Summary of updated report on unanswered COVID-19 vaccines and vaccination priority questions for future trials

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Identified Priority Questions

Vaccine administration

1. How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection?
2. What is the comparative advantage of heterologous vs. homogenic vaccination in terms of efficacy, safety and duration of protection?
3. Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route and possibly with only one dose?
4. What should the vaccination strategy be for recovered patients?

Vaccination in immunocompromised

5. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
6. How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised for the immunocompromised group to ensure maximum protection?

Pediatric vaccination

7. What is the efficacy and the specific immune response to the vaccine in children, including immunocompromised pediatric population?
8. What are the long-term safety considerations of vaccination in children?
9. What is the relationship in terms of protection between vaccination and immuno-mediated diseases such as MIS-C?

Long-term protection and immunity

10. How long does immunity (humoral-cellular) last after vaccination with current vaccines?
11. 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?
12. What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?

Protection against new variants

13. 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? *

Long-term vaccine safety/side effects

14. What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?

Infection transmission prevention

15. Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?

Public health/policy

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

VACCELERATE Survey to identify Public Health priority questions for future COVID-19 vaccine trials - November 2021

In November 2021 a new survey was circulated among the VACCELERATE Consortium focused on the revision of the initial list of priority questions identified in D7.4 First report on unanswered COVID-19 vaccines and vaccination priority questions for future trials was finalised in September 2021.

The survey aimed to rank the list of the 17 priority questions and identify the top 3 most important unanswered questions for potential upcoming COVID-19 vaccines clinical trials to address as well as collect any new emerging questions.

The slides below contain the breakdown of those responses.

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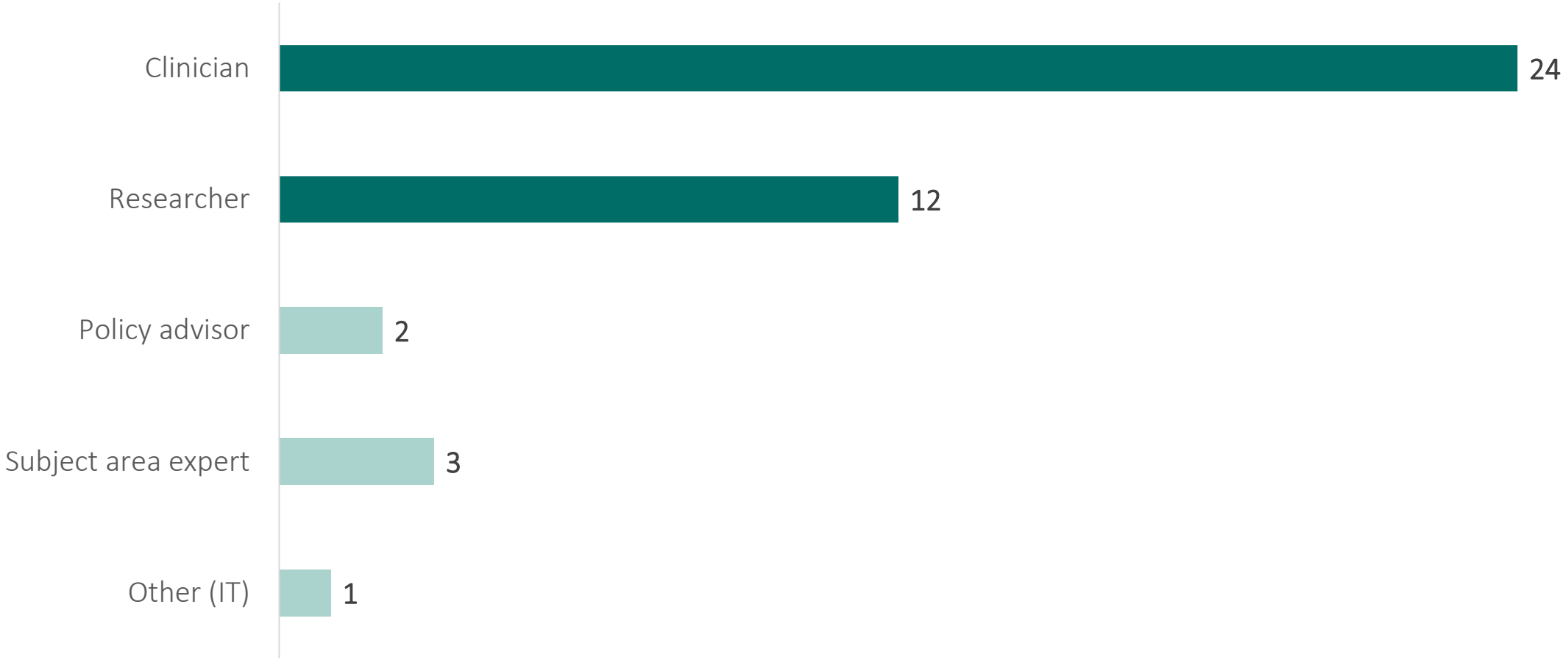
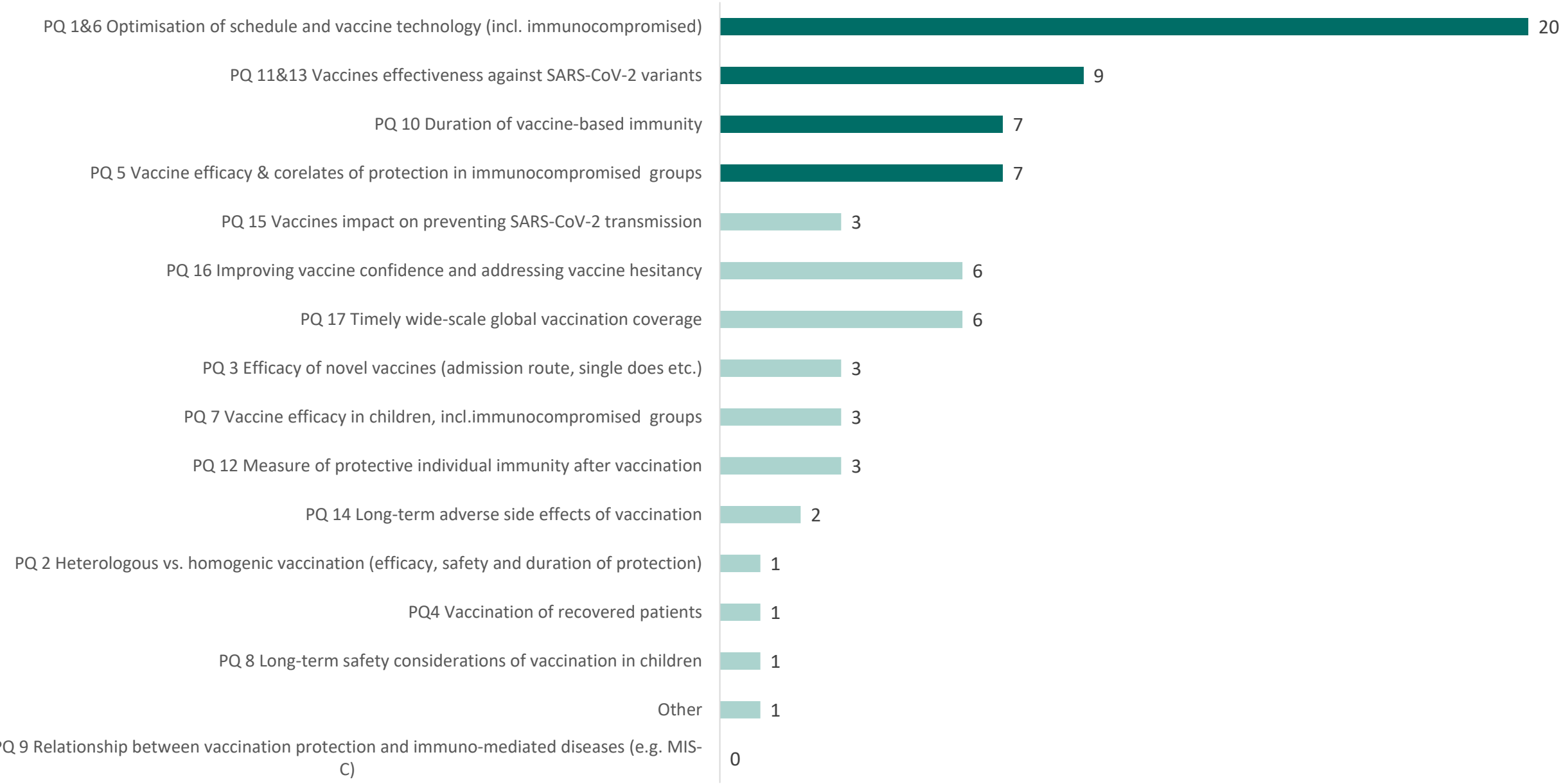
Responses collected from the VACCELERATE Consortium

Professional background of the survey responders



The responders to the survey represented mainly clinicians and researchers, with limited input from policy advisers (n=2) and area experts (n=3). There were significant differences in the priority questions identified by the clinicians and researchers. The slides below specify the responses collected in the main groups.

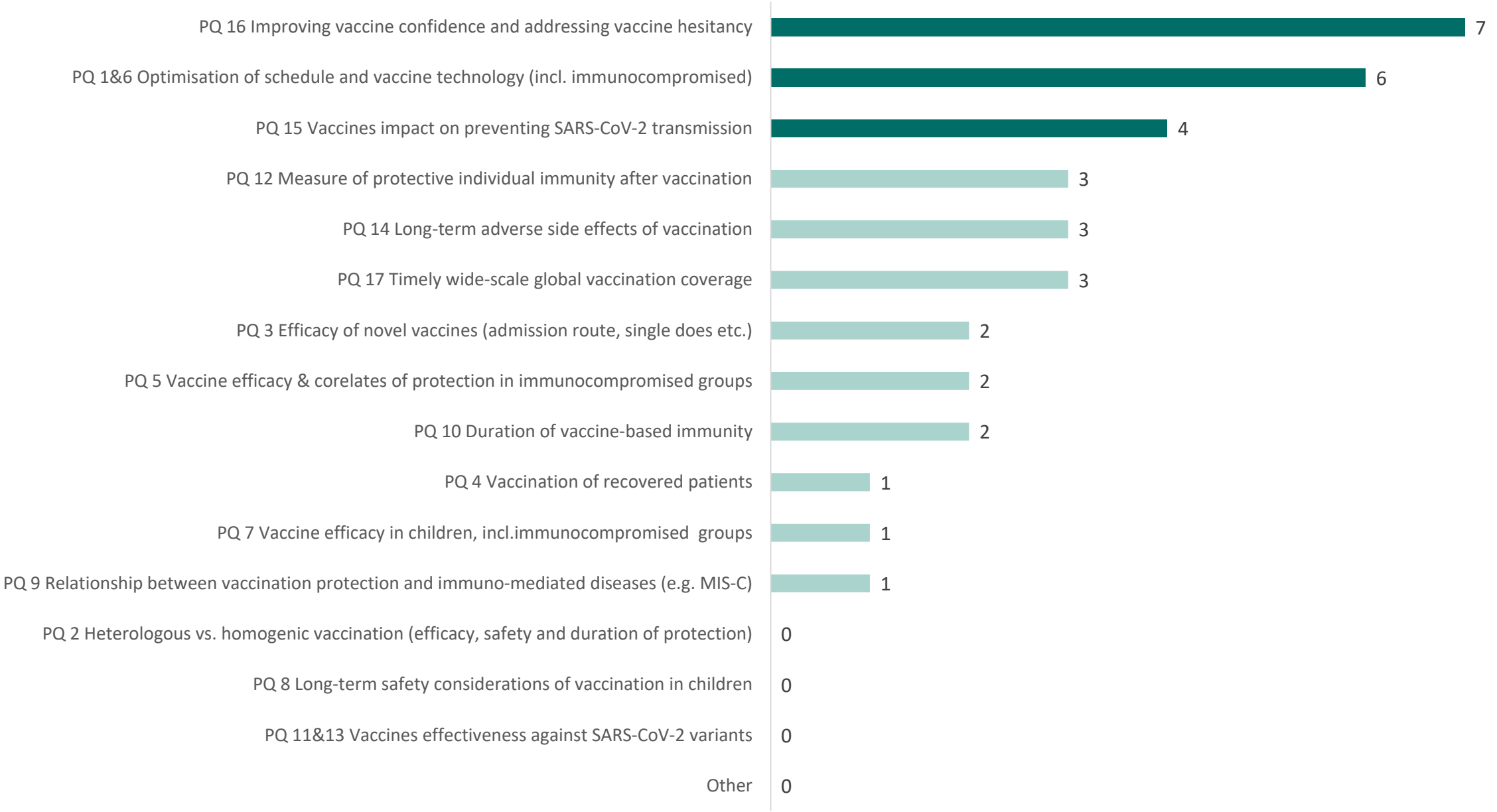
Public Health priority questions for future COVID-19 vaccine trials (Clinicians)



Full list of questions (Clinicians)

VOTES	PUBLIC HEALTH PRIORITY QUESTIONS FOR FUTURE COVID-19 VACCINE TRIALS
20	1. - 6.How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?
9	11.-13. 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?
7	10. How long does immunity (humoral-cellular) last after vaccination with current vaccines?
7	5. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
3	15. Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?
6	16. How can awareness of and confidence in vaccine programmes be improved to address vaccine hesitancy and misinformation with focus on specific population groups?
6	17. How can wide-scale global vaccination coverage be ensured within reasonable timelines, especially in resource-limited settings?
3	3. Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route and possibly with only one dose?
3	7. What is the efficacy and the specific immune response to the vaccine in children, including immunocompromised pediatric population?
3	12. What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?
2	14. What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?
1	2. What is the comparative advantage of heterologous vs. homogenic vaccination in terms of efficacy, safety and duration of protection?
1	4. What should the vaccination strategy be for recovered patients?
1	8. What are the long-term safety considerations of vaccination in children?
1	**Other - Studies into vaccines for nasal administration and their effect on limiting transmission through effects in the nasal mucosa**
0	9. What is the relationship in terms of protection between vaccination and immuno-mediated diseases such as MIS-C?

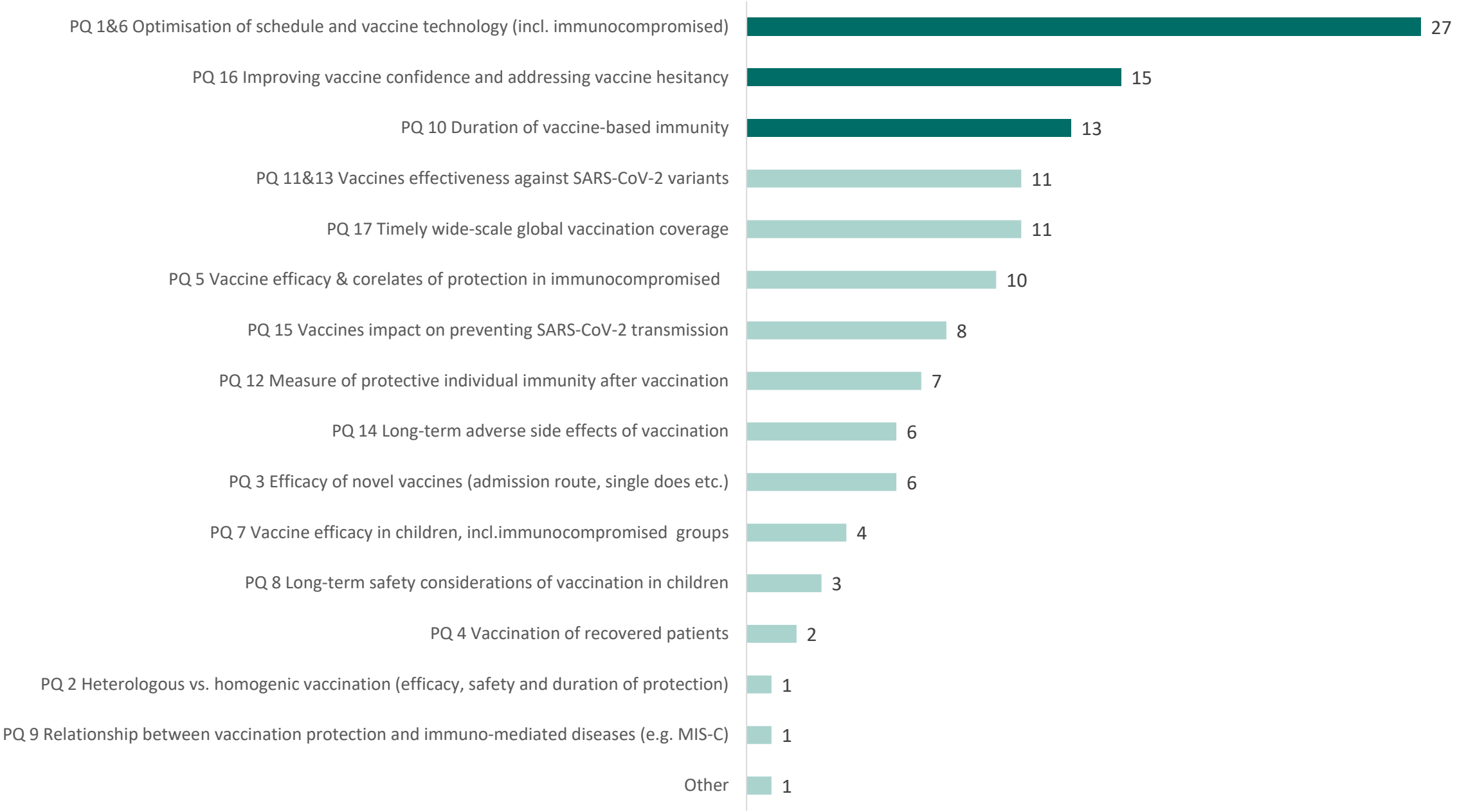
Public Health priority questions for future COVID-19 vaccine trials (Researchers)



Full list of questions (Researchers)

VOTES	PUBLIC HEALTH PRIORITY QUESTIONS FOR FUTURE COVID-19 VACCINE TRIALS
7	16. How can awareness of and confidence in vaccine programmes be improved to address vaccine hesitancy and misinformation with focus on specific population groups?
6	1. - 6.How can immunisation schedule (booster timing and number) and technologies (vaccine dose and type) be optimised to ensure maximum protection (incl. immunocompromised groups)?
4	15. Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?
3	12. What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?
3	14. What are the long-term adverse side effects of vaccination in terms of vaccine-related or vaccine-induced diseases (autoimmune, oncologic, fertility etc.)?
3	17. How can wide-scale global vaccination coverage be ensured within reasonable timelines, especially in resource-limited settings?
2	3. Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route and possibly with only one dose?
2	5. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?
2	10. How long does immunity (humoral-cellular) last after vaccination with current vaccines?
1	4. What should the vaccination strategy be for recovered patients?
1	7. What is the efficacy and the specific immune response to the vaccine in children, including immunocompromised pediatric population?
1	9. What is the relationship in terms of protection between vaccination and immuno-mediated diseases such as MIS-C?
0	2. What is the comparative advantage of heterologous vs. homogenic vaccination in terms of efficacy, safety and duration of protection?
0	8. What are the long-term safety considerations of vaccination in children?
0	11.-13. 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?
0	Other

Public Health priority questions for future COVID-19 vaccine trials



Overview of the identified questions

VOTES	PUBLIC HEALTH PRIORITY QUESTIONS FOR FUTURE COVID-19 VACCINE TRIALS	IDENTIFIED CLINICAL TRIALS*
27	1. - 6.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 – 77 (incl. high risk – 8) Vaccine schedule – 119 (incl. high risk – 5)
15	16. How can awareness of and confidence in vaccine programmes be improved to address vaccine hesitancy and misinformation with focus on specific population groups?	Not applicable (policy question)
13	10. How long does immunity (humoral-cellular) last after vaccination with current vaccines?	Filter not available **Search**: *"Cellular immunity" – 9* *"Humoral immunity" – 5*
11	11.-13. 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) – 22 VOC (omicron) - 0
11	17. How can wide-scale global vaccination coverage be ensured within reasonable timelines, especially in resource-limited settings?	Not applicable (policy question)
10	5. What is the vaccine efficacy and are there other immunological correlates of protection than antibodies in various immunocompromised groups?	Filter not available (search not successful)
8	15. Are current vaccines and vaccine strategies effective in preventing SARS-CoV-2 transmission?	Filter not available (search not successful)
7	12. What is the best measure of protective immunity after vaccination at the individual level and when after vaccination should it be taken?	Filter not available (search not successful)
6	14. 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)
6	3. Can novel vaccines achieve non-inferiority efficacy and safety by non-parenteral route and possibly with only one dose?	Filter not available (search not successful)
4	7. What is the efficacy and the specific immune response to the vaccine in children, including immunocompromised pediatric population?	**Filter**: Under 18 y.o. – 74 (incl. high risk – 7)
3	8. What are the long-term safety considerations of vaccination in children?	Filter not available (search not successful)
2	4. What should the vaccination strategy be for recovered patients?	**Filter**: Recovered patients – 5
1	2. What is the comparative advantage of heterologous vs. homogenic vaccination in terms of efficacy, safety and duration of protection?	**Filter**: Heterologous - 95
1	9. What is the relationship in terms of protection between vaccination and immuno-mediated diseases such as MIS-C?	Filter not available (search not successful)
1	Other - Studies into vaccines for nasal administration and their effect on limiting transmission through effects in the nasal mucosa	Filter not available (search not successful)

*Source: https://covid-nma.com/vaccines/mapping/# (accessed on 14th January 2022)

Potential new emerging questions identified from ongoing public discussion*

- **Studies into vaccines for nasal administration and their effect on limiting transmission through effects in the nasal mucosa**
- Developing vaccines which are protective against a broad range of coronaviruses (e.g. **pan-sarbecovirus vaccine**)
- Vaccination and Menstrual disorders (no pattern, emerging studies - transient)
- Vaccination in the pregnant women (especially 1st trimester) and feeding mothers (no concerns, just data limitations)
- Adapting COVID-19 vaccine platforms for other infections in the future
- Precision medicine approach to vaccination
- How can immunisation schedule (booster timing and number) be optimised for the pediatric population to ensure maximum protection?

**Topics identified from WHO, EMA, CEPI presentations, meetings and press-briefing*