Attitudes towards booster, testing and isolation, and their impact on COVID-19 response in winter 2022/2023 in France, Belgium, and Italy: a cross-sectional survey and modelling study

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Summary

Background European countries are focusing on testing, isolation, and boosting strategies to counter the 2022/2023 winter surge due to SARS-CoV-2 Omicron subvariants. However, widespread pandemic fatigue and limited compliance potentially undermine mitigation efforts.

Methods To establish a baseline for interventions, we ran a multicountry survey to assess respondents' willingness to receive booster vaccination and comply with testing and isolation mandates. Integrating survey and estimated immunity data in a branching process epidemic spreading model, we evaluated the effectiveness and costs of current protocols in France, Belgium, and Italy to manage the winter wave.

Findings The vast majority of survey participants (N = 4594) was willing to adhere to testing (>91%) and rapid isolation (>88%) across the three countries. Pronounced differences emerged in the declared senior adherence to booster vaccination (73% in France, 94% in Belgium, 86% in Italy). Epidemic model results estimate that testing and isolation protocols would confer significant benefit in reducing transmission (17–24% reduction, from R = 1.6 to R = 1.3 in France and Belgium, to R = 1.2 in Italy) with declared adherence. Achieving a mitigating level similar to the French protocol, the Belgian protocol would require 35% fewer tests (from 1 test to 0.65 test per infected person) and avoid the long isolation periods of the Italian protocol (average of 6 days vs. 11). A cost barrier to test would significantly decrease adherence in France and Belgium, undermining protocols' effectiveness.

Interpretation Simpler mandates for isolation may increase awareness and actual compliance, reducing testing costs, without compromising mitigation. High booster vaccination uptake remains key for the control of the winter wave.

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Research in context

Evidence before this study

We searched PubMed and medRxiv for articles published in the past year (January 2022–January 2023) using the terms ("COVID-19" AND "isolation" AND "booster" AND ("adherence" OR "compliance" OR "willingness")) and identified a total of five studies matching these inclusion criteria. Adding the term "modeling" to the search filters provided zero results. We excluded two articles as they were out of topic (a narrative review on the benefits of physical activity before and during the COVID-19 pandemic, and an epidemiological investigation of transmission characteristics of the Delta variant in South Korea). Among the remaining three articles, two studies were based on modeling work and only one designed a questionnaire on compliance to COVID-19 measures. One study provided prospective estimates of effectiveness of various screening protocols on virus transmission in the first months of 2022 in Canada, but none provided estimates for the 2022/2023 winter or focused on European countries. Two works focused on screening protocols, but without assessing isolation and exit test strategies. No study provided a multicountry assessment of attitudes towards booster uptake and compliance to testing and isolation protocols, or assessed the public health impact of these attitudes on the effectiveness and costs of different national protocols.

Added value of this study

This is the first study to use adherence data obtained from a multicountry survey in France, Belgium, and Italy to parametrize a mathematical model for Omicron spread in the 2022/2023 winter and assess the effectiveness and costs of current testing and isolation protocols in these three countries. We found that, with the declared high adherence (>91% to testing, >88% to rapid isolation), current protocols would contribute significantly to reducing transmission in the community (17–24% estimated reduction of the effective reproductive number). However, introducing costs for testing would largely reduce protocols' effectiveness because of considerable loss of compliance. The Belgian protocol stands out as it achieves a mitigation level similar to the French one, but it reduces by one third the testing resources needed, while also avoiding the large individual and social costs of long isolation periods imposed by the Italian protocol.

Implications of all the available evidence

In a context where COVID-19 mandates are being eased since the beginning of 2022, gaps in compliance jeopardize successful mitigation of COVID-19 waves. Our findings have immediate implications to adapt countries' response to such an evolving context of the pandemic. Simpler mandates for self-isolation would achieve similar mitigating effects as more complex ones, while reducing by one third the testing resources needed, and avoiding the individual and societal burden of long isolation periods. Booster vaccination remains fundamental to manage the winter wave and protect the vulnerable population.

Introduction

As the COVID-19 pandemic is in its third winter season in Europe, the World Health Organization recommends that countries should strategically prepare for a possible surge in cases, hospitalizations, and deaths.[1] Despite an estimated moderate risk that the SARS-CoV-2 Omicron variant XBB.1.5 will become dominant in Europe, the pandemic continues to cause a considerable burden, with 1311 COVID-19 deaths reported in Europe in week 3, 2023.[2] Given the largely immunized population (65% of 18+ in Europe with a first booster by the end of January 2023[2]), the response needs to adapt to a shifting phase of the pandemic.[1,3–5]

Contact tracing and quarantine have been progressively eased due to their costs and disruption on the workforce and individual life.[6,7] Case isolation, however, remains key to reduce SARS-CoV-2 spread and protect the health system. Countries adopted different lengths of isolation, with some cutting it short if symptoms subside or the person tests negative (Table 1). Vaccination with an additional booster dose is currently ongoing for the fall 2022 campaign.[8] But it is hard to anticipate its uptake,[9,10] after several vaccine doses and the marked decline in coverage reported for the booster doses administered in the summer 2022 to vulnerable individuals (median uptake across European countries of 11.6% among 60+ by early July 2022[8]).

In this study we evaluated the expected performance of the testing and isolation strategies currently adopted in France, Belgium, and Italy to manage COVID-19 through winter 2022/2023. We inferred the vaccine-induced immunity profile of the population of the three countries at the start of the winter season based on vaccination data and accounting for immunity waning. We ran a multi-country survey to anticipate individual behavior from 4594 survey participants from France, Belgium, and Italy on booster vaccination, adherence to testing and isolation, under a range of protocols (isolation of different durations, with or without exit tests) and conditions (in the presence or absence of recommendations, with free access to tests or at a given cost). We then used a mathematical model of SARS-CoV-2 infection dynamics parameterized to Omicron sub-variants and to survey results on expected individual compliance to evaluate the performance of the testing and isolation protocols adopted by the three countries.

	France	Belgium	Italy
Winter 2021/2022 protocols	*January-February 2022* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated individuals test on days 0, 2 and 4 from tracing and isolate if positive; unvaccinated individuals quarantine for 7 days with exit test (if positive, exit on day 10). **Isolation[a]:** vaccinated individuals isolate for 5 days with exit test (if positive, exit on day 7); unvaccinated individuals quarantine for 7 days with exit test (if positive, exit on day 10).	*January - April 2022* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated individuals do not need to quarantine nor to test; unvaccinated individuals quarantine for 10 days, with daily exit tests starting from day 7 (partially vaccinated individuals quarantine for 7 days, with daily exit tests starting from day 4). **Isolation:** vaccinated and unvaccinated individuals isolate for 7 days.	*December 2021 - March 2022* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated individuals test only if they develop symptoms (test on day 0 and on day 5 from symptom onset) and isolate, if positive; unvaccinated individuals quarantine for 10 days with exit test (if positive, test again until negative). **Isolation:** vaccinated individuals isolate for 7 days with exit test (if positive, test again on day 14, if positive, exit on day 21); unvaccinated individuals quarantine for 10 days with exit test (if positive, exit on day 21).
Spring 2022 protocols	*Since March 2022 (still in place)* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated and unvaccinated individuals test on day 2 and isolate, if positive. **Isolation[a]:** vaccinated individuals isolate for 5 days with exit test (if positive, exit on day 7); unvaccinated individuals isolate for 7 days with exit test (if positive, exit on day 10).	*Since May 2022 (still in place)* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated and unvaccinated individuals do not test nor quarantine. **Isolation:** vaccinated and unvaccinated individuals isolate for 7 days.	*Since April 2022 (new one since September 2022**)* **If symptomatic:** vaccinated and unvaccinated individuals test and isolate, if positive. **If traced:** vaccinated and unvaccinated individuals test only if they develop symptoms (test on day 0 and day 5 from symptom onset) and isolate, if positive. **Isolation:** vaccinated individuals isolate for 7 days with exit test (if positive, test again on day 14, if positive, exit on day 21); unvaccinated individuals isolate for 10 days with exit test (if positive, exit on day 21). ** **Isolation:** vaccinated and unvaccinated individuals isolate for 5 days with exit test (if positive, test again until negative or exit on day 14)

[a]The requirement on isolation exit based on the presence or absence of symptoms is not mentioned in the table as it cannot be accounted for by the model.

Table 1: Protocols for testing, tracing and isolation adopted in France, Belgium, and Italy in 2022.

Methods

Influenzanet multicountry survey and analysis

We used the existing European platform Influenzanet for online participatory surveillance of influenza-like-illness in the general population,[11] adapted to COVID-19 during the pandemic crisis.[12,13] Three countries participated in the study: France, Belgium and Italy. Each country ran its own website, to which participants registered on a voluntary basis, completing an intake survey covering demographical, socio-economic and health-related factors. Recruitment occurred through press releases of the supporting institutions, communications on the Internet, radio, TV, newspapers, and through emails and word of mouth.[12] An email was sent to participants with a personal link to the survey on prospective vaccination, testing and isolation, on June 25, 2022 in France, July 7 in Italy, July 14 in Belgium. Data collection was closed on July 1, July 18, July 25 in the three countries, respectively. The survey was kept open for longer in Belgium and in Italy because of a holiday within the data collection period in Belgium (typically reducing participation) and with the aim to increase the number of participants in the two countries with the lower sample size. No specific events regarding the COVID-19 pandemic occurred in that period that were likely to affect participants' response. In case of multiple submissions by a single participant, only answers submitted last were considered in the study. The surveys asked questions on the participants' willingness to test for COVID-19, self-isolate and get an additional dose of vaccine, during the upcoming winter. Prospective levels of adherence were investigated under various conditions of symptom status, test cost and in presence or absence of recommendations from health authorities. Surveys used a test cost of 20 Euros corresponding to the typical price of an antigenic test in subject countries. The full survey text is provided in the Supplementary Information.

Participants who indicated their sex, age, education level, and vaccination status were included in the study, provided their age met the age/sex/education stratification available for each country (see below). "Undefined" sex type in Belgium was excluded from the analysis.

The Influenzanet sample differed from the general population (Table 2). We therefore adjusted the French, Italian, and Belgian survey data on age, sex, and level of education, as in previous work,[13,14] using data from the French National Institute of Statistics and Economic Studies (Institut National de la Statistique et des Études Économiques, INSEE[15]), the Belgian National Institute of Statistics and Census Data (STATBEL[16]), and the Italian National Institute of Statistics (Istituto nazionale

Population characteristics	Data from the InfluenzaNet survey			Population data (%)
	Raw number	Raw percentage (%)	Weighted percentage (%)	
Sex				
Female	2076 (France), 434 (Belgium), 127 (Italy)	58.7 (France), 58.6 (Belgium), 39.8 (Italy)	52.4 (France), 51.3 (Belgium), 51.8 (Italy)	52.4 (France), 51.3 (Belgium), 51.8 (Italy)
Male	1458 (France), 307 (Belgium), 192 (Italy)	41.3 (France), 41.4 (Belgium), 60.2 (Italy)	47.6 (France), 48.7 (Belgium), 48.2 (Italy)	47.6 (France), 48.7 (Belgium), 48.2 (Italy)
Age				
Young adult	239 (France), 123 (Belgium), 43 (Italy)	6.8 (France), 16.6 (Belgium), 13.5 (Italy)	26.2 (France), 35.9 (Belgium), 25.9 (Italy)	26.2 (France), 35.9 (Belgium), 25.9 (Italy)
Adult	1171 (France), 335 (Belgium), 150 (Italy)	33.1 (France), 45.2 (Belgium), 47.0 (Italy)	35.9 (France), 37.0 (Belgium), 36.9 (Italy)	35.9 (France), 37.0 (Belgium), 36.9 (Italy)
Elderly	2124 (France), 283 (Belgium), 126 (Italy)	60.1 (France), 38.2 (Belgium), 38.5 (Italy)	37.9 (France), 27.1 (Belgium), 37.2 (Italy)	37.9 (France), 27.1 (Belgium), 37.2 (Italy)
Level of education				
≤ A-levels	1041 (France), 194 (Belgium), 157 (Italy)	29.5 (France), 26.2 (Belgium), 49.2 (Italy)	69.6 (France), 59.8 (Belgium), 89.7 (Italy)	69.6 (France), 59.8 (Belgium), 89.7 (Italy)
> A-levels	2493 (France), 547 (Belgium), 162 (Italy)	70.5 (France), 73.8 (Belgium), 50.8 (Italy)	30.4 (France), 40.2 (Belgium), 10.3 (Italy)	30.4 (France), 40.2 (Belgium), 10.3 (Italy)

Table 2: Socio-demographic characteristics of survey respondents.[15–20]

di statistica, ISTAT[17]). Based on available data from these sources, we considered the following age classes (young adults, adults, seniors, respectively): [20, 39], [40, 59], 60+ for France and Italy; [25, 44], [45, 64], 65+ for Belgium. For the level of education, we considered the categories: ≤ A-levels and >A-levels (the full correspondence with the educational levels in each country is provided in the SI, Table S1). Survey participants who did not belong to any of these classes were excluded from the study.

Ethics statement

GrippeNet.fr/COVIDnet.fr was reviewed and approved by the French Advisory Committee for research on information treatment in the health sector (CCTIRS), and by the French National Commission on Informatics and Liberty (CNIL) - the authorities ruling on all matters related to ethics, data, and privacy in France. Infectieradar.be was reviewed and approved by the Committee for Medical Ethics of Antwerp University (EC UZA-UA). Influweb.it was reviewed and approved by the IRB of the ISI Foundation. All use takes place in compliance with the rules contained in the GDPR. Informed consent was obtained online from all participants of the three platforms at enrollment according to regulations, enabling the collection, storage, and treatment of data, and their publication in anonymized, processed, and aggregated forms for scientific purposes. All three websites have a "Privacy Statement" section in which the users who decide to enroll in the study can find all the information on who is responsible for the data acquisition and processing in each country.

Model structure, testing and isolation

We adapted a branching process model previously introduced by Hellewell et al.[21] The model distinguished between symptomatic and asymptomatic cases, and considered their vaccination status. The number of secondary cases generated by each infected individual was drawn from a negative binomial distribution to account for the large individual variation observed in SARS-CoV-2 transmission.[22,23] The mean of the distribution was set to the chosen value of the reproductive number, in the absence of testing and isolation (see the following subsection). We parameterized the model with the distributions of the generation time and of the incubation period estimated for the Omicron (B.1.1.529) subvariant of SARS-CoV-2.[24] Each potential new case was assigned a time of infection drawn from the distribution of generation time, the possibility to develop symptoms,[25,26] and a time of symptoms onset drawn from the incubation period distribution. The number of secondary cases accounted for the reduced infectiousness of asymptomatic individuals[27] and the vaccine effectiveness against transmission.[28] We considered the vaccine effectiveness against SARS-CoV-2 Omicron symptomatic infection[29] in reducing the probability to develop symptomatic forms of the

disease, and considered that the vaccine effectiveness against infection was 10% lower.[30] We considered only the Pfizer-BioNTech BNT162b2 vaccine, which was predominantly used in the three countries in the COVID-19 vaccination campaign (79% in France, 74% in Belgium, 67% in Italy as of January 2023). The estimates for the vaccine effectiveness accounted for the number of doses and the waning in time since the last administration (see next subsection). The vaccine-induced immunity profile of the population in the model was inferred from the reported vaccine coverage and the timing of the vaccination campaigns in each of the three countries considered (see next subsection). Natural immunity from prior SARS-CoV-2 infections and hybrid immunity were accounted for by setting the value of the effective reproductive number of the winter wave (see next subsection).

Infected individuals in the model could enter isolation because they tested positive (see the last subsection of the Methods). We considered adherence to testing if symptomatic, in the presence of recommendations to do so, parameterized with the responses of the Influenzanet survey participants. Those not testing or testing negative did not enter isolation. Individuals testing negative in the presence of symptoms in the model were allowed to repeat the test one or more times, as we considered a certain level of awareness regarding test sensitivity after symptoms onset.[31] This awareness was informed by survey responses. Individuals testing positive (at any of these tests after symptoms onset) could isolate themselves, according to the adherence to isolation recorded in the survey in each country. We allowed for an onset-to-isolation delay drawn from an exponential distribution with average value taken from survey responses. We considered a 75% reduction of transmission in isolation, close to the estimates of Ref.[32] and considering that isolation may be less effective during the third COVID-19 winter because of pandemic fatigue[33] and a lower perceived risk of infection and severe outcome due to widespread vaccination.[34] We also explored 60% and 90% isolation effectiveness for sensitivity. Some protocols required a negative exit test to terminate isolation, and in the model we simply assumed full adherence to the exit test. However, individuals could exit isolation before its prescribed duration and we informed this probability from survey responses in each country, considering an anticipation with respect to the due date drawn from an exponential distribution with average value being a fixed fraction (3/4) of the recommended isolation duration. We considered lateral flow tests (or rapid antigenic tests) and their temporal diagnostic sensitivity to reproduce the observed rate of LFT test positivity over time after the infection from SARS-CoV-2 Omicron subvariants[31,32,34,35] (Fig. S4). Lateral flow tests were more widely used compared to PCR tests (e.g. >80% of tests were rapid antigen tests in Belgium and Italy[36,37]).

We assumed that in the 2022/2023 winter contact tracing will not be adopted anymore by authorities, as it is largely costly in terms of resources and carries a heavy social impact due to the imposed quarantine.[6,7] However, we considered a residual informal contact tracing self-performed by individuals who would alert their known contacts (relatives, friends, co-workers) that they tested positive to COVID-19. We assumed that this residual contact tracing amounts to tracing 5% of the occurred infections.

A visualization of the branching process model is provided in Fig. S2 of the Supplementary Information. Model parameters and sources are provided in Table S2.

2022/2023 winter COVID-19 scenarios

We considered a winter wave due to SARS-CoV-2 Omicron subvariants occurring in the three countries. The vaccine-induced immunity profile of each population was estimated based on vaccination coverage reported in France, Belgium, and Italy up to summer 2022, immunity waning, and uptake of the fall 2022 booster campaign for the elderly as declared by Influenzanet survey participants. By September 1, 2022, the coverage of primary vaccination with a first booster in the 18+ individuals was 55% in France, 62% in Belgium, 68% in Italy (Fig. S3). The fall booster vaccination campaign was recommended for the elderly group, and then made available to the general population. The booster vaccination campaign started on 5/10/2022 in France, and on 12/09/2022 in Belgium and in Italy, with bivalent vaccines available.

To account for the reduction of vaccine protection over time, we considered the following waning process[29]: 2 vaccine doses at 1–6 months since the second dose, at 7–9 months, and at 10+ months; 3 vaccine doses at 1–3 months since the third dose, 4–6 months, or 7+ months; 4 vaccine doses within 3 months from the fourth dose (see Table S3 for point estimates in each waning category). From the reported coverage in each country on September 1, 2022 (Fig. S3), we estimated the probability density of vaccine-induced protection against symptomatic infection for the French, Belgian, and Italian populations at that date. Applying four months of waning, we estimated this probability density at the start of the 2022/2023 winter. Considering the share of the elderly survey respondents willing to get vaccinated with the fall 2022 booster, we computed the expected vaccine-induced protection in each population given the reported coverage and the prospective uptake of the fall booster dose in each country at the start of the 2022/2023 winter.

We considered a winter wave characterized by an effective reproductive number R = 1.6 in the absence of testing and isolation. This value is within the range of time-varying reproductive number Rt values experienced by the three countries during the Omicron waves since its emergence in December 2021 (Section S2 of

the Supplementary Information). Additional values of R in the range 1.3–2.1 were explored in the sensitivity analysis. The intrinsic transmissibility of the virus is parameterized to reproduce an average number of secondary cases equal to the chosen value of R, in a population characterized by the vaccine-induced immunity profile described above, and in absence of testing and isolation. R therefore adjusts already for the other elements not explicitly considered in the model, namely the natural immunity of the population from prior SARS-CoV-2 infection, the hybrid immunity, the variants' immunity escape, the use of masks and adoption of other preventive behaviors. Finally, we also tested a scenario in absence of the fall booster campaign to evaluate its impact.

Testing and isolation protocols
We implemented the testing and isolation protocols adopted by France, Belgium, and Italy in the 2021/2022 winter and spring 2022[38–40] (Table 1). The 2021/2022 winter protocols, currently not in use, were considered for comparison and to assess the impact of the changes in protocols throughout 2022. In all protocols, symptomatic individuals were required to test immediately upon symptom onset and to isolate, if positive. Protocols differed in the duration of the isolation periods and in the exit test strategies. For example, 2021/2022 winter protocols required 5 days with a negative exit test and absence of symptoms in the last 48h or 7 days (with no test) in France, 7 days (with no exit test) in Belgium, 7 days with a negative exit test or 14 days with a negative exit test or 21 days (with no test) in Italy. Other differences referred to distinct isolation mandates depending on vaccination status (in France and in Italy), and to protocols for contact tracing impacting the testing of contacts and their quarantine duration.

In all countries, spring 2022 protocols relaxed certain restrictions foreseen by previous protocols, notably simplifying the contact tracing. As of December 2022, France and Belgium still adopt the spring 2022 protocols (in Belgium, with some regional variations), whereas Italy revised it in early September 2022 (see Table 1), in particular to reduce the length of isolation up to 5 days with a negative exit test, or 14 days with no test in case of persistent positivity, for both vaccinated and unvaccinated individuals.[40] As this last protocol is rather similar to the French spring protocol, we considered in the study the 3 protocols adopted during spring 2022 and commented on the implications of this change in the Discussion section.

Role of the funding source
The funders had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, and decision to submit. The first author and the corresponding author had full access to all the data in the study.

Results

Attitudes towards vaccination, testing, and isolation in the 2022/2023 winter season
We used the three national platforms of the digital surveillance system Influenzanet in France, Belgium, and Italy (GrippeNet.fr/COVIDnet.fr, Infectieradar.be, Influweb.it, respectively) to investigate prospective behavior on booster uptake, testing, and isolation in the 2022/2023 winter season. Data collection took place in the summer 2022, resulting in 3534 respondents in France, 741 in Belgium, and 319 in Italy, after accounting for the inclusion criteria (see Methods). In the following, results for the three countries will be listed according to decreasing sample size. After adjusting for age, sex, and education, countries displayed a marked difference in the participants' propensity to receive an additional booster dose in the fall of 2022 (72.5% of the elderly in France, vs. 93.9% and 86.4% in Belgium and Italy, respectively; Fig. 1A). Prospective testing behavior showed very high adherence to testing if symptomatic (92.7% in France, 91.2% in Belgium, 97.3% in Italy), and 8 to 15 percentage points lower adherence if asymptomatic (78.2% in France, 82.3% in Belgium, 89.6% in Italy; Fig. 1B). More than half of the participants declared they would test twice after a first negative result if symptoms still persisted (50.9% in France, 56.7% in Belgium, 68.2% in Italy), whereas few would repeat the test at least a third time (5.8% in France, 12.2% in Belgium, 15.7% in Italy). If access to the test was at a given cost (<20 Euros), then only 42.2% of individuals in France and 47.2% in Belgium would get tested in the presence of symptoms, compared to 72.5% in Italy (Fig. 1C). Lower values were found if individuals were asymptomatic.

Participants from all countries reported a high propensity to comply with recommendations for rapid isolation if symptomatic (96.2% would isolate in France, and among them 91.8% would enter isolation on the day of symptoms onset, corresponding to 88% of French respondents; similar values were obtained for Belgium and Italy; Fig. 1D). Lower values were reported in France for asymptomatic infections compared to the other two countries (88.3% would isolate if asymptomatic in France vs. 93.4% in Belgium and 97.2% in Italy). If isolated, almost full compliance to recommendations on the isolation duration was declared by participants in the three countries (98.3% in France, 99.2% in Belgium, 97.9% in Italy), with no difference between symptomatic and asymptomatic infection.

Impact of expected booster uptake, adherence to testing and isolation protocols
The fall 2022 booster campaign with declared adherence was estimated to allow the population of each country to restore, during the winter 2022/2023, levels of vaccine-conferred immunity higher than those achieved during the summer of 2022, when the last booster campaign occurred (Fig. 2). Most importantly, as
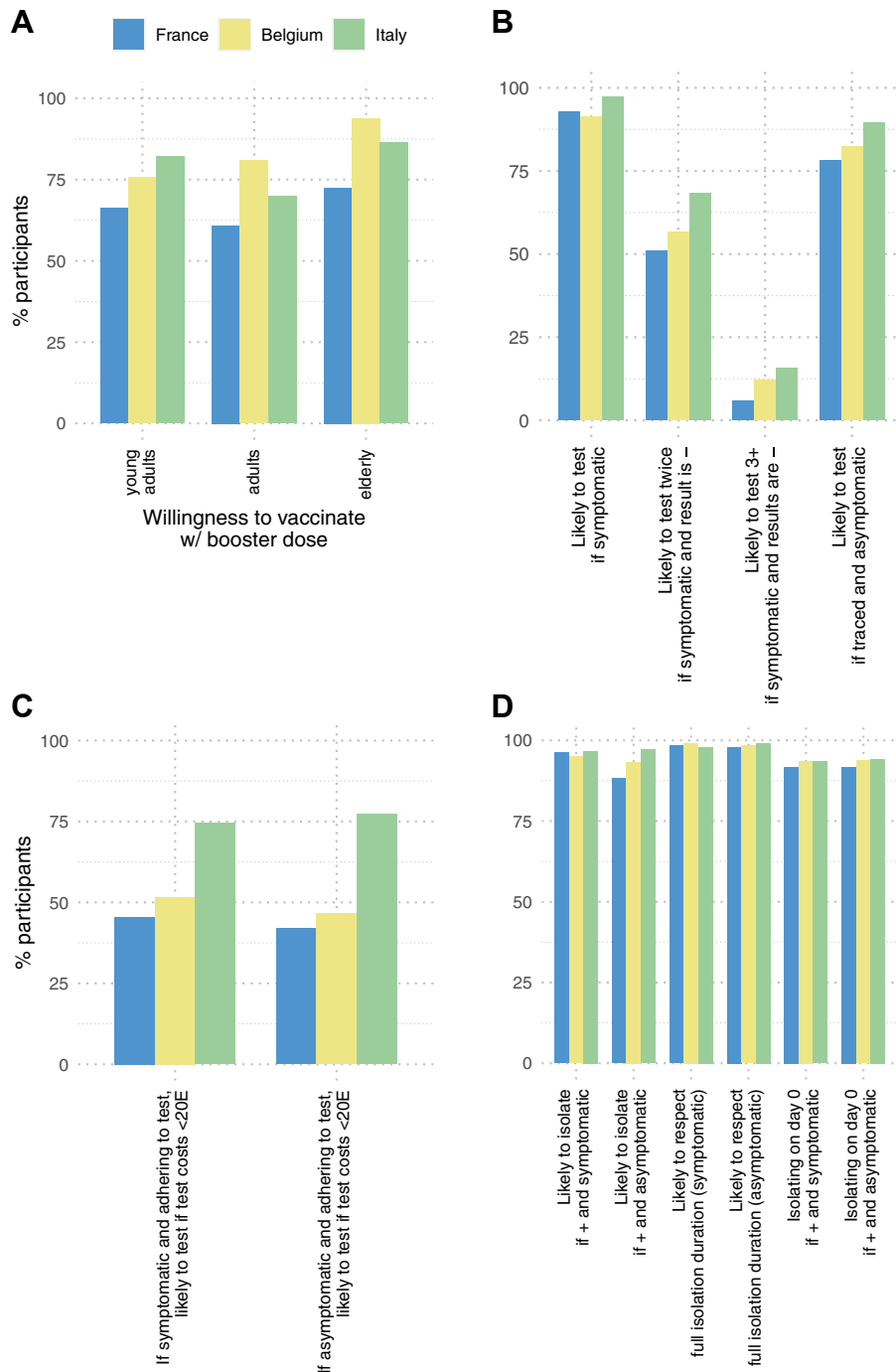
Fig. 1: Survey responses on propensity to vaccinate, testing and isolate in the 2022/2023 winter. A) Willingness to vaccinate with a booster dose in the fall 2022 campaign, if recommended, by age class and by country. Age classes correspond to (young adults, adults, elderly, respectively): [20, 39], [40, 59], 60+ for the French and Italian data; [25, 44], [45, 64], 65+ for the Belgian data. B) Adherence to testing during the 2022/2023 winter wave, if recommended, by country. C) Adherence to testing during the 2022/2023 winter wave, if recommended, by country, if tests cost less than 20 Euros. D) Adherence to isolation during the 2022/2023 winter wave, if recommended, by country. Responses on isolation duration and day of entry into isolation are conditional to a positive response about isolation.
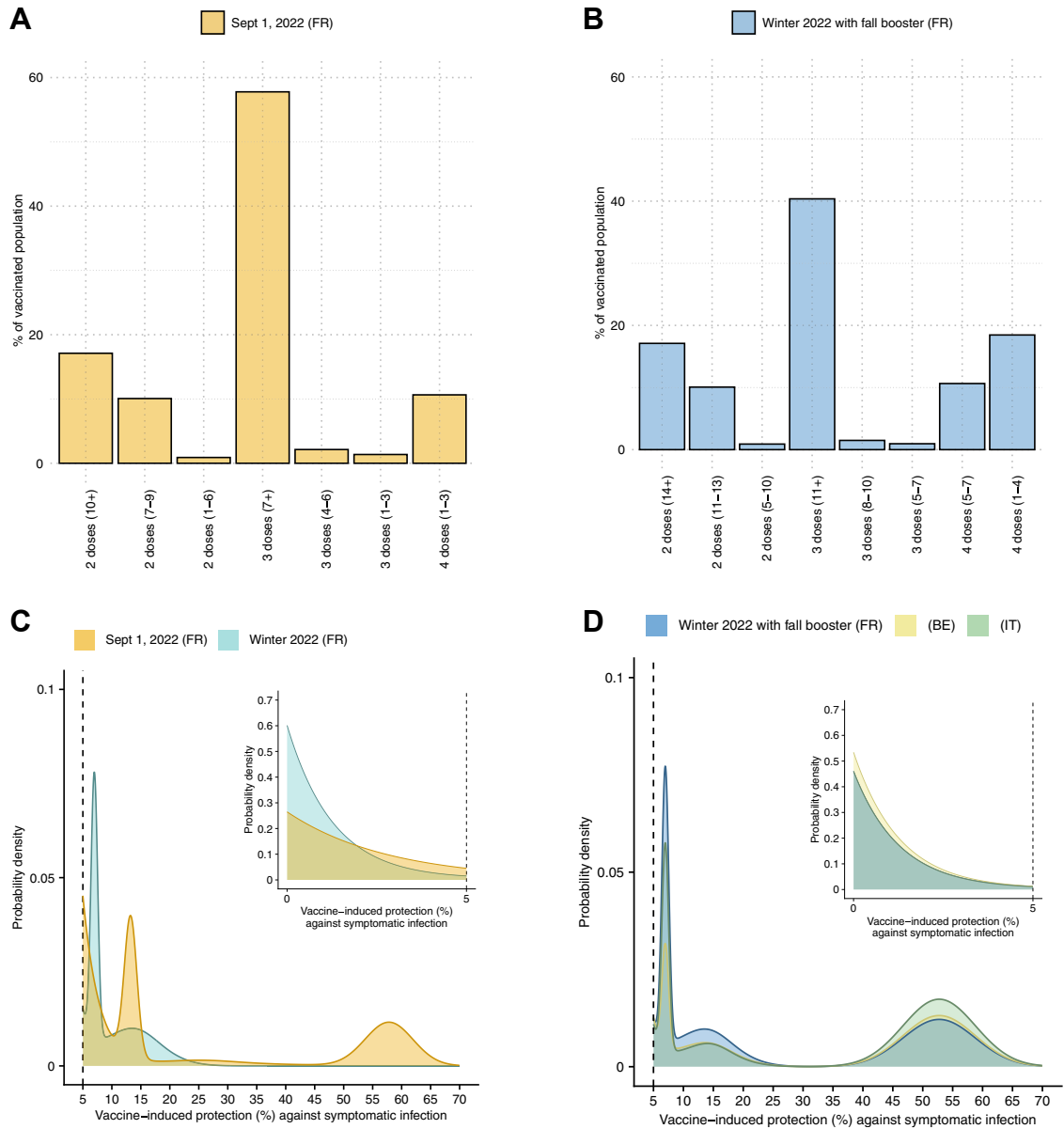
Fig. 2: Estimated vaccine-induced immunity in the population. A) Percentage of vaccinated individuals (2+ doses) in the French population in each waning category (time periods expressed in months), as of Sept. 1, 2022. B) Expected percentage of vaccinated individuals (2+ doses) in the French population in each waning category, with a fall booster informed by French survey respondents. C) Density of probability of population-level vaccine-induced protection against symptomatic infection inferred for September 1, 2022, and for the start of the 2022/2023 winter in the absence of the fall 2022 booster campaign. Results refer to France. D) Density of probability of population-level vaccine-induced protection against symptomatic infection inferred for the start of the 2022/2023 winter in the presence of the fall 2022 booster campaign. Adherence to the campaign is informed by the InfluenzaNet survey responses for France, Belgium and Italy.

immunity decreases over time, these levels would be substantially higher than those estimated for the start of the winter 2022/2023 in the absence of the booster campaign. According to senior respondents' willingness to get vaccinated with a booster, the mean vaccine-conferred protection against symptomatic infection inferred for the overall population of a given country would increase from 3.3% (standard deviation (SD) 0.3%) before the booster to 13% (SD 4%) after the booster in France (i.e. +294%), from 2.4% (SD 0.2%) to 13% (SD 5%) in Belgium (+442%), and from 3.8% (SD 0.3%) to 16% (SD 6%) in Italy (+321%).

As the vaccine-induced immunity profiles of the populations, the testing protocols and the prospective

adherence to such protocols differed among the three countries under study, we first focused on the French population, and evaluated the expected impact of the three national protocols as if they were applied in France. This allowed us to compare the effectiveness and costs of the three protocols applied to the same population, i.e. discounting the differences in uptake and immunity of the population of the three countries. We used a branching process mathematical model for SARS-CoV-2 diffusion parameterized to SARS-CoV-2 Omicron subvariants circulating in France with an effective reproductive number R = 1.6 in the absence of interventions (see Methods). Assuming a 75% reduction in transmissibility during the isolation period, we predicted that testing and isolation would reduce R by 18.4% (95% bootstrap confidence interval (CI) 18.1–18.8%) with the French protocol. If, instead, French authorities were to adopt the Belgian or Italian protocol, that would reduce R by 17.2% (16.8–17.4%) and 24.4% (24.0–24.9%), respectively (Fig. 3A). This corresponds to the Belgian protocols being 2% less effective than the French one, and the Italian protocol being 7% more effective (Fig. 3B). Given R = 1.6, none of the protocols alone would therefore be enough to fully control SARS-CoV-2 Omicron spread by reducing the effective reproductive number below 1. These results were based on the expected adherence to testing and isolation declared by French participants in the survey (Fig. 1) given current access to testing: those vaccinated may get tested at any pharmacy and clinic free of charge, and without prescription (Table 1). Negligible differences were estimated when comparing currently active protocols with those in place last winter (2021/2022 winter, Fig. 3). If tests were to cost up to 20 Euros, the decline in adherence to testing declared by survey participants would be responsible for approximately 60% lower predicted effectiveness of the three testing strategies compared to free access (Fig. 3A).

The three protocols implied different testing resources, with on average 1 diagnostic test per infected person using the French protocol, compared to 0.65 and 1.22 per infected person using the Belgian and Italian protocols, respectively (Fig. 3D). These testing needs would be reduced approximately by 60% if a moderate cost was introduced.

Small variations in the effectiveness and costs of protocols were observed when each testing and isolation protocol was evaluated as applied in its corresponding country, i.e. considering the adherence to interventions declared by the country's participants, under the same scenario of R = 1.6 (Fig. S8 of the Supplementary Information). The higher willingness of Italian survey participants to get tested even if they have to pay out-of-pocket (74.6% vs. 51.7% in Belgium and 45.5% in France if symptomatic, Fig. 1C) would however increase the predicted effectiveness of the Italian protocol in this context compared to the other countries (19% reduction of R considering the Italian adherence to pay for testing, Fig. S8, vs. 11% considering the French adherence, Fig. 3).

A higher isolation effectiveness (90%) would improve the control of the winter wave leading to a 21–29% reduction of community transmission across the three countries (Fig. S10), however still leaving the effective reproductive number larger than 1 under the R = 1.6 scenario considered here. A less effective isolation of infectious individuals (60% reduction of the viral transmissibility) would lower control, yielding a mitigation effort in the range of 15–22% reduction of R (Fig. S9).

Additional values of R in the range 1.3–2.1 were explored for sensitivity. We found little change in the impact of protocols, if expressed in terms of relative reduction of the effective reproductive number (Fig. S7). The only exception was the scenario with R = 1.3 and the Italian protocol, as testing and isolation were able in this case to reduce community transmission below the threshold (i.e. R < 1) in some stochastic simulations. A scenario with no booster campaign would increase the effective reproductive number from R = 1.6 to R = 2.1, corresponding to a relative increase of 31% in the three countries, respectively.

Despite different rules on exit from isolation, the French and Belgian protocols were predicted to impose a similar average length of isolation (about 6 days, after accounting for delays in entry and possible anticipated exits, as declared by survey participants), while releasing similarly high percentages of individuals while still infectious (approximately 60%; Fig. 4). This percentage would be much smaller (8%) with the Italian protocol because of the higher probability that individuals would isolate for longer (average isolation length of about 11 days, Fig. S5). The predicted fraction of infected individuals under isolation exiting after 7 days was indeed 13%, 0%, 68% in the French, Belgian, and Italian protocols, respectively. As a consequence, the predicted share of post-isolation transmission was around 19% in the French and Belgian protocols, while it was significantly lower in the Italian protocol (around 8%; Fig. S6).

Discussion

While contact tracing has been largely abandoned, several European countries still maintain testing and isolation protocols to mitigate COVID-19 in the next phase of the pandemic. Adapting these strategies to this shifting context means accounting for the expected compliance of a population that is increasingly more exhausted by the health crisis.[33,41] Using responses from 4594 individuals of a multi-country survey in Europe on their prospective adherence to testing and isolation, our study predicted that current protocols applied in France and Belgium would contribute with a 17–18% reduction of community transmission in the winter wave caused
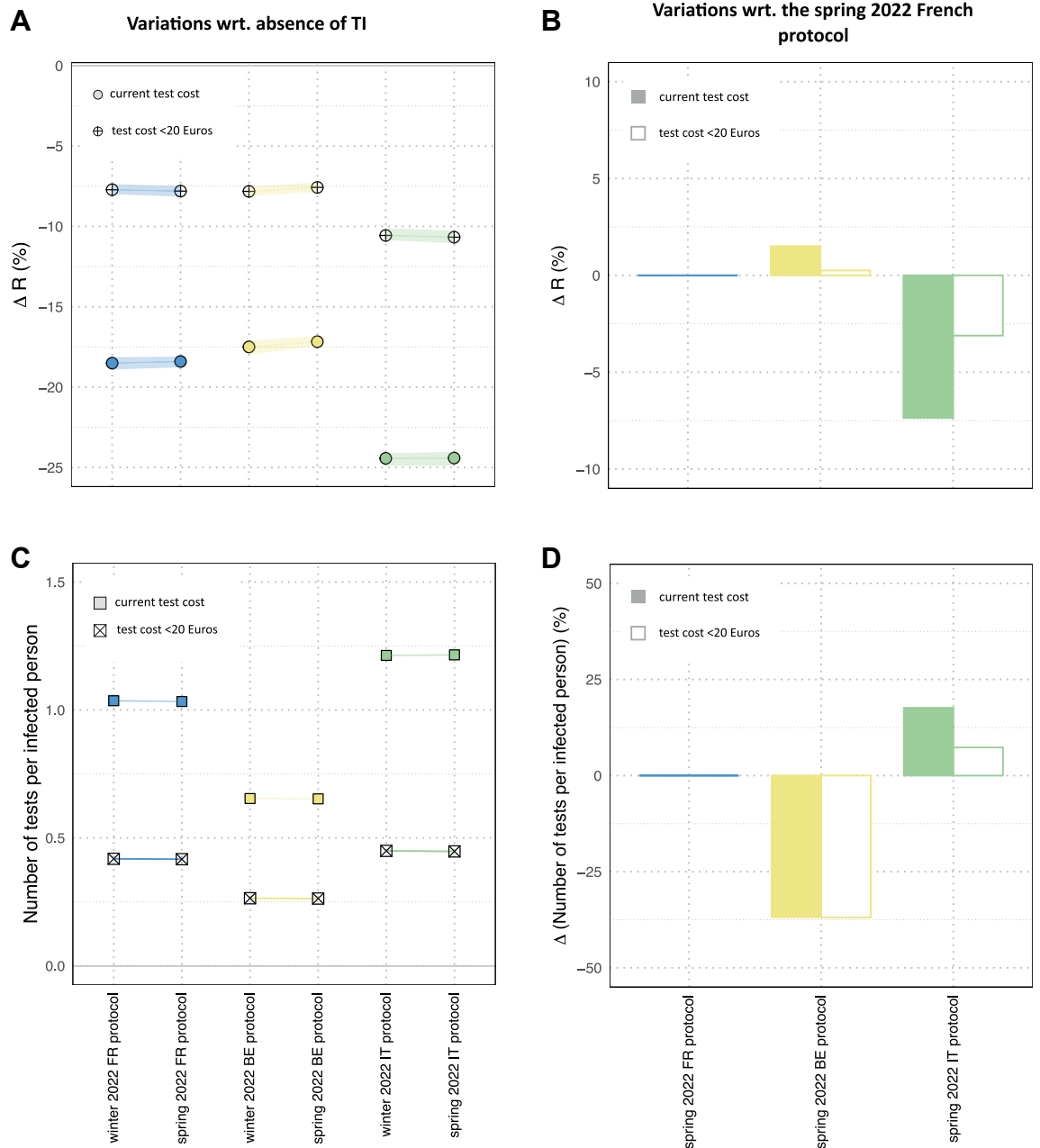
Fig. 3: Expected performance of the French, Belgian, and Italian protocols in the 2022/2023 winter. A) Relative variation of the effective reproductive number compared to the no intervention case (absence of TI, testing and isolation) for each protocol. Medians and 95% bootstrap confidence interval. B) Relative variation of the effective reproductive number compared to the spring 2022 French protocol (currently applied). Medians and 95% bootstrap confidence interval. C) Mean number of diagnostic tests per infected case. D) Mean relative variation of the number of diagnostic tests per infected case compared to the spring 2022 French protocol (currently applied). All results refer to the three protocols as if applied in France.

by the SARS-CoV-2 Omicron subvariants. Simpler guidelines on isolation duration would decrease the needed testing resources without affecting the performance of these protocols. The Italian protocol would be 7% more effective than the others, but at a higher social

cost in terms of days lost in isolation. The protocols alone would however not be enough to bring R below 1 even in the case of the high adherence declared by survey participants. Lower adherence to testing and isolation, due to a lower perceived need of such public
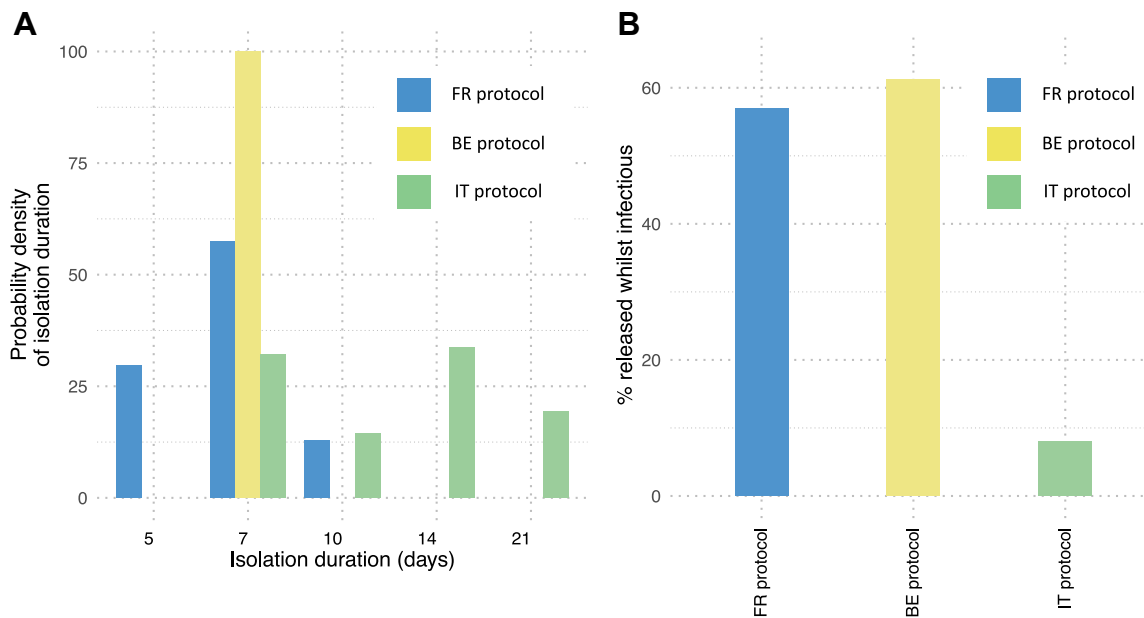
Fig. 4: Impact of the duration of isolation. A) Probability density of isolation duration in the French, Belgian, and Italian protocols. B) Percentage of individuals who are released from isolation while still infectious in the French, Belgian, and Italian protocols. All results refer to the three protocols as if applied in France.

health measures or because of the introduction of a cost barrier, would considerably decrease the mitigating impact of these measures. In any scenario, achieving high coverage of the fall booster vaccine dose remains imperative to obtain effective control of the winter wave.

Among the three national protocols studied here, the Italian protocol yielded the largest reduction of the effective reproductive number (24%) compared to the French and Belgian protocols (17–18%), for a moderate effectiveness of isolation (75%). This is due to a longer mandated isolation period, and in particular to isolation being constrained to fixed weekly durations in case of positive exit test. For example, according to the Italian protocol implemented in April 2022,[40] vaccinated individuals with a positive exit test at day 7 were required to continue isolation until day 14, and were allowed to exit only with a negative exit test; otherwise, they had to remain in isolation for an additional week. Only the modifications to the protocol further applied in the fall 2022[40] relaxed the constraint of the weekly wait, allowing individuals to exit with a negative test after the initial mandatory isolation period. For a 7% loss in mitigating effects, the French and Belgian protocols would ensure shorter isolations - a desirable outcome given the toll of pandemic fatigue building over almost three years.[33,41] Moreover, adopting simpler guidelines on isolation as in the Belgian protocol (with a fixed isolation duration for all individuals) would yield similar durations of isolation compared to the French protocol, but 35% fewer tests required per infected person. This is due to

the absence of the exit test that is instead required in France[38] to shorten isolation (on day 5 if vaccinated, on day 7 if unvaccinated). Simplifying the rules on isolation has the potential to (i) largely reduce the huge costs of the surveillance system[6] or the costs for households purchasing self-tests; and (ii) encourage higher compliance among pandemic-weary individuals through clear communication of a simplified message.[42]

The changes of protocols that occurred in the three countries from winter 2021/2022 to spring 2022 mainly simplified and relaxed the rules on contact tracing, without affecting the requirements for isolation. This change was motivated by the high economic costs of the contact tracing system[6] and the limited adherence observed in the population - e.g. not declaring contacts or sharing details of contacts. Our findings predicted that this protocol change has a negligible impact on community transmission.

Earlier modeling works[43,44] predicted a larger potential of testing and isolation to reduce onward transmission compared to our estimates, e.g. larger than 30%. However, these studies focused on an early phase of the pandemic and assumed perfect adherence to isolation and 100% isolation effectiveness. In contrast, in the current phase, greater fatigue and an evolving perception of risk will likely affect these two aspects. Our main findings were obtained considering the responses on prospective attitudes towards testing and isolation provided by the survey participants in the three countries. Survey data were adjusted to account for the

socio-demographic differences observed between the Influenzanet digital cohorts and the corresponding national populations. Previous work showed that adjusted trends of estimated influenza-like-illness incidence from Influenzanet reports compare well with those of national sentinel systems,[11] proving the accuracy of the Influenzanet participatory system despite its lack of representativeness. However, we cannot exclude that the cohort under study suffers from a self-selection bias towards increased interest in health topics that could possibly also boost willingness to comply with preventive behaviors. Data from 37 nationally representative surveys in the UK between March 2020 and January 2021 reported that only 20% of respondents would seek a diagnostic test if they had symptoms, and that duration-adjusted adherence was around 50%.[45] These behaviors may however be context-specific and induced by the financial and practical support in place[46] (or lack thereof), so that they can hardly be generalizable elsewhere. Indeed, recent data from a nationally representative survey reported that 94% of French respondents who tested positive for COVID-19 since September 2022 complied with isolation mandates,[47] thus showing no gap between the declared willingness of our online cohort and the actual compliance in France.

Another issue is that support and access varied over time. For example, in the period following the first wave in France, seeking a general practitioner to obtain a mandatory prescription to testing was a major barrier to testing and isolation undermining the effectiveness of the surveillance and control system,[12] and was later lifted. Similarly, in our multicountry survey we found that adherence to testing would be reduced by more than half in French and Belgian respondents if tests were to cost up to 20 Euros, even in the presence of COVID-like symptoms. This would halve the effectiveness of testing and isolation in reducing community transmission, showing that such policy change may substantially affect the capacity to control the winter wave. In contrast, a larger fraction of Italian survey participants would agree to test despite the cost barrier. This may possibly be due to habits developed in the Italian context with individuals buying tests at the pharmacies to avoid lengthier and less directly accessible procedures to access free tests through local health authorities. Providing adequate and comprehensive support, including e.g. paid sick leave to encourage and enable self-isolation when sick, remains an important aspect for the management of COVID-19 even beyond the pandemic phase. This would allow the reduction of health disparities[48] and of the overall costs of absenteeism[49] from work due to the spread of winter infections.

While prospective compliance to testing and isolation was rather homogeneous across countries, with the few exceptions discussed above, the willingness to get the booster dose recommended to at-risk individuals in the fall 2022 was markedly different. Among senior respondents (60+ individuals in French and Italian datasets and 65+ in the Belgian dataset), we found a higher propensity to vaccinate with the booster dose in Belgium, followed by Italy, and then France, with an uptake overall larger than 72%. The actual coverage reported by early December 2022 for the fall booster campaign that started in October–November 2022, varies considerably across countries: 11% in France,[50] 52% in Belgium,[51] 17% in Italy[52] in seniors. Fall booster coverage in adults was negligible (e.g., <2% in France[50] as of December 7, 2022). These discrepancies may be due to a social desirability bias in responding to surveys.[53] While the authorities and the scientific community continue to support recommendations to get vaccinated with a booster dose in prevention for the winter wave, it is possible that the changing threat with respect to the previous two winters is deterring individuals. A change in the message delivery, from central authorities to local health care providers, GPs, and pharmacists may help in boosting vaccination choices. Direct recommendations from healthcare workers have proven to be a strong determinant of vaccination uptake against influenza,[54] improving the quality of information provided and increasing patients' trust. Compared to the scenario considered in the main analysis, the low vaccination coverages reported so far in France and in Italy would correspond to a higher effective reproductive number, compromising the ability of testing and isolation strategies to slow down the case surge in the winter wave. Waiting for possible increases of vaccination uptake over the winter, preventive measures such as masking[55] in closed settings become again essential to reduce onward transmission.

This study has a set of limitations. First, the model is not age-stratified. This is due to the branching process approximation, typically used to study the effects of testing, tracing and isolation in detail.[21,56–59] However, we do consider seniors' response to booster uptake in the multi-country survey to infer the population-level vaccine-induced immunity for the 2022/2023 winter. Second, our approach does not consider the healthcare impact in terms, for example, of hospital admissions and saturation. Similarly to the first limitation, this is related to the modeling framework and the absence of age stratification that characterizes the severity of the infection. Though our study does not characterize the epidemiological conditions putting pressure on the healthcare system, its findings can be used to anticipate the expected reduction of the effective reproductive number to slow down the viral circulation, with consequent effects on the hospital admissions. Third, we fixed the effectiveness of isolation to 75%, corresponding to a 75% reduction of transmissibility while the individual is isolated. Previous works[43,44] generally assumed higher values, including full compliance, but they also referred to the acute phase of the pandemic when more severe

variants circulated in a less immunized population, and non-pharmaceutical interventions were the key response to the pandemic. In that context, high compliance to isolation to reduce contacts within households was expected. In a post-crisis phase, where individuals received several vaccine doses and were possibly exposed to previously circulating variants, it is plausible to assume a lower effectiveness of isolation. In the sensitivity analysis we showed that higher values of isolation effectiveness would increase the resulting mitigating impact on COVID-19 circulation, as expected, while preserving the overall conclusions. Fourth, we evaluated protocols in terms of the number of tests per infected person, however our modeling choice prevents us from performing a standard cost-analysis. Fifth, for testing we considered exclusively the use of the antigenic tests as they were more widely used.[36,37] Antigenic tests compensate for their lower sensitivity, compared to PCR tests, with more rapid results, which are critical to anticipate isolation.[60] For the vaccination, we considered only the administration of the Pfizer-BioNTech BNT162b2 vaccine and its corresponding estimated vaccine effectiveness, since it was by large the most commonly used one in the three countries. We did not distinguish between monovalent and bivalent vaccines, as the difference in vaccine effectiveness is absorbed in the parameterization of the effective reproductive number R under study. Finally, regarding the survey, although our analysis is based on estimates from a multi-country study whose sample size is relatively small for Belgium and Italy (Table 2), we have not propagated the uncertainties on survey estimates to the output of the model. Doing so, however, would not increase the accuracy of our results as these uncertainties are considerably smaller than the ones induced by the other literature-based modeling assumptions, whose impact we tested for sensitivity.

As European countries enter their third winter since SARS-CoV-2 emergence with a generalized feeling that the pandemic is over, it is important to evaluate in this shifting context the tradeoff between applicable mitigation measures and the expected compliance to them. Our findings show that simpler guidelines for testing and isolation protocols, similar to the Belgian protocol, would be as efficient as more elaborate guidelines (e.g. the French protocol) while reducing the cost of testing resources needed. Longer isolation periods found in the Italian protocols may not be sustainable in this phase of the pandemic. Booster uptake remains a fundamental element of the response to manage COVID-19 through spring 2023.

Contributors
VC conceived and designed the study. GdM and VC designed the initial survey draft. EV, CC, MD, CKK, HN, DP, LH, NH contributed to revising and finalizing the survey. MD, CKK, CT, LH, DP implemented the survey in the national Influenzanet platforms. GdM developed the code and analyzed the data. All authors interpreted the results. GdM and VC wrote the initial manuscript draft. All authors edited and approved the final version of the Article.

Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2023.100614.

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