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V1.0	21/06/2022	Final report	Shared with the Coordination Office to be uploaded to EU Portal	

Legal Disclaimer

Disclosure Statement

Abbreviations

CDC	Center for Disease Control
CEPI	Coalition for Epidemic Preparedness Innovations
CHIP	Center of Excellence for Health, Immunity and Infections
CLEO	Kentro Klinikis Epidimiologias Kai Ekvasis Nosimaton, Greece
CPME	Standing Committee of European Doctors
EC	European Commission
ECDC	European Center for Disease Control
ECRIN	Ecrin European Clinical Research Infrastructure Network, France
EMA	European Medicines Agency
EUC	European University Cyprus
EUVAP	European Vaccine Trial Accelerator Platform
KUH	Karolinska University Hospital
MIS-C	Multisystem inflammatory syndrome in children
NITAG	National Immunization Technical Advisory Group
PRQ	Priority question
PHIRI	Population Health Information Research Infrastructure
RegionH	Capital Region, Denmark
SERMAS	Servicio Madrileno De Salud
TCB	Trial Coordination Board
UHC	University Hospital Cologne
UP	Université de Paris
VOCs	Variants of Concern
WHO	World Health Organisation
WP	Work Package
REDCap	Research Electronic Data Capture
RCTs	Randomized Controlled Trials
ICTRP	International Clinical Trials Registry Platform

1 Executive summary

Two key network objectives of VACCELERATEs, are identifying and filling public health knowledge gaps in COVID-19 vaccine development that have also been included as the work streams within VACCELERATE. Within the scope of Work Package (WP) 7 – Public Health Needs– under the auspices of VACCELERATE and RegionH, in collaboration with several partners (SERMAS, CLEO, KUH, EUC, UHC, and UP) lead the work of Task 7.2 that focuses on the identification of unanswered public health and clinical research questions in relation to vaccine safety, efficacy and vaccination schemes. The goal of this task is to assess the gaps and prioritise topics where clinical trials are most urgently needed.

The work of Task 7.2 is based on close collaboration with other work streams within VACCELERATE which focus on general public outreach, among others. It is also anchored in a broad European and international dialogue concerning new COVID-19 vaccine trials aiming to inform both ongoing and future studies through a living document with priority questions that reflects knowledge gaps and emerging priorities from the public health perspective. As such, the main task objective is to *develop and maintain a living document of unanswered priority questions for future COVID-19 vaccine trials from the public health perspective.*

The work of the task includes the following concrete actions:

- Engage with partners from VACCELERATE and synergistic initiatives, including vaccine development stakeholders, through regular meetings in the Trial Coordination Board (TCB)[1].
- Collect input from a broad stakeholder group regarding knowledge gaps and unanswered questions through an open-ended survey; repeat the survey at regular intervals (every 6 months), potentially targeting more respondent groups, depending on the evolvement of the pandemic.
- Analyse, categorise, and synthesise survey responses to develop an initial list of unanswered questions; cross-check with Task 7.1. COVID-NMA database to follow up on the existing and changing landscape of ongoing vaccine trials.
- Present the prefinal list of priority questions in the TCB for discussion; the final list is subsequently made publicly available via the VACCELERATE website (https://vaccelerate.eu/).
- Ensure the continuous relevance by revising and updating the list of priority questions regularly (based on discussions with VACCELERATE partners and regular searches on emerging/changing priorities through the official websites and news channels of leading public health agencies (CEPI, ECDC, EMA, WHO Europe, ECRIN, CDC and other key organisations).
- Ensure synergies with WP4 and WP10 by using the developed educational material to reach the general public and underrepresented groups in the repeated stakeholder surveys.
- Assess and re-evaluate the regularity of required updates, as the pandemic progresses.

The current report outlines the work completed between February 2022 and June 2022 which focused on revising the list of priority questions (PRQ) identified through *"D7.4 First report on unanswered COVID-19 vaccines and vaccination priority questions for future trials"* finalised in September 2021 and "*D7.6 Updated report on unanswered COVID-19 vaccines and vaccination priority questions for future trials"* finalised in January 2022.

[1] The TCB is a joint task/WP from 4 ongoing EU-funded projects: Recover, EU-Response, Ecraid-Prime and VACCELERATE. The board includes a therapeutics pillar and a vaccine pillar. From the VACCELARATE consortium, PIs of the VACCELARATE clinical trials and members working on public health needs (WP7) are invited to join the TCB.

2 Deliverable content

With the objective to prioritise the identified emerging and unanswered public health and clinical research questions in relation to vaccine safety, efficacy and vaccination schemes, a survey was circulated in March 2022. The survey attempted to rank the list of questions compiled in September 2021 and identify the 3 questions frequently left unanswered, to ensure they are not overlooked in potential upcoming COVID-19 vaccine trials.

The received responses were analysed in order to identify the priority topics where vaccine trials are most urgently needed. The method, analytical process and results are described below.

The report also includes a list of new emerging questions identified by survey respondents.

2.1 Methods

- Survey

The survey aimed to rank according to priority the questions identified in the initial stakeholder survey in "*D7.4 First report on unanswered COVID-19 vaccines and vaccination priority questions for future trials"* that was finalised in September 2021 and updated in "*D7.6 Updated report on unanswered COVID-19 vaccines and vaccination priority questions for future trials"* finalised in January 2022. The updated survey was circulated among the members of the VACCELERATE and EUVAP consortiums and collaboration NITAG[2] network, with the purpose of shortlisting the top 3 most important unanswered questions that could potentially be addressed in future vaccine trials. VACCELERATE Consortium is maintaining close contact with EC, EMA and ECDC to obtain their input on the emerging public health questions concerning the COVID-19 vaccine trial.

The list of PRQs was updated according to the results of the previously mentioned survey, finalised in January 2022. The initial list of PRQs contained 17 questions of which 5 were removed as they received the least number of votes and 2 questions that have been deemed irrelevant as they referred to policy questions therefore lay outside the scope of clinical trials. Instead, 5 newly identified priority questions were added to the survey, based on the topics identified in D7.6 Updated report on unanswered COVID-19 vaccines and vaccination priority questions for future trials finalised in January 2022.

The survey distributed in March 2022 concluded of 15 predefined priority questions for future COVID-19 vaccine studies and has also included an open-ended format question allowing stakeholders to submit new topics they considered to be a priority. All priority questions were evaluated against each other.

A copy of the survey distributed in March 2022 is available in Appendix 1. The survey has been developed and administered via the Research Electronic Data Capture (REDCap, https://projectredcap.org/) tools hosted at RegionH/CHIP - Centre for Health & Infectious Disease Research and was circulated via email with a link.

Top priority questions for future COVID-19 vaccine studies in the immediate future identified in the previous survey in November 2021.

These questions received the highest number of votes in the previous survey in November 2021.

1. How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?

[2] EU/EEA National Immunisation Technical Advisory Groups (NITAG) collaboration https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/national-immunisation-technical-advisory-groups-nitag

2. How long does immunity (humoral-cellular) last after vaccination with current vaccines?

New priority questions for future COVID-19 vaccine studies added to the survey in March 2022

These questions were identified as new emerging questions (see in D7.6 Updated report on unanswered COVID-19 vaccines and vaccination priority questions for future trials, 2022) and included in the survey disseminated in March 2022.

1. Developing vaccines which are protective against a broad range of coronaviruses (e.g., pansarbecovirus vaccine)
2. How can immunisation schedule (booster timing and number) be optimised for the paediatric population to ensure maximum protection?
3. What are the individual or sub-population genetic or metabolic differences in response to vaccines (precision medicine approach)?
4. Vaccination strategy in pregnant women?
5. Integration of new types of COVID-19 vaccines (e.g., Nuvaxovid) in EU vaccination programs

Other priority questions for future COVID-19 vaccine studies included in the survey in March 2022

These priority questions were first identified in spring 2021 and have received enough votes to remain included in the survey disseminated in March 2022.

1. Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route (e.g., nasal vaccines) and possibly with only one dose?
2. Are currently available vaccines effective against SARS-CoV-2 variants in the short- and long-term and is there a need to develop new vaccines to protect against the VOCs?
3. What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?
4. What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?
5. What are the long-term safety considerations of vaccination in children?
6. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
7. Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?
8. What is the efficacy and the specific immune response to the vaccine in children, (incl. immunocompromised pediatric population)?

List of the priority questions excluded from the survey in March 2022

These priority questions have received the least number of votes in the survey carried out in November 2021 and were excluded from the survey in March 2022.

1. What should the vaccination strategy be for recovered patients?
2. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
3. What is the efficacy and the specific immune response to the vaccine in children, including immunocompromised pediatric population?
4. What are the long-term safety considerations of vaccination in children?
5. What is the relationship in terms of protection between vaccination and immuno-mediated diseases such as MIS-C?

List of the priority questions excluded from the survey due their irrelevancy

These priority questions were concerning the topics of vaccination policies and could not be answered by COVID-19 vaccine trials. Due to this they have been identified as irrelevant and were excluded from the survey in March 2022.

1. How can awareness of and confidence in vaccine programmes be improved to address vaccine hesitancy and misinformation with focus on specific population groups?
2. How can wide-scale global vaccination coverage be ensured within reasonable timelines, especially in resource-limited settings?

- Collaboration with Task 7.1 on potential incorporation of priority topics into the COVID-NMA initiative

Analysis of the survey responses has been supported through discussions during regular WP7 meetings and sub-task meetings of Task 7.1 due to natural synergies between the two tasks. The discussion has enabled us to address the best way of using the COVID-19 NMA (covid-nma.com) tool/ website to explore and identify registered clinical trials that potentially can answer some of the questions and knowledge gaps.

- Regular searches on emerging/changing priorities

In parallel with the survey, CHIP/RegionH has been regularly monitoring ongoing public discussion on the official websites, presentations, meetings and press briefings of leading public health agencies (CEPI, ECDC, EMA and WHO) to identify potential new emerging questions.
For the period from January to June 2022, the ongoing publica discussion was focusing on the questions similar to the ones posed in the circulated survey. The main topics discussed at the multistakeholder meetings organised by WHO[3] included:

- Advancing the development of pan-sarbecovirus vaccines.
- Developing a framework for evaluating new COVID-19 vaccines.

[3] Summary of the meetings are available on the R&D Blueprint and COVID-19 page: https://www.who.int/teams/blueprint/covid-19

2.2 Results – Survey

- Survey respondent profile

In total 64 responses were collected. Contrary to the previous surveys, the most significant group by profession were researchers (n=24) followed by clinicians (n=21), with limited input from policy advisors (n=6) and subject area experts (n=6) as shown in Figure 1 below.

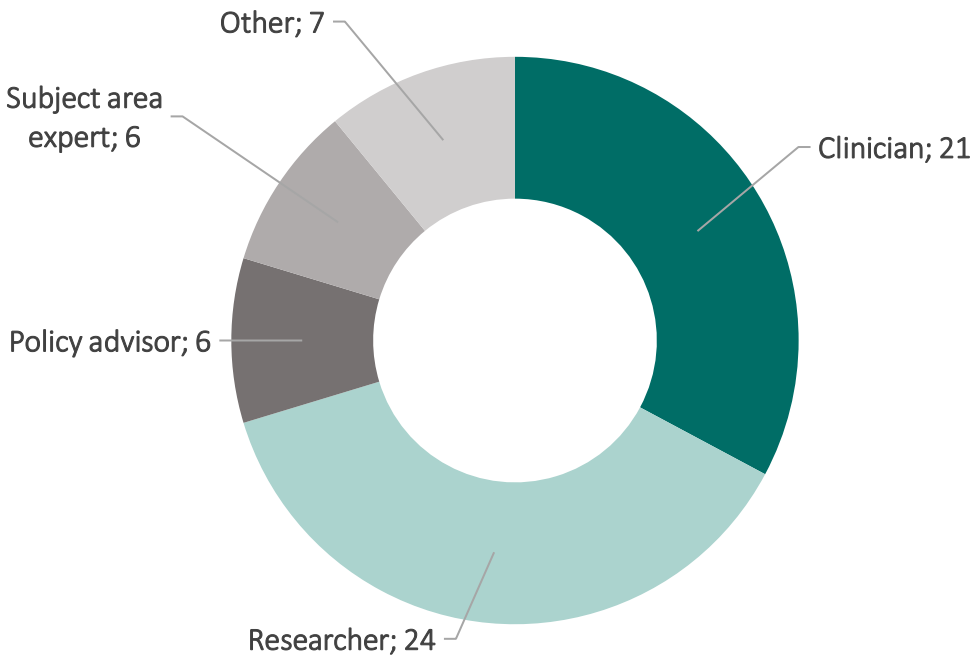

Figure 1: Professional background of the survey respondents (n=64)

Building upon the previous suggestions from ECDC, we have also approached members of the NITAG network in Europe. To identify input from the NITAG representatives, we have included affiliation question in this survey, allowing respondents to indicate their affiliation with VACCELARATE, EUVAP consortia and/or the NITAG network. Out of 64 survey respondents, 13 have indicated their affiliation with the NITAG network. This allowed expanding the survey respondents pull in the attempt to identify new priority questions. We observed a difference in the priority questions identified by the respondents affiliated with the NITAG compared to the rest of the survey respondents.

In most European countries, decisions around vaccines and their use are based on evidence-based recommendations made by national immunisation technical advisory groups (NITAG) or equivalent expert committees. Therefore, input from these stakeholders is crucial in evaluating priority of the vaccine research questions from a public health perspective.

- Top priority questions identified by NITAG representatives (n=13)

Figure 2 specifies the responses collected in the respondent group affiliated with NITAG.

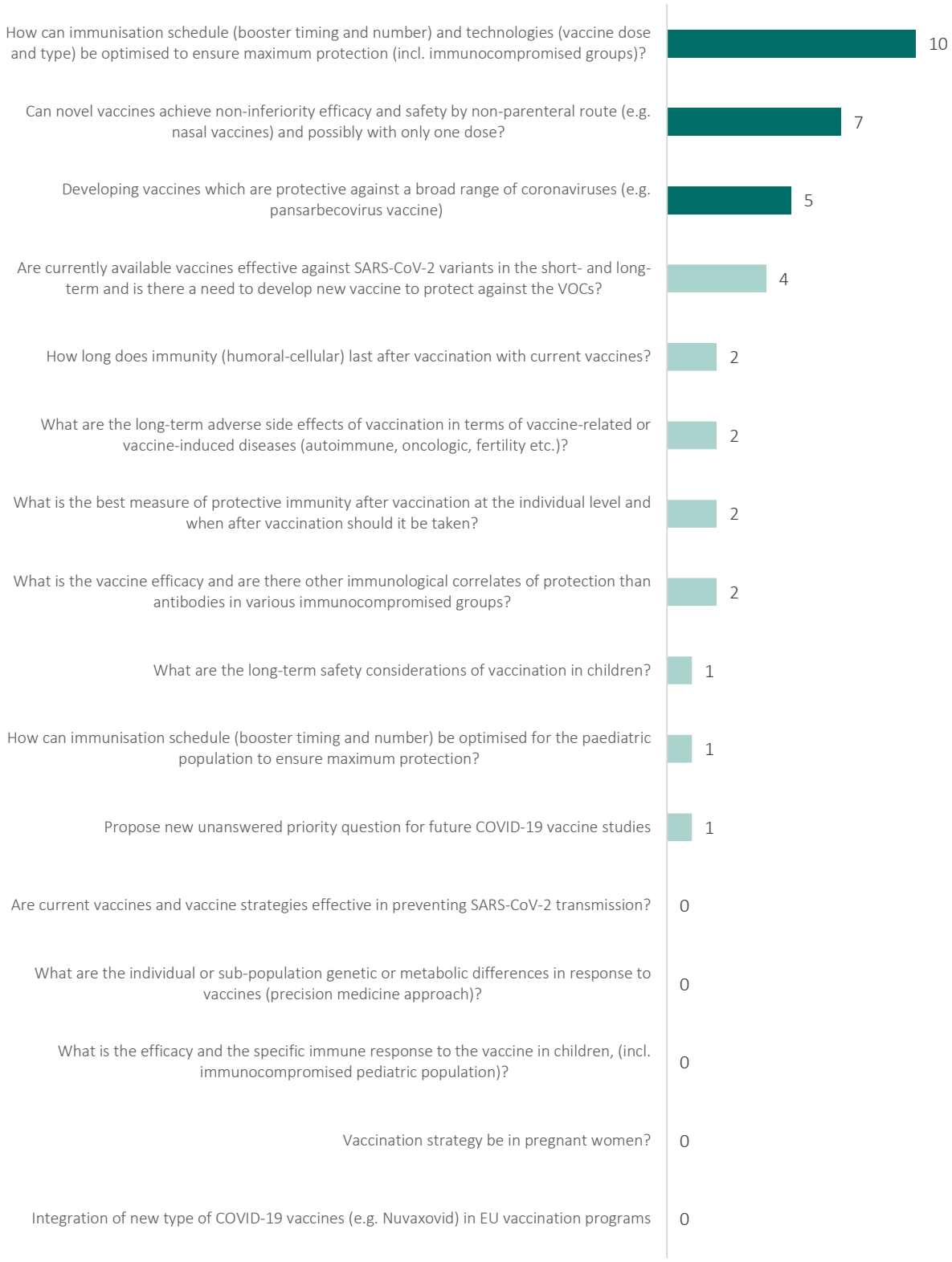

Figure 2: Responses by affiliation of the survey respondents (NITAG)

The top 3 questions identified by the NITAG affiliated survey respondents are listed below.

Table 1: Top public health priority questions identified by the NITAG affiliated respondents

Votes	Public health priority questions for future COVID-19 vaccine trials
10	How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?
7	Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route (e.g., nasal vaccines) and possibly with only one dose?
5	Developing vaccines which are protective against a broad range of coronaviruses (e.g., pansarbecovirus vaccine)

- Top priority questions identified by the survey respondents not affiliated with NITAG (n=51)

Figure 3 below specifies the responses collected from the survey respondents not affiliated with the NITAG Network.

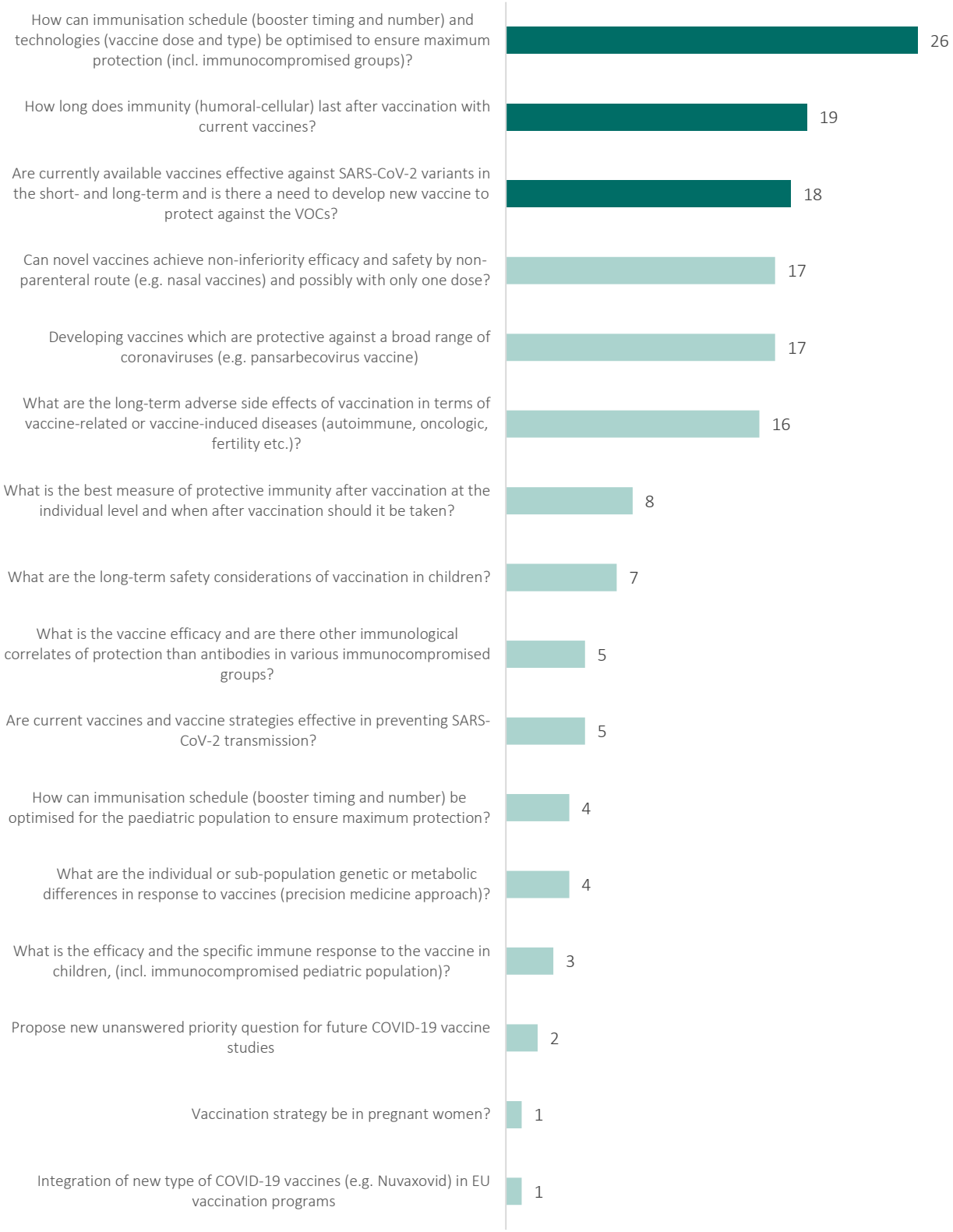

Figure 3: Responses by affiliation of the survey respondents (not affiliated with NITAG)

Overall, from the initial list of priority questions, responses provided by participants not affiliated with NITAG identified the same 3 top priority questions as the survey carried out in November 2021.

Table 2: Top public health priority questions identified by the respondents not affiliated with NITAG

Votes	Public health priority questions for future COVID-19 vaccine trials (Researchers)
26	How can immunisation schedule (booster timing and number) & technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?
19	How long does immunity (humoral-cellular) last after vaccination with current vaccines?
18	Are currently available vaccines effective against SARS-CoV-2 variants in the short- and long-term and is there a need to develop new vaccines to protect against the VOCs?

- The final list of priority questions

After combining responses from all survey participants, we have rearranged the identified priority questions according to the number of votes that they received.

Figure 4 below specifies the responses collected from all survey participants.

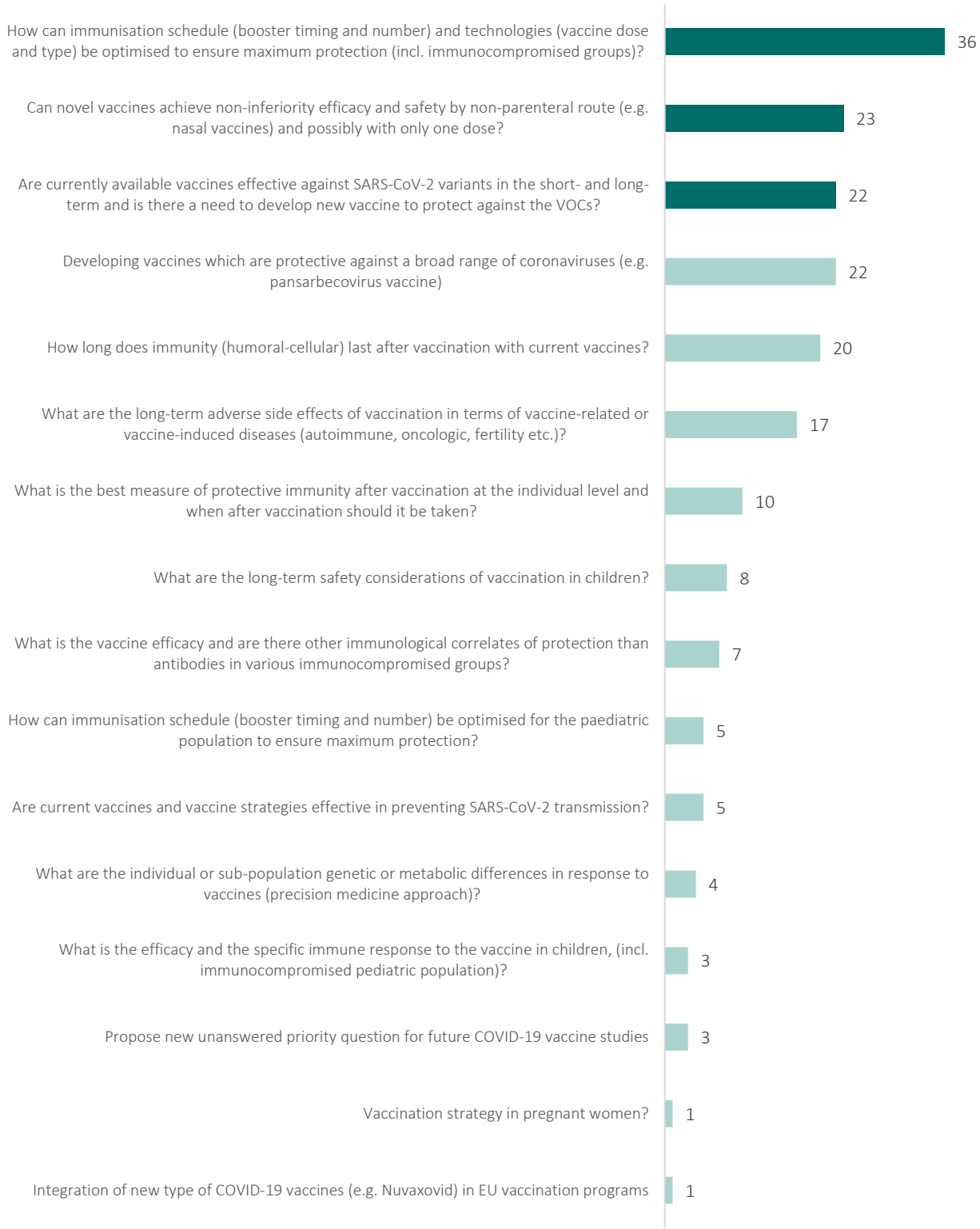

Figure 4: Public Health priority questions (by number of responses).

One question remained the top priority across all 3 surveys focused on identifying Public health priority questions for future COVID-19 vaccine trials, conducted by Task 7.2.

Table 3: Top Public health priority question identified in all surveys

Public health priority question for future COVID-19 vaccine trials
How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?

2.3 Results – Collaboration with Task 7.1 on potential incorporation of priority topics into the COVID-NMA initiative

The up-to-date living mapping of planned, active, completed and published registered trials assessing COVID-19 vaccines is conducted in Task 7.1. The COVID-NMA mapping is developed with the purpose of helping stakeholders plan future vaccine trials.
All randomized controlled trials (RCTs) and non-randomized studies registered in the WHO International Clinical Trials Registry Platform (ICTRP), clinicaltrials.gov and the European clinical trials register (https://www.clinicaltrialsregister.eu/) are searched weekly.

After the publication of our previous report, several new search filters have been added to the COVID-NMA mapping.

1) Age groups

Previously it was only possible to filter by <= 18 years old or > 18 years old. Now, users have access to more detailed subcategories:

- Newborn/neonates (up to 28 days) (11 studies)
- Infants (29 days to 1 year) (12 studies)
- Children (2 to 9 years) (59 studies)
- Adolescents (10 to 17 years) (106 studies)
- Adults (18 to 64 years) (833 studies)
- Elderly (65 to 79 years) (638 studies)
- Older people (80+) (546 studies)
- N/A (1 studies)

Please note that a study could be in multiple categories. For example, if a study has a minimum age of 18 and a maximum age of 75, this study will be classified into two categories: adults and elderly.

2) Pregnant women

It is now possible to identify clinical trials that recruited pregnant women.

3) Immunosuppressed participants

This group is also called immunocompromised and can be characterised by a weaker immune response both to infection and vaccination. It's therefore crucial to understand vaccine efficacy in this population group.

The data are made available on a platform through interactive data visualisation (https://covid-nma.com/vaccines/mapping/). Studies can be filtered by several variables such as the country in which they are taking place, study design, group participants belong to and type of vaccine, among others. The data are updated weekly on the platform. As of the 1st of June 2022, 880 trials were published on the COVID NMA website (https://covid-nma.com/).

We have searched the COVID NMA website database to estimate the potential number of vaccine trials investigating the topics included in the 15 PRQs from our survey circulated in March 2022. The results of this search are provided in the table below in the column: "IDENTIFIED CLINICAL TRIALS Initial search on 10th of June 2022".

The search results are marked in the following colours:

Colour	Explanation
Green	Information is easily found in the interactive data visualization (https://covid-nma.com/vaccines/mapping/) with the use of a **data filter**.
Yellow	Information is partially available, but a specific filter is not available, only a free text search option. Potentially more trials are not identified.
Red	Information was not found; a specific data filter was not available and a free text search did not identify any potential trials.

Compared to the analysis of the identified clinical trials in the D7.6, the COVID NMA database has been expanded to include new search filters. Of 15 priority questions, only 6 could not be searched in the database.

Table 4 List of identified public health priority questions for future COVID-19 vaccine trials and COVID-NMA mapping search results

VOTES	PUBLIC HEALTH PRIORITY QUESTIONS FOR FUTURE COVID-19 VACCINE TRIALS	IDENTIFIED CLINICAL TRIALS Searched on 10th of June 2022[4]
26	*How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?	**Filter**: 'Booster' – 190 trials identified (incl. immunosuppressed patients – 11) 'Vaccine schedule' – 131 trials identified (incl. immunosuppressed patients – 4)
19	*How long does immunity (humoral-cellular) last after vaccination with current vaccines?	Search option: **Free text search**: *"Cellular immunity" – 8 and "Humoral immunity" – 7*
18	Are currently available vaccines effective against SARS-CoV-2 variants in the short- and long-term and is there a need to develop new vaccine to protect against the VOCs?	**Filter**: 'VOC' (alpha, beta, gamma, delta) – 26 'VOC' (omicron) – 14
17	Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route (e.g., nasal vaccines) and possibly with only one dose?	Search option: **Free text search** 'intranasal' or synonyms. **2 trials found.** This search will miss a lot of relevant trial as the route information is collected manually in our database and not presented
17	Developing vaccines which are protective against a broad range of coronaviruses (e.g., pansarbecovirus vaccine)	Filter not available (search not successful)
16	What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?	Filter not available (search not successful)
8	What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?	Search option: Free text search for 'protective' and synonyms. **8 trials to screen**.
7	What are the long-term safety considerations of vaccination in children?	Search option: **Free text search** for 'long-term safety' and synonyms combined with 'Under 18 y. o. filter'. No results found.
5	What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?	Search option: **Free text search** for 'immunological correlates' and synonyms combined with immunosuppression status filter.

[4] Search conducted using COVID-NMA mapping website https://covid-nma.com/vaccines/mapping (accessed on 10th of June 2022).

5	Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?	Search option: **Free text search** for 'transmission' and synonyms. No results found, but a surveillance on this type of search could be relevant.
4	How can immunisation schedule (booster timing and number) be optimised for the paediatric population to ensure maximum protection?	**Filter**: 'Booster' & 'Under 18 y. o. filter' – 19 trials identified (incl. immunosuppressed patients – 3) 'Vaccine schedule' & 'Under 18 y. o. filter' – 13 trials identified (incl. immunosuppressed patients –0)
4	Precision medicine approach to COVID-19 vaccination	Filter not available (search not successful)
3	What is the efficacy and the specific immune response to the vaccine in children, (incl. immunocompromised pediatric population)?	**Filter**: 'Under 18 y. o. filter' – 107 trials identified (incl. immunosuppressed patients – 7)
1	Vaccination strategy be in pregnant women?	**Filter**: 'Pregnant women' – 8 trials identified
1	Integration of new type of COVID-19 vaccines (e.g., Nuvaxovid) in EU vaccination programs	Filter: 'Type of vaccine: Protein subunit' & 'Heterologous regimen' – 38 trials identified

2.4 Potential new emerging questions identified by the survey respondents

In addition to the existing lists, several new unanswered questions have been listed by the survey respondents. These will be discussed further with the WP7 members to evaluate if they should be added to the list of unanswered questions for future COVID-19 trials.

Following are the potential new emerging questions, as listed by the survey respondents:

- Longevity of immunity (humoral-cellular) in naturally infected individuals vs vaccinated and vaccinated & naturally infected (vaccination of recovered patients & hybrid immunity)
- Comparative vaccine studies (incl. booster response of mRNA vaccines against protein-based vaccines)
- Studies to assess a 5th dose (likely to be provided in the autumn by many if a 4th dose is administered this spring).
- Co-administration with influenza & pneumococcal vaccines for the elderly and pregnant women.
- Broader vaccines including the new multivalent vaccine candidates possibly even pansarbecovirus vaccines one day.

2.5 Discussion

The ongoing COVID-19 pandemic is putting an unprecedented strain on the global health system, and vaccine-induced immunity is the only viable solution to achieve large-scale, long-term protection for the entire European population. COVID-19 vaccine trials are still needed to address questions that that have not been addressed in the first vaccine trials, including vaccine efficacy and safety against emerging VOCs and among groups that were previously underrepresented in the studies (e.g. pregnant women, persons with weakened immunity and youngsters).

While opinions on the priorities may diverge, ongoing monitoring of the emerging knowledge gaps in a standardized and regular process could help promote promptly the public health perspective in future COVID-19 vaccine trials and beyond that are relevant for large-scale protection at the population level against emerging infectious diseases threats in the European region and globally.

Although preliminary knowledge gaps have been anticipated, the specific questions resulting from the stakeholder survey shed further light on the public health needs for vaccine development. The ongoing discussion with relevant EU stakeholders has also confirmed the relevance of the identified unanswered questions and a need for an overview of the emerging evidence that could fill these knowledge gaps.

The identified priority questions could feed into the ongoing update of the COVID MNA tool/website in the form of specific search filters and visualization, allowing different stakeholders the opportunity to identify the topics where clinical trials are needed.

The repeated survey has demonstrated that the topic of vaccination schedule and booster doses remains the top priority question. The repeated search of the COVID-19 vaccine trial mapping tool has demonstrated that this question has the highest number of registered vaccine trials (see Table 4), whereas the number of trials looking into the underrepresented groups remains low.

For the second top priority question regarding the duration of vaccine-induced immunity, the situation remained the same since our previous report (see D7.6). We could identify 15 potential vaccine trials looking into humoral and/or cellular immunity. Further monitoring of the trials registered on the COVID MNA website will help to assess if new trials are looking to answer this question.

For the third most popular priority question regarding vaccine effectiveness against emerging VOCs, the number of vaccine trials has increased from 22 to 26 trials for alpha, beta, gamma, and delta variants of SARS-CoV-2 and from 0 to 14 clinical trials looking into protection from the omicron variant.

In order to further assess these questions, the following topics can be considered for the upcoming analyses of the existing/planned clinical trials.

- Industry-initiated vs investigator-initiated vaccine trials

Although the number of clinical trials on COVID-19 vaccines is vast, we have observed that the majority of the unanswered questions could not be answered by the industry-initiated trials and would be better targeted by the investigator-initiated trials.

This issue was also commented on by one of the survey respondents in the quote below:

> *"This consortium must complement the work done by the vaccine industry.*

The developers [of pansarbecovirus vaccines] all need solid consortia that can conduct complicated trials and I do think Vaccelerate may be able to play a role in building upon the first experience you are now building.

The longer-term goal needs to be a vaccine against a broad range of coronaviruses, keeping in view that the last three pandemics in the world over the past two decades were coronaviruses (SARS-CoV-1 & 2, MERS) and so will probably be most in the recent future.

Otherwise, we will end up funding clinical trials whose outcome is useless by the time we get it."

- Underrepresented groups in vaccine trials

Overall, the participants of the COVID-19 trials have overwhelmingly represented healthy populations, while a number of population groups have been majorly underrepresented, specifically:

- Pregnant and breastfeeding women
- Immunocompromised patients
- Patients with comorbidities
- Elderly population
- Migrant communities

The causes of low number of trials in recovered patients, high-risk groups and other underrepresented groups need to be better and in depth investigated. In addition, access to all citizens in vaccine trials should be supported in future trials. Among other efforts, the WP10 Group have established the first transnational registry of future volunteers, which is open to all citizens both adults and children, with currently 40.000 registration across Europe. WP10 has just completed a survey focused on patient advocacy groups to track their view and perspective related to trials and is currently designing an extensive survey addressing the causes of limited access to vaccine trials and participation for individuals from hard-to-reach groups in different countries.

- Interactive visualization of the survey results for the project website

A dashboard containing a summary of surveys on unanswered COVID-19 vaccines and vaccination priority questions for future COVID-19 vaccine trials has been developed to improve the dissemination and communication of the survey results online.

The visualization was developed using a free version of the Infrogram suite and can be accessed at https://infogram.com/vaccelarate-covid-19-vaccine-research-priority-questions-1h8n6m35nm7mz4x. See Figure 5 for a preview of the summary dashboard.

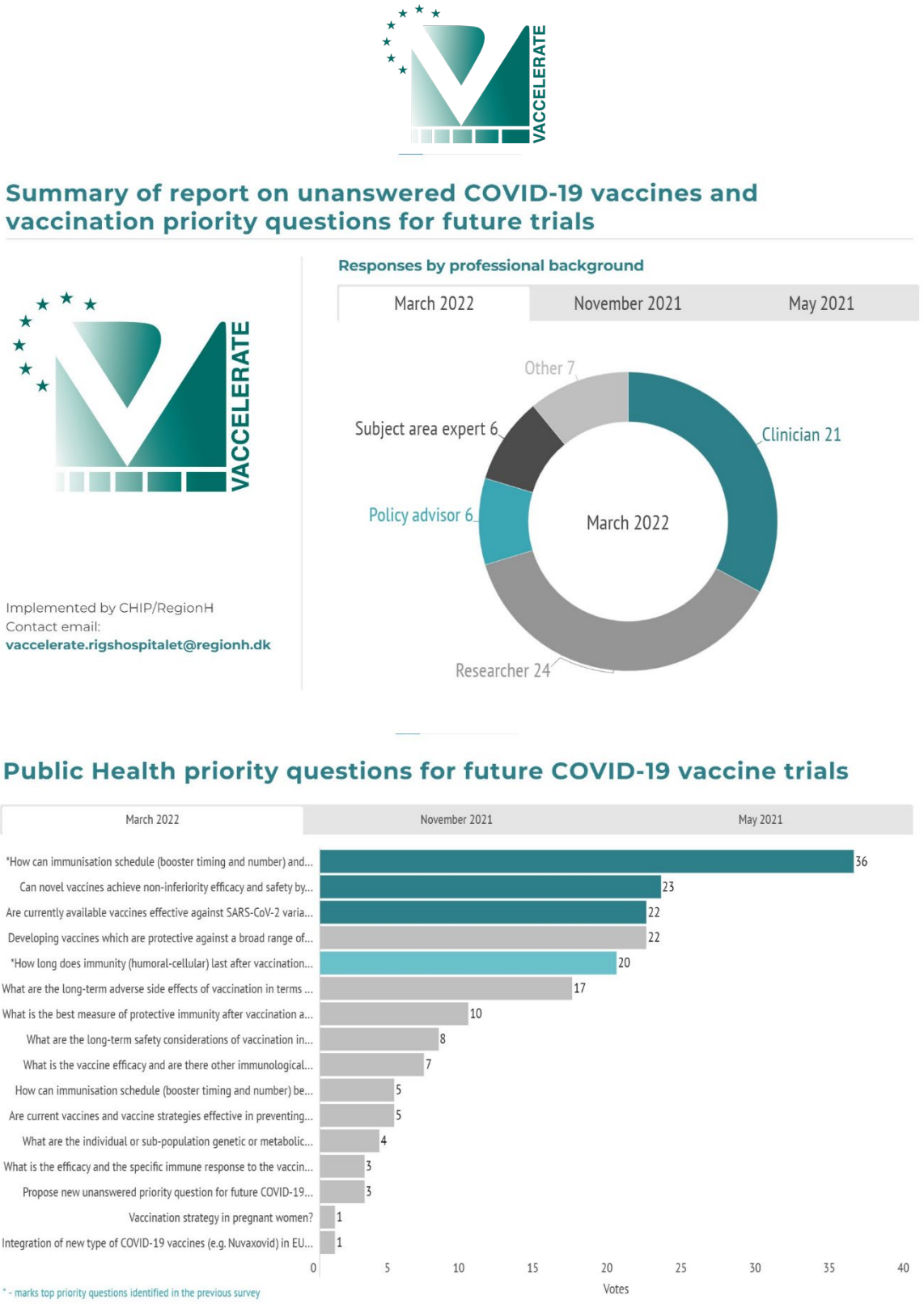

Figure 5: Screenshot of an interactive dashboard of a summary of surveys on unanswered COVID-19 vaccines and vaccination priority questions for future COVID-19 vaccine trials

2.6 Next steps

The initial list of knowledge gaps developed within VACCELERATE in August 2021 has been re-evaluated by the second and third surveys in November 2021 and March 2022. The previous report has indicated an aim of attracting more public health specialists and for this survey, we have shared the invitation to contribute with the European NITAG network. Their input was crucial for the review of public health priority questions for future COVID-19 vaccine trials because it has upvoted the new research topics that were added to the survey in March 2022.

Ongoing communication with the partners involved in the development and upkeep of the COVID-NMA mapping (Task 7.1) is also paramount, as the update of the search filters implies a change in the data extraction form and the need to extract new data. It is feasible if the number of new filters is limited and is identified early in the process otherwise, it involves retrospective data extraction of the studies already registered which involves important resources.

The report will be updated every 6 months throughout the duration of the project and the following steps will be the focus of the next phase of the process:

- Conduct a review of the ongoing studies included in Task 7.1. database to assess their linkage to and relevance for providing answers to the identified questions.
- Investigate the feasibility of the introduction of new identified research questions as a search filter for clinical trials registered in COVID-NMA mapping, e.g.:
    - Pansarbecovirus vaccine (planned to be implemented in the nearest future)
    - 3rd booster shot (5th vaccine dose)
    - Co-administration of COVID-19 vaccine with other vaccines
- Ensure the continuous relevance by revising and updating the list of priority questions regularly based on discussions with VACCELERATE partners and regular searches on emerging/changing priorities through the official websites and news channels of leading public health agencies (CEPI, ECDC, EMA, WHO Europe, ECRIN, CDC and other key organisations).
- Engage with other relevant stakeholders, including PHIRI Consortium and their Rapid Exchange Forum (REF) on COVID-19 developments.
- Assess and re-evaluate the regularity of updates needed as the pandemic progresses.

It is suggested to provide space in the consortium for discussion of how the list of the identified priority questions is utilized in the process of identifying additional vaccine trials to be conducted within VACCELERATE.

3 Deviations from the Description of the Action (DoA) and/or original deliverable

There are no deviations from the Description of the Action.

4 Appendices

Appendix 1: Survey to identify public health priority questions for future COVID-19 vaccine trials distributed in March 2022

Survey to identify public health priority questions for future COVID-19 vaccine trials - 2022

Identifying and filling public health knowledge gaps in COVID-19 vaccine development has been deemed one of the key network objectives and included as one of the workstreams VACCELERATE.

This survey will be repeated every 3 months and aims to help us continuously identify public health knowledge gaps in relation to COVID-19 vaccines and identify where clinical vaccine trials are most urgently needed.

You can read more about the methodology and previous survey results on the VACCELERATE website.

We thank you in advance for your participation. If you have any questions about the survey, please e-mail vaccelerate.rigshospitalet@regionh.dk.

Respondent details (please fill in your affiliation details below)

Are you affiliated with the following (check all that apply):

- ☐ Part of VACCELERATE Consortium
- ☐ Clinical trial site participating in EUVAP (European Vaccine Trial Accelerator Platform) network
- ☐ Part of NITAG collaboration network
- ☐ No, not affiliated with any of the above

Type of institutional affiliation (check one that applies best):

- ◯ University or research Institute/centre
- ◯ National public health institute
- ◯ Government ministry or agency
- ◯ Expert group or clinical society
- ◯ International organisation or network (expert or policy)
- ◯ Pharmaceutical company/vaccine developer
- ◯ Patient group representative
- ◯ Other (please specify)

If 'other' type of institutional affiliation, please specify: _____

Professional background (check one that reflects best the capacity in which you are responding to this survey):

- ◯ Clinician
- ◯ Researcher
- ◯ Policy advisor
- ◯ Subject area expert (national or international level)
- ◯ Other (please specify)

If 'other' professional background, please specify: _____

Country:
(please indicate the country where you are currently working)

◯ Albania
◯ Andorra
◯ Armenia
◯ Austria
◯ Azerbaijan
◯ Belarus
◯ Belgium
◯ Bosnia and Herzegovina
◯ Bulgaria
◯ Croatia
◯ Cyprus
◯ Czechia
◯ Denmark
◯ Estonia
◯ Finland
◯ France
◯ Georgia
◯ Germany
◯ Greece
◯ Hungary
◯ Iceland
◯ Ireland
◯ Israel
◯ Italy
◯ Kazakhstan
◯ Kyrgyzstan
◯ Latvia
◯ Liechtenstein
◯ Lithuania
◯ Luxembourg
◯ Malta
◯ Moldova
◯ Monaco
◯ Montenegro
◯ Netherlands
◯ North Macedonia
◯ Norway
◯ Poland
◯ Portugal
◯ Romania
◯ Russia
◯ Serbia
◯ Kosovo
◯ Slovakia
◯ Slovenia
◯ Spain
◯ Sweden
◯ Switzerland
◯ Tajikistan
◯ Turkey
◯ Turkmenistan
◯ Ukraine
◯ United Kingdom
◯ Uzbekistan
◯ Other (please specify)
(Type to search)

If 'other' country, please specify:

_____

Email address
Your email address will be stored exclusively for the purpose of contacting you in case clarification regarding your survey response is needed. It will not be shared with any other entity or used for any other purpose than stated here.

_____
(By providing my email address, I agree to be contacted in case of validation questions related to my survey responses.)

Top three priority questions for future COVID-19 vaccine studies in the immediate future (i.e. the next 6 months)
Please select max 3 questions that should be prioritised at the European level or in your country in future COVID-19 vaccine trials/studies in the immediate future (i.e. the next 6 months).
*** - marks top priority questions identified in the previous survey**

- ○ *How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?
- ○ Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route (e.g. nasal vaccines) and possibly with only one dose?
- ○ What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
- ○ What is the efficacy and the specific immune response to the vaccine in children, (incl. immunocompromised pediatric population)?
- ○ What are the long-term safety considerations of vaccination in children?
- ○ How can immunisation schedule (booster timing and number) be optimised for the paediatric population to ensure maximum protection?
- ○ *How long does immunity (humoral-cellular) last after vaccination with current vaccines?
- ○ Are currently available vaccines effective against SARS-CoV-2 variants in the short- and long-term and is there a need to develop new vaccine to protect against the VOCs?
- ○ What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?
- ○ What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?
- ○ Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?
- ○ Developing vaccines which are protective against a broad range of coronaviruses (e.g.pansarbecovirus vaccine)
- ○ Vaccination strategy be in pregnant women?
- ○ Precision medicine approach to COVID-19 vaccination
- ○ Integration of new type of COVID-19 vaccines (e.g. Nuvaxovid) in EU vaccination programs

Write here additional unanswered priority question/topic:

General comments

Please include any other comments you would like to provide: