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Associations of COVID-19 risk perception with vaccine hesitancy over time for Italian residents

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ABSTRACT

Rationale: Many countries were and are still struggling with the COVID-19 emergency.

Despite efforts to limit the viral transmission, the vaccine is the only solution to ending the pandemic. However, vaccine hesitancy could reduce coverage and hinder herd immunity.

Objective: People's intention to get vaccinated can be shaped by several factors, including risk perception which, in turn, is influenced by affect. The present work aimed at investigating how risk perception and some factors associated with the decision to comply with vaccination modulated vaccine acceptance for COVID-19 as compared to seasonal influenza, and how these have varied during the lockdown phases.

Method: The study followed the main phases of the emergency in Italy, investigating the intention to get vaccinated against flu and against SARS-CoV-2 (if a vaccine was available) before, during and after the first national lockdown, covering the period from the end of February to the end of June 2020. We investigated the effect of risk perception and other predictors on the decision of getting vaccinated.

Results: Compared to the pre-lockdown phase, during the lockdown more people were willing to get vaccinated for COVID-19, regardless of their beliefs about vaccines, and as

risk perception increased, so did the intention to accept the vaccine. The acceptance of the flu vaccine increased after the re-opening phase. In addition, the intention to get vaccinated against COVID-19 and against flu increased if there was previous flu vaccination behavior but decreased with increasing doubts about the vaccines in general.

Conclusions: The observation of vaccination intentions across the three main phases of the emergency allows important considerations regarding psychological, affect, and demographic determinants useful to tailor public health communication to improve public response to future epidemics.

Keywords: COVID-19; Risk perception; Vaccine acceptance; Flu vaccine; SARS-CoV-2 vaccine.

Introduction

The SARS-CoV-2 emergency severely hit and, at the time of writing, is still affecting the entire world. The majority of the Governments had to enforce extraordinary virus containment measures and strictly regulate private, public and working life by limiting the mobility of the population. However, the compliance with these prescribed behavioral norms and the implementation of preventive and protective measures is also steered by the perception of risk related to new viruses (Dryhurst et al., 2020; Ibuka et al., 2010; Wise et al., 2020). In the early stages of the outbreak, especially before it was declared a pandemic, many people, including some experts and politicians, were not particularly worried by the new coronavirus as they considered it similar to a seasonal influenza (flu). Only when the characteristics of the new coronavirus became better known, revealing its systemic range of symptoms (European Centre for Disease Prevention and Control, 2020), it became clearer that the development of a vaccine is the essential tool to fight the pandemic (WHO, 2020). Thus, in comparison to previous emergencies where the pandemic has been avoided, for example with the epidemic of SARS in 2002-2004, now experts are trying to develop an effective vaccine at pandemic speed (Lurie et al., 2020). A vaccination program against COVID-19 could substantially alleviate the problems related to the spread of the virus but, then, the challenge for the policy makers will be to encourage people to receive the vaccine. Indeed, the majority of vaccine skeptics seems to be reluctant to undergo it (Fadda et al., 2020). This is a consistent risk since vaccine hesitancy, namely the delay in acceptance or refusal of vaccines despite availability of vaccination services (MacDonald, 2015, but see Bedford et al., 2018), has increased to the point that it was declared one of 10 major global health threats (WHO, 2019) and could result in a low prevalence of available vaccination for a high-risk infection (Reintjes et al., 2016). Although many people agreed to receive the vaccine, a high rate of non compliant people could undermine herd immunity. Understanding

people's general attitude towards vaccination is therefore crucial to the successful implementation of a large-scale vaccination program.

Previous studies have shown a relationship between previous flu vaccinations and pandemic vaccinations showing that the best predictor of the uptake of a pandemic vaccine is having received the flu vaccine in the previous season (Chor et al. 2011; Seale et al., 2010). It is worth noting, however, that the uptake of vaccination for seasonal flu is globally rather low. For instance, in the United States, in the 2018-19 vaccine season, the rate of flu vaccinations among people whose age ranged from 18 to 64 years was about 36% (Center for Disease Control and Prevention, 2020). Similarly, in Italy, the vaccination rate remains low: In the 2018/19 season, 53.1% in the age group > 65 years, and just 15.8% in the general population got the seasonal vaccine (Ministry of Health, 2019). In this perspective, the combination of the claims affirming that COVID-19 is similar to flu, especially common in the first phase of the emergency, and the findings showing that the best predictor of a vaccine against a pandemic virus is previous flu vaccine uptake (Chor et al. 2011; Seale et al., 2010), might make one assume that the low uptake just described for flu could affect people's willingness to get vaccinated against COVID-19, too. This could be particularly worrying, according to experts, as it is estimated that for a COVID-19 vaccine to stop the pandemic, coverage should probably be 75-80% (Bartsch et al., 2020; Cohen, 2020). However, a US study conducted between May 14th and 18th, 2020, showed that less than 50% of Americans are committed to receiving a SARS-CoV-2 vaccine (Neergaard & Fingerhut, 2020). Moreover, a recent poll (July 28th - 30th, 2020), as reported by WebMD Health News (2020), showed that only 42% of American people would get a COVID-19 vaccine, that's the lowest percentage so far. Furthermore, and directly related to our own study, it has been reported that the acceptance percentages have decreased from 55% in early May to 50% in late May, and 46% in early July, showing a decreasing temporal trend. Meantime, similar data were

collected in Italy, highlighting that in May only 25% of the population was likely to get vaccinated against SARS-CoV-2 (Barello et al., 2020).

In order to ensure a sufficiently high vaccination rate, it is important to consider that also in the previous pandemic there was some degree of hostility toward vaccines (Chor et al., 2011; Hong & Collins, 2006; Setbon & Raude, 2010). In fact, in 2009, although a vaccine against influenza H1N1 was available close to the second wave of the pandemic, vaccination rates were lower than expected, with population coverage ranging from 0.4 to 59% in 22 countries (Mereckiene et al., 2012). As for influenza vaccination, a low risk-perception, doubts about the effectiveness of vaccines, and fear of side-effects were the most common reason for rejection (Lehmann et al., 2014). Several other studies showed that risk perception plays a crucial role in the intention to get vaccinated (Hong & Collins, 2006; Schmidet al., 2017; Setbon & Raude, 2010; Weinstein et al., 2007) and in vaccination behavior (Brewer et al., 2007; Freimuth et al., 2017). Thus, this paper aims at investigating whether risk perception modulates the acceptance of a potential vaccine against SARS-CoV-2 in comparison to the acceptance of the flu vaccine, and to assess people's intention to uptake the vaccines, separately. In fact, during the 2020-2021 season a co-circulation of influenza viruses and SARS-CoV-2 is more than likely. Both of them lead to life-threatening illness and death and, despite relevant differences between COVID-19 and seasonal influenza, symptoms overlap. Achieving high rates of influenza vaccination is therefore particularly important in these circumstances. In the present study, we kept track of the first four months of the pandemic in Italy, the first country with a domestic contagion after China, studying the effect of the different phases of the outbreak (pre-lockdown, lockdown, and re-opening) on risk perception and the resulting effect on the willingness to get vaccinated against seasonal flu and COVID-19. Finally, we investigated the relationship of mutual influence between the two.

Theoretical background

The risk-as-feelings model describes people's reactions to danger as instinctive and intuitive (Slovic et al., 2002, 2004; Slovic & Peters, 2006) showing that people's responses vary depending on the specific characteristic of a hazard. Specifically, risks are perceived as more dangerous when they are uncommon, unknown to science, characterized by a catastrophic nature, or killing many people at once (Slovic, 1987, 1992). Besides, an important role in the perception of risk is played by affect: it demarcates a stimulus or a context as positive or negative, depending on its specific goodness or badness (Slovic et al., 2004). Thus, affect impacts the decision-making process (Slovic et al., 2004) with fast assessments, automated and rooted in experiential thinking (Slovic et al., 2002), enabling efficient management of complex, uncertain or dangerous contexts, shaping preferences and choices (Peters et al., 2004). The affect heuristic indicates that people consider the riskiness of an event, not only on the basis of objective information, but also on the basis of the feelings they experience. When people have a positive attitude toward an event or stimulus, they tend to perceive low risk and high benefit associated with it, whereas the opposite happens when people have a negative attitude toward an event or stimulus (Finucane et al., 2000). Thus, regardless of the statistics and data about the severity of the consequences, seasonal flu is likely to induce a low risk perception, as people are familiar with, presumably they have also experienced it, directly or indirectly, it is a common illness with a predictable course, and it is not catastrophic; as a consequence, it does not evoke strong feelings. On the contrary, COVID-19 is likely to induce a high risk perception as it is a new disease, for which both science and people have little or no information and experience, with a catastrophic nature, thus evoking strong feelings. Additionally, as Fischhoff suggested (2020), people have a more limited understanding of new viruses than old viruses that they have known for a long time, and for this reason the low predictability of the COVID-19 course could increase

the perception of risk. In western countries, COVID-19, as other emergencies like Ebola Virus Disease (EVD), has been initially perceived as psychologically and physically remote, while deadly. Whereas some emergencies like EVD remain geographically far and are never experienced in western countries and could therefore be perceived as less concerning than COVID-19, the perceived risk of SARS-CoV-2 has changed since the first domestic contagion in Italy (February the 21st, 2020; Rubaltelli et al., 2020; Spina et al., 2020), making COVID-19 psychologically and physically close, with an unpredictable course and a catastrophic nature. If knowing how a risk is perceived is essential for developing an effective plan to persuade people to adopt preventive behaviors, then, measuring people's risk perception for this novel disease and comparing it with other health-related threats, like seasonal influenza and EVD, may provide useful information when preparing an effective plan aimed to improve public response to such a situation. Furthermore, people get used to risks when they are exposed to them for a long time due to habituation (Slovic, 1987) and their perceived risk decreases. In fact, people tend to underestimate the influence of emotional states on decision-making while they overestimate their ability to focus on objective information ("hot-cold empathy gap" bias; Loewenstein, & Schkade, 1999; Loewenstein, 2005; Sayette et al., 2008) leading to suboptimal long-term impact decisions. Namely, regardless of one's state (cold or hot) they will always underestimate the impact of their emotion ending up misjudging their behavior. Thus, contextualizing the "hot-cold empathy gap" bias in the COVID-19 emergency, the lockdown phase (when many new cases and deaths were reported daily, and when extraordinary virus containment measures were enforced; see Table 1) might represent a situation of hot affect, while the pre-lockdown phase might represent the cold state, in which lay people could underestimate the risk associated with the new virus.

Risk perception and vaccine acceptance

Once we understand the role that affect plays in risk perception and in decision making, it is important to delve deeper into how risk perception modulates the acceptance of a potential vaccine. It has been shown that the emotional side of risk perception guides the decision to take preventive action for influenza (Chapman & Coups, 2006; Weinstein et al., 2007), as predicted by the risk-as-feeling hypothesis. Chapman and Coups (2006) investigated whether concern and regret mediated the relationship between risk assessment and vaccination choice suggesting that risk perception, meant as the concern of the disease, guides the vaccination's choice, encouraging preventive health behavior. Comparing the vaccine acceptance for influenza and pandemic diseases, a study investigated the factors influencing the acceptance of the H1N1 vaccine once the 2009 swine influenza pandemic had moved into the post-pandemic phase (Chor et al., 2011). Results showed that previous seasonal influenza uptake predicted vaccination for H1N1 and that overestimating the side effects of influenza vaccination reduced acceptance of the H1N1 vaccine. For our purposes, it should be noted that data collection was run in 2010, one year after the pandemic emergency, and the low uptake (between 13.5% and 41.3%) could be due to the fact that people saw the pandemic as resolved and no longer threatening health. Another study had paid particular attention to the role of temporal and spatial distance in risk perceptions related to H1N1 influenza (Ibuka et al., 2010). Almost 1,300 participants from the United States completed the survey that remained available for one month starting at the initial stage of the outbreak in 2009. Results indicated that even if the perceived likelihood of getting infected increased over time, the interest in preventive pharmaceutical interventions and commitment to certain precautionary activities decreased over time (Ibuka et al., 2010), suggesting that perceived risk of infection and precautionary behavior can vary through time, impacting the effectiveness of disease control measures. Moreover, this study underlined how the

perception of risk and being already engaged in precautionary activities, as previous influenza vaccination, increased the acceptance of an H1N1 vaccine (Ibuka et al., 2010).

Considering the aforementioned literature, this paper investigated whether the perceived risk associated with COVID-19 affects the intention to vaccinate in the upcoming vaccination season against the SARS-CoV-2 (if a vaccine was available) and against the seasonal flu, as a comparison. Moreover, the study aimed at investigating whether the variation of the severity since the beginning of the epidemic in Italy affected the perceived risk and the intention to get vaccinated. Specifically, particular attention was paid to the early phase of the emergency, when the virus diffusion was not yet declared a pandemic (Italy was the first country with a domestic contagion after China), to the lockdown phase (when the entire Italian population was forced to shelter at home by a Government mandate, with the exception of proven cases of necessity or specific permits) and to the re-opening phase (when the more restrictive measures were lifted). We expected that during the lockdown phase the perception of risk would increase, and, in turn, also the intention to be vaccinated against COVID-19, relative to the pre-lockdown phase. In the re-opening phase, we expected people's risk perception to remain high but decrease relative to the lockdown phase. In the reopening phase, we expected people's risk perception to remain high but decrease relative to the lockdown phase. Furthermore, with regard to the influenza, we hypothesized that there should be no difference of perceived risk across the three phases and that there should be no variation in the intention to get vaccinated against it.

Specifically, we hypothesize:

H1.a: Risk perception associated with COVID-19 should increase in the lockdown, compared to pre- and post-lockdown phases.

H1.b: The perceived risk of flu and EVD across the three phases should not change.

H2.a: The intention to get vaccinated against COVID-19 should increase during the lockdown and re-opening phase, as compared to the pre-lockdown phase.

H2.b: The intention to get vaccinated against the flu across the three phases should not change.

H3: The intention to get vaccinated against COVID-19 should be predicted by the perception of risk associated with the new virus.

Method

Participants

Data was collected in Italy by sharing the study link with students and posting it on various institutional and personal social channels related to the research team, following vaccination acceptance from the first cases of the outbreaks to the re-opening phase. Out of 3,691 participants who started the questionnaire, 24 did not provide informed consent and 1,400 dropped out. Thus, 2,267 questionnaires were considered in the analyses (see Table S1 of the Supplementary Material for selection criteria). The overall inclusion rate is 61.4%, with a significant difference by period (pre-lockdown = 60.7%, lockdown = 59.8%, re-opening = 66.8%, *p-value* = 0.006). Participants who dropped out had similar values of risk perception and vaccine hesitancy compared to those who completed the entire questionnaire, except for a slightly lower risk perception for flu (see Table S2 of the Supplementary Material). As reported in Figure 1, the survey's temporal window lasted from the end of February to the end of June 2020.

--- Insert Figure 1 about here ---

Specifically, we collected 844 (69.0% female, mean±SD age = 39.5±13.8 years) participants in the pre-lockdown data collection, 978 (70.2% female, mean± SD age = 38.8±13.7 years) during the lockdown phase, and finally 445 (70.8% female, mean± SD age = 33.8±14.0 years) through the first weeks of the re-opening phase. The respondents were

predominantly females (n = 1,575, 69.9%) with an equal proportion among the sampling periods (Table 1). The average age was 38.1 years old (SD = 14.0 years), and it appeared to vary quite substantially across the window time, with a higher proportion of people aged less than 25 years old during the re-opening (p < 0.001). There was a significantly different distribution concerning the geographical area of residence (p < 0.001) among the sampling periods with a higher percentage of residents in North Italy during the lockdown (p < 0.001).

The project was approved by the ethical committee of the researchers' host university, with the protocol number 3596.

--- Insert Table 1 here---

Materials and Procedure

The questionnaire investigated participants' vaccine attitudes by asking the intention to get vaccinated against flu and against SARS-CoV-2 (if a vaccine was available), on a numeric scale ranging from 0 (*not at all likely*) to 100 (*very likely*) and the level of vaccine hesitancy was calculated by the complement to 100. The order of the questions related to the two diseases was randomized. Subsequently, participants were asked whether they would be willing to pay for the vaccine if the National Health System could not guarantee coverage for the SARS-CoV-2 vaccine, neither to people at risk nor to people over 65 years old (who are offered free flu vaccines in Italy). The survey included three questions on respondent's risk perception toward three diseases: COVID-19 (new disease, unknown to science, no prior experience, potential catastrophic nature), flu (known disease, common, prior experience) and EVD (known disease, a threatening but physically remote risk). Similarly to previous studies, one question investigated the perceived likelihood of being infected by each disease (0 = not at all likely to 100 = extremely likely; Ibuka et al., 2010; Rubaltelli et al., 2020), a second question assessed the perceived severity of each disease (0 = not at all severe to 100 =

extremely severe; Ibuka et al., 2010), and the third question gauged the emotional side of risk perception by asking how scared people felt about each disease (0 = not scared at all to 100 = extremely scared; Yıldırım & Güler, In press). Participants then self-reported whether they received the flu shot in the 2019 season and their level of general attitude toward vaccination with a question asking how doubtful they considered themselves to be about vaccines in general (0 = not at all doubtful to 100 = extremely doubtful); this latter scale was included in the analysis categorized in quintiles with the first quintile fixed to the 0 value (no doubts). Finally, we asked participants to report a series of demographic information: gender, age, municipality of residence and the zip code. We performed a linkage using the municipality of residence to derive an Italian deprivation index (Caranci et al, 2010) for all the participants: the Italian Deprivation Index was categorized in binary form considering as deprived those respondents living in highly deprived and almost deprived areas.

Statistical methods

Descriptive statistical analysis relied on tables (frequency for categorical variables, Median and InterQuartile Range (IQR) for continuous variables), histograms and boxplots. Data was tested for normality using a Shapiro-Wilk test, and a Wilcoxon rank sum test was computed to compare the distribution across two strata given the non-normal distribution of the continuous data. With more than two strata, a Kruskal-Wallis test was considered. Categorical variables were compared using chi-squared or Fisher's exact test where expected frequencies in any combination were less than 10. Statistical significance was assumed at the 5% level. Statistical analysis was performed using R (R Core Team, 2020).

Perceived risk by disease type - exploratory factor analysis

Three different explorative factorial analyses were performed on the respondent's scores of scariness, likelihood of being infected, and severity, one for each disease (COVID-19, flu, and EVD); in each case, a single factor was estimated (see Table S3 of the Supplementary

Material) which represented the overall perceived risk. The amount of variance explained by the one factor solution was acceptable. The factor loadings for COVID-19 and flu reported a high relevance of the scariness and severity with less importance of the likelihood of being infected, especially for the flu, while for the EVD, only the scariness was relevant for the perceived risk (Figure 2). The factor score represented the individual perceived risk, and it was categorized in tertiles (1°tertile = low risk; 2°tertile = medium risk; 3°tertile = high risk).

--- Insert Figure 2 about here ---

COVID-19 vaccine hesitancy - hurdle model

Due to the exceedance of 100 values and a J shape (Figure 3, left box), we measured the hesitancy or reluctance to get vaccinated against COVID-19 considering the complement to 100 of participants' intention to get vaccinated against SARS-CoV-2. The resulting hesitancy was modelled by means of a hurdle model, which can be interpreted as two-part models. The first part of the hurdle model is a logistic regression model which considers the presence of zero (no hesitancy vs. hesitancy > 0), while the second part is a truncated-at-zero count model (Cameron & Trivedi, 2013). In our application, we used a negative binomial regression model for the second part of the model, in order to guarantee a better fit than a Poisson regression model in terms of deviance explained and fitting residuals. Covariates were included in both models, with a forward selection criteria considering the AIC (Akaike Information Criterion) index. Results are presented using Odds Ratios (ORs) and Incidence Rate Ratios (IRRs) obtained by exponentiating the coefficients from the logistic regression model and the negative binomial regression model, respectively.

Flu vaccine hesitancy - logistic model

The intention to get vaccinated for flu had a U-shape distribution (Figure 3, right box). In this context there is an excess of zero and ceiling values. In order to compare the results with the previous hurdle model, we modelled the presence of flu hesitancy (the complement

to 100 for participants' intention to get vaccinated for flu) in a binary form (no hesitancy vs. hesitancy > 0) employing a logistic regression model, including covariates on the basis of AIC index and a forward selection criteria. The results are presented using Odds Ratios (ORs) by exponentiating the estimated coefficients from the logistic regression.

--- Insert Figure 3 about here ---

Results

Descriptive statistics

Our results indicated that vaccine hesitancy for COVID-19 and flu decreased during the lockdown period compared to before (Table 2, p < 0.001), returning to pre-lockdown levels only for the flu vaccine. Overall, a large part of respondents reported the intention to pay for the COVID-19 vaccine if it was available (n = 1782, 78.6%), and this was especially true during the lockdown period (86.2%, p < 0.001) compared to the pre-lockdown, and then it dropped in the re-opening phase (69.7%, p < 0.001). Overall, only a few people reported they had the flu shot in 2019 (n = 369, 16.3%). Participants had few doubts about vaccines in general (Mean \pm SD = 18.7 \pm 25.7) and these were higher during the lockdown period and lower thereafter (p < 0.001). The raw judgments of scariness, likelihood of infection, and severity changed overtime for all the diseases (COVID-19, flu, and EVD) increasing during the lockdown and then decreasing moderately during the re-opening phase. The only exception was the flu likelihood of infection that remained constant (see Figure S4 of the Supplementary Material). The perceived risk, calculated by the combination of the raw judgments of scariness, likelihood of infection, and severity for each disease, varied over time with a higher perceived risk for the 3 diseases during the lockdown period followed by a decrease thereafter (p < 0.001, Table 2).

--- Insert Table 2 here ---

Vaccine hesitancy for COVID-19 and seasonal flu

As reported in Figure 3, the hesitancy to get vaccinated for COVID-19 showed a zero-inflated distribution with the presence of the 40.1% of the questionnaires (n = 909) indicating no hesitancy. Conversely, a U-shape distribution was found for the flu vaccine hesitation, with a similar proportion of non-hesitant people (18.7%, n = 423) and people with no intention to get vaccinated (20.7%, n = 470). Thus, due to the different shape of the marginal distribution, the hesitancy for COVID-19 and seasonal influenza were modeled by means of a hurdle model and a logistic regression, respectively (Table 3).

The coefficients estimated by the first part of the hurdle model applied to the COVID-19 vaccine hesitancy (using a logistic regression model of no hesitancy vs. hesitancy > 0) reported a clear evidence of a higher percentage of respondents that intended to get vaccinated against COVID-19 during the lockdown (OR: 1.37; 95% CI: 1.06-1.77), which increased during the re-opening phase (OR: 2.07; 95% CI: 1.50-2.86) compared with the prelockdown period, taken as reference category. The perceived risk of COVID-19 increased the number of participants that would get the COVID-19 vaccine for sure with an increase of two and a half times (OR: 2.46; 95% CI: 1.08-1.94) for those perceiving a medium risk with respect to the low-risk category, taken as reference. Moreover, the increase was even more pronounced for those who perceived a high risk for COVID-19 (OR: 4.86; 95% CI: 3.53-6.74). In addition, respondents reporting having received the flu shot in 2019, compared to those who did not, were more likely to get vaccinated for sure against SARS-CoV-2 with almost a three-fold increase (OR: 2.83; 95% CI: 2.14-3.76). Similarly, those who were willing to pay for the COVID-19 vaccine were more likely to get vaccinated for sure (OR: 4.04; 95% CI: 2.92-5.70). Conversely, being doubtful about vaccines in general decreased the number of participants willing to get vaccinated for sure against COVID-19 even among those who reported fewer doubts (2nd quintile OR: 0.63; 95% CI: 0.47-0.84), with a sharp

decrease reported by the last quintile of vaccine doubts (5th quintile OR: 0.13; 95% CI: 0.09-0.18). Compared to the age-class (25-45) taken as a reference category, the age-classes (≤ 25) and (45-65) years reported a significant increase of about 50% of the number of participants who intended to get vaccinated for sure against COVID-19. In addition, the order of presentation of questions about flu and COVID-19 was also significant: participants who were asked to think about the flu vaccine first were less likely to get vaccinated for sure against COVID-19, than those who were asked to think about the COVID-19 vaccine first (OR: 0.80; 95% CI: 0.65-0.98).

In the second part of the hurdle model, in which is modeled the level of hesitancy in hesitant participants, the hesitancy decreased during the lockdown period (IRR: 0.87; 95% CI: 0.80-0.96) but returned to the pre-lockdown levels at the re-opening phase (IRR: 0.97; 95% CI: 0.88-1.08). The perceived risk of COVID-19 progressively decreased the hesitancy of people willing to get vaccinated against COVID-19 (low risk as reference; medium risk IRR: 0.72; 95% CI: 0.66-0.79; high risk IRR: 0.60; 95% CI: 0.53-0.67). A high level of perceived risk for flu and EVD implied a light drop on the hesitancy to get vaccinated against COVID-19 (flu IRR: 0.89; 95% CI: 0.80-0.98; EVD IRR: 0.90; 95% CI: 0.82-0.99). Those who got the flu vaccination in 2019 (IRR: 0.66; 95% CI: 0.58-0.76) and those who were willing to pay for the COVID-19 vaccine (IRR: 0.73; 95% CI: 0.68-0.79) reported lower levels of hesitancy. On the contrary, high levels of doubts about vaccines increased COVID-19 vaccine hesitancy (4th quintile IRR: 1.18; 95% CI: 1.06-1.31; 5th quintile IRR: 1.51; 95% CI: 1.35-1.69). Compared to the reference category (25-45), younger respondents (≤ 25 years age class) reported a lower COVID-19 vaccine hesitancy (IRR: 0.76; 95% CI: 0.70-0.83). Looking at the order of presentation of the question about flu and COVID-19 vaccine, participants who were asked to think about the flu vaccine first showed higher levels of

vaccine hesitancy for the COVID-19 vaccine, compared to asking for the COVID-19 vaccine first (IRR: 1.21; 95% CI: 1.13-1.30).

The intention to get vaccinated against flu for sure increased in the post-lockdown period with respect to the pre-lockdown temporal window (OR: 1.82; 95% CI: 1.16-2.87). People who perceived a high risk for flu reported a higher intention to get vaccinated (OR: 2.08; 95% CI: 1.40-3.11); those who got vaccinated against flu in 2019 were also much more willing to do so again in the future (extremely high OR: 38.55; 95% CI: 27.81-54.15). However, among those reporting doubts about vaccines in general, there was a progressive reduction of intention to get vaccinated against flu (5th quintile, OR: 0.20; 95% CI: 0.11-0.35). The intention to pay for COVID-19 vaccine was also positively associated with the plan to get vaccinated against the flu (OR: 2.03; 95% CI: 1.24-3.44). Moreover, the decision to get the flu shot was also influenced by respondents age, with a higher willingness among the age-classes 45-65 (OR: 2.46; 95% CI: 1.71-3.54) and above 65 years old (OR: 2.97; 95% CI: 1.48-5.99), than in the reference category (25-45 years old). Finally, the order of presentation of questions about vaccines was also significant, showing that participants who were asked to think about the flu vaccine first were less likely to get vaccinated against flu, than those who were asked to think about the COVID-19 vaccine first (OR: 0.70; 95% CI: 0.51 - 0.94).

--- Insert Table 3 here ---

Discussion

Thanks to a repeated cross-sectional design, we showed that the intention to get the COVID-19 and the flu vaccines changed during the pandemic development. While previous studies on the intention to get vaccinated against SARS-CoV-2 focused on relatively short temporal window (e.g., one week or less; Barello et al., 2020; Neergaard & Fingerhut, 2020;

Wang et al., 2020; WebMD Health News, 2020; Wise et al., 2020), this project monitored the evolution of the intention to get vaccinated against the new virus, and assessed a measure of perceived risk, from the early days of the outbreak throughout the main phases of the pandemic.

Considering the perceived risk, calculated from the combination of raw judgements of scariness, likelihood of infection, and severity for each disease, we observed a similar variation in risk perception for the three diseases over time, conflicting with our hypothesis H1.b. Specifically, risk perception increased in the lockdown phase and decreased in the reopening phase, for all the three diseases, although the flu and EVD have shown minimal variations. While in the pre-lockdown phase the number of participants who perceived COVID-19 as highly risky was the lowest among the three diseases, during the lockdown, there was a substantial increase in the number of participants perceiving COVID-19 as highly risky (H1.a). A possible interpretation of these results is linked to the fact that, at least initially, COVID-19 was often associated with flu by mass media, experts, and politicians, having made it probably perceived as less frightening. However, this assumption changed during the national lockdown, which clearly defined the state of emergency. This result is consistent with the risk as feeling theory (Slovic et al., 2002, 2004; Slovic & Peters, 2006), according to which the perception of risk depends on specific characteristics of a hazard. In the case of COVID-19, in the transition from pre-lockdown to lockdown, this has become a physically and psychologically close threat, although mostly unknown to science, with limited therapeutic interventions and an unpredictable course. Although it needs further investigation, the unexpected (but small) increase in flu and EVD risk perception may be due to an increased general sensitivity to disease hazards during the lockdown.

The three phases are therefore linked to a different perception of risk associated with COVID-19, with important implications. In particular, during the lockdown, compared to

pre-lockdown, not only a higher percentage of people were willing to get vaccinated against COVID-19 for sure, but also a higher percentage of hesitant people were interested in getting vaccinated. Moreover, in line with our hypothesis (H2.a), in the re-opening phase, there was a further increase with respect to the intention to get vaccinate against COVID-19 but only for those who want to get vaccinated for sure, while for hesitant participants the level returned to the pre-lockdown phase. This different trend could be explained by the "hot and cold empathy bias" (Loewenstein, 2005): People give less importance to their emotional reactions during "cold" decisions than "hot" decisions, and this leads to asymmetries between their beliefs and their choices. Namely, this bias can lead people to make inaccurate predictions about their preferences in the hot state (e.g., during the lockdown) and to fail to follow through in the cold state (e.g., re-opening phase). Thus, we suggest that the hot and cold empathy bias could explain the change in vaccine preferences shown by hesitant participants, who were scared and influenced by their emotional state during the lockdown and made decisions about their own health that were not aligned with their beliefs. During the lockdown (hot affective state), when people were more concerned and were feeling more vulnerable (Brooks et al., 2020; Li et al., 2020; Moccia et al., 2020), they seemed more likely to accept the COVID-19's vaccine than they were in the re-opening phase (cold affective state). On the contrary, this effect did not emerge for the flu vaccine (H2.b), and this could be understood as a further confirmation that flu is not considered to be particularly risky, as it is familiar, and it usually corresponds to a cold state. Despite this, in the re-opening phase, we found a limited marginal increase of the intention to get vaccinated against seasonal flu. This could be due to an effect of prevention campaigns at the national level (Ministry of Health, 2020) on the usefulness of the flu vaccine to reduce hospital overload and its role in allowing for a differential diagnosis.

Moreover, considering the intention to get vaccinated against COVID-19, perceiving a higher risk linked to the new virus predicted the intention to get vaccinated against it, confirming our hypothesis (H3). In line with recent studies, the new virus leads to psychological distress caused by concerns and fears (Brooks et al., 2020; Li et al., 2020; Moccia et al., 2020), which leads to an increase in the vaccine uptake. As the perceived risk for COVID-19 increased, so did the intention to get vaccinated for sure (first part of the hurdle model), while the hesitancy decreased (second part of the hurdle model). In line with the risk as feelings model (Slovic et al., 2002, 2004; Slovic & Peters, 2006), those results confirmed the role of risk perception on judgement and decision making in health care for a disease associated with serious consequences, uncertain outcome and limited scientific knowledge, showing how the perceived risk drives the decision to immunize.

Additionally, our results are in line with previous studies (Chor et al., 2011; Seale et al., 2010), showing that having received a vaccine against seasonal flu in 2019 increased the likelihood to get vaccinated for the new pandemic disease. Furthermore, our findings also showed that the more doubtful people are about vaccines in general, the less willing they were to get vaccinated, no matter the specific vaccine. Although vaccine hesitancy has been defined as context- and vaccine-specific (MacDonald, 2015), it seems reasonable that the more people have doubts about vaccines in general, the less they are likely to be willing to undergo vaccines of any kind.

Finally, age has been considered in the model as a confounding variable, but still, it seems interesting to comment on the result. In fact, our data were consistent with what it emerges when looking at the Italian national trend (Ministry of Health, 2019), which shows that the intention to get vaccinated for the flu increases with age. This trend, though, is reversed if we consider the intention to immunize against SARS-CoV-2, as we have found a greater willingness to vaccinate in younger groups of the population (< 25 years), both

hesitant and not, compared to older people (> 65 years). Given that the distribution of participants by age in the three phases of the study was not equally representative, these results need to be further investigated in order to be properly interpreted and generalized. Understanding in more detail the relationship between age and the willingness to get vaccinated for different vaccines could play a very important role in the planning of tailored vaccination campaigns: In fact, a tailored communication would lead to more satisfactory results in promoting vaccine acceptance (European Centre for Disease Prevention and Control, 2017). Additionally, considering insights for more effective communication, our study also showed an interesting effect in the randomization order of the questions about the intention to get the seasonal flu and the COVID-19 vaccines. Our findings suggest that mentioning flu vaccines when promoting a COVID-19 vaccine (when available) might hinder uptake of the latter. At the same time, when people were asked about their intention to vaccinate against COVID-19 first, they were more likely to be sure about getting the flu shot compared to when they were asked about the vaccine against flu first. This finding may arise due to the comparison between the two diseases: We know that people's judgments are rarely absolute and are often constructed in comparison (Hsee & Zhang, 2010; Slovic, 1995), also in the context of vaccines (Maltz & Sarid, 2020). For example, the flu vaccine can be made more attractive when framed as a choice between vaccinate early or vaccinate late (Maltz & Sarid, 2020). Similarly, our data shows that having thought about the COVID-19 vaccine first provides a frame of reference that makes the flu vaccine more attractive. Although this result deserves to be studied more in-depth, it is important to consider it when it comes to promoting the flu vaccine in the winter season, which is particularly important due to the reasons mentioned previously (i.e., to facilitate differential diagnosis and to reduce the burden on health systems).

Of course, this research is not without limitations. The interpretation of the results must be carefully considered since we did not reach a representative sample of the population. Specifically, age and gender were not equally distributed across data collections, so that our results must be interpreted carefully, although our models of vaccine hesitancy controlled for age and gender when estimating the parameters. Another limitation concerns the fact that participants who dropped out had a slightly lower risk perception for flu and tended to have a slightly lower risk perception for COVID-19, than those who completed the questionnaire. While it is possible that the more people were concerned about the diseases, the more likely they were to complete the questionnaire, it is important to note that the differences were small, and that vaccine hesitancy did not differ. Finally, we have to acknowledge that the initial project aimed to investigate the perception of the risk of COVID-19 and the corresponding intention to accept a possible vaccine against the coronavirus. However, given the rapid and unpredictable evolution of the pandemic, we promptly decided to monitor these variables over time using a cross-sectional design. This choice on the flow allowed us to monitor the variation in risk perception, whether and how it modulates the intention to vaccinate, during the first four months that characterized the dynamic nature of the pandemic, from the pre-lockdown to the re-opening phase.

To conclude, this study monitored the variation of vaccine acceptance for COVID-19 and seasonal flu, throughout the first four months of the pandemic outbreak in Italy, allowing us to keep track of the changes in risk perception at different stages of the crisis. Risk perception played a key role in the choice of getting vaccinated, increasing the willingness to undergo COVID-19 vaccine even for the more hesitant participants. The perception of COVID-19-related risk may provide relevant information to future risk communication and infection control. Despite the importance of the vaccine is unquestionable, given the uncertain timing on the vaccination schedules, it is important to study the role of risk

perception in responses to preventive behavior. As we have seen, different phases of the pandemic lead to a different response to the situation. Therefore, it is plausible to think that the attention to the prescriptions on preventive health regulations undergoes fluctuations that should be prevented. It would also be interesting to assess whether the role of risk perception is similar during the second and subsequent waves of SARS-CoV-2, as it is possible that the disease has become more familiar compared to how it was perceived during the first wave.

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