine types.

**Conclusions.** These findings may be useful to further investigate the drivers of vaccine safety perceptions and their relationship with vaccine hesitancy and may help to develop more effective communication campaigns in the future.

## Key words

- vaccination
- SARS-CoV-2
- subunit vaccines
- viral-vector vaccines
- mRNA vaccines

## INTRODUCTION

On March 11th, 2020, the World Health Organization (WHO) declared a pandemic due to the new SARS-CoV-2 virus (severe acute respiratory syndrome-coronavirus 2), first identified in December 2019 in Wuhan, China [1].

By March 2023, the world had surpassed 759 million documented cases of COVID-19 [2] and 6.8 million deaths [3]. The pandemic has not only had direct health consequences but has also threatened health system stability, disrupted routine services, and indirectly impacted community health [4]. In Italy, more than 25 million cases and over 188,000 deaths have been recorded due to COVID-19, mainly affecting the older segments of the population and the frailest individuals in the same period [5]. Unsurprisingly, these two categories of people were the first to receive the anti-COVID-19 vaccine. COVID-19 does, in fact, cause less severe disease in young people, but the risk of severe illness and death remains high in people aged 60 years and older and those with underlying health conditions

[6]. The “Vaccine-day” (December 27, 2020) is the date that marked the official start of the vaccination campaign against COVID-19 all over Europe [7]. In Italy, the distribution of the vaccine began on 31 December 2020 [8]. Achieving high acceptance and uptake rates is crucial for the success of such campaigns [9]. Globally, as of February 2024, approximately 70.6% of the world population, including 86.3% of Italians, has received at least one dose of a COVID-19 vaccine while 64.1% of the global population, including 81.2% of Italians, was fully vaccinated [10].

Along with the global spread of vaccines, “no-vax” movements have arisen, consisting of people who don’t trust vaccines, particularly the new mRNA technology, or are afraid of adverse reactions [11]. Determining factors include the loss of trust in institutions regarding pandemic management, the rapid development of available vaccines and the spread of misinformation [12, 13]. Indeed, what characterized the COVID-19 pandemic was the presence of a massive infodemic, which the WHO describes as an “overabundance of in-

formation – some accurate and some not – that occurs during an outbreak” [14]. Due to misinformation and infodemic, the risks of COVID-19 have been trivialized, or misinformation has been spread about alleged anti-COVID-19 treatments (e.g., hydroxychloroquine) whose efficacy has never been proven, as has the simultaneous and conflicting emergence of opinions of so many public health experts [15].

The WHO has recognized vaccine hesitancy as one of the top ten threats to global health [16]. Vaccine hesitancy refers to the delayed acceptance or refusal of vaccination despite the availability of vaccines and vaccination services. According to the WHO’s 3 Cs model, the propensity for vaccine hesitancy is a function of three factors: confidence, complacency and convenience.

In particular, complacency corresponds to the perceived risk of getting sick versus the perceived risk of experiencing adverse events after vaccination and determines the belief that vaccines are unnecessary; instead, convenience concerns the individual’s ease of access to vaccination. Confidence is defined as trust in the efficacy and safety of vaccines, trust in the system that provides them (competence of health workers and services), and trust in immunization policies adopted by institutions [17]. Trust issues constitute the predominant reason for vaccine hesitancy [18]. Other factors contributing to vaccine hesitancy are many and partly overlap with those of trust: misperceptions of vaccine-preventable disease risk (based on prior experience or lack of experience), access to information and misinformation, media and social media exposure and social norms [19].

In Italy, nearly one in five people has expressed beliefs that vaccines are harmful, often accompanied by a lack of trust in the scientific community and limited engagement in political or cultural activities [20]. During the COVID-19 pandemic, these concerns became even more pronounced, with the rapid development of vaccines fueling doubts about their safety and efficacy. A survey conducted across seven European countries at the end of 2020 revealed that in Italy, 66% of respondents were willing to accept a COVID-19 vaccine – a higher rate than in some countries but still indicative of significant hesitation. Factors such as trust in healthcare institutions and clear, accurate information emerged as critical in shaping public attitudes [21, 22]. These findings emphasize the need for targeted strategies to rebuild trust and counter misinformation, especially in the context of new vaccine technologies.

Hesitation towards vaccines represents a significant challenge in the fight against SARS-CoV-2 [23]. Indeed, infodemic and misinformation cause an increase in vaccine hesitancy and a decrease in vaccine confidence [24]. Strong confidence in COVID-19 vaccines leads to an increase in immunizations for all age groups and vaccine trust is considered to be the main factor affecting COVID-19 vaccine uptake [25].

For these reasons, several important issues were addressed, including vaccination safety, public trust in the government, and sources consulted for information [26].

More than a year after the beginning of the vaccine campaign, evidence of the public’s willingness to accept COVID-19 vaccines still deserves further investigation,

and the role that determinants may play in vaccine confidence needs to be better understood. In addition, according to the best information we have, different types of anti-COVID-19 vaccine might have different impacts relative to vaccine hesitancy [27].

For this reason, our research aims to assess perceptions of vaccine safety in different anti-COVID-19 vaccine formulations (mRNA, protein subunits and viral-vector vaccines) and factors associated in the context of the pandemic.

## METHODS

This study was conducted in a convenience sample of the general adult population residing in Italy one year after the introduction of the anti-COVID-19 vaccine. An anonymous online survey was conducted among the general adult population from 20 April 2022, to 23 July 2022.

The survey was disseminated via social platforms (Facebook, Instagram, WhatsApp, Telegram) and was especially disseminated through commenting on online newspaper posts that were closely related to information about anti-COVID-19 vaccines and the vaccination campaign. The questionnaire was also posted on a regional website aimed at improving vaccination knowledge and awareness in the general population [28].

Participants aged 18 years and older and residing in Italy were considered eligible. All participants provided online informed consent to be included in the study. Only questionnaires completed by Italians residents in Italy were included. Participation in the study was voluntary.

## Questionnaire

The anonymous questionnaire could be filled out only after viewing the information note on the purpose of the survey and agreeing to a statement of consent to participate. Most of the questions included dichotomous answers (YES/NO), while two questions included open-ended answers.

The first part of the questionnaire addressed general socio-demographic characteristics (age group, sex, geographic area, education, type of employment, employment status, type of healthcare professional, trust in institutions).

The second part examined trust in vaccines and anti-COVID-19 vaccines in their different formulations (mRNA, viral vector and protein subunit). Specifically, the confidence in the protein subunit vaccine was assessed with respect to the mRNA vaccine and the viral vector vaccine, as the protein vaccine was released later than the others.

The last section assessed possible determinants of trust in the COVID-19 vaccine, such as perceived risk related to vaccination versus infection and trust in institutions. In this scenario, respondents were asked whether they knew individuals who had experienced severe adverse reactions, defined as reactions that resulted in hospitalization.

The main source of information regarding vaccination was investigated using a closed question which allowed more than one answer.

The questionnaire underwent a thorough internal validation process. In particular, the questionnaire was reviewed and tested by approximately 50 residents in Hygiene and Preventive Medicine at the University of Florence (Italy) to ensure its relevance and clarity. Although we did not conduct further validation with an external population, we relied on the School's professional expertise and extensive experience to improve the robustness and applicability of the questionnaire.

The questionnaire is available in the *Supplementary File 1* available online as *Supplementary Materials*.

### Statistical analysis

Descriptive statistics were conducted to generate summary tables for study variables. Based on median values, the continuous variable "age" was transformed in two age groups.

In order to assess the predictors of the outcomes indicating vaccine confidence, we performed single and multivariate modified Poisson regression models. Poisson regression can be used for the analysis of cross-sectional studies with binary outcomes. When the outcome event is common [29], it is often more desirable to estimate a prevalence ratio since there is an increasing differential between the RR (relative risk) and OR (odds ratio) with an increasing incidence ratio. Anyway, for binary data Poisson regression model produces CIs (confidence intervals) that tend to be too wide. To correct this potential limitation, Zou *et al.* proposed a modified Poisson regression approach (Poisson regression with a robust error variance) [30]. The effect estimates are presented as relative risks (RRs) with their 95% confidence intervals (CIs).

For all the analyses, a *p*-value <0.05 was considered statistically significant. Statistical analyses were conducted using STATA 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

## RESULTS

Out of the 1,350 completed questionnaires, 1.5% (*n*=21) were excluded because responders reported living abroad. Finally, a total of 1,329 questionnaires were included. Sociodemographic characteristics of the sample are shown in *Table 1*.

Women represent 65.5% (*n*=870) of the sample, while the median age was 47 years (95% CI: 46.7-48). Additionally, 34.1% (*n*=453) were healthcare professionals, and 76.5% (*n*=1,020) declared to be employed at the time of the administration of the survey administration. Half of the responders (*n*=665) reported living in Northern Italy, 38.2% (*n*=508) in Central Italy, and 11.8% (*n*=156) in Southern Italy. Regarding the level of education, the majority of respondents (65% *n*=864) held a bachelor's or master's degree. These characteristics highlight a sample that is not representative of the general population but rather skewed towards individuals with higher education and professional involvement in healthcare. A majority of the sample, specifically 62.6% (*n*=832) reported having sufficient trust in institutions (e.g., Ministry of Health, National Institute of Health, Italian Drug Agency, etc.).

**Table 1**

Sociodemographic features of Italian respondents in the COVID-19 vaccine safety study

	NA	N or median	% or IQR
<b>Age (year)</b>		47	46.7-48.1
<b>Sex</b>	19		
Male		440	33.1
Female		870	65.5
<b>Geographic area</b>	0		
North of Italy		665	50
Center of Italy		508	38.2
South of Italy		156	11.8
<b>Education</b>	0		
Primary school		2	0.2
Secondary school		52	3.9
High school		411	30.9
Bachelor's degree		549	41.3
Master's degree/PhD		315	23.7
<b>Type of employment</b>	309		
Employee		702	52.8
Self-employed		318	23.9
<b>Employment status</b>	45		
Currently employed		1,020	76.5
Currently unemployed/retired		264	19.8
<b>Healthcare professional</b>	0		
Yes		453	34.1
No		876	65.9
<b>Trust in institutions</b>	0		
Yes		832	62.6
No		497	37.4

NA: not available; N: number of valid responses; IQR: inter quartile range.

Personal beliefs about vaccination and perceived safety of different COVID-19 vaccine formulations are shown in *Table 2*.

The majority of respondents, 63.9% (*n*=849), think vaccines are safe, while 39.5% (*n*=525), 32.9% (*n*=437), and 39% (*n*=518) consider vaccines with mRNA technology, viral vectors, and protein subunits safe, respectively. About 10.6% (*n*=142) and 9.1% (*n*=122) of the respondents reported higher confidence in the protein-subunit vaccine compared to the mRNA vaccine and the viral-vector vaccine, respectively.

Among the preferred sources of information on vaccines, scientific books or journals (59%), attending physicians, medical officers and health professionals (52%), and institutional sites (e.g., Ministry of Health, National Institute of Health, Italian Medicines Agency) (35%) were the most selected options. The local health unit (LHU) is a reference for 30% of the participants: 17% and 13% through the vaccination service and region's

**Table 2**

Personal beliefs about vaccinations and perceived safety of different COVID-19 vaccines formulations

	NA	N	%
<b>Do you think vaccines are safe?</b>	0		
Yes		849	63.9
No		480	36.2
<b>Do you think that mRNA vaccines against COVID-19 are safe?</b>	0		
Yes		525	39.5
No		804	60.5
<b>Do you think that protein subunit vaccines against COVID-19 are safe?</b>	0		
Yes		518	39
No		811	61
<b>Do you think that viral-vector vaccines against COVID-19 are safe?</b>	0		
Yes		437	32.9
No		892	67.2
<b>Do you know anyone who have suffered from severe reactions to the mRNA technology COVID-19 vaccines?</b>	0		
Yes		753	43.4
No		576	56.6
<b>Do you know anyone who have suffered from severe reactions to the viral vector COVID-19 vaccines?</b>	0		
Yes		620	46.6
No		709	53.4
<b>Do you think that the risk you are exposed by being vaccinated against COVID-19 is greater than the risk caused by the disease itself?</b>	0		
Yes		738	55.5
No		591	44.5
<b>Do you think that the protein subunits vaccine is safer than mRNA vaccine?</b>			
Yes		122	9.1
No		35	2.6
<b>Do you think that the protein subunits vaccine is safer than viral vector vaccine?</b>			
Yes		142	10.5
No		33	2.4

NA: not available; N: number of valid responses.

website or LHM respectively. In our sample, 16% of participants reported using sites/blogs/forums that are against vaccinations in case of doubt about a vaccine's risks or actual benefits.

Knowing someone who suffered from a serious adverse reaction to vaccines was reported by 43.4% (n=753) of subjects in the case of the mRNA vaccine and by 46.6% (n=620) in the case of the viral-vector vaccine. In this study, a serious adverse reaction is de-

finied as an event that causes death, is life-threatening, requires hospitalisation or results in significant disability [31]. The exploration of personal beliefs about COVID-19 revealed that 55.5% (n=738) of respondents reported a higher perceived risk related to vaccination than to contracting COVID-19 disease.

The results of the single regression analysis are reported in Table 3.

Perceived vaccine safety is associated with being younger than 47 years (RR 1.34; 95% CI: 1.24-1.45;  $p<0.001$ ), working as a healthcare professional (RR 1.18; 95% CI: 1.09-1.28;  $p<0.001$ ), having a bachelor's degree or higher (RR 1.13; 95% CI: 1.03-1.24;  $p<0.008$ ), geographical area of residence in Central Italy (RR 1.34 95% CI: 1.22-1.46;  $p<0.001$ ) or Southern Italy (RR 1.36; 95% CI: 1.21-1.53;  $p<0.002$ ) and trust in institutions (RR 2.25; 95% CI: 2.08-2.43;  $p<0.001$ ).

According to the multivariate analysis (Table 4), factors independently associated with higher vaccine confidence were age lower than 47 years (RR 1.12; 95% CI: 1.02-1.23), residing in Central Italy (RR 1.10; 95% CI: 1.01-1.20), and having trust in institutions (RR 2.16; 95% CI: 1.96-2.37).

Analysis of opinions about the different COVID-19 vaccine technologies produced interesting results. Trust in institutions remained the strongest predictor of vaccine confidence for both the mRNA vaccine (RR 6.66; 95% CI: 4.13-10.74) and the viral vector vaccine (RR 9.22; 95% CI: 6.10-13.99), as well as the protein subunit vaccine (RR 6.92; 95% CI: 5.44-8.81). Being younger than 47 years was specifically associated with higher confidence in the protein subunit vaccine (RR 1.15; 95% CI: 1.01-1.31). On the other hand, knowing someone who suffered a serious adverse reaction was a predictor of lower vaccine confidence in both mRNA vaccines (RR 0.31; 95% CI: 0.19-0.48) and viral vector vaccines (RR 0.35; 95% CI: 0.24-0.52).

Finally, being younger than 47 years (RR 0.92; 95% CI: 0.86-0.98), being an employee (RR 0.92; 95% CI: 0.86-0.98), living in Central Italy (RR 0.88; 95% CI: 0.82-0.96) or Southern Italy (RR 0.86; 95% CI: 0.76-0.98) and having trust in institutions (RR 0.05; 95% CI: 0.03-0.08) were predictors that reduce the possibility of a higher perceived risk associated to vaccination compared to COVID-19 disease.

## DISCUSSION

This study was conducted more than a year after the start of the anti-COVID-19 vaccination campaign in Italy. The objective was to assess confidence in vaccination in general, confidence in anti-COVID-19 vaccination in particular, confidence in different vaccine formulations, and the factors influencing it.

The importance of anti-COVID-19 vaccination is demonstrated by numerous studies testifying to the effectiveness of vaccines, especially in protecting against severe illness, hospitalization, and death, despite the spread of the latest variants known to be more contagious [32]. At least five different vaccine technology platforms have been licensed and used for anti-COVID-19 vaccines in Italy: two mRNA vaccines (Comirnaty BNT162b2, Pfizer-BioNTech; Spikevax mRNA-1273, Moderna)



**Table 3**

Single regression analysis of variables associated with personal beliefs about the safeness of COVID-19 vaccines

Variables	n	Perceived vaccines safety				Perceived mRNA COVID-19 vaccines safety				Perceived protein subunit COVID-19 vaccines safety			
		RR	Lower	Upper	p value	RR	Lower	Upper	p value	RR	Lower	Upper	p value
		95% CI		95% CI		95% CI		95% CI		95% CI		95% CI	
<b>Sex</b>	1,310	0.98	0.89	1.06	0.6	0.92	0.8	1.06	0.25	0.99	0.86	1.14	0.97
<b>Age</b>													
Younger than 47		1.34	1.24	1.45	<0.001	1.8	1.56	2.1	<0.001	1.76	1.53	2.02	<0.001
<b>Geographic area</b>	1,329												
Center of Italy		1.34	1.22	1.46	<0.001	2.07	1.77	2.42	<0.001	1.96	1.68	2.29	<0.001
South of Italy		1.36	1.21	1.53	<0.002	2.37	1.97	2.85	<0.001	2.18	1.8	2.63	<0.001
<b>Education level</b>	1,329												
Bachelor's degree or higher		1.13	1.03	1.24	0.008	1.17	1.01	1.36	0.03	1.34	1.15	1.56	<0.001
<b>Type of employment</b>	1,020												
Employee		0.98	0.89	1.08	0.78	0.99	0.83	1.17	0.913	0.97	0.81	1.14	<0.71
<b>Working as healthcare professional</b>	1,329	1.18	1.09	1.28	<0.001	1.39	1.22	1.59	<0.001	1.5	1.32	1.72	<0.001
<b>Knowing someone who had suffered from severe reaction after mRNA COVID-19 vaccination</b>						0.08	0.06	0.1	<0.001				
<b>Knowing someone who had suffered from severe reaction after viral vector COVID-19 vaccination</b>													
<b>Having trust in institution</b>	1,329	2.25	2.08	2.43	<0.001	14.6	11.02	18.3	<0.001	7.2	6	8.7	<0.001

  

Variables	n	Perceived viral-vector COVID-19 vaccines safety				Perceived COVID-19 vaccination as a higher risk than the disease itself			
		RR	Lower	Upper	p value	RR	Lower	Upper	p value
		95% CI		95% CI		95% CI		95% CI	
<b>Sex</b>	1,310	1.08	0.92	1.26	0.34	1.1	0.99	1.21	0.08
<b>Age</b>									
Younger than 47		1.91	1.62	2.23	<0.001	0.67	0.6	0.74	<0.001
<b>Geographic area</b>	1,329								
Center of Italy		2.2	1.84	2.63	<0.001	0.61	0.55	0.68	<0.001
South of Italy		2.25	1.8	2.82	<0.001	0.51	0.42	0.64	<0.001
<b>Education level</b>	1,329								
Bachelor's degree or higher		1.31	1.1	1.6	0.002	0.91	0.82	1	0.06
<b>Type of employment</b>	1,020								
Employee		0.97	0.8	1.18	0.801	0.95	0.84	1.06	0.365
<b>Working as healthcare professional</b>	1,329	1.55	1.34	1.8	<0.001	0.8	0.72	0.9	<0.001
<b>Knowing someone who had suffered from severe reaction after mRNA COVID-19 vaccination</b>									
<b>Knowing someone who had suffered from severe reaction after viral vector COVID-19 vaccination</b>		0.1	0.076	0.14	<0.001				
<b>Having trust in institution</b>	1,329	16.6	12.24	22.52	<0.001	0.04	0.03	0.07	<0.001

n: number; RR: relative risk; CI: confidence interval.

[33, 34], two viral vector vaccines (Vaxzevria ChAdOx1 nCoV-19, Oxford-AstraZeneca; Janssen Ad26.COV2-S recombinant, Janssen-Cilag International NV) [35], and one protein subunit vaccine (Nuvaxovid NVX-CoV2373, Novavax) [36]. Overall, mRNA vaccines were the most widely used in the vaccination campaign in Italy [37]. Randomized and observational studies have demonstrated the high efficacy of mRNA vaccines in reducing morbidity and mortality from SARS-CoV-2 infection [38-40]. In addition, a systematic review evaluated the

efficacy and safety of vaccines against SARS-CoV-2 in general, showing high certainty evidence for mRNA vaccines and moderate certainty evidence for the protein subunit vaccine in reducing the incidence of symptomatic COVID-19 compared to placebo [41].

Regarding the three different anti-COVID-19 vaccine technology platforms available in Italy, 39.5% of participants had confidence in the mRNA vaccine, 32.9% in the viral vector vaccine, and 39% had confidence in the protein subunit vaccine. The protein subunit vac-

**Table 4**

Multiple regression analysis of variables associated with personal beliefs about the safeness of COVID-19 vaccines

Variables	Perceived vaccines safety				Perceived mRNA COVID-19 vaccines safety				Perceived protein subunit COVID-19 vaccines safety			
	RR	Lower	Upper	p value	RR	Lower	Upper	p value	RR	Lower	Upper	p value
		95% CI				95% CI				95% CI		
<b>Age</b>												
Younger than 47	1.12	1.02	1.23	<b>0.009</b>	1.08	0.99	1.18	0.074	1.16	1.03	1.33	<b>0.019</b>
<b>Geographic area</b>												
Center of Italy	1.1	1	1.2	<b>0.039</b>	1.16	1.05	1.28	<b>0.001</b>	1.29	1.11	1.49	<b>0.001</b>
South of Italy	0.98	0.87	1.11	0.833	1.13	1.1	1.27	<b>0.034</b>	1.26	1.06	1.48	<b>0.006</b>
<b>Education level</b>												
Bachelor's degree or higher	1	0.91	1.11	0.862	0.99	0.91	1.09	0.976	1.09	1.12	1.26	0.195
<b>Type of employment</b>												
Employee	0.99	0.9	1.08	0.953	1.01	0.94	1.1	0.756	0.98	0.87	1.1	0.788
<b>Knowing someone who had suffered from severe reaction after mRNA COVID-19 vaccination</b>					0.31	0.19	0.48	<b>&lt;0.001</b>				
<b>Knowing someone who had suffered from severe reaction after viral vector COVID-19 vaccination</b>												
Working as healthcare professional	1	0.93	1.09	0.891	1.04	0.96	1.11	0.334	1.07	0.94	1.17	0.359
Having trust in institution	2.16	1.96	2.37	<b>&lt;0.001</b>	6.66	4.13	10.69	<b>&lt;0.001</b>	6.7	5.39	8.74	<b>&lt;0.001</b>

  

Variables	Perceived viral-vector COVID-19 vaccines safety				Perceived COVID-19 vaccination as a higher risk than the disease itself			
	RR	Lower	Upper	p value	RR	Lower	Upper	p value
		95% CI				95% CI		
<b>Age</b>								
Younger than 47	1.13	0.99	1.29	<b>0.065</b>	0.91	0.85	0.98	<b>0.009</b>
<b>Geographic area</b>								
Center of Italy	1.2	1.05	1.4	<b>0.01</b>	0.88	0.82	0.96	<b>0.04</b>
South of Italy	1.13	0.93	1.35	0.187	0.86	0.76	0.98	<b>0.035</b>
<b>Education level</b>								
Bachelor's degree or higher	1.07	0.91	1.22	0.356	1.02	0.94	1.08	0.694
<b>Type of employment</b>								
Employee	0.97	0.8	1.18	0.801	0.91	0.76	0.98	<b>0.012</b>
<b>Knowing someone who had suffered from severe reaction after mRNA COVID-19 vaccination</b>								
<b>Knowing someone who had suffered from severe reaction after viral vector COVID-19 vaccination</b>	0.35	0.24	0.52	<b>&lt;0.001</b>				
Working as healthcare professional	1.09	0.98	1.2	0.166	0.99	0.92	1.06	0.774
Having trust in institution	9.2	6.01	13.8	<b>&lt;0.001</b>	0.05	0.03	0.08	<b>&lt;0.001</b>

RR: relative risk; CI: confidence interval. Bold values indicate statistically significant results, with p-values less than 0.05 considered significant.

cine was licensed and used about a year after the others. In our sample, 10.6% and 9.1% reported greater confidence in the protein subunit vaccine than in the mRNA vaccine and the viral vector vaccine, respectively. This could be explained since it uses a traditional vaccine technology platform.

Our study showed that 63.9% of respondents had confidence in vaccines in general, but less than half reported confidence in COVID-19 vaccines. This may be due to the rapid development and approval of COVID-19 vaccines [42] which may have reduced the population's trust in their safety and efficacy. Indeed, trust is

the main factor that contrasts vaccine hesitancy and influences vaccine acceptance [43]. Although the survey found a high percentage of people who do not believe in the safety of the anti-COVID-19 vaccination, Italy is one of the European countries with the highest percentage of the population that has received a full cycle (two doses of vaccine). A possible explanation for this discrepancy could be attributed to the mandatory vaccination that was introduced by the Italian government [44]. Furthermore, the way the benefits of vaccination were communicated, particularly to those who were undecided, may have played a role in shaping public

confidence. Research conducted in Italy indicates that clear communication can significantly improve perceptions of vaccine safety and efficacy, addressing concerns and uncertainties that may arise [21, 45].

Predictors of higher perceived safety for vaccines in general and anti-COVID-19 vaccine, in particular, include living in Central Italy compared to Northern Italy. This is consistent with the exceptionally low vaccination coverage in some regions, most notably Friuli Venezia Giulia or the province of South Tyrol [46], although it should be noted that these two regions collectively have a small population compared to the total population of Northern Italy (1,800,000 compared to 27,500,000 inhabitants).

Individuals in Central and Southern Italy reporting higher vaccine confidence may be influenced by various factors, such as cultural attitudes, local public health campaigns, or differences in healthcare infrastructure. Historically, these regions might have experienced more targeted outreach or communication strategies emphasizing vaccine benefits, particularly during recent public health emergencies. Additionally, sociopolitical dynamics or trust in local healthcare authorities might vary, contributing to these regional disparities.

Other predictors of greater perceived safety regarding vaccines in general and anti-COVID-19 in particular relate to young age (under 47 years) and having trust in institutions. In particular, in our survey, trust in institutions appears to be the most important factor positively associated with vaccine acceptance and with the belief that contracting the disease represents a greater risk than getting vaccinated. Indeed, in line with the WHO's 3 Cs model, vaccine confidence affects not only vaccines as drugs (vaccine safety) but also trust in vaccinators and health professionals (health worker competence) and politicians responsible for public health decisions and is intimately related to vaccine hesitancy (adequacy of the delivery system) [17, 47].

Lack of confidence is related to the level of importance and effectiveness attributed to vaccines; on the other hand, perceived risk relates to a lack of confidence in vaccine safety and concern about adverse events following immunization, which plays a role in vaccine hesitancy and uptake [48, 49].

Indeed, a significant finding concerns the negative association between those who have personally known individuals who have developed serious adverse reactions following the administration of one of the anti-COVID-19 vaccines and their feeling of trust in the same vaccine. In our survey, many people apparently know people who have had a serious reaction to the vaccination; however, this perception is not confirmed by the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA) pharmacovigilance data. According to the report on the surveillance of anti-COVID-19 vaccines produced by AIFA in 2022, most of the reported adverse events are classified as non-serious (about 81.3%) and to a lesser extent serious (18.7%). The finding that a significant proportion of respondents know someone who has suffered a serious adverse reaction underscores a critical aspect of vaccine perception. Personal connections to such events can amplify fears about vaccination,

fostering increased hesitation. Social networks further exacerbate this phenomenon, as awareness of adverse reactions within one's social circle often decreases trust in vaccines and health authorities. This highlights the importance of addressing personal narratives in public health communication to mitigate fear and misinformation effectively. Understanding how these dynamics influence vaccine perception is crucial for developing targeted communication strategies [50].

The distribution of reports by vaccine type follows the distribution of administrations: 81.3% for mRNA vaccines, 18.6% for viral vector vaccines, and 0.1% for protein subunit vaccines [51].

Vaccine hesitancy among health workers can be harmful for several reasons. In our survey, being a healthcare worker in univariate analyses showed an association with a positive perception towards vaccine safety. However, this same association fails in multivariate analysis. Action to improve health workers' trust in institutions and in the safety of vaccines could lead to a higher acceptance rate [52]. Our study showed that people hesitant about vaccination seem to have certain characteristic traits, among which we found, in addition to distrust of institutions, a low perception of danger towards the disease and an extreme fear of adverse events. These aspects have also emerged in other studies [47, 53]. Factors contributing to vaccine trust are multiple: trust in health systems, manufacturers, institutions, information, and perceptions of the importance, safety, and efficacy of vaccines [54]. Analyzing factors related to vaccine acceptance is crucial to guide public health activities, which is the reason we decided to conduct a study based on an online questionnaire to assess in an adult population sample vaccine hesitancy and confidence.

WHO recently stated how infodemic and misinformation are able to negatively influence people's health behaviors [55]. It is a fact that those who did not vaccinate were those who suffered the most severe consequences of COVID-19 disease, constituting the majority of hospitalized cases [56]. Those who filled out this online survey are the same people who seek information through websites, social networks, and online search engines. Therefore, it is hoped that the effects of the infodemic and online health misinformation can be countered by improving awareness campaigns and, above all, by enhancing people's digital and health literacy. This task is precisely fulfilled by institutions, although the population does not always have full trust in them. Those who do not trust institutions probably do not trust the health authorities' decisions regarding health either. Primary prevention, particularly vaccination, represents the most powerful tool available to local and global health decision-makers for preventing the spread of disease and improving the outcome of those infected. The promotion and dissemination of reliable health information are of paramount importance for governments and health authorities to counter false or misleading health information spread on social media. It is critical to counter false or misleading information.

Our study has several limitations. It is necessary to consider the possibility of selection bias. Our ques-

tionnaire was distributed predominantly online, using social platforms and comments on posts regarding anti-COVID-19 vaccination. This approach may have attracted a sample that was not representative of the general population, favoring the participation of individuals with a particular interest, opinion or emotional involvement regarding vaccines. Consequently, the level of trust expressed in our sample, especially towards anti-COVID-19 vaccines, may not accurately reflect the perception of the entire Italian population. It is therefore plausible that this bias influenced our results, underlining the need to conduct further research with more representative samples and different data collection methods to verify our conclusions. Finally, ours is a cross-sectional study, which takes a snapshot of the community response at a specific time in the SARS-CoV-2 pandemic. The feelings and beliefs about COVID-19 vaccines might change over time. A further limitation of the study is that the survey focused on perceptions of vaccine safety and did not include comprehensive measures of vaccine hesitancy, such as complacency and convenience. Still, we evaluated vaccine safety perception as a proxy for vaccine hesitancy. Further studies are needed and should incorporate validated multi-item scales to assess these additional dimensions. The questionnaire was administered one year after the start of the vaccination campaign in Italy, so news about vaccination, alleged adverse reactions, and the evolution of the pandemic may have influenced perceptions toward vaccines.

Despite these limitations, including the non-representativeness of the sample due to the high percentage of healthcare workers and highly educated individuals, our findings are novel and interesting. By exploring the level of confidence in vaccine formulations, we incorporated the concept of an individual's experience, which is related to the feeling of trusting in the good qualities of vaccines. While our data do not represent the general population, they highlight an important phenomenon that deserves further research and attention. In this way, our findings can contribute to a better understanding of people's attitudes towards different vaccine technologies and inform future studies. However, it is essential to balance this individualised perspective with a broader public health approach. While recognition of individual concerns and preferences can improve vaccine uptake at the micro level, public health strategies must emphasise equity of access, consistency of communication and evidence-based guidelines for vaccine safety and efficacy. This dual perspective ensures that individual confidence in vaccines is strengthened with-

out compromising the collective goal of achieving widespread immunity by balancing public health resources and priorities. With the evolution of the epidemic, it will be increasingly important to understand people's attitudes toward vaccinations and their level of confidence in order to construct well-designed communication campaigns.

## CONCLUSIONS

Factors related to vaccine confidence and vaccine hesitancy indicate that among people who generally consider vaccines safe, there is a proportion who do not place the same trust in anti-COVID-19 vaccines. These findings underscore the need for further research into the drivers of vaccine perceptions, especially regarding different vaccine technologies, and should be considered primarily as an indicator of a phenomenon rather than a comprehensive representation of the general population.

There are factors, especially trust in institutions, associated with perceptions of safety toward anti-COVID-19 vaccines; therefore, it will also be important to take these aspects into account to guide future communication activities aimed at achieving SARS-CoV-2 pandemic control and public health goals.

It is important for policymakers to understand the factors related to vaccine confidence and hesitancy. Although our data are not representative of the general population, they provide an initial exploration of a critical phenomenon and stress the need for more extensive research. This study can help in understanding how to target vaccination and communication campaigns more effectively to counter the circulating infodemic and ensure the highest possible vaccination coverage.

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## Ethical approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee of the University of Florence, Italy (Protocol code 0081791, 13/04/2022). The acronym of the questionnaire disseminated online is: PERSIC-VACCINICOVID-19.

## Conflict of interest statement

The Authors declare no conflict of interest.

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