



From COVID-19 vaccine candidates to compulsory vaccination: The attitudes of Italian citizens in the key 7-month of vaccination campaign



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ABSTRACT

Introduction: The aim of the study is to understand the evolution of COVID-19 vaccine acceptance over the key 7-month vaccine campaign in Italy, a period in which the country moved from candidate vaccines to products administered to the public. The research focus points to evaluate COVID-19 vaccine attitudes in adults and their children, propensity towards compulsory vaccination, past and present adherence to anti-flu and anti-pneumococcal vaccines, and the reasons for trust/mistrust of vaccines.

Methods: Italian residents aged 16–65 years were invited to complete an online survey from September 2020 to April 2021. The survey contained 13 questions: 3 on demographic data; 8 on vaccine attitudes; and 2 open-ended questions about the reasons of vaccine confidence/refusal. A preliminary word frequency analysis has been conducted, as well as a statistical bivariate analysis.

Results: Of 21,537 participants, the confidence of those in favor of the COVID-19 vaccine increases of 50 % and the number of people who wanted more information decreases by two-third. Willingness to vaccinate their children against COVID-19 also increased from 51 % to 66.5 %. Only one-third of the strong vaccine-hesitant participants, i.e. 10 %, remained hostile. Compulsory vaccination showed a large and increasing favor by participants up to 78 %, in a way similar to their propensity for children's mandatory vaccination (70.6 %). Respondents' past and present adherence to anti-flu and anti-pneumococcal vaccines does not predict their intentions to vaccinate against COVID-19. Finally, a semantic analysis of the reasons of acceptance/refusal of COVID-19 vaccination suggests a complex decision-making process revealed by the participants' use of common words in pro-and-cons arguments.

Conclusion: The heterogeneity in the COVID-19 vaccine hesitancy, determinants and opinions detected at different ages, genders and pandemic phases suggests that health authorities should avoid one-size-fits-all vaccination campaigns. The results emphasize the long-term importance of reinforcing vaccine information, communication and education needs.

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1. Introduction

Vaccines are one of the most effective tools for preventing infectious diseases. Especially during pandemics, widespread public uptake of the vaccine is crucial to control the contagion, reduce mortality and control the disease [1–3]. Vaccine hesitancy (henceforth, VH), i.e. the delay, reluctance or refusal of vaccination despite their availability, led to increases in disease outbreaks in multiple countries in the past decade and today is a growing global

public health threat. The WHO declared it to be one of the ten main health threats in 2019. Previously, we studied the difficulty of carrying out vaccination campaigns on a global scale [4], the impact of VH for routine vaccination in one of the Italian regions with the lowest vaccination rate [5], as well as the neuro-cognitive determinants which are at the base of VH [6,7].

In the wake of the COVID-19 pandemic, different population sub-groups of various nations have revealed different levels of hesitancy towards COVID-19 vaccines [8,9]. When the production of different vaccines against SARS-CoV-2 was on the horizon, data revealed that in Europe approximately 1 person out of 4 was not willing to be vaccinated [10], but after a series of national lockdown measures, the approval of some COVID-19 vaccines and the start of the global vaccination programmes, VH has gradually

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lessened. Nevertheless, the evolution of factors influencing the hesitancy and/or acceptance of COVID-19 vaccines before and during the vaccination campaign remains unclear. Several determinants of hesitancy may have indeed influenced the social attitude towards COVID-19 vaccines [11–13]. In particular, according to SAGE VH Matrix [14–16], “contextual influences” such as extensive media exposure, “individual/group influences” such as vaccine safety, demographic characteristics of individuals and perceptions of vaccination risks/benefits, or “vaccine-specific issues” such as the introduction of innovative vaccines, delivery programs (mass vaccination campaign) and strength of recommendation (compulsory or not) might have played some role on vaccine confidence, especially in a pandemic context [17,18]. More recently, other analyses integrated these three categories of determinants with two others: one concerning systematic errors of judgment (cognitive bias) towards both vaccines and infectious disease risks, typically present in individuals whose vaccination decision-making is inadequately associated with factors such as perceived risk, ambiguity, uncertainty, and feeling of loss, and who are prone to conspiracy theories; the other regarding the mistrust in institutions and experts, typically present in individuals who adhere to anti-establishment views and have scarce propensity towards some democratic and collectivist goals [19–23].

Beginning in December 2020, the Italian COVID-19 vaccination campaign aimed at covering the entire population by using two m-RNA (Comirnaty, Pfizer/BioNTech, and Spikevax mRNA-1273, Moderna) and two DNA (Vaxzevria, AstraZeneca, and Ad26.COV2.S, J&J²) vaccines [24]. Given the arrival of second waves of the pandemic in absence of any candidate vaccine on the immediate horizon in September 2020, the aim of the study was to understand the evolution over the key 7-month vaccine campaign in Italy of the attitudes and intentions towards candidate and existing COVID-19 vaccines for adults and their children [25–29], by comparing these with both respondents’ attitudes towards adults and children’s mandatory vaccines [30–33] and past and current propensity for seasonal flu and pneumococcal vaccines [34–36], as well as to analyze the trust/mistrust reasons of acceptance/refusal of COVID-19 vaccination.

2. Methods

The survey was conducted by the CNR Interdepartmental Center for Research Ethics and Integrity as a part of a larger research project on vaccine hesitancy (Vaccine Hesitancy Forum). The questionnaire was administered to Italian residents (>16yo) between September 18th 2020 and April 13th 2021, corresponding to the following pandemic epidemiological phases: low transmission intensity (September 2020), progressive increase in the transmission intensity (October 2020), high transmission intensity and 2nd COVID-19 lockdown period (from November 6th 2020 to January 15th 2021), high transmission intensity with social restrictions (from January 16th 2021 to April 13th 2021). These phases were the key 7-months for COVID-19 vaccines attitudes, as we moved from promising experimental candidates to actually available vaccines, administered to the public.

The questionnaire has been developed and published through the EUSurvey platform, the European Commission’s multilingual opensource online survey management tool which complies with

privacy regulations.³ The survey was anonymous, no personal information of any kind was entered into the open question boxes, only technical cookies were activated and no IP address was identified or tracked.⁴ Researchers were not able to identify individuals filling out the questionnaire. The information collected has been used solely for scientific purposes. A study description has been provided to participants, detailing research aspects and the nature of the collected data. Invitations have been sent through social media (WhatsApp, Facebook) and mailing lists available to the CNR for similar surveys.

The survey contained 13 questions: 3 on demographic data such as gender, age and Italian region of residence; 8 on vaccine attitudes; and 2 open-ended questions about the reasons of vaccine confidence/refusal.

A preliminary word frequency analysis has been conducted, as well as a statistical bivariate analysis using advanced excel formulas and functions.

Two ethical reviews were issued respectively by the National Ethics Committee for COVID-19 Clinical Trials (n. 70/2020) and by the CNR Research Ethics and Integrity Committee (n. 0038539/2022).

3. Results

As shown in Table 1, a total of 21,537 questionnaires were collected during a period of seven-months, from September 18th 2020 to April 13th 2021, but we report here data divided into three temporal phases to analyze the different public perceptions corresponding to three different periods of the Italian vaccine campaign: phase 1 (from September 19th 2020 to December 26th 2020) spans from a period of poor media coverage of COVID-19 vaccine candidates to the official inauguration of the campaign with EU Vaccination Day; phase 2 (from December 27th 2020 to February 8th 2021) covers the early national vaccination programme with two m-RNA vaccines (Comirnaty and Spikevax) exclusively available for physicians and health care workers; phase 3 (from February 9th 2021 to April 13th 2021) starts, by including a third DNA (Vaxzevria) vaccine, with the public campaign targeted to elders (>80 yo), fragile people and school/university teachers, and ends with an expansion of the categories of elderly people involved (>70 yo) and about 12.5 % of the Italian population vaccinated.⁵ On April 1st 2021, two weeks before the conclusion, Italy was the first country in Europe to make vaccination against COVID-19 mandatory for healthcare workers by imposing restrictions in cases of non-compliance⁶.

Among the participants, women were prevalent compared to men in all three phases (W. 62.7 % vs M. 37.3 %), with a large prevalence (76.3 %) of middle-aged participants (31–65 yo). The regional distribution of participants, although showing a general predominance of the center-north Italy and of the islands, remained constant in all regions in all phases, except three regions (Lombardia, Veneto, Emilia-Romagna) which, having been mostly affected by the pandemic, showed an increase of about 4 times in the residents’ participation between phase 1 and 2. Since Lombardy is the region with the highest number of participants, to evaluate any bias and deviations we separated this region from all the others and checked the results of the answers: they did

³ <https://ec.europa.eu/eusurvey/home/welcome>.

⁴ <https://ec.europa.eu/eusurvey/home/privacystatement>; https://ec.europa.eu/info/cookies_en.

⁵ Ministero della Salute: Monitoraggio settimanale Covid-19, report 12–18 Aprile 2021 (Ministry of Health: Weekly Covid-19 monitoring, report 12–18 April 2021); <https://www.salute.gov.it/portale/nuovocoronavirus/dettaglioNotizieNuovoCoronavirus.jsp?lingua=italiano&menu=notizie&p=dalministro&id=5442>.

⁶ Italian Law Decree 2021, April 1, No. 44.

² The two European and Italian regulatory agencies, EMA and AIFA, approved the Comirnaty vaccine on 23 December 2020, the mRNA-1273 vaccine between 5 and 6 January 2021, and the Vaxzevria vaccine between 29 and 30 January: all the first 3 vaccines were made available to the Italian population a few days after approval. On the other hand, the Ad26.COV2.S vaccine was approved between 11 and 12 March, but was made available for distribution on 21 April 2021, and therefore is not among those present in this survey concluded on April 13th 2021.

Table 1
Characteristics of survey respondents.

Respondents	n = 21537	
Sex		
Female	n = 13619	63.24 %
Male	n = 7889	36.61 %
I prefer not to say	n = 34	0.16 %
No answer	n = 0	0 %
Age		
16–30	n = 2059	9.56 %
31–50	n = 8693	40.36 %
51–65	n = 7754	36 %
Over 65	n = 3031	14.07 %
No answer	n = 0	0 %
Italian region		
Lombardia	n = 7005	32.53 %
Lazio	n = 2435	11.31 %
Piemonte	n = 2352	10.92 %
Emilia Romagna	n = 2040	9.47 %
Veneto	n = 1606	7.46 %
Toscana	n = 1550	7.2 %
Others	n = 4549	21.13 %
No answer	n = 0	0 %
Seasonal flu vaccine (past years)		
Yes	n = 7484	34.75 %
No	n = 14053	65.25 %
No answer	n = 0	0 %
Pneumococcal polysaccharide vaccine (past years)		
Yes		
No	n = 1991	9.2 %
No answer	n = 19546	90.7 %
	n = 0	0 %

not change, i.e. with or without Lombardy they differ between 0 and 1 %.

In the seven-month period analyzed, in all ages the strong and clear willingness (see Table 2 answers 4.1, 4.2) to be vaccinated against COVID-19 increased constantly from 57.9 % in phase 1, to 84.6 % and 87 % in phase 2 and 3, whereas the mild willingness (answer 4.3) fell sharply by two-third (30.2 %, 11.1 %, 9 %). Furthermore, in all ages an increasing favor towards compulsory vaccination against COVID-19 vaccine was also observable for the same phases from 70.8 % in phase 1, to 72.6 %, and 78.1 % in phase 2 and 3. Compared to all the other age groups, the support of compulsory vaccination was less significant in adult men and women (51–65 yo): in particular, in phase 1 the opposition of this group was double (17.3 % vs 9 % all ages), although tending to align to the other age groups in phase 3 (8.6 % vs 6.6 % all ages).

From phase 1 to 3, the participants with strong and clear willingness to vaccinate their children against COVID-19 (answers 12.1, 12.2) increased on average from 51 % to 66.5 %, whereas the moderate willingness (answer 12.3) diminished from 26.5 % to 10.2 % and the contrary almost halved from 9 % to 4.1 %. As for compulsory vaccination for their children, participants also showed to be largely in favor to it in all three phases (66.3 %, 64.6 %, 70.6 %), albeit to a minor extent, and with a lesser increase over time, if compared to the propensity for adult mandatory vaccination (71 %, 72 %, 78 %). Noteworthy, adult women (51–65 yo) halved their opposition to the obligation for children from 16 % to 8 % from phase 1 to 3.

By correlating the propensity to be vaccinated with the one towards compulsory vaccination, we noticed that among respondents willing to vaccinate (answers 4.1, 4.2, 4.3) against COVID-19, three-quarters (75.1 %) of men and women of all ages were also in favor of mandatory vaccination (in all three phases), while the 17.8 % were uncertain and the remaining (7.1 %) were against. In this correlation, the less favorable group (61.6 %) was represented by young and adult women (31–65 yo) during phase 1, i.e. before the availability of any vaccine.

The same correlation focused on mandatory vaccine for children showed that respondents of all ages were steadily in favor of both, rising from 65.4 % in phase 1 to 70 % in phase 3. The group that was less favorable to the obligation for children in all phases (54 %, 54 %, 58 %) was again represented by women, in particular adult ones (31–50yo). Interestingly, even among those who were not in favor of vaccines (answers 4.4, 4.5, 4.6) there was a small percentage of 4.4 % in favor of compulsory vaccination for adults and of 2.2 % for children.

Moreover, we correlated the propensity for the anti-COVID-19 vaccine with the present (answer 6.1, 6.2, 6.3) and past (7.1, 7.2) propensity for anti-flu vaccines, as well as with the present (8.1, 8.2, 8.3) and past (9.1, 9.2,) propensity for anti-pneumococcal vaccine. As expected, participants used in the last years to be vaccinated against seasonal flu showed a similar propensity to get vaccinated against COVID-19. We also noticed, especially between phase 1 and 2, a decrease in propensity for the anti-flu vaccine in young and adult respondents (16–65 yo), while in seniors (>65 yo) this trend is reversed. Noteworthy, from 20 % to 50 % of the young and adult respondents (16–50yo) who in the past were not vaccinated for the seasonal flu (answer 6.2, 6.3) expressed willingness to vaccinate against COVID-19.

The trend of propensity for anti-pneumococcal vaccine for participants favorable to COVID-19 vaccination was similar to that of anti-flu vaccine but lower of about 25–30 %, i.e., between 8 and 15 % for young and adult (16–50yo) and about 15–50 % for senior (>51yo). A similarity that can also be found in the seasonal trend of propensity from phase 1 to 3, decreasing in young and adult respondents (16–65 yo) and increasing in seniors (>65).

Finally, qualitative analysis on the two open-ended questions (answers 10–11 and 14–15) reveals that 8 out of 10 of the respondents (81.4 %) provided arguments about their vaccine confidence or refusal. Significantly, one fifth (20.5 %) of them, i.e. 3600 respondents, completed both the field “I trust vaccines because...” (answer 10) and “I don’t trust vaccines because...” (answer 11) or the field “Concerning my children, I trust vaccines because...” (answer 14) and “Concerning my children, I don’t trust vaccines because...” (answer 15), with lists of pro-and-cons reasons, although the great majority of them was in favor of vaccine, in line with the general results of the survey. We conducted a preliminary Word Frequency Analysis through NVivo 12 Plus, which provided an overall idea of the most common concepts used in our corpus of responses (see Table 3). We found that the two lists of the 20 high frequency words used by participants when commenting on the opposite ideas (trust vs don’t trust) were almost the same, i.e. with ‘trust’, ‘disease’ and ‘science’ at the top of both lists, even if in different positions. The lexical analysis found that pro-and-cons arguments referred to the same semantic areas with the sole change of the structure between affirmative and negative sentences or vice versa (i.e., I trust or I do not trust), a result we intend to better investigate in the ongoing new survey. Furthermore, we noticed that in the “trust” group there was a prominence of concepts that refer to science, its methods and procedures (e.g. “approved”, “prevention”, “scientifically”, “instrument”), while in the “don’t trust” group medical and clinical aspects of COVID-19 prevailed (e.g. “secondary effects”, “long term outcome”, “adverse reactions”).

The answer “I prefer not to answer” was negligible (less than 0.2 %) and the “no answer” option is substantially absent.

4. Discussion

Started on September 18th 2020, when COVID-19 vaccines were still hypothetical vaccine candidates almost ignored by main Italian and international media, our study on VH shows that as

Table 2
Questions administered (original in Italian) [Word version].

-
- 1. - Gender:**
1) Female; 2) Male; 3) I prefer not to answer
- 2. - Age:**
1) 16–30 yo; 2) 31–50 yo; 3) 51–65 yo; 4) > 65 yo
- 3. - Region where I normally reside:**
1. Abruzzo; 2) Basilicata; 3) Calabria; etc . . . (list of the 20 Italian regions).
- 4. - When a vaccine against Covid-19 becomes available:**
1) I will definitely get the vaccine, even multiple vaccines against Covid-19 if available.
2) I will definitely get the vaccine.
3) I will probably get the vaccine, but I will get more information first.
4) I probably will not get the vaccine, but I will get more information first.
5) I will not get the vaccine.
6) In no case I will get the vaccine.
7) I cannot answer at this moment.
- 5. - Concerning the mandatory vaccination against Covid-19, I am:**
1) In favour.
2) Contrary.
3) Uncertain.
- 6. - Concerning the seasonal flu vaccine, this year:**
1) I will get vaccinated or have already been vaccinated.
2) I will not vaccinate.
3) I do not know yet whether to get vaccinated.
- 7. - Over the past years:**
1) I have already been vaccinated against seasonal flu.
2) I have never been vaccinated against seasonal flu.
- 8. - With respect to the pneumococcal (pneumonia) vaccine, this year:**
1) I will vaccinate or have already been vaccinated.
2) I will not vaccinate.
3) I don't know yet whether to get vaccinated.
- 9. - Over the past years:**
1) I was already vaccinated against pneumococcal disease (pneumonia).
2) I have never been vaccinated against pneumococcal disease (pneumonia).
- 10. - I trust vaccines because . . . (Enter text with minimum 3 and maximum 1500 characters)**
- 11. - I don't trust vaccines because . . . (Enter text with minimum 3 and maximum 1500 characters)**
- 12. - When a Covid-19 vaccine becomes available:**
1) I will definitely have my child vaccinated, even with multiple Covid-19 vaccines if available.
2) I will definitely have my child vaccinated.
3) I will probably have my child vaccinated, but I will get more information first.
4) I will probably not vaccinate my child, but I will get more information first.
5) I will not vaccinate my child.
6) I will not vaccinate my child under any circumstances.
7) I don't know how to answer at this moment.
- 13. - Concerning the mandatory vaccination of children and adolescents against Covid-19, I am:**
1) In favour.
2) Contrary.
3) Uncertain.
- 14. - Concerning my children, I trust vaccines because . . . (text min. 3 and maximum 1500 characters)**
- 15. - Concerning my children, I don't trust vaccines because . . . (text min. 3 and maximum 1500 characters)**
-

early as in the 1st phase (from September to December 2020) almost 1 out of 4 of the survey participants (23.5 %) were available to “definitely get the vaccine” and “even multiple vaccines against COVID-19, if available” (respectively, answers 4.2 and 4.1). Therefore, before the approval of the vaccines there was a group of people *a priori* willing to adhere to the administration of several vaccines or doses: an unusual circumstance indeed. A strong citizens' attitude that should be remembered for future epidemics in order to properly launch campaigns with new, multiple and heterologous vaccines.

During the 1st phase, such a strong propensity towards COVID-19 vaccines is gender biased: it is almost 30 % higher in men than in women of all ages, but the latter reach the same general propensity of men if we also add the group of those who are in favor (without any reference to several vaccines) and of those who are in favor only after having received more information. Both genders reach the same propensity in the 2nd phase (95.8 %) with a dramatic increase in women's trust in vaccines, probably due to a thorough understanding of the vaccines, their efficacy and limited side effects after the early phase of vaccine campaign. Women were also more prevalent than men in participating in the survey,

confirming that engagement in active seeking of vaccine and online health-related information is higher for women [37–40].

Support for COVID-19 vaccination remains very high and non-gender-biased even in the 3rd phase (96.1 %), which temporally precedes the period of decline of COVID's transmission intensity and therefore of diminished public perception of its necessity. A similar increase, albeit to a lesser degree (from 51 % to 66.5 %), also emerges in the participants' strong and clear willingness to vaccinate their children against COVID-19 from phase 1 to 3.

During the three phases there was an overall decrease, from 3.2 % to 1.7 %, in the portion of the participants who showed soft refusal but were looking for more information (answer 4.4). However, interestingly, here too there was a peculiar gender bias: male respondents grew from 0 % to 1.9 %, while female respondents halved from 3.2 % to 1.5 %, shifting to the group in favor of vaccines.

Overall, we observed an increase in vaccination adherence and a decrease in request for information. Between phase 1 and 3, the confidence of those in favor of the COVID-19 vaccine increases of 50 %, the number of people who will certainly get the vaccine increases by two-third, and the number of people who wanted more information decreases by two-third. In the latter case, we

Table 3
Word Frequency Analysis (NVivo 12).

n.	20 High Frequency Words (“I trust vaccines”)				20 High Frequency Word (“I don’t trust vaccines”)			
	Word (Italian)	English translation	Count	Weighted Percentage (%)	Word (Italian)	English translation	Count	Weighted Percentage (%)
1	malattie	diseases	4130	2,03	fido	I trust	1478	2,17
2	scienza	science	3028	1,49	vaccini	vaccines	1096	1,61
3	fido	I trust	2992	1,47	effetti	effects	836	1,23
4	sicuri	safe	1913	0,94	collaterali	secondary	575	0,84
5	vaccini	vaccines	1850	0,91	vaccino	vaccine	560	0,82
6	testati	tested	1474	0,73	covid	covid	354	0,52
7	ricerca	research	1247	0,61	lungo	long	344	0,51
8	scientifica	scientific	1191	0,59	termine	term	300	0,44
9	salute	health	873	0,43	testati	tested	250	0,37
10	vita	life	847	0,42	interessi	interests	245	0,36
11	gravi	serious	840	0,41	reazioni	adverse reactions	223	0,33
12	debellare	eradicate	720	0,35	farmaceutiche	pharmaceutical companies	216	0,32
13	efficaci	effective	654	0,32	tempo	time	202	0,30
14	vaccino	vaccine	644	0,32	economici	inexpensive / low-cost	179	0,26
15	proteggono	protecting	633	0,31	case	case	176	0,26
16	fiducia	trust	631	0,31	paura	fear	170	0,25
17	utili	useful	618	0,30	rischio	risk	166	0,24
18	effetti	effects	559	0,28	temo	I am afraid	166	0,24
19	vite	lives	554	0,27	salute	health	160	0,24
20	comunità	community	533	0,26	fidarmi	to trust	157	0,23

Lists of the 20 high frequency words used by participants when commenting on the trust/mistrust reasons for acceptance/refusal of COVID-19 vaccination (see Table 2, answers 10–11 and 14–15).

note a clear transfer of respondents who wanted more information into the two most pro-vaccination responses, suggesting that two-third of the vaccine-hesitant respondents of phase 1 either received the requested information or have increased their fears of the epidemic and increased their willingness to be vaccinated.

Generally, there was an increase of confidence in COVID-19 vaccination among those who had first shown hesitation, perplexity, and prejudice. Only one-third of the vaccine strong opponents present in the 1st phase were still hostile to vaccinations in the 3rd phase. This part of the population, equal to about 10 %, is therefore the one that has been resistant to the increase in information and to risk perception during the Italian vaccination campaign and can be regarded as being represented by strong vaccine-hesitant individuals.

As for the relationship between respondents’ propensity for the COVID-19 vaccines versus their past and present propensity for both anti-flu and anti-pneumococcal vaccines, we outline that in the general population the compliance for the latter cannot be a reliable indicator of whether they intend to get the COVID-19 vaccine. Indeed, from half to two-third (50–78 %) of the young and adult respondents (16-65yo), who typically had never been vaccinated against seasonal flu, were equally willing to get COVID-19 vaccines. The same happened if we look at the case of pneumococcal vaccine (73–89 %). This suggests that vaccine hesitancy determinants are often linked to a specific vaccine, especially during a pandemic [41]. On the other hand, it is true that in the Italian general population the propensity to the COVID-19 vaccines has been a promoter of >50 % to the flu vaccine if compared to the last 4 years, but we argue that this phenomenon was probably due to the need of the people to facilitate the differential diagnosis in respiratory diseases and to nonspecifically protect the respiratory tract [42–44].

As for adult compulsory vaccination, participants showed a large and increasing favor to it up to 78 % in the 3rd phase, in a way similar, although less extensive and growing, to their propensity for children’s mandatory vaccination, which reaches 70.6 % in the final phase of the analysis. Despite having stated resistance to vaccines, a tiny portion of people support mandatory vaccination for adults and children (4.4 % and 2.2 %). These individuals may

be those who want to leave the choice of vaccination to the government, although further research is required to confirm this hypothesis. We have then found an unexpected favor towards the compulsory vaccination of minors since the beginning of the vaccination campaign, a favor that can be linked to Italy’s already-existing required mandatory policy for routine pediatric immunizations [45].

Finally, concerning the two open-ended questions we noticed that the vast majority of respondents (81 %) answered the questions about the trust/mistrust of vaccinations, a sign of a strong desire to express their opinion. In particular, doubts and hesitations were present in those who expressed their final adherence to vaccination for COVID-19, since they also filled in both the fields “I don’t trust vaccines because ...” and “Concerning my children, I don’t trust vaccines because ...”, confirming that the decision-making process towards vaccination remains a challenge. The words preferentially used by the group which trusted vaccination seem to express more abstract and scientific concepts, whereas the “I do not trust” group seems to express concepts related to their fears.

5. Conclusion

The heterogeneity in the COVID-19 vaccine hesitancy, determinants and opinions detected at different ages, genders and pandemic phases suggests that health authorities should avoid one-size-fits-all vaccination campaigns [46]. Future analysis will need to understand whether the progressive decrease in the request for vaccine-related information by participants is due to an effective availability of information offered by the media and health institutions, and/or to increasing confidence in pandemic vaccination and/or to an alignment with social norms characterized by global adhesion to the vaccination campaign. The results emphasize the long-term importance of reinforcing vaccine information, communication and education needs in preparation for health emergencies such as the current pandemic. Notably, over the course of time, we can claim that the data of those in favor, against, and hesitant toward vaccines correlate with what actually occurred in a more advanced stage of the pandemic program

[47–49], indicating that the survey did have some predictive value.⁷

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No potential conflicts of interest were disclosed.

Availability of data and materials

All data are accessible by request.

Ethical statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All authors attest they meet the ICMJE criteria for authorship.

Authors' contributions

AG, RMZ, MA, CC* CC conceived the study and was in charge of overall direction and planning. CC and AG designed the questionnaire and defined the study methodology, with a contribution of RMZ. RMZ collected the data. CC, AG, and RMZ reviewed and edited the data. CC and AG analyzed the data and drafted the manuscript. MA provided statistical analysis. All authors have approved the manuscript and agree with its submission.

Data availability

Data will be made available on request.

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.

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References

- Meslé MM, Brown J, Mook P, et al. Estimated number of deaths directly averted in people 60 years and older as a result of COVID-19 vaccination in the WHO European Region, December 2020 to November 2021. *Euro Surveill* 2021; 26: 10.2807/1560-7917.ES.2021.26.47.2101021.
- Steele MK, Couture A, Reed C, et al. Estimated Number of COVID-19 Infections, Hospitalizations, and Deaths Prevented Among Vaccinated Persons in the US, December 2020 to September 2021. *JAMA Netw Open* 2022;5:e2220385.
- ISS 2022 Istituto Superiore di Sanità. Infezioni da SARS-CoV-2, ricoveri e decessi associati a COVID-19 direttamente evitati dalla vaccinazione. Italia, 27 dicembre 2020 – 31 gennaio 2022. Nota tecnica [National Institute of Health. SARS-CoV-2 infections, hospitalizations and deaths associated with COVID-19 directly avoided by vaccination. Italy 27/12/2020 – 31/01/2022. Technical Note.]; https://www.iss.it/documents/20126/6703853/NT_Eventi+evitati+COVID19_LAST.pdf/a140e155-bd62-adcd-1b29-d1be3464ed48?t=1649832260103.
- Arnaudo L, Caporale C, Costa E, Locatelli F, Magrini Lezioni da una pandemia N. Per uno sviluppo condiviso e un accesso equo a cure essenziali e vaccini. *Mercato Concorrenza Regole, Rivista quadrimestrale* 2021;2:343–66. <https://www.rivisteweb.it/issn/1590-5128>. <https://doi.org/10.1434/102666>.
- Melot B, Bordin P, Bertoni C, Tralli V, Zuccali M, Grignolio A, et al. Knowledge, attitudes and practices about vaccination in Trentino, Italy in 2019. *Hum Vaccin Immunother* 2020 Jun;12:1–10. <https://doi.org/10.1080/21645515.2020.1763085>.
- Grignolio A. Understanding Vaccine Hesitancy as a Neuro-evolutionary Problem. *Notizie di POLITEIA* 2018;130 (XXXIV):8–18. ISSN 1128–2401.
- Grignolio A. Vaccines: Are they Worth a Shot? 2018. 10.1007/978-3-319-68106-1.
- Salomoni MG, Di Valerio Z, et al. Hesitant or Not Hesitant? A Systematic Review on Global COVID-19 Vaccine Acceptance in Different Populations. *Vaccines (Basel)* 2021;9(8). <https://doi.org/10.3390/vaccines9080873>.
- Gagneux-Brunon A, Detoc M, Bruel S, Tardy B, Rozaire O, Frappe P, et al. Intention to get vaccinations against COVID-19 in French healthcare workers during the first pandemic wave: a cross-sectional survey. *J Hosp Infect* 2021 Feb;108:168–73.
- Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, et al. Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. *Eur J Health Econ* 2020;21(7):977–82. <https://doi.org/10.1007/s10198-020-01208-6>.
- Betsch C, Schmid P, Heinemeier D, et al. Beyond confidence: Development of a measure assessing the 5C psychological antecedents of vaccination. *PLoS One* 2018;13.
- Geiger M, Rees F, Lilleholt L, et al. Measuring the 7Cs of Vaccination Readiness. *Eur J Psychol Assess* 2021;38:261–9.
- Kafadar AH, Tekeli GG, Jones KA, et al. Determinants for COVID-19 vaccine hesitancy in the general population: a systematic review of reviews. *Z Gesundh Wiss* 2022;1–17.
- Larson HJ, Jarrett C, Schulz WS, et al. Measuring vaccine hesitancy: The development of a survey tool. *Vaccine* 2015;33:4165–75.
- MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. *Vaccine* 2015;33:4161–4.
- Butler R, MacDonald NE. Diagnosing the determinants of vaccine hesitancy in specific subgroups: The Guide to Tailoring Immunization Programmes (TIP). *Vaccine* 2015;33(34):4176–9. <https://doi.org/10.1016/j.vaccine.2015.04.038>.
- Blasi F, Aliberti S, Mantero M, Centanni S. Compliance with anti-H1N1 vaccine among healthcare workers and general population. *Clin Microbiol Infect* 2012;18:37–41. <https://doi.org/10.1111/j.1469-0691.2012.03941.x>.
- Fraser MR. Lessons Relearned? H1N1, COVID-19, and Vaccination Planning. *J Public Health Manag Pract* 2021;27 Suppl 1. COVID-19 and Public Health: Looking Back, Moving Forward:S106–S10.
- Murphy J, Vallieres F, Bentall RP, Shevlin M, McBride O, Hartman TK, et al. Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom. *Nat Commun* 2021 Jan 4;12(1):29.
- Lindholt MF, Jørgensen F, Bor A, et al. Public acceptance of COVID-19 vaccines: cross-national evidence on levels and individual-level predictors using observational data. *BMJ Open* 2021;11:e048172.
- Azarpanah H, Farhadloo M, Vahidov R, et al. Vaccine hesitancy: evidence from an adverse events following immunization database, and the role of cognitive biases. *BMC Public Health* 2021;21:1686.
- Bucchi M. To boost vaccination rates, invest in trust. *Nature Italy* 2021 Jan 12. <https://doi.org/10.1038/d43978-021-00003-y>.
- Falcone R, Ansani A, Coli E, et al. Trusting COVID-19 vaccines as individual and social goal. *Sci Rep* 2022;12:9470.
- Marziano V, Guzzetta G, Mammone A, et al. The effect of COVID-19 vaccination in Italy and perspectives for living with the virus. *Nature. Communications* 2021;12:7272.
- Kreps S, Prasad S, Brownstein JS, Hswen Y, Garibaldi BT, Zhang B, et al. Factors Associated With US Adults' Likelihood of Accepting COVID-19 Vaccination. *JAMA Netw Open* 2020 Oct 1;3(10):e2025594.
- Dror AA, Eisenbach N, Taiber S, Morozov NG, Mizrahi M, Zigron A, et al. Vaccine hesitancy: the next challenge in the fight against COVID-19. *Eur J Epidemiol* 2020 Aug;35(8):775–9.
- Alley SJ, Stanton R, Browne M, To QG, Khalesi S, Williams SL, et al. As the Pandemic Progresses, How Does Willingness to Vaccinate against COVID-19 Evolve? *Int J Environ Res Public Health* 2021 Jan 19;18(2).
- Olusanya OA, Bednarczyk RA, Davis RL, et al. Addressing Parental Vaccine Hesitancy and Other Barriers to Childhood/Adolescent Vaccination Uptake During the Coronavirus (COVID-19) Pandemic. *Front Immunol* 2021;12:663074.
- Ruiz JB, Bell RA. Parental COVID-19 Vaccine Hesitancy in the United States. *Public Health Rep* 2022;137:1162–9.
- Douglas T, Forsberg L, Pugh J. Compulsory medical intervention versus external constraint in pandemic control. *J Med Ethics* 2020;47:e77.
- Sprengholz P, Korn L, Eitze S, et al. Attitude toward a mandatory COVID-19 vaccination policy and its determinants: Evidence from serial cross-sectional surveys conducted throughout the pandemic in Germany. *Vaccine* 2022.
- Giannakou K, Kyprianidou M, Heraclides A. Attitudes and Determinants of Mandatory Vaccination against COVID-19 among the General Population of Cyprus: A Nationwide Cross-Sectional Study. *Vaccines (Basel)* 2022;10.
- Gibelli F, Ricci G, Sirignano A, et al. COVID-19 Compulsory Vaccination: Legal and Bioethical Controversies. *Front Med (Lausanne)* 2022;9:821522.
- Mercadante AR, Law AV. Will they, or Won't they? Examining patients' vaccine intention for flu and COVID-19 using the Health Belief Model. *Res Social Adm Pharm* 2021 Dec 30.
- Goldman RD, McGregor S, Marneni SR, Katsuta T, Griffiths MA, Hall JE, et al. Willingness to Vaccinate Children against Influenza after the Coronavirus Disease 2019 Pandemic. *J Pediatr* 2021 Jan;228(87–93):e2.

⁷ The complete data describing the weekly trend of the anti-COVID-19 vaccination coverage of the Italian population can be consulted both on the website of the National Institute of Health (<https://www.iss.it/en/vaccini-covid-19>) and the website of the Ministry of Health (<https://www.salute.gov.it/portale/nuovocoronavirus/archivioNotizieNuovoCoronavirus.jsp>).

- [36] Grech V, Gauci C. Vaccine hesitancy in the University of Malta Faculties of Health Sciences, Dentistry and Medicine vis-a-vis influenza and novel COVID-19 vaccination. *Early Hum Dev* 2020 Nov;12:105258.
- [37] Ibuka Y, Chapman GB, Meyers LA, et al. The dynamics of risk perceptions and precautionary behavior in response to 2009 (H1N1) pandemic influenza. *BMC Infect Dis* 2010;10:296.
- [38] Nikoloudakis IA, Vandelanotte C, Rebar AL, et al. Examining the Correlates of Online Health Information-Seeking Behavior Among Men Compared With Women. *Am J Mens Health* 2018;12:1358–67.
- [39] Wang X, Shi J, Kong H. Online Health Information Seeking: A Review and Meta-Analysis. *Health Commun* 2020;36:1163–75.
- [40] Covolo L, Guana M, Bonaccorsi G, et al. Exploring the Online Health Information-Seeking Behavior in a Sample of Italian Women: The “SEI Donna” Study. *Int J Environ Res Public Health* 2022;19.
- [41] Merkley E, Loewen PJ. The correlates and dynamics of COVID-19 vaccine-specific hesitancy. *Vaccine* 2022;40:2020–7.
- [42] Kong G, Lim NA, Chin YH, et al. Effect of COVID-19 Pandemic on Influenza Vaccination Intention: A Meta-Analysis and Systematic Review. *Vaccines (Basel)* 2022;10.
- [43] Domnich A, Grassi R, Fallani E, et al. Changes in Attitudes and Beliefs Concerning Vaccination and Influenza Vaccines between the First and Second COVID-19 Pandemic Waves: A Longitudinal Study. *Vaccines (Basel)* 2021;9.
- [44] Domnich A, Orsi A, Trombetta CS, et al. COVID-19 and Seasonal Influenza Vaccination: Cross-Protection, Co-Administration, Combination Vaccines, and Hesitancy. *Pharmaceuticals (Basel)* 2022;15.
- [45] D’Ancona F, D’Amario C, Maraglino F, et al. The law on compulsory vaccination in Italy: an update 2 years after the introduction. *Euro Surveill* 2019;24.
- [46] Steinert JI, Sternberg H, Prince H, et al. COVID-19 vaccine hesitancy in eight European countries: Prevalence, determinants, and heterogeneity. *Sci Adv* 2022;8:eabm9825.
- [47] Gozzi N, Chinazzi M, Davis JT, et al. Anatomy of the first six months of COVID-19 vaccination campaign in Italy. *PLoS Comput Biol* 2022;18:e1010146.
- [48] Reno C, Sanmarchi F, Stoto MA, et al. The impact of health policies and vaccine rollout on the COVID-19 pandemic waves in Italy. *Health Policy Technol* 2022;11:100604.
- [49] Zarbo C, Candini V, Ferrari C, et al. COVID-19 Vaccine Hesitancy in Italy: Predictors of Acceptance, Fence Sitting and Refusal of the COVID-19 Vaccination. *Front Public Health* 2022;10:873098.