



World Health Organization

**Department of Immunization, Vaccines
and Biologicals (IVB)**

IVIR-AC – August 2021

**Meeting of the Advisory Committee
on Immunization and Vaccines-
related Implementation Research
(IVIR-AC)**

MICROSOFT TEAMS - VIRTUAL MEETING

WHO HEADQUARTERS, GENEVA, SWITZERLAND

30 August - 3 September 2021

About the IVIR-AC pink book

This booklet contains key background documents for the meeting of the Advisory Committee on Immunization and Vaccines-related Implementation Research (IVIR-AC)
01 – 05 March 2021

This book will be published after the IVIR-AC meeting at the following link

<https://www.who.int/groups/immunization-and-vaccines-related-implementation-research-advisory-committee>

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Current IVIR-AC – Advisory Committee Members

Walter Orenstein (Chair), Professor, Emory Global Health Institute, Emory University, Atlanta, **United States of America**

Habib Hasan Farooqui, Additional Professor, Public Health Foundation of India, Delhi, **India**

Mark Jit, Professor Vaccine Epidemiology, Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London, **United Kingdom of Great Britain & Northern Ireland**

Julie Leask, Professor, Susan Wakil School of Nursing and Midwifery, Sydney Nursing School, Faculty of Medicine and Health, Camperdown NSW 2050, Sydney, **Australia**

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Joseph Wu, Professor, Division of Epidemiology and Biostatistics, School of Public Health, The University of Hong Kong, Pok Fu Lam, **Hong Kong SAR, China**

IVIR-AC Terms of References

The IVIRAC Terms of References
can be accessed at the following link:

<https://www.who.int/groups/immunization-and-vaccines-related-implementation-research-advisory-committee/membership>

DOI and Confidentiality undertakings

DECLARATION OF INTERESTS FOR WHO EXPERTS

WHO's work on global health issues requires the assistance of external experts who **may have interests related to their expertise**. To ensure the highest integrity and public confidence in its activities, WHO requires that experts serving in an advisory role disclose any circumstances that could give rise to a potential conflict of interest related to the subject of the activity in which they will be involved.

All experts serving in an advisory role must disclose any circumstances that could represent a **potential conflict of interest** (i.e., any interest that may affect, or may reasonably be perceived to affect, the expert's objectivity and independence). You must disclose on this Declaration of Interests (DOI) form any financial, professional or other interest relevant to the subject of the work or meeting in which you have been asked to participate in or contribute towards and any interest that could be affected by the outcome of the meeting or work. You must also declare relevant interests of your immediate family members (see definition below) and, if you are aware of it, relevant interests of other parties with whom you have substantial common interests and which may be perceived as unduly influencing your judgement (e.g. employer, close professional associates, administrative unit or department). Please note that not fully completing and disclosing all relevant information on this form may, depending on the circumstances, lead WHO to decide not to appoint you to WHO advisory bodies/functions in the future.

Please complete this form and submit it to WHO Secretariat if possible at least 4 weeks but no later than 2 weeks before the meeting or work. You must also promptly inform the Secretariat if there is any change in this information prior to, or during the course of, the meeting or work. All experts must complete this form before participation in a WHO activity can be confirmed. Please note that not fully completing and disclosing all relevant information on this form may, depending on the circumstances, lead WHO to decide not to appoint you to WHO advisory bodies/functions in the future.

Answering "Yes" to a question on this form does not automatically disqualify you or limit your participation in a WHO activity. Your answers will be reviewed by the Secretariat to determine whether you have a conflict of interest relevant to the subject at hand. One of the outcomes listed in the next paragraph can occur depending on the circumstances (e.g. nature and magnitude of the interest, timeframe and duration of the interest).

The Secretariat may conclude that no potential conflict exists or that the interest is irrelevant or insignificant. If, however, a declared interest is determined to be potentially or clearly significant, one or more of the following three measures for managing the conflict of interest may be applied. The Secretariat (i) allows full participation, with public disclosure of your interest; (ii) mandates partial exclusion (i.e., you will be excluded from that portion of the meeting or work related to the declared interest and from the corresponding decision making process); or (iii) mandates total exclusion (i.e., you will not be able to participate in any part of the meeting or work).

All potentially significant interests will be **disclosed** to the other participants at the start of the activity and you will be asked if there have been any changes. A summary of all declarations and actions taken to manage any declared interests will be **published** in resulting reports and work products. Furthermore, if the objectivity of the work or meeting in which you are involved is subsequently questioned, the contents of your DOI form may be made available by the Secretariat to persons outside WHO if the Director-General considers such disclosure to be in the best interest of the Organization, after consulting with you. Completing this DOI form means that you agree to these conditions.

If you are unable or unwilling to disclose the details of an interest that may pose a real or perceived conflict, you must disclose that a conflict of interest may exist and the Secretariat may decide that you be totally recused from the meeting or work concerned, after consulting with you.

Name:
Institution:
Email:

Date and title of meeting or work, including description of subject matter to be considered (if a number of substances or processes are to be evaluated, a list should be attached by the organizer of the activity):

Please answer each of the questions below. If the answer to any of the questions is "yes", briefly describe the circumstances on the last page of the form.

The term "you" refers to yourself and your immediate family members (i.e., spouse (or partner with whom you have a similar close personal relationship) and your children). "Commercial entity" includes any commercial business, an industry association, research institution or other enterprise whose funding is significantly derived from commercial sources with an interest related to the subject of the meeting or work. "Organization" includes a governmental, international or non-profit organization. "Meeting" includes a series or cycle of meetings.

EMPLOYMENT AND CONSULTING

Within the past 4 years, have you received remuneration from a commercial entity or other organization with an interest related to the subject of the meeting or work?

- 1a Employment Yes No
- 1b Consulting, including service as a technical or other advisor Yes No

RESEARCH SUPPORT

Within the past 4 years, have you or has your research unit received support from a commercial entity or other organization with an interest related to the subject of the meeting or work?

- 2a Research support, including grants, collaborations, sponsorships, and other funding Yes No
- 2b Non-monetary support valued at more than US \$1000 overall (include equipment, facilities, research assistants, paid travel to meetings, etc.) Yes No

Support (including honoraria) for being on a speakers bureau, giving speeches or training for a commercial entity or other organization with an interest related to the subject of the meeting or work?

INVESTMENT INTERESTS

Do you have current investments (valued at more than US \$5 000 overall) in a commercial entity with an interest related to the subject of the meeting or work? Please also include indirect investments such as a trust or holding company. You may exclude mutual funds, pension funds or similar investments that are broadly diversified and on which you exercise no control.

- 3a Stocks, bonds, stock options, other securities (e.g., short sales) Yes No
- 3b Commercial business interests (e.g., proprietorships, partnerships, joint ventures, board memberships, controlling interest in a company) Yes No

INTELLECTUAL PROPERTY

Do you have any intellectual property rights that might be enhanced or diminished by the outcome of the meeting or work?

- 4a Patents, trademarks, or copyrights (including pending applications) Yes No
- 4b Proprietary know-how in a substance, technology or process Yes No

PUBLIC STATEMENTS AND POSITIONS (during the past 3 years)

- 5a As part of a regulatory, legislative or judicial process, have you provided an expert opinion or testimony, related to the subject of the meeting or work, for a commercial entity or other organization? Yes No
- 5b Have you held an office or other position, paid or unpaid, where you represented interests or defended a position related to the subject of the meeting or work? Yes No

ADDITIONAL INFORMATION

- 6a If not already disclosed above, have you worked for the competitor of a product that is the subject of the meeting or work, or will your participation in the meeting or work enable you to obtain access to a competitor's confidential proprietary information, or create for you a personal, professional, financial or business competitive advantage? Yes No
- 6b To your knowledge, would the outcome of the meeting or work benefit or adversely affect interests of others with whom you have substantial common personal, professional, financial or business interests (such as your adult children or siblings, close professional colleagues, administrative unit or department)? Yes No
- 6c Excluding WHO, has any person or entity paid or contributed towards your travel costs in connection with this WHO meeting or work? Yes No

6d Have you received any payments (other than for travel costs) or honoraria for speaking publicly on the subject of this WHO meeting or work? Yes No

6e Is there any other aspect of your background or present circumstances not addressed above that might be perceived as affecting your objectivity or independence? Yes No

7. **TOBACCO OR TOBACCO PRODUCTS** (answer without regard to relevance to the subject of the meeting or work)

Within the past 4 years, have you had employment or received research support or other funding from, or had any other professional relationship with, an entity directly involved in the production, manufacture, distribution or sale of tobacco or tobacco products or representing the interests of any such entity?

Yes No

EXPLANATION OF "YES" RESPONSES: If the answer to any of the above questions is "yes", check above and briefly describe the circumstances on this page. If you do not describe the nature of an interest or if you do not provide the amount or value involved where relevant, the conflict will be assumed to be significant.

Nos. 1 - 4: Type of interest, question number and category (e.g., Intellectual Property 4.a copyrights) and basic descriptive details.	Name of company, organization, or institution	Belongs to you, a family member, employer, research unit or other?	Amount of income or value of interest (if not disclosed, is assumed to be significant)	Current interest (or year ceased)

Nos. 5-6: Describe the subject, specific circumstances, parties involved, time frame and other relevant details

CONSENT TO DISCLOSURE. By completing and signing this form, you consent to the disclosure of any relevant conflicts to other meeting participants and in the resulting report or work product.

DECLARATION. I hereby declare on my honour that the disclosed information is true and complete to the best of my knowledge.

Should there be any change to the above information, I will promptly notify the responsible staff of WHO and complete a new declaration of interests form that describes the changes. This includes any change that occurs before or during the meeting or work itself and through the period up to the publication of the final results or completion of the activity concerned.

Date: _____

Signature _____

Attachment 1

Memorandum of Agreement Terms and Conditions for Temporary Advisers

I, the undersigned, in accepting to act as a Temporary Adviser to the World Health Organization (WHO), agree to the following:

1. RELATIONSHIP BETWEEN THE PARTIES

The execution of the work as Temporary Adviser does not create any employer/employee relationship as between WHO, on the one hand, and me and/or persons claiming under me, on the other hand. Thus, WHO shall not be liable to me or any other person whatsoever for any damage, loss, accident, injury, illness and/or death sustained by me in connection with, or as a result of, my assignment as Temporary Adviser to WHO, including travel.

2. TRAVEL COSTS, PER DIEM AND INCIDENTALS

I understand that my travel, per diem and incidentals will be paid by WHO, in accordance with WHO rules described in Annex 1 attached hereto.

3. CONFLICT OF INTERESTS

I agree to truthfully complete the Declaration of Interests for WHO Experts and disclose any circumstances that may give rise to a real, potential or apparent conflict of interest in relation to my work as Temporary Adviser. I will ensure that the disclosed information is correct and will truthfully declare that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to promptly inform WHO of any change in these circumstances, including if an issue arises during the course of my work as Temporary Adviser. I understand and agree that this Memorandum of Agreement may be cancelled by WHO if WHO determines that the information disclosed by me in the Declaration of Interests requires modification or cancellation of the invitation extended to me to serve as Temporary Adviser to WHO.

4. INSURANCE

I agree that the insurance arrangements set forth below are being made by WHO without any prejudice whatsoever to section 1 above. Thus, I agree that WHO shall not be liable for any damage, loss, accidents, injury, illness and/or death sustained by me in connection with, or as a result of, my assignment as Temporary Adviser to WHO, including travel.

While travelling, my baggage and personal effects will be insured by WHO up to an amount of US\$ 5000 (five thousand United States dollars). This insurance covers all hand baggage carried by me with the exception of documents, travel tickets, currency/cash/travellers cheques, stamps, stamped paper, identity papers, household goods and objets d'art (art works). Personal computers and accessories are also not included in WHO's personal baggage insurance cover unless it is noted on the travel authorization that a personal computer is required during the journey. Laptops must be hand-carried on board airplanes and not checked as registered baggage. Fees to replace stolen travel tickets, credit cards and official documents may be claimed under the insurance policy.

I understand that I will also be covered by an accident and emergency* insurance policy. (A description of the coverage pursuant to this insurance policy and an information booklet containing other information, including with regard to the procedure for submission and reimbursement of claims, are available on the website of Cigna <http://www.cignahealthbenefits.com> Under 'Plan members' the standard reference number **378/WHCPVE** should be entered and on the next screen the standard date of birth **31/01/1977**.)

I understand that the aforementioned insurance policy does not include general 'illness insurance' (medical insurance) for which I should obtain and maintain coverage under my national, institutional or private health insurance scheme, or from the insurance provider proposed by WHO in accordance with the following paragraph, that is valid in all locations in which I shall undertake the assignment on behalf of WHO.

I understand that I may purchase additional voluntary complementary insurance coverage directly from the insurance provider proposed by WHO, for compensation in case of death due to illness and medical expenses for general (non-emergency*) illness during the contract period, and that further information concerning the voluntary complementary insurance is available on the website of Cigna: <http://www.cignahealthbenefits.com>. Under 'Plan members' the standard reference number **378/WHCPVE** should be entered and on the next screen the standard date of birth **31/01/1977**.

I further understand that if I opt to purchase such additional voluntary complementary insurance, I must contact the insurance company directly and pay the applicable premiums for the whole contract period prior to the start date of the contract.

Finally, I understand, with regard to both (i) the accident and emergency* illness insurance policy, and (ii) the voluntary complementary insurance coverage, referred to herein that:

- all interactions relating to such insurance coverage shall be between the insurance company and myself, without the involvement of WHO.
- any insurance claims under either of the aforementioned policies must be submitted by me directly to the insurance company, which will review and process the claim without the involvement of WHO;
- WHO assumes no responsibility for non-payment by the insurance company of all or part of a claim that may be submitted by me; and
- WHO assumes no responsibility or liability with regard to any expenses which may be incurred by me in connection with any illness contracted in the location of my assignment with WHO which exceeds the amount of the insurance coverage (compulsory and/or voluntary) referred to in this letter or as a result of any failure on my part to ensure that I have adequate insurance coverage for general (non-emergency*) illness during the contract period.

* *Note: "Emergency" (as used herein) means a life-threatening situation or situation where the patient must start treatment within 48 hours and for whom travel is not possible for medical reasons.*

5. SMOKING POLICY

I understand and agree that smoking is not permitted in WHO premises or in any designated meeting areas outside WHO premises.

6. CONFIDENTIALITY UNDERTAKING

I undertake to exercise the utmost discretion in all matters relating to my assignment as Temporary Adviser to WHO. In this regard, I shall treat all information and documentation (in whatever format) to which I may gain access in connection with, or as a result of, my assignment as Temporary Adviser to WHO, as confidential and proprietary to WHO and/or parties collaborating with WHO, and agree to take all reasonable measures to ensure that such information and documentation (hereinafter jointly referred to as "Information"):

- i) is not used for any purpose other than the performance of my work as Temporary Adviser to WHO; and
- ii) is disclosed and provided only to persons who have a need to know for the aforesaid purpose and are bound by like obligations of confidentiality and non-use as contained in this Memorandum of Agreement.

This undertaking does not cease upon completion of my work as Temporary Adviser. However, there shall be no obligation of confidentiality if and to the extent: (i) information is publicly available, or becomes publicly available through no fault of my own; or (ii) information was already known to me (as evidenced by written records) prior to its receipt by me; or (iii) information is received from a third party not in breach of an obligation of confidentiality.

I agree to promptly return any and all copies of the aforesaid information and documentation to WHO at the conclusion of my work as Temporary Adviser to WHO or upon earlier termination of this Memorandum of Agreement.

7. INDEPENDENCE

I agree to respect the impartiality and independence required of WHO. In this regard, I shall not seek or accept instructions regarding the work performed by me as Temporary Adviser to WHO from any Government or from any authority external to WHO.

8. RIGHTS

I agree that any and all rights in the work performed by me in connection with, or as a result of, my assignment as Temporary Adviser to WHO shall be exclusively vested in WHO. I hereby irrevocably and unconditionally assign all such rights to WHO and waive any moral rights attached to such work.

I understand and agree that WHO reserves the right (a) to revise such work, (b) to use it in a different way from that originally envisaged, or (c) not to use or publish it at all.

9. COMPLIANCE WITH WHO CODES AND POLICIES

By entering into this Memorandum of Agreement, I acknowledge that I have read, and hereby accept and agree to comply with, the WHO Policies (as defined below). In connection with the foregoing, I shall not engage in any conduct that would constitute a violation of the standards of conduct, as described in the WHO Policies. Without limiting the foregoing, I shall promptly report to WHO, in accordance with the terms of the applicable WHO Policies, any actual or suspected violations of any WHO Policies of which I become aware. For purposes of this Memorandum of Agreement, the term “WHO Policies” means collectively: (i) the WHO Code of Ethics and Professional Conduct; (ii) the WHO Policy on Sexual Exploitation and Abuse Prevention and Response; (iii) the WHO Code of Conduct for responsible Research; and (iv) the WHO Policy on Whistleblowing and Protection Against Retaliation, in each case, as amended from time to time and which are publicly available on the WHO website at the following link and at <http://www.who.int/about/ethics/en/>

10. ZERO TOLERANCE FOR SEXUAL EXPLOITATION AND ABUSE

WHO has zero tolerance towards sexual exploitation and abuse. In this regard, and without limiting any other provisions contained herein, I undertake (i) not to engage in any conduct that would constitute sexual exploitation or abuse as described in the WHO Policy on Sexual Exploitation and Abuse Prevention and Response; and (ii) to promptly report to WHO, in accordance with the terms of the Policy, any actual or suspected violations of the Policy of which I becomes aware.

11. ANTI-TERRORISM AND UN SANCTIONS; FRAUD AND CORRUPTION

I warrant for the entire duration of my assignment as Temporary Advisor that:

- (i) I am not and will not be involved in, or associated with, any person or entity associated with terrorism, as designated by any UN Security Council sanctions regime, that I will not make any payment or provide any other support to any such person or entity and that I will not enter into any employment or subcontracting relationship with any such person or entity;
- (ii) I shall not engage in any illegal, corrupt, fraudulent, collusive or coercive practices (including bribery and theft) in connection with the execution of this Memorandum of Agreement; and
- (iii) I shall take all necessary precautions to prevent the financing of terrorism and/or any illegal corrupt, fraudulent, collusive or coercive practices (including bribery, and theft) in connection with the execution of this Memorandum of Agreement.

12. BREACH OF ESSENTIAL TERMS

I acknowledge and agree that each of the provisions of paragraphs 9, 10 and 11 hereof constitutes an essential term of this Memorandum of Agreement, and that in case of breach of any of these provisions, WHO may, in its sole discretion, decide to:

- (i) terminate this Memorandum of Agreement, and/or any other contract concluded by WHO with me, immediately upon written notice to me, without any liability for termination charges or any other liability of any kind; and/or
- (ii) exclude me from entering into any future contractual or collaborative relationships with WHO.

WHO shall be entitled to report any violation of such provisions to WHO's governing bodies, other UN agencies, and/or donors.

13. USE OF WHO NAME AND EMBLEM

Without WHO's prior written approval, I shall not, in any statement or material of an advertising or promotional nature, refer to this Memorandum of Agreement or my relationship with WHO, or otherwise use the name (or any abbreviation thereof) and/or emblem of the World Health Organization.

14. PUBLICATION OF AGREEMENT

Subject to considerations of confidentiality, WHO may acknowledge the existence of this Memorandum of Agreement to the public and publish and/or otherwise publicly disclose my name and general information with respect to my assignment as Temporary Advisor. Such disclosure will be made in accordance with WHO's Information Disclosure Policy and shall be consistent with the terms of this Agreement.

15. SURVIVING PROVISIONS

Those provisions of this Memorandum of Agreement that are intended by their nature to survive its expiration or earlier termination shall continue to apply.

16. SETTLEMENT OF DISPUTES

Any matter relating to the interpretation or application of this Memorandum of Agreement which is not covered by its terms shall be resolved by reference to the laws of Switzerland. Any dispute relating to the interpretation or application of this Memorandum of Agreement shall, unless amicably settled, be subject to conciliation. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The parties shall accept the arbitral award as final.

17. PRIVILEGES AND IMMUNITIES OF WHO

Nothing in or relating to this Memorandum of Agreement shall be deemed a waiver, express or implied, of any of the privileges and immunities of WHO, whether under the Convention on the Privileges and Immunities of the Specialized Agencies approved by the General Assembly of the United Nations on November 21, 1947, or otherwise, and no provision of this Memorandum of Agreement shall be interpreted or applied in a manner, or to an extent, inconsistent with such privileges and immunities.

By signing this Memorandum of Agreement, I confirm that I accept my assignment as Temporary Adviser, in accordance with and subject to the terms and conditions contained in the invitation letter and this Memorandum of Agreement and its annexes

Place and date:

Name:

Signature:

Received by WHO:

Date: _____
Dr Philipp Lambach
Medical officer
Initiative for Vaccine Research

Signature: _____

Annex 1 to Attachment 1 - Memorandum of Agreement Terms and Conditions for Temporary Advisers

TRAVEL COSTS, PER DIEM AND INCIDENTALS

WHO will be responsible for my airfare and/or first-class train fare from my place of residence to the place of the work and return. In view of the financial stringencies being faced by WHO, I agree to cooperate in reducing airfare costs through the use of cheapest available tickets on the most economical route.

The standard of airline accommodation for which WHO will bear the cost is:

The lowest available economy class ticket by the least expensive route, with the condition it does not exceed the most direct itinerary by 4 hours or more.

Should I wish to upgrade my ticket, or change the airline or route, I may do so at my own expense, but, in accordance with WHO travel policy, WHO's liability will not exceed the limits mentioned above.

WHO will send me the travel authorization when WHO has received the counter-signed invitation letter and signed Memorandum of Agreement and completed and signed Declaration of Interests for WHO Experts, and is able to send me written notification that the information disclosed by me in the Declaration of Interests does not require modification or cancellation of WHO's invitation.

In order to take advantage of the most competitive air fares, I will make reservations as quickly as possible through the travel agency mentioned in the invitation letter.

"WHO will provide travel cancellation insurance in the event that I am unfit to travel due to medical reasons and a ticket purchased cannot be changed or cancelled."

If I wish to travel by private car, I will ask WHO for specific authorization in advance. In such event, the maximum amount to be reimbursed by WHO will be according to the UN official mileage rate to and from the destination by the most direct route. I will advise WHO if I require details of the amount to be reimbursed. I agree that evidence must be provided that travel by car was in fact undertaken, together with the distance travelled.

SUBSISTENCE ALLOWANCE

WHO will pay me a daily subsistence allowance (DSA), according to the UN's standard published DSA rates for the location concerned, for the duration of any travel during my assignment and for travel time from my place of residence to the place of the work and return, except for the last day of travel (for which no daily subsistence allowance will be paid). An allowance of 50% of the per diem applicable to the city of departure will be paid to travellers for an overnight stay on an airplane. An additional travel allowance of US\$ 47* per city of departure and arrival to cover miscellaneous expenses and local transport will also be paid. I agree and accept that the total allowance as described herein is intended to cover all costs related to my assignment, such as accommodation, meals and all other incidental expenses. Accordingly, charges for airport taxes, ground transportation from airport to hotel or vice versa will not be separately reimbursed, and I am not required to submit a travel claim.

WHO policy on the reimbursement of accommodation depends upon whether the traveller stays in a hotel, or other commercial establishment, or makes his or her own private arrangements and does not incur lodging costs. Travellers staying in a hotel will receive the full applicable DSA; travellers that do not incur expenses for lodging will receive 50% of the applicable DSA rate.

I agree to advise WHO which of the above accommodation options I decide upon and will provide details of my bank account if I would like the payment for DSA to be made to this account.

WHO HOTEL PROGRAMME

WHO has implemented a Preferred Hotel Programme in 20 cities:

Addis Ababa – Accra – Atlanta - Amman – Bangkok – Beirut - Brazzaville – Cairo – Copenhagen – Dakar – Geneva – Jakarta - Johannesburg – Hanoi - Libreville – London – Manila – Nairobi – Paris – Rome

In all of the above cities, WHO has selected and agreed rates with selected properties. WHO travellers going to any of these cities must stay at one of the preferred hotels:

The list of available hotels and descriptions at each location are accessible using the following link: <https://hoteldirectory.lanyon.com/Login.aspx?authToken=6fc76fd9-fe20-47f0-88d4-e2c7bf10408f>.

As a result of the preferential room rates in the selected hotels, travellers to these cities will receive an adjusted DSA.

SWITZERLAND

Applicable rates

WHO will pay a daily subsistence allowance (DSA), according to the official WHO daily subsistence allowance rates in force, at the date of the Travel, as per current policy, up to a maximum ceiling of CHF 3,000 per month, i.e. per consecutive periods of 30 calendar days. The DSA would then be applied at a rate of CHF 100 per extra day during my assignment and for travel time from my place of residence to Switzerland and return, except for the last day of travel (for which no DSA will be paid). An allowance of 50% of the DSA applicable to the city of departure will be paid to travellers for an overnight stay on an airplane. An additional travel allowance of US\$ 47 per city of departure and arrival, and return* to cover miscellaneous expenses and local transport will also be paid.

Other provisions:

- a. Only one month's DSA will be advanced to me at a time. The following month's DSA will only be advanced if I provide WHO, proof of accommodation charges incurred (*such as copy of a hotel booking, proof of payment, or other suitable evidence*) for the previous TR period.
- b. Any excess DSA paid will be adjusted on the next Travel Request (TR).
- c. The final month's DSA will only be paid once accommodation receipts have been received by WHO, evidencing the DSA entitlement for all prior months.
- d. Travel Claim(s) will be submitted if an adjustment to the previously paid amount on TR

needs to be made.

- e. If DSA has been paid for the city where I am assigned primarily, DSA paid for any travel to another duty station during the same period must be adjusted to ensure that no double payment occurs, and DSA already paid must be deducted if I take leave for personal reasons during the period.

I agree and accept that the total allowance as described above is intended to cover all costs related to my assignment, such as accommodation, meals and all other incidental expenses. Accordingly, charges for airport taxes, ground transportation from airport to hotel or vice versa will not be separately reimbursed, and I am not required to submit a travel claim.

WHO policy on the reimbursement of accommodation depends upon proof of accommodation charges incurred (such as copy of a hotel booking/commercial establishment, proof of payment, or other suitable evidence) for the previous TR period. Or whether the traveller makes his or her own private arrangements and does not incur lodging costs. Travellers staying in a hotel will receive the full applicable DSA; travellers that do not incur expenses for lodging will receive 50% of the applicable DSA rate.

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* *The travel allowance for New York is \$ 78.*

For a return trip, travel allowances are payable on both ways. e.g. departure Washington - \$47, arrival Geneva - \$47, departure Geneva - \$47, arrival Washington - \$47, total travel allowance - US\$ 188)

Agenda and List of Participants

**Meeting of the Advisory Committee on Immunization
and Vaccines-related Implementation Research (IVIR-AC)**

Microsoft Teams - Virtual Meeting
WHO Headquarters, Geneva, Switzerland
30 August -3 September 2021



Background reading materials available at:

[Meeting of the Advisory Committee on Immunization and Vaccines-related Implementation Research \(IVIR-AC\)](#)

Chair: Walt Orenstein

30 August				
Duration	Title	Content	Purpose	Proposed speaker
12:00 - 12:05 5'	Opening of Meeting	<ul style="list-style-type: none"> Update on global strategies and issues of relevance to WHO 	For information	K O Brien, Director, Department of Immunization, Vaccines and Biologicals
12:05 - 12:15 10'	Introduction/ Objectives of the meeting	<ul style="list-style-type: none"> Administrative issues Objectives of IVIR-AC meeting and outline of the 1st day 		P Lambach W Orenstein
COVID 19 vaccine impact modelling				
12:15 - 12:30 15'	Background	<ul style="list-style-type: none"> This session serves to discuss the multiple efforts that have been made in follow up to last IVIR-AC meeting's session on COVID 19 vaccine modelling 		R Hutubessy, S Pallas, N Grassly

		<ul style="list-style-type: none"> • Eight research groups identified in a previously published RfP will briefly present their work on the five RfP topics to IVIR-AC: <ul style="list-style-type: none"> ○ Topic I: Vaccination strategies to maximize in-person schooling provision ○ Topic II: Vaccination strategies to keep health system use below maximum capacity ○ Topic III: Importation into settings with no cases and outbreak response vaccination ○ Topic IV. Extent to which vaccination can allow non-pharmaceutical interventions to be lifted ○ Topic V. Strategies to maximize impact of available supply of vaccines (dose interval, targeting products to different priority groups) <p>Background reading materials: Eight groups' deliverables (see SharePoint)</p> <ul style="list-style-type: none"> • Expectations of IVIR-AC <ul style="list-style-type: none"> ○ To provide feedback on each group's work ○ To provide feedback on key messages to SAGE across the modeling groups for each of the 5 topics ○ To provide recommendations on the type and degree of future modeling support that may be needed to inform SAGE, WHO/IVB, and country COVID-19 vaccination decision making through 2022 and how to organize such support (e.g., modeling network/consortium/hub, individual modeling groups contracted for ad hoc questions, integrate with other efforts such as VIMC or WHO essential service modeling hub) 	<p>For discussion</p>	
<p>12:30 - 12:50 20'</p>	<p>Topics II (health system capacity), III (settings with no cases), IV (lifting NPIs)</p>	<ul style="list-style-type: none"> • Anticipating combined impacts of vaccines and PHSMs following SARS-CoV-2 introduction into low burden settings • 10 minutes Q&A 		<p>J McVernon, U. of Melbourne</p>

12:50-13:10 20'	Topics II (health system capacity), IV (lifting NPIs)	<ul style="list-style-type: none"> • Impact of vaccination and natural immunity in the context of other public health and social measures in high incidence countries of the Indo-Pacific • 10 minutes Q&A 		E McBryde, James Cook University
13:10-13:30 20'	Topics I (schools), II (health system capacity), III (settings with no cases)	<ul style="list-style-type: none"> • Prioritization of vaccines in Kenya, Zimbabwe and Vietnam to maintain health systems, keep schools open and prevent outbreaks • 10 minutes Q&A 		N Scott, Burnet Institute
13:30 - 13:40 10'	Break			
13:40-14:00 20'	Topics I (schools), II (health system capacity), IV (lifting NPIs)	<ul style="list-style-type: none"> • Network and agent-based models for school reopening and vaccination-NPI interaction in the context of India • 10 minutes Q&A 	For discussion	G Menon, Ashoka University
14:00-14:20 20'	Topics II (health system capacity), IV (lifting NPIs), V (dose interval)	<ul style="list-style-type: none"> • Modelling the Impact of COVID-19 Vaccination Strategies across Income Settings to Inform Global Strategy Development • 10 minutes Q&A 		A Hogan, Imperial College London
14:20-14:40 20'	Topics V (dose interval, product targeting)	<ul style="list-style-type: none"> • Modelling COVID-19 vaccination strategies: optimising dosing intervals and roll-out scenarios • 10 minutes Q&A 		Y Liu, LSHTM
14:40 - 14:50 10'	Break			
14:50-15:10 20'	Topics II (health system capacity), IV (lifting NPIs), V (dose interval)	<ul style="list-style-type: none"> • Modeling the impact of COVID-19 vaccination in LMICs amidst relaxation of non-pharmaceutical interventions and variant transmission • 10 minutes Q&A 	For discussion	A Kraay, Emory University
15:10-15:30 20'	Topics II (health system capacity), IV (lifting NPIs)	<ul style="list-style-type: none"> • Modelling impact of COVID-19 vaccination strategies in six Latin American countries 		A Lopez Osornio & A Pichon Riviere, IECS

		<ul style="list-style-type: none"> 10 minutes Q&A 		
15:30-16:00 30'	Q&A and discussion	<ul style="list-style-type: none"> IVIR-AC discusses issues across presentations, clarifies on content and acknowledges main issues 		J Leask, S Verguet, JD Lelièvre
16:00 - 16:10 10'	Wrap up	<ul style="list-style-type: none"> Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session 	For information	W Orenstein, Chair

31 August

Duration	Title	Content and key questions to IVIR-AC	Purpose	Proposed speaker
12:00 - 12:05 5'	Introduction	<ul style="list-style-type: none"> Recap of previous day and objectives for the day 	For information	W Orenstein, Chair
CDC Measles immunity profiles				
12:05 - 12:15 10'	Background	<ul style="list-style-type: none"> Gavi, WHO Regions and the Measles Outbreak Strategic Response Plan are all relying on CDC Immunity Profiles as a component of their country risk assessment. This methodology may be transferred to WHO in future. IVIR-AC is asked to review, comment upon and validate the methodology applied to assessing the risk of measles at country level. 	For information	N Crowcroft
12:15 - 12:35 20'	Interim update on progress with revised measles CFR estimates	<ul style="list-style-type: none"> CDC will present a static methodology to calculate susceptible populations based on coverage. Penn State will present a SIR model using surveillance data and population mixing patterns in addition to coverage data. <p>Background reading materials: see SharePoint</p>		Xi Li, M Ferrari
12:35 – 12:55 20'	Q&A and discussion to inform IVIR-AC recommendations	<ul style="list-style-type: none"> IVIR-AC discusses presentation, clarifies on content and acknowledges main issues 		P Luz, X Wang



**World Health
Organization**

12:55 - 13:05 10'	Wrap up	<ul style="list-style-type: none">Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session	For information	W Orenstein, Chair
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1 September				
12:00 - 12:05 5'	Introduction	<ul style="list-style-type: none"> Recap of previous day and objectives for the day 	For information	W Orenstein, Chair
Review of vaccine delivery cost projection				
12:05 - 12:10 5'	Background	<ul style="list-style-type: none"> Summary of previous recommendations by IVIR-AC Findings from consensus statement on existing vaccine guidance for retrospective costing Gaps identified 	For recommendation	K Yeung
12:10 - 12:30 20'	Technical presentation	<ul style="list-style-type: none"> Protocol of literature review on vaccine delivery cost projection and development of guidance Background reading materials: see SharePoint 		A Levin
12:30 - 13:00 30'	Q&A and Discussion	<ul style="list-style-type: none"> Is the literature review protocol an appropriate approach to review vaccine delivery cost projection? Is there a need to develop a guidance on vaccine delivery cost projection? 		M Jit and H Habib
13:00 - 14:00 60'	Break			
CAPACITI				
14:00 - 14:10 10'	Background	<ul style="list-style-type: none"> Update on the CAPACITI project and priorities moving forward; Background on the 'Decision Making Resource Catalogue': <ul style="list-style-type: none"> Identified country-level gaps in using the CAPACITI decision-support tool concern i) the selection of decision criteria and ii) selecting the most appropriate evidence sources. The Decision Making Resource Catalogue aims to strengthen criteria selection and identification of high-quality evidence and is a repository of already existing tools, databases, and reports. 	For information	M Jansen

		<ul style="list-style-type: none"> ○ An IVIR-AC subgroup provided feedback on user-friendliness, completeness and correctness of resource mapping. ○ The subgroup is now presenting their findings for information to the plenary. 		
14:10 - 14:20 10'	Decision Making Resource Catalogue	<ul style="list-style-type: none"> ● Presentation of the Decision Making Resource Catalogue, the IVIR-AC subgroup feedback, and revisions made to address the feedback. <p>Background reading materials: Decision Making Resource Catalogue (Excel) see Sharepoint</p>		D Spasenoska
14:20 - 14:40 20'	Q&A and Discussion	<ul style="list-style-type: none"> ● IVIR-AC discusses presentation, clarifies on content and acknowledges main issues 		D Lyimo, V Pitzer
14:40 - 14:50 10'	Wrap up	<ul style="list-style-type: none"> ● Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session 	For information	W. Orenstein, Chair

2 September

IA2030				
12:05 - 12:15 10'	Background	<ul style="list-style-type: none"> The first iteration of IA2030 vaccine impact estimates (number of future deaths averted due to immunization from 2021-2030) has been generated for Impact Goal indicator 1.1. of IA2030 Monitoring and Evaluation framework as well as for advocacy. There is an ongoing effort to validate the estimates, conduct a more comprehensive uncertainty analysis and expand the scope of work to fully capture the impact of vaccination on mortality reduction (number of future deaths averted) in the coming decade. 	For information	Y Sim
12:15 – 12:35 20'	Technical presentation	<ul style="list-style-type: none"> To respond to the previous IVIR-AC recommendations, the project team will present the current status of work on validation of the first iteration of estimates for high income countries and uncertainty analysis. The team would like to request feedback from IVIR-AC members. Questions for IVIR-AC: How can we improve our methods for propagating uncertainty? Are there effective alternatives to draw-level estimation? How should we interpret/communicate about the meaning of the uncertainty in our estimates given our data, methods, and purpose? What criteria should we use for selecting the vaccines to focus on as part of the HIC validation? How best can we standardize across time periods, measures of impact and levels of underlying burden? <p>Background reading materials: See SharePoint</p>		W Msemburi, A Carter
12:35 - 12:55 20'	Q&A and Discussion	<ul style="list-style-type: none"> IVIR-AC discusses presentation, clarifies on content and acknowledges main issues 		S Verguet and J Wu
12:55 - 14:00	Break			

60'				
VIMC				
14:00 - 14:10 10'	Background	<ul style="list-style-type: none"> This for information session serves to update the IVIRAC on new models and ongoing projects of VIMC 	For information	R Hutubessy /Y Sim
14:10 - 14:20 10'	Presentation on updates	<ul style="list-style-type: none"> Update the IVIRAC on ongoing projects of VIMC <p>Background reading materials: See SharePoint</p>		K Gaythorpe
14:20 - 14:40 20'	Q&A and Discussion	<ul style="list-style-type: none"> IVIR-AC discusses presentation, clarifies on content and acknowledges main issues 		J Wu and JD Lelièvre
14:40 - 14:50 10'	Wrap up	<ul style="list-style-type: none"> Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session 	For information	W. Orenstein, Chair

3 September

Closed session: IVIR-AC members only

12:00 - 16:00	IVIR-AC reporting/recommendations
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**Meeting of the Advisory Committee on Immunization and
Vaccines-related Implementation Research (IVIR-AC)**

Microsoft Teams - Virtual Meeting

WHO Headquarters, Geneva, Switzerland

30 August - 3 September 2021

Draft list of participants

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WER summary of last IVIRAC



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Meeting of the Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC), March 2021

The IVIR-AC recommendations are based on discussions during a virtual meeting of the IVIR-AC held 1–5 March 2021.

COVID-19 vaccine modelling

The WHO COVID-19 Vaccine Impact Modelling Subgroup of the WHO Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on COVID-19 Vaccines provides modelling guidance to inform global policy recommendations related to prioritization of COVID-19 vaccines. In September 2020, IVIR-AC reviewed an initial set of modelling questions developed by the Subgroup. These were part of a Request for Information that was shared with modelling groups which have since presented work on these topics to the SAGE Working Group and Subgroup. In January 2021, the Subgroup issued a Request for Proposals (RFP) that addressed priority questions and gaps in modelling evidence. The results of the RFP, expected in mid-2021, will enable SAGE to further develop vaccine product-specific guidance and policy recommendations. To inform this process, IVIR-AC was asked to identify additional priority areas for vaccine modelling and ways to incorporate additional evidence into the SAGE *Evidence to Recommendations* (E2R) process.¹

¹ Evidence to recommendations for COVID-19 vaccines: evidence framework (<https://www.who.int/publications/item/WHO-2019-nCoV-SAGE-Framework-Evidence-2020-1>; accessed March 2021).

Réunion du Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC), mars 2021

Les recommandations de l'IVIR-AC présentées ici sont basées sur les discussions qui ont eu lieu lors d'une réunion virtuelle du Comité qui s'est tenue du 1^{er} au 5 mars 2021.

Modélisation des vaccins contre la COVID-19

Le sous-groupe de l'OMS chargé de la modélisation de l'impact des vaccins anti-COVID-19 au sein du groupe de travail sur les vaccins anti-COVID-19 du Groupe stratégique consultatif d'experts de l'OMS (SAGE) sur la vaccination fournit des conseils en matière de modélisation afin d'éclairer les recommandations stratégiques mondiales relatives à l'établissement des priorités de vaccination contre la COVID-19. En septembre 2020, l'IVIR-AC a examiné une première série de questions de modélisation préparées par le sous-groupe. Celles-ci faisaient partie d'une demande d'information partagée avec des groupes de modélisation qui ont depuis présenté des travaux sur ces sujets au groupe de travail et au sous-groupe du SAGE. En janvier 2021, le sous-groupe a émis un appel à propositions visant à répondre aux questions prioritaires et à combler les lacunes dans les données de modélisation. Les résultats de cet appel à propositions, attendus pour le milieu de l'année 2021, permettront au SAGE de poursuivre l'élaboration d'orientations et de recommandations stratégiques spécifiques aux différents vaccins. A cette fin, il a été demandé à l'IVIR-AC d'identifier d'autres domaines prioritaires pour la modélisation des vaccins et des moyens d'intégrer des données probantes supplémentaires dans le processus du SAGE pour élaborer des recommandations à partir des preuves scientifiques (*Evidence to Recommendations*).¹

¹ Evidence to recommendations for COVID-19 vaccines: evidence framework (<https://www.who.int/publications/item/WHO-2019-nCoV-SAGE-Framework-Evidence-2020-1>; consulté en mars 2021).

Summary of IVIR-AC feedback and recommendations

IVIR-AC commended the tremendous work of the Subgroup in summarizing the outputs from 30 different modelling groups and confirmed that the modelling supports vaccine prioritization as described in the SAGE Roadmap.²

IVIR-AC recommended:

- for SAGE to modify the E2R tables to enable product comparisons, to use product-specific characteristics in models, and to consider prioritizing products for specific populations or countries on the basis of modelled parameters and feasibility of implementation;
- inclusion of additional modelling questions;³
- evaluation of the models' suitability for addressing particular questions and consideration of including more diverse model types (e.g. immune dynamics or population genetics);
- modelling the impact of new variants, prioritizing vaccine effectiveness, and including feasibility of vaccine implementation when determining vaccine formulation priorities;
- maintaining ongoing surveillance systems that collect high-quality data on duration of immunity, vaccine-specific effectiveness, and short- and long-term vaccine safety issues; and
- improving and informing models by filling the evidence gap on social and behavioural drivers of vaccination and interventions to address these (non-pharmaceutical interventions).

Optimizing COVID-19 vaccine costing

The E2R "resource use" criterion required as part of COVID-19 vaccine-specific recommendations utilized by SAGE presents several challenges. IVIR-AC provided feedback on how best to interpret and apply the criterion to global and country-level costing for decision-making on COVID-19 vaccination. IVIR-AC also discussed the most appropriate approaches/tools for estimation of COVID-19 vaccine-related costs.

Résumé des observations et des recommandations de l'IVIR-AC

L'IVIR-AC a salué le travail considérable accompli par le sous-groupe pour résumer les résultats de 30 groupes de modélisation différents et a confirmé que la modélisation aide à l'établissement des priorités de vaccination tel que décrit dans la feuille de route du SAGE.²

L'IVIR-AC a recommandé:

- au SAGE de modifier les tableaux des recommandations élaborées à partir des preuves scientifiques de manière à pouvoir comparer les produits, d'utiliser les caractéristiques spécifiques des différents produits dans les modèles, et d'envisager la priorisation des produits pour des populations ou des pays particuliers sur la base des paramètres modélisés et de la faisabilité de la mise en œuvre;
- d'intégrer des questions de modélisation supplémentaires;³
- d'évaluer l'aptitude des modèles à répondre à des questions particulières et d'envisager la possibilité d'inclure des types de modèles plus divers (par exemple la dynamique immunitaire ou la génétique des populations);
- de modéliser l'impact des nouveaux variants, de hiérarchiser l'efficacité vaccinale et de prendre en compte de la faisabilité de leur mise en œuvre lors de la détermination des priorités en matière de formulations des vaccins;
- de maintenir des systèmes de surveillance continue qui collectent des données de qualité sur la durée de l'immunité, sur l'efficacité spécifique des différents vaccins et sur la sécurité des vaccins à court et à long terme; et
- d'améliorer et d'alimenter les modèles grâce au recueil de données probantes, actuellement insuffisantes, sur les facteurs sociaux et comportementaux de la vaccination et les interventions nécessaires pour y répondre (interventions non pharmaceutiques).

Optimisation de l'établissement des coûts de la vaccination contre la COVID-19

Le critère «utilisation des ressources» des recommandations élaborées à partir des preuves scientifiques, requis dans le cadre des recommandations spécifiques aux différents vaccins anti-COVID-19 et utilisé par le SAGE, pose plusieurs difficultés. L'IVIR-AC a présenté ses observations sur la meilleure façon d'interpréter et d'appliquer ce critère au calcul des coûts aux niveaux mondial et national en vue de la prise de décisions concernant la vaccination contre la COVID-19. Le Comité a également discuté des approches/outils les plus appropriés pour estimer ces coûts.

² WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply (<https://www.who.int/publications/m/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply>; accessed March 2021).

³ For instance: What are the effects of prior infection on vaccine efficacy? What is the acceptable lower limit of vaccine effectiveness for specific priority groups? What is the impact of vaccine hesitancy at the national level? What is the appropriate vaccination strategy for settings with no cases? In the context of supply shortages for 2-dose vaccines, should the focus be on vaccinating as many people as possible with one dose or preserving the vaccine supply to ensure that the second dose can be administered at the recommended interval? What is the benefit and immunological impact of alternative dosing strategies (e.g. 6-month booster), based on clinical evidence of waning immunity? What is the best dosing combination?

² Feuille de route du SAGE de l'OMS pour l'établissement des priorités concernant l'utilisation des vaccins anti-Covid-19 dans un contexte d'approvisionnement limité (<https://www.who.int/fr/publications/m/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply>; consulté en mars 2021).

³ Par exemple: Quels sont les effets d'une précédente infection sur l'efficacité des vaccins? Quelle est la limite inférieure acceptable de l'efficacité vaccinale pour des groupes prioritaires donnés? Quel est l'impact de la réticence à la vaccination au niveau national? Quelle stratégie de vaccination envisager pour les milieux où il n'y a pas de cas? Dans le contexte d'une pénurie de vaccins nécessitant l'administration de 2 doses, faut-il privilégier la vaccination du plus grand nombre de personnes possible avec une seule dose ou gérer le stock de vaccins de manière à pouvoir administrer la seconde dose à l'intervalle recommandé? Quels sont les avantages et l'impact immunologique d'autres stratégies de vaccination (par exemple une dose de rappel tous les 6 mois), d'après les données cliniques disponibles sur la baisse de l'immunité? Quelle est le meilleur schéma posologique?

Summary of IVIR-AC feedback and recommendations

IVIR-AC stressed that the health sector perspective alone is not sufficient to decide vaccine rollout as it will not capture the macroeconomic impact of COVID-19. Consequently, the Advisory Committee recommended:

- to evaluate, interpret and communicate COVID-19 vaccine resources needed within the context of broader cost implications (e.g. global economic impact estimated at US\$ 28 trillion by the International Monetary Fund);
- to consider the breadth of health system's constraints and cost implications; and
- to account for health systems strengthening, at least within the discussion of benefits (including the potential for enhanced testing and treatment, and for strengthening non-COVID-19 essential services).

IVIR-AC provided guidance on estimation approaches and tools, as follows:

- Collect and analyse detailed, case-relevant costs (e.g. delivery and human resources costs) for country-level decision-making.
- Prioritize the use of different types of cost estimates for global-level resource mobilization and budgeting.
- Consider the substantial budget impact in low- and middle-income countries (LMICs), including health system constraints such as limited human resources (in both numbers and skills) and physical infrastructure for vaccine delivery (e.g. cold chain capacity, vaccination sites).
- Consider the potential opportunity costs of vaccine rollout – i.e. that vaccination can significantly take human resources away from their regular duties and may jeopardize the maintenance of essential health services in the short term.
- Consider how COVID-19 vaccination can help strengthen local health systems, including, for instance: the development of adult immunization delivery platforms; the development of responsive testing, diagnosis and treatment capacity; and the strengthening of non-COVID essential services (e.g. current Expanded immunization programmes) in the long term.

IVIR-AC highlighted the importance of cost and resource estimates within economic evaluations at the local, country level, which will depend on local vaccine prices, coverage targets, vaccine delivery strategies (e.g. campaign vs. routine delivery), human resources implications, and cold chain maintenance investments.

Résumé des observations et des recommandations de l'IVIR-AC

L'IVIR-AC a souligné que la perspective du secteur de la santé ne suffit pas à elle seule pour décider du déploiement des vaccins, car elle ne permet pas de saisir l'impact macroéconomique de la COVID-19. Par conséquent, le Comité a recommandé:

- d'évaluer, d'interpréter et de communiquer les ressources nécessaires pour la vaccination contre la COVID-19 en tenant compte d'incidences financières plus larges (par exemple l'impact économique mondial estimé à 28 billions de dollars américains par le Fonds monétaire international);
- de prendre en considération l'étendue des contraintes des systèmes de santé et les incidences financières pour ces derniers;
- de tenir compte du renforcement des systèmes de santé, au moins dans le cadre du débat sur les avantages (notamment la possibilité d'améliorer le dépistage et le traitement, et de renforcer les services essentiels non liés à la COVID-19).

L'IVIR-AC a fourni les conseils suivants concernant les approches et les outils d'estimation des coûts:

- recueillir et analyser les coûts détaillés et pertinents à la situation (par exemple les coûts de la délivrance et des ressources humaines) aux fins de la prise de décisions au niveau national;
- établir des priorités dans l'utilisation de différents types d'estimations des coûts en vue de la mobilisation des ressources et la budgétisation au niveau mondial;
- tenir compte de l'impact budgétaire important dans les pays à revenu faible et intermédiaire, notamment en raison des contraintes des systèmes de santé telles que des ressources humaines limitées (en termes d'effectifs et de compétences) et de l'infrastructure nécessaire pour la délivrance des vaccins (par exemple la chaîne du froid, les sites de vaccination);
- tenir compte des coûts d'opportunité potentiels du déploiement des vaccins: la vaccination peut en effet détourner notablement les ressources humaines de leurs tâches habituelles et peut compromettre le maintien des services de santé essentiels à court terme;
- examiner la manière dont la vaccination contre la COVID-19 peut contribuer à renforcer les systèmes de santé locaux, par exemple par la mise en place de plateformes de vaccination des adultes; le développement de capacités réactives de dépistage, de diagnostic et de traitement; et le renforcement des services essentiels non liés à la COVID-19 (par exemple les programmes élargis de vaccination actuels) sur le long terme;

L'IVIR-AC a souligné l'importance des estimations des coûts et des ressources dans les évaluations économiques locales et nationales, qui dépendront des prix des vaccins au niveau local, des objectifs de couverture, des stratégies d'administration des vaccins (campagnes de vaccination ou vaccination systématique par exemple), des incidences en termes de ressources humaines et des investissements dans la chaîne du froid.

Measles case fatality ratios

Until now, static age- and country-specific case fatality ratios (CFRs), established by expert opinion and informed by a review of CFR studies in LMICs,⁴ have provided the basis for WHO's measles mortality estimates. The review consists of literature with known limitations, including varying case definitions and a lack of representativeness among countries. Newer approaches include a predictive model to estimate CFRs, as outlined in an updated review.⁵ To further optimize CFR estimation, the London School of Hygiene and Tropical Medicine presented a new methodology that builds on the updated review utilizing a Bayesian meta-regression platform with spatial disaggregation. IVIR-AC was asked to advise how best to leverage current methods and to give feedback on fixed versus dynamic model trade-offs, additional primary data needs, future approaches for best outputs, and how to navigate plans for estimates in the short term and beyond.

Summary of IVIR-AC feedback and recommendations

Welcoming the extensive literature review and development of a new methodology, IVIR-AC:

- stated that continued updating of the model/data as new studies become available is challenging but necessary;
- strongly recommended that funds and human resources be made available to support the ongoing literature and data review, model developments and generation of CFRs, predictions and projections;
- agreed there is little value in static age- and country-specific CFRs, and that time-varying and updatable CFRs are needed with incidence terms informed by dynamic models; and
- noted that time-varying CFRs will be sensitive to covariate selection and parameter estimates, which may present future methodological challenges.

With respect to the covariates that inform CFR modeling, IVIR-AC supported:

- a clear rationale for covariates that have an explicit link to CFRs and that represent poverty and socioeconomic inequalities;

Taux de létalité due à la rougeole

Jusqu'à présent, les estimations OMS de la mortalité due à la rougeole reposaient sur les taux de létalité statiques selon l'âge et le pays, établis par des experts et éclairés par une revue des études sur les taux de létalité dans les pays à revenu faible et intermédiaire.⁴ Cette revue porte sur la littérature dont les limites sont connues, notamment des définitions de cas variables et un manque de représentativité parmi les pays. Les approches plus récentes comprennent un modèle prédictif pour estimer les taux de létalité, comme décrit dans une revue actualisée.⁵ Pour optimiser davantage l'estimation des taux de létalité, la London School of Hygiene and Tropical Medicine a présenté une nouvelle méthode qui s'appuie sur la revue actualisée en utilisant une plateforme de méta-régression bayésienne avec désagrégation spatiale. Il a été demandé à l'IVIR-AC de fournir des conseils sur la meilleure façon d'exploiter les méthodes actuelles et de faire des observations sur les compromis entre modèles fixes et dynamiques, sur les besoins supplémentaires en données primaires, sur les approches futures pour obtenir les meilleurs résultats, et sur la façon de guider les plans pour obtenir des estimations à court terme et au-delà.

Résumé des observations et des recommandations de l'IVIR-AC

Se félicitant de cette revue approfondie de la littérature et de l'élaboration d'une nouvelle méthode, l'IVIR-AC:

- a indiqué que l'actualisation continue du modèle et des données au fur et à mesure que de nouvelles études deviennent disponibles est difficile mais nécessaire;
- a fortement recommandé que des fonds et des ressources humaines soient mis à disposition pour appuyer la revue continue de la littérature et des données, le développement de modèles et la génération des taux de létalité, des prédictions et des projections;
- est convenu que les taux de létalité statiques selon l'âge et le pays ont peu d'intérêt et que des taux de létalité variables dans le temps et actualisables sont nécessaires avec des éléments d'incidence éclairés par des modèles dynamiques; et
- a noté que les taux de létalité variables dans le temps seront sensibles au choix des covariables et aux estimations des paramètres, ce qui pourrait poser des difficultés méthodologiques futures.

En ce qui concerne les covariables utiles à la modélisation des taux de létalité, l'IVIR-AC est favorable à:

- une justification claire des covariables qui ont un lien explicite avec les taux de létalité et qui représentent la pauvreté et les inégalités socio-économiques;

⁴ Wolfson LJ et al. Estimates of measles case fatality ratios: a comprehensive review of community-based studies. *Int J Epidemiol.* 2009;38(1):192–205 (<https://pubmed.ncbi.nlm.nih.gov/19188207/>; accessed March 2021).

⁵ Portnoy A et al. Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis. *Lancet Glob Health.* 2019;7(4):E472–81 ([https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(18\)30537-0/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30537-0/fulltext); accessed March 2021).

⁴ Wolfson LJ et al. Estimates of measles case fatality ratios: a comprehensive review of community-based studies. *Int J Epidemiol.* 2009;38(1):192–205 (<https://pubmed.ncbi.nlm.nih.gov/19188207/>; consulté en mars 2021).

⁵ Portnoy A et al. Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis. *Lancet Glob Health.* 2019;7(4):E472–81 ([https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(18\)30537-0/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30537-0/fulltext); consulté en mars 2021).

- possible use of 1) a theoretical model of causal factors that influence disease incidence and progression, and 2) geographical and other markers which represent the most vulnerable populations; and
- possible inclusion of covariates on the short-versus long-term impact of COVID-19 on health-care capacity and the impact on vaccination coverage.

Noting the need for ongoing primary empirical data collection, IVIR-AC encouraged:

- acknowledgement of the importance of vitamin A therapy on CFRs;
- investments in strengthening outbreak investigation and evaluation activities to generate additional primary data;
- creation of a standard CFR study protocol and a structured data collection tool to improve comparability of studies;
- development of a unified research protocol; and
- validation of model predictions against new CFR estimates.

For future approaches IVIR-AC recommended:

- transparency and availability of flexible/analytical methods with user-friendly R⁶ packages, clear documentation in a newsletter including bug fixes, discussion forums and case studies; and
- documentation/publication of the methodology in open access peer-reviewed journals.

Overview of the Vaccine Impact Modelling Consortium

The *Vaccine Impact Modelling Consortium* (VIMC)⁷ is a multinational collaboration of 16 research groups funded by Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation (BMGF). The consortium aims to deliver a more sustainable, efficient and transparent approach to generating estimates of disease burden and vaccine impact. They published a comprehensive modelling study⁸ and data visualization tool⁹ on the impact of vaccination against 10 pathogens in 98 LMICs. The VIMC collaborates with WHO on the *Immunization Agenda 2030 (IA 2030) Vaccine Impact Estimates* and on COVID-19-related projects, including modelling the impact of interruptions in routine and supplementary immunizations on vaccine preventable diseases (VPDs) in the context of COVID-19.

- l'utilisation éventuelle 1) d'un modèle théorique de facteurs de causalité qui influent sur l'incidence et la progression de la maladie, et 2) de marqueurs géographiques et autres qui représentent les populations les plus vulnérables; et
- l'inclusion éventuelle de covariables pour l'impact à court et à long terme de la COVID-19 sur les capacités des soins de santé et sur la couverture vaccinale.

Notant la nécessité d'un recueil continu de données empiriques primaires, l'IVIR-AC a encouragé:

- la prise en compte de l'importance du traitement par la vitamine A pour les taux de létalité;
- des investissements pour renforcer les activités d'investigation et d'évaluation des épidémies afin de générer des données primaires supplémentaires;
- l'élaboration d'un protocole standard pour les études sur les taux de létalité et d'un outil de recueil de données structuré pour améliorer la comparabilité des études;
- l'élaboration d'un protocole de recherche unifié; et
- la validation des prédictions du modèle par rapport aux nouvelles estimations des taux de létalité.

Pour les approches futures, l'IVIR-AC a recommandé:

- la transparence et la disponibilité de méthodes souples/analytiques avec des paquets R⁶ faciles à utiliser, une documentation claire rassemblée dans un bulletin comprenant des corrections de bugs, des forums de discussion et des études de cas; et
- la documentation/publication de la méthode dans des revues à comité de lecture en libre accès.

Aperçu du Vaccine Impact Modelling Consortium

Le *Vaccine Impact Modelling Consortium*⁷ est une collaboration multinationale de 16 groupes de recherche financés par l'Alliance Gavi et la Fondation Bill & Melinda Gates. Ce Consortium vise à fournir une approche plus durable, efficace et transparente de la génération des estimations de la charge de morbidité et de l'impact des vaccins. Il a publié une étude de modélisation⁸ et un outil de visualisation des données⁹ sur l'impact de la vaccination contre 10 agents pathogènes dans 98 pays à revenu faible et intermédiaire. Le Consortium collabore avec l'OMS sur les estimations de l'impact des vaccins dans le cadre du *Programme pour la vaccination à l'horizon 2030* et sur des projets liés à la COVID-19, notamment la modélisation de l'impact des interruptions de la vaccination systématique et des activités de vaccination supplémentaire sur les maladies à prévention vaccinale dans le contexte de la COVID-19.

⁶ See <https://www.r-project.org/> (accessed March 2021).

⁷ See <https://www.vaccineimpact.org/> (accessed March 2021).

⁸ Li X et al. Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study. *Lancet*. 2021;397(10272):398–408 ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32657-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32657-X/fulltext); accessed March 2021).

⁹ See <https://montagu.vaccineimpact.org/2020/visualisation/> (accessed March 2021).

⁶ Voir <https://www.r-project.org/> (consulté en mars 2021).

⁷ Voir <https://www.vaccineimpact.org/> (consulté en mars 2021).

⁸ Li X et al. Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study. *Lancet*. 2021;397(10272):398–408 ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32657-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32657-X/fulltext); consulté en mars 2021).

⁹ Voir <https://montagu.vaccineimpact.org/2020/visualisation/> (consulté en mars 2021).

Summary of IVIR-AC feedback and recommendations

While IVIR-AC members acknowledged VIMC's main objective being to provide GAVI¹⁰ and the Bill & Melinda Gates Foundation¹¹ with estimates of global vaccine impact, the committee still encouraged modelling of indirect impacts – particularly hospitalizations and immunizations – on the health-care system.

IVIR-AC suggested further clarification on:

- how the model accounts for early detection tools with vaccines such as human papillomavirus (HPV) and hepatitis B virus (HBV) which primarily impact adulthood;
- how to ensure that dynamic models are used for diseases for which herd immunity may be important; and
- any group of VPDs for which the effects of vaccinations in different years are interdependent.

IVIR-AC provided feedback on different methodological issues, namely:

VIMC supporting models:

The utility of the Impact Estimates (IE) method depends on how often coverage estimates are revised and the magnitude of changes in coverage.

General Strategy for VIMC:

Since it seems that IE would work only for small perturbations in coverage estimates, members of IVIR-AC asked whether simple analytics could be developed to check if IE is likely to be robust for a given revision of coverage. It would also be helpful to clarify whether mortality rates from United National World Population Prospects (UNWPP) have accounted for deaths due to VPDs when they are used in the VIMC calculations and to know the assumption regarding the impact of vaccines on death rates in UNWPP.

Interim estimates:

Proposed case study: Does IE provide robust approximation of the effect of coverage drop attributable to COVID-19?

Meta-analysis of economic evaluations

Meta-analyses (MA) are useful for quantitative pooling of results from multiple studies to create more reliable estimates of the effectiveness of an intervention. Application of this approach to economic evaluations (EE) is under consideration and may be useful in countries that lack the capacity to do their own cost-effectiveness (CE)

Résumé des observations et des recommandations de l'IVIR-AC

Si les membres de l'IVIR-AC ont reconnu que l'objectif principal du Consortium était de fournir à l'Alliance Gavi¹⁰ et à la Fondation Bill & Melinda Gates¹¹ des estimations de l'impact des vaccins à l'échelle mondiale, le Comité a néanmoins encouragé la modélisation des impacts indirects – en particulier les hospitalisations et les vaccinations – sur le système des soins de santé.

L'IVIR-AC a suggéré de clarifier plus avant:

- la manière dont le modèle tient compte des outils de détection précoce avec des vaccins tels que ceux contre le papillomavirus humain (PVH) et le virus de l'hépatite B (VHB) qui ont principalement un impact à l'âge adulte;
- la façon de s'assurer que des modèles dynamiques sont utilisés pour les maladies pour lesquelles l'immunité collective peut être importante; et
- les groupes de maladies à prévention vaccinale pour lesquels les effets des vaccinations à différents moments (années) sont interdépendants.

L'IVIR-AC a présenté des observations sur différentes questions méthodologiques, présentées ci-après.

Modèles pour le Consortium

L'utilité de la méthode pour établir les estimations d'impact dépend de la fréquence de la révision des estimations de la couverture et de l'ampleur de l'évolution de la couverture.

Stratégie générale pour le Consortium

Puisque les estimations d'impact semblent ne s'appliquer que pour des changements minimes dans les estimations de la couverture, les membres de l'IVIR-AC ont demandé s'il était possible de développer une méthode analytique simple pour vérifier la robustesse des estimations d'impact pour une révision donnée de la couverture. Il serait également utile de préciser si les taux de mortalité issus des United National World Population Prospects (UNWPP) ont pris en compte les décès dus aux maladies à prévention vaccinale lorsqu'ils sont utilisés dans les calculs du Consortium et de connaître l'hypothèse concernant l'impact des vaccins sur les taux de mortalité utilisée dans les UNWPP.

Estimations provisoires

Proposition d'étude de cas: Les estimations d'impact fournissent-elles une approximation robuste de l'effet de la baisse de la couverture attribuable à la COVID-19?

Méta-analyses des évaluations économiques

Les méta-analyses sont utiles pour le regroupement quantitatif des résultats de plusieurs études afin de créer des estimations plus fiables de l'efficacité d'une intervention. L'application de cette approche aux évaluations économiques est à l'étude et pourrait s'avérer utile dans les pays qui n'ont pas la capacité de réaliser leurs propres études coût-efficacité.

¹⁰ See <https://www.gavi.org/> (accessed March 2021).

¹¹ See <https://www.gatesfoundation.org/> (accessed March 2021).

¹⁰ Voir <https://www.gavi.org/> (consulté en mars 2021).

¹¹ Voir <https://www.gatesfoundation.org/> (consulté en mars 2021).

studies. However, the utility of MA for EE is subject to scientific debate following publication of the first methodology paper by Crespo *et al*¹² in 2014 and a systematic review on the use of MA for EE studies¹³ in 2019. IVIR-AC considered several examples (rotavirus vaccine, anticoagulants, diabetes medications) and provided feedback on the value and limitations of using MA for EE.

Summary of IVIR-AC feedback and recommendations

IVIR-AC agreed that:

- MA for EE could facilitate decision-making in countries without context-specific EEs.
- The EE literature is heterogeneous, highly dependent on input parameters, methodological and with modelling choices in each study, which can make it difficult for informing global-level decision-making and policy.
- MA of CE studies is not straightforward, as the incremental cost-effectiveness ratio (ICER) is not normally distributed, 95% confidence intervals for the ICER cannot be validly estimated, and interpretation of the ICER is not straightforward (e.g. a negative ICER could indicate a cost-saving or dominated strategy).

IVIR-AC recommended that:

- High-quality, locally-produced and context-/country-specific EE should be maintained as the priority for decision-making over MA for EE.

Harmonization of inputs across studies:

- Consistent currency years should be used for costs (e.g. 2021 \$).
- There should be a focus on scenarios in order to extract variance/covariance of incremental costs and incremental effectiveness separately.
- Caution is required when assuming that incremental effectiveness is distributed normally because this may not be the case for infectious disease interventions.
- Contextual differences in the stratification of EEs should be considered.

Toutefois, l'utilité des méta-analyses des évaluations économiques fait l'objet d'un débat scientifique depuis la publication du premier article méthodologique de Crespo *et al*.¹² en 2014 et d'une revue systématique sur l'utilisation des méta-analyses pour les études d'évaluations économiques¹³ en 2019. L'IVIR-AC a examiné plusieurs exemples (vaccin contre le rotavirus, anticoagulants, médicaments pour le diabète) et a présenté des observations sur la valeur et les limites de l'utilisation des méta-analyses pour les évaluations économiques.

Résumé des observations et des recommandations de l'IVIR-AC

L'IVIR-AC est convenu de ce qui suit:

- les méta-analyses des évaluations économiques pourraient faciliter la prise de décisions dans les pays ne disposant pas d'évaluations économiques spécifiques au contexte;
- la littérature sur les évaluations économiques est hétérogène et ces évaluations dépendent fortement des paramètres d'entrée, de la méthodologie et des choix de modélisation de chaque étude; l'exploitation de ces évaluations pour éclairer la prise de décisions et les politiques peut donc s'avérer difficile;
- les méta-analyses des études coût-efficacité ne sont pas simples, car le rapport coût-efficacité différentiel (ICER) ne suit pas une distribution normale, les intervalles de confiance à 95% pour l'ICER ne peuvent pas être estimés de manière valable, et l'interprétation de l'ICER est délicate (par exemple un ICER négatif peut indiquer une stratégie d'économie ou une stratégie dominée).

Recommandations de l'IVIR-AC:

- continuer à privilégier des évaluations économiques de qualité, produites localement et spécifiques au contexte/pays dans la prise de décisions par rapport aux méta-analyses des évaluations économiques.

Harmonisation des données d'entrée utilisées dans les études

- Utiliser des années monétaires cohérentes pour les coûts (par exemple \$ 2021).
- Mettre l'accent sur les scénarios afin d'extraire séparément la variance/covariance des coûts différentiels et de l'efficacité différentielle.
- Faire preuve de prudence lorsqu'on suppose que l'efficacité différentielle suit une distribution normale, car cela peut ne pas être le cas pour les interventions en matière de maladies infectieuses.
- Prendre en compte les différences contextuelles dans la stratification des évaluations économiques.

¹² Crespo C et al. Comparative efficiency research (COMER): meta-analysis of cost-effectiveness studies. *BMC Med Res Methodol.* 2014;14:139.

¹³ Systematic review journal: submitted 2019; *BMJ Open Diabetes Res Care.* 2020;8(1):e001020; *Open Forum Infect Dis.* 2019;6(4):ofz117; *Value Health.* 2019;22(12):1458–69.

¹² Crespo C et al. Comparative efficiency research (COMER): meta-analysis of cost-effectiveness studies. *BMC Med Res Methodol.* 2014;14:139.

¹³ Systematic review journal: submitted 2019; *BMJ Open Diabetes Res Care.* 2020;8(1):e001020; *Open Forum Infect Dis.* 2019;6(4):ofz117; *Value Health.* 2019;22(12):1458–69.

Synthesis of EE estimates:

- When pooling estimates of incremental net benefits across studies, the estimates should be unweighted or weighted by study quality instead of by inverse variance.
- Develop a grid of criteria for assessing study quality to enable quantitative assessment and weighting.
- Exclude poor-quality studies from sensitivity analyses.

Additional desirable outputs:

- Document and explain major sources of variation and heterogeneity in the CE/ICER estimates, as well as uncertainty about the selected sample of studies, in order to identify regions where more studies are needed.
- To the extent that it is feasible, provide estimates for typical country groupings.

As a “public good” IVIR-AC recommended:

- An open-access data-sharing repository should be created to gather all underlying inputs, data sources, codes and detailed documentation.
- Synergies with other efforts/groups should be considered.

Full Public Health Value of Vaccines – influenza vaccine

In order to inform the implementation of a seasonal influenza vaccine programme and to drive innovative research for next-generation influenza vaccines for LMICs, WHO aims to develop a Full Public Health Value of Vaccines (FPHVV) assessment for influenza vaccines. As a first step, WHO developed methods and approaches for developing use cases and country archetypes for seasonal influenza vaccine. IVIR-AC provided feedback on the overall methodology for developing and validating these draft use cases and country archetypes.

Summary of IVIR-AC feedback and recommendations

IVIR-AC agreed that:

- Country decision-making processes are relevant to consider and are unique to each country. Seasonal influenza vaccine is one of several new vaccines being recommended for introduction in many countries and for which principles and scenarios exist to guide both the decision-making and the process. Use cases and country archetypes are other innovative approaches.
- The approach to developing use cases addresses an important policy need and is important for informing country programme strategies, market-shaping

Synthèse des estimations des évaluations économiques

- Lors du regroupement des estimations des avantages nets différentiels issues des études, il convient de ne pas pondérer les estimations ou de les pondérer par la qualité de l'étude plutôt que par l'inverse de la variance.
- Elaborer une grille de critères d'évaluation de la qualité des études pour permettre une évaluation quantitative et une pondération.
- Exclure les études de mauvaise qualité des analyses de sensibilité.

Autres résultats souhaitables

- Documenter et expliquer les principales sources de variation et d'hétérogénéité dans les estimations des données coût-efficacité/ICER, ainsi que l'incertitude concernant l'échantillon d'études sélectionné, afin d'identifier les régions où davantage d'études sont nécessaires.
- Dans la mesure du possible, fournir des estimations pour des groupes de pays types.

Considérant qu'il s'agit d'un «bien public», l'IVIR-AC a recommandé:

- la création d'un référentiel de partage de données en libre accès pour rassembler tous les intrants sous-jacents, les sources de données, les codes et les documents détaillés;
- la mise en place de synergies avec d'autres travaux/groupes.

La pleine valeur des vaccins pour la santé publique – vaccin contre la grippe

Afin d'éclairer la mise en œuvre d'un programme de vaccination contre la grippe saisonnière et de stimuler une recherche innovante sur les vaccins antigrippaux de nouvelle génération pour les pays à revenu faible et intermédiaire, l'OMS cherche à mettre en place une évaluation de la pleine valeur des vaccins pour la santé publique concernant les vaccins antigrippaux. Dans un premier temps, l'OMS a élaboré des méthodes et des approches pour développer des scénarios d'utilisation et des archétypes de pays pour le vaccin contre la grippe saisonnière. L'IVIR-AC a fourni des observations sur la méthodologie globale de développement et de validation de ces projets de scénarios d'utilisation et d'archétypes de pays.

Résumé des observations et des recommandations de l'IVIR-AC

L'IVIR-AC est convenu de ce qui suit:

- il est pertinent de prendre en compte les processus de décision nationaux, qui sont propres à chaque pays. Le vaccin contre la grippe saisonnière est l'un des nombreux nouveaux vaccins dont l'introduction est recommandée dans de nombreux pays et pour lesquels il existe des principes et des scénarios pour guider à la fois la prise de décisions et le processus. Les scénarios d'utilisation et les archétypes de pays constituent d'autres approches innovantes;
- l'élaboration de scénarios d'utilisation répond à un besoin politique important et est très utile pour éclairer les stratégies des programmes nationaux, la structuration du

and possibly short-term product development. This approach should be undertaken. However, as the value proposition is developed further there will need to be clarification as to how the approach informs a value proposition for universal influenza vaccines (even as first step), as well as broader country-level and global strategic goals.

IVIR-AC recommended that:

- Concerns about the conceptual framework, the dimensions and the country archetypes/use cases should be clarified.
- The conceptual framework and the pathway should be elaborated from a use case for current influenza vaccines to universal influenza vaccines.
- The public health goals of seasonal influenza vaccines in different countries should be understood before considering the product characteristics and target population.
- The definition of geographical location should be considered.
- The use of data-clustering techniques to define archetypes should be explored; in this regard it could be helpful to include a data scientist in the team.
- Market, policy and programmatic factors should be considered – including procurement mechanisms, strength of the National Immunization Technical Advisory Group, service delivery, decision-making factors, cold chain and vaccine hesitancy. A country's delivery capacity could also be taken into account – such as high capacity (e.g., annual adult influenza vaccine given prior to pandemic; high access; multiple service points; trained workforce), low capacity (e.g., no previous adult influenza vaccination prior to pandemic; limited service access with remote communities; significant workforce limitations or need for training), and medium capacity.
- There must be consideration of how COVID-19 vaccine implementation may change the overall approach, use case and future availability of seasonal and pandemic influenza vaccines.

Immunization Agenda 2030 (IA 2030) – vaccine impact estimates

In September 2020, IVIR-AC gave recommendations on the framework and methods proposed for estimating future deaths averted due to vaccination, as part of the *IA2030 Agenda: A Global Strategy to Leave No One Behind*.¹⁴ At its March 2021 meeting, IVIR-AC evaluated follow-up to previous recommendations, reviewed

marché et éventuellement le développement de produits à court terme. Cette approche doit être entreprise. Toutefois, au fur et à mesure de l'élaboration de la proposition de valeur, il conviendra de clarifier la manière dont cette approche éclaire une proposition de valeur pour les vaccins antigrippaux universels (même dans un premier temps), ainsi que des objectifs stratégiques plus larges aux niveaux national et mondial.

Recommandations de l'IVIR-AC:

- il convient de clarifier les préoccupations concernant le cadre conceptuel, les dimensions et les archétypes de pays/scénarios d'utilisation;
- le cadre conceptuel et le cheminement doivent être élaborés à partir d'un scénario d'utilisation des vaccins antigrippaux actuels jusqu'aux vaccins antigrippaux universels;
- il est nécessaire de comprendre les objectifs de santé publique des vaccins contre la grippe saisonnière dans les différents pays avant d'envisager les caractéristiques des produits et la population cible;
- il convient d'envisager la définition de l'emplacement géographique;
- l'utilisation de techniques de regroupement de données pour définir les archétypes mérite d'être explorée; à cet égard, il pourrait être utile d'inclure un spécialiste en science des données dans l'équipe;
- les facteurs liés au marché, aux politiques et aux programmes doivent être pris en compte, notamment les mécanismes d'achat, la solidité des groupes consultatifs techniques nationaux sur la vaccination, la prestation de services, les facteurs décisionnels, la chaîne du froid et la réticence à l'égard des vaccins. La capacité de prestation d'un pays pourrait également être prise en compte: capacité élevée (par exemple un vaccin annuel contre la grippe chez l'adulte administré avant la pandémie; un large accès; de multiples points de service; une main-d'œuvre formée), faible capacité (par exemple aucune vaccination contre la grippe chez l'adulte avant la pandémie; un accès limité aux services dans les communautés éloignées; une main-d'œuvre très limitée ou insuffisamment formée) et capacité moyenne;
- il faut examiner la manière dont la mise en œuvre des vaccins contre la COVID-19 peut modifier l'approche globale, le scénario d'utilisation et la disponibilité future des vaccins contre la grippe saisonnière et pandémique.

Programme pour la vaccination à l'horizon 2030 – estimations de l'impact des vaccins

En septembre 2020, l'IVIR-AC a formulé des recommandations sur le cadre et les méthodes proposés pour estimer les futurs décès évités grâce à la vaccination, dans le cadre du *Programme pour la vaccination à l'horizon 2030: Une stratégie mondiale pour ne laisser personne de côté*.¹⁴ Lors de sa réunion de mars 2021, l'IVIR-AC a évalué le suivi des recommandations précé-

¹⁴ Immunization Agenda 2030: A Global Strategy to Leave No One Behind. <https://www.who.int/teams/immunization-vaccines-and-biologicals/strategies/ia2030> (accessed 26 March 2021).

¹⁴ Programme pour la vaccination à l'horizon 2030: Une stratégie mondiale pour ne laisser personne de côté. <https://www.who.int/fr/publications/m/item/immunization-agenda-2030-a-global-strategy-to-leave-no-one-behind> (consulté le 26 mars 2021).

updates to proposed methodologies, and evaluated preliminary results.

Summary of IVIR-AC feedback and recommendations

- For the statistical modelling, IVIR-AC recommended giving more details on:
 - the different input covariates; variance of the covariates; explanations of observed uncertainties; and the advantages and disadvantages of the different models tested;
 - how the model accounts for the attributable reduction in mortality that is not due to vaccines (e.g. the differences in health-care services across VPDs, between countries and over time);
 - how the IA2030 impact model accounts for herd immunity.
- IVIR-AC further recommended presenting vaccine impact estimates for high-income countries separately as it was unclear whether use of the IA2030 statistical model to extrapolate the VIMC estimates to these countries would produce results consistent with existing high-income country estimates (i.e. from WHO's Regional Office for Europe, the Centers for Disease Control and Prevention in the USA and Public Health England). Validation was needed to ensure consistency.
- IVIR-AC reiterated the importance of communicating information on key WHO websites in a clear and accessible manner. The “deaths averted” figure currently available is widely used but its sources and references are hard to find.
- IVIR-AC stressed the need to clarify whether the mortality rates from UNWPP have accounted for deaths due to VPDs when they are used to parameterize the IA2030 impact model.

IA 2030 costing

WHO collaborates with the International Vaccine Access Center (IVAC) at Johns Hopkins University to generate global and regional cost estimates for implementing the IA2030 Global Strategy from 2021 to 2030. These estimates include vaccine costs (vaccine price, cost of injection supplies, freight costs) and immunization delivery costs (labour, storage, transportation, other capital costs and other recurrent costs). IVIR-AC gave feedback on the proposed costing methodology and identification of data gaps between IVAC's previous model¹⁵ and IA2030 objectives.

dentés, examiné les mises à jour des méthodes proposées et évalué les résultats préliminaires.

Résumé des observations et des recommandations de l'IVIR-AC

- Pour la modélisation statistique, l'IVIR-AC a recommandé de donner plus de détails sur:
 - les différentes covariables d'entrée; la variance des covariables; les explications des incertitudes observées; et les avantages et inconvénients des différents modèles testés;
 - la manière dont le modèle tient compte de la fraction attribuable de la réduction de la mortalité qui n'est pas due aux vaccins (par exemple les différences dans les services de soins de santé pour les différentes maladies à prévention vaccinale, entre les pays et dans le temps);
 - la manière dont le modèle d'estimation de l'impact tient compte de l'immunité collective.
- L'IVIR-AC a également recommandé de présenter séparément les estimations de l'impact des vaccins pour les pays à revenu élevé, car il n'est pas certain que l'utilisation du modèle statistique du Programme pour la vaccination 2030 pour extrapoler les estimations pour le Consortium à ces pays produise des résultats cohérents avec les estimations existantes pour les pays à revenu élevé (c'est-à-dire celles du Bureau régional OMS de l'Europe, des *Centers for Disease Control and Prevention* aux États-Unis d'Amérique et de *Public Health England*). Une validation est nécessaire pour garantir la cohérence.
- L'IVIR-AC a réitéré l'importance de communiquer les informations sur les sites Web clés de l'OMS de manière claire et accessible. Le chiffre des «décès évités» actuellement disponible est largement utilisé, mais ses sources et références sont difficiles à trouver.
- L'IVIR-AC a souligné la nécessité de préciser si les taux de mortalité issus des UNWPP ont pris en compte les décès dus aux maladies à prévention vaccinale lorsqu'ils sont utilisés pour paramétrer le modèle d'impact du Programme pour la vaccination 2030.

Etablissement des coûts du Programme pour la vaccination à l'horizon 2030

L'OMS collabore avec l'International Vaccine Access Center (IVAC) de l'Université Johns Hopkins pour générer des estimations mondiales et régionales des coûts de la mise en œuvre de la stratégie mondiale du Programme pour la vaccination pour la période 2021-2030. Ces estimations comprennent les coûts des vaccins (prix du vaccin, coût du matériel d'injection, frais de transport) et les coûts de la délivrance des vaccins (main-d'œuvre, stockage, transport, autres coûts d'investissement et autres coûts récurrents). L'IVIR-AC a présenté ses observations sur la méthode de calcul des coûts proposée et sur l'identification des lacunes dans les données entre le modèle précédent¹⁵ de l'IVAC et les objectifs du Programme pour la vaccination à l'horizon 2030.

¹⁵ Sim YS et al. Return on investment from immunization against 10 pathogens in 94 low- and middle-income countries, 2011–30. *Health Aff.* 2020;39(8): (<https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00103>; accessed March 2021).

¹⁵ Sim YS et al. Return on investment from immunization against 10 pathogens in 94 low- and middle-income countries, 2011–30. *Health Aff.* 2020;39(8): (<https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00103>; consulté en mars 2021).

Summary of IVIR-AC feedback and recommendations

The Advisory Committee noted that:

- The proposed plan for analysis is comprehensive and methodologically robust with sensitivity and scenario analysis; the scope, scale and perspective are clearly defined; and the distinction between vaccine cost and delivery cost is helpful in terms of resource generation and allocation.
- Updating the analysis with the latest vaccine demand, coverage and price estimates is a step in the right direction.
- It is important to ensure model availability, transparency and accessibility.

In addition:

- IVIR-AC suggested that future analyses should account for costs incurred by the beneficiaries who are immunized (e.g. transportation, lost productive time due to immunization sessions) in both the public and private sectors. These costs will have implications for potential interventions such as conditional cash transfers or country strategies to strengthen health systems.
- IVIR-AC recommended that future work should incorporate detailed information about public and private sector-specific contributions to coverage rates and variation in prices.
- The communication team should link cost estimates to the vaccine impact estimates as part of the IA2030 Global Strategy.
- IVIR-AC reiterated the importance of timely release of updated costing and impact estimates, including updated methods or source data and limitations. ■

Résumé des observations et des recommandations de l'IVIR-AC

Le Comité consultatif a noté que:

- le plan d'analyse proposé est complet et méthodologiquement solide, avec l'analyse de la sensibilité et des scénarios; la portée, l'échelle et la perspective sont clairement définies; et la distinction entre le coût des vaccins et le coût de la délivrance des vaccins est utile en termes de génération et d'allocation des ressources;
- la mise à jour de l'analyse avec les dernières estimations de la demande, de la couverture et du prix des vaccins est un pas dans la bonne direction;
- il est important de garantir la disponibilité, la transparence et l'accessibilité des modèles.

En outre:

- l'IVIR-AC a suggéré que les analyses futures tiennent compte des coûts supportés par les personnes vaccinées (par exemple le transport, le temps de travail perdu en raison des séances de vaccination) dans les secteurs public et privé. Ces coûts auront des répercussions sur les interventions potentielles telles que le versement conditionnel d'une somme d'argent ou les stratégies nationales de renforcement des systèmes de santé;
- l'IVIR-AC a recommandé que les travaux futurs intègrent des informations détaillées sur les contributions spécifiques des secteurs public et privé aux taux de couverture et à la variation des prix;
- l'équipe chargée de la communication doit établir un lien entre les estimations des coûts et les estimations de l'impact des vaccins dans le cadre de la stratégie mondiale du Programme pour la vaccination 2030;
- l'IVIR-AC a réitéré l'importance de la publication en temps utile des estimations actualisées des coûts et de l'impact des vaccins, y compris les méthodes ou les données sources actualisées et leurs limites. ■

How to obtain the WER through the Internet

- (1) WHO WWW server: Use WWW navigation software to connect to the WER pages at the following address: <http://www.who.int/wer/>
- (2) An e-mail subscription service exists, which provides by electronic mail the table of contents of the WER, together with other short epidemiological bulletins. To subscribe, send a message to listserv@listserv.who.int. The subject field should be left blank and the body of the message should contain only the line subscribe wer-reh. A request for confirmation will be sent in reply.

Comment accéder au REH sur Internet?

- 1) Par le serveur Web de l'OMS: A l'aide de votre logiciel de navigation WWW, connectez-vous à la page d'accueil du REH à l'adresse suivante: <http://www.who.int/wer/>
- 2) Il existe également un service d'abonnement permettant de recevoir chaque semaine par courrier électronique la table des matières du REH ainsi que d'autres bulletins épidémiologiques. Pour vous abonner, merci d'envoyer un message à listserv@listserv.who.int en laissant vide le champ du sujet. Le texte lui-même ne devra contenir que la phrase suivante: subscribe wer-reh. Une demande de confirmation vous sera envoyée en retour.

www.who.int/wer

Email • send message **subscribe wer-reh** to listserv@listserv.who.int

Content management & production • wantzc@who.int or werreh@who.int

www.who.int/wer

Email • envoyer message **subscribe wer-reh** à listserv@listserv.who.int

Gestion du contenu & production • wantzc@who.int or werreh@who.int

WHO web sites on infectious diseases – Sites internet de l'OMS sur les maladies infectieuses

Avian influenza	https://www.who.int/influenza/human_animal_interface	Grippe aviaire
Buruli ulcer	http://www.who.int/buruli	Ulcère de Buruli
Child and adolescent health and development	http://www.who.int/child_adolescent_health	Santé et développement des enfants et des adolescents
Cholera	http://www.who.int/cholera	Choléra
COVID-19	https://www.who.int/emergencies/diseases/novel-coronavirus-2019	Maladie à coronavirus 2019 (COVID-19)
Dengue	http://www.who.int/denguecontrol	Dengue
Ebola virus disease	https://www.who.int/health-topics/ebola/#tab=tab_1	Maladie à virus Ebola
Emergencies	https://www.who.int/emergencies	Situations d'urgence sanitaire
Epidemic and pandemic diseases	https://www.who.int/emergencies/diseases	Maladies épidémiques et pandémiques
Eradication/elimination programmes	http://www.who.int/topics/infectious_diseases	Programmes d'éradication/élimination
Fact sheets on infectious diseases	http://www.who.int/topics/infectious_diseases/factsheets	Aide-mémoires sur les maladies infectieuses
Filariais	http://www.filariosis.org	Filariose
Global Foodborne Infections Network (GFN)	http://www.who.int/gfn	Réseau mondial d'infections d'origine alimentaire
Global Health Observatory (GHO) data	https://www.who.int/gho	Données de l'Observatoire de la santé mondiale
Global Influenza Surveillance and Response System (GISRS)	https://www.who.int/influenza/gisrs_laboratory	Système mondial de surveillance et d'intervention en cas de grippe (GISRS)
Global Outbreak Alert and Response Network (GOARN)	https://www.who.int/ihr/alert_and_response/outbreak-network/en/	Réseau mondial d'alerte et d'action en cas d'épidémie (GOARN)
Health topics	http://www.who.int/topics/en	La santé de A à Z
Human African trypanosomiasis	http://www.who.int/trypanosomiasis_african	Trypanosomiase humaine africaine
Immunization, Vaccines and Biologicals	http://www.who.int/immunization	Vaccination, Vaccins et Biologiques
Influenza	https://www.who.int/influenza	Grippe
International Health Regulations	http://www.who.int/ihr	Règlement sanitaire international
International travel and health	http://www.who.int/ith	Voyages internationaux et santé
Leishmaniasis	http://www.who.int/leishmaniasis	Leishmaniose
Leprosy	http://www.who.int/lep	Lèpre
Lymphatic filariasis	http://www.who.int/lymphatic_filariais	Filariose lymphatique
Malaria	http://www.who.int/malaria	Paludisme
Middle East respiratory syndrome coronavirus (MERS-CoV)	https://www.who.int/emergencies/mers-cov	Coronavirus du syndrome respiratoire du Moyen-Orient (MERS-CoV)
Neglected tropical diseases	http://www.who.int/neglected_diseases	Maladies tropicales négligées
Onchocerciasis	http://www.who.int/onchocerciasis	Onchocercose
OpenWHO	https://openwho.org/	OpenWHO
Outbreak news	http://www.who.int/csr/don	Flambées d'épidémies
Poliomyelitis	http://www.polioeradication.org	Poliomyélite
Rabies	http://www.who.int/rabies	Rage
Schistosomiasis	http://www.who.int/schistosomiasis	Schistosomiase
Smallpox	http://www.who.int/csr/disease/smallpox	Variole
Soil-transmitted helminthiasis	http://www.who.int/intestinal_worms	Géohelminthiases
Trachoma	http://www.who.int/trachoma	Trachome
Tropical disease research	http://www.who.int/tdr	Recherche sur les maladies tropicales
Tuberculosis	http://www.who.int/tb and/et http://www.stoptb.org	Tuberculose
Weekly Epidemiological Record	http://www.who.int/wer	Relevé épidémiologique hebdomadaire
WHO Lyon Office for National Epidemic Preparedness and Response	http://www.who.int/ihr/lyon	Bureau OMS de Lyon pour la préparation et la réponse des pays aux épidémies
WHO Pesticide Evaluation Scheme (WHOPES)	https://www.who.int/whopes/resources	Schéma OMS d'évaluation des pesticides
Yellow fever	http://www.who.int/csr/disease/yellowfev	Fièvre jaune
Zika virus disease	https://www.who.int/emergencies/diseases/zika	Maladie à virus Zika

Background information to the sessions

Session 1

COVID 19 vaccine impact modelling

Session COVID 19 vaccine impact modelling – Presentation summaries –

J McVernon, U. of Melbourne

- **Title of presentation:** Anticipating combined impacts of vaccines and PHSMs following SARS-CoV-2 introduction into low burden settings
- **Summary of content**
 - Countries that have successfully limited SARS-CoV-2 importation through border measures face the challenge of defining vaccine thresholds and accompanying social measures to enable reopening, while minimising disease impacts
 - We introduce ‘transmission potential’ (TP) as a useful metric for such settings and quantify proportional reductions in this measure for Delta variants achievable with vaccination alone (for different vaccines, coverage thresholds and strategies), as well as the overlaid impacts of bundled social measures (of different durations and intensities)
 - Alternative strategies to achieve TP reduction will have differing consequences for clinical outcomes by age group and vaccine status, which must also be mapped to country demography and health sector capacity to define local tolerance for cases
- **IVIRAC advice needed on the group’s work/methodology**
 - We will submit a technical report in advance of the meeting, TP has been socialised as a metric with WHO based on our existing PHSM work but publishing has been constrained by our policy focus.
 - We will aim to demonstrate how we believe our approaches map to LMIC settings based on regional experience in the Pacific where transmission genuinely appears to be lower (eg localised targeting to specific regions/sectors for countries with limited supply to enable focal easing of measures and maximise economic gains) but further advice regarding applicability/utility would be welcome to inform next steps.
- **Key resulting message** (that may be relevant to inform SAGE, if applicable): While vaccines are an important component of strategies to support a reopening pathway for low burden countries, reinforcing social measures will almost certainly be required to support cautious easing of border restrictions, particularly given constraints on supply and achievable immunisation coverage.

E Mc Bryde, James Cook University

- **Title of presentation:** Impact of vaccination and natural immunity in the context of other public health and social measures in high incidence countries of the Indo-Pacific
- **Summary of content:** We examine both static and dynamic models of disease transmission and include age-specific contacts, clinical fraction and disease severity, to optimize vaccine distribution under many changing situations.

- **IVIRAC advice needed on the group's work/methodology**
 - Age specific sero-prevalence rates would be very useful for our key countries of Indonesia, the Philippines, Sri Lanka and Malaysia.
 - Evidence of waning immunity from either natural infection or vaccines would be valuable
- Key resulting message (that may be relevant to inform SAGE, if applicable)
 - Vaccine choice matters: Sinovac is not as effective as either AstraZeneca or Pfizer at reducing deaths from COVID
 - Age distribution matters: when the effective reproduction number is approaching one, then targeting transmitters is the best policy, whereas when it is far from one -for example 5, then targeting the elderly is far more effective, as they have the highest morbidity and mortality.

N Scott, Burnet Institute

- **Title of presentation:** Prioritization of vaccines in Kenya, Zimbabwe and Vietnam to maintain health systems, keep schools open and prevent outbreaks

- **Summary of content**
 - We worked with country teams to calibrate the Covasim agent-based model to Kenya, Zimbabwe and Vietnam.
 - Across these contexts, we assessed (1) the impact of vaccinating key population groups in different orders; (2) how the benefits of optimal prioritization compare to the benefits of increased supply; (3) the benefits of vaccinating teachers and teaching staff compared to the rest of the population; (4) how vaccines in schools can reduce reliance on other school-based NPIs; and (5) how vaccination can be used to minimize or mitigate a resurgence in delta cases.

- **IVIRAC advice needed on the group's work/methodology**
 - Confirmation that these findings are consistent with other scientific advice received (i.e. non modelling)

- **Key resulting message (that may be relevant to inform SAGE)**
 - Vaccines should be prioritized to people over 60 years before other groups:
 - This includes people with comorbidities, who in general are best targeted after people over 60, although there may be exceptions for particular comorbidities
 - Aside from people over 60, additional prioritization has minimal overall benefit compared with vaccination speed
 - This suggests that additional key populations should be prioritized based on achieving faster rollout, or objectives other than population-level control
 - The first ~20% vaccine coverage has the greatest impact on mortality and health system capacity
 - If the aim is to keep schools open, vaccinating teachers provides greater benefit than other groups and can reduce the need for NPIs in schools
 - With current vaccines, herd immunity against delta variant is unlikely to be achieved
 - Long-term health system capacity for COVID is likely to be required
 - NPIs will still be required, though higher vaccination coverage means less reliance on them
 - Vaccinating teachers and school staff is approximately equivalent to NPIs in schools of about 50% efficacy
 - Once a delta resurgence has started, vaccination as a response is unlikely to be able to contain it, though vaccination coverage when it begins can have a greater impact

G Menon, Ashoka University

- **Title of Presentation:** Network and agent-based models for school reopening and vaccination-NPI interaction in the context of India
- **Summary of Content:**
 - We describe network and agent-based models that we use to examine ways in which schools can reopen within the background of an evolving epidemic.
 - Our results suggest that schools can reopen in the conditions prevalent currently in India, with large levels of background seroprevalence (> 60%), given that school-going children have been found to have seropositivities comparable to that of adults.
 - We also present results for different vaccine allocation strategies and their interactions with various NPIs.
- **IVIRAC advice needed:**
 - What do we know from other LMIC settings that could be useful to put into our models to make them more widely applicable?
 - Our models do not include the possibility of long-COVID in children, but this should potentially be a worry in deciding when it is safe for schools to open
 - Are there vaccine allocation strategies that are of particular interest to IVIRAC?
- **Key resulting message (that may be relevant to inform SAGE, if applicable)**
 - The extent of seropositivity in the community, as determined by serosurveys, can be one factor in determining the optimal time to reopen schools. Beyond a critical vaccination rate of about 0.4% - 0.5% of the population per day, NPI's do not appear to make a difference.

A Hogan, Imperial College London

- **Title of presentation:** “Modelling the Impact of COVID-19 Vaccination Strategies across Income Settings to Inform Global Strategy Development”
- **Summary of content**
 - Show our work on the impact of vaccination of age-based priority groups by broad income setting, which is being used to inform the “WHO Global COVID-19 Vaccination Strategy: July 2021 Update” [Topic II]
 - Demonstrate the extent to which vaccination allows NPIs to be lifted for a generic illustrative setting, across different transmission (R_t) levels [Topic IV]
 - Provide an update on our methodology to examine the impact of varying the timing between doses in order to vaccinate younger populations, in supply-constrained settings [Topic V]
- **IVIRAC advice needed on the group’s work/methodology**
 - We would welcome guidance on specific scenarios/questions to explore relating to our work on Topic V
- **Key resulting message (that may be relevant to inform SAGE, if applicable)**
 - Even a vaccine with “sub-optimal” efficacy can have substantial impact on public health and avert many deaths
 - Across all scenarios considered, it is always most efficient to continue to prioritise the oldest or most at risk of severe disease and mortality, and there is always additional benefit in vaccinating more age groups
 - Timing of vaccination roll-out relative to the epidemic curve is important to consider, in terms of anticipating vaccine impact (and noting that future waves may be expected beyond the immediate epidemic)

Y Liu, LSHTM

- **Title of presentation:** Modelling COVID-19 vaccination strategies: optimising dosing intervals and roll-out scenarios

- **Summary of content**
 - Results for related policy questions:
 - (i) For different assumptions about waning, what is the optimal interval for minimising COVID-19 burden?
 - (ii) Given different roll-out scenario options to prioritise first-dose among different age-groups, what is the optimal scenario for minimising COVID-19 burden?

- **IVIRAC advice needed on the group's work/methodology**
 - Feedback on scenario analysis of presented results will be valuable

- **Key resulting message (that may be relevant to inform SAGE)**
 - For different seroprevalence settings, and vaccination rate and vaccine supply constraints, project the impact of different dosing intervals and roll-out scenarios to identify optimal policy options (we plan to have some clear messages on this).

B Lopman, Emory University

- **Title:** Modeling the impact of COVID-19 vaccination in LMICs amidst relaxation of non-pharmaceutical interventions and variant transmission
- **Summary:** We modeled the impact of vaccination in 12 LMICs. Overall, we found that disease incidence can be substantially reduced by combining rapid vaccination rollout with delayed relaxation of non-pharmaceutical interventions. Extending the inter-dose interval to 24 weeks to mitigate supply constraints is unlikely to greatly increase incidence, but failing to administer the second dose could lead to dramatic increase in deaths and health system burden. While these patterns are similar by country, the ultimate number of deaths and peak health system burden varies and is largely dependent on the level of natural immunity at the time of vaccine introduction.
- **Questions for IVIRAC:**
 - Is the committee aware of any additional data on the level of baseline immunity and its distribution by variants of concern for individual countries?
 - Are our modeled rates of vaccine introduction achievable?
 - Does the committee think that the level of social distancing is correct and is it realistic to maintain NPIs in LMICs as vaccines roll out?
- **Key message:** Aggressive vaccine rollout and delaying the rollback of NPIs until higher levels of vaccine coverage are achieved is likely to be the most effective way to reduce the public health impacts of the COVID-19 epidemic. Extending the inter-dose interval to 24 weeks in order to maximize distribution is unlikely to greatly increase risk.

A Rubinstein, IECS

- **Title of presentation:** Modelling impact of COVID-19 vaccination strategies in six Latin American countries
- **Summary of content**
 - Description of model features, characterized by the age and immunity state compartmentalization, vaccination transitions and stages, and contact matrices and transmission rates by age groups, social interactions, and settings (3 minutes). Description of parameters, inputs, and sources of information (2 minutes) and presentation of the results (different scenarios) for the six selected countries through an interactive tool.
- **Key resulting message (that may be relevant to inform SAGE)**
 - The model will help Latin American countries to make decisions on times were the supply of vaccines is still restricted in most of them, specially about the balance between vaccines uptake and NPI lifting possibilities

Session 2

CDC Measles immunity profiles

Measles immunity profiles: a brief description

April 30, 2021

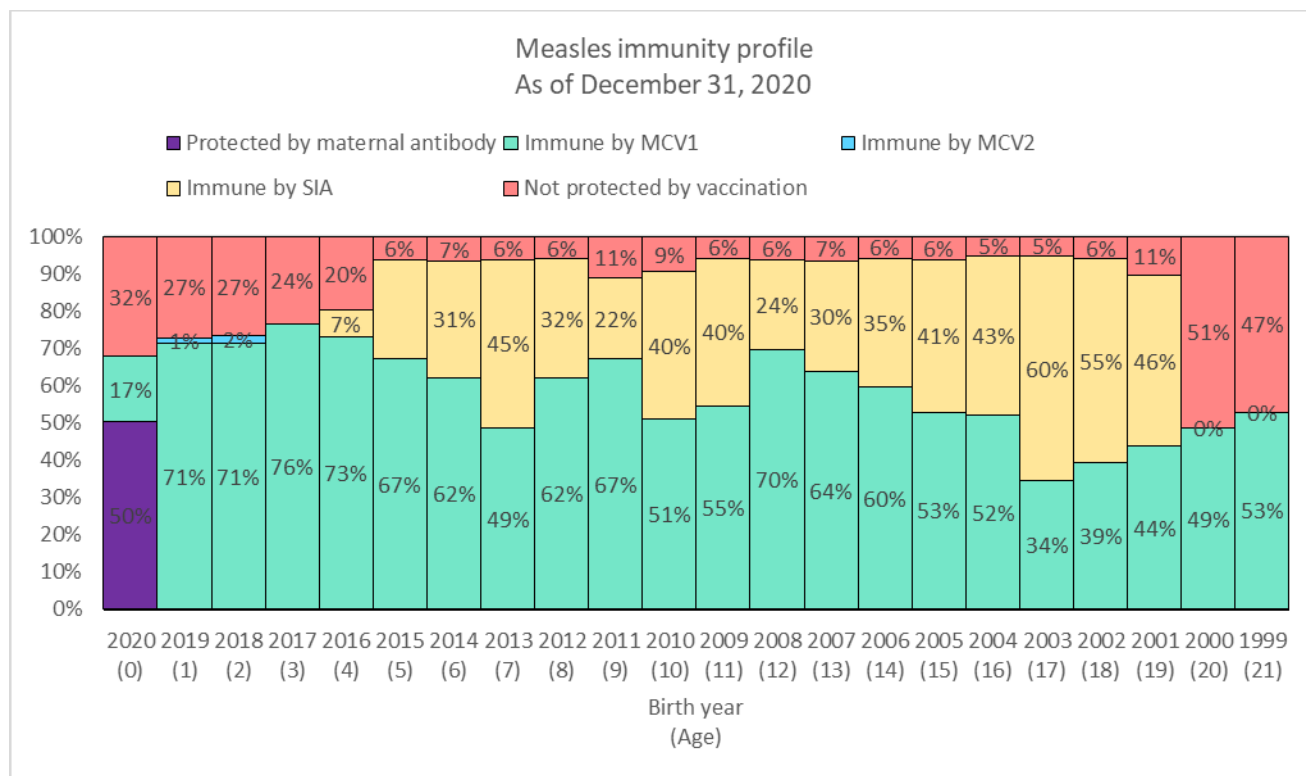
Background

Identifying measles immunity gaps can help immunization programs monitor program performance, determine the period when the next supplementary immunization activity (SIA) should be planned and implemented, identify age groups that have large immunity gaps for targeting by intensification of routine or additional supplemental vaccination activities, and help assess outbreak risk and prevent outbreaks. In countries where routine immunization cannot maintain high levels of immunity to measles, the WHO recommends monitoring the risk of measles outbreaks by estimating the accumulated number of measles-susceptible preschool-aged children, and conducting SIAs before that number reaches the size of one birth cohort¹. This approach has been programmatically useful for preventing large measles outbreaks.

Measles immunity gaps can also be identified through population-based serosurveys. However, serosurveys are time and resource intensive and are usually not conducted frequently. In contrast, measles immunity profiles estimate immunity gaps using readily available data such as annual number of births and previously collected vaccination coverage data. The profiles estimate the percentage of each birth cohort protected by immunization based on coverage with the routine first dose of measles-containing vaccine (MCV1), routine second dose of measles-containing vaccine (MCV2), and SIAs. The results can be easily visualized in a stacked bar chart. Figure 1 shows an example of the graph of the estimated measles immunity profile for a hypothetical country at the end of 2020. It is a quick and simple way to identify birth cohorts with large immunity gaps. For program decision-making, measles immunity profiles should be triangulated with surveillance and other relevant program data.

¹ WHO Measles Position Paper. <http://apps.who.int/iris/bitstream/10665/255149/1/WER9217.pdf?ua=1>

Figure 1. Example of measles immunity profile in a hypothetical country



Measles immunity profiles have been developed and used by countries and partners for many years, traditionally using Microsoft Excel. Previous versions were based on a variety of assumptions and formulas, often producing inconsistent results. A formal tool, the Measles Strategic Planning (MSP) tool, was developed in Excel by WHO, PATH and Stanford University to show the impact of various strategies for accelerating measles control on the estimated immunity profile and the number of measles cases estimated through a static model². A key assumption of the tool was independence between routine and SIA doses, so that every child had the same chance of being vaccinated in SIAs, regardless of previous vaccination by routine or earlier SIAs. This assumption, and the fact that administrative data frequently over-estimated true SIA coverage data, often estimated very small immunity gaps, even in countries where outbreaks continued to occur.

In order to produce profiles that triangulate better with surveillance data, and recognizing that many countries offered a second dose 6-12 months after the first dose, we developed methods to estimate immunity profiles assuming dependence between doses, as described below, using a Microsoft Excel spreadsheet tool. The calculations were then replicated in R software for higher throughput efficiency and reliability. These gains allowed us to rapidly and reliably generate profiles for all WHO member states based on publicly available data. The formulas in R were further refined to more accurately follow cohorts over time, using age-dependent vaccine effectiveness estimates for routine and SIAs, an accurate chronological sequence of routine and SIA doses, and estimates of the proportion of each cohort included in SIAs based on exact SIA start and end dates. The formulas were also refined to better estimate SIA impact at subnational level. The key differences between the Excel and R versions are in Table 1 below. A set of tools for generating

² Simons E, Mort M, Dabbagh A, Strebel P, Wolfson L. Strategic Planning for Measles Control: Using Data to Inform Optimal Vaccination Strategies. J Infect Dis 2011;204(suppl1):S28-S34.

and visualizing measles immunity profiles are currently under development, including a Power BI dashboard and a Shiny R app. We recommend using the R version as it produces more accurate estimates.

Table 1. Assumptions and methods of the measles immunity profile tool based on Microsoft Excel and R

	Excel version	R version (in Shiny R app and Jupyter notebook, Power BI dashboard)
Main considerations	<ul style="list-style-type: none"> Calculations laid out, allowing the average Excel user to follow them. 	<ul style="list-style-type: none"> Provide profiles more accurately reflecting the timing of vaccination opportunities and age-specific SIA VE. Possible to rapidly generate profiles for all countries.
Assumptions and methods		
Correlation between doses	<ul style="list-style-type: none"> Only total dependence assumption is implemented in this version, that is, MCV2 and SIA doses are given first to children who have been previously vaccinated, and when coverage is higher, then given to those previously unvaccinated. 	<ul style="list-style-type: none"> Total dependence or total independence options are available, allowing users to see and compare profiles calculated using either assumptions. The total dependence is the recommended default assumption.
Temporal granularity	<ul style="list-style-type: none"> Routine and SIA coverage applied to whole year birth cohorts. For example, an SIA in 2020 with a target age range of 9–59 months would cover 2016–2019 birth cohorts. 	<ul style="list-style-type: none"> Routine and SIA coverage applied to daily birth cohorts that are eligible for vaccination, based on the routine immunization schedule and SIA implementation dates and target age group.
Vaccine effectiveness (VE)	<ul style="list-style-type: none"> VE is dependent on age of administration: 58% for MCV1 given at 6–8 months of age or earlier, 84% at 9–11 months, 92.5% at ≥12 months of age; and 95% for MCV2 given at ≥12 months of age. For SIAs, the same VE (95%) is used for all age groups targeted by the SIA. 	<ul style="list-style-type: none"> VE for MCV1 and MCV2: same as the Excel version. Age-specific VE estimates used for SIAs: 58% for children 6–8 months of age, 84% for children 9–11 months of age, and 95% for children ≥12 months of age.
Sequence of routine and SIA doses	<ul style="list-style-type: none"> Assumes SIA doses are always given after MCV1 and MCV2. 	<ul style="list-style-type: none"> Routine doses and SIA doses are put in sequence according to age of administration for each birth cohort at the time of SIA implementation. For example, SIA targeting 6–59 months of age will deliver vaccine to some children before MCV1, between MCV1 and MCV2, or after MCV2 based on age of eligibility according to the national immunization schedule.

Phased SIAs	<ul style="list-style-type: none"> • Users need to manually combine multiple phases of SIAs into one entry. Users also have to manually combine all subnational SIAs done in different areas in one calendar year. 	<ul style="list-style-type: none"> • The coverage and implementation dates of each phase are accurately applied to the target population in each phase.
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Key data, assumptions, and formulas

Input data

Routine immunization coverage data are based on the WHO and UNICEF Estimates of National Immunization Coverage (WUENIC).

SIA data are based on data publicly available on WHO’s website³. Whenever post-campaign coverage surveys are conducted, the survey coverage estimate is used; if survey coverage is not available, then reported administrative coverage is used. Administrative coverage for SIAs is capped at 95% unless a post-campaign coverage survey suggested the coverage was greater than 95%. This cap is to avoid over-estimation of administrative coverage due to population denominator issues and vaccination of children outside the target age range.

Population estimates of the number of persons by one-year of age (i.e., <1 year, 1 year to less than 2 years, etc.) are those published in World Population Prospects, 2019 Revision published by UN Population Division⁴.

Correlation between doses:

Correlation between doses represents the probability that a child is reached by subsequent immunization services, given the prior vaccination history.

For routine immunization, WHO recommends a dose should be recorded as MCV2 only if the child has the documented first dose of MCV1^{5, 6}, and therefore MCV2 is dependent on MCV1.

If every child has the equal chance of being vaccinated during each SIA, then the chance of vaccination is independent of the vaccination status before the SIA (the “independent scenario”). This assumption contrasts with the common observation that children who have been reached by previous health services are often reached first by subsequent SIAs. To better capture the dependency between vaccination opportunities, we instead assumed that each vaccination opportunity results first in re-vaccinating children who have been vaccinated before, and then, only if the vaccination coverage is higher than previous opportunities,

³ WHO Immunization Data, statistics and graphics. Available at <https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/data-statistics-and-graphics>

⁴ United Nations. World Population Prospects 2019. Available at <https://population.un.org/wpp/Download/Standard/CSV/>

⁵ World Health Organization (2013). A Guide to Introducing a Second Dose of Measles Vaccine into Routine Immunization Schedules. Page 35. Available at <https://www.who.int/publications/i/item/WHO-IVB-13.03>

⁶ World Health Organization (2018). Establishing and strengthening immunization in the second year of life: Practices for immunization beyond infancy. Pages 20, 68, and 94-95. Available at https://www.who.int/immunization/documents/WHO_IVB_ISBN9789241513678/en/

vaccinating previously unvaccinated children (the “dependent scenario”). The “independent scenario” and “dependent scenario” represent the boundaries of a range of reporting practices and of where the real-world correlation between previous vaccination status and the probability of receiving a subsequent dose lies.

We used the “dependent scenario” to provide a conservative estimate of immunization program impact, and to reduce the chance of overestimation of immunity and delayed response activities as administrative vaccination coverage data are frequently higher than actual coverage. Formulas of this assumption are shown in Figure 2.

Figure 2. Formulas based on the assumption that previously vaccinated children are first reached by a subsequent vaccine dose

$$\% \text{ of persons immune from MCV1} = MCV1 * MCV1 \text{ VE}$$

$$\% \text{ of additional persons immune from MCV2} = \begin{cases} (MCV1 - MCV1 * MCV1 \text{ VE}) * \frac{MCV2}{MCV1} * MCV2 \text{ VE}, & \text{when } MCV2 < MCV1, \\ (MCV1 - MCV1 * MCV1 \text{ VE}) * MCV2 \text{ VE} + (MCV2 - MCV1) * MCV2 \text{ VE}, & \text{when } MCV2 \geq MCV1 \end{cases}$$

$$\text{Cumulative percentage vaccinated after SIA}_n = \begin{cases} \text{cumulative percentage vaccinated before SIA}_n, & \text{when SIA}_n < \text{cumulative \% vaccinated before SIA}_n \\ \text{SIA}_n \text{ coverage} * \% \text{ population targeted} + \text{cumulative percentage vaccinated before SIA}_n * (1 - \% \text{ population targeted}) & \text{when SIA}_n \text{ coverage} \geq \text{cumulative \% vaccinated before SIA}_n \end{cases}$$

$$\% \text{ of additional persons immune from SIA}_n = \begin{cases} (\text{cumulative \% vaccinated before SIA}_n - \text{cumulative \% immune before SIA}_n) * \frac{\text{SIA}_n \text{ coverage}}{\text{cumulative \% vaccinated before SIA}_n} * \text{SIA} \text{ VE} * \% \text{ population targeted}, & \text{when SIA}_n \text{ coverage} < \text{cumulative \% vaccinated before SIA}_n, \\ (\text{SIA}_n \text{ coverage} - \text{cumulative \% immune before SIA}_n) * \text{SIA} \text{ VE} * \% \text{ population targeted}, & \text{when SIA}_n \text{ coverage} \geq \text{cumulative \% vaccinated before SIA}_n \end{cases}$$

MCV1: first routine dose of the measles-containing vaccine
 MCV2: second routine dose of the measles-containing vaccine
 SIA: supplementary immunization activities
 VE: vaccine effectiveness

Impact of subnational SIAs and phased SIAs

We calculated the additional percentage of children immunized by a subnational SIA based on the subnational SIA coverage and the proportion reached in earlier opportunities for vaccination, and then multiplied that by the proportion of the country where the subnational SIA was conducted to estimate the additional percentage immunized at national level. Similarly, for phased SIAs, we calculated the percentage of additional children immune in the areas targeted by each phase separately in the R version and aggregated the impact at the national level.

Vaccine effectiveness

The vaccine effectiveness (VE) of a measles vaccine dose is dependent on the age of administration. A literature review found the median VE of a single dose of MCV1 to be 84% if administered at 9–11 months of age, and 92.5% if administered at 12 months and above, based on trials that verified vaccination history and

confirmed cases by laboratory methods⁷. Among children who do not develop immunity after MCV1, roughly 95% will develop immunity with a second dose. The VE is lower when the vaccine is given before 9 months of age, estimated by separate literature review to be 58%⁸. Our assumptions of the VE of MCV1 and MCV2 are based on the recommended age of vaccine administration in the national immunization schedule.

SIAs usually cover children of a wide age range, from 9 months up to 14 years of age, and in outbreak settings, as low as 6 months of age. The SIA target age was split according to previous vaccination status and age at the time of the SIA, and the age-appropriate estimate of VE was used.

Limitations

The measles immunity profile method does not account for geographical heterogeneity within a country. While immunity profiles could be developed for subnational areas, such analyses are often not feasible because of the unavailability of routine immunization and SIA coverage and population data at subnational levels, in particular the lack of coverage survey estimates. Because of the lack of accurate coverage and population data at subnational levels, the impact of each SIA is averaged at national level, the equivalent to assuming a complete mixing of the population in the country after each SIA. However, this homogeneous mixing is not likely to occur. Furthermore, the immunity profile does not consider immunity acquired through natural measles infection, potentially underestimating the proportion of persons who are immune to measles especially in older age groups born when measles was highly endemic. The accuracy of the analysis also relies on the quality of input data and on the frequency and quality of nationally representative population-based coverage surveys.

⁷ Uzicanin A and Zimmerman L. Field effectiveness of live attenuated measles-containing vaccines: a review of published literature. *J Infect Dis.* 2011 Jul;204 Suppl 1:S133–148.

⁸ Nic Lochlainn LM, de Gier B, van der Maas N, Strebel PM, Goodman T, van Binnendijk RS, de Melker HE, Hahné SJM. Immunogenicity, effectiveness, and safety of measles vaccination in infants younger than 9 months: a systematic review and meta-analysis. *Lancet Infect Dis.* 2019 Nov;19(11):1235-1245.



Measles immunity profile method and tools

Xi Li

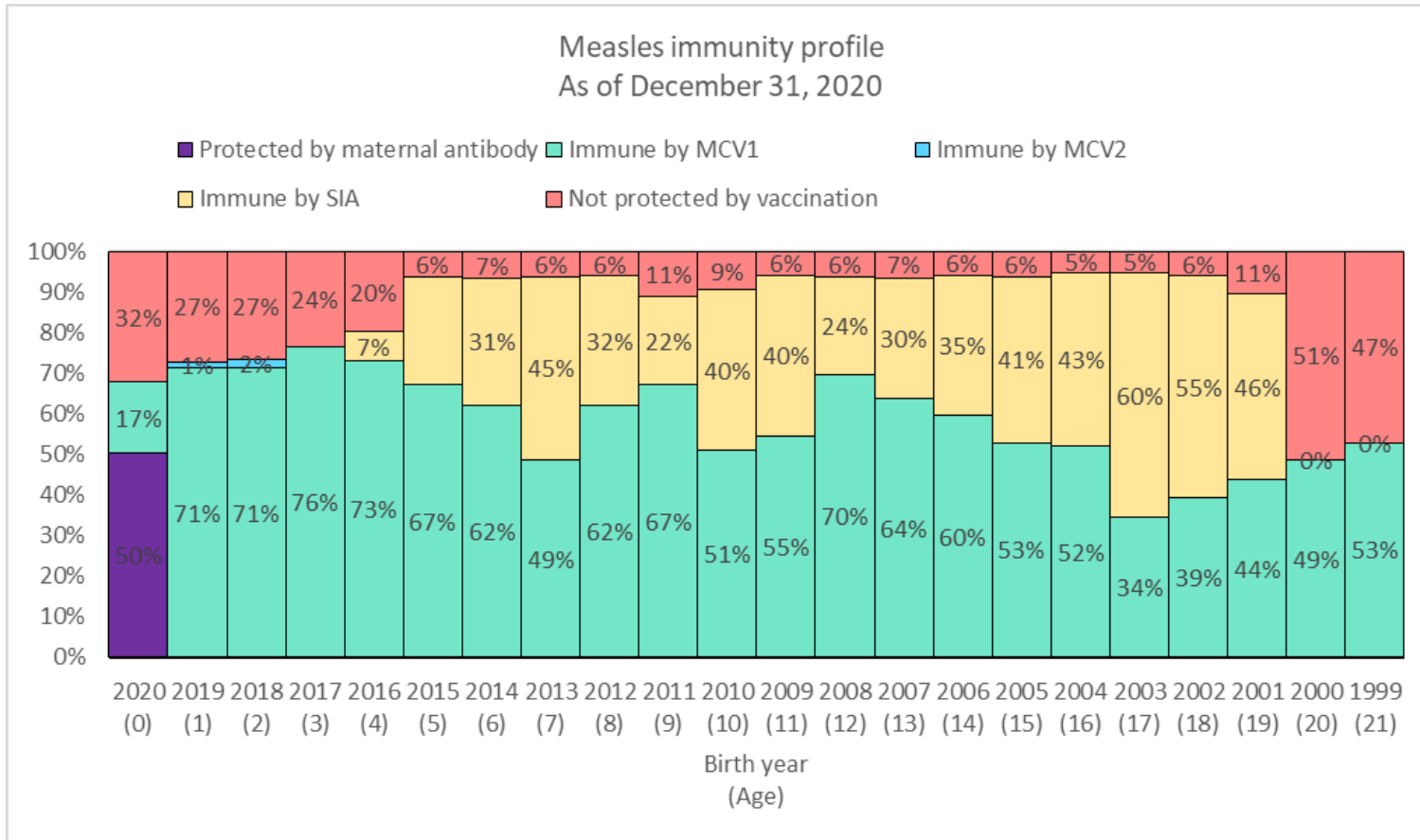
James Goodson

Robert Perry

Measles Elimination Team, Accelerated Disease Control Branch

Global Immunization Division, Center for Global Health

What is Measles Immunity Profile?



Used by epidemiologists for many years

% of persons immune by each vaccination opportunity
 $= \% \text{ of population susceptible} \times \text{vaccination coverage among susceptible} \times \text{vaccine effectiveness}$

Triangulation with surveillance data, serosurvey and modelling results

A component of risk assessment

In a cohort that an SIA was conducted after MCV2 age:

% of persons immune by MCV1 = MCV1 coverage * MCV1 VE

% of persons immune by MCV2 = % of persons susceptible before MCV2 * MCV2 coverage among susceptible * MCV2 VE

% of persons immune by SIA = % of persons susceptible before SIA * SIA coverage among susceptible * SIA VE

Issues and objectives




- **Issues**

- Multiple informal versions of Excel spreadsheets used different assumptions and parameters, producing inconsistent results
- Measles Strategic Planning Tool: SIA is independent of routine immunization

- **Objectives**

- Standardize and better document assumptions and methods.
- Make immunity profiles available to all countries based on publicly available data, updated at least annually.
- Promote use of profiles by countries and partners for planning preventive SIAs.
- Provide a set of tools that are suitable for different scenarios

A set of tools

Formulas written in	Microsoft Excel	R		
Software				
Intended use	Illustration for comprehension of basic methods for estimating measles immunity. Hands-on field training	View readily made measles immunity profiles	Interactive dashboard that users could review and edit input data and generate the profiles or analyze measles susceptibility in hypothesized scenarios.	View and modify annotated source codes if users are interested

Microsoft Excel

Measles Immunity Profile

Background
This tool creates a profile of immunity against measles in a country or subnational area. It provides estimates of the number and percentage of the population immune to measles, by year of birth and by age group. The quality of these estimates depends largely on the quality of the coverage data that are used, and the validity of the assumption that previously unvaccinated persons will be only be reached after previously vaccinated persons have been vaccinated with MCV2 or during a supplementary immunization activity (SIA). This tool should be useful to estimate the size of population susceptible to measles and the age groups most likely affected. These estimates should help to plan if and when a vaccination campaign should be held, and indicate the target age group to include. This tool is based on many preceding tools, including the Measles Strategic Planning tool developed by WHO, PATH, and Stanford University in 2009.

How to use this workbook?

- 1. Input data**: Enter data in sheets 1A and 1B
- 2. Calculation**: Calculations are done in sheets 2A, 2B, 2C
- 3. Output**: Output data in tables in sheets 3A, 3B
- Graphs**: Results are plotted in Chart 1, 2, 3

Instructions and resources

- For links to public data sources, go to sheet Data sources.
- For instructions on data entry, go to sheet Data entry instructions.
- For detailed instructions on SIA data, go to SIA data worksheet.
- Go to sheet Assumptions, formulas for description of the methods, limitations and explanations of the formulas.
- For additional information including version history, go to sheet Additional info.

Microsoft Power BI

Country name: Chad

Age range for the profile: 0 to 29

Assumptions on correlation between doses

- MCV2 and SIA first reach previously vaccinated children (assuming receiving MCV2 and SIA doses are dependent on previous vaccination status)
- MCV2 and SIA reach children with equal chance, regardless of vaccination status (assuming independence between receiving MCV1, MCV2 and SIA doses)

Immunity by birth cohort (as of Jan 1, 2020)

Number of susceptible under 5: **995.92K**
Ratio of <5 susceptible to one birth cohort: **1.63**

Number of susceptible under 15: **1.24M**
Ratio of <15 susceptible to one birth cohort: **2.03**

MCV1 (%) in 2019: **41**
MCV2 (%) in 2019: **0**

Supplementary immunization activities

Country	Extent	Year	Start date	Status	Activity	Age group	Target population	Reached pop.
Chad	Sub-National	2019	4/9/2019	done	FollowUp	6 M-9 Y	606318	620355
Chad	Sub-National	2018	11/17/2018	done	Outbreak Response	6 M-9 Y	2415484	2421067
Chad	Sub-National	2017	3/12/2017	done	CatchUp	9-59 M	693526	707103
Chad	Sub-National	2016	11/21/2016	done	FollowUp	9-59 M	2083306	2342341

Routine immunization schedule

Vaccine	Schedule	Entire country
Measles	9 months	Yes

Shiny R app

Country: Afghanistan

Start and end dates of birth of the cohorts covered: 01/01/1960 to 12/31/2019

Relationship between doses: MCV2 and SIA first reach previously vaccinated children (Recommended default choice)

Planned SIA coverage

MCV1 and MCV2	A1 (Best case)	A2	A3	A4
A: 0% decrease	81	82	83	84
B: 25% decrease	61	62	63	64
C: 50% decrease	41	42	43	44
D: 75% decrease	21	22	23	24
E: 100% decrease	01	02	03	04

Source codes

```

R version 4.0.3 (2020-10-10) -- "Bunny-Wunnies Freak Out"
Copyright (C) 2020 The R Foundation for Statistical Computing
Platform: x86_64-w64-mingw32/x64 (64-bit)

R is free software and comes with ABSOLUTELY NO WARRANTY.
You are welcome to redistribute it under
Type 'license()' or 'licence()' for
Natural language support but running in
Type 'demo()' for some demos, 'help()'
Type 'help.start()' for an HTML browser interface
Type 'q()' to quit R.

[Previously saved workspace restored]

independent<-function(priorState,singleDose){
  singleDoseAdditionalPercentImmune<-(1-priorStateCumulativeImmune)*singleDose
  postState<-data.frame(CumulativeVaccinated=priorStateCumulativeVaccinated+(
  return(list('postState'=postState,'singleDose'=singleDose))
}

parallel<-function(priorState,parallelSIA,independence){
  immunityByParallelSIA<-data.frame(intervention=character(),coverage=double())
  postStateParallelSIA<-data.frame(CumulativeVaccinated=double(),CumulativeImm
  for(i in rownames(parallelSIA)){
    singleDose<-parallelSIA[i,c('coverage','nationalPercentTarget','SubActivity
    if(singleDose$selective==TRUE){
      immunityBySIA<-selective(priorState,singleDose)
    } else if(singleDose$independence==TRUE){
      immunityBySIA<-independent(priorState,singleDose)
    }
  }
}

in [5]: M mcv1 <- read_excel("Input/coverage.xlsx")
in [6]: M sia <- read_excel("Input/SIAs.xlsx",sheet="
in [7]: M lastNationalSIA <- read_excel("Input/SIAs.xlsx",sheet="
in [8]: M population <- read_excel("Input/population.xlsx",sheet="
in [9]: M MCV1_MCV2_Ages <- read_excel("Input/MCV1_MCV2_Ages.xlsx",sheet="
in [10]: M vaccineEffectiveness <- read_excel("Input/vaccineEffectiveness.xlsx",sheet="
in [11]: M sia$selective <- FALSE
in [12]: M sia <- cleanSIA(sia,population)
in [13]: M sia
  
```

Major updates

- **Dependence between MCV1, MCV2, and SIAs**

- Previous versions: independence between routine and SIA doses leading to overestimation of vaccination impact.
- Now: fully dependent as default. Optional independent scenario in R.

- **Subnational SIAs and phased SIAs**

- Previous versions: lack instructions on combining SIAs targeting different subnational areas, resulting in underestimation of vaccination impact.
- Now: non-overlapping subnational SIAs and phased SIAs vaccinate different segments of the population

Advantages of using R codes

- **Improved precision**
 - High granularity: calculation done for each daily birth cohort
 - Age dependent vaccine effectiveness in SIAs
 - Sequence of MCV1, MCV2 and SIAs for each daily birth cohort
- **Improved efficiency**
 - Generated profiles for all 194 WHO member states
- **Ease of system integration**
 - Codes and web-based dashboards that could be integrated with other systems

Limitations

- **Lack of subnational data**
 - National profiles assume complete population mixing after each SIA
 - Subnational heterogeneity not considered in national profiles
- **Inaccurate input data**
 - Relies on administrative coverage of SIAs when survey estimates are unavailable
 - WUENIC may be interpolation/extrapolations based on recent surveys, trends in doses administered, and information on program performance
 - Exact dates of vaccination for routine or SIAs at individual level are unavailable
- **Immunity acquired through national infection is not considered**
 - The profiles could be the starting point of advanced modelling

Recent use cases

- A component of comprehensive risk assessment
 - Assessing measles outbreak risks during the COVID-19 pandemic in 5 AFRO countries
 - Complement Measles Programmatic Risk Assessment Tool
- Generated profiles for countries applying to Gavi SIA funding
- Estimated number of under-5 susceptible children for country prioritization in the Global Measles Outbreak Strategic Response Plan
- Generated profiles for EMRO countries for outbreak response plans

Future plans

- **Model validation and comparison**
 - Serosurveys
 - Cohort analyses of case-based surveillance data
 - Comparison of methods on dose dependence with modelers
- **Disseminating readily made immunity profiles**
 - For countries applying to Gavi SIA support
 - For all countries (possibly through sharing the Power BI dashboard)
- **Finalizing “self-service” tools**
 - Excel for hands-on training
 - Shiny R app for more accurate results

Session 3

Review of vaccine delivery cost projection

Consensus Statement on Vaccine Delivery Costs

April 2021

Authors

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1. Background

This consensus statement was developed in response to a request from the World Health Organization (WHO) Immunization and Vaccines related Implementation Research Advisory Committee (IVIR-AC). They requested that ‘guidance be developed for standardization of micro-costing and planning tools, on new vaccine introduction on where to obtain data, at what level it should be collected, how to conduct sampling, and methods used in vaccine delivery costing.’ (Weekly Epidemiological Record, No. 24, 15 June 2018). In response to this request, an *ad hoc* Working Group was created to oversee the development of this guidance for WHO.

The Working Group identified that multiple efforts, either in process or completed, each partly addressed or are addressing the original IVIR-AC request on data collection, sampling, and methods to be used in vaccine delivery costing. Each of these efforts has different purposes. With this new information, in March 2019, IVIR-AC modified their request to instead review and document the various workstreams that are being conducted in immunization costing. In July 2019, the Working Group met to discuss the vaccine delivery costing work taking place through different organizations. They noted some differences in terminology and principles among the organizations. As a result, they agreed to develop this consensus statement to harmonize key terminology and clarify the scope of the various methods. Annex 1 shows a figure that illustrates the chronology of presentations to IVIR-AC on vaccine delivery costing and other meetings to develop the Consensus Statement.

The target audience for the consensus statement is the developers of costing tools or guidance, vaccine delivery cost researchers, and funders of costing tools, guidance and studies. The expectation is that the terminology and methods utilized in the future for developing new tools or guidance, undertaking delivery cost studies, interpreting findings on vaccine delivery costs, or reviewing studies/research/tools will be consistent with this Consensus Statement. It recognizes that retroactive changes to published costing tools and guidance documents that differ from the recommended terminology and methods may not be feasible. The Consensus Statement summarizes similarities and differences in data collection and sampling methods among costing approaches as well as gaps in guidance documents.

2. Objectives of the Consensus Statement for the Immunization Costing Community

The objectives of the consensus statement are the following:

- To highlight and explain commonalities and differences across different costing approaches, tools, and guidelines;
- To highlight the objectives of different costing approaches, tools, and guidelines;
- To encourage improvement and innovation in methods and tools that are fit for purpose;
- To advance the immunization economics community of practice by committing to follow certain principles and common definitions (as detailed in Annex) that will make the collective costing work more easily interpretable and useful, while acknowledging that some deviations may occur due to limits to standardization of approaches with different objectives.

To achieve these objectives, the Working Group reviewed terminology, definitions, and principles of guidance documents and costing tools for vaccination delivery. Recommendations for costing principles and terminology were developed.

For the purpose of this document, the definition of vaccine delivery costing is the following: all costs associated with delivering immunizations to target populations, noting whether is inclusive or exclusive of vaccine costs, and including recurrent and capital costs. Vaccine delivery costs can be disaggregated into financial and economic delivery costs (see cost definitions below).

3. Vaccination Delivery Cost Analyses

Efforts to estimate the costs of immunization programs, strategies, and new vaccine introductions have utilized various methodological approaches as described below. The approach selected is usually based on the purpose of the analysis and the type of information that decision-makers need. The Working Group qualitatively characterized workstreams based on their knowledge of groups currently working in the field following a 2019 International Health Economics Association pre-congress session on vaccine economics in Basel, Switzerland. These characterizations were intended to help elucidate where and why differences in definitions and methods were occurring and were not derived from any prior framework.

Major workstreams on costing of vaccine delivery and immunization program costing identified by the Working Group are the following:

- i. **Retrospective routine immunization (multiple vaccines) cross-sectional costs:** The first workstream is focused on estimating retrospective (i.e., already incurred) routine immunization, cross-sectional costs of service delivery units at a single point in time, typically using a full costing approach. This method provides a range of unit costs (cost per dose, cost per person, cost per fully immunized person [FIP]) by facility, district, and higher levels in the health system for total routine immunization delivery costs. Costs are economic and/or financial costs. It includes, for example, the work conducted in the Expanded Programme on Immunization Costing (EPIC) studies (see www.immunizationeconomics.org) and other work by groups, such as the Harvard School of Public Health, Wits University, Curatio Foundation, PAHO, ThinkWell, UNICEF, Johns Hopkins University, and PATH (see Annex 2 for details). The purposes are to determine delivery costs of the entire routine immunization program as it currently operates for benchmarking and/or to explain variation in facility costs and unit costs (e.g., cost determinants, efficiency).
- ii. **Retrospective single-vaccine costs:** The second approach is to estimate retrospective costs for a specific vaccine, typically using incremental costing. Retrospective estimation of incremental vaccine-specific campaign and new vaccine introduction costs differs from full costing of routine immunization in requiring some implicit or explicit estimation of counterfactual resource use in the absence of that campaign or vaccine introduction. This is often done through data collection at a single point in time (post-campaign or post-introduction) with reference to documents and recall by key informants to estimate which

resource use was specifically incremental. Examples of such studies are being applied by groups such as ThinkWell, Harvard School of Public Health (EPIC studies), International Vaccine Institute (IVI), WHO, UNICEF and Centers for Disease Control and Prevention (CDC). Costing tools used to estimate retrospective costs include, but are not limited to (see Annexes for websites for these tools):

- the IVI/WHO CHOLTOOL
- the WHO Cervical Cancer Prevention and Control Costing Tool (C4P)
- the WHO Seasonal Influenza Immunization Costing Tool (SIICT)
- the WHO/IVI Typhoid Vaccine Costing Tool (TCVCT)
- the PATH Malaria Vaccine Immunization Costing Tool (MVICT)
- the PAHO ProVac/COSTVAC

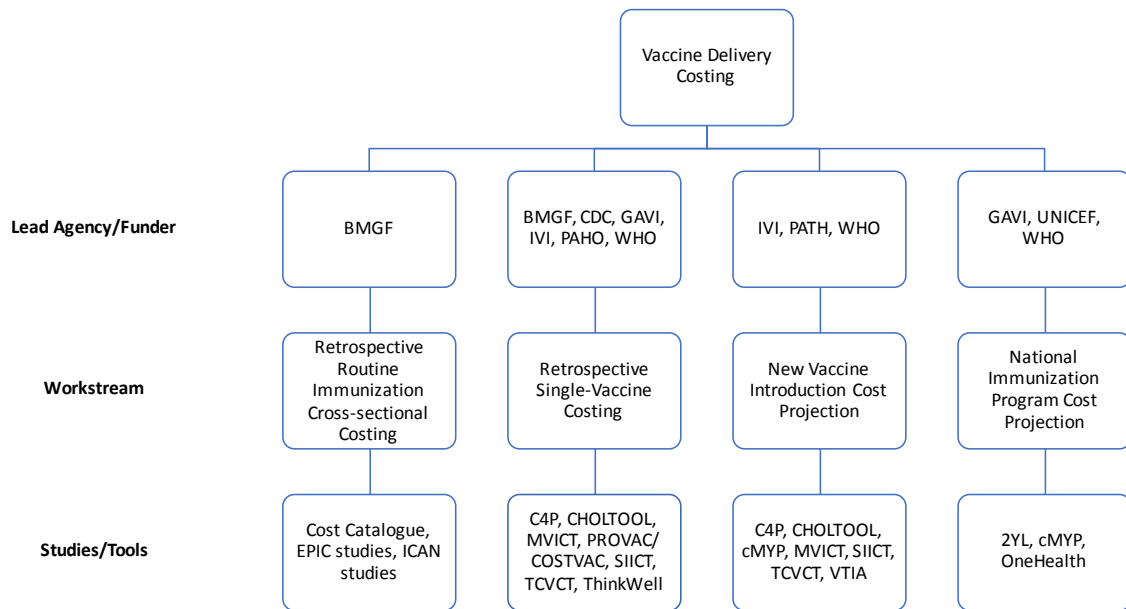
Incremental costing of a specific vaccine, whether delivered through campaign or routine, differs substantially from full costing of routine immunization because it involves not only estimating the proportion of shared health system resources used for immunization, but also the extra step of allocation by vaccine. In particular, campaign delivery may differ in frequency, administrative levels (sometimes sub-national rather than national), whether these are preventive or in response to outbreaks (e.g., oral cholera vaccine [OCV] provision), for catch-up, and whether these involve populations other than young children and pregnant women, such as health workers, adolescent girls, or all ages over one year for OCV. When conducted for a campaign, the purpose of these cost analyses may be for retrospective evaluation of campaign costs (including as an input to cost-effectiveness analyses), explaining variation in costs by strategy and venue, and cost projections for planning and decision-making on conducting campaigns. When estimating retrospective costs of new vaccine introduction, whether via campaign or routine immunization, the purpose of these analyses may be to inform country planners and decision makers, and global funders on the costs of introduction and recurrent costs over time. Both financial and economic costs are estimated.

- iii. **Projection of new vaccine introduction costs:** The third approach is estimation of new vaccine introduction costs through the projection of the price and quantity of ingredients (e.g., time, equipment, vaccines, etc.) needed for vaccine introduction, typically using incremental costing for a specific period, e.g., one or five years. The prices and quantities of ingredients are obtained through interviews with program managers and facility visits to obtain current information on for instance personnel time, supplies, and equipment. The projections are often conducted with the same costing tools as found in the second workstream: C4P, SIICT, TCVCT, CHOLTOOL, and MVICT. Examples of such studies have been funded by BMGF through EPIC, WHO, UNICEF, IVI, CDC, and PATH. Another tool, the Vaccine Technology Costs and Health Impact Assessment Tool (VTIA), is used to compare the commodity and system costs for a new vaccine technology (e.g. temperature stability vaccines) with the current one. The purpose of these cost projections is for planning and decision-making on new vaccines during the introduction period. Costs are shown for both financial and economic costs and include cost per dose and FIC as well as total annual costs.

- iv. **Projection of national immunization program costs:** The fourth workstream is immunization program cost projection (e.g., comprehensive multi-year plan [cMYP], 2nd Year of Life (2YL), OneHealth tool) where the cost of a national program is approximated for a baseline year and then the costs of future years are projected. This is a type of costing for strategic planning to assist in budgeting, resource planning, and mobilization over a strategic period. These projections estimate fiscal costs; also, both annual and three to five-year costs are estimated.

Figure 1 shows the four workstreams, their lead agencies/funders, and associated studies/tools.

Figure 1. Major Current Workstreams in Vaccine Delivery Costing identified by Working Group



Note: 2YL = 2nd Year of Life; BMGF = Bill & Melinda Gates Foundation; C4P = Cervical Cancer Prevention and Control Costing; CDC = United States Centers for Disease Control and Prevention; CHOLTOOL = Oral Cholera Vaccine Costing Tool; cMYP = comprehensive multi-year plan; EPIC = Expanded Programme on Immunization Costing; ICAN = Immunization Costing Action Network; IVI = International Vaccine Institute; MVICT = Malaria Vaccine Immunization Costing Tool; SICT = Seasonal Influenza Immunization Costing Tool; TCVCT = Typhoid Conjugate Vaccine Costing Tool; VTIA = Vaccine Technology Costs and Health Impact Assessment Tool; WHO = World Health Organization

4. Review of existing Guidance Documents and Costing Tools

Annex Tables A2a and A2b show the eleven existing guidance documents and eleven tools for costing vaccine delivery and immunization programs. These were identified by the Working Group as of July 2020. Note that this list is based on Working Group members' personal knowledge and prior reference to them in conducting immunization delivery costing and may not be exhaustive. A few of these guidance documents and tools are for costing health services more generally, such as the OneHealth Tool and the Community Health Planning and Costing Tool (CHPCT).

The review showed that some gaps in costing guidance for the workstreams exist on how to consider slackness of resources, estimation of shared resources for the interventions and specific vaccines, and sampling and respondent selection, particularly for the cost projections for vaccine introduction.

Terminology and definitions of costs in workstreams

Annex Table A3 shows definitions of costing terminology found in the guidance documents. The guidance documents have similar definitions of financial and economic costs, and recurrent and capital costs, but vary in the level of details of the definitions. Most guidance documents do not describe in detail issues of interactions¹ between terminology, perspective, financial vs. economic costs², and how incremental costing affects financial vs. economic costing³. For example, incremental costs for financial costs will differ depending on the perspective of the analysis; if the perspective is of the public health provider, resources donated by external entities will not be included.

Annex Table A4 compares the costing principles in the guidance documents with the Global Health Cost Consortium (GHCC) Principles and Methods Reporting Checklist (GHCC 2017). Guidance documents vary in the extent to which costing principles are discussed. Most guidance documents refer to study purpose, classification of costs, the time horizon of data collection, presentation of costing methods, and depreciation of capital costs. Other principles such as describing the timing of data collection and listing sources for price data are only discussed by one or two of the guidance documents (see discussion in annex).

Annex Table A5 compares the level of data collection, activities/cost categories, perspective, and definitions of cost terms and perspective among the workstreams and shows the variations among these. Annex Table A6 shows differences in data sources, sampling, and characterization of uncertainty by workstream.

¹ An Interaction is the action or influence of things on one another (Merriam-Webster.com).

² Financial costs only include resources paid for by the 'buyer' or 'provider' and will therefore be affected by the perspective chosen for the analysis.

³ The definitions are not clear about whether resources that already exist before the intervention (e.g. cold chain equipment) should be included in economic costs and how excess capacity should affect these (e.g., whether the costs should only be included if there is no slack capacity to absorb the new intervention resource requirements).

Areas for clarification and harmonization

Based on the review, some specific areas that need further clarification and harmonization have been identified in terms of data collection, sampling, and characterization of uncertainty. These are shown in Annex 6.

5. Recommendations for Costing Terms by Working Group

The Working Group reviewed costing term definitions in the existing guidance documents. Based on the definitions shown in Table A2, they developed recommendations for costing terms to be used in estimates of vaccine delivery cost.

The following definitions of costing terms are recommended by the Working Group:

1. **Vaccine delivery costs**
Costs associated with delivering immunization programs to target populations, exclusive of vaccine costs.
2. **Vaccine cost**
At a minimum includes the cost of the vaccine and diluent (if applicable); the analysis should include accounting for wastage rates; the analyst should specify whether this also includes injection supplies (syringes), international shipment, insurance, and customs/duties
3. **Financial cost**
Monetary outlays, with straight-line depreciation for capital goods; does not include opportunity costs for use of resources or donated goods and services from sources other than the payer(s) defined in the analysis. Definition is dependent on perspective since monetary outlays are specific to the payer(s) defined in the analysis.
4. **Economic cost**
The value of all resources utilized, regardless of the source of financing. Includes opportunity costs for use of existing resources and any donated goods or services from any source. Capital costs are annualized and discounted.
5. **Fiscal cost**
Financial costs without depreciation of capital costs. (Note: Such fiscal costs have been termed “initial investment” in some costing tools.)
6. **Recurrent cost**
Value of resources that last less than one year. Start-up activity costs may include recurrent costs.
7. **Capital cost**
Value of resources lasting more than one year such as equipment, buildings, and trainings. Start-up activity costs may include capital costs.
8. **Incremental cost**
Cost of adding a new service/intervention or a package of services/interventions over and above an existing program; inclusion of existing resources will depend on assumptions made about excess capacity (i.e., whether resources are underemployed; if there are no slack resources (e.g., all personnel time is fully allocated before the addition of the new service/intervention), then

their use for the new service or intervention incurs an opportunity cost that should be included – either by measurement or assumption).

9. **Full cost**

Baseline cost as well as the additional cost of the new intervention, including vaccine cost.

10. **Cost projection**

Estimation of future costs of both recurrent and capital inputs.

11. **Prospective data collection**

Direct observation of resource use during data collection, i.e., data are collected concurrently with intervention implementation.

12. **Retrospective data collection**

Data collection after resource use is completed.

13. **Start-up cost**

Cost of initial one-time programmatic activities. Examples may include initial micro-planning, initial training activities, and initial sensitization/ social mobilization/ information, education and communication (IEC); does not include routine or repeated programmatic activities such as refresher training or annual microplanning. Start-up activities may include both recurrent and capital costs; they are defined by the non-repeating nature of the activity, not the type of input.

14. **Micro-costing**

Focuses on granular accounting of input prices and quantities; disaggregates costs of particular output into specific goods and services consumed.

15. **Bottom-up costing**

Measures input quantities at the client or activity level.

16. **Top-down costing**

Divides overall program cost or expenditures, often including those above service level, by number of outputs to calculate unit cost.

17. **Perspective**

The point of view considered for costs (and benefits, if included) in a costing study, by whom the costs were incurred. Payers are the disbursing agents for a good or service, and may differ from the original source of funding. A provider perspective includes costs incurred by health service providers (can be limited to the government), a payer perspective includes costs to the payer(s), such as government or an external partner, while the societal perspective includes all costs incurred by providers as well as clients.

18. **Shared cost**

Shared resources that are not used only for immunization, but also for other productive activities.

6. Recommendations for Costing Principles for the Methodological Approaches

The Working Group reviewed costing principles in the various guidance documents and compared these to the GHCC reference case since this document has the most comprehensive set of principles for health service costing. Based on a review of similarities and differences among the guidance documents, they developed recommendations for the costing principles to be used in future costing studies.

The recommended costing principles include the following.

1. Definitions of terms used in studies of vaccine delivery costing should conform closely to the recommended definitions in this Consensus Statement.
2. The study scope in terms of its purpose, audience, target population, time horizon, and service/output should be clearly stated. It should also state whether data collection will be prospective or retrospective, and whether the analysis will be retrospective or a cost projection.
3. The perspective of the cost estimation should be stated and justified.
4. Types of costs to be generated should be clearly defined in terms of startup/introduction or non-startup/introduction, recurrent and capital, fiscal, financial or economic, and incremental or full. Capital costs should be appropriately annualized and depreciated for financial and economic costs and the discount rate justified.
5. The scope of the inputs to be estimated should be defined, justified and if needed referenced. For example, do the costs include national and sub-national costs or only facility-level service delivery costs? Are non-immunization costs included?
6. The 'units' in the unit costs for strategies, services and interventions should be defined – e.g., cost per dose administered.
7. If incremental costing is conducted, any assumptions made regarding existing health system capacity should be described. (See GHCC reference case, pg. 64).
8. The selection of the data sources, including any adjustments to price data (e.g., inflation or currency conversion) should be described and referenced.
9. The methods for estimating the quantity of inputs should be described – whether top-down or bottom-up, methods of allocation, use of shadow prices and the opportunity cost of time, and, methods for excluding research and evaluation costs.
10. Costs should be mapped and reported as either inputs or activities:
 - i. Resource inputs include, for example, personnel time, vaccines, injection and safety supplies, vehicles, fuel, per diem and travel allowances, cold chain equipment, stationery, laboratory equipment, and buildings;
 - ii. Program activities include, for example, vaccine procurement, service delivery, training, micro-planning, social mobilization and advocacy and communication, monitoring and evaluation, surveillance, AEFI monitoring, and supervision.
11. Some boundaries around costs included in the analysis may be employed to keep the costing scope feasible and will depend on the purpose of the costing study, with the rationale for any exclusions provided; use discretion about including one-time costs that are unique or unlikely to be replicated or transferable across settings (for example, new vaccine launches with the President. Clarify definition and threshold for small costs that have expected small (e.g., <\$25) contribution to total costs in aggregate across all sampled units, such as the use of existing office supplies by health facility staff.
12. The sampling strategy employed should aim for internal and external validity of the data⁴. Sampling strategy should be stated, described, and justified, depending on the workstream and costing objectives. Sampling of different service delivery units is desirable as it provides a more

⁴ Internal validity refers to the extent of systematic bias in an estimate while external validity is the extent to which the cost estimate can be directly applied to other programmatic setting. (GHCC, pg. A15-A16).

representative picture of costs and highlights cost variation and cost drivers for a strategy or vaccine.

13. Variation in the cost of the intervention by site/organization, sub-population, or by other drivers of heterogeneity should be explored and reported for retrospective analyses when possible.
14. The uncertainty around the cost estimates should be appropriately characterized when feasible, (e.g., sensitivity analyses; ranges of results for different input parameter scenarios for cost projections; mean and standard deviation for non-representative samples with multiple units; and confidence intervals or credible intervals for retrospective analyses).
15. Inclusion and exclusion criteria: 'stopping rules'⁵ should be defined, explaining which costs are included and the respective rationale.
16. Cost estimates should be communicated clearly and transparently to enable decision-makers to interpret and use the results relevant to the original policy and/or programmatic question.

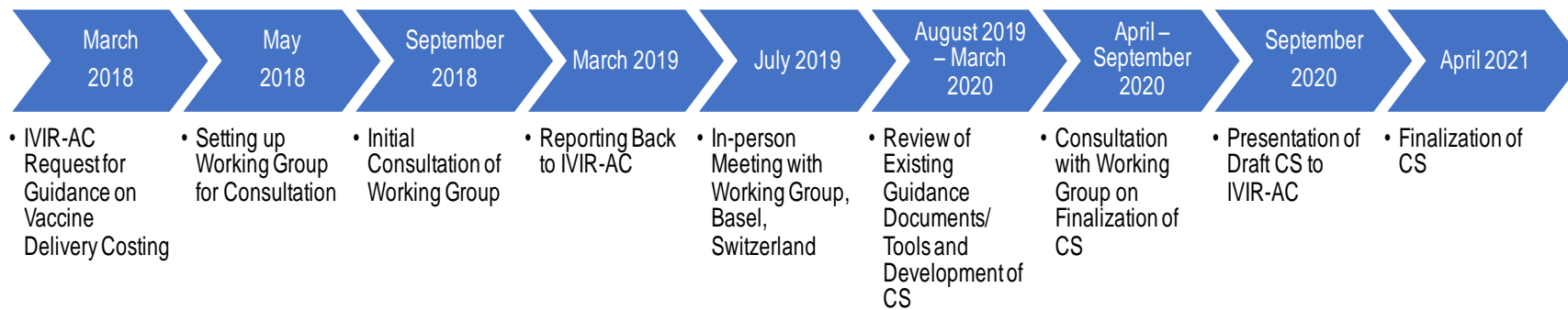
⁵ A 'stopping rule' defines and explains which costs are included, and how the line is drawn between inclusions and exclusions. (GHCC reference case, pg. B-2)

Annexes for the Consensus Statement on Vaccine Delivery Costs (April 2021)

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Annex 1. Timeline for developing a Vaccine Delivery Costing Consensus Statement (CS)



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Annex 2. List of Existing Guidance and Costing Tools for Vaccination Delivery Costing

Table A2a presents the list of guidance documents with their year of publication, target interventions, and purpose as identified by the advisory group. One document is a training manual for costing primary health care services, one document is a reference case for costing global health care interventions, and the rest are specifically about costing of vaccine delivery. Note that some publications such the textbook on vaccine economics are forthcoming and are not shown in the table.

Table A2a. List of guidelines by publication year, target interventions, and purposes

Developer	Guidelines	Publication years	Target Interventions	Purposes	Link
WHO	Cost analysis in primary health care: A training manual for program managers	1994	Primary health care	Assist health program managers to cost their services for planning and evaluating efficiency	https://apps.who.int/iris/handle/10665/40030
WHO	Guidelines for estimating costs of introducing new vaccines into the national immunization system	2002	New vaccine programs	Assist countries in planning for introduction of new vaccines	https://apps.who.int/iris/handle/10665/67342
	WHO guide for standardization of economic evaluations of immunization programs	2008 (edition I), 2019 (edition II)	Existing and new vaccine programs	Methodology for cost and cost-effectiveness analyses of vaccines	https://apps.who.int/iris/bitstream/handle/10665/69981/WHO_IVB_08.14_eng.pdf;jse https://apps.who.int/iris/rest/bitstreams/retrieve
EPIC	Common Approach for the costing and financing analyses of routine immunization and new vaccine introduction costs	2013	Existing and new vaccine programs	Methods for data collection for routine programs and new vaccine introduction (including delivery costs) and financial flows	http://static1.squarespace.com/static/556deb8ee4b08a534b8360e7/t/55970258e4b03cf942da51ac/1435959896232/WEBSITE_Common+Approach.pdf
	How to Cost Immunization Programs - A practical guide on primary data collection and analysis	2020		Practical guidance on how to conduct a facility-based exercise on immunization program costs, including sampling and analytical techniques	http://immunizationeconomics.org/recent-activity/2019howtocost
Global Health Cost Consortium (GHCC)	GHCC Reference Case	2017	Health interventions in general	Improve quality of cost estimates	https://ghcosting.org/pages/standards/reference_case

Developer	Guidelines	Publication years	Target Interventions	Purposes	Link
WHO	Comprehensive Multi-Year Planning (cMYP): A Tool and User Guide for cMYP Costing and Financing	2014	Immunization Programs	To facilitate costing and finance estimation of a cMYP	https://www.who.int/immunization/programmes_systems/financing/tools/cmyp_costing_tool_manual.pdf
ICAN	Methodology note for systematic review, cost catalogue, and analytics How to conduct the cost of a campaign: methodological guidance” to be completed in 2020	2019	Immunization delivery costs	Designed for users of data, including national and sub-national planners and policymakers, researchers, and international partners supporting country immunization and health system policy, planning, and financing	http://immunizationeconomics.org/ican-idcc-methodology
IVI/WHO	CHOLTOOL User Guide	2015	Cholera-specific vaccination programs, including campaigns	Instructions for users of costing tools	https://www.tandfonline.com/doi/full/10.1080/21645515.2020.1747930
WHO	C4P User Guide, Vaccination Module	2012-2019	HPV vaccination programs	Instructions for users of costing tool	TBD
WHO	Flutool plus (SIICT): introduction planning and costing	2017	Seasonal influenza vaccination, including campaigns	Instructions for users of costing tool	https://www.who.int/immunization/research/development/Influenza_economics/en/

Table A2b shows the characteristics of costing tools ⁶ that have been developed for costing vaccine delivery or immunization programs that were identified by the advisory group. It includes five tools for costing the introduction of single antigens, three to estimate immunization program costs, one for estimating the cost-effectiveness of introducing a new vaccine or vaccine technology, one for estimating vaccine technology costs and health impact, and one for estimating costs of vaccination in the second year of life. Characteristics were self-reported by the tool developers on the advisory group.

⁶ Costing tools perform analysis and some have accompanying data forms such as the IVI CHOLTOOL

Table A2b. List of Costing Tools for Vaccine Delivery or Immunization Program

	Delivery Modality	Antigens included	Retrospective vs. Cost projection data collection	Retrospective vs. projection analysis	Full or incremental costs	Economic vs. financial (or fiscal)	Intended Perspective	Intended Data Sources	Sampling	Intended Use of Results
WHO C4P	Health facility; School; Multiple	HPV	Retrospective	Retrospective; Projection	Incremental	Economic; Financial; Initial Investment	Government; Provider; or Payer	Interviews; Financial records; Expert opinion	No guidance	Planning; RM; CEA
IVI CHOLTOOL	SIA/ campaign	Oral Cholera Vaccine	Retrospective	Retrospective; Projection	Incremental	Economic; Financial	Government; or Payer	Interviews; Financial records; Expert opinion	No guidance	Planning; RM; CEA
WHO SIICT	Health facility; SIA/ Campaign; Outreach; Multiple	Influenza	Retrospective	Retrospective Projection	Incremental	Economic; Financial	Government; Provider; or Payer	Interviews; Financial records; Expert opinion	No guidance	Planning; RM; CEA
WHO/IVI TCVCT	Health facility; SIA/ Campaign; Outreach; Multiple	Typhoid Conjugate	Retrospective	Retrospective; Projection	Incremental	Economic; Financial	Government; Provider; or Payer	Interviews; Financial records; Expert opinion	No guidance	Planning; RM; CEA
PATH MVICT	Health Facility; Outreach	RTS,S	Retrospective	Retrospective Projection	Incremental	Economic; Financial; Initial Investment	Government; or Provider	Interviews; Financial records; Expert opinion	No guidance	Planning; RM; CEA
WHO cMYP	Health facility; SIA/ Campaign; Outreach; Multiple	All	Retrospective	Retrospective Projection	Full	Fiscal	Government	Interviews; Financial records; Expert opinion	No guidance	Planning; RM
UN OneHealth Tool	Health Facility; Outreach; Multiple	All	Retrospective Prospective	Projection	Incremental	Financial	Government	Interviews; Financial records;	No guidance	Planning; Budgeting; RM; CEA

	Delivery Modality	Antigens included	Retrospective vs. Cost projection data collection	Retrospective vs. projection analysis	Full or incremental costs	Economic vs. financial (or fiscal)	Intended Perspective	Intended Data Sources	Sampling	Intended Use of Results
								Expert opinion		
PAHO ProVac/ Costvac	Health Facility; Outreach	All	Retrospective	Retrospective	Full	TBD	Government Provider Payer	Interviews; Financial records; Expert opinion	Random selection; Convenience	Budgeting; Efficiency
PAHO ProVac/ UNIVAC	Health Facility/ Outreach	All	Retrospective	Retrospective	Full	TBD	Government Provider Payer	Interviews; Financial records; Expert opinion	Random selection; Convenience	Budgeting; CEA
PATH VTIA	Health Facility; Outreach	All	Retrospective	Projection	Incremental	Economic	N/A	Interviews; Financial records; Expert opinion	Convenience	Planning; Decision-making
UNICEF second year of life (2YL)	Health Facility	All	Retrospective	Projection	Incremental	Economic; Financial	Health sector Government	Interviews; Financial records; Expert opinion	No guidance	Planning

Abbreviations: C4P = Cervical Cancer Prevention and Control Costing (https://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/); CHOLTool = Oral Cholera Vaccine Costing Tool; SIICT = Seasonal Influenza Immunization Costing Tool; TCVCT = Typhoid Conjugate Vaccine Costing Tool; MVICT = Malaria Vaccine Immunization Costing Tool; cMYP = Comprehensive Multi-Year Plan; 2YL = Second Year of Life; VTIA = Vaccine Technology Impact Assessment; RM = Resource Mobilization; CEA = Cost-Effectiveness Analysis

Annex 3. Definition of Costing Terminology

Table A3 shows the definition of costing terms presented in the various guidance documents. Most of the guidance documents have similar definitions of financial and economic costs, capital costs, and incremental costs but differ in the level of detail in their explanations. Fewer documents (less than three) have definitions of cost projections, prospective and retrospective costing, perspective, and bottom-up and top-down costing. The GHCC guidance document has the most definitions while other guidance documents focused on methods.

Other differences among the guidance documents are variations in definitions of vaccine delivery cost and prospective costing. The EPIC and ICAN definition of vaccine delivery are that it includes costs of delivering vaccines, exclusive of vaccines. The costing tools, however, use the term service delivery for operational costs of delivering vaccines, exclusive of vaccines, while ‘vaccine delivery cost’ includes all the value of all resources involved in the immunizations. Prospective costing is defined as ‘direct observation’ in EPIC and as projection of costs in the costing tools.

Table A3. Definitions of Costing Terms in Guidance Documents

	WHO 1994	WHO 2002	ICAN & EPIC (including ‘How to Cost Immunization Programs’ and The Common Approach)	GHCC	Costing Tools’ User Manuals	cMYP Guideline	Recommendation
Vaccine delivery cost	NA	NA	Costs associated with delivering immunizations to target populations, exclusive of vaccine costs (ICAN Methodology Note, pg.11) All resources used, whether immunization-specific, or ‘shared, and whether consumed at immunization delivery ‘sites’ or above the level of service delivery, with and	NA	Vaccine delivery includes startup costs, service delivery (personnel time, supplies and transport/allowance), vaccine procurement, monitoring and supervision, and other costs (C4P guide, pg. 262)	NA	Use ICAN/EPIC definition, specify whether is inclusive or exclusive of vaccines and that includes recurrent and capital costs.

	WHO 1994	WHO 2002	ICAN & EPIC (including 'How to Cost Immunization Programs' and The Common Approach)	GHCC	Costing Tools' User Manuals	cMYP Guideline	Recommendation
			without the new vaccine (How to cost immunization programs, pg. 4)				
Financial cost	NA	Actual expenditure for resources used for goods or services purchased. Does not include cost of existing health personnel time or donated goods (pg. 2)	Financial outlays, usually with straight-line depreciation of capital items (ICAN Methodology Note, pg. 31) A financial costing is concerned with accounting transactions (i.e., monetary outlays or expenditures). (How to cost immunization programs, pg. 7)	Capture the resources that are 'paid' for (pg. A-8)	Actual monetary flows of the buyer such as the Ministry of Health. Does not include the value of resources already paid for, such as personnel time. (SIICT guide, pg. 21)	NA	Composite of three definitions, noting that perspective affects the specification of the ingredients.
Economic cost	Value of resources used to produce something, including a specific health service or a set of services (pg. 13)	Resources that have been foregone for alternative uses, or opportunity costs (pg. 2)	A valuation of all inputs needed for the routine immunization program including valuation of time, supplies, equipment, and annualization of costs that adjusts for a discount rate. (Common Approach, p. 6) Financial outlays plus opportunity costs such as health worker time and any donated items such as vaccines (ICAN Methodology Note, pg. 56)	The value of the highest alternative health intervention opportunity forgone; captures the full value forgone of all resources used. (pg. A-8)	Estimates all costs of an intervention, regardless of the source of funding, so that the opportunity cost of all resources is accounted for in the analysis, includes in-kind and donor contributions. (SIICT guide, pg. 21)	NA	ICAN/EPIC definition, with clarification that includes resources from all payers/resource providers.

	WHO 1994	WHO 2002	ICAN & EPIC (including 'How to Cost Immunization Programs' and The Common Approach)	GHCC	Costing Tools' User Manuals	cMYP Guideline	Recommendation
			An economic costing values resources based on their opportunity cost, regardless of whether a financial transaction occurred. (How to cost immunization programs, pg. 7)				
Fiscal Costs (called initial investment in costing tool guides)	NA	NA	Financial outlays, usually without depreciation of capital items (ICAN Methodology Note, pg. 31)	NA	Initial upfront resource requirements (C4P guide, pg. 268)	NA	ICAN/EPIC definition
Start-up or introduction costs	NA	NA	Costs that are incremental to the routine immunization system and specifically incurred as a result of introduction of the new vaccine (Common Approach, pg.17) All resources used for one-time activities (e.g. social mobilization, cold chain capacity mobilization expansion) in a defined time period around the introduction (How to Cost Immunization, pg. 4)	NA	Initial one-time programmatic activities and include micro-planning, initial training activities, and initial sensitization/ social mobilization/ IEC (SIICT guide, pg.21)	NA	Costing tool User Manual definition, with clarification on difference between initial and continuing activities.

	WHO 1994	WHO 2002	ICAN & EPIC (including 'How to Cost Immunization Programs' and The Common Approach)	GHCC	Costing Tools' User Manuals	cMYP Guideline	Recommend ation
Recurrent cost	NA	Items that are used up during a year (pg. 3)	Recurrent items include labor and consumable items such as vaccines doses, supplies and travel costs (How to cost immunization, pg. 11)	Value of resources/inputs with useful lives of less than one year (pg. 61)	Goods or items used in the delivery of a service or intervention that last less than a year, e.g. personnel salaries. (SIICT guide, pg. 21)	Costs of resources consumed within one year (CMYP guide, pg. 19)	Composite definition.
Capital cost (sometimes called investment cost)	Inputs that last for more than one year (pg. 6)	Items that last longer than one year and are therefore incurred only every few years rather than annually (pg. 3)	Capital items are durable items such as building, equipment, and vehicles ((How to cost immunization, pg. 11)	One-time costs for items that have a useful life of over one year (pg. B-23)	Goods that last for longer than one year, such as equipment (SIICT guide, pg. 21)	An input that has a useful life of more than one year. (cMYP guide, pg. 19)	Composite definition.
Incremental cost	NA	Only looks at the cost of an addition, e.g. a new vaccine, to existing services (pg. 2)	Additional costs associated with introducing new vaccines or making changes in delivery (ICAN Methodology Note, pg. 32) Make assumptions about what particular resources were affected by the intervention, and only measure those resources. (How to cost immunization, pg. 8)	Cost of adding a new or a batch of services or intervention over and above an existing program (pg. 59)	Additional resources required to add an intervention to an existing immunization program (CHOLTOOL guide, pg. 6)	NA	Composite of definitions, with clarification that if resources are not slack, then have to account of opportunity cost
Full costs	NA	NA	Full costs include baseline cost as well as the additional cost of the new intervention. (How to cost immunization, pg. 8)	NA	NA	NA	ICAN/EPIC definition, with clarification that includes vaccines and basic infrastructure.

	WHO 1994	WHO 2002	ICAN & EPIC (including 'How to Cost Immunization Programs' and The Common Approach)	GHCC	Costing Tools' User Manuals	cMYP Guideline	Recommendation
			The sum of all costs associated with vaccination delivery (ICAN Methodology Note, pg. 31)				
Prospective	NA	NA	Direct observation (How to Cost Immunization Programs, pg. 21)	Direct observation of resource use (pg. B-18)		NA	Composite of definitions, with clarification that costs are collected concurrently with interventions implementation
Retrospective	NA	NA		Data collection takes place after resource use (pg. B-18)		NA	GHCC definition
Cost projections		NA	NA	NA	NA	Total future costs of both recurrent and capital inputs to the NIP (cMYP guide, pg. 108)	cMYP definition with clarification that is for intervention or program
Micro-costing/Ingredients	NA	NA	Approach in which prices and quantities of resources are measured (How to Cost Immunization Programs, pg. 4)	Focuses on granular accounting of inputs; Disaggregates costs of particular output into specific items consumed (pg. A-13)	NA	NA	GHCC definition
Bottom-up Costing vs Top-down Costing	NA	NA	NA	Bottom-up measures input quantities at the client or activity level; Top-down divides overall program cost or expenditures, often including those above	NA	NA	GHCC definition

	WHO 1994	WHO 2002	ICAN & EPIC (including 'How to Cost Immunization Programs' and The Common Approach)	GHCC	Costing Tools' User Manuals	cMYP Guideline	Recommend ation
				service level, by number of outputs to calculate unit cost (pg. A-13)			
Perspective	NA	NA	The point of view considered for costs (and benefits, if included), in a costing study; to whom the costs were incurred. Common perspectives include provider, government, healthcare, insurer and societal. (ICAN Methodology Note, pg. 32) Perspective has to do with which costs we care about. A study from the "societal" perspective should include all costs, no matter who in society pays them. The more commonly used "health sector" perspective is narrower. (How to Cost Immunization Programs, pg. 7)	Describes which payers' costs are included in the estimate. For example, a provider perspective may include costs incurred by health service providers, non-health service providers, and be limited to specific payers. (pg. B-2)	NA	NA	Composite definition

Sources: WHO 1994 Training Manual (<https://apps.who.int/iris/handle/10665/400300>); WHO Cervical Cancer screening and treatment module user manual (https://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/); ICAN (<http://immunizationeconomics.org/ican-idcc-methodology>); GHCC (https://ghccosting.org/pages/standards/reference_case); WHO 2013 cMYP

Guidelines (https://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en/#:~:text=cMYP%20Guidelines&text=Better%20alignment%20of%20immunization%20and,than%20by%20disease%20or%20initiative)

In addition, most guides define incremental costing but not full costing. Only one of the documents (EPIC) had nuanced discussions of how perspective affects financial costs, incremental costing affects economic costs, and how the purpose of the analysis affects what cost ingredients should be included. Specifically, the perspective of the costing affects the designation of which inputs/resources are donated – e.g. vaccines in GAVI-eligible countries are donated if the perspective is the government and therefore would appear only as an economic cost, whereas if the study were conducted from a health sector perspective these might be included as financial costs. It is critical to clarify if the perspective is defined in terms of the payer (i.e., the organization outlaying the funds directly to the provider of goods or services) or the funding source; for example, when donor funds are channeled to the government and the government conducts the monetary outlay, this would be considered both an economic cost if the government perspective is used but a financial and economic cost if defined in terms of the payer (donor). Thus, the perspective will affect which resources are included in financial costs. For incremental costs, the guides define these as additional costs incurred with the introduction of a new vaccine or other technology but don't indicate what inputs/resources should be included in economic costs – i.e., which recurrent and existing capital costs should be included.

Annex 4. Costing Principles

Table A3 compares the costing principles in the guidance documents with the GHCC Principles and Methods Reporting Checklist. The guidance documents focus on five of the principles: 1) defining the purpose of the study (GHCC principle 1); 2) classifying the costs as recurrent/capital and financial/economic (GHCC principle 3) ; 3) specifying the time horizon of data collection (GHCC principle 5) ; 4) presenting costing methods (GHCC principle 7); and 5) depreciating the capital costs (GHCC principle 12).

Other GHCC principles were only discussed in one or two of the other guidance documents: 1) importance of stating the perspective (GHCC principle 2); 2) scope of costing (GHCC principles 5 and 6); 3) sampling strategy (GHCC principle 8); 4) timing of data collection (GHCC principle 10); 5) sources for price data (GHCC principle 11); 6) selection of discount rate (GHCC principle 13); 7) use of shadow prices (GHCC principle 14); and 8) characterization of uncertainty (GHCC principle 16). The recommended costing principles are also found in Section 5 of the Consensus Statement.

Table A4. Comparison of Costing Principles among Guidance

GHCC Principle #	WHO 1994	EPIC/Common Approach/Reference Guide	Costing Tools	cMYP	Recommendation in Consensus Statement (CS) (Section 5)
1 The purpose, the population, and the intervention and/or service/output of the cost estimation should be clearly defined.	NA	At the earliest stage of planning a costing exercise, one should consider objectives and rationale.	User should assess whether financial or economic costs are most appropriate based on the objective (C4P, SIICT, CHOLTOOL, SIICT, TCV, MVICT)	The objectives are to analyze program costs, financing and financing gaps and these should be linked to the program objectives.	Combined GHCC principles 1 and 5 (CS Principle # 2): The study scope in terms of its purpose, audience, target population, time horizon, and service/output should be clearly stated. It should also state whether data collection will be prospective or retrospective, and whether the analysis will be retrospective or a cost projection.
2 The perspective of the cost estimation should be stated and justified.	NA	Perspective is an important concept that is somewhat unique to economic studies, as compared to other types of health service research.	NA	NA	Applied GHCC principle (CS Principle # 3): The perspective of the cost estimation should be stated and justified.

GHCC Principle #	WHO 1994	EPIC/Common Approach/Reference Guide	Costing Tools	cMYP	Recommendation in Consensus Statement (CS) (Section 5)
<p>3 The type of cost should be clearly defined, in terms of economic vs. financial, incremental vs full cost, and whether the cost is ‘net of future cost.’</p>	<p>Costs should be classified by inputs: recurrent and capital; Can also be classified by function/activity, level, source, and type of currency; Economic costing should be used for cost-effectiveness analyses.</p>	<p>It is important to make the distinction between financial and economic costs.</p>	<p>Costs are classified as financial and economic as well as recurrent and capital in the costing tools. (C4P, SIIC, CHOLTOOL, TCV, MVICT)</p>	<p>Costs are defined as recurrent and capital.</p>	<p>Composite of definitions(CS Principle # 4): Types of costs to be generated should be clearly defined in terms of startup/ introduction or non-startup/introduction, recurrent and capital, fiscal, financial or economic, and incremental or full. Capital costs should be appropriately annualized and depreciated for financial and economic costs and the discount rate justified.</p>
<p>4 The ‘units’ in the unit costs for strategies, services and interventions should be defined.</p>	<p>Explains general nature of unit costs and gives examples of unit costs.</p>	<p>All resources used in an intervention divided by number vaccination</p>	<p>Unit costs are measured as cost per dose administered, child or girl fully vaccinated</p>	<p>NA</p>	<p>Composite of definitions (CS Principle # 6): The ‘units’ in the unit costs for strategies, services and interventions should be defined – e.g., cost per dose administered or cost per FIC.</p>
<p>5 The time horizon of data collection should be explicit and of sufficient length to capture costs relevant to the purpose, and consideration should be given to disaggregating costs into separate time periods where they vary over time.</p>	<p>Should choose the most recent year for which cost data are available for one full year.</p>	<p>When collecting primary data retrospectively, one must set boundaries of the time horizon in which resource use occurred.</p>	<p>The user should specify whether the estimates are cost projection or retrospective analyses. (C4P, CHOLTOOL, MVICT)</p>	<p>Planning horizon is five years or less.</p>	<p>Combined GHCC principles 1 and 5 (CS Principle # 2)</p>
<p>6 The scope of the inputs to include in the cost estimation should be defined and justified relevant to purpose.</p>	<p>Need to be clear about scope of the costing.</p>	<p>The decisions about scope should be made when planning the exercise, before data is collected.</p>	<p>NA</p>	<p>NA</p>	<p>Composite of definitions (CS Principle # 5): The scope of the inputs to be estimated should be defined, justified and if needed referenced. For example, do the costs include national and sub-national</p>

GHCC Principle #	WHO 1994	EPIC/Common Approach/Reference Guide	Costing Tools	cMYP	Recommendation in Consensus Statement (CS) (Section 5)
					costs or only facility service delivery costs? Are non-immunization costs included?
7 The methods for estimating the quantity of inputs should be described, including methods, data sources and criteria for allocating resources.	NA	Presents methods for recurrent and capital costs.	Presents methods of calculation and suggests data sources. (C4P, SIICT, CHOLTOOL, TCV, MVICT)	Ingredients approach is used to estimate costs – quantities x price x % used in immunization.	Composite of definitions (CS Principle # 9): The methods for estimating the quantity of inputs should be described – whether top-down or bottom-up, methods of allocation, use of shadow prices and opportunity cost of time, and, methods for excluding research and evaluation costs.
8 The sampling strategy used should be specified and designed to minimize bias.	It is necessary to choose a sample and use one of four types: either random, cluster, systematic, or stratified.	Published guidance for sampling health facilities that was developed for health facility data collection alongside DHS household surveys can be applied to immunization costing studies.	NA	NA	Combined definitions and edits by advisory group (CS Principle # 12): The sampling strategy employed should aim for internal and external validity of the data. Sampling strategy should be stated, described, and justified, depending on the workstream and costing objectives. Sampling of different service delivery units is desirable as it provides a more representative picture of costs and highlights cost variation and cost drivers for a strategy or vaccine.
9 The selection of the data source(s) and methods for estimating service use should be described, and potential biases reported in the study limitations.	Methods are described.	Recommend being aware of the quality of available data sources and reporting systems and comparing data sources.	Data sources and methods for estimating service use are described. (C4P, SIICT,	NA	Composite of definitions (CS Principle # 8): The selection of the data sources, including any adjustments to price data (e.g., inflation or currency

GHCC Principle #	WHO 1994	EPIC/Common Approach/Reference Guide	Costing Tools	cMYP	Recommendation in Consensus Statement (CS) (Section 5)
			CHOLTOOL, TCV, MVICT)		conversion) should be described and referenced.
10 Consideration should be given to the timing of data collection to minimize recall bias and, where relevant, the impact of seasonality and other differences.	NA	Notes that the major advantage of direct observation methods is lack of recall bias.	NA	NA	Not included
11 The sources for price data should be listed by input, and clear delineation should be made between local and international price data sources, and tradeable, non-tradeable goods.	NA	The Common Approach lists the sources of information for unit vaccine prices. The HOW TO COST... document lists sources of data for prices.	Sources for price data should be noted in the designated worksheets. (C4P, SIICT, CHOLTOOL, TCV, MVICT)	NA	Included in CS Principles # 8 and 9
12 Capital costs should be appropriately annuitized or depreciated to reflect the expected life of capital inputs	Recommends straight line depreciation.	For economic cost evaluation, all capital costs need to be annualized based on a discount rate and estimates of useful life.	Straight line depreciation is calculated for financial costs, and annualization and discounting for economic costs. (C4P, SIICT, TCV, MVICT)	NA	Included in CS Principle # 4
13 Where relevant, an appropriate discount rate, inflation and exchange rates should be used, and clearly stated.	NA	Recommends using a 3% discount rate unless there is another justification.	NA	NA	Include in CS Principle # 4
14 The use and source of shadow prices for goods and the opportunity cost of time should be reported.	NA	NA	NA	NA	Include in CS Principle # 9
15 Variation in the cost of the intervention by site/organization, sub-populations, or by other drivers of heterogeneity	NA	iOne of the main questions of the Common Approach is to assess the factors that drive the variation between facility total and unit costs. EPIC has	NA	NA	Included in CS Principle # 13

GHCC Principle #	WHO 1994	EPIC/Common Approach/Reference Guide	Costing Tools	cMYP	Recommendation in Consensus Statement (CS) (Section 5)
should be explored and reported.		an analytical tool and database to facilitate comparisons across facilities.			
16 The uncertainty associated with cost estimates should be appropriately characterized.	NA	Standard statistical approaches can be used to calculate an unbiased measure of mean, and the uncertainty in this mean estimated.	NA	Recommends scenario-building to take in account uncertainty; also risk assessment.	Combined two principles in CS Principle 14: The uncertainty around the cost estimates should be appropriately characterized,(e.g., sensitivity analyses; ranges of results for different input parameter scenarios for cost projections; mean and standard deviation for non-representative samples with multiple units; and confidence intervals or credible intervals for retrospective analyses.
17 Cost estimates should be communicated clearly and transparently to enable decision-maker(s) to interpret and use the results.	NA	Section in the Common Approach focuses on writing up results	NA	It is essential to communicate the results clearly.	Combined two principles in CS Principle # 16: Cost estimates should be communicated clearly and transparently to enable decision-makers to interpret and use the results.

Annex 5. Characteristics of Costing Workstreams

Table A5 shows characteristics of the four costing workstreams identified based on recent work known to the advisory group. It shows that the activities/cost categories used in costing are largely similar within the guidance documents for immunization costing. However, in a few cases, the terminology differs – e.g. vaccines/injection supplies for program costing, vaccine procurement for cost projections and retrospective campaign costing, and vaccine, collection, distribution and storage for retrospective routine immunization costing. In addition, some workstreams use the term service delivery to encompass health personnel time, supplies, and transport while other workstreams separate these into individual components. Also, two of the workstreams, program costing and retrospective routine costing, explicitly mention surveillance as an activity while the other workstreams include surveillance under the monitoring activity/cost category. Similarly, two of the workstreams include micro-planning, cost projections and retrospective campaign costing, while this activity is not included in the other workstreams.

Table A5. Characteristics of Costing Workstreams

	Level of Data Collection	Activities/Cost categories	Perspective	Incremental or full	Similarities and Differences in workstream guidance in definitions of terms and perspective
Retrospective routine immunization cross-sectional costs	Facility with some data collection at higher levels	Vaccine (procurement), collection, distribution, storage Facility-based service delivery (personnel, time and resources) Monitoring and evaluation Supervision Training Social mobilization Surveillance Program management Cold chain maintenance Other capital	Health sector, i.e., ignored costs accruing to patients	Full or Incremental	<ul style="list-style-type: none"> - Similar definitions of financial and economic costs and recurrent and capital costs - Uses health sector perspective
Retrospective single-vaccine costs	Program and facility with sampling or interviews with program managers	Vaccine procurement Service Delivery (personnel and transport) Distribution Supervision Micro-planning Training Other Recurrent Cold Chain AEFI Surveillance Other capital	Payer or health system/ government	Incremental	<ul style="list-style-type: none"> - Similar definitions of financial and economic costs and recurrent and capital costs - Uses government and payer perspectives - Costing tools assume incremental economic costs do not include existing equipment since these have available capacity (excess capacity)

	Level of Data Collection	Activities/Cost categories	Perspective	Incremental or full	Similarities and Differences in workstream guidance in definitions of terms and perspective
Projection of new vaccine introduction costs	Program and facility	Vaccine procurement Service Delivery (personnel and transport) Distribution Supervision Micro-planning Training Other Recurrent Cold Chain AEFI Surveillance Other capital	Government or payer perspective	Incremental	<ul style="list-style-type: none"> - Similar definitions of financial and economic costs and recurrent and capital costs - Uses government and payer perspectives - Assumes incremental economic costs do not include existing equipment since these have available capacity (excess capacity)
Projection of immunization program costs	Program	Vaccines/injection supplies Personnel Transport Social Mobilization/IEC Training Supervision Monitoring (includes surveillance) Cold chain equipment Other capital	Provider (could include external funding)	Full or Incremental	<ul style="list-style-type: none"> - Similar definitions of recurrent and capital costs except for US\$100 requirement for capital costs per item; uses straight line depreciation - Cost projections also similar to other definitions - Perspective is government but includes value of donated goods and personnel time

Variation among Workstreams

The workstreams shows the different approaches on data sources, sampling, and characterization of uncertainty, as shown in Table A6. This makes sense given the different recommended uses of the different workstreams. For example, cost projections of new vaccine introduction or an five-year immunization program are by definition an exercise in assumptions about an unknown future program with hypothetical information on costs and quantities; therefore, larger or more representative sampling of sites may not reduce uncertainty about this future program, whereas exploration of a range of scenario input parameters can help identify influential programmatic and cost elements and the range of possible cost results.

Table A6. Data sources, sampling and characterization of uncertainty, and terminology by Workstreams

	Recommended Use	Perspective	Data Sources	Sampling	Characterizing Uncertainty
Retrospective routine immunization cross-sectional costs	Compare costs of vaccine delivery for benchmarking and to explain variation in facility costs and unit costs and evaluate efficiency and equity	Provider, Payer, or Societal	Health facility records; interviews with national and sub-national program managers	Representative sampling of health facilities (stratified, random)	Characterized based on number of sites in sample, stratification of units, and basis of probability of selection; one-way sensitivity testing or scenario analysis
Retrospective single-vaccine costs	Estimate costs of campaigns or routine health facility delivery for benchmarking and to explain variations by strategy and venue	Provider payer, or Societal	Interviews with national and sub-national program managers	Representative sampling of health facilities or campaign sites; Convenience samples	Characterized based on number of sites in sample, stratification of units, and basis of probability of selection
Projection of new vaccine introduction costs	Estimate costs to assist program managers in planning and decision-making on vaccine introduction	Provider, payer, or Societal	No guidance provided; Practice is to use expert opinion; conduct visits to selected health facilities; and hold workshops with stakeholders	No guidance provided; Practice is to conduct visits to selected facilities – urban and rural, etc.	Results based on estimated parameters; conduct scenario analysis to have a range of estimates
Projection of Immunization program costs	Estimate costs to assist in budgeting, planning and resource mobilization over a five-year period	Provider	Interviews with national and sub-national program managers; visits to selected health facilities sometimes	Can collect data at the sub-national as well as national levels	Results based on estimated parameters and necessarily have uncertainty; conduct scenario analysis to have a range of estimates

Annex 6. Areas for clarification and harmonization

Areas for clarification and harmonization are defined as problem areas or areas without a consensus. The following are the areas that have been identified from the review of guides and costing tool manuals.

1. Definitions on terminology among and within workstreams differ and need to be harmonized, where appropriate, acknowledging the different workstream purposes. See Annex 6 for recommended terms
2. The options for study perspective should be agreed upon by advisory group, including use of perspective in financial vs. economic costing.
3. Inconsistent labeling of program activities vs. resource inputs as cost categories, inconsistent nesting of resource inputs inside program activities and vice versa without regard for the perspective of the analysis.
4. Definition of incremental and full costing is not consistent.
5. Sampling and uncertainty: What are the appropriate sampling approaches (random, purposive) for different costing objectives (assuming time and money are not the limitations)? What level of uncertainty is appropriate?
6. Gaps in practical guidance on aggregating costs across levels of the health system and clarity on level of activity vs. level of payer.

Session 3: Review of Vaccine Delivery Cost Projection

Karene Yeung

**Value of Vaccines, Economics, and Modeling
Immunization Analysis & Insights, IVB**



**World Health
Organization**

Timeline

- 2018 March IVIR-AC requested for a guidance on vaccine delivery costing
- 2019 March IVIR-AC recommended setting up a workshop with all partners involved in vaccine costing methodology to have detailed discussion and potentially develop a joint guideline
- 2019 Sep Provided update to IVIR-AC on the development of consensus statement with the redefined scope of review, and continued efforts to harmonize terminology and principles of vaccine delivery costing
- 2020 Sep Presented draft Consensus Statement to IVIR-AC
- 2021 April Finalization of Consensus Statement



Finalized Consensus Statement on Vaccine Delivery Costs

- 11 guidelines
- 11 costing tools

Consensus Statement on Vaccine Delivery Costs

April 2021

Authors

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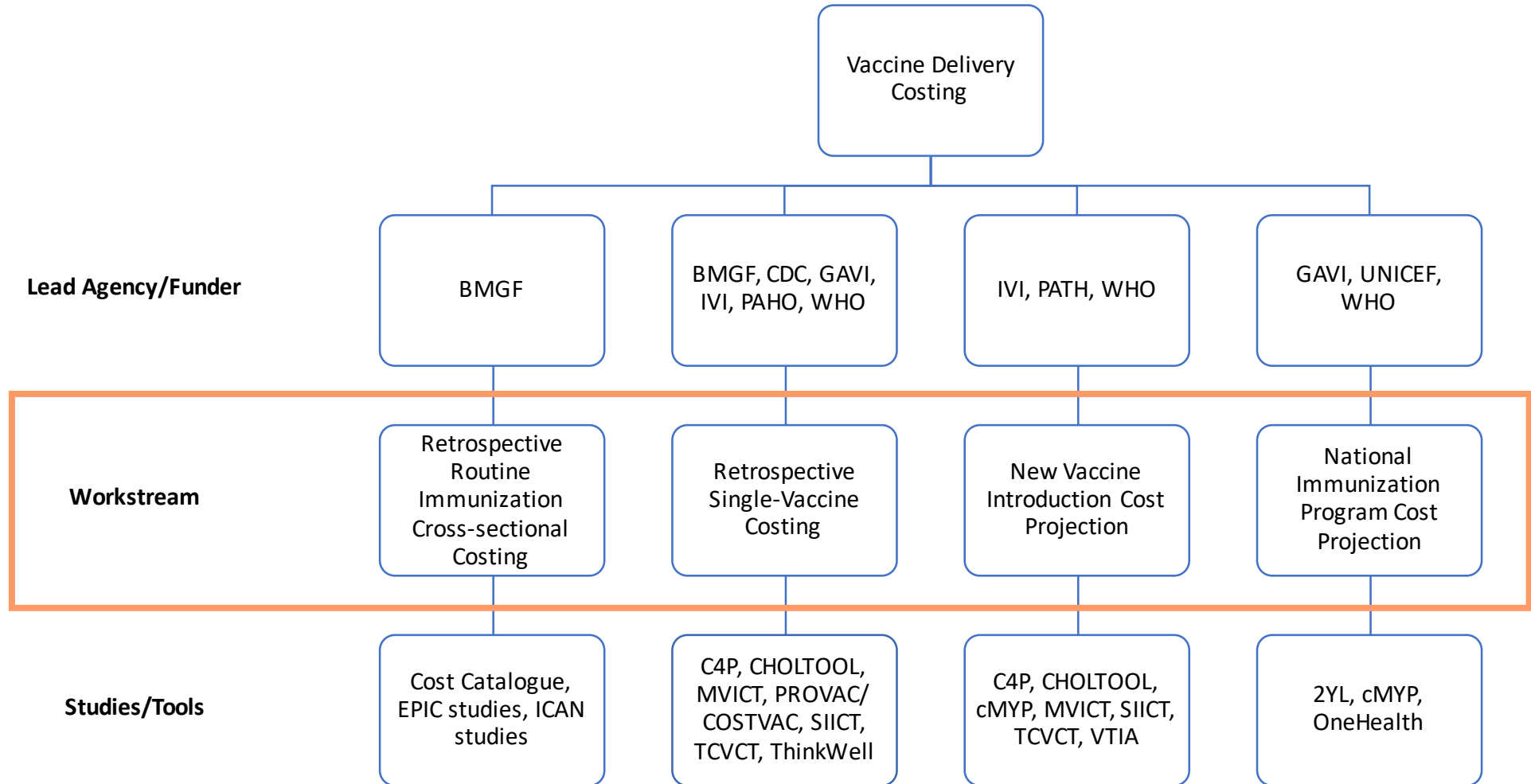
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Major Current Workstreams in Vaccine Delivery Costing identified



Findings from Consensus Statement

- Review of existing guidance documents and costing tools
- Identified terminology and definitions of costs in workstreams
- Identified areas of clarification and harmonization
- Provided recommendations for costing terms
- Provided recommendations for costing principles for methodological approaches



Gaps Identified

- Guidance documents already developed for retrospective costing
- Insufficient guidance on methods to project vaccine delivery costs
 - Data collection
 - Sampling and respondent selection
 - Method for dealing with uncertainty
 - Analysis of findings



Questions to IVIR-AC

- Is the literature review protocol an appropriate approach to review vaccine delivery cost projection?
- Is there a need to develop a guidance on vaccine delivery cost projection?



Vaccine delivery cost projection review and guidance

Ann Levin, PhD



**LEVIN &
MORGAN**
GLOBAL HEALTH CONSULTANTS



Agenda

- Protocol for Systematic Literature Review on Vaccine Delivery Cost Projection
- Process to develop a guidance document on vaccine cost projections for single vaccines

Background

- IVIRAC requested WHO to develop a guidance document on vaccine delivery costing
- An ad hoc working group was formed, comprised of 8 organizations working in vaccine delivery costing
 - Found four workstreams on vaccine delivery costing with different objectives and methods of analysis
 - Reviewed eleven guidance documents on vaccine delivery cost identified by W.G.
 - Differences found in costing terminology and methodological principles
- Modified plan to develop guidance document, instead wrote consensus statement to harmonize differences in costing terminology and methodological principles

Background (continued)

	Perspective	Data Collection	Sampling	Characterizing Uncertainty
Retrospective routine immunization cross-sectional costs	Provider, payer, or societal	Health facility records, interviews with program managers	Representative sampling of health facilities	Based on number of sites in sample, stratification, and probability selection
Retrospective single-vaccine costs	Provider, payer, or societal	Interviews with national and sub-national managers	Representative sampling of health facilities or campaign sites; convenience samples	Based on number of sites in sample, stratification, and probability selection
Projection of new vaccine introduction costs	Provider, payer, or societal	Practice is to use expert opinion; interview program managers	No guidance provided	Conduct scenario analysis but no characterization of uncertainty
Projection of immunization program costs	Provider	Interviews with national/sub-national program managers	Collect data at national and sub-national levels	Conduct scenario analysis but no characterization of uncertainty

Findings

- Found that guidance is well-developed for retrospective vaccine delivery costing
- Gap exists in guidance for vaccine delivery cost projections



Proposed Protocol

Literature review on vaccine delivery cost projection



Purpose

- Conduct systematic literature review on vaccine cost projections guidance
- Potentially inform the development of a guidance document on vaccine delivery cost projection

Questions to be answered through this review.

- What are the objectives of vaccine delivery cost projection studies?
- What data collection and sampling methods are being used?
- What methods of analysis are used for vaccine delivery cost projections?
- How is data uncertainty being characterized in the studies?

Literature Search Strategy

- Reference searches of papers that match eligibility criteria
 - Database Searches
 - PUBMED
 - LISTA EBSCO

Literature Search Strategy

- Search Terms
 - Illustrative vaccine types
 - HPV, Influenza, MCV, Polio, PCV, RCV, TCV, OCV, COVID-19
 - Delivery Costing
 - Cost projection
 - Costing
 - Vaccine terms
 - Vaccine
 - Vaccination
 - Immunization

Literature Selection and Review

1. Remove articles that do not meet inclusion criteria or meet exclusion criteria

Eligible

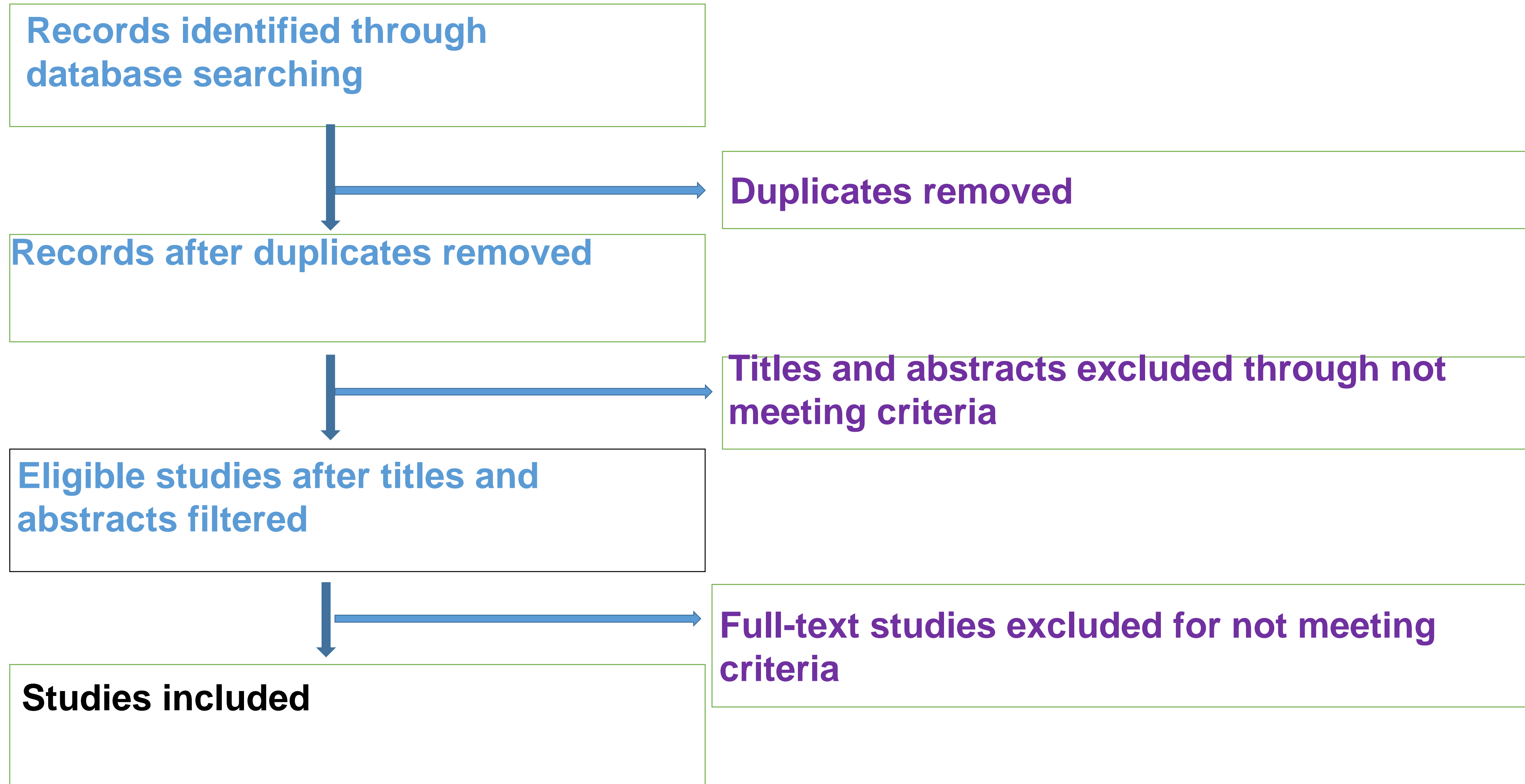
- Vaccine delivery cost projection
 - Single vaccine (could include more than one antigen)

Noneligible

- Retrospective vaccine delivery costing
- Vaccination programme costing

2. Review full papers that meet inclusion criteria

Flow Diagram of Study Selection for Systematic Review



Results of Literature Review

- Summarized and developed into a report/manuscript
 - Types of data collection
 - Cost projection methods
 - Types of analysis analyzed

Development of Guidance for Cost Projection

- Based on:
 - Literature review
 - Previous review of guidance documents on vaccine delivery costs
 - Consensus Statement
 - Working Group comprised of persons that previously conducted cost projections

Session 4: CAPACITI

| CAPACITI |

Country-led Assessment for Prioritization on Immunization

A systematic approach to support decision-making



Progress update IVIR-AC plenary

Maarten Jansen (jansenm@who.int)

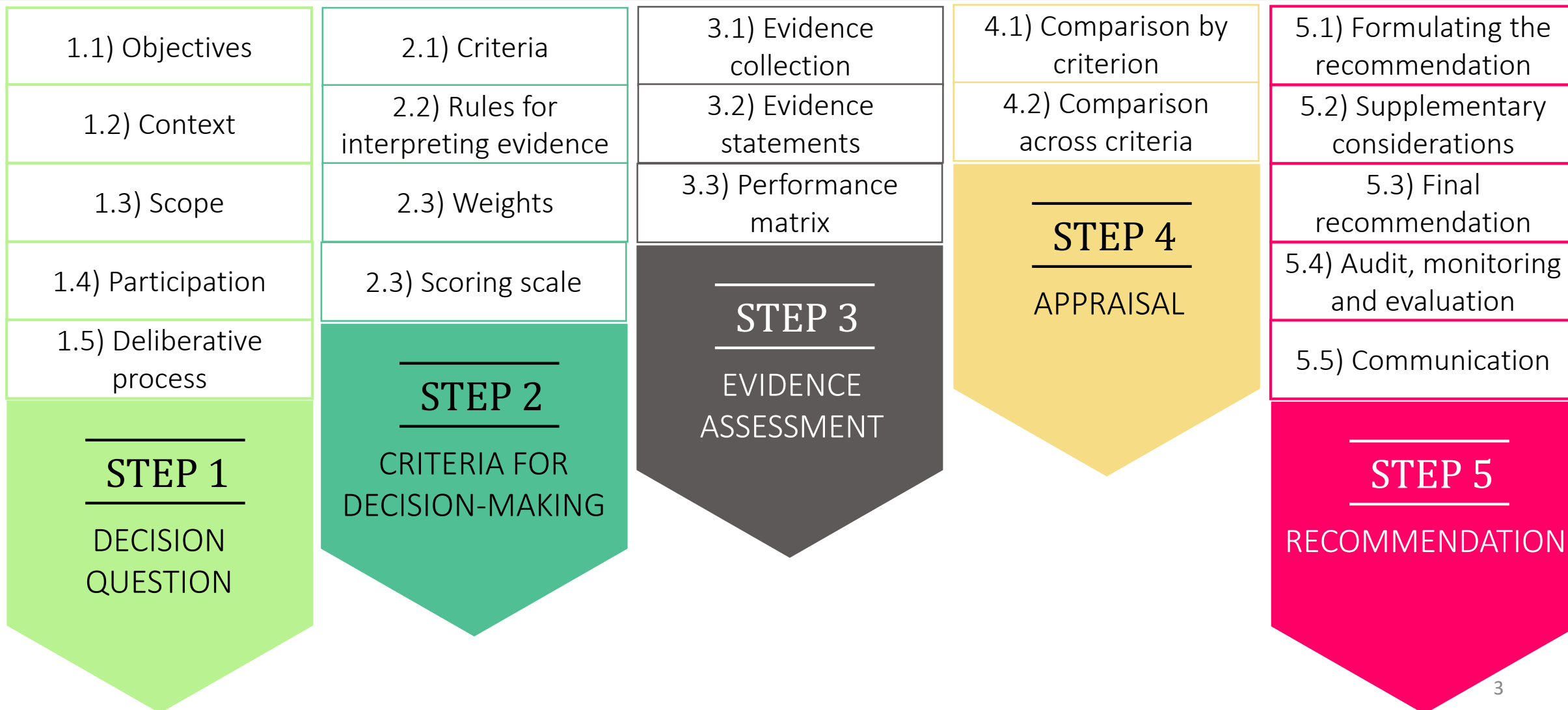
Dijana Spasenoska (spasenoskad@who.int)

01-09-2021

What is the goal of CAPACITI?

To strengthen the ability of LMICs to **evaluate immunisation products, services and/or strategies** according to their priorities and programme context, both for national immunisation programme decisions and to inform vaccine supply, research and development

Overview of the framework



IVIR-AC review of CAPACITI

IVIR-AC has been involved from the beginning in reviewing the CAPACITI decision-support tool and training materials.

Dec 2020 – Recommendation:

“... the decision-support tool is ready to be made publicly available.”



Weekly epidemiological record
Relevé épidémiologique hebdomadaire

4 DECEMBER 2020, 95th YEAR / 4 DÉCEMBRE 2020, 95^e ANNÉE

No 49, 2020, 95, 609–628

<http://www.who.int/wer>

Country support

Currently providing online support to:

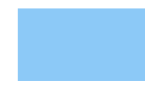
- **Zambia:** started Q1 2020, delayed due to COVID-19, ready to proceed
- **Indonesia:** started Q4 2019, completion was delayed due to COVID-19. As of 05/2021 ready to continue with the evidence review workshop
- **Ethiopia:** following a training in December 2020, online technical support for the implementation of the decision-support tool was requested in Q1 2021

In close coordination with the CHOICES project:

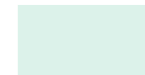
- CHOICES will promote CAPACITI in the countries

List of CHOICES countries

Tanzania
Lao PDR
Senegal
Angola
Nicaragua
Rep of Congo
Ethiopia
Zambia
Côte d'Ivoire
Armenia
Ghana

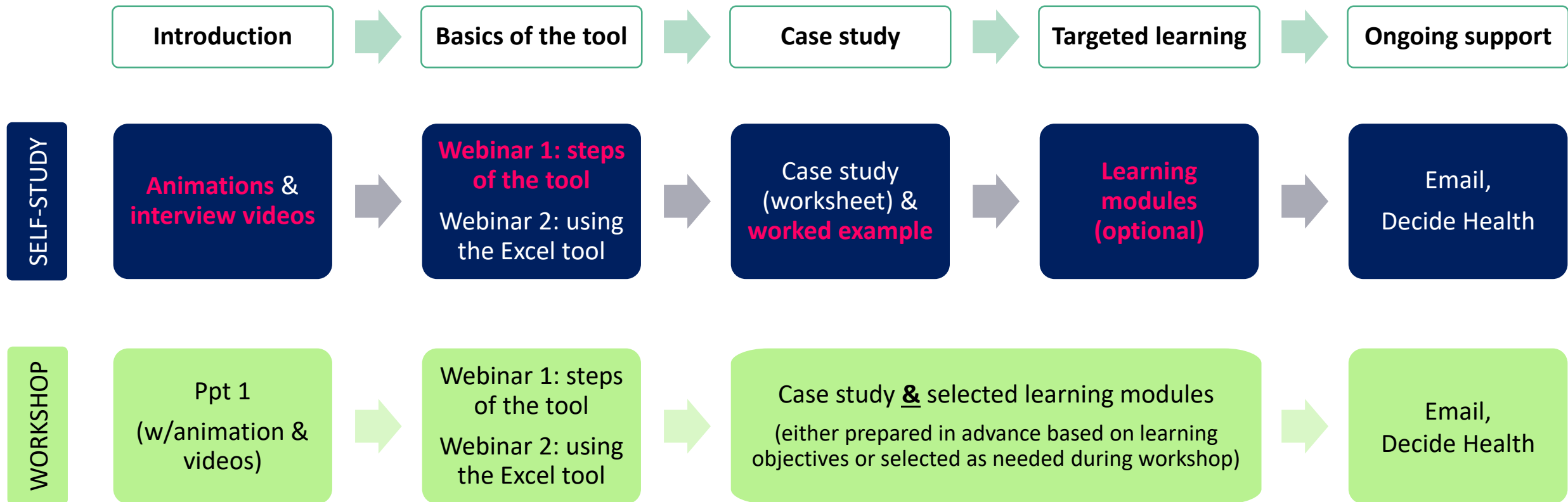


Uses CAPACITI



Expressed interest to use CAPACITI

Country support and training materials



Training materials development

Interview videos



Made available in July 2021

Webinar 1:
Introducing the
steps of the
CAPACITI tool



Revised webinar published in July 2021

Animation 2: An
illustrative
example



The animation is at the production stage.
Expected completion: Sept 2021

Training materials development

Worked examples



The worked example is undergoing final revisions. **Expected completion: Sept 2021**

Training modules
for self-study

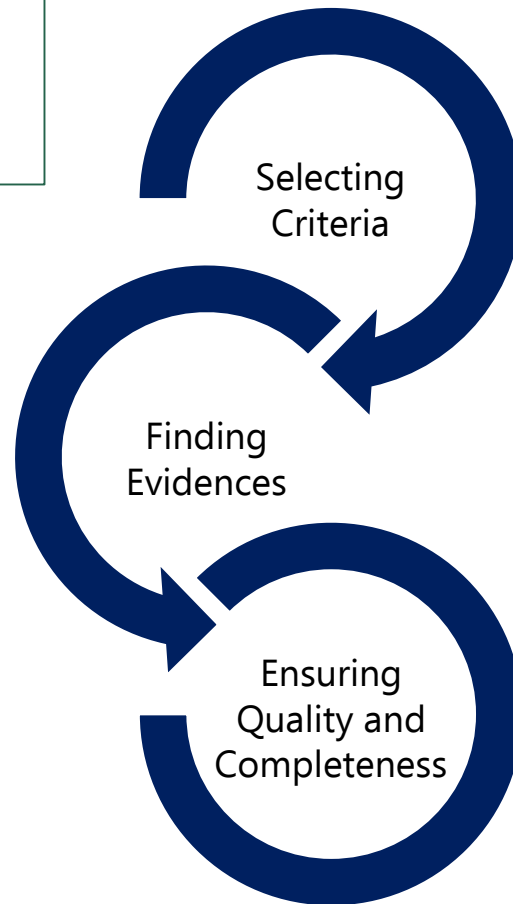


The English language versions have been translated into **French, Spanish and Portuguese.**

Country-level gaps identified:

To address these gaps it is important to strengthen the process of criteria selection and identification of high quality evidence.

Selecting the most appropriate evidence sources for the identified metrics.



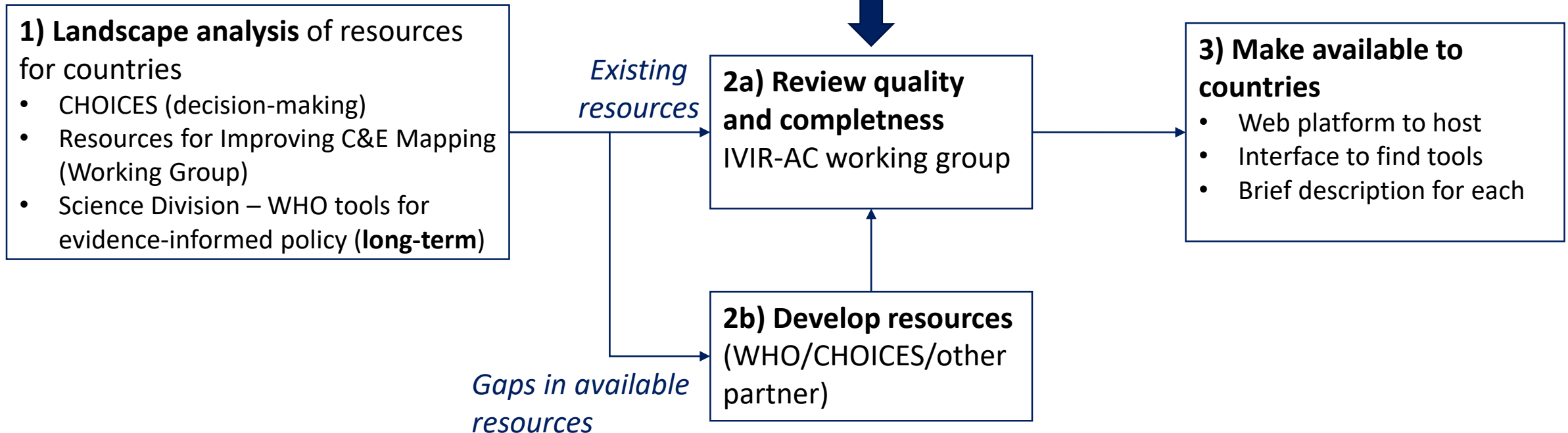
Identifying a set of criteria suitable for the recommendation process.

Reviewing the identified criteria and collected evidences for the completeness and quality.

Decision Making Resource catalogue

informing country decision making for immunization

LONG-TERM: best practice for evidence-based decision-making (based on WHO HGF 3D framework) forms basis of IVIR-AC sub-group review



Purpose

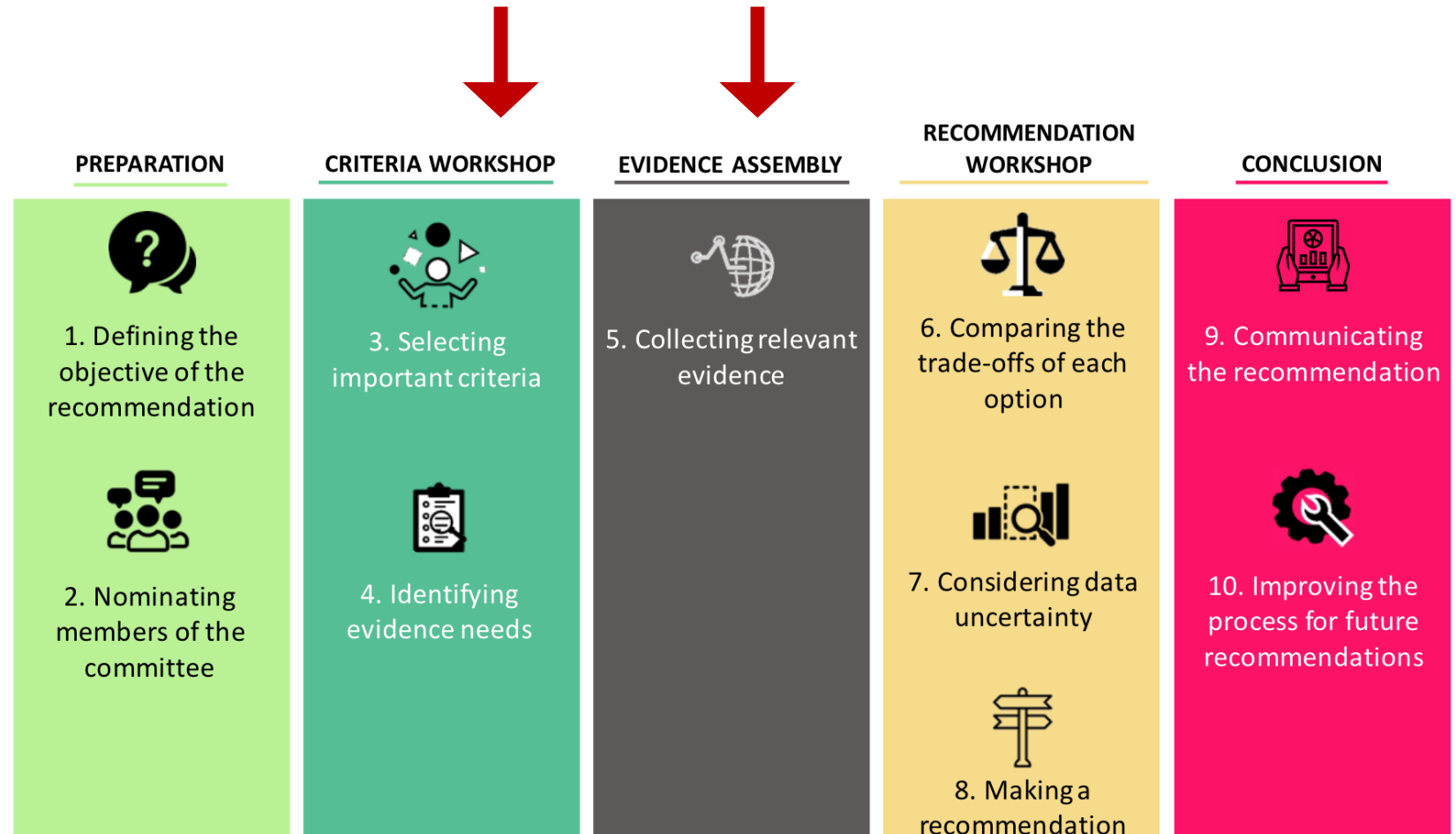
- The Decision Making Resource Catalogue aims to develop **a repository of already existing tool, databases and guidance documents** that can be used as **the base for selecting criteria** and the **collection of high quality evidence** to support the identified criteria.

Key concepts:

- ✓ Information sources are classified per criteria category to allow for easy browsing;
- ✓ Synopsis is provided for each of the sources to allow quick identification of relevant information;
- ✓ Examples of criteria that can be extracted from each source are provided.

When would it be used in CAPACITI?

- Format: Initially Excel-based, in the long term an online database.
- Users: in the context of CAPACITI, the committee selecting the criteria and collecting relevant evidence.



Landscaping

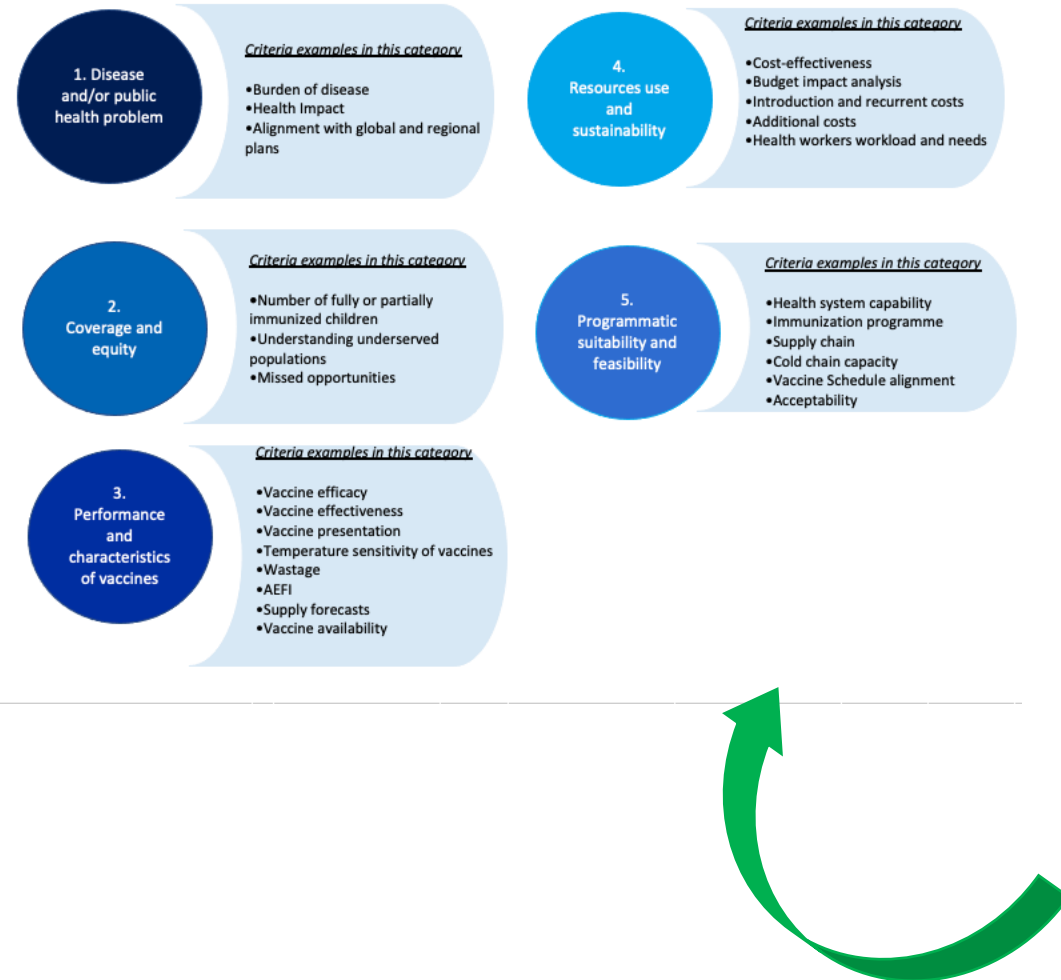
- Includes tools, databases, reports, documents:
 - Published by WHO and partner organizations.
- Building on landscaping work done by CHOICES on decision-making tools and other relevant resources (e.g. UNIVAC, COSTVAC).
- Building on other resource mapping work done in the department:
 - Desk review of immunization program performance (e.g. SARA, SPA);
 - Resources for Improving C&E Mapping (e.g. EQUIST, Health Equity Assessment Toolkit, EPI Review)
- ***Expert recommendations (IVIR-AC, CAPACITI SC and CHOICES Advisory board).***

IVIR-AC CAPACITI subgroup - 4 June

Feedback and revisions following the sub-group meeting

- ✓ Revised the entry and navigation page based on decision-making criteria
- ✓ Added tags for quicker navigation
- ✓ Quality of resources -> Development notes comments, and included constraints/limitations
- ✓ Referenced other decision-making tools

For additional feedback: Use the Microsoft Form [link](#).



Decision Making Resource Catalogue

Informing country decision making for immunization

DECISION MAKING RESOURCE CATALOGUE

informing country decision making for immunization

Introduction

The Decision Making Resource Catalogue is a repository of already existing tools, databases, and guidance documents that can be used as the base for selecting criteria for the decision-making process, e.g. when using the CAPACITI decision-support tool, and the collection of high quality evidence to support the criteria. The catalogue is organized by decision-making criteria and for each of the resources a synopsis is provided to allow quick identification of the available information sources that are best suited for purpose. The synopsis includes information on the purpose, type of source, date of publishing, publisher, tag to signify relevance only to a specific vaccine, description, example of criteria that each resource can inform, as well as an example of evidence that can be extracted, and if available notes on the development process. For each resource we highlight in the synopsis which criteria categories it can help inform, using the following criteria categories: disease and/or public health problem; coverage and equity; performance and characteristics of vaccines; resources use and sustainability; programmatic suitability and feasibility. The criteria categories ascribed to each resource in the synopsis should not be limiting, the user can use the resource for other criteria if suitable. This is the first draft of the catalogue and we would like to gather feedback on the user experience and technical content.

To access the CAPACITI decision-suport tool [click here](#)

We appreciate your feedback. Complete the feedback form [click here](#)

This workbook has been developed by the World Health Organization WHO. For support using this workbook, please contact:

Dijana Spasenoska (spasenoskad@who.int)

Maarten Jansen (jansenm@who.int)

CAPACITI email (tse_tool@who.int)

To explore other decision-making tools [click here](#)

Instructions

Each of the circles below is one criteria relevant to decision making, and for each of the criteria on the side is show a list of sub-criteria examples that can be extracted from the resources included in that criteria. Click on the circle to explore the criteria.

1. Disease and/or public health problem

Criteria examples in this category

- Burden of disease
- Health Impact
- Alignment with global and regional plans

2. Coverage and equity

Criteria examples in this category

- Number of fully or partially immunized children
- Understanding underserved populations
- Missed opportunities

3. Performance and characteristics of vaccines

Criteria examples in this category

- Vaccine efficacy
- Vaccine effectiveness
- Vaccine presentation
- Temperature sensitivity of vaccines
- Wastage
- AEFI
- Supply forecasts
- Vaccine availability

4. Resources use and sustainability

Criteria examples in this category

- Cost-effectiveness
- Budget impact analysis
- Introduction and recurrent costs
- Additional costs
- Health workers workload and needs

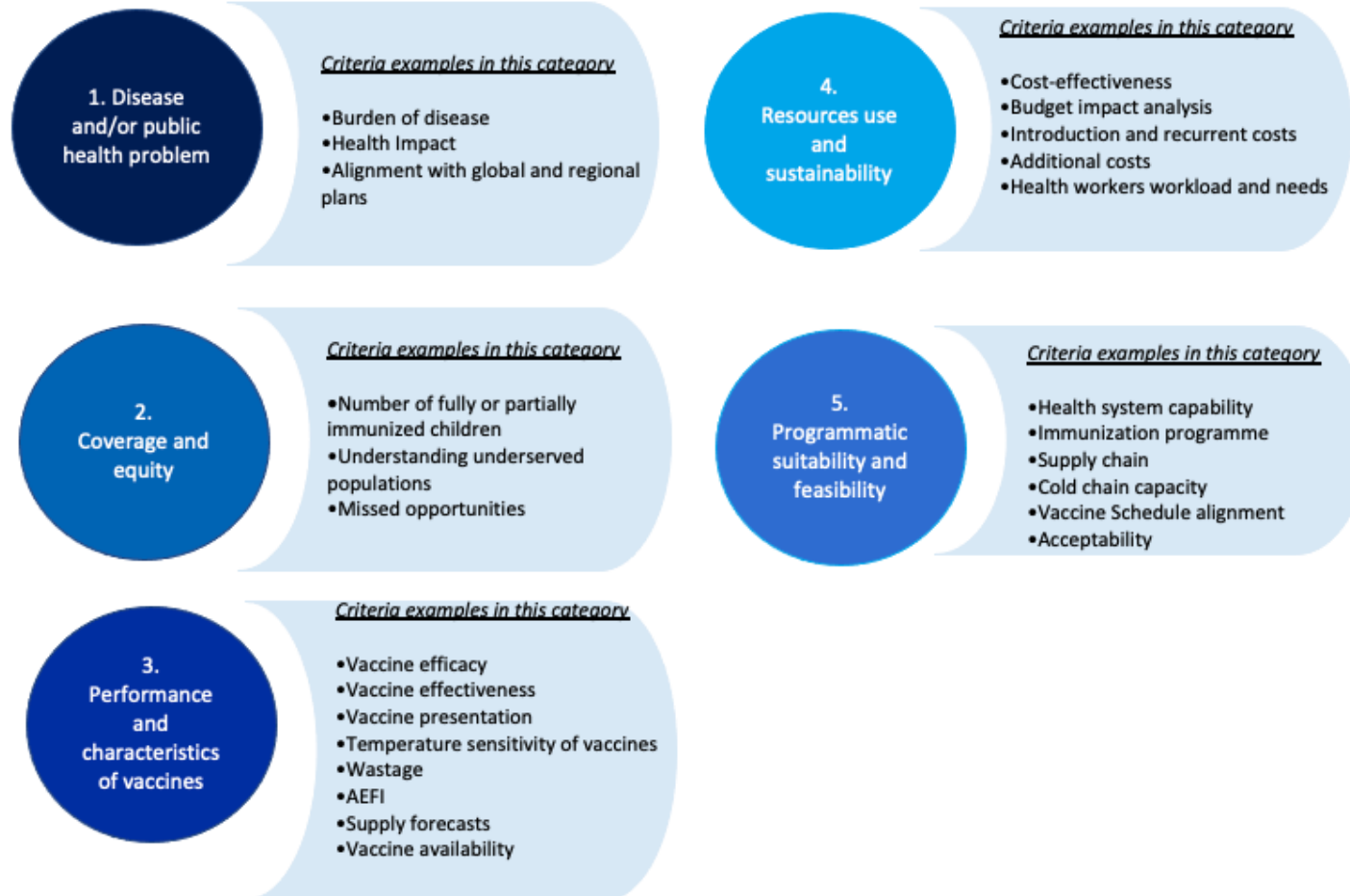
5. Programmatic suitability and feasibility

Criteria examples in this category

- Health system capability
- Immunization programme
- Supply chain
- Cold chain capacity
- Vaccine Schedule alignment
- Acceptability

Instructions

Each of the circles below is one criteria relevant to decision making, and for each of the criteria on the side is show a list of sub-criteria examples that can be extracted from the resources included in that criteria. Click on the circle to explore the criteria.



The user can click on any of the criteria to access the list of relevant resources

Joint Reporting Forms (JRF) WHO UNICEF Estimated National Immunization Coverage (WUENIC) estimates WHO VPD Monitoring System	Demographic Health Survey (DHS) Multiple Indicators Cluster Survey (MICS)	WHO EPI Coverage Surveys National Survey Data	Health Equity Assessment Toolkit (HEAT and HEAT Plus Tools)	Global Health Observatory (GHO)
World Bank Data	Organisation for International Migration (OIM) Migration data portal	Urban Immunisation Toolkit	Missed Opportunities for Vaccination (MOV)	DHIS 2 Immunisation Analysis App
Immunization Equity Reference group papers (Gender and Immunization, Urban populations and Immunization)				

[Click to compare
them](#)

END PAGE

By clicking on one of the criteria, the user is taken to a list of resources that are relevant to that criterion. The 'click to compare them' button will take the user a resource synopsis page.

	Joint Reporting Forms (JRF) WHO UNICEF Estimated National Immunization Coverage (WUENIC) estimates WHO VPD Monitoring System	Demographic Health Survey (DHS) Multiple Indicators Cluster Survey (MICS)	WHO EPI Coverage Surveys National Survey Data	Health Equity Assessment Toolkit (HEAT and HEAT Plus Tools)
Purpose	•To report national immunization coverage, reported cases of vaccine-preventable diseases, immunization schedules, and indicators of immunization system performance.	•Nationally representative household survey that provides data for wide range of monitoring and impact evaluation indicators in the areas of population, health and nutrition.	•To provide coverage estimate for selected vaccines or a set of vaccines (fully vaccinated for age) among infants, children, and/or women of childbearing age, etc.	•To enable the interactive exploration and comparison of health inequalities in countries over time.
Tag	•N/A	•BCG, Polio 1-4, DTP1-3, Measles, Hep B (Birth dose, 1-3).	•N/A	•N/A
Document type	•Data	•Data	•Data	•Tool
Publication date	•Data submitted on annual basis, WHO AFRO region data submitted every month	•Different dates depending on the country, usually every 5-6 years	•Different dates depending on the country. WHO Guidance published in 2018	•Latest update 2021
Source	•Nationally generated data •WUENIC estimates published by WHO and UNICEF	•DHS is published by the DHS Programme funded by USAID •MICS is published by UNICEF	•WHO produced the guidance document. Data generated by country	•WHO
Category	•Coverage and equity	•Coverage and equity	•Coverage and equity	•Coverage and equity
Content	•The WHO and UNICEF jointly collect information on immunization coverage through a standard Joint Reporting Form (JRF) sent to all Member States. The JRF includes estimates of national immunization coverage, reported cases of vaccine-preventable diseases (VPDs), immunization schedules, as well as indicators of immunization system performances. It is completed by national immunization programme staff in collaboration with WHO and UNICEF country office, and the completed forms are returned to the WHO/UNICEF HQs, where data are extracted, reviewed for completeness and consistency; queries could be sent to countries to clarify absent information and inconsistencies. The nationally reported immunization coverage data (official, administrative) and survey data are used to come up with WHO UNICEF Estimated National Immunization Coverage (WUENIC) estimates. On the WHO/IVB website information is available by WHO Member State, as well as summarized by WHO region. All countries report their national coverage rates for multiple antigens, while 140 countries (mostly LMICs) also report data for the second sub-national level (available for 2016-2018). Also useful are indicators on 1) DTP1 drop-out rates (# of districts reporting drop out >10%) and 2) # of districts reporting DTP3, MCV1 and MCV2 coverage rates in various percentage categories. The # of districts with coverage <50% or <80% is a useful indicator.	•The Demographic Health Survey (DHS) is a nationally-representative household survey that provides data for a wide range of monitoring and impact evaluation indicators in the areas of population, health, and nutrition. The standard DHS has a large sample size and is conducted usually every 5 years, so country comparisons over time are possible. The DHS survey topics include child health, education, environmental health, family planning, gender/domestic violence, HIV prevalence, maternal health, nutrition, etc. •The Multiple Indicator Cluster Survey (MICS) is a large-scale, nationally representative household survey that collects data through standardized, face-to-face interviews with women aged 15-49 years in LMICs. The surveys include information on coverage, and data is disaggregated per demographic characteristics. The coverage data available is for BCG, Polio 1-4, DTP1-3, Measles, Hep B (Birth dose, 1-3), complete vaccination and no vaccinations at all. The demographic characteristics per which the coverage is disaggregated are: coverage per district, sex, urban/rural, mother's education, wealth index quintile, ethnicity of household head. DHS indicators other than immunization are also potentially useful. For example, national and subnational percentages for "Assistance during delivery from skilled provider" is informative relative to administration of birth doses of vaccines.	•It provides high-quality coverage data for programme monitoring and evaluation with results that are credible to national and international policymakers. The data is representative, of high quality and the estimates of vaccination coverage are reproducible. In addition, the EPI coverage survey assesses barriers to vaccination. The data can be used to understand and monitor the performance of routine vaccination services at subnational and national levels, to measure the effectiveness of interventions to increase coverage, to evaluate how well a supplementary immunization activity or vaccination campaign has reached the target population. It can also be used to estimate the rate of dropout and frequency of missed immunization opportunities due to non-simultaneous vaccination, as well as the impact of vaccination on disease burden.	• It facilitates the assessment of within-country health inequalities. It is available in two editions: HEAT, Built-in Database edition- which comes pre-installed with the Health Equity Monitor database. HEAT Plus, Upload Database edition- which allows users to upload and work with their own database. Both HEAT and HEAT Plus are organized around two main components: 1) Explore inequality, which enables users to explore the situation in one setting of interest (e.g. country, province or district) to determine the latest situation of inequality and the change in inequalities over time. 2) Compare inequality, which enables users to benchmark, i.e. compare the situation in one setting of interest with the situation in other settings. The tools use DHS and MICS data to overlay socio-economic indicators on vaccination coverage. This allows comparison of inequality trends over multiple DHS/MICS. Currently contains disaggregated data for over 30 reproductive, maternal, newborn and child health indicators for 118 low- and middle-income countries. Some of the indicators included are: adolescent fertility rate, antenatal care coverage, BCG immunization, births attended by skilled health personnel, full-immunization coverage among one-year-olds, infant mortality rate, neonatal mortality rate, under-five mortality rate.
Use	•Does not require user input. Data is available	•Does not require user input. Data is available	•Does not require user input. Data is available.	•Does not require user input. The user just needs to select what should be visualised. •HEAT Plus allows for user input for database.
Constraints/Limitations	•These estimates are based on the reported administrative data. However, there is potential for bias in the reported data due to over- or under-estimation of denominator populations or overreporting of doses administered. Possible outdated survey data.	•Cross-sectional data, which means only one point in time is captured. •When vaccination cards are not present, the information is collected from the mother's report.	•Quality of data might vary depending on how the survey was designed, conducted and the data analysed (e.g. sampling, weighted analysis, extracting vaccination data from records).	•As with other databases, the data reflects states of health associated with social or geographic exposures, but cannot provide in depth analysis of determinants of health. •Information may not always be up to date, and there may be some large time gaps between data points.
Sub-category criteria	•Number of fully or partially immunized children	•Number of fully or partially immunized children; understanding underserved populations	•Number of fully or partially immunized children; understanding underserved populations; missed opportunities.	•Understanding underserved populations
Example criteria this resource could address	•Can extract data on coverage through out the years, for different vaccines. •Equality data on district coverage, and for certain years also information for coverage on the second sub-national level.	•Coverage data disaggregated by vaccine and demographic characteristics.	•Coverage data can be used to understand the performance of routine vaccination services, or the data can be used to estimate the rate of drop out.	•Can visualize data over time disaggregate by different inequality dimensions (age, wealth quintile, education, place of residence, sex, subnational region) to understand the most prominent inequality dimensions in the country.
If available, notes on the development process	•The WHO and UNICEF jointly collect information on immunization coverage through a standard Joint Reporting Form (JRF) sent to all Member States. It is completed by national immunization programme staff in collaboration with WHO and UNICEF country office, and the completed forms are returned to the WHO/UNICEF HQs, where data are extracted, reviewed for completeness and consistency; queries could be sent to countries to clarify absent information and inconsistencies. The nationally reported immunization coverage data (official, administrative) and survey data are used to come up with WHO UNICEF Estimated National Immunization Coverage (WUENIC) estimates.	•Information available: DHS: in the past 5 years, 47 countries have conducted at least one, and in the past 10 years 63 countries in total. MICS: in the past 5 years, 40 countries have conducted at least one, and in the past 10 years 76 countries in total.	•Usually conducted in the country by Ministries of Health (such as immunization programme managers, communicable diseases epidemiologists and surveillance officers) and their partners who are considering an EPI coverage survey.	•The software, contains the WHO Health Equity Monitor database, was beta-tested in 2015 as part of ongoing capacity building workshops on health inequality monitoring.
References and Links to Access the Resource	http://apps.who.int/immunization_monitoring/globalsummary/	https://dhsprogram.com/publications/PublicationSearch.cfm	Data available at the country level. The WHO Guidance link is available through the link below.	https://www.who.int/data/gho/health-equity/assessment_toolkit

The synopsis for each resource includes information on purpose, tag, document type, publication date, source, category, content, use, constraints/limitations, sub-category criteria, example criteria this resource could address, access link and if available, notes on the development process.

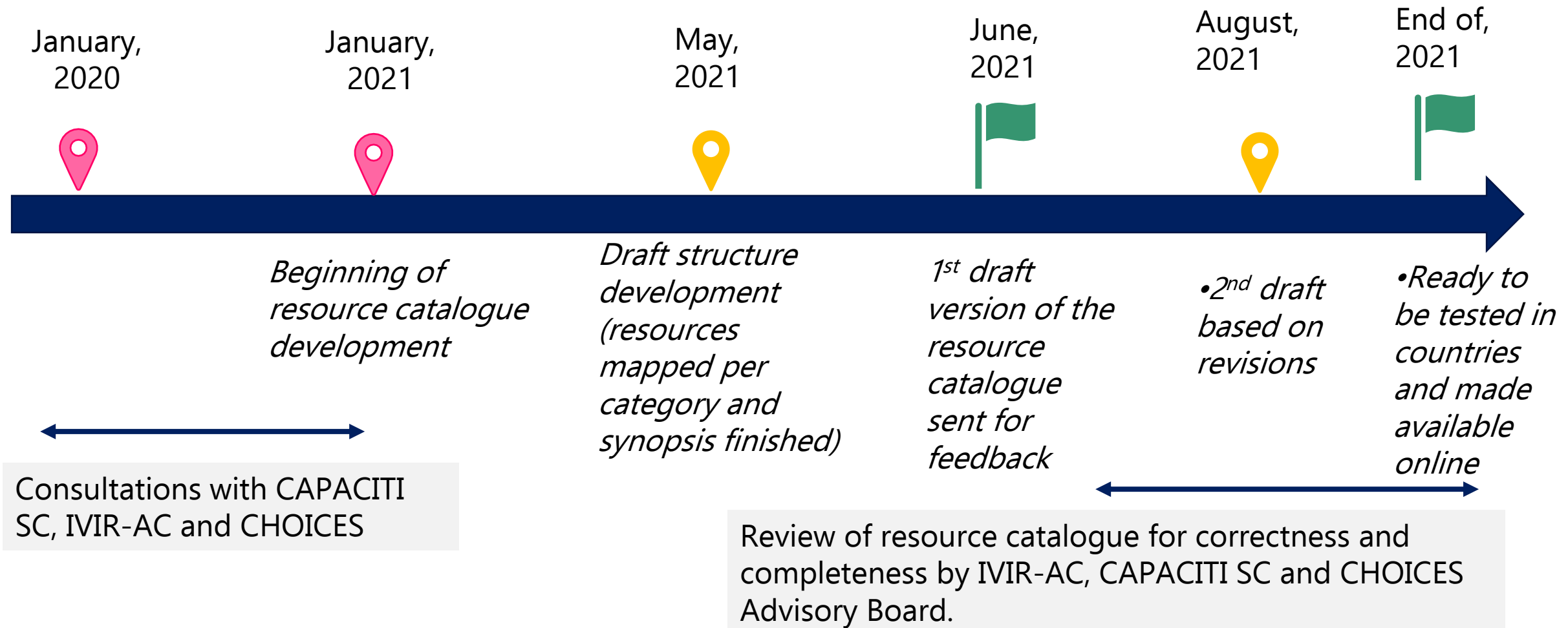
Return to Home

Document type
Publication date
Source
Main Structural Classification
Purpose
Content
Criteria that can inform
Example of information extracted
References and Links to Access the Resource

	PriorityVax	Malaria Vaccine Decision-Making Framework	Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC)	Partnership for Influenza Vaccine Introduction (PIVI)
Document type	•Tool	•Tool	•Initiative	•Partnership
Publication date	•2020 (latest version of the SMART Vaccines Platforms)	•2020		•2020
Source	•Sabin Vaccine Institute	•Malaria Center Initiative PATH, in collaboration with WHO and the health ministries of several African countries	•Agence de Médecine Préventive (AMP), in partnership with the International Vaccine Institute (IVI) of Seoul and in collaboration with WHO	•The Task Force for Global Health
Main Structural Classification	•Use for decision-making process	•Use for decision-making process	•Use for decision-making process	•Use for decision-making
Purpose	•Prioritizing vaccine development	•To prepare African countries to decide, in a timely manner, if and how a vaccine should be introduced to complement existing malaria control strategies.	•To support countries in the establishment or strengthening of National Immunization Technical Advisory Groups (NITAGs)	•To support policy makers that are interested in and ready to introduce or expand influenza vaccination.
Content	<p>•The target audience for this tool are immunization decision-makers. PriorityVax promotes auditable and rigorous deliberations; enables and captures the decision matrix of users; and generates shareable documentation of the process. The tool is especially useful in highlighting the sensitivity of decisions to inherent bias and uncertainty in the evidence. The platform is designed to capture deliberations around prioritisation, to explicitly evidence the importance of different criteria and produce a consistent documented process that supports transparent EIDM. This improved platform, supported by the Sabin Vaccine Institute, has a more streamlined user experience and a clearer selection and use of attributes. Users can easily tailor PriorityVax to incorporate local evidence-to-recommendation processes. It is a customizable, web-based tool in which users can employ the national and subnational data they have identified as best-suited to inform their priority-setting decisions and to place equity at the center of vaccine selection, allocation and distribution. In a stepwise process the tool guides the user to define the target population, the disease and vaccine characteristics, and to identify the country vaccine needs, attributes and criteria that can guide the decision making. Weighting can be applied, and the evidence that should be used can be both qualitative and quantitative. The output is a report on the available evidence, and how the decision was made.</p>	<p>•The African governments, their partners at the national, regional and global levels. Those involved in the planning process include ministries of health, policy, finance and planning, international organizations, malaria vaccine scientists and donors. This framework helps countries to understand the disease burden, likely impact of future malaria vaccine, impact of current malaria interventions and financing options. The planning tool promotes preparation for a new vaccine at the national level. One of the key aspects in the planning process for country decisions on malaria vaccine introduction is the early identification and gathering of the necessary data. The planning tool outlines a range of data that would inform country decisions- from the malaria disease burden, the likely impact of future malaria vaccine, the impact of current malaria interventions, financing options. The tool supports countries to put processes in place, if a decision is made to adopt a vaccine, many groups and people would have to act on the information for successful introduction.</p>	<p>•The approach is a step-by-step, country-driven process that provides sustainable support to a selection of countries to help them create their own NITAGs or to reinforce the capacities of the existing NITAG scientific and technical secretariat. It provides specific support activities established in consultation with the country and other international partners. SIVAC and partners have built an electronic platform, the NITAG Resource Centre, that provides information, tools and briefings to NITAGs and the immunization community.</p>	<p>•To provide technical assistance and readiness assessment, helping to build a strong foundation for sustainable influenza vaccine programs. Through technical assistance, PIVI supports country workflow related to developing or strengthening pandemic preparedness and seasonal influenza vaccination programs. PIVI may assist with work such as: Estimation of disease and economic burden of influenza, Development of acceptability surveys, communication campaigns, and training initiatives, Vaccine program implementation and evaluation activities, including adverse event and vaccine coverage monitoring, National Immunization Technical Advisory Group (NITAG) support and strengthening</p>
Criteria that can inform	•The tool allows the user to select from a wide range of criteria, thus it can be used to explore many areas.	•The data collection can focus on any of the criteria areas.	•Different types of criteria areas can be included in the	
Example of information extracted				
References and Links to Access the Resource	https://spark.adobe.com/page/7k8BDB1kHlp7Y/	https://www.malariavaccine.org/malaria-and-vaccines/access/data-decision-making/decision-making-framework http://malvacdecision.net	https://www.nitag-resource.org/sites/default/files/39b511fa6a9e58ea453aea6df7b8_1.pdf https://www.nitag-resource.org/	

In addition to CAPACITI decision-making tool, a list of other decision-making resources is also included. This section will be further developed by CHOICES.

Timeline



CAPACITI - next steps

Dissemination of
the resource
catalogue



A dissemination plan will be developed with input of the CAPACITI SC and partners, with ongoing collection of feedback by end-users.

LMICs
implementation of
CAPACITI



Supporting LMICs in collaboration with CHOICES in decision making providing materials and technical support when requested, and collecting feedback to improve resources.

CAPACITI - next steps

Developing training materials based on needs of LMICs



Based on feedback from LMICs using the CAPACITI materials **an additional training module for self-study will be developed to support stakeholder involvement.**

CAPACITI
Innovation
Framework



The CAPACITI Innovation Framework is envisioned to be an established process to partner with country immunization stakeholders to contribute to a robust understanding of perceived benefit, or value, of novel vaccine products from the country perspective. It builds on the recently published situational analysis workbook. We are currently exploring how we can best proceed with developing the Innovation Framework.

Discussion

- What should be a priority for the CAPACITI project moving forward?
- Does the Decision Making Resource Catalogue complement the CAPACITI decision-support tool effectively?
- Should additional training materials be developed for the use of the Decision Making Resource Catalogue?

Session 5

IA2030

Vaccine Impact Estimates for Immunization Agenda 2030: For IVIR-AC recommendation

WHO IVB&DDI Project Team

2 September 2021

Agenda

1. Project updates
2. Recap of IVIR-AC Recommendations (February/March 2021)
3. Questions for IVIR-AC
4. Method updates: uncertainty analysis
5. Method updates: validation of estimates for high income countries

Project updates

Project objectives

WHO IVB & DDI aim to update the modeled vaccine impact estimates and document the methodology in a transparent manner to inform two use cases:

1

Robust ways to **measure the impact** of Immunization Agenda 2030

- The vision of IA2030 provides impetus for advancing the effort to capture full impact of vaccination across the globe leveraging the latest analytical developments
- The estimates will be used for Impact Goal indicator 1.1 “number of future deaths averted through immunization”

2

Advocacy and resource mobilization efforts by the global community

- It has been frequently cited that 2.5 million lives are saved every year due to vaccination.
- However, limited documentation of data sources requires us to update the figure and communicate the methodology in a transparent manner.
- Along with costing analysis, impact estimates can be used as an investment case for IA2030

Phase 1 timeline

Project timeline

IA2030 M&E timeline

2020	July	Work plan, scoping exercises and selection of the Stakeholder Committee (SC) members
	August	Analytical framework presented to IA2030 M&E taskforce
	September	Kick-off meeting with SC Analytical framework & methodologies presented to IVIR-AC
	October	2 nd meeting: project updates presented to SC
	November	
	December	3 rd meeting: project updates presented to SC
2021	January	4 th meeting: project updates presented to SC
	February	Methods and preliminary results presented to SC (5 th meeting), IVIR-AC , M&E taskforce, IA2030 M&E, O&A and C&A joint groups
	March	Final deliverables submitted to WHA
	April	Manuscript submitted to Vaccine (pre-print available on SSRN) World Immunization Week (April 26 – 30)
	May	6 th meeting project updates presented to SC
	June	IA2030 rolling launch: Events around/after WHA

Finalization of IA2030 strategic priority and impact goal indicators & outline of the framework presented to SAGE

Draft Framework for Action through Coordinated Planning Monitoring & Evaluation, and Ownership & Accountability

IA2030 Draft M&E framework to be reviewed by SAGE, regions, SB, EB and core partners

IA2030 final M&E framework submitted to the World Health Assembly

74th World Health Assembly

IA2030 rolling launch & advocacy

[Home](#) / [News](#) /

Immunization services begin slow recovery from COVID-19 disruptions, though millions of children remain at risk from deadly diseases – WHO, UNICEF, Gavi

Immunization services begin slow recovery from COVID-19 disruptions, though millions of children remain at risk from deadly diseases – WHO, UNICEF, Gavi

Ambitious new global strategy aims to save over 50 million lives through vaccination

26 April 2021 | News release | Reading time: 5 min (1221 words)

New UN-led global immunization push aims to save more than 50 million lives



© UNICEF/Jannatul Mawa | A young boy is vaccinated against measles and rubella during a national vaccination campaign in Bangladesh.

Modeling the Impact of Vaccination for the Immunization Agenda 2030: Deaths Averted Due to Vaccination Against 14 Pathogens in 194 Countries from 2021-2030

41 Pages • Posted: 26 Apr 2021 • Last revised: 6 May 2021

Pre-print: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3830781



SEVENTY-FOURTH WORLD HEALTH ASSEMBLY
Provisional agenda item 13.8

A74/9 Add.4
21 May 2021

Immunization Agenda 2030

Report by the Director-General

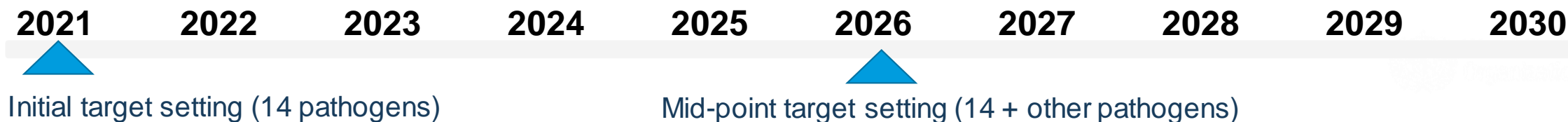
EXECUTIVE SUMMARY

1. In August 2020, the Seventy-third World Health Assembly, through the written silence procedure, adopted decision WHA73(9), in which it endorsed the new global vision and overarching strategy for vaccines and immunization: Immunization Agenda 2030 (IA2030). The IA2030 provides the strategic framework to tackle key issues related to immunization within primary health care and universal health coverage during 2021–2030.
2. Decision WHA73(9) requests the Director-General to finalize the operational elements outlined in the IA2030, in consultation with Member States and other relevant stakeholders, for consideration by the Seventy-fourth World Health Assembly, through the Executive Board at its 148th session.
3. Following the 148th session of the Executive Board in January 2021 and further consultations with Member States held on 8 April, the operational elements have been finalized and made available on the Internet as a living document entitled “**Implementing the Immunization Agenda 2030: A Framework for Action through Coordinated Planning, Monitoring & Evaluation, Ownership & Accountability, and Communication & Advocacy**”.¹

IMPLEMENTING THE IMMUNIZATION AGENDA 2030:

A Framework for Action through Coordinated
Planning, Monitoring & Evaluation,
Ownership & Accountability, and
Communications & Advocacy

Next steps: Phase 2



From 2021-2025:

- Annual updates of vaccine impact estimates based on WUENIC data using the existing model
- Annual reporting to SAGE
- Biennial reporting to the World Health Assembly

By 2026:

- Expansion of the scope of pathogens for updated target setting
- Method and model updates:
 - Validate the first iteration of estimates
 - Expand uncertainty analysis
 - Establish a process to incorporate new models
 - Develop tools to update results with new data and methods
 - Implement tools for decomposition of changes in the estimates

Recap of IVIR-AC Recommendations (February/March 2021)



**World Health
Organization**

Organisation mondiale de la Santé

Weekly epidemiological record Relevé épidémiologique hebdomadaire

30 APRIL 2021, 96th YEAR / 30 AVRIL 2021, 96^e ANNÉE

No 17, 2021, 96, 133–144

<http://www.who.int/wer>

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- 133 Meeting of the Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC), March 2021

Sommaire

- 133 Réunion du Comité consultatif sur la vaccination et la recherche sur la mise en

Meeting of the Immunization and Vaccine- related Implementation Research Advisory Committee (IVIR-AC), March 2021

The IVIR-AC recommendations are based on discussions during a virtual meeting of the IVIR-AC held 1–5 March 2021.

Réunion du Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC), mars 2021

Les recommandations de l'IVIR-AC présentées ici sont basées sur les discussions qui ont eu lieu lors d'une réunion virtuelle du Comité qui s'est tenue du 1^{er} au 5 mars 2021.

IVIR-AC recommendation (1/2)

1. For the statistical modelling, IVIR-AC recommended giving more details on:
 - the different input covariates; variance of the covariates; explanations of observed uncertainties; and the advantages and disadvantages of the different models tested;
 - how the model accounts for the attributable reduction in mortality that is not due to vaccines (e.g. the differences in health-care services across VPDs, between countries and over time);
 - how the IA2030 impact model accounts for herd immunity.

IVIR-AC recommendation (2/2)

2. IVIR-AC further recommended presenting vaccine impact estimates for high-income countries separately as it was unclear whether use of the IA2030 statistical model to extrapolate the VIMC estimates to these countries would produce results consistent with existing high-income country estimates (i.e. from WHO's Regional Office for Europe, the Centers for Disease Control and Prevention in the USA and Public Health England). Validation was needed to ensure consistency.
3. IVIR-AC reiterated the importance of communicating information on key WHO websites in a clear and accessible manner. The “deaths averted” figure currently available is widely used but its sources and references are hard to find.
4. IVIR-AC stressed the need to clarify whether the mortality rates from UNWPP have accounted for deaths due to VPDs when they are used to parameterize the IA2030 impact model

Questions for IVIR-AC

Questions for IVIR-AC

- How can we improve our methods for propagating uncertainty? Are there effective alternatives to draw-level estimation?
- How should we interpret/communicate about the meaning of the uncertainty in our estimates given our data, methods, and purpose?
- What criteria should we use for selecting the vaccines to focus on as part of the HIC validation?
- How best can we standardize across time periods, measures of impact and levels of underlying burden?

Methodology updates: Uncertainty analysis

Initial uncertainty methods

Single sources of uncertainty for each group

Group 1: VIMC countries/pathogens

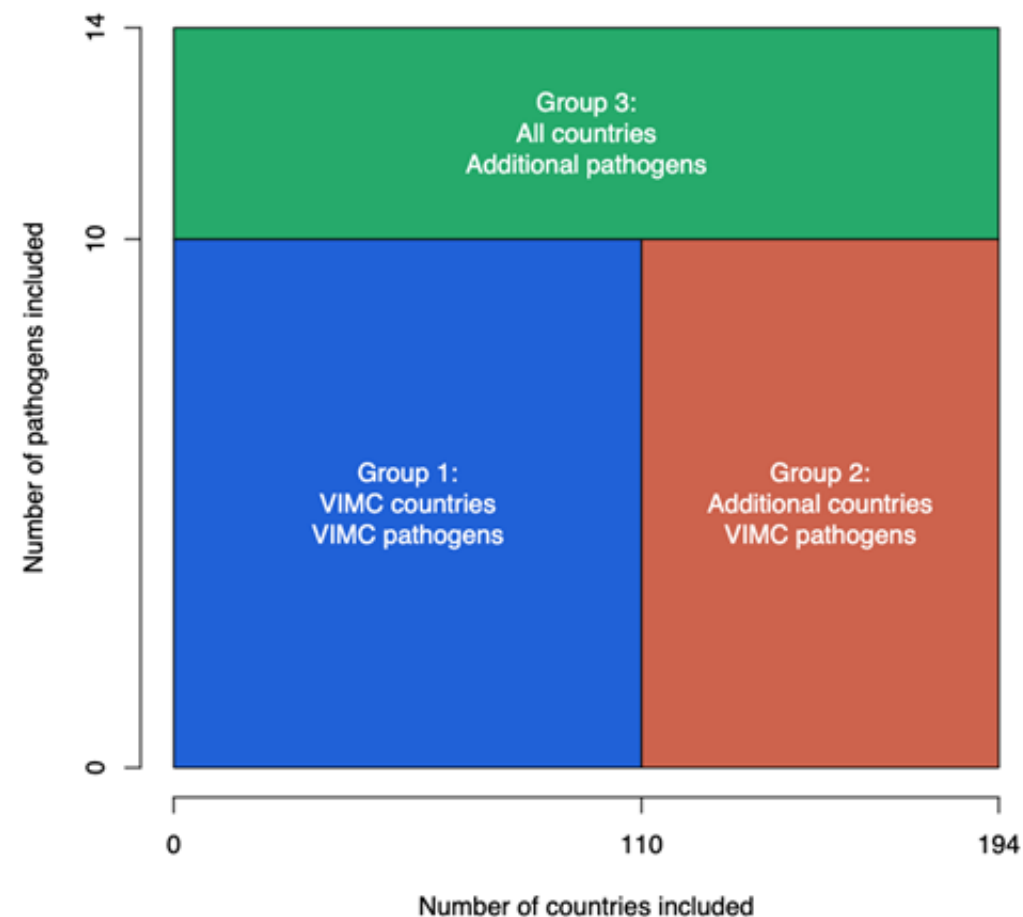
- Scale the location/vaccine-specific interquartile range from VIMC estimates to align with a normal distribution centered at the mean estimates

Group 2: Additional countries for VIMC pathogens

- Estimate a standard deviation from the coefficient of variation in the alignment scalars used to shift estimates for VIMC locations to match estimates from the VIMC and center a normal distribution at the mean

Group 3: All countries for additional pathogens

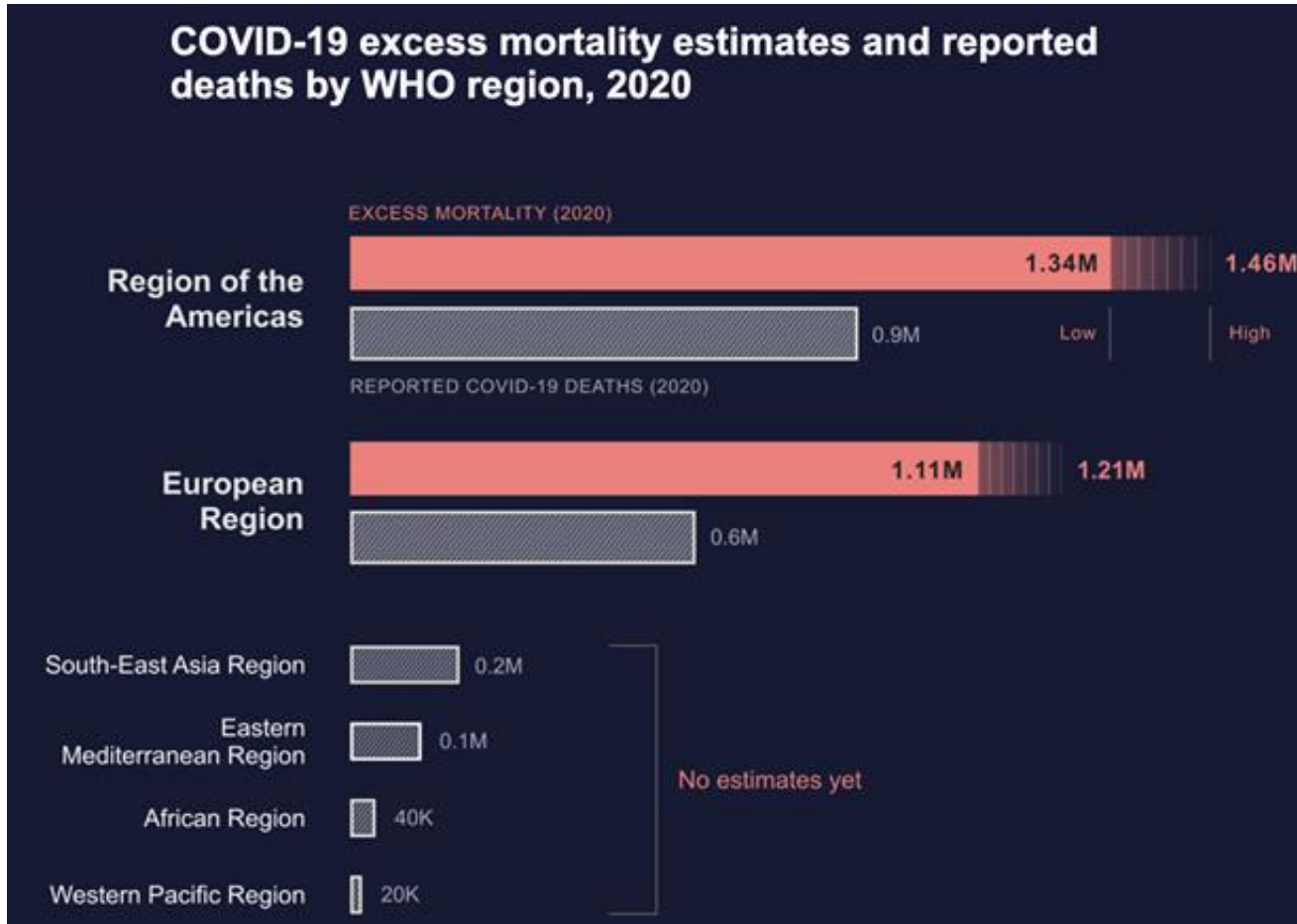
- Fit a beta distribution to the vaccine efficacy mean and lower/upper confidence intervals extracted from literature and use draws from the distribution to produce a distribution of vaccine impact



Planned uncertainty methods

Draw-level analysis	Input uncertainty	Sensitivity analysis
<ul style="list-style-type: none"> • Propagate multiple sources of uncertainty, including predictive uncertainty from modeling • Secured computational capacity for running draw-level analysis in parallel 	<ul style="list-style-type: none"> • GBD <ul style="list-style-type: none"> • Cause-specific mortality • Covariates • VIMC <ul style="list-style-type: none"> • Utilize impact factor draws • Demography • Improved vaccine efficacy distributions from meta-analysis 	<ul style="list-style-type: none"> • Decompose overall uncertainty into contributions from each of uncertain inputs (Sobol method) • Report on the potential impact of uncertain factors for which we don't have uncertainty through scenarios

Communicating about uncertainty



Source: <https://www.who.int/data/stories/the-true-death-toll-of-covid-19-estimating-global-excess-mortality>

Purpose of estimates: Advocacy, not country-level resource allocation

Purpose of reporting uncertainty: Communicate the strength of evidence for estimates across locations and pathogens

Primary focus: Mean or uncertainty intervals (à la COVID-19 excess mortality data story)

Methodology updates: Validation of estimates for high income countries

Background

- Current methodology fits model using data from LIC and LMIC for most of the pathogens (VIMC-10).
- Available data can be used to validate the fit of the model using standard in-sample model validation techniques (e.g. training data vs test data).
- The model has been used to extrapolate to a global estimate including generating estimates of impact for HIC and UMIC.
- We require a systematic approach for validation of the estimates of immunization that have been derived for some of the HIC/UMIC.

Approach

- **Contact researchers:** directly contact researchers who may have modeled impact in some HIC using the VIMC network
- **Literature review:** search online databases to find relevant studies in HIC
- **Estimate total deaths averted** with vaccination based on these studies
- **Validate the predictions** of the logistic model with data from the previous step
- **Adjust the prediction model/approach** for HIC accordingly.

Literature review

Searches have been performed on multiple databases including Pubmed, cochrane and google scholar.

The search process has been automated using the python packages PyMed, Entrez.

So far, after filtering, a maximum of 50 potential relevant studies have been found. These studies are targeted to only a handful of the 14 pathogens.

Only a few of these studies include the estimation of the number of deaths averted. Some other estimate or report the following outcomes:

- Percentages of cases averted
- Reduction in severe cases
- Reduction in incidence
- Reduction of hospitalization rate
- Percentage of death averted
- QALY/DALY

Example of literature search:

Country	Pathogen	Model	Vaccine Coverage	Outcome	Source
Netherland	Diphtheria, Poliomyelitis, mums, Rubella	Poisson Regression	Mass vaccination	% of Case averted	[1]
Oman	Rotavirus	Markov model	Universal vaccination	<ul style="list-style-type: none">• Reduction of hospitalizations, ED visits, outpatients• QALY and the number of death in the base scenario	[2]

[1] Van Wijhe M, Tulen AD, Altes HK, McDonald SA, de Melker HE, Postma MJ, Wallinga J. Quantifying the impact of mass vaccination programmes on notified cases in the Netherlands. *Epidemiology & Infection*. 2018 Apr;146(6):716-22.

[2] Al Awaidy ST, Gebremeskel BG, Al Obeidani I, Al Baqlani S, Haddadin W, O'Brien MA. Cost effectiveness of a pentavalent rotavirus vaccine in Oman. *BMC infectious diseases*. 2014 Dec;14(1):1-9.

Literature review: Type of Models Used in the Studies

So far we have identified the following types of models:

- i. Static cohort models (mainly for progression of disease);
 1. Decision tree,
 2. Markov model.
- ii. Population models;
 - a. Static model,
 - b. Dynamic model (mostly for transmission of the pathogen):
 1. Compartmental transmission dynamic models,
 2. Discrete-event models.

Questions for IVIR-AC

Questions for IVIR-AC

- How can we improve our methods for propagating uncertainty? Are there effective alternatives to draw-level estimation?
- How should we interpret/communicate about the meaning of the uncertainty in our estimates given our data, methods, and purpose?
- What criteria should we use for selecting the vaccines to focus on as part of the HIC validation?
- How best can we standardize across time periods, measures of impact and levels of underlying burden?

Appendix: updates based on IVIR- AC recommendations (Sep 2020)

IVIR-AC recommendation on the project

Prioritization:

- Given that the agenda is complex and the proposed timeline aggressive, prioritization should be exercised with respect to the level of uncertainties anticipated in the many different impact estimates. It was suggested that the initial focus be on mortality estimates and on vaccines with a higher anticipated impact and more reliable data.

Use cases:

- Use cases of the estimates should be carefully defined to ensure that the results are not misused. For example, the availability and use of estimates at the country level could be minimized and global and regional estimates prioritized.

Prioritization of vaccines

2021 2022 2023 2024 2025 2026 2027 2028 2029 2030

VIMC10 + Tier 1:

Hep B, Hib, HPV, measles, rubella, pneumococcal, rotavirus, yellow fever, MenA, JE, Diphtheria, Tetanus, Pertussis, TB(BCG)

Tier 2 + New vaccines:

Polio, Typhoid, Influenza, Cholera, Multivalent meningitis, COVID-19

Tier 3 + Other new vaccines:

Varicella, Dengue, Mumps, Rabies, Hep A, Hep E, Other new vaccines

Other new vaccines

- Phased approach to generating estimates for 194 Member States
- Assessment criteria and scoring scheme based on global strategic priorities, availability of coverage data and feasibility

Use cases

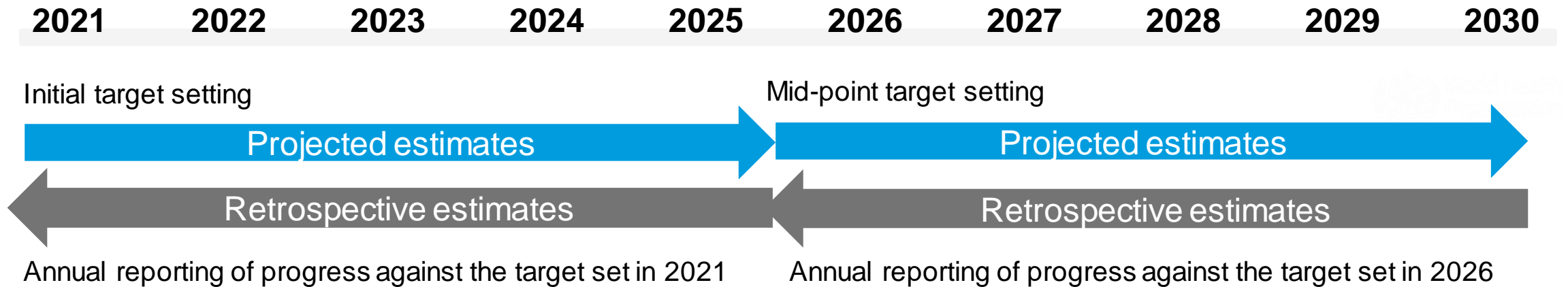
Impact Goals	Proposed Indicators	Proposed Targets	
1 Disease	Save lives	1.1 Number of deaths from vaccine-preventable diseases averted	TBD (based on coverage targets & ongoing modelling)
	Control, eliminate & eradicate VPDs	1.2 Number of countries that have achieved global or regional VPD control, elimination and eradication targets	TBD (based on updates of regional & global commitments)
	Reduce VPD outbreaks	1.3 Number of large outbreaks of vaccine-preventable diseases	Annual improvement
2 Equity	Leave no child behind	2.1 Number of zero dose children	Reduce by 50%
	Deliver across the life course	2.2 Coverage of vaccines included in national immunization schedules (DTP3, MCV2, HPVc, PCV3)	Global target: 90% Country target: limit drop-out from DTP1 to <5%; introduce vaccines not included in national schedule
3 PHC/UHC	Strengthen PHC/UHC coverage	3.1 Difference between DTP3 coverage and Universal Health Coverage Service Coverage index	TBD (based on analysis of historical trends for UHC index of service coverage)

- Impact Goal 1.1. focuses on mortality estimates
- Primary use for advocacy
- Reporting at the global and regional level

Source: Implementing the Immunization Agenda 2030: A Framework for Action through Coordinated Planning, Monitoring & Evaluation, and Ownership & Accountability (Version: 25 January 2021)

Appendix: plans for Phase 2

Target setting & monitoring/reporting



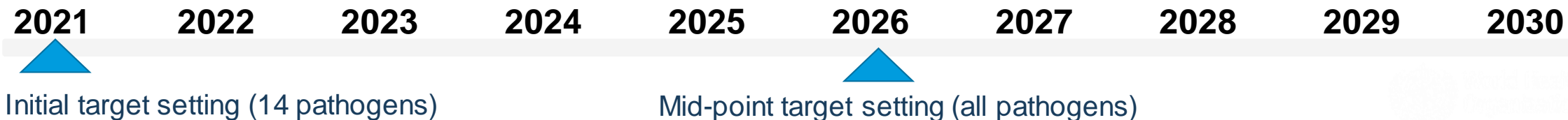
• Target setting

- Future projection modeling
- Goal: set ambitious targets to be achieved by 2030
- Coverage: IA2030 coverage scenario
- Frequency: twice (starting point, mid-point)

• Monitoring/reporting

- Retrospective modeling
- Goal: compare the estimates based on actual data against targets
- Coverage: historical WUENIC updates
- Frequency: annual reporting

Scope of pathogens



14 priority pathogens

Hep B, Hib, HPV, measles, rubella, pneumococcal, rotavirus, yellow fever, MenA, JE, Diphtheria, Tetanus, Pertussis, TB(BCG)

Gradually add new pathogens to the model using a systematic approach

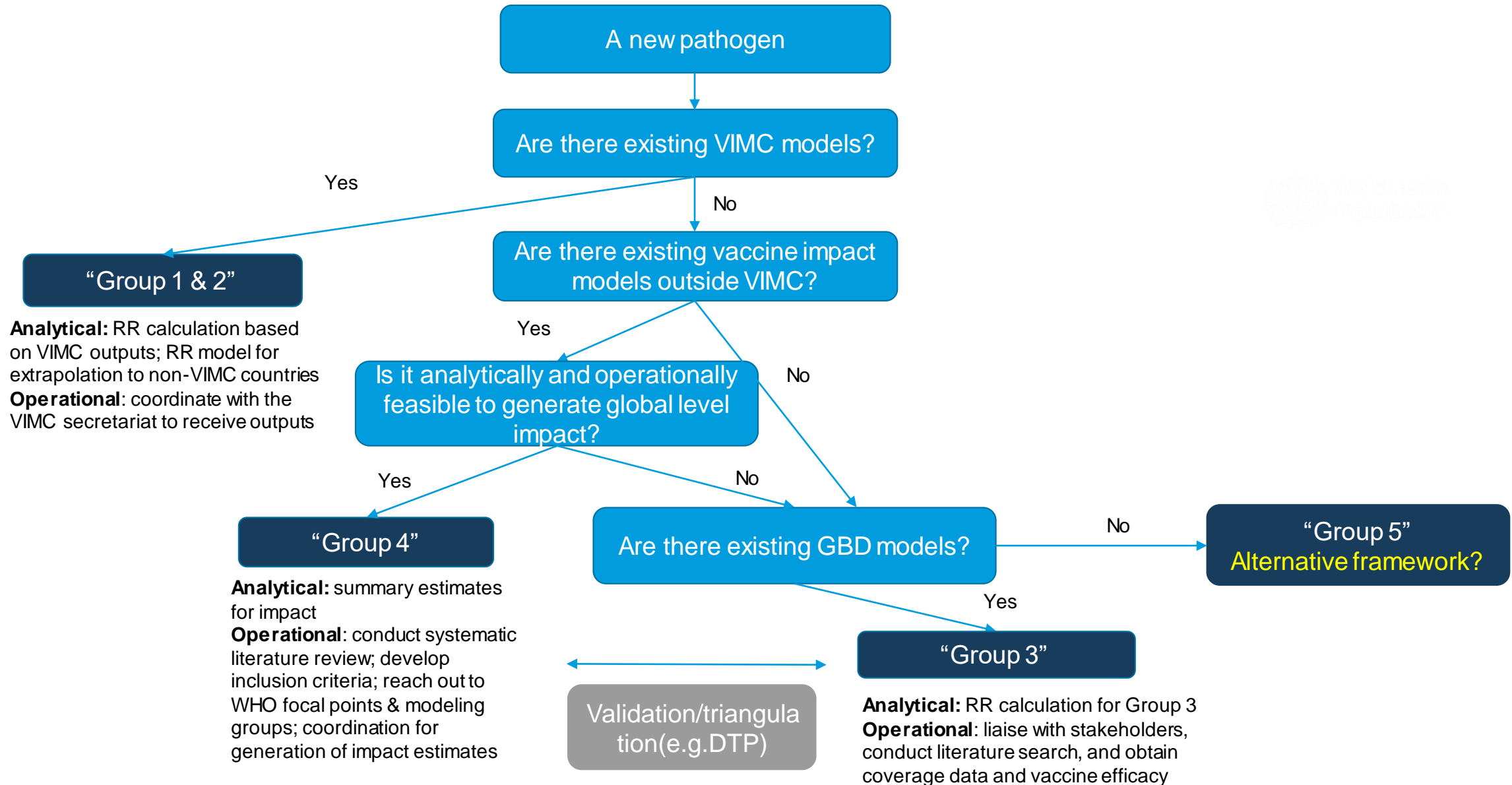
Other pathogens for existing vaccines:

Polio, Typhoid, Influenza, Cholera, Multivalent meningitis, Varicella, Dengue, Mumps, Rabies, Hep A, Hep E, SARS-CoV-2

Other pathogens for new vaccines:

RSV, GBS, HIV, Malaria, New TB, E.E.coli, Shigella, etc.

Phase 2: Decision tree for a new pathogen



Plans for methods updates

1. **Expansion of uncertainty analysis**
 - Run entire analysis at the draw-level to enable propagation of uncertainty from multiple processes
 - Enable model runs within WHO Azure ML tool to expand computational capacity
2. **Establish a process for integration of new models**
 - While we have methods for pathogens that are included in VIMC and GBD estimates, we need to establish how we will integrate models identified in literature that estimate vaccine impact for a limited geography
3. **Utilize tools for efficient updating of results after new data becomes available and new methods are implemented**
 - When new WUENIC, VIMC, WPP, and GBD data becomes available, we want to ease the process of updating our estimates to reflect updated data
 - Implement our analytic pipeline within the *orderly* framework for reproducible analyses
4. **Implement tools for decomposition of changes in impact estimates**
 - Enabled by clear documentation of changes in data and methods, we plan to implement tools that allow for clear communication of the sources of changes in our impact estimates

Plans for sharing results

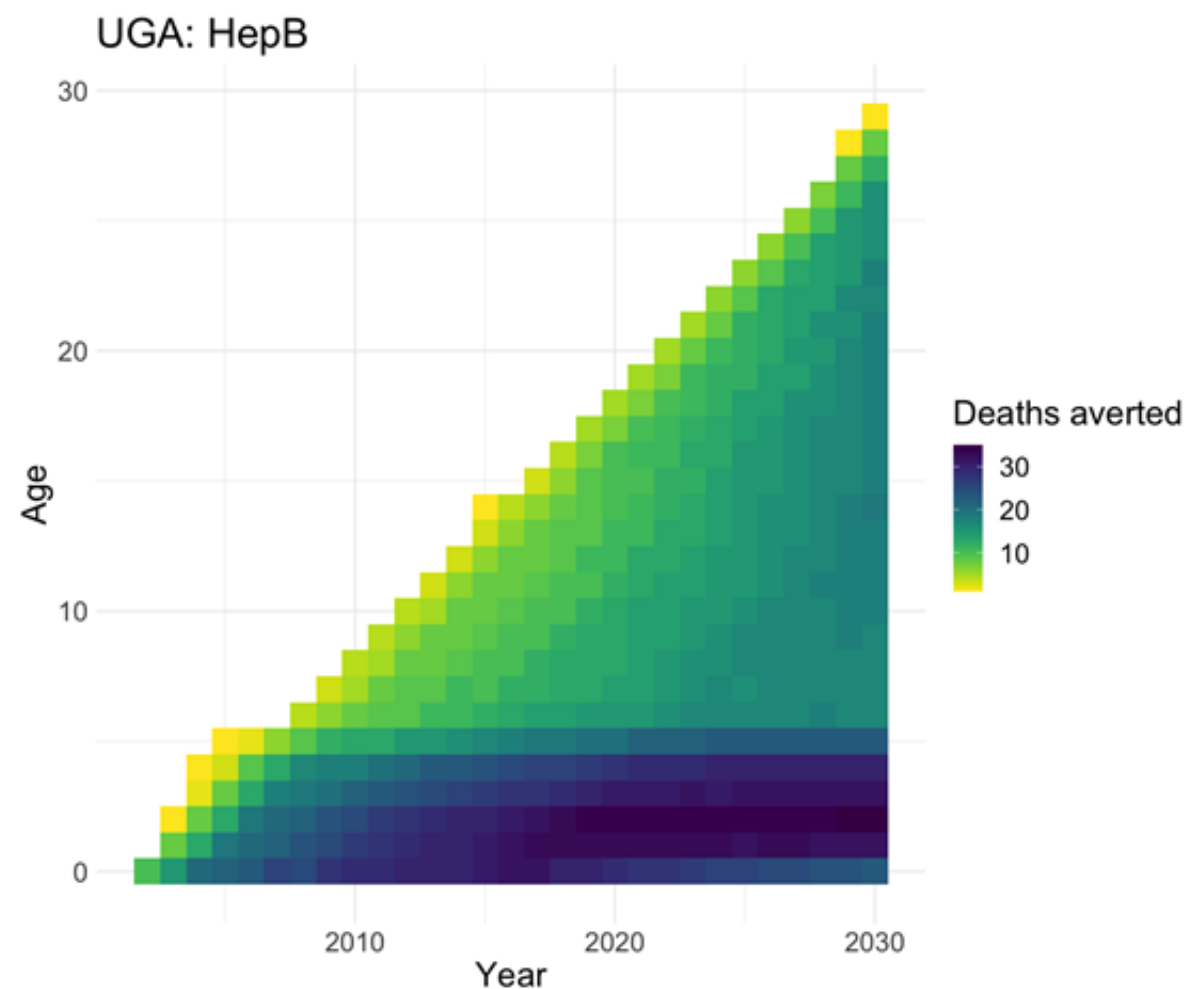
We are working on establishing a website where users can access:

- Tables with all estimates
- An archive of reports generated during iterations of data and methods updates
- Interactive data visualizations

Location:
UGA ▼

Vaccine:
HepB ▼

Log transform



Project team & Stakeholder Committee

Project team

- **Supervision:** Raymond Hutubessy
- **Analytics:** William Msemburi, Austin Carter, Maryam Sadeghimehr
- **Project management:** Yoonie Sim
- **VIMC focal point:** Katy Gaythorpe

WHO focal points

- **M&E:** Jan Grevendonk
- **IVIR-AC:** Philipp Lambach
- Other WHO colleagues on an as-needed basis

Stakeholder Committee

- **BMGF:** Emily Dansereau
- **CDC:** Mike Lynch
- **Gavi:** Dan Hogan
- **IHME:** Jon Mosser
- **VIMC*:** Katy Gaythorpe
- **VIMC* Scientific Advisory Board:**
 - Cherry Kang (**Christian Medical College, Vellore, India**)
 - Ulla Griffiths (**UNICEF**)
- **IVIR-AC:** Walt Orenstein
- **WHO DDI:** Somnath Chatterji
- **WHO IVB:** Ann Lindstrand, Raymond Hutubessy

*VIMC: Vaccine Impact Modelling Consortium

Session 6

VIMC

Vaccine Impact Modelling Consortium

Updates on VIMC

IVIR-AC September 2021

Dr. Katy Gaythorpe



Imperial College
London



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VIMC's goals

💧 Provide vaccine impact estimates to Gavi and BMGF

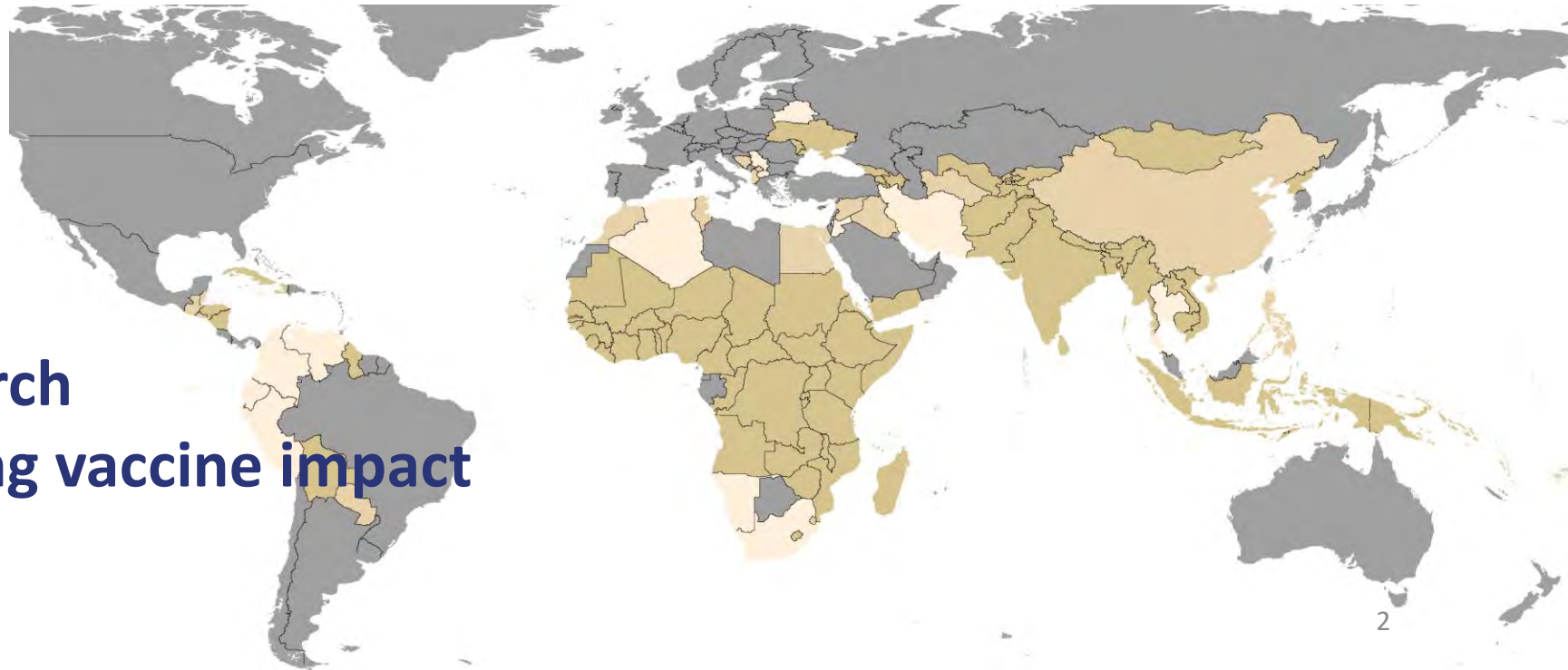
- 💧 12 diseases (cholera, hepatitis B, Hib, HPV, Japanese encephalitis, measles, meningitis A, pneumococcal disease, rotavirus, rubella, typhoid and yellow fever)
- 💧 112 countries (shown in light/dark beige on the map)

💧 Further analyses as required by the funders

💧 Focus on

- 💧 Consistency
- 💧 Efficiency
- 💧 Quality

💧 Advance the research agenda in modelling vaccine impact



Latest publication



Epidemiology and Global Health




Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world



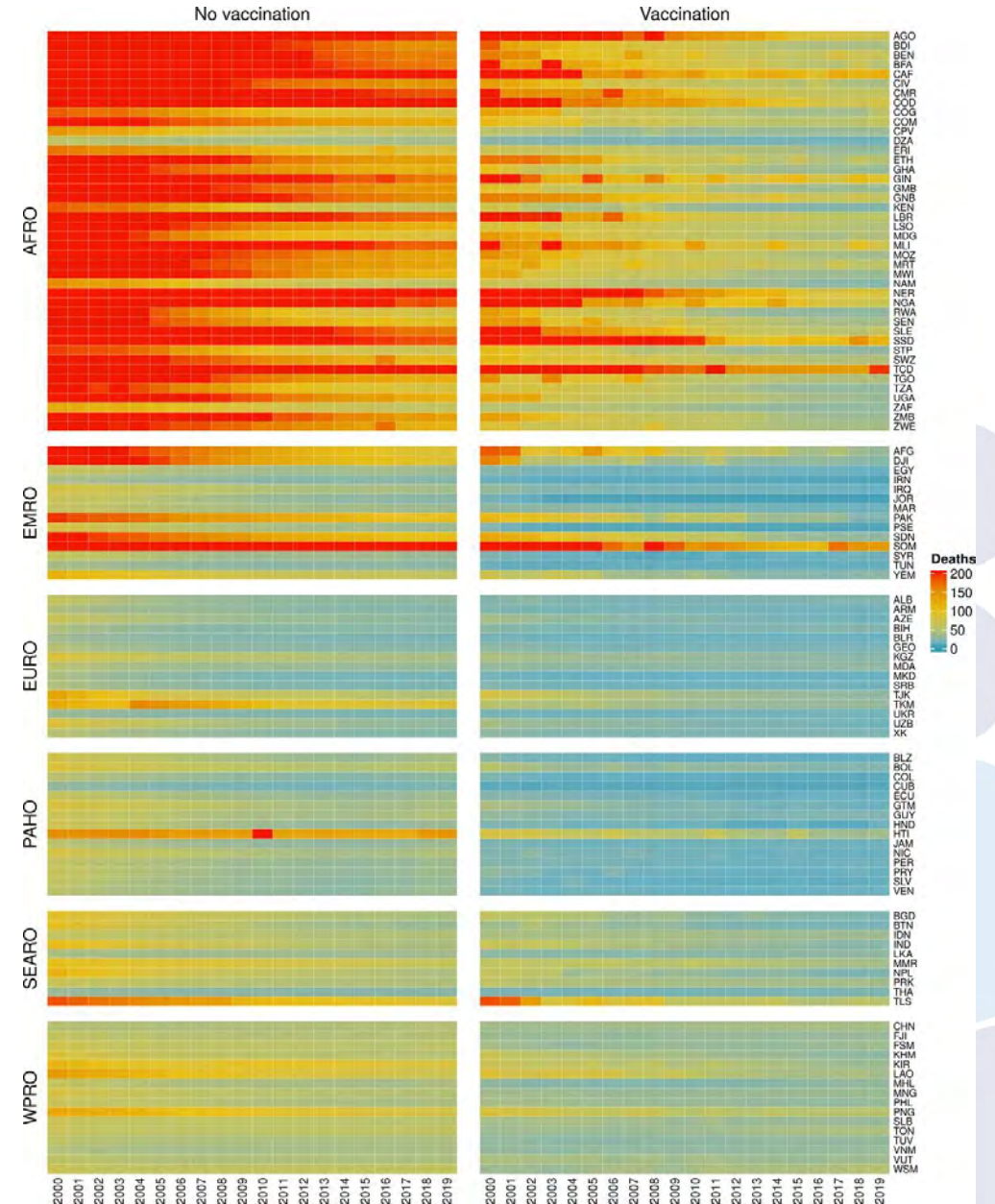
Jaspreet Toor, Susy Echeverria-Londono, Xiang Li, Kaja Abbas, Emily D Carter, Hannah E Clapham, Andrew Clark, Margaret J de Villiers, Kirsten Eilertson [see all](#) »

MRC Centre for Global Infectious Disease Analysis; and the Abdul Latif Jameel Institute for Disease and Emergency Analytics (J-IDEA), School of Public Health, Imperial College London, United Kingdom; London School of Hygiene and Tropical Medicine, United Kingdom; Bloomberg School of Public Health, Johns Hopkins University, United States; Saw Swee Hock School of Public Health, National University of Singapore, Singapore; Oxford University Clinical Research Unit, Vietnam; Nuffield Department of Medicine, Oxford University, United Kingdom; Colorado State University, United States; Pennsylvania State University, United States; Center for Disease Analysis Foundation, United States; Gavi, the Vaccine Alliance, Switzerland; Department of Biological Sciences, University of Notre Dame, United States [see all](#) »

Research Article · Jul 13, 2021

 Latest consortium-wide publication out now in eLife: [\[link\]](#)

 Accompanying [data visualisation tool](#)



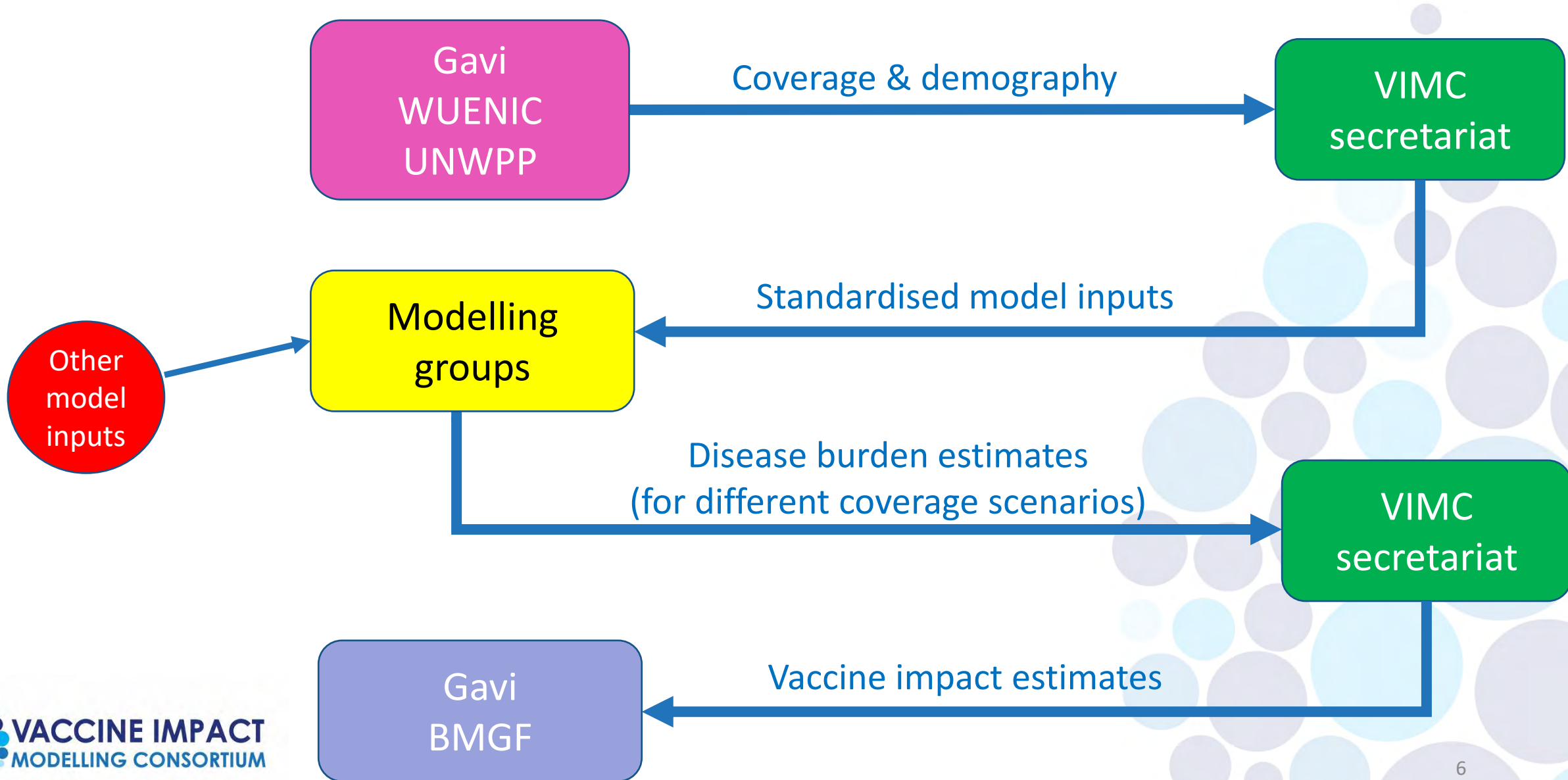
2021 focus



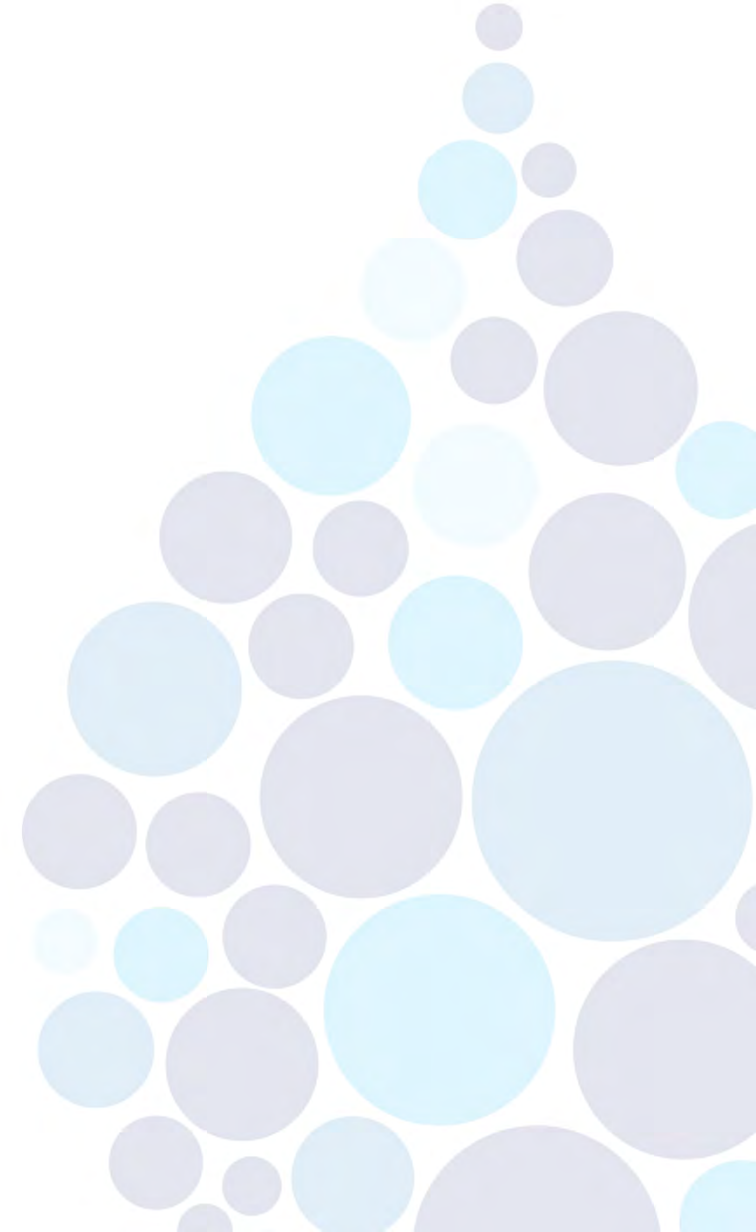
VIMC 2021 model runs

- 🌿 Producing estimates of vaccine impact for 12 pathogens in 112 countries
- 🌿 Will depend on WUENIC 2021 release, IA2030 coverage projections, available vaccination campaign data for 2021 and discussions with Gavi, WHO and BMGF
- 🌿 Estimates to be released first half of 2022

VIMC workflow for full model runs



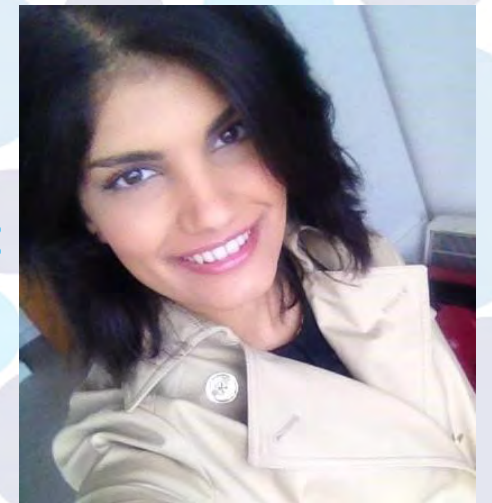
Ongoing workstreams



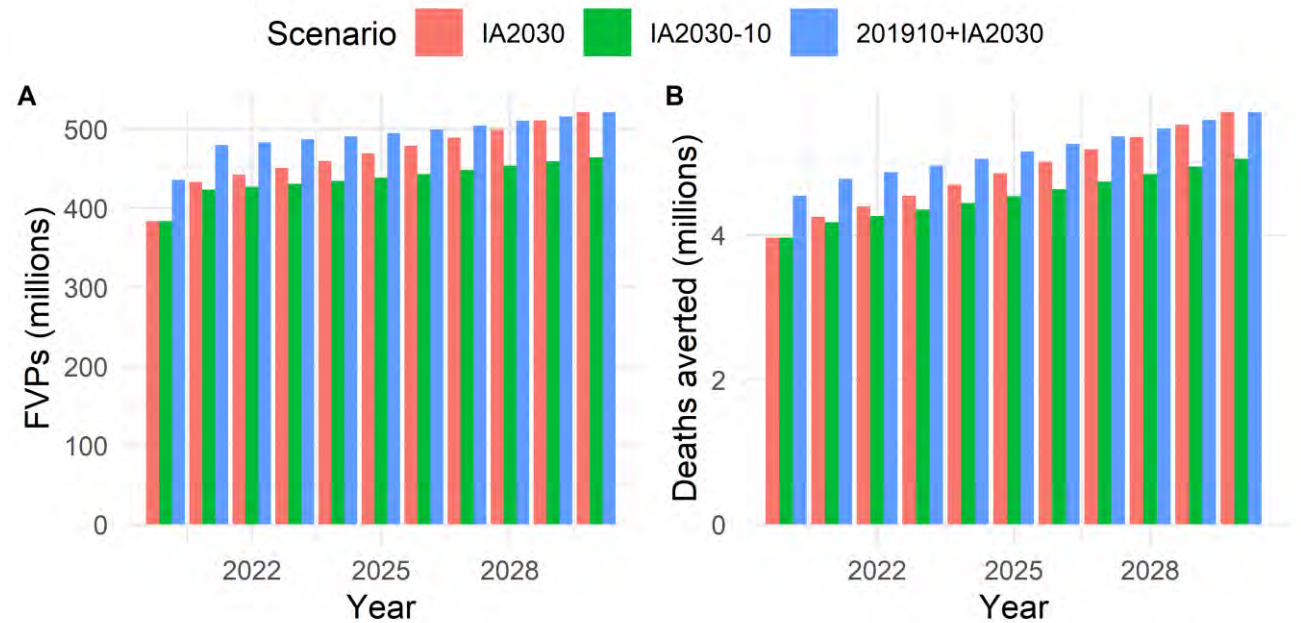
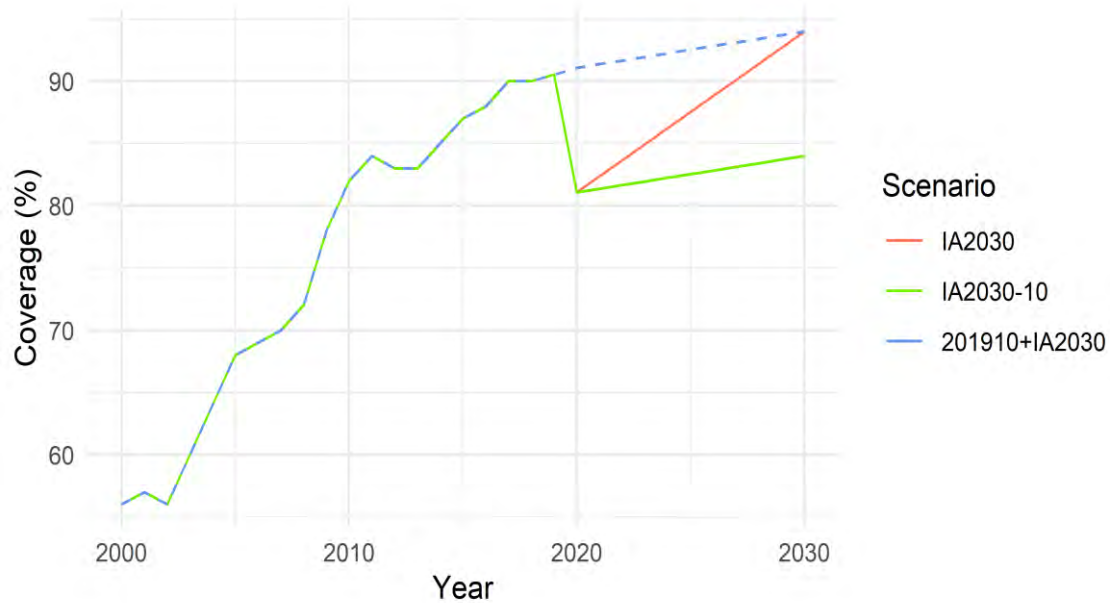
Projecting impact post-2021

- Using the VIMC interim update [Echeverria-Londono et al. 2021], we aim project the vaccination impact given drops in coverage in 2020
- Coverage relies on existing VIMC projections [Toor et al. 2021], IA2030 coverage projections, WUENIC 2020 and IHME estimates of coverage disruption
- Focus is on routine immunisation disruption only
- Investigate the impact of different return strategies
- Three scenarios:
 - One without COVID-19 disruptions
 - Two with different resumptions following COVID-19 disruptions:
 - One reaching IA2030 coverage
 - One with a slower return

Dr. Jaspreet Toor



Projecting impact post-2021



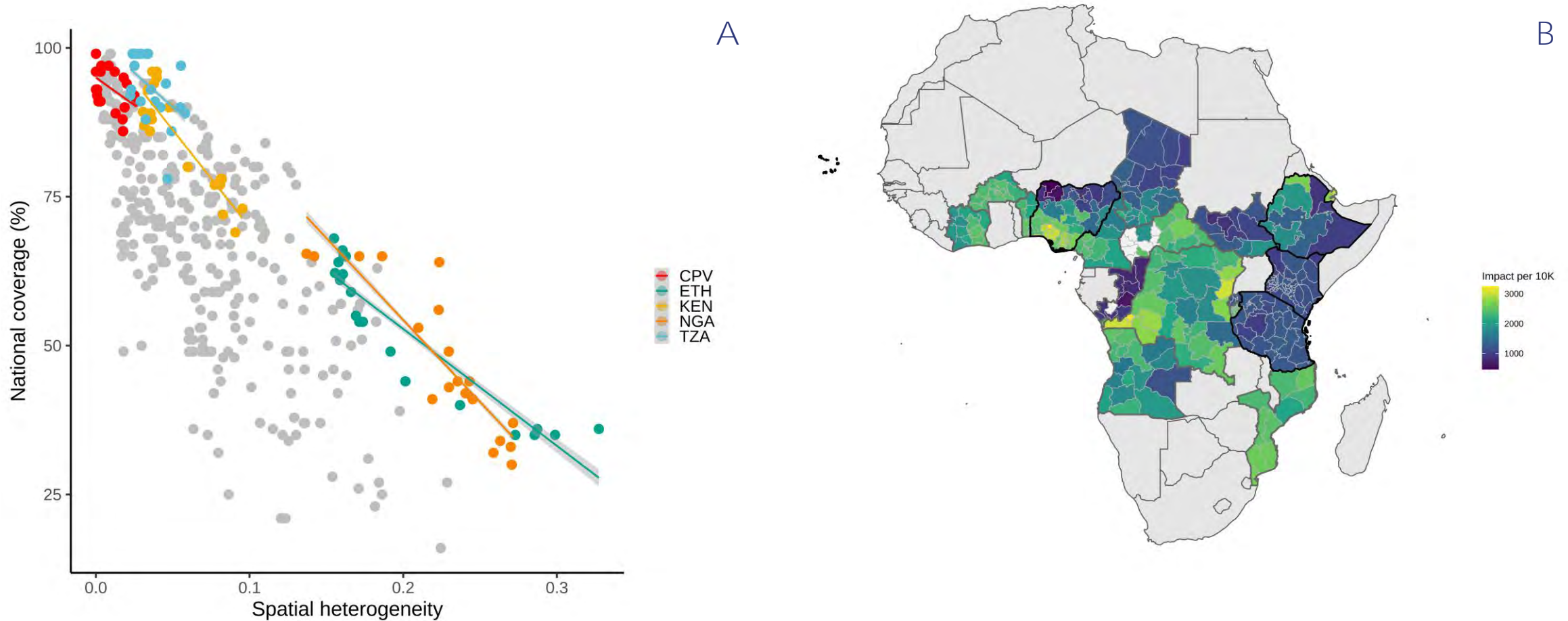
Subnational heterogeneity in impact

- Using recent estimates of MCV1, DTP1 and DTP3 subnational vaccination coverage [*Sbarra et al. 2021; Mosser et al. 2019*]
- Examine heterogeneity within countries across sub-Saharan Africa over time
- Project vaccine impact given subnational coverage using VIMC interim update approach [*Echeverria-Londono et al. 2021*]
- Compare best and worse-case scenarios of heterogeneity
- Evaluate how changes in spatial heterogeneity can affect the overall national impact

Dr. Susy Echeverria-Londono



Subnational heterogeneity in impact



The effect of clustering in coverage and indirect benefits

- Partition a population by whether individuals are effectively protected by vaccination against infection
- For each partition, we estimate their probability of survival in a no-vaccination and a with-vaccination scenario.
- Comparing survivals in different scenarios results in the attribution of direct vaccine impact and indirect benefits
- The proposed methodology makes a useful tool for the understanding of vaccine's direct impact and indirect benefits

Dr. Xiang Li



The impact of demographic uncertainty

- UNWPP produce both median and confidence interval projections of population sizes in the future
- We will use these to project the range in possible routine immunisation impact due to variation in population size alone
- Initial analysis has focused on understanding the particular sources of uncertainty in their projections , and producing uncertainty estimates targeted to single years and single-year ages that are consistent with the methods and results previously used with five-year age groups and five-year periods

Dr. Jeremy Roth



Thank you to all our members



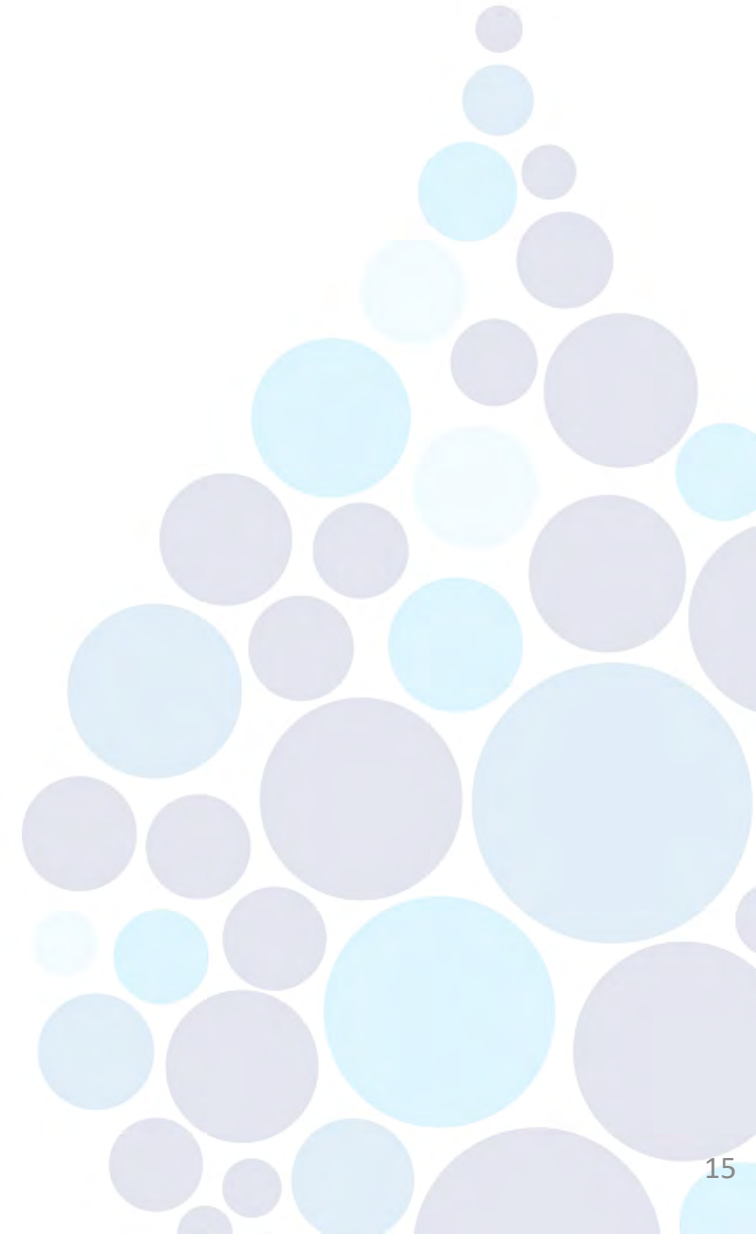
VACCINE
IMPACT
MODELLING
CONSORTIUM

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Discussion



Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world

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†These authors contributed equally to this work

Competing interest: See page 14

Funding: See page 14

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Abstract

Background: Vaccination is one of the most effective public health interventions. We investigate the impact of vaccination activities for *Haemophilus influenzae* type b, hepatitis B, human papillomavirus, Japanese encephalitis, measles, *Neisseria meningitidis* serogroup A, rotavirus,

rubella, *Streptococcus pneumoniae*, and yellow fever over the years 2000–2030 across 112 countries.

Methods: Twenty-one mathematical models estimated disease burden using standardised demographic and immunisation data. Impact was attributed to the year of vaccination through vaccine-activity-stratified impact ratios.

Results: We estimate 97 (95%CrI[80, 120]) million deaths would be averted due to vaccination activities over 2000–2030, with 50 (95%CrI[41, 62]) million deaths averted by activities between 2000 and 2019. For children under-5 born between 2000 and 2030, we estimate 52 (95%CrI[41, 69]) million more deaths would occur over their lifetimes without vaccination against these diseases.

Conclusions: This study represents the largest assessment of vaccine impact before COVID-19-related disruptions and provides motivation for sustaining and improving global vaccination coverage in the future.

Funding: VIMC is jointly funded by Gavi, the Vaccine Alliance, and the Bill and Melinda Gates Foundation (BMGF) (BMGF grant number: OPP1157270 / INV-009125). Funding from Gavi is channelled via VIMC to the Consortium's modelling groups (VIMC-funded institutions represented in this paper: Imperial College London, London School of Hygiene and Tropical Medicine, Oxford University Clinical Research Unit, Public Health England, Johns Hopkins University, The Pennsylvania State University, Center for Disease Analysis Foundation, Kaiser Permanente Washington, University of Cambridge, University of Notre Dame, Harvard University, Conservatoire National des Arts et Métiers, Emory University, National University of Singapore). Funding from BMGF was used for salaries of the Consortium secretariat (authors represented here: TBH, MJ, XL, SE-L, JT, KW, NMF, KAMG); and channelled via VIMC for travel and subsistence costs of all Consortium members (all authors). We also acknowledge funding from the UK Medical Research Council and Department for International Development, which supported aspects of VIMC's work (MRC grant number: MR/R015600/1).

JHH acknowledges funding from National Science Foundation Graduate Research Fellowship; Richard and Peggy Notebaert Premier Fellowship from the University of Notre Dame. BAL acknowledges funding from NIH/NIGMS (grant number R01 GM124280) and NIH/NIAID (grant number R01 AI112970). The Lives Saved Tool (LiST) receives funding support from the Bill and Melinda Gates Foundation.

This paper was compiled by all coauthors, including two coauthors from Gavi. Other funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Introduction

Vaccines play a vital role in immunising populations worldwide to provide protection against a wide range of diseases. In 1974, the World Health Organisation (WHO) launched the Expanded Programme on Immunisation (EPI) with a goal of universal access to all relevant vaccines for all at risk (*Keja et al., 1988*). To further increase momentum on vaccine coverage, Gavi, the Vaccine Alliance, was created in 2000 with a goal of providing vaccines to save lives and protect people's health (*Bill & Melinda Gates Foundation, 2020; Zerhouni, 2019*). Over the past two decades, vaccination programmes have expanded across low- and middle-income countries (LMICs), significantly reducing morbidity and mortality related to vaccine preventable diseases (VPDs). As of 2019, Gavi has helped immunise over 822 million children through routine programmes and provided over 1.1 billion vaccinations through campaigns in supported countries (*Gavi, the Vaccine Alliance, 2019*). Despite this immense progress, almost one in five (15.2 million) children in Gavi-supported countries remain under-immunised with the third dose of the essential childhood vaccination containing diphtheria-tetanus-pertussis vaccine (DTP3), 10.6 million of these children are zero-dose children, that is, having not received their first dose of DTP (*Zerhouni, 2019*).

The beneficial effect of vaccination programmes cannot be assessed directly as the counterfactual, that is, the situation without vaccination, cannot be observed. Hence, models of disease risk and the impact of vaccination activities play a vital role in assessing the current burden, examining the effect of previous activities and projecting the future situation. The Vaccine Impact Modelling

Consortium (VIMC), established in 2016, aims to deliver an effective, transparent and sustainable approach to generating disease burden and vaccine impact estimates (*Imperial College London, 2021*). The VIMC consists of twenty-one independent research groups which provide estimates of disease burden and vaccine impact across 112 LMICs for 10 pathogens, namely hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella, and yellow fever (YF).

There are various ways of calculating the impact of vaccination (*Echeverria-Londono et al., 2021*). The burden averted by vaccination can be estimated in terms of the number of cases, deaths and disability adjusted life years (DALYs) averted. Vaccine impact is commonly presented by calendar year, that is, the number of lives saved by vaccination in a particular year or by birth cohort, that is, the number of lives saved by vaccination over the lifetime of individuals born in a particular year. Previous work by the VIMC on these 10 pathogens estimated that 69 million deaths would be averted by vaccination over calendar years 2000–2030 across 98 LMICs, with 120 million deaths averted over the lifetime of birth cohorts born between 2000 and 2030 (*Li et al., 2019*). The WHO estimates that immunisation currently prevents 2–3 million deaths every year (*World Health Organization, 2021*), similarly *Ehreth, 2003* estimated 3 million deaths averted due to vaccination for pathogens such as measles, YF, HepB, diphtheria, Hib, pertussis, neonatal tetanus and poliomyelitis.

Although attributing vaccine impact to calendar year or birth cohort is intuitive and commonly used, these methods fail to capture the impact of a specific year's vaccination activities traced over the lifetime of those vaccinated. It is beneficial to examine the impact corresponding to a vaccination activity so that the cost and benefit of each intervention can be appropriately calculated. The impact by year of vaccination activity method, developed by the VIMC, estimates the number of individuals that will be saved due to a particular year's vaccination activities (*Echeverria-Londono et al., 2021*). This method addresses the issue of attributing impact to the vaccination activity that caused it without repeatedly rerunning modelling scenarios which, whilst the optimal approach, is extremely computationally intensive. As such, we can approximate the potential effect of one year's worth of activity.

The first human case of coronavirus 2019 (COVID-19) was reported in December 2019 and has subsequently affected vaccination and healthcare worldwide. Whilst the effect of COVID-19 is not the focus of the current study, we acknowledge the huge influence the global pandemic has had and will have for years to come. Preliminary work has begun on quantifying the effect of disruption on vaccination activities and on assessing the benefit of continuing routine infant immunisation in times of COVID-19 (*Abbas et al., 2020a; Gaythorpe et al., 2021b*). There is also evidence that the rise in non-pharmaceutical interventions (NPIs, e.g. social distancing) associated with the pandemic may reduce the transmission of certain pathogens, such as those that cause bacterial meningitis (*Taha and Deghmane, 2020*). However, there is also a risk that NPIs may result in a build up of susceptible individuals in the population, particularly for outbreak prone diseases, such as measles, but catch-up activities may be able to prevent this. Currently, there is little data to inform how the pandemic may have influenced long-term population health and vaccine coverage. In order to assess this, we need to firmly understand the impact of vaccination before the pandemic; only then will it be possible to assess changes due to this global disruption.

In this paper, we estimate the impact of immunisation by year of vaccination for the 10 pathogens modelled by the VIMC across 112 LMICs over the years 2000–2030. Burden averted is investigated in terms of deaths and DALYs averted in synthetic coverage scenarios (with vaccination) compared to counterfactual coverage scenarios (with no vaccination). Although the current COVID-19 pandemic may have hindered vaccination activities, our analyses focus on the projections given what has happened in the past (2000–2019) and given no disruption (from 2020 onward) thus presenting vaccine impact estimates prior to COVID-19.

Materials and methods

Models

The VIMC consists of multiple modelling groups. These provide disease-specific vaccine impact projections to a central Secretariat based at Imperial College London who then synthesise these

estimates. Twenty-one mathematical models were used to inform the estimates with two models per pathogen (except HepB which has three models) thereby increasing robustness and capturing structural uncertainty within the analyses. There is substantial variation in modelling approach due to both the differences in pathogen dynamics and inherent uncertainties in modelling disease risk. The model characteristics vary in their type, from static cohort to transmission-dynamic models; their complexity, for example in their representation of age effects; and their calibration and validation methods. A brief overview of pathogens is provided in **Table 1** with detailed model descriptions provided in Appendix 2.2 (HepB [Nayagam et al., 2016], HPV [Goldie et al., 2008; Abbas et al., 2020b], Hib [Clark et al., 2019a; Walker et al., 2013a], JE [Quan et al., 2020], Measles [Chen et al., 2012], MenA [Karachaliou et al., 2015; Tartof et al., 2013], PCV [Walker et al., 2013a; Clark et al., 2019a], Rota [Pitzer et al., 2012; Clark et al., 2019a], Rubella [Boulianne et al., 1995; Vynnycky et al., 2019], YF [Gaythorpe et al., 2021a]).

Each modelling group provided estimates of age-stratified disease burden at national level for three scenarios: no vaccination, only routine vaccination (routine immunisations; RI) and, where appropriate, both RI and non-routine vaccination (non-routine immunisations; NRI, such as multi-age cohort vaccinations for HPV, and catch-up campaigns for measles). Disease burden was quantified in terms of deaths and DALYs. DALYs measure the years of healthy life lost due to premature death and disability from the disease, and are the sum of years of life lost (YLLs) through premature mortality and years lived with disability (YLDs). No discounting or weighting was applied in the calculation of DALYs. For rubella, only disease burden from congenital rubella syndrome (CRS) was included and the models differed in the inclusion of deaths due to stillbirths.

For every pathogen, the modelling teams were asked to provide 200 samples of their burden estimates for each year, vaccination scenario, and country constructed from the probabilistic ranges of their model parameters. The same randomly sampled sets of parameters were used for the no vaccination and with vaccination model runs allowing the direct comparison of the estimates. In order to calculate the mean and credible interval (CrI) for each pathogen, the full probabilistic distributions of impact are combined from all models for a pathogen, then the mean and 95% CrI are calculated from the full distribution. Similarly, when calculating the aggregated impact across pathogens, bootstrap sampling was used. In these bootstraps, a sample of interest was taken from the individual model; this was then averaged across models of the same pathogen and then summed across all pathogens; finally, the mean and 95% CrIs were calculated from 1000 bootstrap samples.

Table 1. Vaccine Impact Modelling Consortium (VIMC) pathogen-specific details.

RI denotes routine immunisations and NRI denotes non-routine immunisations. RI schedule details the number of doses given and the ages (in years, y) targeted. Vaccination over 2000 - 2030 shows whether vaccination has been occurring over the years 2000 to 2030; years are shown where the vaccines have been introduced in later years. Countries included shows the maximum number of VIMC countries that had coverage in specific year(s) (coverage information in supplementary spreadsheet and countries listed in Appendix 6.1).

Pathogen	Countries included	Activity type	RI schedule	Vaccination over 2000 - 2030
Hepatitis B (HepB)	112	RI	Birth dose + Infant 3 doses (<1y)	Yes
Human papillomavirus (HPV)	112	RI + NRI	Adolescent girls 2 doses (9-14 y)	2014–2030
Haemophilus influenzae type B (Hib)	112	RI	Infant 3 doses (<1y)	Yes
Japanese encephalitis (JE)	17	RI + NRI	Infant dose (<1y)	2005–2030
Measles	112	RI + NRI	1st dose (<=1 y) + 2nd dose (<2 y)	Yes
<i>Neisseria meningitidis</i> serogroup A (MenA)	26	RI + NRI	Infant dose (< 1 y)	2010–2030
<i>Streptococcus pneumoniae</i> (PCV)	112	RI	Infant 3 doses (<1y)	2009–2030
Rotavirus (Rota)	112	RI	Infant 2 doses (<1y)	2006–2030
Rubella	112	RI + NRI	1st dose (< 1 y) + 2nd dose (< 2 y)	Yes
Yellow fever (YF)	36	RI + NRI	Infant dose (< 1 y)	Yes

Data and vaccination scenarios

Standardised, national-level, age-stratified demographic data was provided to all modellers from the 2019 United Nations World Population Prospects (UNWPP) for years 2000 to 2100 (*World Population Prospects, 2019*). The 112 countries considered here include 73 currently and formerly Gavi supported countries and 39 other countries that are of interest due to high burden and/or potential vaccine introduction. These 112 countries represent 99% of the total mortality attributed to measles for children under-5 using the WHO child causes of death 2000–2017 estimate (*World Health Organization, 2020*) and 96% of the total deaths attributed to measles, HepB, Hib, MenA, PCV, and YF of all ages using the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease Study (GBD) 2017 estimates (*GHDx, 2019*). Therefore, there has been a greater focus on supporting vaccine introduction and implementation in these countries, mainly through Gavi. Pathogens endemic only in certain regions such as JE, MenA, and YF have estimates for 17, 26, and 36 countries, respectively (*Table 1*).

For the vaccination scenarios, standardised vaccine coverage data were provided at a national level where past RI coverage (1980–2018) was obtained from WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) as published in July 2019 (*WHO UNICEF coverage estimates, 2020*). Historical campaign coverage (2000–2018) was taken from Gavi's data repository, which included data from various sources, mainly Gavi and WHO. For HPV, JE, MenA, PCV and Rota, RI and NRI were introduced later, from 2005 onward (*Table 1*). Future coverage estimates, both RI and NRI, from 2019 to 2030 were taken from default scenario forecasts, developed with Gavi, for all 112 countries (countries listed in Appendix 6.1). Projection for future (2030–2100) RI is done by assuming a 1% annual increment up to a threshold of 90% (95% for the first dose of measles containing vaccine, MCV1) or historical highest. We assume no campaigns post-2030 to avoid predicting future campaign coverage beyond the default scenario forecasts, see supplementary material for further details on coverage assumptions. Estimates of numbers of vaccines received per child were calculated based on these coverage estimates and projections assuming independence between vaccines.

In the no vaccination (counterfactual) scenario, zero coverage is assumed for all years from 1980 to 2100 except for YF which has historical reactive campaigns for outbreaks.

Impact by year of vaccination

We calculate deaths and DALYs averted by year of vaccination using impact ratios stratified by vaccine activity type (*Echeverria-Londono et al., 2021*). In this way, we attribute the deaths averted due to vaccination to the year in which the vaccination activity took place. We stratify the impact ratios by activity type in order to account for the different effects of RI compared to NRI which has been found to better capture model projections (*Echeverria-Londono et al., 2021*). Hence, this method assumes vaccine impact varies between RI and NRI but does not vary across birth cohorts. This method averages the effects of any temporal changes in disease incidence or population health over the time period modelled. We present results using 'fully vaccinated persons (FVPs)' which refer to the total number of doses provided by a vaccination activity. Where separate coverage figures are provided, one vaccine dose results in one FVP. However, for diseases such as HepB, coverage figures are based on the completed courses of multi-dose vaccinations. More specifically, we also show deaths and DALYs averted per 1000 FVPs. Notably, for some of the pathogens, the different models assume varying levels of dose dependency. For example, the measles dynaMICE model assumes that NRI doses are weakly dependent on RI doses whereas the measles Pennsylvania State University model assumes that NRI doses are independent from prior RI doses and that the second dose (MCV2) is only given to those who received the first dose (MCV1) (further model details in Appendix 2.2). When assuming NRI doses are distributed randomly and thus may re-vaccinate some individuals, the relative benefit of NRI compared to RI, which will always vaccinate a naive individual, is affected.

As we model disease-specific mortality under different vaccination scenarios, when aggregating estimates of deaths averted across all 10 pathogens per calendar year or birth cohort, double counting can arise whereby an individuals' death is accounted for more than once. Under the year of vaccination method, we do not adjust death estimates for double counting.

Impact by birth year for children under five

To investigate the impact of vaccination in children under-5, we calculate deaths and DALYs averted by birth cohort. Here, we aggregate the impact over the first 5 years of life of birth cohorts born within the years of interest and then calculate the difference in the no vaccination and with vaccination scenarios. Furthermore, in [Appendix 5—figure 1](#) and [Appendix 5—figure 2](#), we present vaccine impact by calendar year and by birth cohort in line with [Li et al., 2019](#) which shows the impact in a particular year or the total impact over an individuals' lifetime, respectively. These methods are directly calculated through comparison of the focal scenario with vaccination (both RI and NRI where appropriate) to the counterfactual scenario without vaccination.

Within the birth cohort method when investigating the impact of vaccination in children under-5, we account for double counting of deaths attributable to the 10 VIMC pathogens. This is done by clustering a population or birth cohort by vaccine coverage and evaluating the proportion of disease burden in those un-vaccinated and vaccinated, respectively; via which the total deaths across all 10 pathogens is re-estimated with double counting removed. A full description of the method is given in [Echeverria-Londono et al., 2021](#); [Li et al., 2019](#).

Results

Estimated burden

The modelling groups produced estimates of deaths attributable to the pathogens for years 2000–2100 for the given vaccination scenarios. In the focal scenario with vaccination, coverage has improved over time leading to more FVPs ([Figure 2](#) and [Appendix 5—figure 3](#)). We find that given these improvements in coverage over time, there is a general decline in the mean number of predicted deaths due to the 10 VIMC pathogens in each of the 112 countries. The decline in deaths averted due to vaccination varies by country, largely due to variations in vaccination coverage over time as well as variation in the epidemiology, treatment assumptions, health access, case fatality ratio (CFR), pathogen-specific mortality and demographic parameters (e.g. life expectancy) of some pathogens by country. Without vaccination, there is still some reduction in deaths over time in some countries due to these latter factors ([Figure 1](#)). Notably, the total burden caused by these diseases disproportionately lies within the WHO African region where the greatest decline in burden is predicted ([Figure 1](#) and [Appendix 5—figure 4](#)).

The ages at which the greatest mortality risks are faced varies across the pathogens with mortality related to Hib, measles, Rota, rubella, and PCV mostly focused in children under-5 ([Appendix 5—figure 5](#) shows a corresponding decline in deaths in the under-5s when vaccination occurs). Mortality attributable to HepB and HPV is focused in those over 40, and for YF, MenA and JE this is focused in those under 30 (due to natural immunity acquired with age in older adults).

Impact by year of vaccination

Due to vaccination activities over the years 2000–2030 for all 10 VIMC pathogens, 97 (95%CrI[80, 120]) million future deaths and 5100 (95%CrI[4100, 6300]) million DALYs are estimated to be averted. Focusing on the years prior to the COVID-19 pandemic, i.e. 2000 to 2019, 50 (95%CrI[41, 62]) million deaths and 2700 (95%CrI[2200, 3500]) million DALYs are estimated to have been averted. The remaining numbers averted arise from the years 2020 to 2030, which may be affected by COVID-19 and other changes to future vaccine introductions and coverage as well as changes in access to health care ([Table 2](#)). Note: although the first human case of COVID-19 was reported in December 2019, any effects of this on vaccination activities in 2019 would be negligible.

The Global Vaccine Action Plan (GVAP) target for 2011–2020 is to avert between 24 and 26 million future deaths with vaccination for the 10 pathogens over 94 countries ([World Health Organization, 2013](#)). Over 2011–2019, we estimate that 23 (95%CrI [19, 27]) million deaths will be averted, with this increasing to 26 (95%CrI [21, 31]) million deaths averted over 2011–2020 (without COVID-19-related disruptions in 2020). Hence, the achievement of the GVAP target will depend on how the year 2020 is impacted by COVID-19.

The years in which vaccination activities occur, the types of activities carried out, the coverage and the number of FVPs achieved varies by pathogen. Measles and HepB have activities occurring over the entire time period of interest from 2000 to 2030 and achieve higher coverage and FVPs

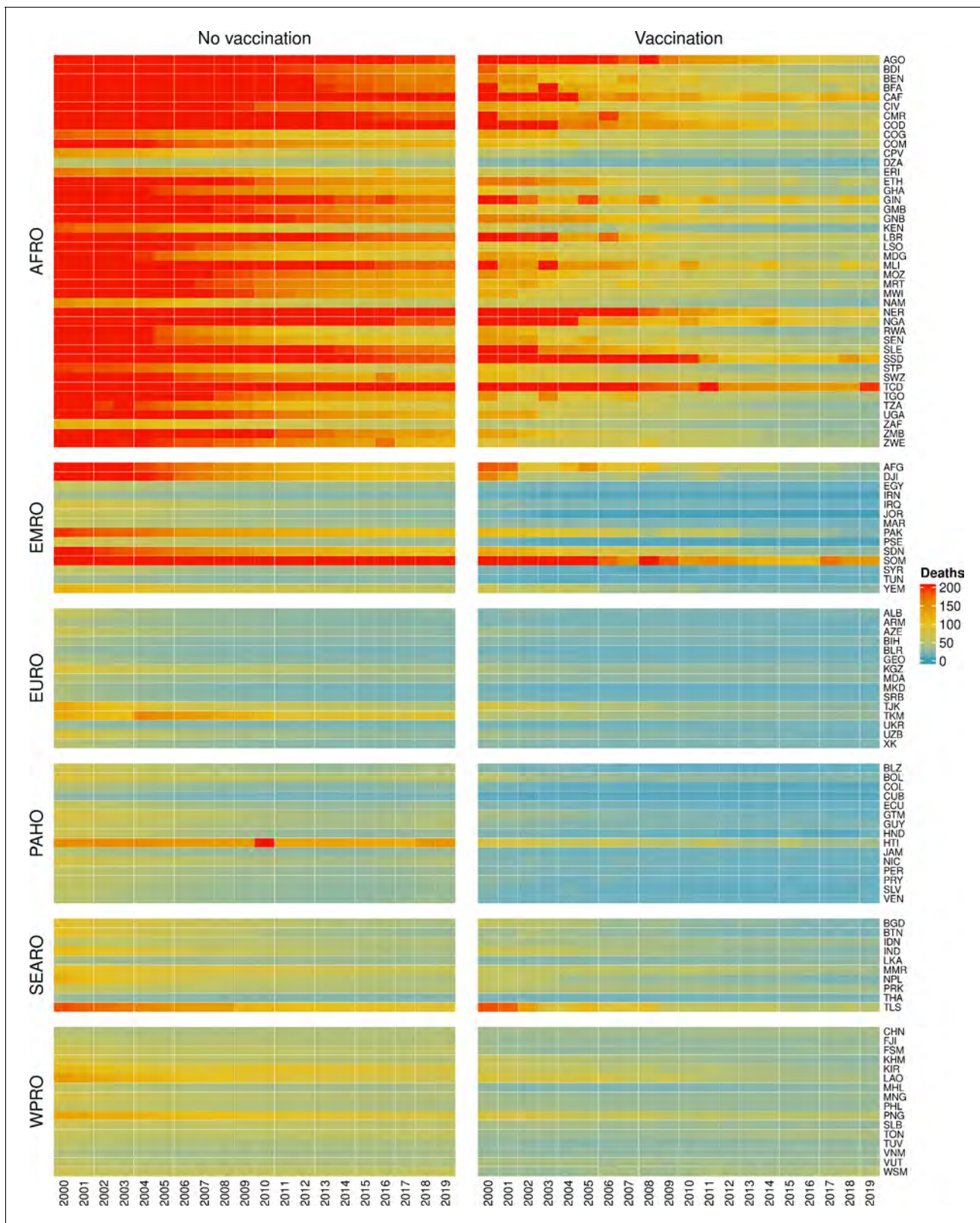


Figure 1. Mean predicted deaths due to the 10 Vaccine Impact Modelling Consortium (VIMC) pathogens per 100,000 population per country for years 2000–2019 under the no vaccination and with vaccination (routine immunisations; RI only) scenarios. Countries are arranged by World Health Organisation (WHO) African (AFRO), Eastern Mediterranean (EMRO), European (EURO), Pan American (PAHO), South-East Asian (SEARO), and Western Pacific (WPRO) regions. The difference (i.e. deaths averted) between these two scenarios are shown in **Table 2** and **Figure 2**.

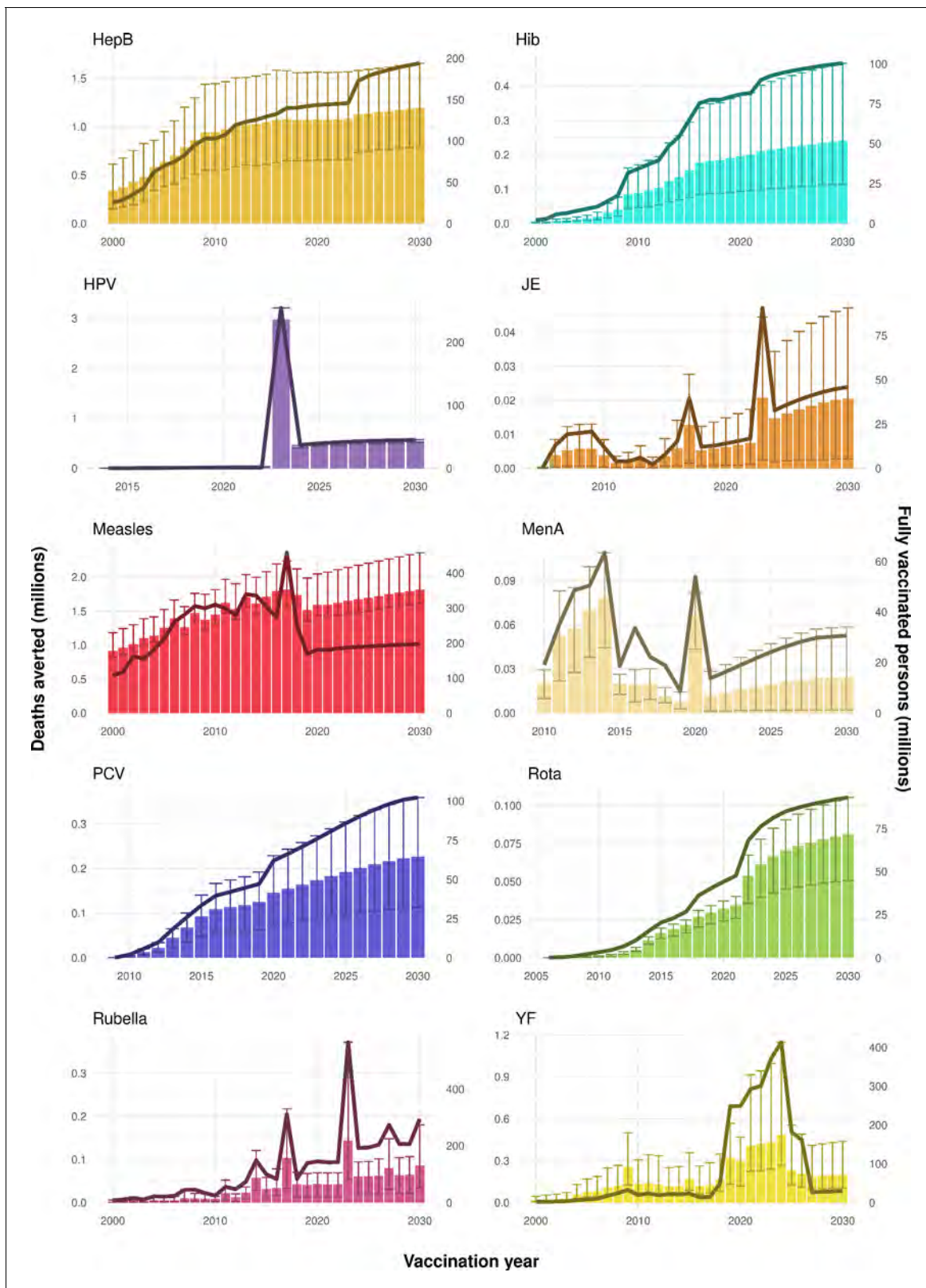


Figure 2. Deaths averted per year of vaccination for hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella, and yellow fever (YF). The bars show the number of deaths averted (in millions) in each vaccination year. Error bars indicate 95% CI. The line shows the number of fully vaccinated persons (FVPs; in millions) achieved in each year's vaccination activities.

Table 2. Deaths and disability-adjusted life years (DALYs) averted (in millions), and deaths and DALYs averted per 1000 fully vaccinated people (FVPs) due to vaccination activities in each time period. Numbers within brackets correspond to 95% credible intervals.

Time period	Deaths averted (in millions)	Deaths averted per 1000 FVPs	DALYs averted (in millions)	DALYs averted per 1000 FVPs
2000–2019	50 [41, 62]	4.8 [3.9, 5.9]	2700 [2200, 3500]	260 [210, 330]
2020–2030	47 [39, 56]	3.7 [3.1, 4.4]	2300 [1900, 2900]	180 [150, 230]
2000–2030	97 [80, 120]	4.2 [3.5, 5]	5100 [4100, 6300]	220 [180, 270]

than the other pathogens (**Figure 2** and **Appendix 5—figure 3**). Overall, from 2000 to 2030, measles vaccination activities have the largest impact with 47 (95%CrI[42, 60]) million deaths and 3100 (95%CrI[2700, 3900]) million DALYs averted, followed by 29 (95%CrI[17, 43]) million deaths and 1000 (95%CrI[560, 1800]) million DALYs averted due to HepB vaccination activities (**Figure 2** and **Table 3**). Most of the mortality reduction from measles is attributable to routine MCV1, for which procurement is not directly funded by Gavi. As we attribute impact to the year of vaccination, we capture the impact for pathogens where the mortality occurs later in life, such as HepB, whereas, when comparing impact by calendar year (see **Appendix 5—figure 1**), we miss these long-term benefits. As measles-related mortality is focused in children under-5, a large number of DALYs are averted when immunising against this disease. In comparison, as HepB-attributable deaths are primarily focused in those over 40 years of age, there are fewer YLLs but morbidity contributes to higher numbers of YLDs.

Rubella and YF have RI and NRI occurring over the entire time period from 2000 to 2030. With disease burden from CRS modelled for rubella, an estimated 1.2 (95%CrI[0.47, 2.1]) million deaths and 86 (95%CrI[56, 170]) million DALYs are averted. Over the relatively fewer (36) countries endemic for YF, 5.6 (95%CrI[2.9, 13]) million deaths and 210 (95%CrI[110, 510]) million DALYs are estimated to be averted (**Figure 2** and **Table 3**).

For Hib, which is based only on RI, there are an estimated 4.1 (95%CrI[1.9, 7.9]) million deaths and 280 (95%CrI[120, 540]) million DALYs averted over 2000 to 2030 (**Figure 2** and **Table 3**).

Further vaccines for the 10 pathogens have been introduced from 2005 onward, contributing to more lives saved (**Table 1**). From 2014, introductions of RI and NRI for HPV over 112 countries avert an estimated 6.6 (95%CrI[6.1, 7.1]) million deaths and 140 (95%CrI[130, 150]) million DALYs by 2030 (**Figure 2** and **Table 3**). RI were introduced for PCV in 2009, resulting in a further 2.8 (95%CrI[1.4, 4.4]) million deaths and 190 (95%CrI[94, 300]) million DALYs averted by 2030, and for Rota in 2006

Table 3. Deaths and disability-adjusted life years (DALYs) averted (in millions), and deaths and DALYs averted per 1000 fully vaccinated people (FVPs) per disease from vaccination activities occurring from 2000 to 2030.

Disease abbreviations: hepatitis B (HepB), human papillomavirus (HPV), yellow fever (YF), *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), *Neisseria meningitidis* serogroup A (MenA), and Japanese encephalitis (JE). Numbers within brackets correspond to 95% credible intervals.

Disease	Deaths averted (in millions)	Deaths averted per 1000 FVPs	DALYs averted (in millions)	DALYs averted per 1000 FVPs
Measles	47 [42, 60]	6.5 [5.9, 8.2]	3100 [2700, 3900]	420 [380, 540]
HepB	29 [17, 43]	7.7 [4.7, 12]	1000 [560, 1800]	270 [140, 460]
HPV	6.6 [6.1, 7.1]	12 [11, 13]	140 [130, 150]	250 [230, 270]
YF	5.6 [2.9, 13]	2.1 [1.1, 4.6]	210 [110, 510]	81 [43, 200]
Hib	4.1 [1.9, 7.9]	2.4 [1.1, 4.5]	280 [120, 540]	160 [74, 310]
PCV	2.8 [1.4, 4.4]	2.3 [1.1, 3.7]	190 [94, 300]	160 [79, 260]
Rubella	1.2 [0.47, 2.1]	0.3 [0.1, 0.5]	86 [56, 170]	22 [14, 44]
Rota	0.84 [0.56, 1.1]	0.8 [0.5, 1]	46 [36, 56]	44 [35, 54]
MenA	0.62 [0.47, 0.86]	1 [0.8, 1.4]	36 [24, 45]	59 [39, 73]
JE	0.23 [0.03, 0.52]	0.4 [0, 0.8]	24 [2.6, 46]	40 [4.2, 76]

resulting in 0.84 (95%CrI[0.56, 1.1]) million deaths and 46 (95%CrI[36, 56]) million DALYs averted by 2030 (**Figure 2** and **Table 3**). MenA is endemic in 26 countries with RI and NRI introduced from 2005 onward resulting in 0.62 (95%CrI[0.47, 0.86]) million deaths and 36 (95%CrI[24, 45]) million DALYs averted by 2030 (**Figure 2** and **Table 3**). JE is endemic in fewer (17) countries with RI and NRI also introduced from 2005 onward resulting in 0.23 (95%CrI[0.03, 0.52]) million deaths and 24 (95%CrI[2.6, 46]) million DALYs averted by 2030 (**Figure 2** and **Table 3**).

When examining deaths averted per 1000 FVPs, HPV vaccination activities are estimated to have the largest impact with 12 (95%CrI[11, 13]) deaths averted per 1000 FVPs. This is followed by HepB with 7.7 (95%CrI[4.7, 12]) deaths averted per 1000 FVPs and measles with 6.5 (95%CrI[5.9, 8.2]) deaths averted per 1000 FVPs (**Table 3**). In terms of DALYs averted per 1000 FVPs, measles is estimated to have the largest impact with 420 (95%CrI[380, 540]) DALYs averted per 1000 FVPs as it mainly affects children under-5 (**Table 3**).

Generally, for each of the pathogens, as the number of FVPs (or number of vaccine doses distributed) increase over time, the number of deaths averted increases (**Figure 2**). For the pathogens with RI-only (HepB, Hib, PCV, and Rota), there is an increasing trend of FVPs from 2000 to 2030 leading to a steady increase in deaths averted over this time period. When NRI also occur (HPV, JE, measles, MenA, rubella, and YF), more variation is seen as the FVPs and in turn the deaths averted rise in years for which both activities occur. For example, we expect to see the largest impact due to vaccination activities occurring in the year 2023 for HPV and rubella which project a sharp increase in the number of FVPs arising from NRI in addition to RI in that year (**Figure 2**).

Impact in children under five

Several of the pathogens, namely Hib, measles, Rota, rubella and PCV, have mortality heavily focused in children under-5. To determine the impact of vaccination for these ages, we aggregate by birth cohort rather than by year of vaccination as this allows us to calculate the disease burden across the first 5 years of life for each yearly birth cohort (born between 2000 and 2030) (**Echeverria-Londono et al., 2021**). We also account for the double counting of mortality when we aggregate mortality across all diseases.

For the 2000–2030 birth cohorts, we estimate that 52 (95%CrI[41, 69]) million deaths and 3400 (95%CrI[2700, 4600]) million DALYs are averted in children under-5. Of these, 33 (95%CrI [27, 43]) million deaths and 2100 (95%CrI[1700, 2800]) million DALYs are estimated to be averted over the years 2000–2019 prior to COVID-19 (**Table 4**). The proportional change due to the removal of double counting is relatively small at 2.36% (95% CI[2.00%, 2.83%]) for all cohorts born between 2000 and 2030 and this reduces to 1.07% (95% CI[0.90%, 1.32%]) for children under-5.

Impact in comparison to other studies

Our results have focused on the impact by year of vaccination. However, as in the previous VIMC-wide study **Li et al., 2019**, we also investigated the impact of vaccination (deaths and DALYs averted) by calendar year and by birth cohort (**Echeverria-Londono et al., 2021**; **Appendix 5—figure 1** and **Appendix 5—figure 2**). There are differences when comparing the impact estimates, largely driven by changes in coverage/FVPs (**Appendix 5—figure 3**) and/or further developments of model structures, particularly for HepB, HPV, measles and YF. Additional models have also been added, namely, the Emory University Rota model and the University of Notre Dame YF model. Furthermore since the previous study, the uncertainty ranges/confidence intervals for many of the pathogens have narrowed (**Appendix 5—figure 1** and **Appendix 5—figure 2**).

Table 4. Deaths and disability-adjusted life years (DALYs) averted (in millions), and deaths and DALYs averted per 1000 fully vaccinated people (FVPs) in children under-5 for birth cohorts born between each time period. These are adjusted for double counting. Numbers within brackets correspond to 95% credible intervals.

Time period	Deaths averted (in millions)	Deaths averted per 1000 FVPs	DALYs averted (in millions)	DALYs averted per 1000 FVPs
2000–2019	33 [27, 43]	3.9 [3.2, 5]	2100 [1700, 2800]	250 [200, 330]
2020–2030	20 [14, 26]	1.9 [1.3, 2.5]	1300 [960, 1800]	130 [95, 180]
2000–2030	52 [41, 69]	2.8 [2.2, 3.7]	3400 [2700, 4600]	190 [140, 250]

Mortality estimates from our results were compared to the IHME GBD 2019 (*Institute for Health Metrics and Evaluation, 2019*) on a global level and for four high burden countries (Pakistan, India, Nigeria and Ethiopia) for HepB, measles and YF. Note, estimates for GBD 2019 are global and for VIMC are for 112 countries. The GBD 2019 did not estimate deaths averted. Comparison between the mortality estimates from VIMC and GBD 2019 show significant overlap in the overall values between 2000 and 2019 for HepB and measles (*Table 5*). Globally, measles mortality estimates from VIMC tend to be higher than those from GBD 2019 between 2000 and 2010 with an increasing overlap in recent years (*Appendix 5—figure 8*). For HepB, the trend is reversed with overlapping estimates between 2000 and 2010 and divergent estimates in recent years (*Appendix 5—figure 6*). For measles, VIMC has greater variability in the mortality estimates in countries with a high burden such as Pakistan, India, Nigeria, and Ethiopia compared to GBD 2019 estimates (*Appendix 5—figure 9*). For HepB, we see considerable agreement between the VIMC and GBD 2019 mortality in Pakistan, India and Nigeria (*Appendix 5—figure 7*). Unlike measles and HepB, the global mortality estimates for YF from VIMC do not show any overlap with those from GBD 2019, with significantly higher VIMC estimates (*Table 5* and *Appendix 5—figure 10*). Nevertheless, when looking at the mortality estimates for a high burden country such as Ethiopia, we do see overlap between the estimates but with great uncertainty (*Appendix 5—figure 11*). The differences between VIMC and GBD 2019 estimates are generally due to differences in treatment assumptions and parameter values, such as the CFR estimates for YF.

Discussion

We present the first estimates of vaccine impact to be attributed to the year in which the vaccination activity occurred for 10 pathogens in 112 countries. This alternative view of impact allows us to directly assess the influence of a particular year's vaccination efforts over the lifespans of all individuals affected, better capturing the full long-term benefits of vaccination. This is an advance both in methodology and scope with the countries and pathogens considered representing the vast majority of VPD burden globally.

Stratifying the impact of vaccination activities over the years 2000–2019 and 2020–2030 allows us to estimate the immense progress made to date, and to estimate future advances which may be affected by the COVID-19 pandemic as well as other variations in transmission or healthcare. Without vaccination activities between 2000 and 2019, there would be an additional 50 (95%CrI[41, 62]) million deaths, with a further additional 47 (95%CrI[39, 56]) million deaths without vaccination activities between 2020 and 2030 due to these 10 pathogens over the 112 countries. If vaccination proceeds per the default scenario forecast through 2030, the greatest reductions in deaths are predicted to be for measles with 47 (95%CrI[42, 60]) million deaths averted from vaccination activities occurring in 2000 to 2030. HepB, HPV and YF also see large predicted reductions with 29 (95%CrI[17, 43]), 6.6 (95%CrI[6.1, 7.1]) and 5.6 (95%CrI[2.9, 13]) million deaths averted, respectively. In children under-5, we examine the impact per birth cohort and find that an estimated 33 (95%CrI[27,

Table 5. Global mortality estimates (in thousands) from the Vaccine Impact Modelling Consortium (VIMC) and the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME) attributed to Hepatitis B (HepB), measles and yellow fever (YF) for all ages and for children under-5 over the years 2000–2019.

Estimates for GBD 2019 are global and for VIMC are for 112 countries. 95% CI shown for VIMC estimates (see *Appendix 5—figures 6–11*).

Disease	Time period	All ages		Under-5	
		VIMC 2019	GBD 2019	VIMC 2019	GBD 2019
HepB	2000–2010	7200 [5100, 10000]	5200	100 [21, 360]	72
	2011–2019	7200 [5300, 9800]	4200	33 [5.4, 110]	43
Measles	2000–2010	5600 [4100, 9500]	4200	5300 [3800, 9400]	3600
	2011–2019	920 [620, 1700]	1200	870 [560, 1700]	1100
YF	2000–2010	600 [320, 1500]	84	100 [54, 250]	10
	2011–2019	450 [240, 1100]	47	63 [32, 150]	5.7

43]) million child lives were saved by vaccination between 2000 and 2019, 20 (95%CrI[14, 26]) million thereafter.

In comparison to other studies, we generally find less uncertainty and lower median deaths averted estimates relative to the previous VIMC-wide study (*Li et al., 2019*) and similar overall mortality estimates to the IHME GBD 2019 (*Institute for Health Metrics and Evaluation, 2019*). The differences compared to the previous VIMC-wide study which examined the same pathogens but for a subset of countries (98 of the 112 countries), are mostly driven through differing assumptions around FVPs, affecting HPV, developments to model structure which influence the results for HepB, measles and YF, and additional models for Rota and YF. In comparison to GBD 2019 for HepB and measles, we find similar magnitude estimates of mortality both globally and for particular high-burden countries (Nigeria, Pakistan, India, and Ethiopia). However, YF estimates diverge from the GBD 2019 due to differences in assumed CFR values and parameter estimates.

In this study, we attribute the impact to the year in which the vaccination activity occurred through calculating an impact ratio. We stratify this impact ratio by vaccine activity type (assuming vaccine impact does not vary between birth cohorts), thereby averaging the effects of any improvements in disease incidence or population health over the entire time period modelled. However, a recent study examined different ratio stratifications and found varying support for each dependant on the question, pathogen and model examined (*Echeverria-Londono et al., 2021*). As such, whilst we have shown the impact in one format, this could underestimate characteristics such as the change in population demography, transmission or healthcare over time which may mean that one cohort has a different experience of vaccination compared to another. Similarly, the assumptions around vaccination post-2030 may have implications for the impact of earlier activities, for example in rubella the number of CRS cases depend on infections among women of child-bearing age, thus later vaccination activities could affect the incidence of CRS over the lifetime of vaccinated individuals. As a result, for long-term disease burden due to pathogens such as HepB or HPV, we may underestimate the uncertainty in vaccine impact. This may be particularly relevant when assessing the changes in healthcare due to COVID-19 and the introduction of SARS-COV-2 vaccines.

We account for uncertainty in model structure and parameterisation by including at least two models per pathogen sampling from the full uncertainty distribution of both models. However, we do not consider uncertainties within demography or immunisation coverage data. Demographic uncertainty will affect both our estimates of vaccination coverage and the disease dynamics themselves. For example, although the UNWPP population data takes migration into account, we do not account for this explicitly. As such, we may lose a key influencing factor for disease transmission from one country to another. Furthermore, estimating current vaccine uptake is often complicated by changes in assumed population size and issues around dose wastage. This is one reason that the coverage estimates for RI and NRI are uncertain, affecting any measure of vaccine impact. The correlation and dependency between doses varies by disease modelled and can influence the relative effects of campaign versus routine immunisation. Although vaccines such as measles and rubella may be given together, we considered them to be independent.

Inclusion of different model structures allows us to capture some of the inherent unknowns within the epidemiology of these pathogens. However, in some cases, data are limited and validation of models is not possible. This is a focus of constant work as more data becomes available. Conversely, as we focus on 112 countries, a limitation of our study is that not all countries are modelled globally. However, our analyses include the countries with the highest burden relating to the pathogens (representing 99% of the total mortality attributed to measles for under-5s [*World Health Organization, 2020*] and 96% of the total deaths attributed to HepB, Hib, measles, MenA, PCV, and YF of all ages [*Institute for Health Metrics and Evaluation, 2019*]).

Following vaccine introductions, future coverage has been assumed to increase over time. However, there is the risk of decline in coverage, or delays to activities without sustained focus. Disruptions to health services caused by the COVID-19 pandemic have been an example of such disruption and in April 2020, Gavi estimated that at least 13.5 million people may have missed vaccinations with disruption likely to continue (*Gavi, the Vaccine Alliance, 2020*). Similarly, *Chandir et al., 2020* estimated that one in every two children in Sindh province, Pakistan have missed their routine vaccinations during lockdown associated with the pandemic. Disruption to vaccine and health care services may influence our estimates of lives saved from 2020 onward, particularly if the risk of outbreak or disease emergence is increased. However, this disruption in immunisation might be partially offset

by decreased disease transmission due to NPIs implemented to help control COVID-19, as has been shown for influenza and norovirus ([Jones, 2020](#); [Kraay et al., 2020](#)). In the longer-term, there is a risk that NPIs may result in a build up of susceptible individuals in the population for outbreak prone diseases, such as measles, but catch-up activities may be able to prevent this. To date, many vaccination activities have restarted and catch-up vaccination campaigns have begun to ensure the immunity gap due to disruption is as small as possible.

Despite improvements in vaccine coverage, universal vaccination coverage is not yet achieved and there are areas in many countries where coverage remains low ([World Health Organization, 2021b](#); [Hamlet et al., 2019](#); [Kundrick et al., 2018](#); [Takahashi et al., 2017](#); [Vanderslott et al., 2013](#)). The model estimates presented in this study do not account for such geographic or socioeconomic clustering of vaccine coverage, which could increase disease transmission. Hence, sub-populations with low access to vaccines and/or high exposure to the pathogens are not presented in our results ([Gavi, the Vaccine Alliance, 2020](#); [Chandir et al., 2020](#)). However, some of the models included are estimated subnationally and can examine questions around heterogeneity in health access and transmission (Appendix 2.2). A combined, cross-pathogen approach to these heterogeneities is an area of continued research.

When attributing vaccine impact to the year of vaccination, and aggregating mortality across all 10 pathogens, we do not adjust for double counting, thereby counting an individual's death more than once when mortality arises by more than one pathogen ([Li et al., 2019](#)). However, this is accounted for when aggregating vaccine impact over a calendar year and birth cohort. The issue of double counting can be viewed from two perspectives- either a person's life is saved from different pathogens multiple times or their death is averted from different pathogens multiple times. Intuitively, the former makes sense, it is important to capture each time an individual's life is saved. The latter is a more difficult perspective as each person will only die once. When focusing on the under-5s using the birth cohort method, the proportional change due to double counting adjustment was found to be 2.36% (95% CI[2.00%, 2.83%]) for cohorts born between 2000 and 2030 and reduced to 1.07% (95% CI[0.90%, 1.32%]) for under-5s. Thus, whilst the majority of double counting occurs in the under-5s, the overall difference is minimal.

Although we do not account for the current COVID-19 pandemic, our analyses provide a vital baseline against which comparison can be made. Studies assessing the impact of COVID-19 on VPDs are ongoing. [Abbas et al., 2020a](#) assessed the benefit of continuing routine childhood immunisation in Africa given the ongoing pandemic. They found the benefits outweighed the costs with 84 (95% uncertainty interval 14-267) child deaths averted by sustained childhood immunisation per 1 excess COVID-19 death even with the risks associated with vaccination clinic visits. The VIMC Working Group on COVID-19 Impact on VPDs analysed the effect of COVID-19 disruption on measles, MenA and YF through modelling scenarios of routine immunisation service disruptions and mass vaccination campaign suspensions in a subset of countries ([Gaythorpe et al., 2021b](#)). They found that the nature of the disease affects the impact of vaccination activity disruption; for example, YF and measles affect younger age groups and are prone to outbreaks, thus short-term disruption will likely increase burden. However, protection afforded by previous vaccination activities for MenA can mitigate the short-term effects due to COVID-19 disruption. A global analysis of the impact of COVID-19 on vaccination activities is not yet available and it is unclear how the continued disruption, and likely impact of distributing a future SARS-COV-2 vaccine, will affect vaccination in the future. Conversely, we also do not know to what extent transmission has been perturbed due to NPIs instigated to mitigate COVID-19 for the pathogens mentioned here.

Overall, our results provide a thorough assessment of the impact of vaccination activities prior to COVID-19, from 2000 to 2019, and from 2020 thereafter. These results are subject to change as our understanding of the transmission and epidemiology of these pathogens continues to grow. Additionally, future coverage, particularly during and following the pandemic, is uncertain. This study paints a picture of the immense progress to date and the tremendous health impacts that could be obtained over the next decade due to vaccination activities.

Conclusion

Our largest VIMC-wide study for 10 pathogens across 112 countries showcases the immense impact of vaccination activities over 2000–2030 with 97 (95%CrI[80, 120]) million lives estimated to be saved in a pre-COVID-19 world. Though the wide-spread COVID-19 pandemic has caused disruption to

vaccination activities, currently it is difficult to assess the impact. Nonetheless, our study shows the substantial progress to date and as we look to the future, it continues to show the benefits of vaccination and motivates efforts to sustain and improve coverage of vaccination globally.

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Additional files

Supplementary files

- Transparent reporting form

Data availability

Data is available through a publicly available tool at <https://montagu.vaccineimpact.org/2021/visualisation/>.

The following dataset was generated:

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Appendix 1

Vaccine coverage forecasts

Vaccine coverage forecasts were generated for every country-antigen combination for years 2019 to 2030. For existing routine programs, future coverage was modelled using Generalised Additive Models (GAMS), with historical WUENIC coverage as an input, to forecast the country- and antigen-specific time-series of coverage (*WHO UNICEF coverage estimates, 2020*).

For countries that had not yet introduced a specific vaccine by 2018, all countries were assigned the same future year of introduction for that vaccine based on projections from an accelerated failure time model. The vaccine introduction year and coverage were forecasted for each vaccine based on the association between time to introduction and coverage of existing vaccines (DTP3, MCV1 and Pol3) in countries where the vaccine had been introduced, controlling for Gavi support. Coverage scale-up was then modeled for each country on the basis of annual rates of increase in coverage for existing vaccines at the time of their introduction. For regional vaccines, namely yellow fever (YFV), meningitis A (MenA) and Japanese Encephalitis (JE), vaccine introductions were forecasted only in countries where the respective disease is endemic.

Non-routine activities, such as supplementary Immunisation activities (SIAs) and multi-age cohort vaccinations (MACs), and their associated fully immunised persons (FVPs) were forecasted for the regional vaccines, measles/measles-rubella (M/MR) and HPV, according to the specific characteristics of the individual vaccine program and the related WHO recommendations, see table **Appendix 1—table 1** for summary.

Appendix 1—table 1. Vaccine, non-routine immunisation activity type and target population for coverage forecasts.

Vaccine	Type of non-routine immunisation activity	Target population
HPV	Multi-age cohorts (MACs)	Girls 10–14 year-olds
MR	Catch-up	9 months- 15 year-olds
M/MR	Follow-up	9 months- 5 year-olds
JE	Catch-up	9 months –14 year-olds
Men A	Initial catch-up	1–29 year-olds
	Mini-catch-up	Country dependent
YFV	Preventive mass campaigns	At risk population older than 9 months

For MR, HPV, and JE, introductions of the vaccines in the routine program are generally preceded with catch-up campaigns or MACs for HPV. Thus, the analysis outlined above also predicts campaigns as they relate to the routine introductions, according to the specifications outlined in table below.

For Men A, the WHO recommends an initial introductory campaign targeting 1 to 29 year-olds and a mini catch-up campaign targeting all the missed cohorts between the initial catch-up and the introduction of the vaccine into routine. Thus, in countries where introductory campaigns had been conducted by 2018, mini catch-up campaigns were forecasted at the time of routine introduction, and the target populations were calculated as the number of cohorts missed between the initial introductory campaign and the routine introduction date. Where introductory campaigns had not been conducted by 2018, we assumed these would be conducted in 2019.

Measles and measles-rubella (M/MR) follow-up campaigns were forecasted on the basis of WHO guidance on the frequency of these types of campaigns, that is, every 2 years in countries where MCV1 coverage is less than 60%, every 3 years in countries where MCV1 coverage is between 60% and 79% , and every 4 years in countries where MCV1 coverage is over 80%.

National mass preventive campaigns for yellow fever were included in the forecasts for relevant countries according to proposed sequencing in the WHO EYE Strategy Eye (*Weekly Epidemiol Record, 2017*).

Appendix 2

Model review process and model descriptions

2.1 Model review process

All VIMC models were reviewed against pre-defined model standards in early 2018. Three pre-defined minimum standards and seven desirable standards set out the criteria for models' inclusion in VIMC. The three essential criteria are (1) the models can produce required outputs: deaths, cases and DALYs for all countries and years; (2) the models used standardised demography data provided by the VIMC and (3) the models are well documented. The seven desirable criteria were: (1) rigorous fitting to epidemiological data; (2) appropriate model complexity for the data available; (3) suitable data used for model fitting; (4) out-of-sample validation; (5) ability to capture quantifiable uncertainty; (6) representation of indirect effects of vaccination (herd immunity) where epidemiologically relevant; (7) shared model source code. The 2018 reviews were led by the VIMC management group. These reviews have been repeated annually against the same standards, but with a move towards light-touch peer reviews.

2.2 Model descriptions

Hepatitis B – Centre for Disease Analysis Foundation

PRoGReSs is a deterministic, dynamic disease burden model of HBV infection that calculates the annual HBV prevalence, incidence, and mortality by stage of liver disease, serologic status (low-viral load [LVL], high-viral load [HVL], on-treatment), sex, and age. A detailed description of the model has been previously published (*Polaris Observatory Collaborators, 2018*). Since the last major publication specific to the model, the following progression rates have been revised: chronic hepatitis B (CHB) to hepatocellular carcinoma (HCC), LVL; CHB to HCC, HVL; compensated cirrhosis (CC) to HCC, LVL; CC to HCC, HVL; HCC to HBV-related death, subsequent years; decompensated cirrhosis (DCC) to HBV-related death; CHB to CC, LVL; CHB to CC, HVL. The remaining progression rates have been previously published (*Polaris Observatory Collaborators, 2018*). The HBV-related deaths were calculated by applying stage-, sex-, and age-specific mortality rates to the HBV-infected population. Updated prevalence estimates since the last publication were incorporated in the analysis (*United States Ministry of Health, 2018; Ministry of Health, 2018; Quaglio et al., 2008; Shrestha, 1990; Thompson et al., 2019; Tshering et al., 2020; UPHIA, 2017*).

Uncertainty in a wide range of model inputs, detailed below, was modeled to estimate the uncertainty in all model outputs. The parameters of the probability distributions were obtained from previously reported sources (*Polaris Observatory Collaborators, 2018*).

The share of HBeAg-negative cases among HVL cases, share of HBeAg-positive cases among HVL cases, and HBV transmission rates to infants born to mothers with HVL with and without peripartum antiviral treatment, having received (1) complete HBV vaccine series with timely dose without HBIG, (2) complete HBV vaccine series with timely birth dose with HBIG, (3) timely birth dose of HBV vaccine only, (4) complete HBV vaccine series without timely birth dose, and (5) no vaccination were assumed to be betaPERT-distributed.

Progression rates of (1) CHB to CC, LVL, (2) CHB to HCC, LVL, (3) CHB to CC, HVL, (4) CHB to HCC, HVL, (5) CC to HCC, LVL, (6) CC to HCC, HVL were parametrized using a random variable corresponding to a (1) baseline (50% likelihood), (2) low (25% likelihood), and (3) high (25% likelihood) progression. Progression rates of (1) CC to DCC, HVL, (2) development of fulminant HBV, (3) DCC to HBV-related death, LVL, (4) mortality from fulminant HBV, (5) HCC to HBV-related death, first year, and (6) HCC to HBV-related death, subsequent years were parametrized using betaPERT-distributed scalar multipliers.

Additionally, the treatment schedule was parametrized as a random variable corresponding to (1) baseline (50% likelihood), (2) intermediate (25% likelihood), and (3) optimistic (25% likelihood) treatment coverages.

Lastly, the incidence function was parametrized with a betaPERT-distributed scalar multiplier corresponding to baseline, low, and high prevalence estimates of HBsAg by country. A Monte Carlo simulation with 200 realizations was performed to calculate uncertainty intervals around all modeled outcomes. No correlations between doses of HBV vaccine were assumed.

Hepatitis B – Imperial College London

This population-level, deterministic, dynamic transmission model (*Nayagam et al., 2016; de Villiers et al., 2020*) contains both acute (Severe Acute and Non-severe Acute) and chronic (Immune Tolerant, Immune Reactive, Asymptomatic Carrier, Chronic Hepatitis B, Compensated Cirrhosis, Decompensated Cirrhosis and Liver Cancer) mutually exclusive disease states. The two acute states as well as the Immune Tolerant and the Immune Reactive states are assumed to contain HBsAg+ HBeAg+ individuals, which are assumed to be 15 times more infectious than the HBsAg+ HBeAg- individuals in the other states (*Mendy et al., 1999; Mendy et al., 2008; Keane et al., 2016*). The model also contains separate state variables for susceptible and recovered/vaccinated individuals as well as for individuals on tenofovir antiviral treatment. HBV-related deaths can occur from the Severe Acute, Compensated Cirrhosis, Decompensated Cirrhosis, Liver Cancer and treatment states. The rates of progression through disease stages are informed by literature reviews and assumed to be the same in all settings.

Infection is spread in the population by both vertical and horizontal transmission, the rates of which are informed through fitting. The risk of acute infection becoming chronic is highest in the younger age groups and controlled by an exponential function that ranges in value from 88.5% for vertical infections in infants to less than 5% risk for acute sufferers over 30 years of age (*Edmunds et al., 1993*). Background mortality and migration are applied equally to individuals in all states. Younger age groups are assumed to undergo seroconversion from being HBsAg+ HBeAg+ to HBsAg+ HBeAg- at a faster rate than older age groups. In contrast, older age groups are at greater risk of developing liver cancer than are younger age groups. Since new HBV cases predominantly occur among the younger age groups (infants and 1 to 5 year olds), population make-up and fertility rates heavily influence the rate of spread of the disease in the population.

The model takes into account the effects of the birth-dose (BD) and the infant vaccines. The BD vaccine is assumed to be 95% effective in protecting infants of mothers that are HBsAg+ HBeAg-, and 83% effective in protecting infants of mothers that are HBsAg+ HBeAg+. All infants are equally likely to be given the BD vaccine within 24 hr of birth. The infant vaccine is assumed to be 95% effective in conferring life-long protection to vaccinated individuals. Individuals are assumed to be either unvaccinated or have been given all infant vaccine doses necessary in their first six months of life to confer the full protection specified in the model. All six-month-olds are equally likely to be given the infant vaccine series.

The model is calibrated to country-level, age-specific HBsAg+ prevalence data and HBeAg+/HBsAg+ prevalence data in pregnant women, obtained from the Polaris Observatory and from other sources (*Ott et al., 2012a; Ott et al., 2012b*), as well as to HBV-related cirrhosis and liver cancer death rates, obtained from the Global Burden of Disease Results Tool website (*Institute for Health Metrics and Evaluation, 2019*). The calibrated model parameters include the risk of horizontal transmission to susceptible one to five year-olds and the risk of vertical transmission from HBsAg+ HBeAg- mothers to their infants. Calibration is performed by the Approximate Bayesian Computation Sequential Monte Carlo algorithm (*Toni et al., 2009*).

Other data sources include demographic data (female and male population sizes of one-year age groups, migration, female fertility rates of five-year age groups, sex ratio of infants, female and male life expectancy of five-year age groups, female and male mortality rates of five-year age groups) from the United Nations World Population Prospects (UNWPP) 2019 Revision and infant and BD vaccine coverage data from the WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) and Gavi, the Vaccine Alliance.

Uncertainty in model estimates are due to uncertainties in the prevalence data that are used in the model calibration, as well as uncertainties in historical coverage data, vaccine efficacies and the number of individuals on antiviral treatment. The model structure is regularly updated to reflect the latest understanding of the natural history of HBV.

Hepatitis B – Goldstein

The model was developed by Susan Goldstein, Fangjun Zhou, Stephen Hadler, Beth Bell, Eric Mast and Harold Margolis at the US Centers for Disease Control and Prevention (CDC) (*Goldstein et al.,*

2005). It is a static deterministic model that estimates the global burden of hepatitis B and the impact of hepatitis B immunization programs. The model examines the mortality outcomes due to hepatitis B virus (HBV) infection, including deaths of fulminant hepatitis, and deaths of liver cirrhosis and hepatocellular carcinoma as results of chronic hepatitis B.

The model assumes infections occur in three age periods with different probabilities of developing symptomatic infections and progressing to chronic hepatitis B, which are: perinatal period, early childhood period (under 5 years), and the period over 5 years of age.

The rate of perinatal infection was determined by the prevalence of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) among pregnant women. Infants born to HBsAg positive and HBeAg positive mothers had a 90% chance of perinatal infection, while infants born to HBsAg positive and HBeAg negative mothers had a 10% chance of perinatal infection. The rate of infection in early childhood was determined by the prevalence of antibody to hepatitis B core antigen (anti-HBc) at age five after excluding perinatal infections, and the rate of infections between age 5 and 30 was determined by anti-HBc prevalence at 5 and 30 years of age. The prevalence at 30 years of age was assumed to have reached its peak in lifetime. A literature review was conducted on the prevalence of the hepatitis B seromarkers worldwide, and countries were grouped into 15 strata with stratum-specific prevalence based on the reported prevalence in literature and the geographic proximity of the countries.

The model assumes 99% of the infants infected perinatally were asymptomatic during the acute infection phase, and 90% progressed to chronic hepatitis B, regardless of whether they were symptomatic or not. The model assumed 90% of children infected horizontally before the age of 5 had asymptomatic infection and 70% progressed to chronic hepatitis B. After the age of five, the chance of progressing to chronic hepatitis B was much lower: 70% of infections that occurred after the age of 5 were asymptomatic and only 6% progressed to chronic hepatitis B. Of the acute symptomatic infections, the risks of developing fulminant hepatitis B were 0.1% for perinatal infections, and 0.6% for horizontal infections. The case-fatality rate of fulminant hepatitis was 70% for all ages. Starting from 20 years of age, a small percentage of chronically infected persons (0.5% annually) seroconverted from HBsAg positive to negative, and were no longer at risk of complications related to chronic hepatitis B.

Liver cirrhosis and hepatocellular carcinoma account for the majority of hepatitis B deaths worldwide. The age-specific liver cirrhosis mortality rates were derived from mortality statistics from the United States and Taiwan (China). The age-specific hepatocellular carcinoma incidence was derived by fitting a polynomial function to data from populations with high HBV prevalence, including Alaska Natives, China, the Gambia and Taiwan (China). Given the low survival rates of hepatocellular carcinoma, the death rate of hepatocellular carcinoma was assumed to be the same as the incidence. The rates were adjusted by the prevalence of HBeAg in each country: populations who were HBeAg positive had six times higher the risk of developing hepatocellular carcinoma. The background all-cause mortality rates were from the life table published in the United Nations World Population Prospects.

The lives saved by hepatitis B vaccine were calculated as the difference between predicted deaths of hepatitis B in an unvaccinated cohort and a vaccinated cohort born in a certain year in one country. The vaccination coverages, namely the coverage of the timely birth dose (HepB birth dose within 24 hr of birth) and the coverage of the complete series of at least three doses of hepatitis B vaccine (HepB3) were from the WHO-UNICEF Estimates of National Immunization Coverage (WUENIC) of the past years, and the coverage projection provided by the VIMC secretariat. 95% of infants who received the timely birth dose were assumed to be protected from perinatal infection, and 95% of infants who received the complete series of hepatitis B vaccine (indicated by HepB3 coverage) were assumed to be protected from horizontal infection in their lifetime. The model does not include herd immunity, or the effect of partial vaccination series.

The key uncertainties of the model includes estimates on the prevalence of hepatitis B seromarkers from the pre-vaccination era that are based on limited number of studies in some countries, and the change in mortality of chronic hepatitis B in the long term due to improved access to antiviral treatment. The model used a sensitivity-to-parameters test, rather than a true uncertainty test. It was run with a spread of six parameters that are normally distributed around the original values, with a range of +/- 5%. Two vaccine efficacy parameters (for HepB3 and birth dose respectively) were originally set to 0.95 and then varied together (with the same value for both) between 0.9 and 1.0, normally distributed. These were not country-specific. Four prevalence parameters (HBsAg

prevalence, HBeAg prevalence, anti-HBc prevalence at age 5, anti-HBc prevalence at age 30) all had country group-specific central values, and were varied in unison by +/- 5% around their central values. We assumed the chance of HBV exposure among children who are vaccinated and those who are unvaccinated, and the probability of receiving HepB3 is independent of the birth dose.

Hib, PCV and Rota – Johns Hopkins University

The Lives Saved Tool (LiST) is a deterministic linear mathematical model for estimating the health impact of changes in health intervention coverage in low- and middle-income countries (LMICs) described in *Walker et al., 2013a*. LiST is a publicly available module within the Spectrum suite, a policy modelling system comprised of several software components. LiST contains over 80 health interventions, including vaccines, and has been used for over a decade to assist in public health decision-making and program evaluation. Evidence-based interventions included in the model have been demonstrated to reduce stillbirths, neonatal deaths, deaths among children aged 1–59 months, maternal mortality or risk factors.

The model describes fixed relationships between inputs (intervention coverage) and outputs (cause-specific mortality or risk factor prevalence) specified in terms of the effectiveness of the intervention for reducing the probability of that outcome under the assumptions that (1) country-specific mortality rates and cause of death structure will not change dynamically, (2) changes in mortality occur in response to changes in intervention coverage, and (3) distal factors, such as improvements in wealth, affect mortality by increasing intervention coverage or reducing risk factors.

The model is built on an underlying demographic projection derived from the United Nations Population Division (UNPD) and age structure for children (0–1, 1–5, 6–11, 12–23, 24–59 months) which serves as a theoretical cohort. Each model uses country-specific inputs of demographic growth (*World Population Prospects, 2019*), under-five mortality rates (*World Population Prospects, 2019*), and cause of death structure (*World Health Organisation, 2021; Liu et al., 2016*). Together, these values are used to calculate cause-specific mortality and the potential deaths averted by increasing coverage of interventions. LiST attributes lives saved to changes in coverage of specific interventions, attributing impact first to preventative and then curative interventions, ordered sequentially from periconception, through pregnancy, delivery, followed by the specific age group. By using cause-specific efficacy and applying each intervention to the residual deaths remaining after the previous intervention, LiST ensures that double counting is avoided, and the potential impact of multiple interventions is not erroneously inflated.

Estimates of intervention efficacy are derived from existing reviews, many of which were published in five journal supplements (*Fox et al., 2011; Walker et al., 2013a; Clermont and Walker, 2017; Walker and Friberg, 2017*) National and subnational level impact estimates modelled by LiST have been validated against measured mortality reduction in various LMIC settings and for various packages of interventions (*Amouzou et al., 2010; Friberg et al., 2010; Hazel et al., 2010; Larsen et al., 2011; Ricca et al., 2011; Victora et al., 2013*).

LiST is used to generate estimates of cases and deaths averted for 0, 1, 2, 3 and 4 years of age due to coverage scale-up of pneumococcal conjugate vaccines (PCV), Hemophilus influenza type b (Hib) vaccine, and rotavirus vaccines. Deaths and cases are calculated separately in LiST. Incidence of diseases (number of cases per child per year) is used instead of cause-specific mortality as a baseline input to calculate cases. Cases and deaths averted by vaccination were calculated by applying estimates of scale-up in coverage in each of the countries. The model accounts for impact of other interventions in each country that could lower the risk of pneumonia, meningitis, or diarrhoea incidence (e.g. clean water and sanitation), or reduce mortality from pneumonia, meningitis, or diarrhoea (e.g. antibiotic treatment) using country-specific coverage of interventions drawing primarily on data from the Demographic and Health Survey (dhsprogram.com) and/or Multiple Indicator Cluster Survey (mics.unicef.org). The specific associations between interventions, risk factors, and mortality within LiST can be accessed via an interactive tool ([LiSTVisualizer.org](https://listvisualizer.org)). Deaths and cases averted were calculated holding coverage of all other interventions constant.

The LiST uncertainty bounds are produced using a Monte Carlo approach. For each of the key assumptions in the model we have developed distributions around those values. These include efficacy of interventions, mortality rates, causes of death, relative risks of risk factor for mortality and incidence for severe pneumonia, meningitis and diarrhoea. In general, beta distributions were used

for effectiveness of interventions, correlated normal distribution for mortality rates, Dirichlet distribution for death causes, and log-normal distribution for relative risks. Further information regarding rationale for sampling distributions can be provided upon request.

For the estimates presented here we were asked to only vary efficacy of Hib, PCV, and Rotavirus vaccines, and causes of death of pneumonia, meningitis, and diarrhoea in our uncertainty analysis. For each scenario we were provided 200 sets of varied vaccine efficacies and causes of death from the VIMC Scientific and technical team, based on the 95% confidence intervals of the vaccine efficacies and causes of death. The distribution of model outputs from the 200 runs were then used to produce the uncertainty bounds, which here were set to capture 95% of the distribution of results.

PCV-specific assumptions

LiST generates estimates of pneumococcal pneumonia and meningitis cases and deaths averted by the coverage scale-up of PCV. The potential envelope of deaths and cases averted by PCV was derived by applying a proxy for the proportion of pneumonia (product of proportion of *S. pneumoniae* among chest x-ray positive episodes of pneumonia, and proportion of *S. pneumoniae* due to PCV13 serotypes by region) (*Rudan et al., 2013; Johnson et al., 2010*) and meningitis (product of proportion of *S. pneumoniae* among severe bacterial meningitis cases, and proportion of *S. pneumoniae* due to PCV13 serotypes by region) (*Johnson et al., 2010; Davis et al., 2013*) deaths due to *S. pneumoniae* in the pre-vaccine era to the country-specific estimates of pneumonia and meningitis mortality. Country-specific incidence of severe pneumonia pre-vaccine introduction was derived from an analysis by Rudan and colleagues (*Rudan et al., 2013*). The country-specific incidence of bacterial meningitis was calculated using the proportions of bacterial meningitis deaths due to *S. pneumoniae* and Hib from *Davis et al., 2013*, the *S. pneumoniae* case-fatality rates from *O'Brien et al., 2009*, and Hib case-fatality rates from *Watt et al., 2009*, divided by the total population 1–59 months of age. The proportion of pneumonia and meningitis cases and deaths averted was calculated by applying the 3-dose coverage of PCV scaled by the 80% efficacy of PCV in preventing PCV13 serotypes of invasive pneumococcal disease (*Lucero et al., 2004*), and 84% efficacy of PCV in preventing severe bacterial meningitis (*Davis et al., 2013*), to the fraction of deaths due to *S. pneumoniae*. The model includes only the direct effect of complete three-dose vaccination coverage.

Hib vaccine-specific assumptions

LiST generates estimates of Hib pneumonia and meningitis cases and deaths averted by the coverage scale-up of Hib vaccine. The potential envelope of deaths and cases averted by Hib vaccine was derived by applying proxy estimates of proportion of pneumonia (proportion of Hib among chest x-ray positive episodes of pneumonia) and meningitis (proportion of Hib among severe bacterial meningitis cases) deaths due to Hib in the pre-vaccine era to the country-specific estimates of pneumonia and meningitis mortality (*Davis et al., 2013; Rudan et al., 2013*). The same country-specific estimates of the incidence of severe pneumonia and meningitis for the PCV impact analysis were used. The proportion of pneumonia and meningitis cases and deaths averted was calculated by applying the three-dose coverage of Hib scaled the 93% efficacy of Hib in preventing invasive pneumococcal disease (*Griffiths et al., 2012*), and the 94% efficacy of Hib in preventing severe bacterial meningitis (*Davis et al., 2013*), to the fraction of deaths due to Hib. The model includes only the direct effect of complete three-dose vaccination coverage.

Rotavirus vaccine-specific assumptions

LiST generates estimates of rotavirus diarrhoea cases and deaths averted by the coverage scale-up of rotavirus vaccine. The potential envelope of deaths averted by rotavirus vaccine was derived by applying region-specific estimates of the proportion of rotavirus among severe diarrhoea cases and deaths in the pre-vaccine era to the country-specific estimates of diarrhoea mortality (*Walker et al., 2013a*). Region-specific estimates of the incidence of severe diarrhoea were derived from the same source. The proportion of diarrhoea cases and deaths averted was calculated by applying the complete dose coverage of rotavirus vaccine scaled by the region-specific efficacy of rotavirus vaccine in

reducing severe rotavirus gastroenteritis (*Lamberti et al., 2016*) to the fraction of deaths due to rotavirus. The model includes only the direct effect of complete rotavirus vaccination coverage.

Hib, PCV and Rotavirus – London School of Hygiene and Tropical Medicine (LSHTM)

UNIVAC (universal vaccine decision support model) is a static cohort model with a finely disaggregated age structure (weeks of age <5 years, single years of age 5–99 years). A detailed description of the model and the methods for estimating vaccine impact are available in *Clark et al., 2017*. UNIVAC is available as an R script for desk-based multi-country analyses. It is also available as an Excel-based decision-support model, where it has been widely used by national Ministries of Health in low and middle income countries (LMICs) to estimate the potential impact, cost-effectiveness and benefit-risk of alternative vaccine policy options. In the context of the vaccine impact modelling consortium (VIMC), the R version of UNIVAC was used to generate transparent desk-based estimates of the impact (% reduction in cases, clinic visits, hospitalisations, lifelong sequelae, deaths and DALYs) of three vaccines (haemophilus influenza type b - Hib, pneumococcal and rotavirus) over the period 2000–2030 in 112 LMICs.

Interpolated 1 year time and age estimates (*World Population Prospects, 2019*) were used to calculate the number of life-years between birth and age 5.0 years for each of the 31 birth cohorts (2000–2030) in each of the 112 countries. Life-years <5 yrs were multiplied by rates of disease cases and deaths (per 100,000 aged <5 yrs) to estimate numbers of cases and deaths expected to occur without vaccination between birth and age 5.0 years. The rates of disease cases and deaths due to Hib and Pneumococcal were based on estimates generated by *Wahl et al., 2018* for the year 2015. For Hib, these included estimates for non-severe Hib pneumonia, severe Hib pneumonia, Hib meningitis and Hib non-pneumonia/non-meningitis (NPNM) in children aged <5 years. For Pneumococcal, they included estimates for non-severe Pneumococcal pneumonia, severe Pneumococcal pneumonia, Pneumococcal meningitis and severe Pneumococcal non-pneumonia/non-meningitis (NPNM) in children aged <5 years. In addition, the model includes cases of Pneumococcal acute otitis media (AOM) based on estimates by the (*CDC, 2017* and *Monasta et al., 2012*). For both Hib and Pneumococcal, the risk of meningitis sequelae was based on a systematic review and meta-analysis by *Edmond et al., 2010*. For rotavirus, country-specific estimates of rotavirus deaths <5 years were based on the mean of three independent sources of international burden estimates, recently compared in *Clark et al., 2017*. Estimates of rotavirus disease cases (non-severe and severe) were based on systematic reviews and meta-analyses by *Bilcke et al., 2009* and *Walker et al., 2013b*. Granular rotavirus disease age distributions (by week of age <5 years) were based on a recent systematic review and statistical analyses by *Hasso-Agopsowicz et al., 2019*.

Historical time-series estimates of pneumonia and diarrhoea deaths have declined in the absence of vaccination (*Liu et al., 2016*). To avoid over-stating the impact of vaccination, we assume the disease-specific mortality rate will decrease without vaccination at the same rate as the overall under-five mortality rate (*World Population Prospects, 2019*). For consistency, we make the same assumption for Hib/Pneumococcal meningitis and NPNM. We do not assume any decline in the incidence of disease cases, so case fatality ratios (CFRs) decline in each successive year.

Life expectancy estimates by age and year (*World Population Prospects, 2019*) were used to calculate YLLs (years of life lost due to premature mortality) from the age/year of disease death. YLDs (years of life with disease) were calculated by multiplying disability weights by the average duration of illness. DALYs (YLLs + YLDs) were attributed to the year of disease onset.

For all three vaccines, estimates of vaccination impact were restricted to children aged <5 years. The impact was calculated by multiplying the expected number of disease events (cases, clinic visits, hospitalisations, deaths) in each week of age <5 years, by the expected coverage of vaccination in each week of age (adjusted for realistic vaccine delays/timeliness) and the expected efficacy of vaccination in each week of age (adjusted for the waning vaccine protection). The model accounted for partial vaccination by calculating the incremental impact of each dose of vaccination in each week of age. Rotavirus was modelled as a two-dose vaccine co-administered with DTP1 and DTP2 without age restrictions. Hib and Pneumococcal vaccines were modelled as a three-dose vaccine co-administered with DTP1, 2 and 3. For each vaccine, coverage projections by country and year were provided by Gavi, the Vaccine Alliance, over the period 2000–2030 (201910gavi - version 5). Estimates of the timeliness of vaccination (coverage by week of age) were based on the timeliness of DTP1, 2 and 3

reported in USAID Demographic and Health Surveys (DHS) (<https://dhsprogram.com>) and Multiple Cluster Indicator Surveys (MICS) (mics.unicef.org). Methods for estimating vaccine timeliness have been described previously in *Clark and Sanderson, 2009*. For Hib vaccination, dose-specific efficacy was based on a global systematic review and meta-analysis of RCTs by *Griffiths et al., 2012*. For rotavirus, vaccine efficacy by dose and duration of follow-up (year 1 and year 2) was based on a Bayesian meta-regression of RCTs by *Clark et al., 2019b*. For Pneumococcal, efficacy against all serotypes of pneumococcal disease (vaccine type and non-vaccine type) was based on a global meta-analysis by *Lucero et al., 2004*.

UNIVAC is not a transmission dynamic model, and thus excludes indirect effects (both positive and negative). This is likely to lead to substantial under-estimates of impact in some countries, particularly for Hib vaccine. More detailed validation against real-world post-introduction evidence of impact is needed. However, the available data in many of the countries included in this desk-based analysis are insufficient to allow validation of modelled estimates (against real-world estimates of post-introduction vaccine impact) and/or parameterisation of a country-specific transmission dynamic model. As such, there is a good deal of uncertainty in the predicted estimates for many countries.

Human Papilloma Virus (HPV) – Harvard University

The Center for Health Decision Science companion model is a flexible tool that has been developed to reflect the main features of HPV vaccines, and to project the potential (health and economic) impacts of HPV vaccination at the population level in settings where data are very limited (*Goldie et al., 2008*). The model is constructed as a static cohort simulation model based on a structure similar to a simple decision tree and is programmed using R software (*R Development Core Team, 2020*). The model tracks a cohort of girls at a target age (e.g., 9 years) through their lifetimes, comparing health and cost outcomes with and without HPV vaccination programs. Population-level analyses are conducted by running multiple cohorts.

Unlike more complex empirically-calibrated micro-simulation models (*Goldie et al., 2007; Campos et al., 2012; Kim et al., 2007*), the companion model does not fully simulate the natural history of HPV infection and cervical carcinogenesis. Instead, based on simplifying assumptions (i.e., duration and stage distribution of, and mortality from, cervical cancer), which rely on insights from analyses performed with the micro-simulation model, and using the best available data on setting-specific age-specific incidence of cervical cancer and HPV-16/18 type distribution and assumed vaccine efficacy and coverage, the model estimates reductions in cervical cancer risk at different ages. By applying this reduction to country-specific, age-structured population projections incorporating background mortality (*World Population Prospects, 2019*), the model calculates averted cervical cancer cases and deaths, and transforms them into aggregated population health outcomes, years of life saved and disability-adjusted life years (DALYs) averted. DALYs are calculated using the approach adopted by the Global Burden of Disease (GBD) study (*Murray and Lopez, 1996*), using stage-specific disability weights. The model also incorporates five-year stage-specific survival probabilities for untreated and treated cervical cancers (by region) and treatment access proportions (by country). These values are combined into weighted averages to provide country-specific 5 year survival parameters, matched to GLOBOCAN 2020 age-specific mortality rates.

The companion model captures the burden of HPV infection by estimating the number of cervical cancer cases caused by HPV infection based on epidemiological data obtained from various sources (*Goldie et al., 2008*). The model assumes that age-specific cervical cancer incidence, average age of sexual initiation, and the level of other risk factors remain constant over the time horizon of the model. It assumes that girls are fully immunized and that girls effectively immunized against vaccine-targeted HPV types can develop cervical cancer associated with non-vaccine HPV types; also, no cross-protection against non-vaccine types is assumed. Country-specific assumptions are used for the proportion of cancer that is attributed to the vaccine-covered types (HPV-16/18 in this analysis) (*Guan et al., 2012*). Vaccine-induced immunity is assumed to be lifelong. Currently, there are no interactions or correlations between doses as the model assumes fully vaccinated individuals (whether with 1, 2, or three doses). All assumptions are varied in sensitivity analyses.

Four key parameters were identified for probabilistic sensitivity analysis (PSA): HPV-16/18 type distribution, age-specific cervical cancer incidence, stage distribution of cervical cancer, and stage-specific 5 year survival and treatment access (as a combined parameter). Each parameter was

assigned a β -PERT distribution for probabilistic sampling, with the bounds determined by: (1) empirical data for type distribution; (2) confidence intervals estimated from cervical cancer cases in GLOBOCAN 2020 (Ferlay et al., 2020) (3) assumed +/- 10% bounds from the base case for stage distribution; and (4) assumed +/- 10% bounds from the base case for stage-specific probability of death following 5 year survival, if this estimate is contained between zero and one. For stage distribution, for a single parameter set, the value for a single stage (specifically, stage 2, given country-level differences in survival and disability weights) is drawn individually and the remaining stages are normalized to adjusted values in order for the four stages to add up to one. As the stage-specific probability of death cannot exceed 100%, the minimum bound is set to the difference between the base-case value and one, where relevant. Two hundred independent parameter sets were drawn for each country.

Human Papilloma Virus (HPV) – London School of Hygiene and Tropical Medicine (LSHTM)

The Papillomavirus Rapid Interface for Modelling and Economics (PRIME) is a static, proportional impact model that can estimate the impact of HPV vaccination on cervical cancer cases, deaths, and disability-adjusted life years as well as the cost-effectiveness of vaccination programmes at the global, regional, and national levels (Abbas et al., 2020a; Jit et al., 2014). The PRIME model was developed by LSHTM in collaboration with the World Health Organization (WHO), Laval University and Johns Hopkins University. It is designed to estimate the impact and cost-effectiveness of HPV vaccination in low- and middle-income countries (LMICs). In addition to its application in the Vaccine Impact Modelling Consortium (VIMC), it has been used to support vaccine recommendations by WHO, as well as individual countries. It has been validated against published studies using HPV vaccine economic models set in LMICs (Jit et al., 2014). It was also endorsed by the WHO's expert advisory committee, the Immunization and Vaccines Implementation Research Advisory Committee (IVIR-AC) to provide a conservative estimate of the cost effectiveness of vaccinating girls prior to sexual debut.

The Excel-based version of the model and documentation are publicly accessible at <http://prime-tool.org/> for use by country programme managers and planners to facilitate country-specific decision-making in LMICs. The R package of the model (prime) has additional functionality such as multiple cohorts and probabilistic sensitivity analysis and is available at <https://github.com/lshmt-vimc/prime> (copy archived at [swh:1:rev:0da13630968de0863f38294a1c234c5947baf97e](https://www.swh.io/rev/0da13630968de0863f38294a1c234c5947baf97e)); Abbas and Hadley, 2021. It can be used for research, global analyses and to generate the vaccine impact estimates used by VIMC. Data inputs include country and age-specific cervical cancer incidence, prevalence, and mortality among females. The model estimates vaccination impact in terms of reduction in age-dependent incidence of cervical cancer and mortality in direct proportion to vaccine efficacy against HPV 16/18, vaccine coverage, and HPV type distribution. It assumes that vaccinating girls prior to infection with HPV types 16 and 18 fully protects them from developing cervical cancer caused by HPV 16 and 18, in accordance with vaccine trials (Schiller et al., 2012).

The model assumes a two-dose schedule with perfect timeliness at the target ages given in the coverage estimates. Herd effects are not considered meaning that the vaccine impact estimates produced are conservative, although the model can be used in conjunction with transmission dynamic models to project indirect effects. The impact of vaccinating multiple age cohorts is estimated by using the most conservative assumption that 9–14 year old girls who have sexually debuted are not protected, although these assumptions do not change the overall impact estimates significantly (Jit and Brisson, 2018).

Measles – London School of Hygiene and Tropical Medicine (LSHTM)

DynaMICE (DYNAmic Measles Immunisation Calculation Engine) is a measles transmission and vaccination model developed by LSHTM with input from Harvard University and the University of Montreal (Verguet et al., 2015). It has been previously used to inform policies on measles-containing vaccines by WHO; this work has been reviewed by the WHO's Immunization and Vaccines Implementation Research Advisory Committee (IVIR-AC) as well as WHO's Strategic Advisory Group of Experts on Immunization (SAGE)'s measles and rubella working group.

It is an age-structured compartmental transmission dynamic model with compartments for maternal immune, susceptible, infected, recovered, and vaccinated subpopulations. A proportion of infected people will die depending on their age and country characteristics (*Portnoy et al., 2019*). The population is also stratified by age with weekly age classes up to age 3 years, and annual age classes thereafter up to 100 years. The force of infection is calculated by combining an age-dependent social contact matrix from the POLYMOD study (*Mossong et al., 2008*), demographic distribution for each country, and an estimated probability of transmission per contact. The probability of transmission per contact is then estimated from the basic reproduction number of measles using the principal eigenvalue method. Vaccination is incorporated as a pulse function and can be delivered to any age or range of ages and in either routine or through supplementary immunisation activities (SIAs) or campaigns. The ability of SIAs to reach children who miss routine vaccination is determined using analyses of Demographic and Health Survey (DHS) data (*Portnoy et al., 2018*). Vaccine efficacy is dependent on age and the number of doses received (*Hughes et al., 2020*). The model has been previously described in detail (*Verguet et al., 2015*).

Measles – Pennsylvania State University (PSU)

The PSU measles model is a dynamic, age-structured, discrete time-step, annual SIR model. Unlike conventional SIR models, which describe dynamics at the scale of an infectious generation (*Finkenstadt and Grenfell, 2000*) or finer (*Anderson and May, 1991*), it models the aggregate number of cases over one-year time steps. While this is coarse relative to the time scale of measles transmission, it matches the annual reporting of measles cases available for all countries, since approximately 1980, for all countries through the WHO Joint Reporting Form (JRF). To account for the fine-scale dynamics that are being summed over a full year, the model describes the number of infections ($I_{i,t}$) in country i and year t , and age class a as an increasing function of the fraction, $p_{i,t}$, of the population susceptible in age class a at the start of year t , $S_{a,i,t}$:

$$E[I_{a,i,t}] = p_{i,t} * S_{a,i,t},$$

where $E[\cdot]$ indicates the expectation and $p_{i,t}$ is a country and year specific annualized attack rate modeled as:

$$p_{i,t} = \text{invlogit}(-\beta_{0,i} + \beta_{1,i} * \frac{\sum_a S_{i,t}}{N_{i,t}} + e_t),$$

where $\text{invlogit}()$ indicates the inverse logit function, $N_{i,t}$ is the total population size in country i and year t over all age classes, and e_t is a Gaussian random variable with mean 0 and variance σ^2 . The parameters $\beta_{0,i}$, $\beta_{1,i}$, and σ^2 are fit to each country independently using a state-space model fitted to observed annual cases reported through the JRF from 1980 to 2016 as described by *Eilertson et al., 2019*. Inferred cases are not constrained by external mortality estimates. Historical population and vaccination coverage values are provided by WHO as described by *Simons et al., 2012*.

The number of susceptible individuals in each single-year age class a ($a=2, \dots, 100$) is equal to the number not infected in the previous year, nor immunized through supplemental immunization activities (SIAs). The number susceptible is further deprecated by the crude death rate. The efficacy of doses administered through SIAs is assumed to be 99%; SIA doses are assumed to be independent of prior routine immunization. The number of susceptible individuals in age class $a=one$ is assumed to be 50% of the annual live birth cohort; this assumes that all children have protective maternal immunity until 6 months of age. Age class $a=two$ and $a=m$ is assumed to receive a first and second dose (respectively) of routine measles vaccination before the start of the time step. We assume that the second routine dose is delivered only to those who have received the first routine dose. Efficacy is assumed to be 85% and 93% for the first dose in countries delivering at 9 m and 12 m of age, respectively, and assumed to be 99% for the second dose.

Deaths are calculated by applying an age- and country-specific case fatality ratio (CFR) to each country. CFRs for cases below 59 months of age for all countries were taken from *Portnoy et al., 2019*; CFR for cases above 59 months of age are assumed to be 50% lower than those applying to under-5s.

Forward simulations of this model assume random variation in the annual attack rate according to the parameter σ^2 . Future vaccination coverage values, for routine and SIAs, are assumed known and future birth and death rates are assumed known.

MenA - University of Cambridge

The University of Cambridge MenA model is a compartmental transmission dynamic model of *Neisseria meningitidis* group A (NmA) carriage and disease to investigate the impact of immunisation with a group A meningococcal conjugate vaccine, known as MenAfriVac, as published by [Karachaliou et al., 2015](#). The model is age-structured (1 year age groups up to age 100) with continuous ageing between groups. Model parameters were based on the available literature and African data wherever possible, with the model calibrated on an ad-hoc basis as described below.

The population is divided into four states, which represent their status with respect to the meningitis infection. Individuals may be susceptible, carriers, ill or recovered, and in each of these states be vaccinated or unvaccinated, with vaccinated individuals having lower risks of infection (carriage acquisition) and disease (rate of invasion). We assume that both carriers and ill individuals are infectious and can transmit the bacteria to susceptible individuals. The model captures the key features of meningococcal epidemiology, including seasonality, which is implemented by forcing the transmission rate, the extent of which varies stochastically every year.

Since only a small proportion of infected individuals develop the invasive disease, disease-induced deaths are not included in the model. From each compartment, there is a natural death rate from all causes. Carriage prevalence and disease incidence vary with age, and the model parameterised these distributions using a dataset from [Campagne et al., 1999](#); the case:carrier ratio consequently varies with age. The duration of 'natural immunity' is an important driver of disease dynamics in the absence of vaccination but good data on this parameter is lacking; instead, prior estimates are used ([Irving et al., 2012](#)).

The model assumes that mass vaccination campaigns occur as discrete events whereas routine immunisation takes place continuously. We allowed the duration of protection to vary uniformly between 5 years and 20 years for the 0–4 year-olds and 10–20 years for over 5-year-olds. For the 200 runs, we selected pairs of values for these two parameters so that duration of protection for the older age group is not shorter than the duration of protection for 0–4 year-olds ([Yaro et al., 2019](#); [White et al., 2019](#)). Vaccine efficacy against carriage and disease is 90%.

Disease surveillance is not comprehensive across the meningitis belt, so the disease burden is uncertain in several countries. Therefore, the model classifies the countries into three categories, based on the incidence levels using historical data. This classification defines the transmission dynamic parameters. The model generates estimates of case incidence, to which a 10% case-fatality ratio is applied to estimate mortality ([Lingani et al., 2015](#)). To estimate DALYs it is assumed that 7.2% of survivors have major disabling sequelae with a disability weight of 0.26 ([Edmond et al., 2010](#)).

Countries were stratified into high and medium risk, and different infection risks applied based on this stratification. As there was insufficient information to define infection risk on a country-by-country basis, the approach/stratification was agreed upon with experts in the WHO meningitis team. For countries only partly within the meningitis belt, only the (subnational) area at risk was included.

To produce estimates on the impact of vaccination, 200 simulation runs were generated by stochastically varying the baseline transmission rate to reflect between-year climactic or another external variability. Although each individual simulation reflects the reality of irregular and periodic epidemics, as visually compared to time series from Chad and Burkina Faso and analysis of inter-epidemic periods, the resulting averaged estimates give a stable expected burden of disease over time. Uncertainty in other model parameters is currently not quantified.

MenA – Kaiser Permanente Washington

This model is a stochastic, age-structured, compartmental model of the transmission of serogroup A *Neisseria meningitidis* (MenA) ([Jackson et al., 2018](#)). Model compartments track hosts' status with respect to MenA exposure (as Susceptible, Colonized, and Invasive Disease) and adaptive immunity

to infection/disease (as High, Low, or No immunity). Exposure to MenA through colonization leads to the 'low immunity' state, in which individuals are still susceptible to colonization but have a reduced risk of developing invasive disease if colonized. MenA colonization among individuals with low immunity leads to a 'high immunity' state, which is highly protective against both colonization and disease.

Model parameters such as the age-specific force of infection, rates of immune waning, and immune protection against colonization/disease were estimated by approximate (*Marjoram et al., 2003*). Prior distributions for model parameters were taken from the existing literature (*Marjoram et al., 2003*). Simulated prevalence of colonization by age was compared to longitudinal studies of the prevalence of MenA colonization in Burkina Faso (*Traore et al., 2009*) and the expected age distribution of MenA cases (*Campagne et al., 1999*).

In the simulations, mortality burden estimates are obtained in a 'bottom-up' manner, in that case fatality ratios (CFRs) (*Campagne et al., 1999; Boisier et al., 2007; Belcher et al., 1977; Traore et al., 2009; Varaine et al., 1997; World Health Organisation, 2001; World Health Organization, Geneva, 2005*) are applied to simulated case counts.

For estimating the impact of serogroup A polysaccharide conjugate vaccine (MenAfriVac), vaccination is assumed to be superior to natural immunity, based on estimates of vaccine effectiveness and serum bactericidal antibody (SBA) concentrations (*Goldschneider et al., 1969*), an assumption which is shown to better capture the dynamics of NmA in Burkina Faso following mass vaccination campaigns with MenAfriVac, compared to assuming vaccination is equivalent to natural infection (*Jackson et al., 2018*).

Countries were stratified based on risk (hyper-endemic vs. not), and different forces of infection used based on risk group. For countries only partly within the meningitis belt, the model was restricted to the area at risk.

Variability in infection rates is represented by randomly sampling values for the force of infection parameters within $\hat{\pm}20\%$ of their estimated values; new values are sampled annually to reflect annual variation in climate or other external factors. To estimate incidence of MenA disease and death in each modelled vaccination scenario, we run 200 iterations of the simulation. Each simulation randomly samples parameter values from their posterior distributions; mean estimates are taken from the mean values by year and age across the 200 iterations. Key sources of uncertainty not presently included are the expected duration of vaccine-induced protection and the force of infection in countries for which MenA surveillance data are lacking.

Japanese Encephalitis – National University of Singapore

This deterministic dynamic model uses a basic catalytic model for the force of infection (FOI), in which individuals become infected and are then immune. Vaccination is modelled as a removal of susceptibles from the susceptible class. As humans are dead-end hosts for Japanese encephalitis (JE), infection comes from animal reservoirs via mosquitoes. This simple model successfully captures the natural history and transmission dynamics of JE.

A systematic review of all published studies and publicly available JE surveillance data was undertaken to collate a dataset of age-stratified case data. The FOI model is fit to age-stratified national surveillance data that were publicly available and data identified via this systematic review of age-stratified JE case data (*Quan et al., 2020*). Data from a total of 10 countries and 17 studies was used, which gave estimates of a wide range of force of infection parameters, as expected for the wide geographical locations. The model is fit in a Bayesian framework using RStan. This gave FOI estimates for all locations in which data is available. For areas in which data was not available we extrapolated from areas in which it was, using the WHO groupings of transmission intensity (*Campbell et al., 2011*). In order to generate uncertainty in the case burden estimates, all model parameters were sampled from the posterior distributions of the parameter estimates. The symptomatic rate was sampled from uniform distribution (0.002, 0.004) SAGE Working Group on Japanese encephalitis (*World Health Organization, 2014*), the proportion of these symptomatic cases that died was from uniform distribution (0.2, 0.3) and the force of infection from the relevant posterior estimate from the age-stratified case data described above. The vaccine was assumed to be 100% effective, and protection lifelong.

Disease burden was generated from the 'bottom up': i.e. from infection rates applying parameters governing the proportion of infections that are symptomatic and the proportion that die (case fatality ratio). The key uncertainties which affect disease burden estimates are the method of extrapolation of FOI from areas in which there is data to areas in which there is not. Spatial modelling work is on-going to improve this extrapolation and to make estimates on smaller spatial scales. The case fatality ratio is also uncertain, and further work undertaking a systematic review of this is ongoing.

Japanese Encephalitis - University of Notre Dame

We developed a static, stochastic model of Japanese encephalitis virus (JEV) transmission with a constant force of infection (FOI) to estimate the burden of JE and the potential impact of vaccination in JE-endemic countries. JEV is a mosquito-transmitted, zoonotic pathogen that requires an animal host for ongoing transmission, given humans are believed to be a dead-end host (*van den Hurk et al., 2009*). Therefore, JE incidence is limited to geographic regions where there are suitable hosts and vectors to sustain both ongoing transmission in animal hosts and spill-over to humans. To estimate the number of JEV infections, the model first estimates the number of people at risk of infection, and then estimates the transmission intensity in each country. JE burden (including cases, deaths, and DALYs) was then estimated from the number of JEV infections. Key sources of uncertainty in our model are the spatial variation in JEV transmission intensity and the proportion of JEV infections that result in either a severe case or death.

To identify the areas suitable for sustained JEV transmission, and the size of the population living in at-risk areas, a spatial analysis of the risk factors associated with JEV was conducted. Potential JEV-endemic areas were identified using large-scale spatiotemporal datasets related to suitable climate conditions for the vector species, suitable habitat conditions for the vector, and the presence of potential zoonotic hosts. Transmission was assumed to occur only in areas occupied by the primary vector, *Culex tritaeniorhynchus* (*Longbottom et al., 2017*), or where the annual minimum temperature exceeded 20°C and annual precipitation exceeded 150 cm. Suitable habitat conditions included areas with rice cultivation or nearby wetlands (*Gumma, 2011*). Within these suitable areas, people were considered at risk of infection if the density of domestic pigs or fowl exceeded two per km (with uncertainty represented by varying the animal threshold from 0 to 10 per km) (*Robinson et al., 2014*). Risk maps were validated using seroprevalence and surveillance data.

Next, the FOI in each country was estimated from age-specific incidence data using a catalytic model. FOI represents the per-capita rate at which susceptible individuals are infected. Age-specific incidence data was obtained from a literature search, restricted to studies conducted in areas with no history of vaccination (or prior to documented vaccination) to simplify the estimation process. For several countries where no age-specific incidence data was available, FOI estimates were drawn from the posterior estimate of a neighbouring country. FOI estimates for each study were estimated using a maximum likelihood approach, using the observed numbers of JE cases per age class in each year. Study-specific FOI values were estimated using a Bayesian framework via a Markov chain Monte Carlo (MCMC) approach implemented in the software package STAN. The probability of asymptomatic infection and the case fatality ratio for symptomatic infections were assumed to be independent of the FOI.

The annual number of JEV infections for a given study area were then calculated from the FOI estimate and the size of the at-risk population. In the absence of vaccination, the number of infections in age class was calculated by multiplying the age-specific probability of infection by the number of at-risk individuals in the age class. Vaccination reduced the number of at-risk individuals in each targeted age class based on provided coverage estimates. We assume that all vaccinated individuals receive a full vaccine regimen and that routine and campaign-based vaccinations are independent. The number of JE cases and deaths were then estimated from the number of JEV infections based on the proportion of infections that are symptomatic or fatal. The number of JE cases was modelled assuming an asymptomatic to symptomatic (A:S) ratio for JEV infections of 295:1 (95% CI: 83:1 to 717:1), based on the range from published estimates (*van den Hurk et al., 2009*). The case fatality ratio (CFR) from JE was assumed to follow a Beta distribution with a median symptomatic CFR of 0.33 (95% CI: 0.05-0.75), reflecting the large uncertainty in this parameter (*van den Hurk et al., 2009*). The annual burden of JE at the national-level was calculated using

disability-adjusted life years (DALYs) with disability weights taken from the Global Burden of Disease 2016 report (*GBD 2016 DALYs and HALE Collaborators, 2017*).

Rotavirus – Emory University

The Emory model is a dynamic, deterministic, age-structured compartmental transmission model simulates rotavirus transmission and estimates disease incidence/burden in a given country. The model is based on a Susceptible–Infected–Recovered (SIR) structure, with elaborations in order to capture the complexities of rotavirus immunity and transmission. In particular, individuals can be infected up to four times. We model the following age groups: 0–1 months, 2–3 months, 4–11 months, 1 year age bands from 1 to 4 years old, and 5 years and older. We use realistic, age-specific population sizes, aging and death rates.

In the model, infants are born with maternal immunity (*Linhares et al., 1989*). After maternal immunity wanes, infants become susceptible to a primary rotavirus infection. We assume that protection is conferred by previous infections against subsequent infections, such that the proportion of individuals that remain susceptible to re-infection decreases with each subsequent infection (*Gladstone et al., 2011; Velázquez et al., 1996*). Primary, secondary, tertiary, and quaternary infections are assumed to have the same duration of infectiousness, however non-primary infections have lower per-contact infectiousness relative to primary infections (*Pitzer et al., 2012*). Immunity is assumed to be a mix of ‘take type’ where a portion of individuals develop long-term immunity, while others remain fully susceptible to subsequent infections. We assume primary, secondary, tertiary, and quaternary infections had different probabilities for developing rotavirus gastroenteritis (*Velázquez et al., 1996*). We assume only severe rotavirus gastroenteritis cases are reported to surveillance and can result in death. This model incorporates the introduction of vaccines in a specified year, delivered to 2- and 4 month olds. We assume that vaccine doses are independent. We incorporate an immunogenicity parameter that determines whether individuals will respond to the vaccine (*Patel et al., 2009*). If individuals respond to vaccination, we assume that the vaccine acts like a natural infection; the probability of becoming infected, given vaccination and natural history of infections, goes down with each subsequent vaccine dose and natural infection. Values for natural history parameters were set to values identified in birth cohort and challenge studies.

In lieu of fitting this model to estimate country-specific effective contact rates, we used a linear regression model to estimate the mean age of severe rotavirus infection, and subsequently calculated the basic reproduction number. Variables considered for inclusion were: under five mortality rates (*World Bank, 2021*), gross domestic product (GDP) per capita (*World Bank, 2021*), total GDP (*World Bank, 2021*), region, sub-region, birthrate (*World Population Prospects, 2019*), life expectancy (*World Population Prospects, 2019*), and percent of the population living in a rural setting (*World Bank, 2021*). The linear regression model was fit using a training (80%) and validation (20%) data set, with the optimal model for each country being selected to optimize the correlation accuracy and the mean absolute percent error (MAPE). The basic reproduction number was calculated by dividing the life expectancy for each country (*World Bank, 2021*) by the fitted average age of severe infection.

To account for uncertainty, we generated 200 parameter sets by uniformly sampling from the published range of vaccine immunogenicity and the 95% confidence interval of the regression models estimated mean age of infection for each country. The remaining parameters were fixed. We then simulated the model for each set of fixed and sampled parameters. We calculated the central burden/impact estimate as the median of the 200 probabilistic runs. To calculate the number of deaths, we estimated the number of previous rotavirus infections (with first infections being most severe and subsequent infections being less likely to cause severe disease) and then multiplied this quantity by the estimated rotavirus case fatality ratio for each country and age group, based on data from the Global Burden of Disease Study (*Troeger et al., 2018*).

Rubella – Johns Hopkins University

We developed a discrete-time stochastic age-structured compartmental rubella transmission model, building from previous work describing rubella dynamics (*Metcalf et al., 2012a*). The key feature of the model is a matrix that at every time-step defines transitions from every combination of

epidemiological stage (maternally immune 'M', susceptible 'S', infected 'I', recovered 'R', and vaccinated 'V', taken to indicate the effectively vaccinated) and age group (1 month age groups up to 20 years old, then 1 year age groups up to 100 years old) to every other possible combination of epidemiological stage and age group. The discrete time-step was set to about two weeks (i.e. 24 time steps in a year), the approximate generation time of rubella.

Demographic parameters (population size, crude birth rates, and age-specific death rates) and vaccination coverage were time and country-specific, and were supplied by VIMC. We assumed dependence between routine vaccine doses. We adjusted campaign coverage based on the assumptions that a portion of the population may always remain inaccessible to campaigns. We assumed the age and time-specific proportion inaccessible corresponds to WUENIC DTP routine vaccination rates World Health Organization and UNICEF (*World Health Organization and UNICEF, 2015*) if it does not exceed routine coverage. Duration of maternal immunity (*Nicoara et al., 1999*) and vaccine efficacy (*Boulianne et al., 1995*) were assumed from published literature and are constant across time and country. The annual introduction of infected individuals was scaled with the median time-specific population size of each country set to trigger an outbreak if the size of the susceptible population was large enough but small enough to not effect probability of elimination.

Country-specific transmission to individuals in age group a from individuals in age group j for each time-step t is defined by $\beta_{a,j,t} = \overline{\beta_{a,j}}(1 + \alpha \cos(2\pi t))$, where $\overline{\beta_{a,j}}$ is mean transmission from individuals in age group j to age group a , and α is a parameter controlling the magnitude of seasonal fluctuations (assumed 0.15 [*Metcalf et al., 2012b*] and constant over time and country). Mean transmission from individuals in age class j to age class a , $\overline{\beta_{a,j}}$, was estimated by rescaling population-adjusted age-contact rates (time constant and country-specific, *Prem et al., 2017*) to reflect the assumed basic reproductive number (R_0) of rubella. R_0 distributions were country-specific and estimated by fitting a dampened exponential model (*Farrington, 1990*) with likelihood-based MCMC to published rubella immunoglobulin G (IgG) seroprevalence data.

Rubella burden is generated from a 'bottom up' approach in which we calculate CRS cases, and deaths, from modeled output. Country- age- and time-specific CRS cases were estimated by multiplying the country, age and time-specific number of susceptible individuals, the country and time-specific sex ratio of the population, the country- and age-specific fertility rate, the country- age- and time-specific probability of becoming infected over 16 week period, and finally the probability of CRS following rubella infection during the first 16 weeks of pregnancy (estimated ~0.4; *Andrade et al., 2006; Hahné et al., 2009; Grillner et al., 1983; Miller, 1991; Mirambo et al., 2019; Zgórnjak-Nowosielska et al., 1996; Vejtorp and Mansa, 1980*). Fetal deaths were estimated directly from rubella infections among women in the first 16 weeks of pregnancy as 20.7 per 100 (*Mirambo et al., 2019; Cooper and Krugman, 1967; Miller et al., 1982; Siegel et al., 1966a; Siegel et al., 1966b*) and infant deaths were estimated from the number of CRS cases as 8.9 per 100 (*Miller, 1991; Cooper and Krugman, 1967; Saad de Owens and Tristan de Espino, 1989; Panagiotopoulos et al., 1999; Toizumi et al., 2014*).

We simulated 200 stochastic runs for each country from the year 1980 to 2100. Model uncertainty includes process uncertainty for all epidemiological and demographic transition and uncertainty from the R_0 , CRS rate, and CRS death rate distributions. Model input parameters (e.g., R_0) were fit to empirical data, however the mechanistic transmission model itself is not directly fit to data.

Rubella – Public Health England

This is an age and sex-structured, deterministic, compartmental model of the transmission dynamics of rubella (*Vynnycky et al., 2016b; Vynnycky et al., 2019*). The population is stratified into those with maternal immunity (lasting 6 months), susceptible, pre-infectious (infected but not yet infectious), infectious and immune, using annual age bands and a 'Realistic Age Structure' (*Schenzle, 1984*). Country-specific birth and age-specific death rates were fixed at 2010 levels and calculated from UN population survival data for 2010–15 (*UNWPP, 2017*) respectively. The supplement to *Vynnycky et al., 2016a* provides the model's differential equations.

The force of infection (rate at which susceptibles are infected) changes over time and is calculated using the number of infectious individuals and the effective contact rate (rate at which infectious and susceptible individuals come into effective contact). Contact is described using the following matrix of 'Who Acquires Infection From Whom':

$$\begin{pmatrix} \beta_1 & 0.7\beta_2 \\ 0.7\beta_2 & \beta_2 \end{pmatrix}$$

The effective contact rate differs between <13 and ≥ 13 year olds, with its relative size based on contact survey data (*Mossong et al., 2008*). β_1 and β_2 are calculated from the average force of infection in <13 and ≥ 13 year olds, estimated from age-stratified rubella seroprevalence data, which had been collected before rubella containing vaccine (RCV) was introduced (*Vynnycky et al., 2016b*). Seroprevalence data were available for 28 countries (see *Vynnycky et al., 2019*). For countries lacking seroprevalence data, we used data from countries in the same WHO region (*Vynnycky et al., 2016b; Vynnycky et al., 2019*). Confidence intervals (CI) on the force of infection were calculated using 1000 bootstrap-derived-seroprevalence datasets (*Vynnycky et al., 2016b; Vynnycky et al., 2019*). The vaccine doses were assumed to be correlated, with 100% of those vaccinated previously being vaccinated I SIAs, where possible and 50% of those who have received RCV1 receiving RCV2, where possible.

Country-specific numbers of congenital rubella syndrome (CRS) cases in year y during 2001–2080 were calculated by summing the number of CRS cases born each day to women aged 15–49 years. As assumed elsewhere (*Vynnycky et al., 2003; Vynnycky et al., 2016b; Vynnycky et al., 2019*), infection during the first 16 weeks of pregnancy carries a 65% risk of the newborn having CRS. The number of CRS deaths in year y was calculated by multiplying the number of CRS cases born in year y by the assumed case fatality rate (30%). The latter was assumed to have a plausible range of 10–50%, consistent with the number of DALYs for cases in year y was calculated by multiplying the number of CRS cases in year y by the corresponding DALY (*Simons et al., 2016*), which was based on the country-specific World Bank Income group for 2017 (*World Bank, 2017*). Both the DALYs and the assigned World Bank income group remained fixed over time. As rubella infections are mild, rubella-specific deaths are not included and people with rubella infection are assumed to die at the general all-cause, age and sex-specific mortality rate.

Confidence intervals on the outputs for each setting were calculated as the 95% range of the outputs obtained by running the model using 200 combinations of 5 randomly-sampled parameters. The parameters were the pre-vaccination force of infection which was used to calculate the contact parameters (see above), the risk of a child being born with CRS if his/her mother had been infected during pregnancy, the CRS-related case-fatality rate, the vaccine coverage and the vaccine efficacy. The pre-vaccination force of infection was sampled from 1000 bootstrap-derived force of infection estimates, obtained by fitting catalytic models to bootstrap-derived seroprevalence data for that setting, or, if that setting lacked seroprevalence data, from bootstrap-derived force of infection estimates from countries in the same WHO region as the country of interest (*Vynnycky et al., 2016b; Vynnycky et al., 2019*). The remaining parameters were randomly sampled from distributions reflecting their plausible range, as implied by published studies, wherever possible (*Vynnycky et al., 2016a*). For example, the CRS-related mortality was sampled from the uniform distribution in the range 10–50%, consistent with estimates from three studies in Vietnam, Greece and Panama, in which the 95% confidence intervals were 20–51%, 12–50% and 15–40% respectively (*Toizumi et al., 2014; Panagiotopoulos and Georgakopoulou, 2004; Saad de Owens and Tristan de Espino, 1989*). The risk of a child being born with CRS to a mother infected in the first 16 weeks of pregnancy was sampled from the Gamma distribution with shape and scale parameters 37 and 56 respectively. This assumption leads to a median and 95% range of 65% and 47–88% respectively for this risk, consistent with estimates from several studies (*Miller et al., 1982; Grillner et al., 1983; Hahné et al., 2009*) which, as found in a recent review (*Thompson et al., 2016*) were likely to have been more reliable than those in other studies. The sampling was conducted assuming that the parameters were independent.

Yellow Fever – Imperial College London

The Imperial College yellow fever (YF) transmission model is a static force of infection (FOI) epidemiological model. The first iteration was originally published by *Garske et al., 2014*; however, this has been extensively updated by *Gaythorpe et al., 2021a* to provide the 2019 model estimates. The model is fitted at the first administrative level or province level for all countries considered at risk or endemic for YF. In each administrative unit, the force of infection is assumed to be constant across

the observation period and across age groups. This is analogous to assuming that all yellow fever transmission occurs as a result of spillover events from the sylvatic reservoir. As a result, this model variant includes no herd immunity effects.

The model is estimated from multiple data sources which inform separate components. A generalised linear model, based on environmental covariates, is informed by presence/absence of yellow fever reports between 1984 and 2019 at province level. Reports of yellow fever are based on outbreak reports published by the WHO and on cases reported in the Yellow Fever Surveillance Database (YFSD) managed by WHO-AFRO, to which 21 countries in West and Central Africa contribute, and reports from the Brazilian Ministry of Health as well as PAHO (*World Health Organization, 2021a, World Health Organization, 2021b*). The environmental covariates were revisited since the initial 2014 model version and now include substantially updated datasets. Covariates include non-human primate species occurrence, vector occurrence, temperature, land cover type and altitude (*Fick and Hijmans, 2017; Kraemer et al., 2015; LP DAAC NASA, 2001; Xie and Arkin, 1996; IUCN, 2019*). The regression model provides estimates of the probability of yellow fever reports across the endemic zone. In order to preserve structural uncertainty from covariate selection, we average over the 20 best fitting generalized linear models within the Bayesian framework.

These estimates are then translated to the number of infections by further fitting to data obtained from 42 serological surveys performed in Africa (*Chepkorir et al., 2019; Diallo et al., 2010; Kuniholm et al., 2006; Merlin et al., 1986; Omilabu et al., 1990; Tsai et al., 1987; Werner et al., 1985*). In each survey location, a static, age-independent force of infection is fitted. This is also informed by estimates of demography and vaccination coverage including historic vaccination campaigns (*World Health Organization and UNICEF, 2015; Hamlet et al., 2019*). We assume there is no correlation between vaccine doses.

Model components are estimated within a Bayesian framework with adaptive Markov Chain Monte Carlo sampling, this framework was extended in Gaythorpe et al. to lie within a product-space estimation framework (*Gaythorpe et al., 2019*). All estimation was performed in R and convergence of the chains was checked visually. To produce the burden estimates, 200 samples of the posterior predictive distributions of the FOI in each province were taken which we then use to calculate the incidence of infections in each province.

We use published values of the proportion of infections which are severe and of the CFR to calculate the burden of disease. These proportions, estimated by *Johansson et al., 2014*, are that 12% [5%, 26%] of infections are severe and that 47% [31%, 62%] of severe infections result in death. However, these estimates remain uncertain since the disease is notoriously misdiagnosed and under-reported. Another area resulting in uncertainty in burden estimates is the heterogeneity in data availability, specifically serological surveys which are not currently available in West Africa or South America. As such, whilst the updated data and model averaging framework have improved the uncertainty ranges, these are still broad.

Yellow Fever – University of Notre Dame

The University of Notre Dame yellow fever (YFV) model is a static transmission model that assumes a constant force of infection (FOI) for each endemic country. Yellow fever infections in the human population are thus modeled as spillover events from non-human primates, so human-to-human transmission observed in urban outbreaks is not considered. Accordingly, our model is intended to capture long-term changes in YFV burden on account of changes in vaccination coverage rather than to realistically capture interannual variability due to YFV epizootics in non-human primates and occasional outbreaks in humans.

We calibrated our YFV transmission model to multiple sources of epidemiological data collected in sub-Saharan Africa at the first administrative level sub-nationally. First, we quantified past exposure to YFV by estimating the force of infection in 23 administrative units using data collected in serological surveys. We then related the predicted number of YFV infections at each of the 23 administrative units to the corresponding reported outbreak data collated by *Garske et al., 2014* to quantify the extent of underreporting. We then obtained estimates of the total number of infections at each administrative unit in sub-Saharan Africa by relating our estimates of underreporting to the total number of reported cases and deaths in each administrative unit. This allowed us to estimate a posterior distribution of a single FOI for each administrative unit in sub-Saharan Africa. Because the

FOIs that we estimated are sensitive to the number of reported cases and deaths, we smoothed across our estimates by performing a regression analysis with spatial covariates. We considered multiple regression models and generated an ensemble prediction by weighting the predicted FOI from each regression model based on performance in ten-fold cross-validation at the country level. National-level FOI estimates were obtained by weighting the ensemble spatial prediction of FOI according to WorldPop 2015 population density estimates at the first administrative level and then summing to obtain national FOIs.

To project the number of yellow fever cases and deaths in each country under a given vaccination coverage scenario, we first scaled the national-level FOI by the proportion of the population that is unvaccinated. We then used the scaled FOI estimate to project the annual number of YFV infections and multiplied this quantity by the probabilities of disease and death reported by *Johansson et al., 2014* to obtain estimates of the annual number of YFV cases and deaths. We assume a 0.975 probability of protection from infection among those who are vaccinated based on *Jean et al., 2016*, with this level of protection assumed to be lifelong based on a single dose. In the event of campaigns, we assume that individuals are vaccinated randomly and irrespective of prior vaccination through another campaign or routine vaccination.

Appendix 3

3.1 Impact by year of vaccination

Taking an activity perspective, we assume that RI and NRI, which target multiple age groups, have different effects; for example due to dosage clustering. Therefore, there are two activity-specific impact ratios which can then be multiplied by the number of FVPs to calculate impact provided by vaccination occurring in one year.

For RI, the impact ratio is defined as the impact for all cohorts who are vaccinated over time period Y_v per the additional FVPs between the baseline and focal scenarios. The impact for RI, D_R , is given by $D_{b_R-f_R}$, where b_R and f_R are the baseline and focal RI scenarios, respectively. Here, the impact ratio for RI is given by the following:

$$\rho_R(c) = \frac{\sum_{y-a \in Y_v - A_v} D_R(a, c, y)}{\sum_{y \in Y_v} FVP_R(c, y)}, \quad (C.1)$$

where $Y_v - A_v$ are cohorts receiving vaccinations in years Y_v . The impact by year of vaccination is then given by the following:

$$D_R(c, y) = \rho_R(c) \times FVP_R(c, y), \quad (C.2)$$

where FVP_R are FVPs vaccinated through RI.

For NRI, the impact ratio is averaged evenly over all ages across the entire time period (Y_m). This is because we do not attempt to predict future NRI coverage after the final year of credible campaign schedules. Therefore, the only impact due to NRI comes from NRI years Y_v and all campaign impact for birth cohorts born after this period can be attributed back to these vaccination years. The impact of NRI, D_S , is given by $D_{b_S-f_S}$, where b_S and f_S are the baseline and focal NRI scenarios, respectively. The impact ratio is given by the following:

$$\rho_S(c) = \frac{\sum_{y \in Y_m} \sum_{a \in A_m} D_S(a, c, y)}{\sum_{y \in Y_v} FVP_S(c, y)}. \quad (C.3)$$

The impact by year of vaccination is then given by the following:

$$D_S(c, y) = \rho_S(c) \times FVP_S(c, y), \quad (C.4)$$

where FVP_S are FVPs vaccinated through NRI.

The aggregated impact by YoV for both activities is the sum of the impact from RI and NRI, that is sum of Equations C.2 and C.4.

Further analysis on this method has been done ([Echeverria-Londono et al., 2021](#)).

Appendix 4

Specific differences to previous VIMC-wide study

4.1 Fully vaccinated persons

Due to increases in coverage projections for years 2018 onward, the FVPs generally increased between the two model estimates (**Appendix 5—figure 3**). This is particularly seen for HPV where the optimistic assumptions around vaccine introductions leads to large numbers of FVPs, thereby an increase in deaths averted by cohort year, due to campaigns (**Appendix 5—figure 2**). As the models for HPV have remained fairly static, the difference in HPV vaccine impact estimates are due only to this change in FVPs.

4.1 Model structure

The large changes in HepB, measles and YF estimates are due to changes in model structure since the *Li et al., 2019* study.

4.2 Measles

The two measles models both reassessed the case fatality ratios (CFRs) used in their estimates. Previously, the CFRs were derived from *Wolfson et al., 2009*. However, a recent publication re-evaluated the case fatality ratio for measles and predicted how the CFR may change in future (*Portnoy et al., 2019*). They found that the CFR due to measles was likely lower than that of Wolfson et al. and expected to fall towards 2030. This means that deaths due to measles are expected to fall and thus, vaccine impact.

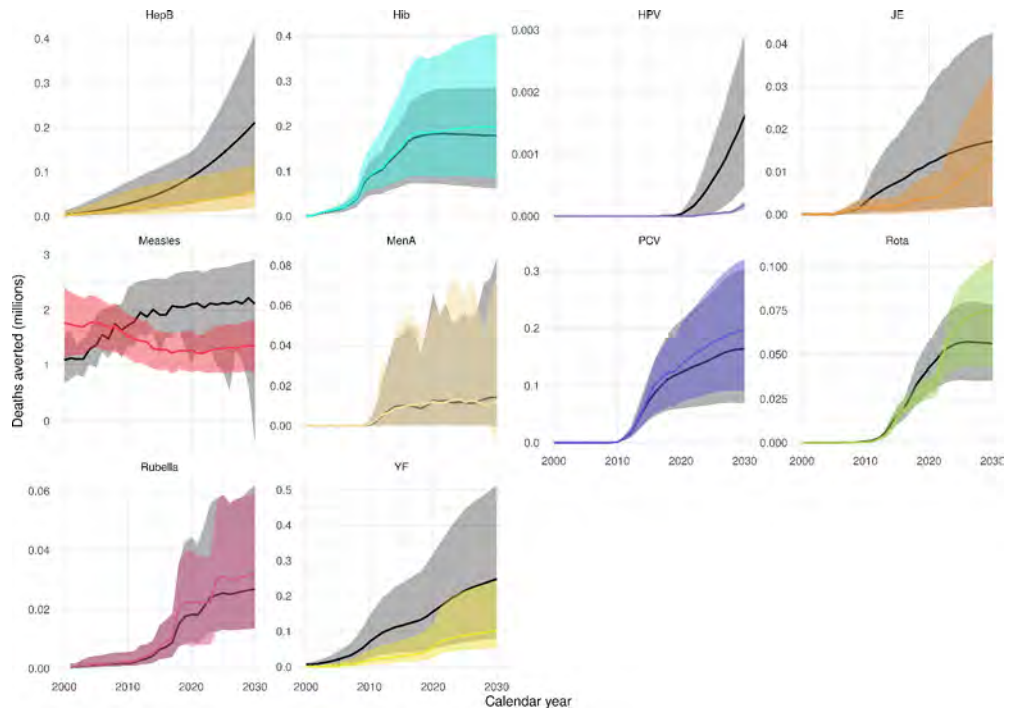
4.3 Hepatitis B

The change in the estimates for HepB are driven by model structure alterations. These changes, detailed in the supplementary material for HepB, Imperial, take into account more optimistic assumptions around treatment in future years. As such, the burden and severe outcomes are reduced and the vaccine impact is also lowered.

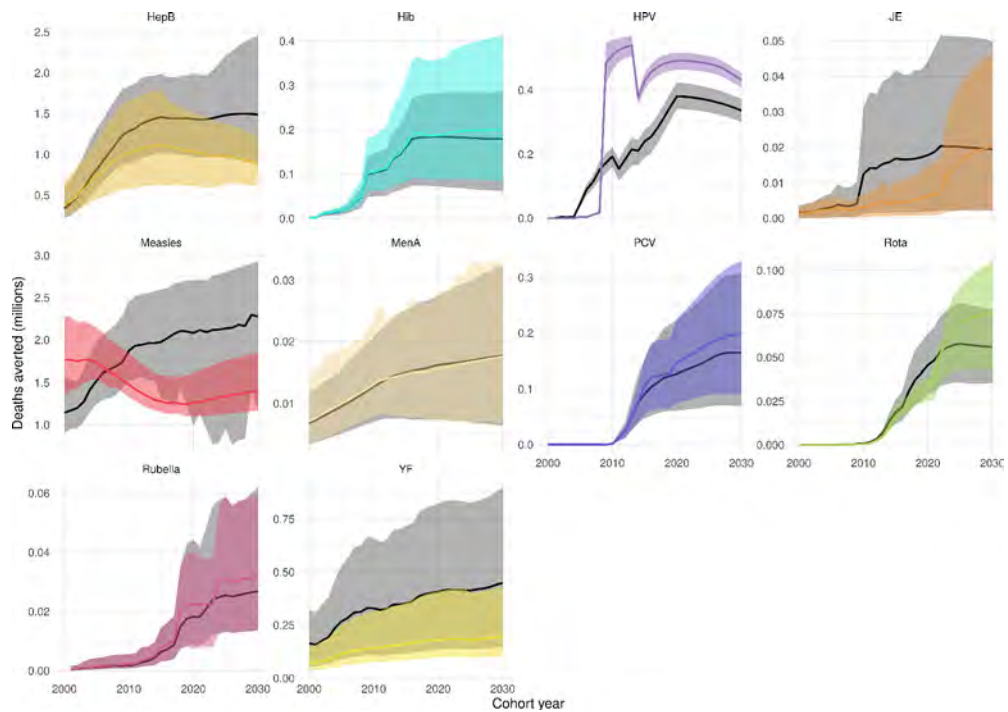
4.4 Yellow fever

In a change to the estimates shown in the previous VIMC-wide study, there are two models included in the current work for YF (*Li et al., 2019*). As such, the mean estimates will be affected by both models. The model described in **Appendix 5—figure 2** for YF, Imperial, was extensively expanded from the original work of *Garske et al., 2014* which included updated serological and outbreak data as well as new environmental covariates (*Gaythorpe et al., 2021a*). This led to a decrease in overall uncertainty and thus a decrease in the mean expected burden and vaccine impact. This also affected the geographic distribution with the Democratic Republic of the Congo particularly highlighted for YF burden.

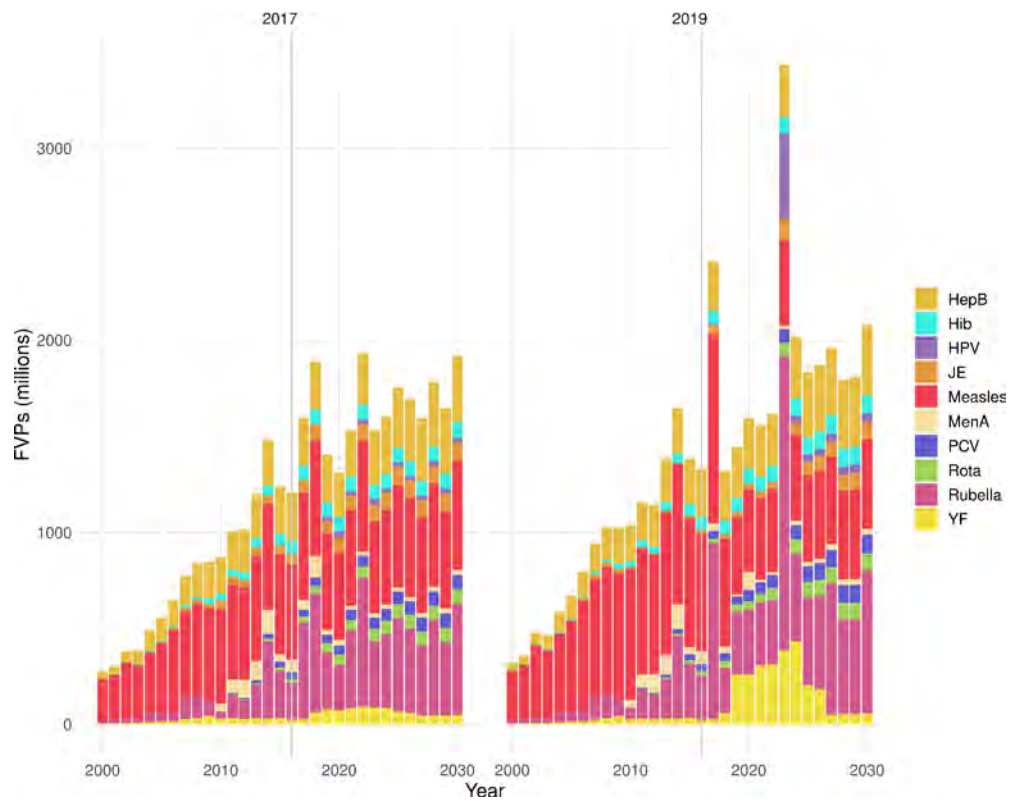
Appendix 5



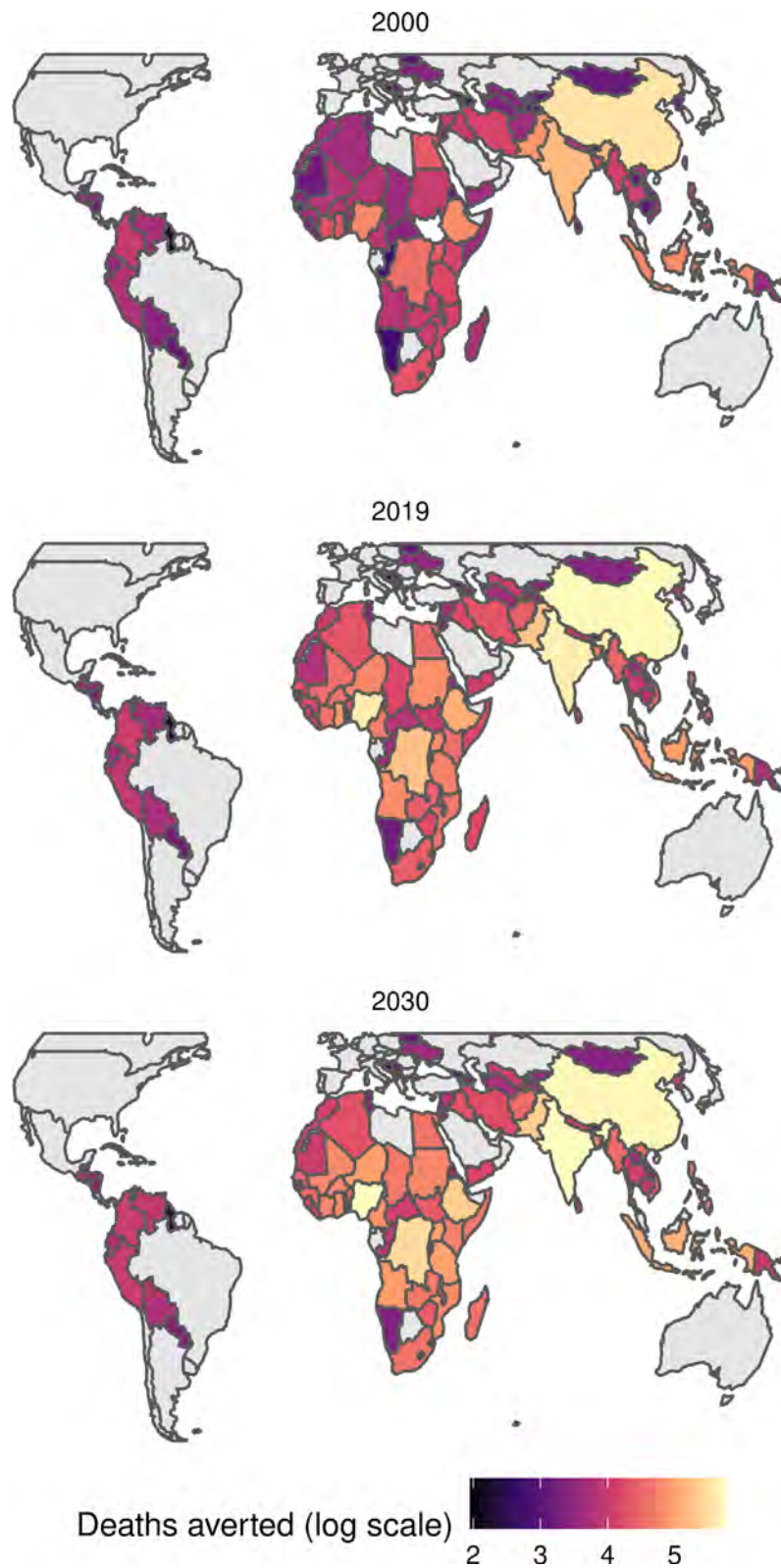
Appendix 5—figure 1. Deaths averted per calendar year for hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella and yellow fever (YF). Coloured lines and areas indicate estimates based on this Vaccine Impact Modelling Consortium (VIMC) study and grey lines and areas indicate estimates based on previous VIMC results (Li et al., 2019). Ribbons indicate 95% CI.



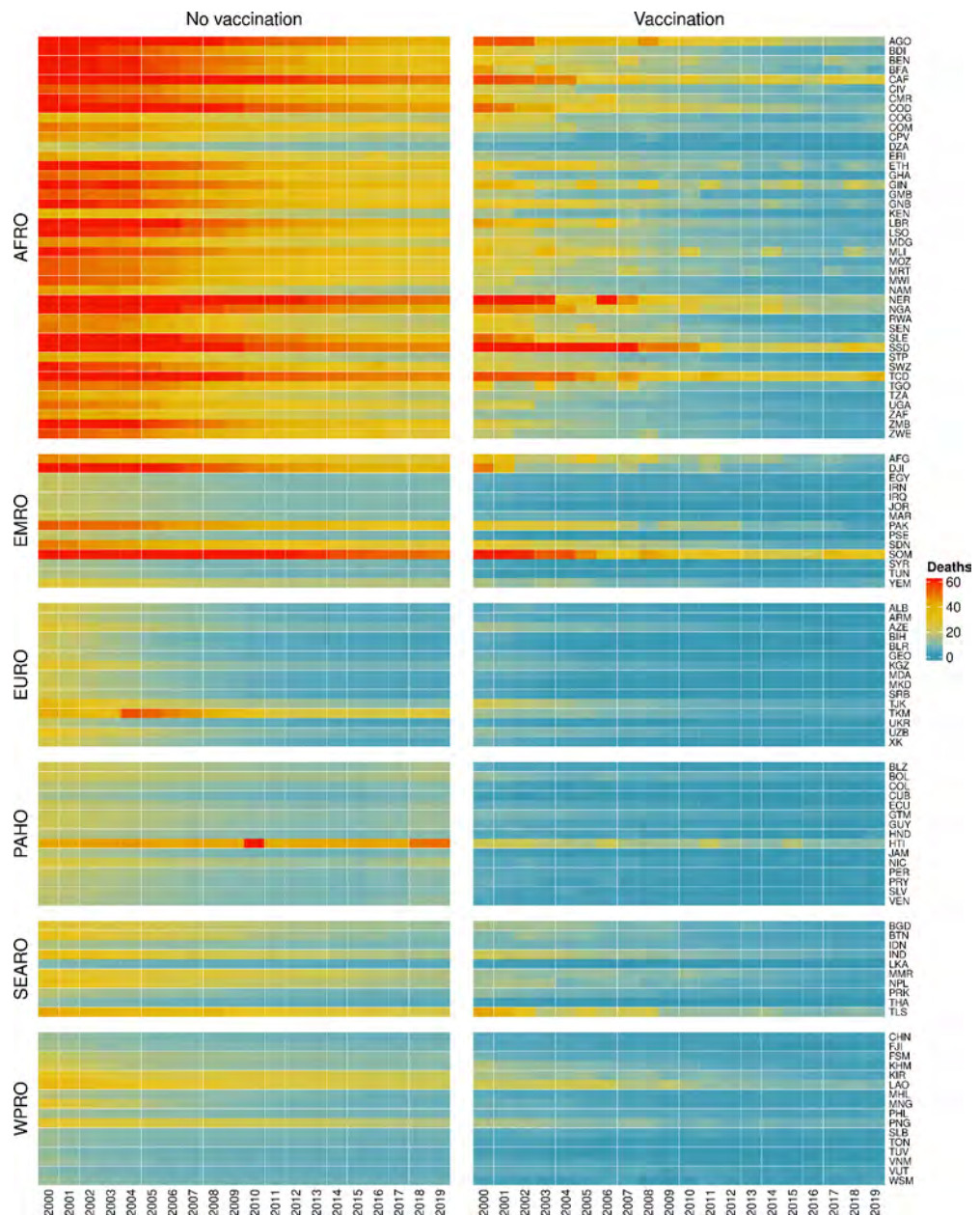
Appendix 5—figure 2. Deaths averted per birth cohort year for hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella and yellow fever (YF). Coloured lines and areas indicate estimates based on this Vaccine Impact Modelling Consortium (VIMC) study and grey lines and areas indicate estimates based on previous VIMC results (Li et al., 2019). Ribbons indicate 95% CI.



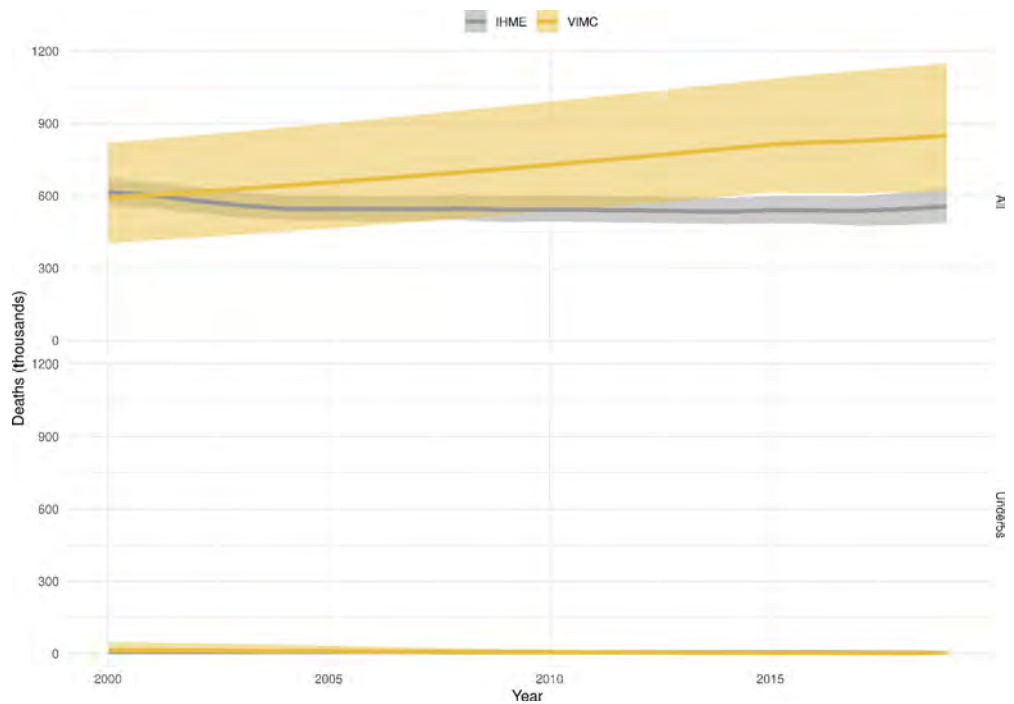
Appendix 5—figure 3. Comparison of fully vaccinated persons (FVPs) in millions between 2017 and 2019 model estimates used within the previous Vaccine Impact Modelling Consortium (VIMC)-wide study *Li et al., 2019* and this study, respectively. FVPs shown for hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella, and yellow fever (YF).



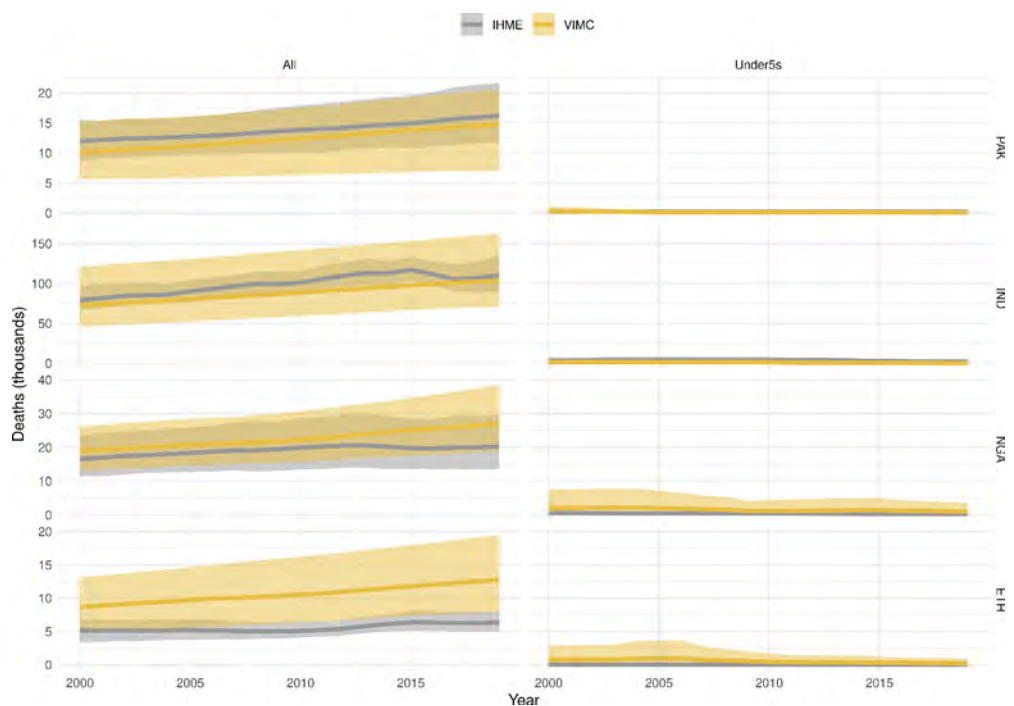
Appendix 5—figure 4. Estimated number of deaths averted per year of vaccination in 2000, 2019, and 2030 for all 10 Vaccine Impact Modelling Consortium (VIMC) pathogens.



Appendix 5—figure 5. Mean predicted deaths for children under-5 with and without vaccination due to the 10 Vaccine Impact Modelling Consortium (VIMC) pathogens per 1000 lives per country for years 2000–2019. Countries are arranged by World Health Organisation (WHO) African (AFRO), Eastern Mediterranean (EMRO), European (EURO), Pan American (PAHO), South-East Asian (SEARO), and Western Pacific (WPRO) regions.



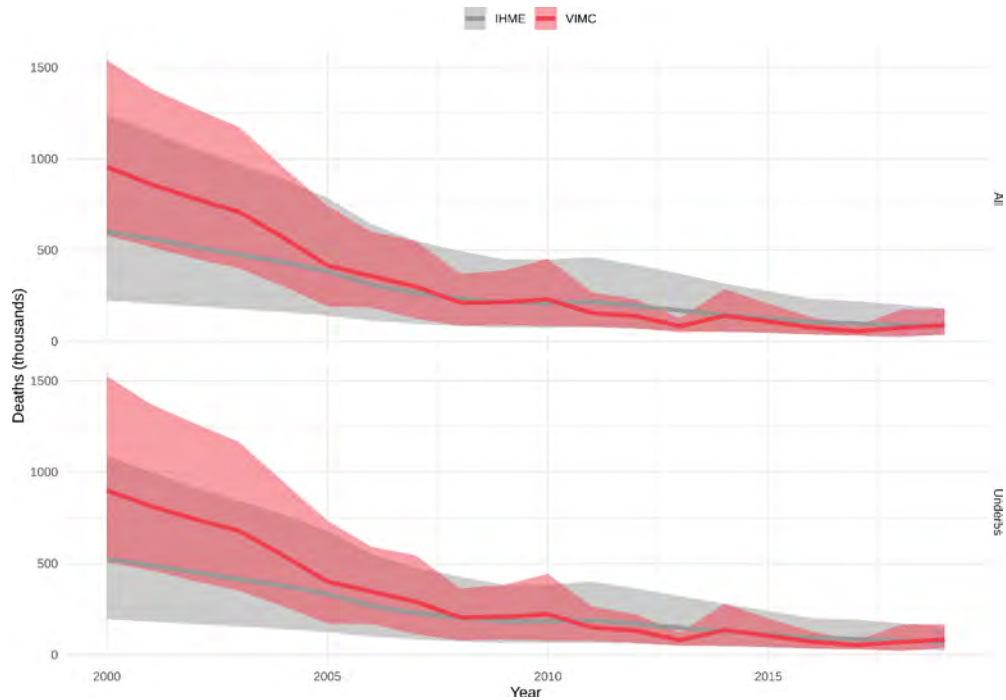
Appendix 5—figure 6. Global deaths for hepatitis B per calendar year (in thousands) for all ages and for children under-5. Orange lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



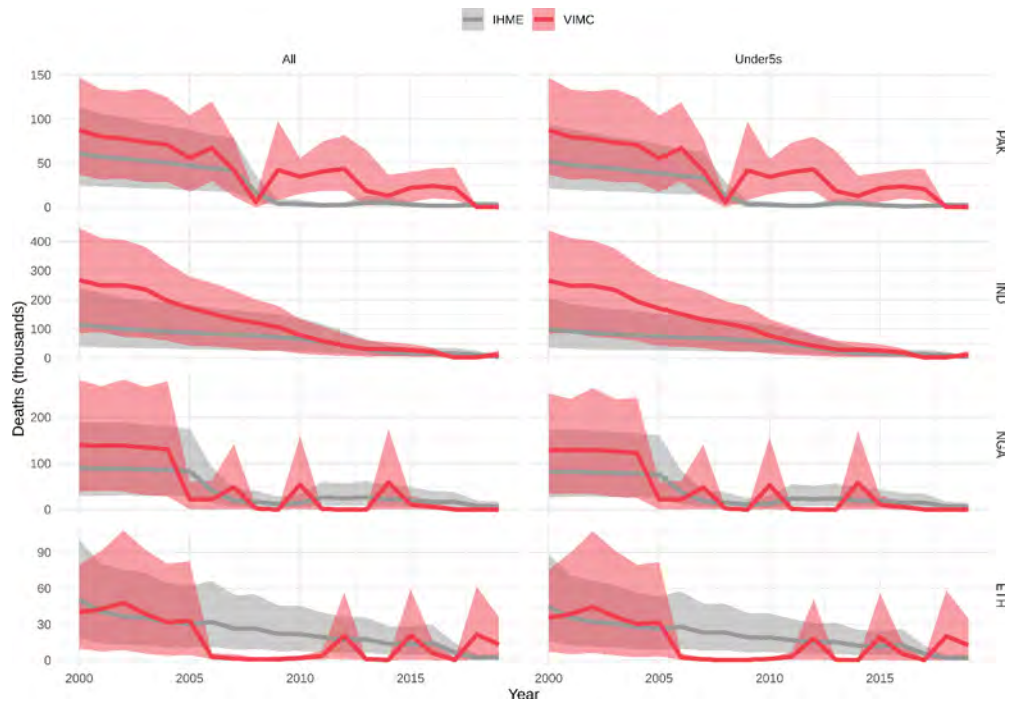
Appendix 5—figure 7. Deaths for hepatitis B in the PINE countries (Pakistan - PAK, India - IND, Appendix 5—figure 7 continued on next page

Appendix 5—figure 7 continued

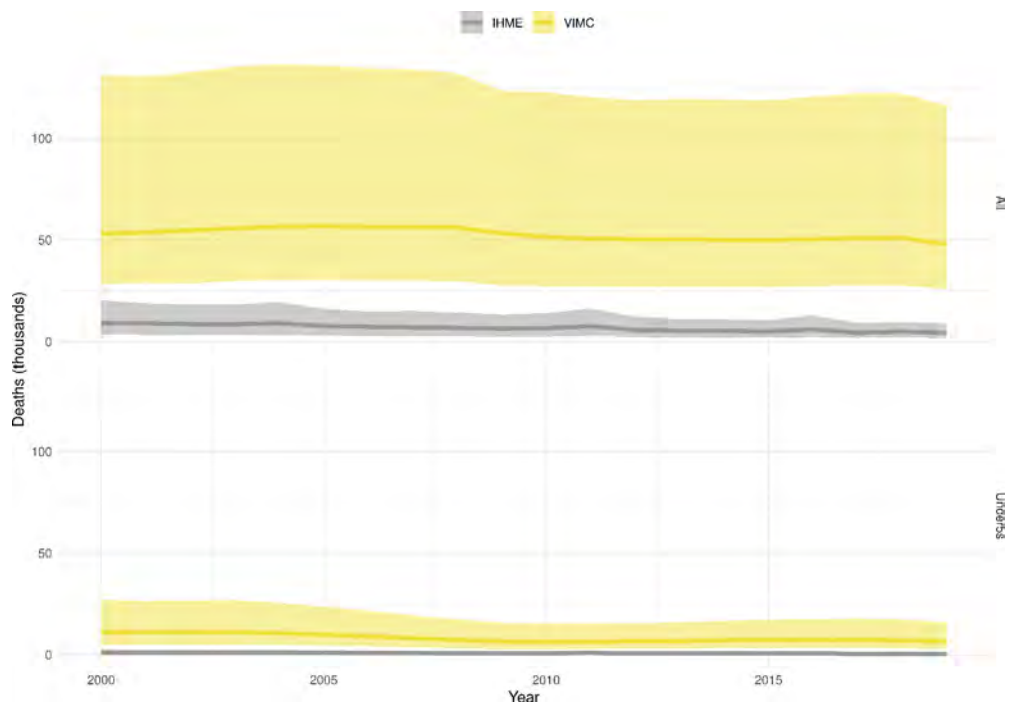
Nigeria - NGA and Ethiopia - ETH) per calendar year (in thousands) for all ages and for under-5s. Orange lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



Appendix 5—figure 8. Global deaths for measles per calendar year (in thousands) for all ages and for children under-5. Red lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



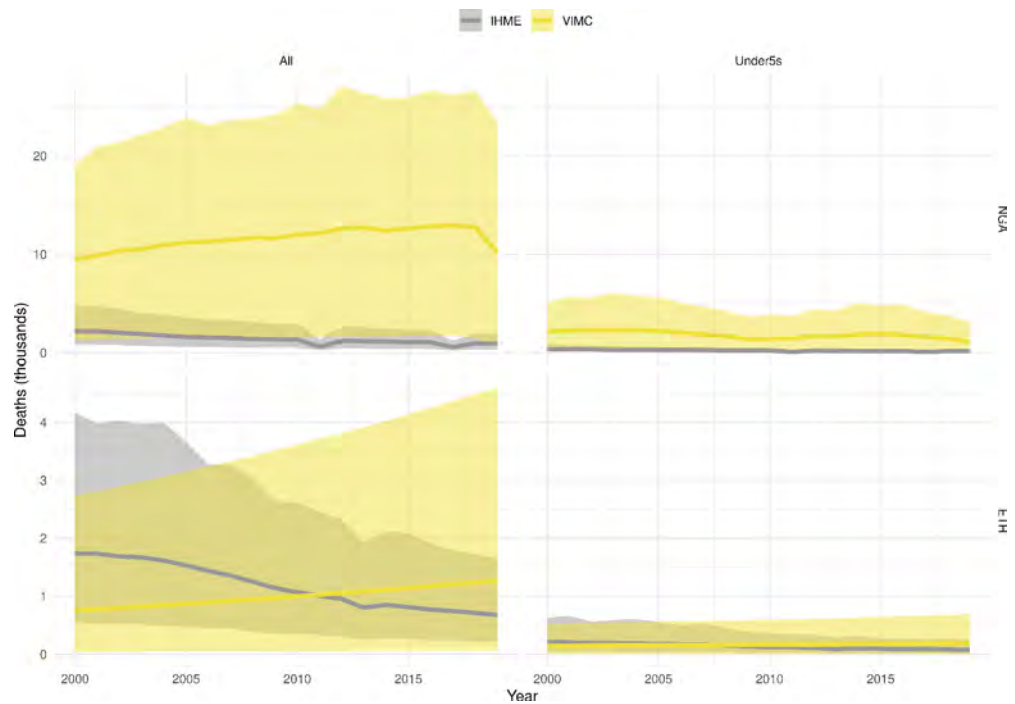
Appendix 5—figure 9. Deaths for measles in the PINE countries (Pakistan - PAK, India - IND, Nigeria - NGA and Ethiopia - ETH) per calendar year (in thousands) for all ages and for children under-5. Red lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



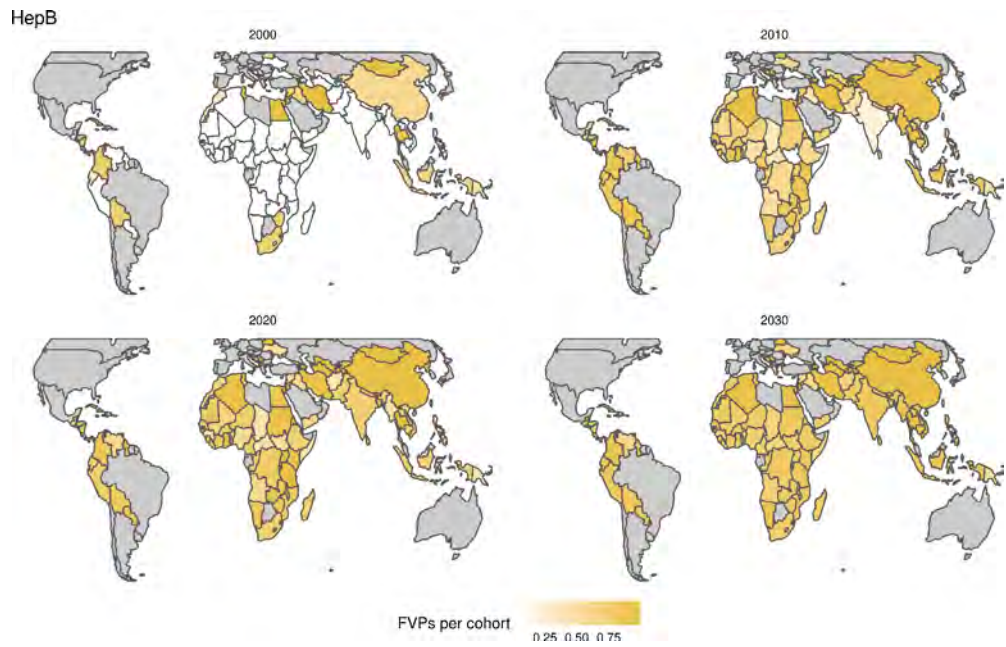
Appendix 5—figure 10. Global deaths for yellow fever per calendar year (in thousands) for all ages
 Appendix 5—figure 10 continued on next page

Appendix 5—figure 10 continued

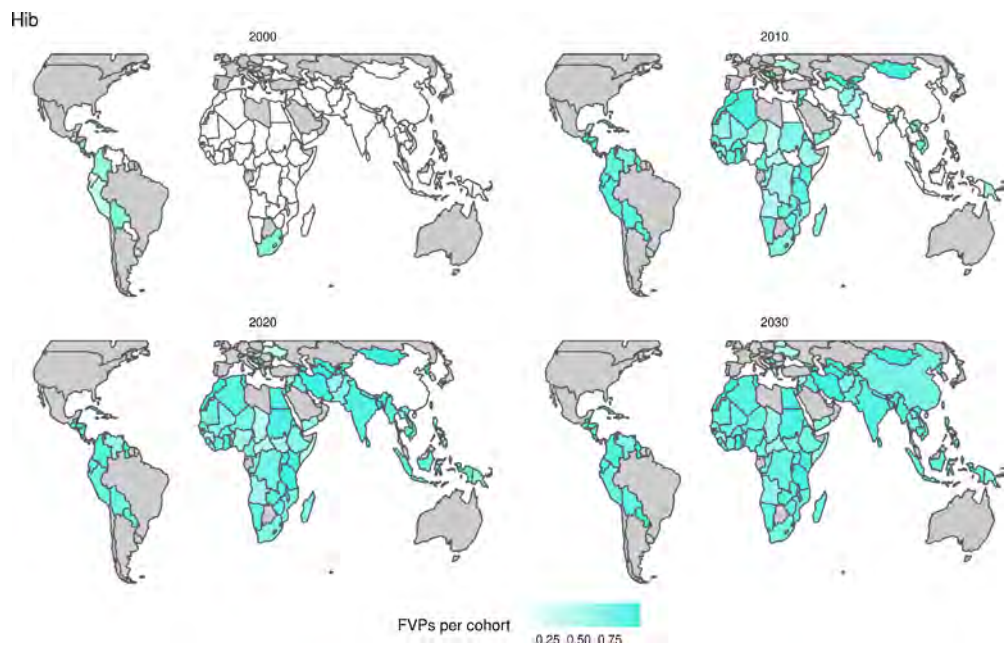
and for children under-5. Yellow lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



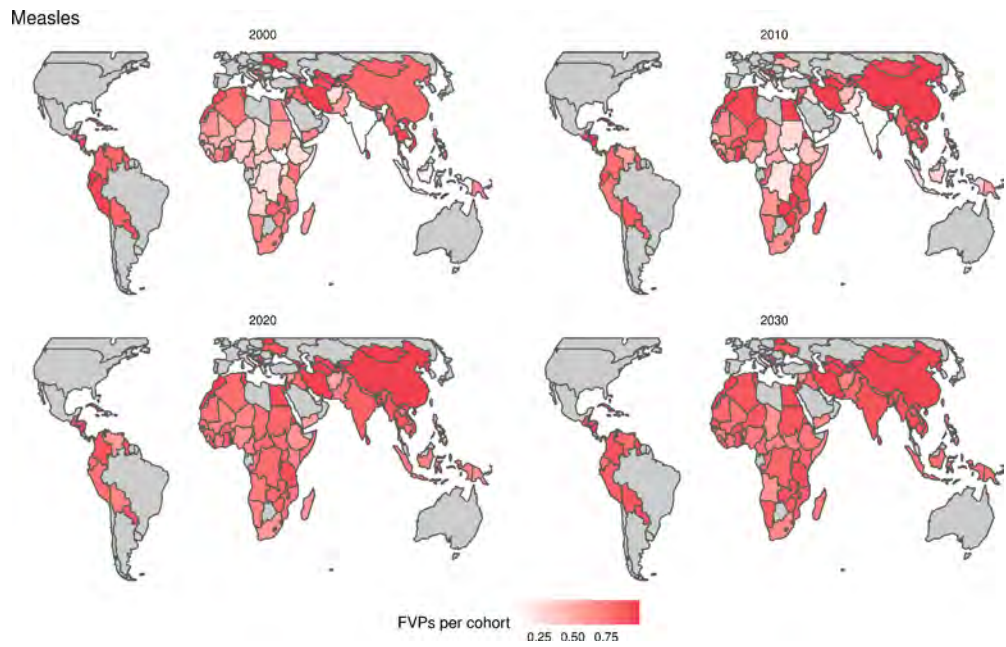
Appendix 5—figure 11. Deaths for yellow fever in Nigeria - NGA and Ethiopia - ETH per calendar year (in thousands) for all ages and for children under-5. Yellow lines and areas indicate estimates from the Vaccine Impact Modelling Consortium (VIMC). Grey lines and areas indicate estimates from the Global Burden of Disease Study (GBD) 2019 from the Institute for Health Metrics and Evaluation (IHME). Ribbons indicate 95% CI.



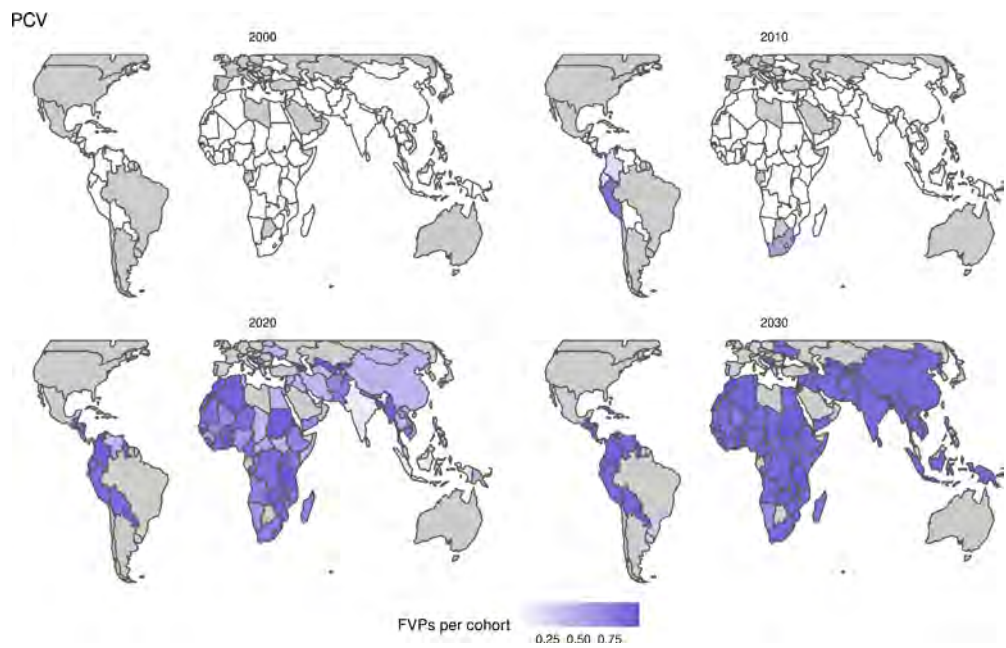
Appendix 5—figure 12. Fully vaccinated persons (FVPs) per vaccination target population for Hepatitis B for years 2000, 2010, 2020, and 2030.



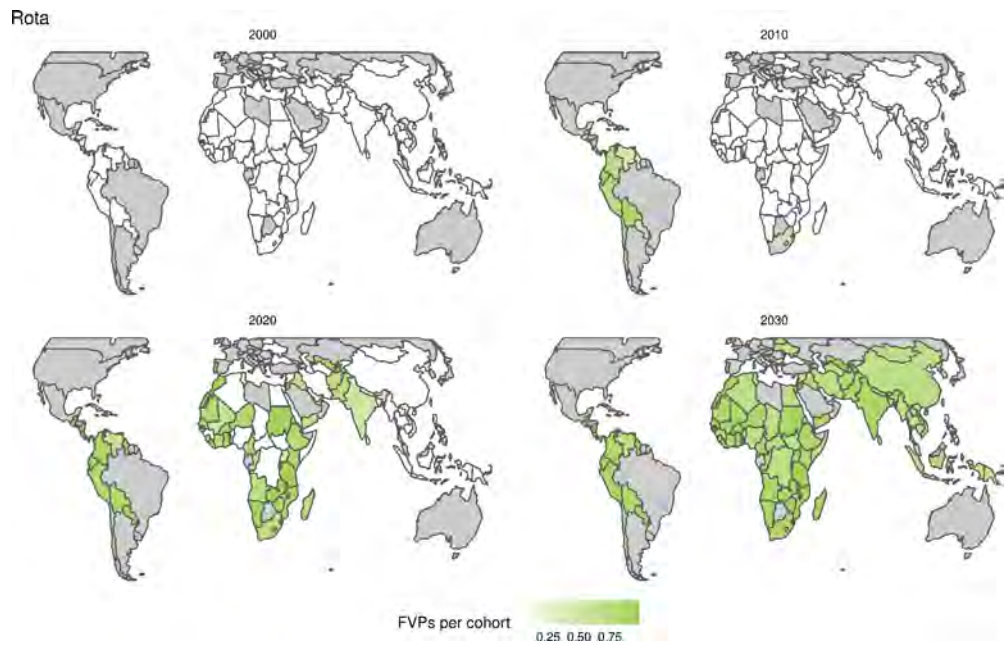
Appendix 5—figure 13. Fully vaccinated persons (FVPs) per vaccination target population for *Haemophilus influenzae* type b (Hib) for years 2000, 2010, 2020, and 2030.



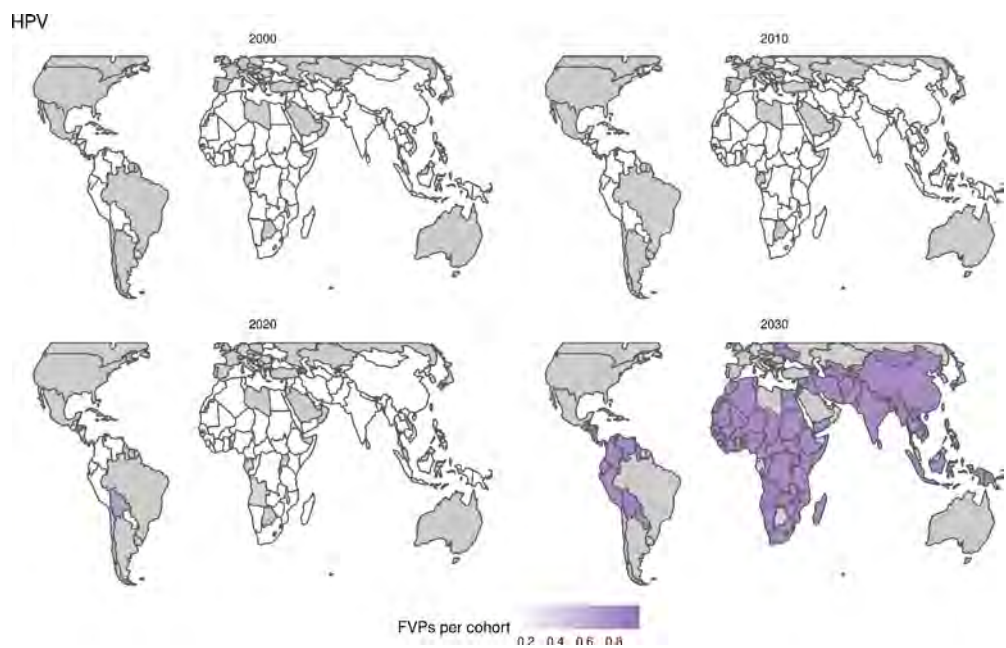
Appendix 5—figure 14. Fully vaccinated persons (FVPs) per vaccination target population for measles for years 2000, 2010, 2020, and 2030.



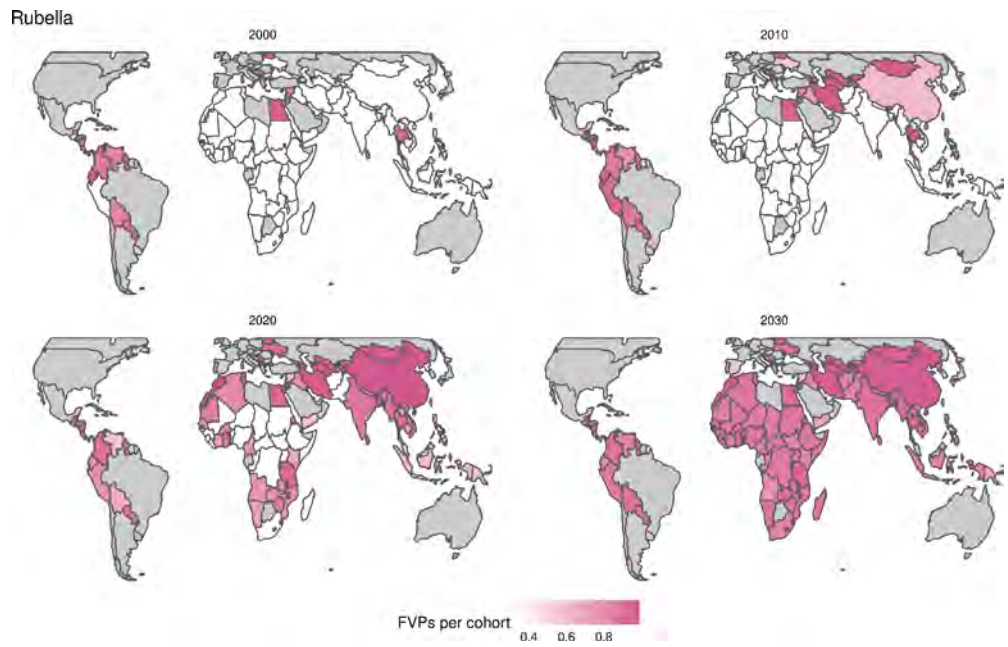
Appendix 5—figure 15. Fully vaccinated persons (FVPs) per vaccination target population for *Streptococcus pneumoniae* (PCV) for years 2000, 2010, 2020, and 2030.



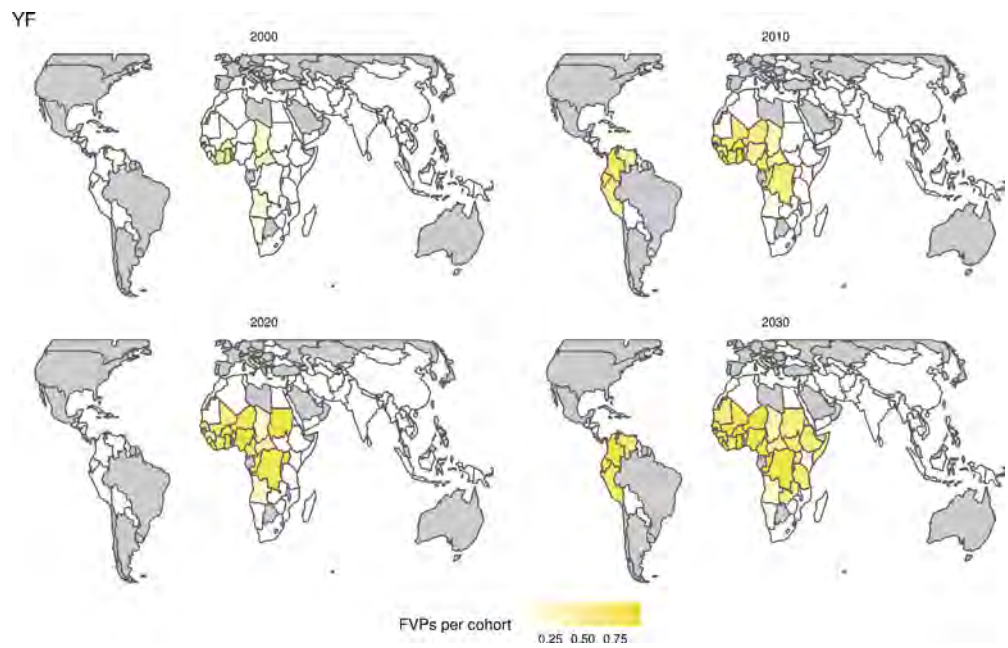
Appendix 5—figure 16. Fully vaccinated persons (FVPs) per vaccination target population for rotavirus for years 2000, 2010, 2020, and 2030.



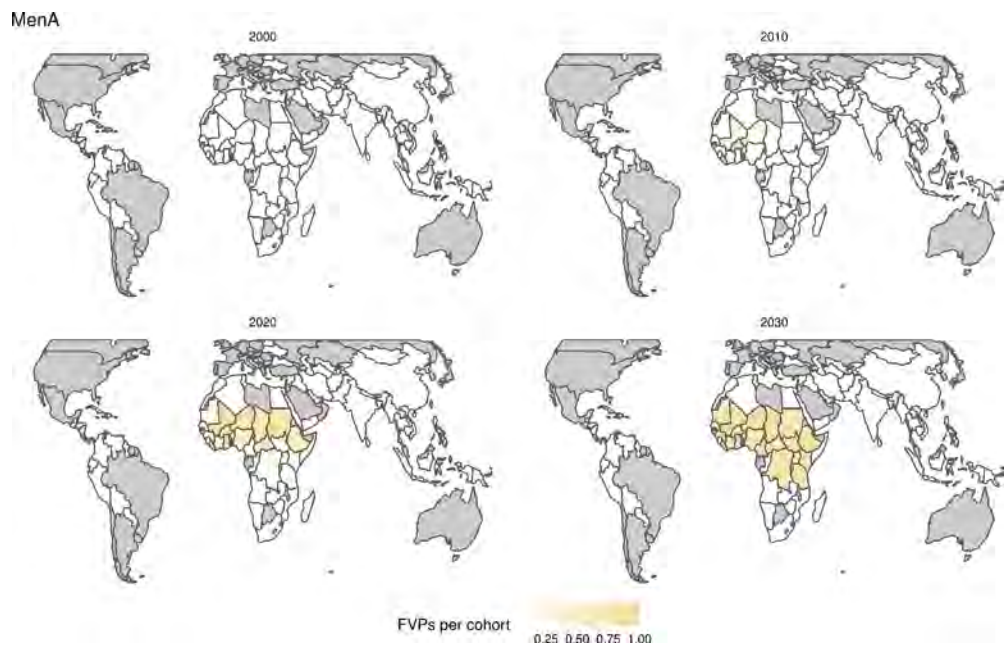
Appendix 5—figure 17. Fully vaccinated persons (FVPs) per vaccination target population for human papillomavirus (HPV) for years 2000, 2010, 2020, and 2030.



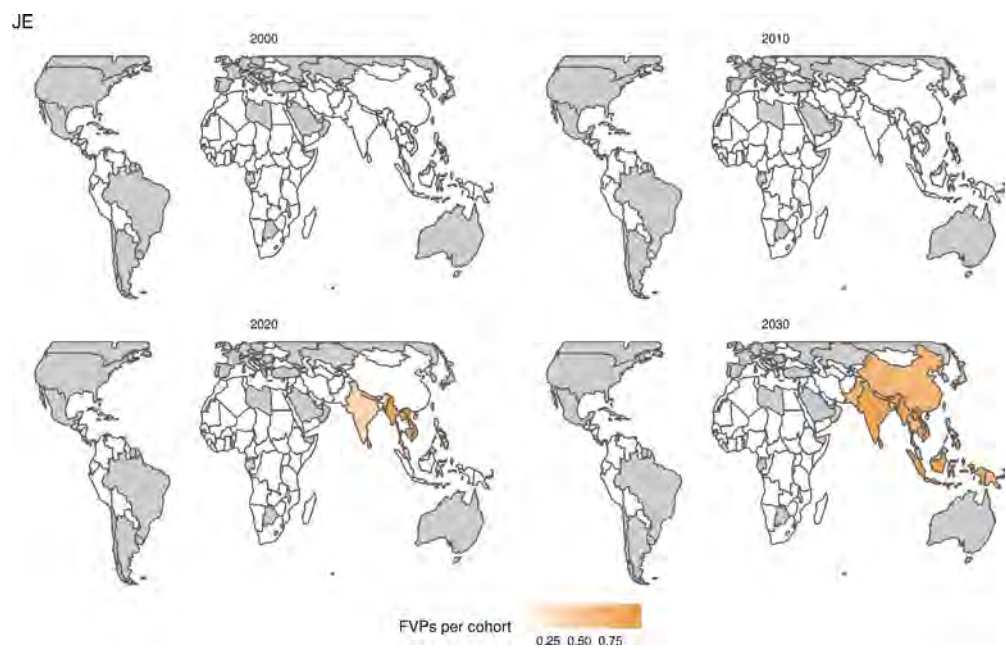
Appendix 5—figure 18. Fully vaccinated persons (FVPs) per vaccination target population for rubella for years 2000, 2010, 2020, and 2030.



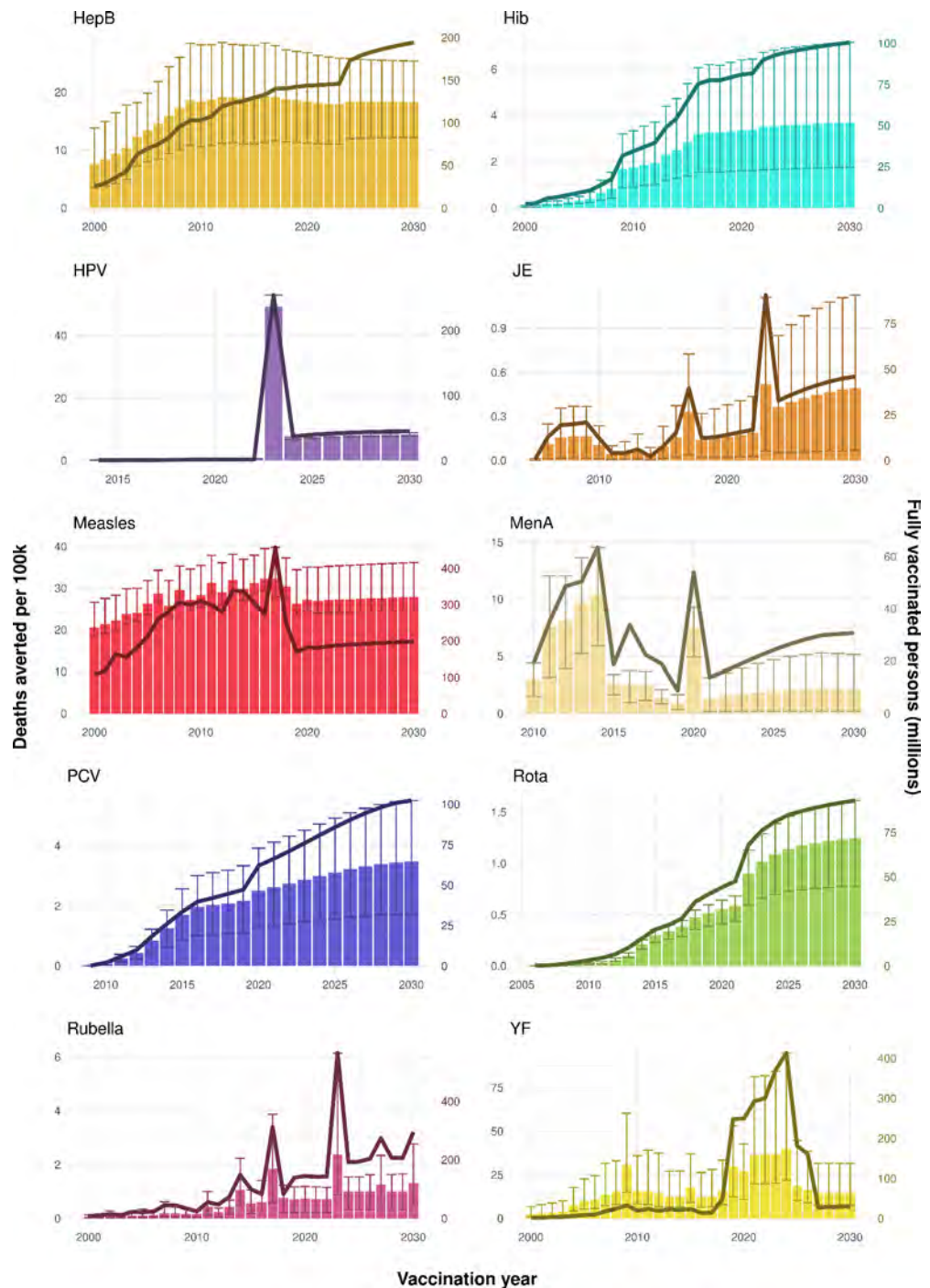
Appendix 5—figure 19. Fully vaccinated persons (FVPs) per vaccination target population for yellow fever (YF) for years 2000, 2010, 2020, and 2030.



Appendix 5—figure 20. Fully vaccinated persons (FVPs) per vaccination target population for *Neisseria meningitidis* serogroup A (MenA) for years 2000, 2010, 2020, and 2030.



Appendix 5—figure 21. Fully vaccinated persons (FVPs) per vaccination target population for Japanese encephalitis (JE) for years 2000, 2010, 2020, and 2030.



Appendix 5—figure 22. Deaths averted per 100,000 population per year of vaccination for hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (PCV), rotavirus (Rota), rubella, and yellow fever (YF). The bars show the number of deaths averted (per 100,000 population) in each vaccination year. Error bars indicate 95% CI. The line shows the number of fully vaccinated persons (FVPs; in millions) achieved in each year's vaccination activities.

Appendix 6

The full list of countries included in this and the previous VIMC studies is provided in table **Appendix 6—table 1**

Appendix 6—table 1. 112 countries included in the analysis.

Those TRUE for gavi73 receive GAVI support; those TRUE for vimc98 were included in the previous VIMC-wide study (*Li et al., 2019*).

Country	Country name	gavi73	vimc98
AFG	Afghanistan	TRUE	TRUE
AGO	Angola	TRUE	TRUE
ALB	Albania	FALSE	TRUE
ARM	Armenia	TRUE	TRUE
AZE	Azerbaijan	TRUE	TRUE
BDI	Burundi	TRUE	TRUE
BEN	Benin	TRUE	TRUE
BFA	Burkina Faso	TRUE	TRUE
BGD	Bangladesh	TRUE	TRUE
BIH	Bosnia and Herzegovina	FALSE	TRUE
BLR	Belarus	FALSE	FALSE
BLZ	Belize	FALSE	TRUE
BOL	Bolivia, Plurinational State of	TRUE	TRUE
BTN	Bhutan	TRUE	TRUE
CAF	Central African Republic	TRUE	TRUE
CHN	China	FALSE	TRUE
CIV	Cote d'Ivoire	TRUE	TRUE
CMR	Cameroon	TRUE	TRUE
COD	Congo, the Democratic Republic of the	TRUE	TRUE
COG	Congo	TRUE	TRUE
COL	Colombia	FALSE	FALSE
COM	Comoros	TRUE	TRUE
CPV	Cabo Verde	FALSE	TRUE
CUB	Cuba	TRUE	TRUE
DJI	Djibouti	TRUE	TRUE
DZA	Algeria	FALSE	FALSE
ECU	Ecuador	FALSE	FALSE
EGY	Egypt	FALSE	TRUE
ERI	Eritrea	TRUE	TRUE
ETH	Ethiopia	TRUE	TRUE
FJI	Fiji	FALSE	TRUE
FSM	Micronesia, Federated States of	FALSE	TRUE
GEO	Georgia	TRUE	TRUE
GHA	Ghana	TRUE	TRUE
GIN	Guinea	TRUE	TRUE
GMB	Gambia	TRUE	TRUE
GNB	Guinea-Bissau	TRUE	TRUE
GTM	Guatemala	FALSE	TRUE

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Appendix 6—table 1 continued

Country	Country name	gavi73	vimc98
GUY	Guyana	TRUE	TRUE
HND	Honduras	TRUE	TRUE
HTI	Haiti	TRUE	TRUE
IDN	Indonesia	TRUE	TRUE
IND	India	TRUE	TRUE
IRN	Iran, Islamic Republic of	FALSE	FALSE
IRQ	Iraq	FALSE	TRUE
JAM	Jamaica	FALSE	FALSE
JOR	Jordan	FALSE	FALSE
KEN	Kenya	TRUE	TRUE
KGZ	Kyrgyzstan	TRUE	TRUE
KHM	Cambodia	TRUE	TRUE
KIR	Kiribati	TRUE	TRUE
LAO	Lao People's Democratic Republic	TRUE	TRUE
LBR	Liberia	TRUE	TRUE
LKA	Sri Lanka	TRUE	TRUE
LSO	Lesotho	TRUE	TRUE
MAR	Morocco	FALSE	TRUE
MDA	Moldova, Republic of	TRUE	TRUE
MDG	Madagascar	TRUE	TRUE
MHL	Marshall Islands	FALSE	TRUE
MKD	Macedonia, the former Yugoslav Republic of	FALSE	FALSE
MLI	Mali	TRUE	TRUE
MMR	Myanmar	TRUE	TRUE
MNG	Mongolia	TRUE	TRUE
MOZ	Mozambique	TRUE	TRUE
MRT	Mauritania	TRUE	TRUE
MWI	Malawi	TRUE	TRUE
NAM	Namibia	FALSE	FALSE
NER	Niger	TRUE	TRUE
NGA	Nigeria	TRUE	TRUE
NIC	Nicaragua	TRUE	TRUE
NPL	Nepal	TRUE	TRUE
PAK	Pakistan	TRUE	TRUE
PER	Peru	FALSE	FALSE
PHL	Philippines	FALSE	TRUE
PNG	Papua New Guinea	TRUE	TRUE
PRK	Korea, Democratic People's Republic of	TRUE	TRUE
PRY	Paraguay	FALSE	TRUE
PSE	Palestine, State of	FALSE	TRUE
RWA	Rwanda	TRUE	TRUE
SDN	Sudan	TRUE	TRUE

Continued on next page

Appendix 6—table 1 continued

Country	Country name	gavi73	vimc98
SEN	Senegal	TRUE	TRUE
SLB	Solomon Islands	TRUE	TRUE
SLE	Sierra Leone	TRUE	TRUE
SLV	El Salvador	FALSE	TRUE
SOM	Somalia	TRUE	TRUE
SRB	Serbia	FALSE	FALSE
SSD	South Sudan	TRUE	TRUE
STP	Sao Tome and Principe	TRUE	TRUE
SWZ	Swaziland	FALSE	TRUE
SYR	Syrian Arab Republic	FALSE	TRUE
TCD	Chad	TRUE	TRUE
TGO	Togo	TRUE	TRUE
THA	Thailand	FALSE	FALSE
TJK	Tajikistan	TRUE	TRUE
TKM	Turkmenistan	FALSE	TRUE
TLS	Timor-Leste	TRUE	TRUE
TON	Tonga	FALSE	TRUE
TUN	Tunisia	FALSE	TRUE
TUV	Tuvalu	FALSE	TRUE
TZA	Tanzania, United Republic of	TRUE	TRUE
UGA	Uganda	TRUE	TRUE
UKR	Ukraine	TRUE	TRUE
UZB	Uzbekistan	TRUE	TRUE
VEN	Venezuela, Bolivarian Republic of	FALSE	FALSE
VNM	Viet Nam	TRUE	TRUE
VUT	Vanuatu	FALSE	TRUE
WSM	Samoa	FALSE	TRUE
XK	Kosovo	FALSE	TRUE
YEM	Yemen	TRUE	TRUE
ZAF	South Africa	FALSE	FALSE
ZMB	Zambia	TRUE	TRUE
ZWE	Zimbabwe	TRUE	TRUE