



Vaccine hesitancy for the COVID-19 vaccine booster dose among nursing home staff fully vaccinated with the primary vaccination course in Belgium

Marina Digregorio^{a,*}, Pauline Van Ngoc^a, Simon Delogne^a, Eline Meyers^b, Ellen Deschepper^c, Nadia Dardenne^d, Els Duysburgh^e, Liselore De Rop^f, Tine De Burghgraeve^f, Anja Coen^g, Nele De Clercq^g, An De Sutter^g, Jan Y. Verbakel^{f,h}, Piet Cools^b, Stefan Heytens^g, Laëtitia Buret^a, Beatrice Scholtes^a

^a Research Unit of Primary Care and Health, Department of General Medicine, Faculty of Medicine, University of Liège, Liège, Belgium

^b Department of Diagnostic Sciences, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

^c Biostatistics Unit, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

^d Biostatistics and Research Method Center, University of Liège, Liège Belgium

^e Department of Epidemiology and Public Health, Sciensano, Brussels, Belgium

^f EPI-Centre, Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium

^g Department of Public Health and Primary Care, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

^h NIHR Community Healthcare Medtech and IVD cooperative, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom

ARTICLE INFO

Keywords:

COVID-19
SARS-CoV-2
Vaccine hesitancy
Booster dose
Nursing home
Staff
Belgium
COVID-19 vaccination
COVID-19 vaccine booster dose

ABSTRACT

In Belgium, nursing home (NH) staff (NHS) and residents were prioritised for the initial COVID-19 vaccination and successive booster doses. The vaccination campaign for the first booster started in September 2021 in Belgian NH. Our first study about vaccine hesitancy towards the COVID-19 vaccine in Belgian NHS already showed a degree of fear for the primary vaccination course (T1). This new study aims to evaluate vaccine hesitancy to get the first booster (T2) in a population of fully vaccinated (with two doses) NHS. A random stratified sample of NHS who received the primary vaccination course ($N = 954$) completed an online questionnaire on COVID-19 booster hesitancy (between 25/11/2021 and 22/01/2022). NHS who hesitated or refused the booster were asked for the main reason for their hesitation/refusal. Overall, 21.0 % of our population hesitated before, were still hesitating or refused the booster, NHS that were not hesitant at T1 being 5.7 times less likely to hesitate to get the first booster dose (Adjusted OR 0.179, 95 % CI: 0.120, 0.267). Although there was a slight reduction (23.5 % to 20.1 %) in the proportion of NHS who hesitated/refused vaccination at T1 compared to T2 ($p = 0.034$), the fear of unknown effects was the principal reason for hesitation/refusal, already mentioned in our first study. NHS were not reassured concerning their initial fears. Given the likelihood that booster vaccinations will be necessary over the coming years, a communication strategy specific to NHS should be implemented.

Introduction

It is well established that community immunity can be achieved through mass COVID-19 vaccination campaigns [1]. This is however only true if at least 70 % of the world's population is fully vaccinated with an effective vaccine [2]. COVID-19 vaccine effectiveness is now well documented, with the demonstration of a decrease in severe cases of COVID-19 and in COVID-19-related mortality [3,4]. In Belgium, the vaccination campaign for the primary vaccination course (the first two

doses) started in December 2020 [5]. Given the vulnerability of nursing home residents (NHR) and the close contact they have with nursing home staff members (NHS), both groups were prioritised for vaccination. Mass vaccination programs in nursing homes (NH) have been decisive in reducing infection rates, morbidity, and mortality from COVID-19 [6]. However, the emergence of new variants and the rapid decline in vaccine-induced immunity over time, has required new vaccination campaigns for booster doses [7]. The particularly rapid decline in vaccine efficacy in NHR also led to the prioritisation of NH for

Abbreviations: NH, nursing home; NHS, nursing home staff members; NHR, nursing home residents.

* Corresponding author at: Research Unit of Primary Care and Health, Department of General Medicine, Faculty of Medicine, University of Liège, Liège, Belgium.

E-mail address: marina.digregorio@uliege.be (M. Digregorio).

<https://doi.org/10.1016/j.jvaxc.2024.100453>

Received 3 April 2023; Received in revised form 25 January 2024; Accepted 29 January 2024

Available online 30 January 2024

2590-1362/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

the first booster dose, the campaign started in September 2021 in Belgium [6,8,9].

As of 14 September 2022, after the campaigns for the primary vaccination course and for the first booster dose and during the campaign for the second booster dose, 78.5 % of the Belgian population has received the primary vaccination course and 62.0 % the first booster dose [8]. There is therefore a difference in vaccination coverage between the primary vaccination course and first booster dose that may increase as campaigns for booster vaccination progress to eventually impact community immunity. A decrease in the likelihood of getting booster doses has been reported by others in various countries [10–12]. Pal S. *et al* also reported limited acceptance of a hypothetical COVID-19 booster dose among US healthcare workers between 1 February 2021 and 31 March 2021 [13]. The acceptability of vaccinations can be influenced by various concerns, such as their safety and efficacy, low risk perception, lack of recommendations and information from healthcare professionals, and socio-economic factors. Vaccine hesitancy was defined by the World Health Organization (WHO) as the “delay in acceptance or refusal of safe vaccines despite availability of vaccination services” and considered as one of the ten major threats to global health in 2019 [14–16]. Our first study about vaccine hesitancy towards the COVID-19 vaccine in Belgian NHS already showed a degree of fear for the primary vaccination course. The three main reasons for refusal and hesitation were: the fear of unknown future effects, the fear of side-effects, and mistrust of vaccinations [17]. We also identified a subgroup of fully vaccinated participants who hesitated at first and finally got vaccinated mainly to protect the most vulnerable people [17]. Uncertainty and unwillingness to be vaccinated with the first dose of COVID-19 vaccine were described as factors that can predict acceptability of booster doses [11].

The present study aims to identify the proportion of NHS fully vaccinated with the first two doses that hesitated or refused to get the first booster dose as well as predictors of hesitancy for the booster dose. We compare the data with results from our first analysis for the primary vaccination course and identify the principal reasons for their hesitation/refusal for the first booster dose. To the best of our knowledge, COVID-19 vaccine hesitancy towards booster doses is poorly reported and not at all in Belgium. Examining the reasons for hesitancy for these additional doses in a population of NHS would allow a better understanding of the concerns of this population, frequently in contact with the elderly, who had already agreed to receive the primary vaccination course.

Methods

Study design and population

The present study is a sub-study of a national study (SCOPE) in which the prevalence of SARS-CoV-2 antibodies was assessed among Belgian NHS and NHR using a rapid antibody test. The study design including sample size calculation has been described in the study protocol and also summarized in our previous papers [17–19]. The present paper reports on a nested study that included only the NHS participating in the SCOPE study. In August (or in October, if the participant was absent at the August testing visit 2021 - timepoint 1 (T1)), all NHS participating in the SCOPE study were invited to answer questions about hesitancy for the primary vaccination course that had been added to the usual questionnaire [17]. Between 25/11/2021 and 22/1/22 (T2) a total of 1,368 participants were invited to answer the survey. NHS that received the primary vaccination course were asked questions about hesitancy towards the first COVID-19 booster dose, we report on those data in this paper.

Ethics approval and consent to participate

The SCOPE study was approved by Ghent University Hospital Ethics

Committee (reference number BC-08719) on the 11/12/2020. An amendment for the nested study was approved on 13/07/21 (reference number BC-08719-AM02). The study was conducted according to the approved protocol and the principles outlined in the Declaration of Helsinki. At the start of the study (February 2021) each participant was informed of the goal of the study, the intended use of the collected data, the pseudonymization of their data and guarantee of their anonymity, all participants signed an informed consent form. Participants did not receive any gift or financial reward for the time invested.

Data collection

In the SCOPE study, an online questionnaire (LimeSurvey version 3.22) was completed by each participant (NHS) within one week following the antibody testing. Reminders were sent through the LimeSurvey platform, approximately one week after the first mail was sent. The study team also reminded the NHS to complete the online questionnaire while they were at the NH to conduct the antibody testing for the wider national study. Approximately one week after testing, the study team sent a coded list to the NH management corresponding to NHS that had not yet completed the questionnaire. Each participant was provided with a unique link to their questionnaire which became invalid once they had successfully filled out the entire questionnaire.

A baseline questionnaire was completed in the SCOPE study between February 1st and March 24th, 2021. In this baseline questionnaire, participants were questioned about various individual characteristics (age, sex, type of job), presence of one of the following comorbidities (cardiovascular disease, diabetes, hypertension, immunosuppression, severe renal/lung/cardiac disease, active cancer), their influenza vaccination status in 2020 and COVID-19 vaccine (including type of vaccine, date of vaccination). The latter information was collected at each visit.

During T1 and T2, single-choice questions about vaccine hesitancy were added to the usual follow up questionnaire. Participants were asked if they had received a primary vaccination course (for T1) and if they had received the first booster dose (for T2) and if so, whether they had hesitated before being vaccinated. During T2, for participants that had not received any doses of the vaccine, the questionnaire ended, and these participants were not included in the analysis of hesitancy about the booster dose. The main reason for hesitation/refusal was explored using single-choice question with thirteen different answer options (detailed in the results section). In the vaccine hesitancy questionnaires, each question was mandatory but contained a ‘prefer not to answer’ option. The questionnaire was inspired by the items described by Larson and colleagues [20]. Although this study was not piloted, several of the authors of this paper (with diverse professional profiles) were directly involved in the elaboration of the questionnaire.

Fig. 1 shows how the questions were organised. Four profiles for vaccine hesitancy were coded as followed: (1) first booster dose received (or soon), no hesitation before; (2) first booster dose received (or soon), hesitation before; (3) not yet received the first booster dose, still hesitating; (4) refused the first booster dose. The complete questionnaire for T2 is available in [Supplementary material file 1](#).

Data and statistical analysis

Descriptive statistics were performed as follows; qualitative variables were summarized by number and percentage and the quantitative variable (age) was summarized using median and interquartile range 25th 75th percentile (IQR 25 and 75).

To test consistency in hesitation across T1 and T2 in NHS that received the primary vaccination course, McNemar’s test with durkalski adjustment for analysis of clustered matched-pair data was used [21].

In order to study the effects of various factors on vaccine hesitancy profile, a new binary variable was created for vaccine hesitancy with non-hesitant participants (NHS that had received the first booster dose

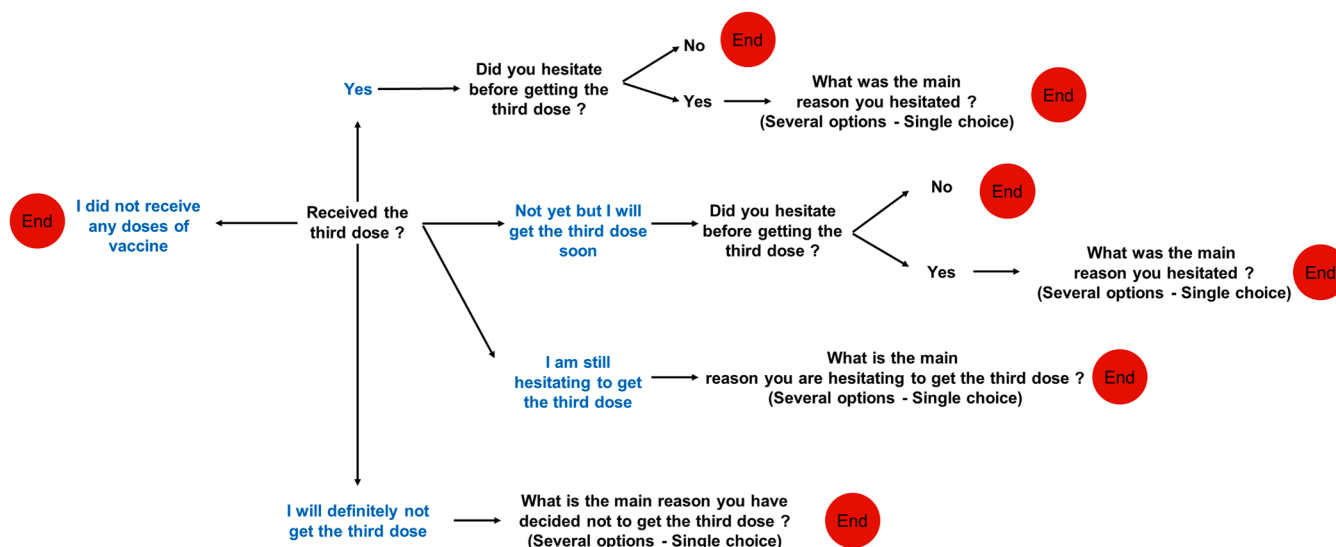


Fig. 1. Schematic representation of questions asked to nursing home staff members about hesitancy concerning the first booster dose between November 25th, 2021 and January 22nd, 2022. Questions are organised taking into account the answers to the previous question. Depending the answer, a new question was asked or the questionnaire ended.

or would receive it soon and did not hesitate to receive it) on one side and hesitant participants (participants that hesitated and had already received the first booster dose or would receive it soon or participants still hesitating or who refused the first booster dose) on the other. Profiles are distributed by individual characteristics as: age (median and IQR 25 and 75), gender (male, female), region (Brussels, Flanders, Wallonia), type of job with jobs divided into medical-related job (Medic.; nursing and paramedical) and non-medical-related job (Non-medic.; cleaning staff, catering, administration, hairdresser/pedicure and other), comorbidity (classified according to whether NHS self-reported zero (No) or one or more (Yes) comorbidities), influenza vaccination status in 2020 (yes = vaccinated; no = not vaccinated) and previous hesitation towards the first and second dose of COVID-19 vaccine (COVID-19 primary vaccination course hesitation). To study the effects of these characteristics on vaccine hesitancy profile, we performed GEE analysis with exchangeable covariance structure, taking the clustered nature of the staff within NHs into account. For this purpose, unadjusted (univariate analysis) and adjusted odds ratio (OR) for all covariates (multivariate analysis), and 95 % confidence interval (95 % CI) are reported. All covariates were included in the model as the use of stepwise selection methods for logistic regression modelling may result in biased estimates and unstable results [22,23].

In the present study, participants were not able to continue to the next question of the questionnaire if they failed to provide a response to an item. However, participants had the possibility to indicate that they prefer not to answer or to propose an answer with the item "other". Hesitation was analysed separately from refusal, when possible. For analysis of the main reason for hesitancy, when participants chose 'other', the reason given was manually analysed with attribution to a proposed item if possible. When the same reason was given frequently a new item was created, this was the case for the item 'pregnancy'.

All tests were two-sided and a p-value of ≤ 0.05 was considered statistically significant. Statistical analyses and graphical representations were performed by using R (version 4.1.1) and Microsoft Excel 2019.

Results

Participation characteristics

The study cohort for T1 was previously described by Digregorio et al

[17]. For T2, of the total cohort ($N = 1,368$), 998 (72.9 %) NHS completed the questionnaire and 954 (69.7 %) NHS that answered questionnaire were fully vaccinated with the first vaccination course and were considered in our analysis for hesitancy regarding the first booster dose. The majority of respondents were over 40 years old ($N = 582$; 61.0 %) with the median equal to mean age being 45 years old (IQR P25 –P75, 36–54), female ($N = 801$, 84.0 %), working in Flanders ($N = 601$; 63.0 %), worked as nurses or care workers ($N = 478$; 50.1 %) and reported not having any co-morbidities ($N = 752$; 78.8 %). Concerning status of influenza vaccination in 2020, the distribution of the NHS was split almost evenly between those who reported being vaccinated and those who reported not being vaccinated. Out of the 954 NHS considered for T2 analysis, 22.5 % ($N = 215$) hesitated for the first vaccination course in T1 (Table 1). The representativity of the sample was guaranteed through the wider national study design where 69 NH, geographically and demographically representative for NH in Belgium, were randomly selected. Moreover, non-respondents' characteristics were similar to our surveyed population (Supplementary material file 2).

Distribution of NHS by vaccine hesitancy question (profile), comparison of proportion of NHS who hesitated/refused vaccination between T1 and T2 and association with individual characteristics

Overall, 72.5 % ($N = 692$) of NHS fully vaccinated with the first two doses reported being vaccinated with the first booster dose of the vaccine against COVID-19. Among the hesitant participants, we identified three profiles; participants who had already received the first booster dose or would receive it soon and had hesitated before (14.5 %, $N = 138$), participants who were still hesitating (4.9 %, $N = 47$) and those who refused to get the first booster dose (1.6 %, $N = 15$). Overall, 21.0 % ($N = 200$) of the total fully vaccinated cohort hesitated, were still hesitating or refused the booster (Table 1).

Considering the population that answered both the first survey on hesitancy about the primary vaccination course (T1) and the second survey on the first booster dose (T2), we can encounter a sample size of 913 participants. Among these participants, at T2, 11.4 % were still hesitating and 67.7 % were still not hesitating. Moreover, 8.8 % of NHS who did not hesitate at first, hesitated before the first booster dose and 12.1 % of participants who hesitated at T1, did not hesitate at T2. There is a significant reduction (23.5 % to 20.1 %) in the proportion of NHS who hesitated/refused vaccination at the primary vaccination course

Table 1

Characteristics of 954 Belgian nursing home staff members fully vaccinated with the first vaccination course responding to the survey about hesitancy regarding the first booster dose of COVID-19 vaccine (between November 25th, 2021 and January 22nd, 2022) in T2.

| | N (%) |
|---|--------------|
| TOTAL | 954 |
| Age | |
| 18–40 | 329 (34.5) |
| > 40 | 582 (61.0) |
| Unknown | 43 (4.5) |
| Gender | |
| Male | 138 (14.5) |
| Female | 801 (84.0) |
| Unknown | 15 (1.5) |
| Region | |
| Brussels | 60 (6.3) |
| Flanders | 601 (63.0) |
| Wallonia | 293 (30.7) |
| Type of job[#] | |
| Nursing | 478 (50.1) |
| Paramedic | 134 (14.1) |
| Cleaning staff | 97 (10.2) |
| Catering | 70 (7.3) |
| Administration | 85 (8.9) |
| Hairdresser/pedicure | 1 (0.1) |
| Other | 57 (6.0) |
| Unknown | 32 (3.3) |
| Comorbidity | |
| Cardiovascular disease | 26 (2.7) |
| Diabetes | 32 (3.3) |
| Hypertension | 107 (11.2) |
| Respiratory disorders | 14 (1.5) |
| Immunosuppression | 19 (2) |
| Cancer | 5 (0.5) |
| None | 752 (78.8) |
| Unknown | 32 (3.3) |
| Influenza vaccination | |
| Yes | 488 (51.1) |
| No | 440 (46.1) |
| Unknown | 26 (2.8) |
| COVID-19 primary vaccination course hesitation | |
| Hesitation | 215 (22.5) |
| No hesitation | 698 (73.2) |
| Unknown | 41 (4.3) |
| COVID-19 booster dose hesitancy | |
| First booster dose (or soon), no hesitation | 754 (79.0) |
| First booster dose (or soon), hesitation | 138 (14.5) |
| Not yet received the first booster dose, still hesitating | 47 (4.9) |
| Refuse first booster dose | 15 (1.6) |

[#] Other type of job includes mainly logistic assistants ($N = 8$), animators ($N = 7$) and supervisors ($N = 25$).

(T1) compared to the first booster dose (T2) (p -value = 0.034) (Table 2).

There were differences in individual characteristics in terms of vaccine hesitancy profiles (Table 3). For this analysis, NHS that did not hesitate and received the first booster dose or would receive it soon were grouped together. In the same way, participants that hesitated and had already received the first booster dose or would receive it soon or participants still hesitating or who refused the first booster dose were also grouped. In addition, participants for whom we had at least one missing data were excluded from this analysis, which gives us a population of 178 hesitant vs 699 non hesitant NHS towards the first booster dose of

Table 2

Vaccine hesitancy status for the primary vaccination course (T1) and for the first booster dose (T2).

| T1/T2 | Yes (%) | No (%) | | McNemar p-value |
|---------|------------|------------|------------|-----------------|
| Yes (%) | 104 (11.4) | 111 (12.1) | 215 (23.5) | 0.034 |
| No (%) | 80 (8.8) | 618 (67.7) | 698 (76.4) | |
| | 184 (20.1) | 729 (79.9) | 913 | |

Data are shown as the number (N) of participants in each category and the percentage (%) of the cohort fully vaccinated for the first vaccination course that answered vaccine hesitancy questionnaire in T1 (vertical) and T2 (horizontal) (excluding missing data). p -value is from McNemar's Chi-squared test with durkalski adjustment for analysis of clustered matched-pair data.

COVID-19 vaccine. NHS working in Wallonia and NHS that did not report influenza vaccination in 2020 had a higher odds of vaccine hesitancy compared to their Flemish counterparts or those who reported themselves to be vaccinated, respectively (Unadjusted OR Wallonia 1.96, 95 % CI: 1.26, 3.05 and Unadjusted OR FluvacNo 2.18, 95 % CI: 1.53, 3.11). However, when considering adjusted OR for all covariates, region and influenza vaccination in 2020 were no longer statistically related to the probability of hesitation (Adjusted OR Wallonia 1.44, 95 % CI: 0.90, 2.29 and Adjusted OR FluvacNo 1.33, 95 % CI: 0.88, 2.00). Moreover, with each increase, by one year of age, the probability of hesitating decreases (Adjusted OR 0.96, 95 % confidence interval (CI): 0.94, 0.97). Finally, NHS that were not hesitant at T1 (for the first two doses of COVID-19 vaccine) had a smaller odds of vaccine hesitancy toward the first booster dose than those who were hesitant at T1, being 5.7 times less likely to hesitate to get the first booster dose (Adjusted OR 0.18, 95 % CI: 0.12, 0.267).

Principal reasons for hesitation/refusal of getting the first booster dose and comparison between the different profiles identified

Those participants that were uncertain about getting the first booster dose ($N = 200$) were asked the main reason for their hesitancy (Fig. 2). The main reason was the fear of unknown future effects in NHS who received the first booster dose and hesitated before ($N = 20$) and in NHS who will be vaccinated soon ($N = 13$). For NHS who were still hesitating, the principal reason was that they felt that they were sufficiently protected with the two doses of the vaccine ($N = 8$). Finally, for the 15 participants who refused to get the first booster dose, the main reason was split almost evenly between answer options, with the first being that they prefer not to answer ($N = 3$).

Although the three principal reasons for hesitation/refusal among all participants were not homogeneous between profiles, all profiles mentioned the fear of side-effects after a bad experience with the primary vaccination course in their top three reasons for hesitancy.

Discussion

Compared to T1, though fewer participants completed the questionnaire during T2 (for the first booster dose $N = 998$ vs $N = 1142$ for T1), population characteristics were similar in both studies [17]. In T2, fewer vaccinated participants reported that they had received the first booster dose (72.5 %) compared with vaccination in T1 where more than 90 % of NHS reported to have been vaccinated with the primary vaccination course at the time of completing the questionnaire. This difference was certainly due to the timing of the completion of the questionnaire. Indeed, participants answered T1 questionnaire after the campaign for the primary vaccination course, while for the questionnaire in T2, NHS completed it during the vaccination campaign for the first booster dose.

In the T2 cohort, we showed that 21.0 % ($N = 200$) of fully vaccinated NHS hesitated, were still hesitating or refused the first booster dose of COVID-19 vaccine in T2. Looking beyond the population of NHS

Table 3Odds of hesitancy concerning the first booster dose of COVID-19 vaccine as a function of individual characteristics ($N = 877$).

| | No hesitation before N (%) | Hesitation before/still hesitating/refusing N (%) | Unadjusted OR [95 % CI] | Adjusted OR [95 % CI] |
|---|-------------------------------|--|-------------------------|-----------------------|
| Age (years) | 699 (79.7) | 178 (20.3) | 0.95 [0.94, 0.97] | 0.96 [0.94, 0.97] |
| Median (IQR 25–75) | 47 (38–56) | 40 (31–49) | | |
| Gender | | | | |
| Female (ref) | 597 (68.1) | 155 (17.7) | 1 | 1 |
| Male | 102 (11.6) | 23 (2.6) | 0.89 [0.55, 1.44] | 1.14 [0.65, 1.99] |
| Region | | | | |
| Brussels | 35(4.0) | 11 (1.2) | 1.52 [0.65, 3.58] | 2.03 [0.83, 4.95] |
| Flanders (ref) | 469 (53.5) | 93 (10.6) | 1 | 1 |
| Wallonia | 195 (22.2) | 74 (8.4) | 1.96 [1.26, 3.05] | 1.44 [0.90, 2.29] |
| Type of job | | | | |
| Medic. (ref) | 460 (52.4) | 128 (14.6) | 1 | 1 |
| Non-medic. | 239 (27.2) | 50 (5.7) | 0.76 [0.53, 1.09] | 0.98 [0.64, 1.48] |
| Comorbidity | | | | |
| No (ref) | 569 (64.9) | 149 (17.0) | 1 | 1 |
| Yes | 130 (14.8) | 29 (3.3) | 0.84 [0.54, 1.31] | 1.01 [0.60, 1.70] |
| Influenza vaccination | | | | |
| Yes (ref) | 397 (45.3) | 65 (7.4) | 1 | 1 |
| No | 302 (34.4) | 113 (12.9) | 2.18 [1.53, 3.11] | 1.33 [0.88, 2.00] |
| COVID-19 primary vaccination course hesitation | | | | |
| Yes (ref) | 107 (12.2) | 101 (11.5) | 1 | 1 |
| No | 592 (67.5) | 77 (8.8) | 0.14 [0.10, 0.21] | 0.18 [0.12, 0.27] |

Vaccines hesitancy profiles are: nursing home staff members (NHS) that received the first booster dose or would receive it soon and did not hesitate before vaccination (No hesitation before = reference profile) and NHS that received the first booster dose and hesitated before vaccination, NHS that did not receive yet the first booster dose and were still hesitating or refusing to get the first booster dose (hesitation before/still hesitating/refusing). Profiles are distributed by individual characteristics as: age (median and interquartile range 25th 75th percentile (IQR 25 and 75), gender, region, type of job with jobs divided into medical-related job (Medic.; nursing and paramedical) and non-medical-related job (Non-medic.; cleaning staff, catering, administration, hairdresser/pedicure and other), Comorbidity (classified according to whether NHS self-reported zero (No) or one or more (Yes) comorbidities), influenza vaccination status in 2020 and previous hesitation towards the first and second dose of COVID-19 vaccine (COVID-19 primary vaccination course hesitation). Data are shown as unadjusted odds ratio (OR) with 95 % confidence interval (95 %CI) and adjusted OR for all covariates (multivariate analysis) with 95 %CI. The ORs are estimated based on a GEE analysis with exchangeable covariance structure, taking the clustered nature of the staff within NHS into account.

our findings are comparable with a population of staff and students of a Belgian university. In their study of 1030 participants, 84.2 % intended to get the COVID-19 booster dose and 15.8 % hesitated or refused [24]. Similarly, a meta-analysis showed that, out of 13 studies, 14 % of the global general population fully vaccinated for the first two doses intended to refuse to get the first booster dose when recommended [25].

The change between initial intention to get the booster dose and the final decision to not get it was also investigated by the Belgian study cited above. They identified determinants negatively associated with the decision not to get the booster dose; having a weaker past intention to get the vaccine, having had a previous COVID-19 infection, and having a higher neutralizing antibody level [24]. In our study, previous hesitation towards the first vaccination course was associated with a vaccine hesitancy profile for the first booster dose. However, unlike T1, gender, type of job, region and previous influenza vaccination were no longer associated with hesitation profiles when all covariates were considered in the multivariate analysis model. Comparatively, in 2022, predictors of participant's willingness to accept a first COVID-19 booster dose were reviewed in a meta-analysis including 14 studies of the general population (vaccinated with the first two doses) where they found that age and previous influenza vaccination were both associated with booster acceptance, unlike gender and chronic comorbidities [25].

COVID-19 vaccine booster acceptability has been studied in various

countries, and more widely in the general population [10,11,25–32]. The meta-analysis mentioned above showed that out of 14 studies, 79 % of the populations studied (fully vaccinated general population) intended to receive the first booster dose when available and recommended [25]. In a population of 443 Polish healthcare workers, 25.5 % hesitated or refused the booster dose, a proportion of hesitant participants comparable to our study [26].

Unlike our T1 analysis, in T2 there was no consensus between groups concerning the three principal reasons for hesitation. Furthermore, in T2, the main reason for hesitation was the fear of unknown future effects for participants who had received the booster and those who would receive it soon. This last information suggests that NHS have not been reassured about their initial fears. The fear of long-term effects was indeed one of the main reasons for hesitation mentioned by NHS for the primary vaccination course. Fear of side-effects was also identified by others as a reason for hesitation/refusal of healthcare workers for the booster dose [26]. In a study that focused on the general population in Poland, participants mentioned similar reasons for hesitation/refusal to those reported in our study; fear of side-effects and feeling of being sufficiently protected with the two doses of vaccine [10]. Others highlighted that reasons to get a booster may vary according to socio-demographic characteristics in a population of older people or with chronic conditions [30]. Mistrust of vaccines was mentioned in our

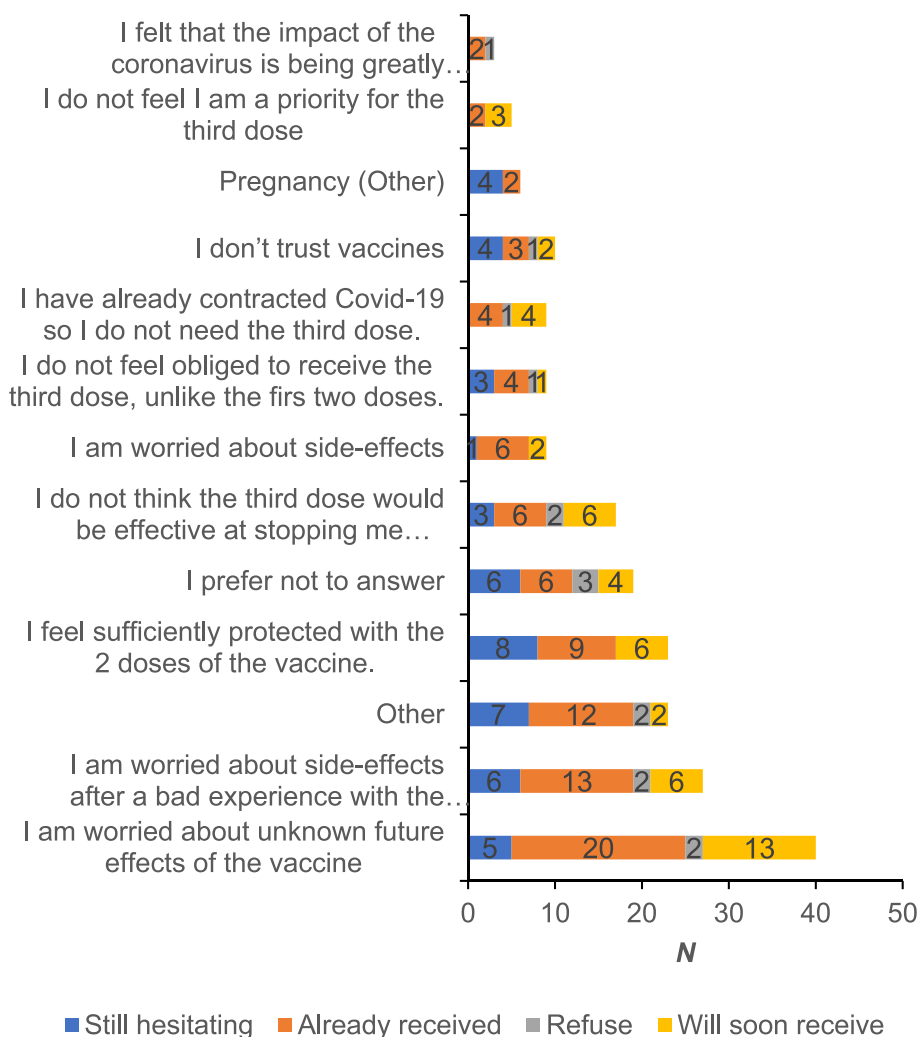


Fig. 2. Main reason for hesitation regarding the first booster dose among nursing home staff members (NHS); distribution by vaccine hesitancy profiles. Profiles are: NHS that received the first booster dose and hesitated before (orange), NHS that would soon receive the first booster dose and hesitated (yellow), NHS still hesitating to get the first booster dose (blue) and NHS that refused to get the first booster dose (grey). Data are shown as the number (N) of answer in each profile. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

previous study in the top three of the main reasons for hesitation/refusal of the primary vaccination course, and also mentioned by others as main reason for hesitation for the booster dose [10], however, in the present study, only 5 % of participants that hesitated/refused indicated this as the main reason for hesitation/refusal. An adverse reaction to a previous vaccination and concerns about serious adverse reactions to booster doses have both been shown to be associated with a decrease in willingness to accept further boosters [25]. In our study, these concerns were identified as reasons for hesitation among NHS. While many countries now recommend further booster doses for populations at risk, communication strategies towards NHS by reassuring and communicating about the current knowledge of the long-term effects of the vaccine and its booster doses should be a priority [25]. Indeed, the willingness to receive the boosters and the maintenance of this acceptability is essential to decrease vaccine hesitancy and to manage the crisis.

Vaccination of NHS and NHR has already proven its efficacy in decreasing COVID-19 infections in NHS and NHR and COVID-19-related deaths in NHR [6,33]. In our study, we found a statistically significant change in the proportion of fully vaccinated NHS that hesitated for the primary vaccination course and for the first booster dose, moving towards a decrease. Our study also shows that NHS who had hesitated for the primary vaccination course in T1 were 5.7 times more likely to

hesitate/refuse the booster dose vaccine than those who had not hesitated at T1. In a study conducted among the general population in Poland, the importance of past experiences and perceptions in vaccine preferences were highlighted as determinants for the willingness to get a booster [31]. These observations add an argument in favor of specific communication for NHS and that measures should be deployed to encourage vaccine uptake among NHS, particularly those who have already hesitated about COVID-19 vaccination and especially for future booster doses, especially since it is known that confidence in vaccination is volatile and closely linked to communication [34]. In a qualitative study conducted in 50 NH in the US, misinformation about the COVID-19 vaccine was identified among NHS [35]. In general, misinformation about safety is known to be associated with vaccine hesitancy [36]. Strategies have been developed to boost COVID-19 vaccine acceptance among the general population in the USA [37]. A recent review also synthesized scientific information to support communication strategies specific to vaccine-hesitant populations [38]. In addition, information regarding the second booster dose, derived from scientific journals, has positively influenced vaccine acceptance within specific population, including special groups such as health care workers [39,40]. Among measures undertaken to address vaccine hesitancy in NHs, some institutions mandated COVID-19 vaccination, as this has already been shown to be effective for influenza vaccination [41,42]. Other studies

suggest that the identification and support of champions among front-line staff, vaccination goals and use of multiple strategies is associated with higher NH-level vaccination coverage [43]. Another qualitative study indicated that peer-positive experiences may also be effective to address vaccine hesitancy [35]. A recent study found that strategies such as a peer counseling and providing sick leave or time off for vaccine symptoms could be effective to increase vaccination rates among NHS in Ohio, USA [44].

To the best of our knowledge, this study is the first to investigate COVID-19 first booster dose hesitancy among NHS randomly recruited among geographically and demographically representative Belgian NH. Most of the methodological strengths and limitations of the first published study can be applied for the present study about hesitation regarding COVID-19 booster dose [17]. Briefly, participants were already familiar with the study team and questionnaires, when they answered questions about vaccine hesitancy during T2. This study design therefore limited social desirability bias in our research. Unlike the T1 design, in T2, participants answered questions during the vaccination campaign that may have limited recall bias mentioned in T1 but may also have had a different effect at that time-point. As the same population answered both T1 and T2, this allowed us to statistically compare the proportion of NHS hesitating between the two time points. Concerning weaknesses of our study, first, a limitation regarding the fixed order of proposed possible answers for the main reason for hesitation applies. Second, although this study was not piloted before data collection, its validity was improved through the participation of a multi-disciplinary group in the elaboration of the questionnaire.

Conclusion

There was a slight reduction (23.5 % to 20.1 %) in the proportion of NHS who hesitated/refused vaccination at the primary vaccination course (T1) compared to the first booster dose (T2). In addition, hesitancy at T1 was positively associated with hesitancy at T2, participants who hesitated for the primary vaccination course were more likely to hesitate for the first booster dose. The main reason for hesitation to get the first booster dose was the fear of unknown effects. In conclusion, this study indicates that NHS still express a certain degree of fear concerning vaccination and that these fears have not yet been allayed. In the context of COVID-19 vaccine booster strategies emerging worldwide, especially for high-risk populations, a communication strategy, specific to NHS and particularly those hesitant, should be conducted to provide information on short, medium and long-term side-effects of COVID-19 vaccination. This should be timed to precede and accompany future vaccination campaigns to fully inform NHS at the right moment.

Funding

The SCOPE study, within which this study was conducted, was funded by the Belgian Scientific Institute of Public Health (SCIENSANO), this nested study did not benefit from additional funding.

Institutional Review Board Statement

The SCOPE study was approved by the Ethical Committee of the Ghent University Hospital (reference number BC-08719) as of 11/12/20 and conducted according to the approved protocol and the principles outlined in the Declaration of Helsinki. An amendment for this nested study was approved on 13/07/21 (reference number BC-08719-AM02).

Informed consent Statement

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Ghent University Hospital (reference number BC-

08719) as of 11/12/20.

CRedit authorship contribution statement

Marina Digregorio: Conceptualization, Investigation, Methodology, Writing – original draft. **Pauline Van Ngoc:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Simon Delogne:** Methodology, Eline Meyers: Methodology, Writing – review & editing. **Ellen Deschepper:** Writing – review & editing. **Nadia Dardenne:** Writing – review & editing. **Els Duysburgh:** Writing – review & editing. **Liselore De Rop:** Methodology, Writing – review & editing. **Tine De Burghgraeve:** Methodology, Writing – review & editing. **Anja Coen:** Methodology. **Nele De Clercq:** Methodology. **An De Sutter:** Writing – review & editing. **Jan Y. Verbakel:** Writing – review & editing. **Piet Cools:** Writing – review & editing. **Stefan Heytens:** Writing – review & editing. **Laëtitia Buret:** Writing – review & editing. **Beatrice Scholtes:** Conceptualization, supervision, Writing – review & editing.

Declaration of competing interest

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

Data availability

Data will be made available on request.

Acknowledgements

We would like to thank all participants for their collaboration.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvaxc.2024.100453>.

References

- [1] Randolph HE, Barreiro LB. Herd Immunity: Understanding COVID-19. Immunity [Internet]. Elsevier; 2020 [cited 2022 Sep 21];52:737. Available from: /pmc/articles/PMC7236739/.
- [2] WHO. Strategy to Achieve Global Covid-19 Vaccination by mid-2022.
- [3] Henry DA, Jones MA, Stehlik P, Glasziou PP. Effectiveness of COVID-19 vaccines: findings from real world studies. Med J Aust [Internet]. Wiley-Blackwell 2021;215: 149 [cited 2022 Sep 21].
- [4] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine [cited 2021 Jun 7] Available from: N Engl J Med [Internet]. Massachusetts Medical Society 2020;383: 2603–15.
- [5] Catteau L, Haarhuis F, Dequeker S, Vandael E, Stouten V, LITZROTH A, et al. THEMATISCH RAPPORT : SURVEILLANCE VAN DE COVID-19 VACCINATIE IN BELGISCHE WOONZORGCENTRA [Internet]. 2021. Available from: https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_THEMATIC_REPORT_SURVEILLANCE_VAN_DE_VACCINATIE_IN_BELGISCHE_WOONZORGCENTRA.pdf.
- [6] Dyer AH, Fallon A, Noonan C, Dolphin H, O'Farrelly C, Bourke NM, et al. Managing the Impact of COVID-19 in Nursing Homes and Long-Term Care Facilities: An Update. J Am Med Dir Assoc [Internet]. Elsevier 2022;23:1590 [cited 2022 Sep 23] Available from: /pmc/articles/PMC9250924/.
- [7] Loubet P, Laureillard D, Martin A, Larcher R, Sotto A. Why promoting a COVID-19 vaccine booster dose? Anaesthesia. Crit Care Pain Med [Internet] Elsevier 2021;40: 100967 [cited 2022 Sep 21]; Available from: /pmc/articles/PMC8675238/.
- [8] Sciensano. Belgium COVID-19 Dashboard - Sciensano) Vaccination [Internet]. [cited 2022 Sep 20]. Available from: https://datastudio.google.com/embed/reporting/c14a5cfc-cab7-4812-848c-0369173148ab/page/p_j1f02pfnp.
- [9] Meyers E, Deschepper E, Duysburgh E, De Rop L, De Burghgraeve T, Van Ngoc P, et al. Declining Prevalence of SARS-CoV-2 Antibodies among Vaccinated Nursing Home Residents and Staff Six Months after the Primary BNT162b2 Vaccination Campaign in Belgium: A Prospective Cohort Study [Internet]. Multidisciplinary Digital Publishing Institute; [cited 2023 Feb 20] Available from Viruses 2022;14: 2361.
- [10] Babicki M, Mastalerz-Migas A. Attitudes of poles towards the COVID-19 vaccine booster dose: An online survey in poland [cited 2022 Sep 21] Available from:

- Vaccines [Internet] Vaccines (Basel) 2022;10. <https://pubmed.ncbi.nlm.nih.gov/35062729/>.
- [11] Paul E, Fancourt D. Predictors of uncertainty and unwillingness to receive the COVID-19 booster vaccine: An observational study of 22,139 fully vaccinated adults in the UK. *Lancet Reg Heal - Eur* [Internet] Elsevier. 2022;14 [cited 2022 Sep 21]; Available from: </pmc/articles/PMC8811487/>.
 - [12] Reifferscheid L, Lee JSW, MacDonald NE, Sadarangani M, Assi A, Lemaire-Paquette S, et al. Transition to endemic: acceptance of additional COVID-19 vaccine doses among Canadian adults in a national cross-sectional survey. *BMC Public Health* [Internet]. BioMed Central. 2022;22:1745 [cited 2022 Sep 21]; Available from: </pmc/articles/PMC9473459/>.
 - [13] Pal S, Shekhar R, Kottewar S, Upadhyay S, Singh M, Pathak D, et al. COVID-19 Vaccine Hesitancy and Attitude toward Booster Doses among US Healthcare Workers [cited 2022 Sep 26]; Available from Vaccines [Internet]. Vaccines (Basel) 2021;9.
 - [14] World Health Organization 2019. Ten threats to global health in 2019 [Internet]. WHO. 2019 [cited 2021 Nov 17]. Available from: <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>.
 - [15] Della Polla G, Napolitano F, Pelullo CP, De Simone C, Lambiase C, Angelillo IF. Investigating knowledge, attitudes, and practices regarding vaccinations of community pharmacists in Italy. *Hum Vaccin Immunother* [Internet] [cited 2023 Oct 4] Available from Hum Vaccin Immunother. 2020;16:2422–8.
 - [16] Dubé É, Farrands A, Lemaitre T, Boulianne N, Sauvageau C, Boucher FD, et al. Overview of knowledge, attitudes, beliefs, vaccine hesitancy and vaccine acceptance among mothers of infants in Quebec, Canada. *Hum Vaccin Immunother* [Internet] [cited 2023 Oct 4] Available from Hum Vaccin Immunother. 2019;15: 113–20.
 - [17] Digregorio M, Van Ngoc P, Delogne S, Meyers E, Deschepper E, Duysburgh E, et al. Vaccine hesitancy towards the COVID-19 vaccine in a random national sample of Belgian nursing home staff members [cited 2022 Sep 20] Available from Vaccines [Internet] Vaccines (Basel) 2022;10. <https://pubmed.ncbi.nlm.nih.gov/35455347/>.
 - [18] Sciensano. protocol : SARS-CoV-2 seroprevalence among nursing home staff and residents in Belgium [Internet]. 2021 [cited 2022 Feb 14]. Available from: https://www.sciensano.be/sites/default/files/v6.2_2021-06-23_proposal_sars-cov-2_seroprevalence_study_in_belgian_nh.pdf.
 - [19] Meyers E, De Rop L, Deschepper E, Duysburgh E, De Burghgraeve T, Van Ngoc P, et al. Prevalence of SARS-CoV-2 antibodies among Belgian nursing home residents and staff during the primary COVID-19 vaccination campaign [cited 2023 Feb 20]; Available from: *Eur J Gen Pract* [Internet] Eur J Gen Pract 2022. <https://pubmed.ncbi.nlm.nih.gov/36440533/>.
 - [20] Larson HJ, Jarrett C, Schulz WS, Chaudhuri M, Zhou Y, Dube E, et al. Measuring vaccine hesitancy: The development of a survey tool. *Vaccine* [Internet] 2015;33: 4165–75. <https://doi.org/10.1016/j.vaccine.2015.04.037>.
 - [21] Durkalski VL, Palesch YY, Lipsitz SR, Rust PF. Analysis of clustered matched-pair data. *Stat Med* [Internet] [cited 2023 Feb 17] Available from John Wiley & Sons, Ltd. 2003;22:2417–28.
 - [22] Whittingham MJ, Stephens PA, Bradbury RB, Freckleton RP. Title: Why do we still use stepwise modelling in ecology and behaviour?
 - [23] Flom P. Stopping stepwise: Why stepwise selection is bad and what you should use instead | by Peter Flom | Towards Data Science [Internet]. [cited 2023 Oct 4]. Available from: <https://towardsdatascience.com/stopping-stepwise-why-stepwise-selection-is-bad-and-what-you-should-use-instead-90818b3f52df>.
 - [24] Paridans M, Monseur J, Donneau A-F, Gillain N, Husson E, Leclercq D, et al. The Dynamic Relationship between the Intention and Final Decision for the COVID-19 Booster: A Study among Students and Staff at the University of Liège, Belgium [Internet]. Multidisciplinary Digital Publishing Institute; [cited 2022 Sep 22] Available from Vaccines. 2022;10:1485.
 - [25] Galanis P, Vraika I, Katsiouroupa A, Siskou O, Konstantakopoulou O, Katsoulas T, et al. First COVID-19 booster dose in the general population: A systematic review and meta-analysis of willingness and its predictors. *Vaccines* [Internet] MDPI 2022; 10 [cited 2022 Sep 26] Available from: </pmc/articles/PMC9323526/>.
 - [26] Dzedzic A, Issa J, Hussain S, Tanasiewicz M, Wojtyczka R, Kubina R, et al. COVID-19 vaccine booster hesitancy (VBH) of healthcare professionals and students in Poland: Cross-sectional survey-based study. *Front Public Heal Frontiers Media SA* 2022;10:2391.
 - [27] Tan KYK, Soh ASE, Ong BWL, Chen MIC, Griva K. Determining the prevalence and correlates of COVID-19 booster vaccine hesitancy in the Singapore population following the completion of the primary vaccination series [cited 2022 Sep 20] Available from Vaccines [Internet] Vaccines (Basel) 2022;10. <https://pubmed.ncbi.nlm.nih.gov/35891252/>.
 - [28] Achrekar GC, Batra K, Urankar Y, Batra R, Iqbal N, Choudhury SA, et al. Assessing COVID-19 Booster Hesitancy and Its Correlates: An Early Evidence from India. *Vaccines* [Internet] Multidisciplinary Digital Publishing Institute (MDPI). 2022;10: 1048.
 - [29] Weitzer J, Birmann BM, Steffelbauer I, Bertau M, Zenk L, Caniglia G, et al. Willingness to receive an annual COVID-19 booster vaccine in the German-speaking D-A-CH region in Europe: A cross-sectional study. *Lancet Reg Heal - Eur* [Internet]. Elsevier Ltd; 2022. Available from: [cited 2022 Sep 20].
 - [30] Miraglia del Giudice G, Folcarelli L, Della Polla G, Napoli A, Angelillo IF. Investigating the reasons for receiving the second booster dose of the COVID-19 vaccine in adults and in people with chronic medical conditions in southern Italy [cited 2023 Oct 4]; Available from Vaccines [Internet]. Vaccines (Basel) 2023;11.
 - [31] Rzymiski P, Poniedziałek B, Fal A. Willingness to receive the booster COVID-19 vaccine dose in Poland. Available from Vaccines [Internet] Vaccines (Basel). 2021; 9.
 - [32] Folcarelli L, Del Giudice GM, Corea F, Angelillo IF. Intention to receive the COVID-19 vaccine booster dose in a university community in Italy, vaccines [Internet] [cited 2022 Sep 21]; Available from Vaccines (Basel). 2022;10.
 - [33] McGarry BE, Barnett ML, Grabowski DC, Gandhi AD. Nursing Home Staff Vaccination and Covid-19 Outcomes. *N Engl J Med* [Internet]. NEJM Group. 2022; 386:397–8 [cited 2022 Sep 23]; Available from: </pmc/articles/PMC8693685/>.
 - [34] Larson HJ, Broniatowski DA. Volatility of vaccine confidence. *Science* (80-). American Association for the Advancement of Science; 2021. p. 1289 [Internet]. [cited 2023 Feb 20] Available from:.
 - [35] Berry SD, Johnson KS, Myles L, Herndon L, Montoya A, Fashaw S, et al. Lessons learned from frontline skilled nursing facility staff regarding COVID-19 vaccine hesitancy. *J Am Geriatr Soc* [Internet] Wiley-Blackwell 2021;69:1140 [cited 2022 Sep 23]; Available from: </pmc/articles/PMC8183564/>.
 - [36] Paul E, Steptoe A, Fancourt D. Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications. *Lancet Reg Heal - Eur Elsevier* 2021;1:100012.
 - [37] Schmitzberger FF, Scott KW, Nham W, Mathews K, Schulson L, Fouche S, et al. Identifying Strategies to Boost COVID-19 Vaccine Acceptance in the United States. Identifying Strateg to Boost COVID-19 Vaccine Accept United States [Internet]. RAND Corporation; 2021 [cited 2022 Oct 21]; Available from:.
 - [38] Kassianos G, Puig-Barberà J, Dinse H, Teufel M, Türeci Ö, Pather S. Addressing COVID-19 vaccine hesitancy. *DRUGS Context* [Internet]. 2022 [cited 2022 Oct 21]; Available from: <https://doi.org/10.7573/dic.2021-12-3>.
 - [39] Della Polla G, Miraglia del Giudice G, Folcarelli L, Napoli A, Angelillo IF. Willingness to accept a second COVID-19 vaccination booster dose among healthcare workers in Italy. *Front Public Heal Frontiers Media SA* 2022;10: 1051035.
 - [40] Miraglia del Giudice G, Della Polla G, Folcarelli L, Napoli A, Punzo R, Peracchini M, et al. Midwives' knowledge, attitudes, and practice regarding COVID-19 vaccination for pregnant women: A nationwide web-based survey in Italy [cited 2024 Jan 24]; Available from Vaccines [Internet]. Vaccines (Basel) 2023;11.
 - [41] Dumyati G, Jump RLP, Gaur S. Mandating COVID-19 Vaccine for Nursing Home Staff: An Ethical Obligation. *J Am Med Dir Assoc* [Internet]. Elsevier 2021;22:1967 [cited 2022 Sep 23]; Available from: </pmc/articles/PMC8387223/>.
 - [42] McGarry BE, Gandhi AD, Syme M, Berry SD, White EM, Grabowski DC. Association of State COVID-19 Vaccine Mandates With Staff Vaccination Coverage and Staffing Shortages in US Nursing Homes. *JAMA Heal forum* [Internet]. JAMA Health [cited 2022 Sep 23]. Available from: *Forum* 2022;3:e222363. <https://pubmed.ncbi.nlm.nih.gov/35983581/>.
 - [43] Berry SD, Baier RR, Syme M, Gouskova N, Bishnoi C, Patel U, et al. Strategies associated with COVID-19 vaccine coverage among nursing home staff. *J Am Geriatr Soc* [Internet] [cited 2022 Sep 23] Available from *J Am Geriatr Soc* 2022; 70:19–28.
 - [44] Kunkel Lmsw MC, Applebaum R, Mgs MN. Strategies to Address COVID-19 Vaccine Hesitancy Among Ohio Nursing Home Staff [cited 2022 Oct 21]; Available from. *Gerontologist* [Internet]. Oxford University Press (OUP); 2022.