



# World Health Organization

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

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**IVIR-AC – March 2021**

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

**MICROSOFT TEAMS - VIRTUAL MEETING**

WHO HEADQUARTERS, GENEVA, SWITZERLAND

1 to 5 March 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**

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**Xuan-yi Wang**, Research Scientist, Shanghai Medical College, Fudan University, **China**

**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:
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**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):**

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*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)*

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## **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**

**1-5 March 2021**

**[Draft list of participants](#)**

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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  
1-5 March 2021

*Background reading materials available at:* [https://worldhealthorg.sharepoint.com/sites/ws-VaccinesResearch/IVIR-AC/IVIR-AC\\_mar21/SitePages/Welcome.aspx](https://worldhealthorg.sharepoint.com/sites/ws-VaccinesResearch/IVIR-AC/IVIR-AC_mar21/SitePages/Welcome.aspx)

**Chair:** Walt Orenstein

1 March				
Duration	Title	Content and key questions to IVIR-AC	Purpose	Proposed speaker
12:00 - 12:05 5'	Opening of Meeting	<ul style="list-style-type: none"><li>Update on global strategies and issues of relevance to WHO</li></ul>	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"><li>Administrative issues</li><li>Objectives of IVIR-AC meeting and outline of the 1<sup>st</sup> day</li></ul>		P Lambach W Orenstein
12:15 - 12:25 10'	Background	<ul style="list-style-type: none"><li>Secretariat view</li><li>Technical background/Information needs from WHO SAGE to estimate impact of COVID-19 on immunization programs (for SAGE WG)</li></ul>		R Hutubessy
COVID 19 vaccine modelling				
12:25 - 12:35 10'	Background	<ul style="list-style-type: none"><li>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</li><li>Questions to IVIR-AC<ul style="list-style-type: none"><li>How should epidemiological and economic modelling evidence on COVID-19 vaccination be incorporated into SAGE's Evidence</li></ul></li></ul>	For decision	A Wilder-Smith

		<p>to Recommendations process, particularly for vaccine-specific recommendations (e.g., in which documents and E2R table criteria should this be reflected)?</p> <ul style="list-style-type: none"> <li>○ What additional modelling questions should the WHO SAGE Working Group and SAGE consider related to COVID-19 vaccination impacts in the short and medium term?</li> <li>○ What are the remaining critical evidence or quality gaps (methodological, data, other) related to COVID-19 vaccination impact modelling, considering the models identified by the Working Group through literature review, Request for Information, and Request for Proposals? How can these gaps be addressed?</li> <li>○ How should modelling of vaccination in combination with other COVID-19 interventions beyond SAGE's remit be addressed?</li> </ul>		
12:35 - 12:55 20'	Modeling advice to SAGE for vaccine prioritisation	<ul style="list-style-type: none"> <li>• Update on model review on prioritization of vaccination under limited vaccine supply based on Request for Information questions from July <ul style="list-style-type: none"> <li>○ Results from model review summarized by question, geography, model features</li> <li>○ Summary of evidence provided to SAGE to date on vaccine prioritisation and remaining evidence gaps</li> </ul> </li> </ul> <p><b>Background reading materials:</b> See Sharepoint</p>		N Grassly
12:55 - 13:10 15'	Q&A and review of modelling advice to SAGE on vaccine prioritisation	<ul style="list-style-type: none"> <li>• IVIR-AC discusses presentation, clarifies on content and provides feedback on strengths and weaknesses of models reviewed to date</li> </ul>		W Ndifon, J Leask
13:10 - 13:25 15'	Request for proposals (RfP) issued in January 2021	<ul style="list-style-type: none"> <li>• Update on the Request for Proposal (RFP) questions, including vaccination strategy questions beyond prioritization</li> </ul> <p><b>Background reading materials:</b> See Sharepoint</p>		N Grassly / S Pallas
13:25 - 13:45 20'	Q&A and review of key vaccine modelling questions	<ul style="list-style-type: none"> <li>• IVIR-AC discusses questions and identifies any additional priority areas for vaccine modelling not included in RfP</li> </ul>		W Ndifon, J Leask
13:45 - 14:30 45'	Break			

### Optimizing COVID 19 vaccine costing

14:30 - 14:40 10'	Background	<ul style="list-style-type: none"> <li>This session serves to inform IVIR-AC of the SAGE Evidence to Recommendations (E2R) "Resource Use" criterion for the vaccine-specific recommendations, and the tools and approaches to estimating resource needs for COVID-19 vaccination identified to date. <ul style="list-style-type: none"> <li>E2R questions: "Are the resources required small?" "Cost effectiveness?" "Is vaccine X a reasonable and efficient use of resources?"</li> <li>Considerations of perspective, intervention, and comparator (currently always placebo/no vaccination)</li> </ul> </li> <li>Questions to IVIR-AC <ul style="list-style-type: none"> <li>How should the Resource Use criterion in the Evidence to Recommendations process be interpreted and applied for SAGE's COVID-19 vaccine-specific recommendations (e.g., perspective, intervention, counterfactual)?</li> <li>Which types of estimation approaches and tools are most appropriate for global- and country-level costing and decision making around COVID-19 vaccination resource use?</li> </ul> </li> </ul> <p><b>Background reading materials:</b> See Sharepoint</p>	For information	R Hutubessy
14:40 - 14:55 15'	Costing	<ul style="list-style-type: none"> <li>For information: Country level and global costing</li> <li>Resource Use estimates: <ul style="list-style-type: none"> <li>ACT-A investment case resource needs estimates</li> <li>COVAX global-level resource needs estimates</li> <li>Country-level COVID-19 vaccination costing tool</li> <li>Other COVID-19 cost estimates from literature</li> </ul> </li> <li>Summary: <ul style="list-style-type: none"> <li>How should the available estimates be incorporated into SAGE COVID-19 vaccine-specific recommendations?</li> </ul> </li> </ul>		S Pallas

		<ul style="list-style-type: none"> <li>What types of cost and resource use estimates are still needed by SAGE?</li> </ul>		
14:55 - 15:25 30'	Q&A and discussion	<ul style="list-style-type: none"> <li>IVIR-AC discusses presentation, clarifies on content and acknowledges main issues</li> </ul>		W Ndifon, J Leask, S Verguet
15:25 - 15:35 10'	Wrap up	<ul style="list-style-type: none"> <li>Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session</li> </ul>	For information	W Orenstein, Chair

## 2 March

Duration	Title	Content and key questions to IVIR-AC	Purpose	Proposed speaker
12:00 - 12:05 5'	Introduction	<ul style="list-style-type: none"> <li>Recap of previous day and objectives for the day</li> </ul>	For information	W. Orenstein, Chair
<b>Measles Case Fatality Ratio (CFR) estimation</b>				
12:05 - 12:15 10'	Background	<ul style="list-style-type: none"> <li>Until now, WHO has used CFRs that have been established by a group of experts. However, in assessments of new data, actual measles CFRs have likely changed over time</li> <li>Several publications present methods for estimating measles CFR</li> <li>To allow for annual measles mortality estimation and measles deaths averted, IVIRAC is asked to provide advice on how to best leverage methods available</li> </ul> <p>Questions to IVIRAC</p> <ol style="list-style-type: none"> <li>What are the trade-offs between utilizing fixed estimates vs. adapting a dynamic methodology that can incorporate new information to provide time-varying, updatable estimates?</li> <li>What additional primary data are needed to refine the assessment of the effect measles vaccination programmes and other factors such as health care and nutritional status have on mortality in high-risk populations?</li> <li>Which future approach would result in best outputs in terms of incorporating new primary data, and what considerations would need to be given in terms of hosting model updates and refinements?</li> <li>In a concrete fashion, how to proceed with mortality estimates and IA203 deaths averted in (i) 2020 (time-sensitive), and (ii) beyond (for possible future discussion)?</li> </ol> <p><b>Background reading materials:</b> See Sharepoint</p>	For decision	K Kretsinger
12:15 - 12:30 15'	Methods and data available	<ul style="list-style-type: none"> <li>Currently available methods</li> <li>Requirements to CFR estimates</li> </ul>		M Ferrari

12:30 - 12:40 10'	Way forward: Possible upcoming methods for CFR estimation	<ul style="list-style-type: none"><li>Description of plan to update and refine recent CFR model, including incorporation of subnational estimates.</li></ul>		M Jit
12:40 - 13:10 30'	Q&A and discussion to inform IVIR-AC recommendations	<ul style="list-style-type: none"><li>Discuss/Recommend possible way forward for Measles CFR estimation</li><li>How could shortcomings of data available to inform CFRs be best managed to inform significant policy outputs.</li></ul>		P Luz, X Wang
13:10 - 14:00 50'	Break			
Overview of Vaccine Impact Modelling Consortium (VIMC)				
14:00 - 14:10 10'	Background	<ul style="list-style-type: none"><li>Vaccine Impact Modelling Consortium (VIMC) is a multinational collaboration of 16 research groups.</li><li>VIMC is funded by Gavi, the Vaccine Alliance and the Bill &amp; Melinda Gates Foundation, and is coordinated by a secretariat based at Imperial College London.</li></ul>	For information	Y Sim
14:10 - 14:30 20'	Technical presentation	<ul style="list-style-type: none"><li>Description of updated methodology and opportunities of alignment</li></ul> <p><b>Background reading materials:</b> see Sharepoint</p>		K Gaythorpe
14:30 - 14:50 20'	Q&A and Discussion	<ul style="list-style-type: none"><li>IVIR-AC discusses presentation, clarifies on content and acknowledges main issues</li></ul>		J Wu and JD Lelièvre
14:50 - 15:00 10'	Wrap up	<ul style="list-style-type: none"><li>Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session</li></ul>	For information	W. Orenstein, Chair

### 3 March

12:00 - 12:05 5'	Introduction	<ul style="list-style-type: none"><li>Recap of previous day and objectives for the day</li></ul>	For information	W. Orenstein, Chair
Meta-analysis of Economic Evaluations				
12:05 - 12:10 5'	Background	<ul style="list-style-type: none"><li>While meta-analyses are quite useful to quantitatively pool effect estimates from different RCTs to create more reliable estimates of the effectiveness of an intervention, their usefulness from a cost-effectiveness perspective is subject to scientific debate</li></ul> <p><b>Background reading materials:</b> See Sharepoint</p>	For information	R Hutubessy
12:10 - 12:30 20'	Meta-analysis of global literature on economic evaluation studies: Strengths and Criticisms	<ul style="list-style-type: none"><li>Based on several examples (Rota vaccine, herpes vaccine, anticoagulant, and diabetes medications) the value and limitations of use and methods of meta-analyses of economic evaluations will be presented</li></ul>		N Chaiyakunapruk A Thakkestian
12:30 - 13:00 30'	Q&A and Discussion	<ul style="list-style-type: none"><li>IVIR-AC discusses presentation, clarifies on content and acknowledges main issues</li></ul>		V Pitzer, S Verguet
13:00 - 13:45 45'	Break			
Influenza vaccine value proposition				
13:45 - 13:55 10'	The need for an influenza vaccine value proposition	<ul style="list-style-type: none"><li>Rationale for influenza vaccine value proposition and description of intended approach to shape the value proposition</li></ul>	For discussion	P Lambach
13:55 – 14:15 20'	Seasonal influenza vaccine use cases and country archetypes	<ul style="list-style-type: none"><li>Presentation of the work initiated (draft use cases for seasonal influenza vaccines and relevant country archetypes)</li></ul> <p><i>Question to IVIRAC: Does IVIRAC agree with the approach to defining use cases and country archetypes for seasonal influenza vaccination?</i></p> <p><b>Background reading materials:</b> See Sharepoint</p>		S Malvoti / C Mantel

14:15 - 14:35 20'	Q&A and Discussion	<ul style="list-style-type: none"> <li>IVIR-AC discusses presentation, clarifies on content and provides feedback/inputs to the use case definitions</li> </ul>		D Lyimo, M Jit
14:35 - 14:45 10'	Wrap up	<ul style="list-style-type: none"> <li>Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session</li> </ul>	For information	W Orenstein, Chair



## 4 March

IA2030 costing				
12:00 - 12:05 5'	Introduction	<ul style="list-style-type: none"> <li>Recap of previous day and objectives for the day</li> </ul>	For information	W. Orenstein, Chair
12:05 - 12:15 10'	Background	<ul style="list-style-type: none"> <li>Understanding the level of investment needed for the next decade is critical to mobilizing resources and developing effective strategies for IA2030</li> <li>WHO IVB is collaborating with partners to generate cost estimates for IA2030 for 194 Member States and target vaccines in alignment with impact estimates.</li> </ul>	For information	Y Sim
12:15 – 12:35 20'	Technical presentation	<ul style="list-style-type: none"> <li>Description of methodology and data</li> <li>Future steps for generating cost estimates to be reported at global and regional level</li> </ul> <p><i>Background reading materials: See Sharepoint</i></p>		B Patenaude
12:35 - 12:55 20'	Q&A and Discussion	<ul style="list-style-type: none"> <li>IVIR-AC discusses presentation, clarifies on content and acknowledges main issues</li> </ul>		JD Lelièvre and H Farooqui
12:55 - 13:05 10'	Wrap up	<ul style="list-style-type: none"> <li>Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session</li> </ul>	For information	W. Orenstein, Chair

5 March	
Closed session: IVIR-AC members only	
12:00 - 16:00	IVIR-AC reporting/recommendations

## **WER summary of last IVIRAC**



**World Health  
Organization**

**Organisation mondiale de la Santé**

# Weekly epidemiological record Relevé épidémiologique hebdomadaire

4 DECEMBER 2020, 95th YEAR / 4 DÉCEMBRE 2020, 95<sup>e</sup> ANNÉE

No 49, 2020, 95, 609–628

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

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- 623 L'OMS appelle à relancer la lutte contre le paludisme

## Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC)

### Summary and recommendations, September 2020

The IVIR-AC recommendations reported below are based on deliberations held during a virtual meeting on 21–25 September 2020. A detailed version of these recommendations and the session background and discussions can be found at: [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.html](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.html)

### Generic recommendation

As at previous meetings, IVIR-AC reviewed successful research projects by multidisciplinary research groups in which multiple institutions who previously worked independently in an area collaborated. As a generic recommendation, IVIR-AC encourages research groups to continue productive collaborations and potentially build further on successful formats, such as those of the *Enteric burden of disease project* and the *Vaccine delivery cost consensus statement initiative*. Specifically, community of practices are encouraged for guideline development to standardize research methods, research workshops and project websites.

### Session 1a: COVID-19: Risk of SARS-CoV-2 transmission with different immunization services

#### Introduction

The global COVID-19 pandemic has disrupted both surveillance and immuni-

## Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC)

### Résumé et recommandations, septembre 2020

Les recommandations de l'IVIR-AC présentées ci-dessous sont fondées sur les délibérations qui se sont tenues lors d'une réunion virtuelle du 21 au 25 septembre 2020. Une version détaillée de ces recommandations ainsi que le contexte et les discussions de la session peuvent être consultés à l'adresse [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.html](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.html)

### Recommandation générale

Comme lors des réunions précédentes, l'IVIR-AC a examiné des projets de recherche menés avec succès par des groupes de recherche multidisciplinaires auxquels ont participé plusieurs institutions qui travaillaient auparavant de manière indépendante dans un domaine donné. À titre de recommandation générale, l'IVIR-AC encourage les groupes de recherche à poursuivre leurs collaborations fructueuses et à s'inspirer éventuellement des formats qui ont fait leurs preuves, comme ceux du projet sur la charge des maladies entériques (*Enteric burden of disease project*) et de l'initiative de déclaration consensuelle sur les coûts de la délivrance des vaccins (*Vaccine delivery cost consensus statement initiative*). Plus précisément, les communautés de pratique sont encouragées à élaborer des lignes directrices afin de standardiser les méthodes de recherche, les ateliers de recherche et les sites Web des projets.

### Session 1a: COVID-19: risque de transmission du SARS-CoV-2 avec différents services de vaccination

#### Introduction

La pandémie mondiale de COVID-19 a perturbé les services de surveillance et de

zation services in nearly all countries. In March 2020, WHO identified immunization as an essential health service<sup>1</sup> to be prioritized and safeguarded for continuity during the COVID-19 pandemic. At the same time, WHO emphasized the need to adapt vaccine delivery strategies in order to conduct them under safe conditions without undue risk of SARS-CoV-2 transmission to health workers (HWs) and the community. In order to clarify the risk of transmission of SARS-CoV-2 to HWs and the community and to inform safe approaches for vaccination, a key question with 3 components was posed for modelling:

What is the risk of SARS-CoV-2 transmission to communities and to HWs?

- 1) in settings with various burdens of COVID-19,
- 2) under different health service delivery conditions (e.g. routine immunization via fixed-site, outreach and schools; mass vaccination campaigns either fixed-site or door-to-door), and
- 3) in consideration of the nature and extent of infection prevention control (IPC) implemented?

The Committee was asked whether the model is robust and whether it fully addresses the question of risk of SARS-CoV-2 transmission to HWs and the community; they were also asked about the assumption of children's transmission risk and how to extrapolate results to other countries.

### Recommendations

- The model partially answers the key analytical question on COVID-19 transmission, within the scope of its design. Knowledge and information are, however, lacking due to limited empirical evidence and understanding of COVID transmission (e.g. the effectiveness of different IPC measures in practice and the relative risk of transmission to HWs). Both empirical and modelling evidence are still required to determine the necessary considerations for delivering vaccines thorough supplementary immunization activities (SIAs) and routine immunization programmes. Some of these issues are being addressed in other work.
- The risk of transmission to HWs depends on their relative exposure to COVID-19 cases (the input parameter *relative acquisition and transmission rate (RATR)* in the model). The model can be used to translate RATR into risk of transmission, but the study is not designed to estimate the likely values of RATR. Location-specific empirical evidence on the relative risk of SARS-Cov-2 transmission to HWs is required to assess the corresponding absolute risk.

vaccination dans presque tous les pays. En mars 2020, l'OMS a identifié la vaccination comme un service de santé essentiel à prioriser et à préserver pour en assurer la continuité pendant la pandémie COVID-19.<sup>1</sup> Dans le même temps, l'OMS a souligné la nécessité d'adapter les stratégies de délivrance des vaccins afin de les mener dans des conditions sûres, sans risque indu de transmission du SARS-CoV-2 aux agents de santé et à la communauté. Afin de clarifier le risque de transmission du SARS-CoV-2 aux agents de santé et à la communauté et d'éclairer les approches sûres en matière de vaccination, une question clé à 3 composantes a été posée en vue de la modélisation:

Quel est le risque de transmission du SARS-CoV-2 aux communautés et aux agents de santé?

- 1) dans des contextes où la charge de la COVID-19 est variable;
- 2) dans différentes conditions de prestation des services de santé (vaccination systématique sur sites fixes, vaccination de proximité, dans les écoles; campagnes de vaccination de masse sur sites fixes ou de porte-à-porte); et
- 3) compte tenu de la nature et de l'étendue des mesures de lutte contre les infections mises en œuvre?

Il a été demandé au Comité si le modèle était robuste et s'il répondait pleinement à la question du risque de transmission du SARS-CoV-2 aux agents de santé et à la communauté; il a également été interrogé sur l'hypothèse du risque de transmission des enfants et sur la manière d'extrapoler les résultats à d'autres pays.

### Recommandations

- Ce modèle répond en partie à la question analytique clé sur la transmission de la COVID-19, dans le cadre de sa conception. Toutefois, les connaissances et l'information font défaut en raison du manque de données empiriques et de compréhension de la transmission du virus de la COVID-19 (par exemple l'efficacité des différentes mesures de lutte anti-infectieuse dans la pratique et le risque relatif de transmission aux agents de santé). Davantage de données empiriques et de données de modélisation sont nécessaires pour déterminer les éléments à prendre en compte pour la délivrance des vaccins dans le cadre des activités de vaccination supplémentaire (AVS) et des programmes de vaccination systématique. Certaines de ces questions sont abordées dans d'autres travaux.
- Le risque de transmission aux agents de santé dépend de leur exposition relative aux cas de COVID-19 (le paramètre d'entrée appelé *taux relatif d'acquisition et de transmission* dans le modèle). Le modèle peut être utilisé pour traduire ce taux en risque de transmission, mais l'étude n'est pas conçue pour estimer les valeurs probables du taux relatif d'acquisition et de transmission. Des données empiriques propres aux différents sites de vaccination sur le risque relatif de transmission du SARS-CoV-2 aux agents de santé sont nécessaires pour évaluer le risque absolu correspondant.

<sup>1</sup> See <https://apps.who.int/iris/handle/10665/331590>

<sup>1</sup> Voir <https://apps.who.int/iris/handle/10665/275799>

- The main conclusions on community impact are robust (i.e. that the risk of additional COVID-19 infections associated with routine immunization or SIAs is small, a <2% increase in incidence of total COVID-19 infections). Yet, this will vary by context and setting.
- Conclusions on HWs should be interpreted as policy guidance rather than precise projections, because of uncertainty in the RATR. RATRs should also be considered important input variables in various scenarios.
- Particular caution should be exercised for SIAs in areas with high COVID-19 prevalence. IPC for HWs should be maximized (subject to the local resources) in order to avoid viral introduction.
- Children were assumed to be 55% less susceptible to infection and 15% less infectious than adults from published estimates. These assumptions are reasonable (i.e. based on the best currently available evidence) but not necessarily conservative. Depending on the percentage of children in the population, the primary outcome (i.e. cumulative number of infections per 1000 vaccinated) could increase by up to 2–3 times if age had no effect on susceptibility and infectiousness (i.e. children are as susceptible and contagious as older people).
- The communication of uncertainties in results, including the range of outcomes and corresponding parameters, should be improved.
- The primary results could be more clearly presented and communicated, e.g. the community impact should be presented as the percentage increase in the cumulative number of infections (in addition to the number of cases per 1000 vaccinations).
- The results for the 6 countries analysed should be summarized and plotted in terms of the percentages of rural and urban and the percentage of the population aged <15 years, with the characteristics of other countries not included in the modelling exercise to facilitate extrapolation to other countries.

## Session 2: Frameworks and methods to guide COVID-19 vaccine development

### Introduction

In the initial phases of COVID-19 vaccine roll-out, vaccine constraints will probably necessitate prioritization of population groups for vaccination. The aim of the COVID-19 Vaccine Impact Modelling Subgroup of the Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on COVID-19 Vaccines is to provide high-quality modelling guidance to inform policy recommendations for prioritization that will achieve the maximum public health impact with a limited vaccine supply.

- Les principales conclusions concernant l'impact sur la communauté sont solides (à savoir que le risque d'infections supplémentaires par le virus de la COVID-19 associées à la vaccination systématique ou aux AVS est faible, l'augmentation de l'incidence des infections étant <2%). Pourtant, cela varie selon le contexte et le site de vaccination.
- Les conclusions relatives aux agents de santé doivent être interprétées comme des orientations stratégiques plutôt que comme des projections précises, en raison de l'incertitude concernant le taux relatif d'acquisition et de transmission. Ce taux doit également être considéré comme une variable d'entrée importante dans les divers scénarios.
- Il convient d'être particulièrement prudent en ce qui concerne les AVS menées dans des zones où la prévalence de la COVID-19 est élevée. La lutte anti-infectieuse pour protéger les agents de santé doit être renforcée (si ressources locales le permettent) afin d'éviter l'introduction du virus.
- Selon les estimations publiées, la sensibilité à l'infection et l'infectiosité des enfants seraient inférieure de 55% et de 15%, respectivement, à celles des adultes. Ces hypothèses sont raisonnables (c'est-à-dire fondées sur les meilleures données actuellement disponibles) mais pas nécessairement prudentes. Selon le pourcentage d'enfants dans la population, le résultat principal (c'est-à-dire le nombre cumulé d'infections pour 1000 personnes vaccinées) pourrait être multiplié par 2 ou 3 si l'âge n'avait aucun effet sur la sensibilité et l'infectiosité (autrement dit si les enfants étaient aussi sensibles et contagieux que les personnes plus âgées).
- La communication des incertitudes dans les résultats, notamment les plages des résultats et les paramètres correspondants, doit être améliorée.
- Les résultats principaux pourraient être présentés et communiqués plus clairement; par exemple l'impact sur la communauté devrait être présenté comme l'augmentation en pourcentage du nombre cumulé d'infections (en plus du nombre de cas pour 1000 personnes vaccinées).
- Les résultats des 6 pays analysés devraient être résumés et rapportés aux pourcentages de la population rurale et urbaine et au pourcentage de la population âgée de <15 ans, en excluant de l'exercice de modélisation les caractéristiques d'autres pays afin de faciliter l'extrapolation à d'autres pays.

## Session 2: Cadres et méthodes pour guider la mise au point de vaccins contre la COVID-19

### Introduction

Au cours des premières phases du déploiement des vaccins anti-COVID-19, l'approvisionnement limité en vaccins nécessitera probablement de déterminer des groupes de population prioritaires pour la vaccination. L'objectif du sous-groupe 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 (SAGE) sur la vaccination est de fournir des conseils de modélisation de qualité pour éclairer les recommandations stratégiques relatives à l'établissement des priorités de vaccination en vue d'obtenir le maximum d'impact sur la santé publique dans le contexte d'un approvisionnement limité en vaccins.



A request for information (RFI) to modellers and economists included an initial set of prioritized modelling questions.<sup>2</sup> More than 20 modelling groups responded to the RFI that could address different use case scenarios in high- and low-to middle-income countries. The Committee was asked to identify any additional criteria for modelling optimal deployment of the vaccine, the pressing knowledge gaps that remain to be addressed and how the IVIR-AC committee could be involved.

## Recommendations

- The Committee recommends that more modelling work on impacts on equity be commissioned. It is important to consider people who are disproportionately affected by COVID-19 because of reduced access to health care, lockdowns, income loss and other impacts. National and global equity are noted as values in the *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination*.<sup>3</sup>
- Model structures should be validated. Decision-makers should prioritize model structures that are demonstrably sufficient to reproduce relevant epidemiological dynamics and (if used as counterfactuals) the effects of non-pharmaceutical interventions.
- Encourage modellers to quantify and report the uncertainty (or inadequacy) of their models whenever possible.
- An objective approach should be used to grade models when synthesizing the outputs of different models, such as assigning posterior probabilities to models given some observations and using the probabilities in a weighting scheme.
- The Committee recommends that models include the impact outcome measures of interest when vaccines are preferentially targeted to the best-connected places in countries and/or the best-connected individuals.
- WHO should take a proactive approach by identifying modellers in RFIs and requesting models that provide the knowledge required for decision-making.
- The Committee can support any future review processes and assessments of the quality of modelling by providing:
  - ongoing review as the work progresses,
  - participation in a working group to be established as necessary,

Une demande d'information adressée aux modélisateurs et aux économistes comprenait une première série de questions de modélisation classées par ordre de priorité.<sup>2</sup> Plus de 20 groupes de modélisation ont répondu à cette demande qui pouvait porter sur différents scénarios d'utilisation dans les pays à revenu élevé et dans les pays à revenu faible ou intermédiaire. Il a été demandé à l'IVIR-AC d'identifier tout critère supplémentaire pour modéliser le déploiement optimal des vaccins, les lacunes pressantes en matière de connaissances qui restent à combler et la façon dont le Comité pourrait être impliqué.

## Recommandations

- Le Comité recommande de faire réaliser d'autres travaux de modélisation des effets sur l'équité. Il est important de tenir compte des personnes qui sont touchées de manière disproportionnée par la COVID-19 en raison d'un accès limité aux soins de santé, du confinement, de pertes de revenus et d'autres répercussions. L'équité nationale et l'équité mondiale sont considérées comme des valeurs dans le *Cadre de valeurs du SAGE de l'OMS pour l'attribution des vaccins anti-COVID-19 et la détermination des groupes à vacciner en priorité*.<sup>3</sup>
- Les structures des modèles doivent être validées. Les décideurs doivent donner la priorité aux structures de modèles dont il est démontré qu'elles sont suffisantes pour reproduire une dynamique épidémiologique pertinente et, s'ils sont utilisés comme éléments de comparaison, les effets des interventions non pharmaceutiques.
- Il convient d'encourager les modélisateurs à quantifier et à communiquer l'incertitude (ou l'insuffisance) de leurs modèles chaque fois que cela est possible.
- Une approche objective doit être utilisée pour classer les modèles lors de la synthèse des résultats des différents modèles, par exemple en attribuant des probabilités postérieures aux modèles en fonction de certaines observations et en utilisant ces probabilités dans un schéma de pondération.
- Le Comité recommande d'inclure dans les modèles les mesures d'impact qui présentent un intérêt lorsque la vaccination cible de préférence les lieux les mieux connectés des pays et/ou les personnes les mieux connectées.
- L'OMS devrait adopter une approche proactive en identifiant les modélisateurs dans les demandes d'information et en requérant des modèles qui fournissent les connaissances nécessaires à la prise de décisions.
- Le Comité peut appuyer les processus d'examen et les évaluations de la qualité de la modélisation futurs en fournissant:
  - un examen continu au fur et à mesure de l'avancement des travaux;
  - la participation à un groupe de travail à mettre en place si besoin;

<sup>2</sup> See [https://www.who.int/immunization/policy/sage/SAGE\\_WG\\_COVID19\\_Vaccines\\_Modelling\\_Questions\\_31July2020.pdf?ua=1](https://www.who.int/immunization/policy/sage/SAGE_WG_COVID19_Vaccines_Modelling_Questions_31July2020.pdf?ua=1)

<sup>3</sup> See [https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE\\_Framework-Allocation\\_and\\_prioritization-2020.1-eng.pdf?sequence=1&isAllowed=y](https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_prioritization-2020.1-eng.pdf?sequence=1&isAllowed=y)

<sup>2</sup> Voir [https://www.who.int/immunization/policy/sage/SAGE\\_WG\\_COVID19\\_Vaccines\\_Modelling\\_Questions\\_31July2020.pdf?ua=1](https://www.who.int/immunization/policy/sage/SAGE_WG_COVID19_Vaccines_Modelling_Questions_31July2020.pdf?ua=1)

<sup>3</sup> Voir <https://apps.who.int/iris/bitstream/handle/10665/336541>

- ad hoc advice from individual IVIR-AC members,
- support in ongoing grading exercises and
- guidance on mathematical approaches for synthesizing outputs from different models to inform policy recommendations by SAGE.

### Session 3: WHO/UNICEF estimates of national immunization coverage (WUENIC 2.0)

#### Introduction

Since 2000, WHO and UNICEF have produced the WHO/UNICEF *Estimates of national immunization coverage* (WUENIC) with a rule-based method first developed in 1999. Although WUENIC has expanded and improved over time, it is still challenged to produce credible estimates for all current use cases. A plan to identify alternative or complementary methods was presented to IVIR-AC in March and September 2019. For the present meeting, 3 modelling approaches to estimating national immunization coverage were evaluated, presented and compared. The Committee was asked to highlight the pros and cons of each modelling approach and to advise which model they would recommend to replace and/or complement WUENIC.

#### Recommendations

- The Committee cannot recommend a single approach, as each has unique benefits.
- Efforts should be made to improve and promote national data collection, quality assurance, analytical capacity, utilization and buy-in.
- Efforts should be made to ensure the transparency and understandability of all approaches, including the current WUENIC approach and the proposed modelling approaches.
- Data inputs should be clear and presented with model estimates.
- Multiple models may be desirable, although forcing model convergence should be avoided. Multiple estimates may cause confusion at country level, which should also be avoided.
- Estimates from the Institute of Health Metrics and Evaluation (IHME), external work to provide coverage estimates in the context of the Global Burden of Disease (GBD)<sup>4</sup> initiative, could serve as good comparators.
- The potential for a “hybrid approach” (rule-based complemented by modelling) should be further explored.

- des conseils ad hoc de membres individuels de l'IVIR-AC;
- un soutien dans les exercices de classement en cours; et
- des conseils sur les approches mathématiques permettant de synthétiser les résultats de différents modèles afin d'éclairer les recommandations stratégiques du SAGE.

### Session 3: Estimations UNICEF/OMS de la couverture vaccinale nationale (WUENIC 2.0)

#### Introduction

Depuis 2000, l'OMS et l'UNICEF produisent les *estimations OMS/UNICEF de la couverture vaccinale nationale* (WUENIC) à l'aide une méthode basée sur des règles, mise au point pour la première fois en 1999. Bien que ces estimations se soient élargies et améliorées au fil du temps, il est toujours difficile de produire des estimations crédibles valables pour tous les cas d'utilisation actuels. Un plan visant à identifier d'autres méthodes ou des méthodes complémentaires a été présenté à l'IVIR-AC en mars et septembre 2019. Dans le cadre de la présente réunion, 3 approches de modélisation pour l'estimation de la couverture vaccinale nationale ont été évaluées, présentées et comparées. Il a été demandé au Comité de mettre en évidence les avantages et les inconvénients de chaque approche de modélisation et d'indiquer le modèle qu'il recommanderait pour remplacer et/ou compléter les WUENIC.

#### Recommandations

- Le Comité ne peut recommander une seule approche, car chacune de ces approches présente des avantages uniques.
- Des efforts doivent être déployés pour améliorer et promouvoir la collecte des données nationales, l'assurance de la qualité, la capacité analytique, l'utilisation et l'adhésion.
- Des efforts doivent être faits pour assurer la transparence et la compréhensibilité de toutes les approches, y compris l'approche actuellement utilisée pour établir les WUENIC et les approches de modélisation proposées.
- Les données d'entrée doivent être claires et présentées avec les estimations des modèles.
- Il peut être souhaitable d'utiliser plusieurs modèles, mais il faut éviter de forcer la convergence des modèles. Les estimations multiples peuvent être source de confusion au niveau des pays, ce qui doit également être évité.
- Les estimations de l'Institute of Health Metrics and Evaluation (IHME), des travaux extérieurs visant à fournir des estimations de la couverture dans le cadre de l'initiative Global Burden of Disease, pourraient constituer de bons comparateurs.<sup>4</sup>
- La possibilité d'une «approche hybride» (approche basée sur des règles complétée par la modélisation) devrait être explorée plus avant.

<sup>4</sup> See <https://www.thelancet.com/gbd>

<sup>4</sup> Voir <https://www.thelancet.com/gbd>



## Session 4: Microarray patches with measles–rubella vaccine

### Introduction

Microarray patches (MAPs) with measles-rubella vaccine (MR) could significantly ease logistical challenges faced by low- and middle-income countries (LMICs) with the existing presentation (5- or 10-dose lyophilized vial, cold chain required, high wastage, needle reconstitution and vaccine administration). MR-MAPs could thus contribute to significant progress towards MR elimination by facilitating delivery and administration to hard-to-reach populations; however, they have been slow to advance to the clinic.

IVIR-AC was presented with the results of an analysis to identify, evaluate and validate cases of delivery of MR-MAPs and a proposed approach to estimating their size. A landscaping analysis was conducted to identify 6 use cases to deliver MR-MAPs. Surveys and interviews were conducted with immunization programme managers in several countries and MR experts to validate the 6 potential use cases. IVIR-AC was asked to evaluate the findings and endorse the proposed approach to identifying, verifying and determining the size of the 6 use cases.

### Recommendations

- The Committee agrees that the use cases for MR-MAPs (U1: Delivery by HW or CHW in fixed post, U2: Outreach delivery by HW, U3: Outreach delivery by CHW, U4: Delivery by CHW in their “home” community, U5: Self-administration with HW or CHW assistance, U6: Self-administration without assistance) are appropriate, and the approach is systematic and scientific.
  - Consider including adults in the definition and potential sizes of use cases of self-administration of MR-MAPs (use cases 5 and 6).
- The description of the method of the survey should include the demographics and the role of the respondents in more detail and give numbers, possibly some quantitative validation of how representative the respondents are and hence the validity of the findings.
- The assessment of use cases, and their relative importance, is dynamic and should be reviewed between now and 2030, when there are shifts in the MR-MAP environment, such as:
  - additional end-user acceptability and feasibility of self-administration studies that may bring a new perspective;
  - changes in measles incidence and progress towards elimination;

## Session 4: Timbres à micro-aiguilles contenant le vaccin antirougeoleux-antirubéoleux

### Introduction

Les timbres à micro-aiguilles contenant le vaccin contre la rougeole et la rubéole (vaccin RR) pourraient atténuer considérablement les difficultés logistiques auxquelles sont confrontés les pays à revenu faible ou intermédiaire avec le conditionnement existant (flacon lyophilisé de 5 ou 10 doses, chaîne du froid requise, gaspillage important, reconstitution des aiguilles et administration du vaccin). Ces timbres à micro-aiguilles pourraient donc contribuer à des progrès significatifs vers l'élimination de la rougeole et de la rubéole en facilitant la fourniture et l'administration des vaccins aux populations difficiles à atteindre; cependant, leur utilisation progresse lentement dans les dispensaires.

Les résultats d'une analyse visant à identifier, évaluer et valider les scénarios d'utilisation des timbres à micro-aiguilles contenant le vaccin RR ont été présentés à l'IVIR-AC, ainsi qu'une proposition d'approche pour estimer leur ampleur. Une analyse du paysage a été effectuée afin d'identifier 6 scénarios d'utilisation des timbres à micro-aiguilles contenant le vaccin RR. Des enquêtes et des entretiens ont été menés avec les responsables des programmes de vaccination dans plusieurs pays et des experts vaccination antirougeoleuse et antirubéoleuse pour valider les 6 scénarios d'utilisation potentiels. Il a été demandé à l'IVIR-AC d'évaluer les résultats et d'approuver l'approche proposée pour identifier, vérifier et déterminer l'ampleur des 6 scénarios.

### Recommendations

- Le Comité convient que les scénarios d'utilisation des timbres à micro-aiguilles contenant le vaccin RR (U1: Administration par un agent de santé ou un agent de santé communautaire sur site fixe, U2: Administration de proximité par un agent de santé, U3: Administration de proximité par un agent de santé communautaire, U4: Administration par un agent de santé communautaire dans leur propre communauté, U5: Autoadministration assistée par un agent de santé ou un agent de santé communautaire, U6: Autoadministration sans assistance) sont appropriés, et que l'approche est systématique et scientifique.
  - Il convient d'envisager d'inclure les adultes dans la définition et l'ampleur potentielle des scénarios d'autoadministration (scénarios d'utilisation 5 et 6).
- La description de la méthode de l'enquête devrait inclure les données démographiques et le rôle des répondants de manière plus détaillée et donner des chiffres, éventuellement une validation quantitative de la représentativité des répondants et donc de la validité des résultats.
- L'évaluation des scénarios d'utilisation et leur ampleur relative sont dynamiques et devraient être réexaminées d'ici à 2030, quand l'environnement des timbres à micro-aiguilles contenant le vaccin RR aura évolué, par exemple:
  - des études supplémentaires sur l'acceptabilité par l'utilisateur final et la faisabilité de l'autoadministration qui peuvent apporter une nouvelle perspective;
  - des changements dans l'incidence de la rougeole et des progrès vers son élimination;

- data on the underlying assumptions;
- supplementary analyses;
- confidence in patch technology and awareness and demand from the community,
- updated data on the conditions of practical use of the vaccines; and
- possible interest from high-income countries in the technology, in view of its unique benefits, which may offset the lower procurement costs expected in LMICs and offer a return in investment.
- IVIR-AC provides insights and suggestions on the overall method for calculating the size of each use case:
  - The choice of countries and proposed groupings may be appropriate and focus on the greatest public health need.
  - Consider the shift from needle-syringe vaccination to MR-MAPs as it evolves over time, rather than incrementally, to assess access to previously unreachable populations with standard technologies.
  - Evaluate the feasibility of establishing novel financing or procurement mechanisms for MR-MAPs to incentivize MR-MAP product development. In particular, consider the implications of a globally or regionally coordinated switch to MR-MAPs (similar to the switch from oral to inactivated polio vaccine), which may release further financing and enable economies of scale.
  - Consider future market research to validate the assumptions derived from the use case, demand size exercise (e.g. SIA versus routine immunization; outreach versus fixed post).
- General comment:
  - The effectiveness of total systems should be considered (e.g. less wastage, easier use, savings in delivery cost vs willingness to pay) to fully assess the economic trade-offs in where and how MR-MAPs are used. This will be crucial to move from a directional demand-sizing exercise that proposes potential ranges, to a demand-forecast model.
  - It will be important to incentivize potential manufacturers with these supplementary data to encourage investment in the development of MAPs, as many are currently profiting from traditional delivery systems (e.g. needle and syringe).
- des données sur les hypothèses sous-jacentes;
- des analyses complémentaires;
- la confiance dans la technologie des timbres, la sensibilisation et la demande de la communauté;
- des données actualisées sur les conditions d'utilisation pratique des vaccins; et
- l'intérêt éventuel des pays à revenu élevé pour cette technologie, compte tenu de ses avantages uniques, qui peuvent compenser la baisse des coûts d'achat prévue dans les pays à revenu faible et intermédiaire et offrir un retour sur investissement.
- L'IVIR-AC fournit des éclairages et des suggestions sur la méthode globale de calcul de l'ampleur de chaque scénario d'utilisation:
  - Le choix des pays et des propositions de regroupements peuvent être appropriés et se concentrer sur les besoins les plus importants en matière de santé publique.
  - Le passage de la vaccination antirougeoleuse et antirubéoleuse au moyen d'une seringue avec aiguille à la vaccination par le timbre à micro-aiguilles doit être envisagé en fonction de son évolution, plutôt que de manière progressive, afin d'évaluer l'accès à des populations auparavant inaccessibles avec des technologies standard.
  - La faisabilité de la mise en place de nouveaux mécanismes de financement ou d'achat pour les timbres à micro-aiguilles contenant le vaccin RR doit être évaluée afin d'encourager le développement de ces produits. En particulier, il convient d'examiner les implications d'un passage coordonné à l'échelle mondiale ou régionale aux timbres à micro-aiguilles contenant le vaccin RR (semblable au passage du vaccin antipoliomyélitique oral au vaccin antipoliomyélitique inactivé), qui peut libérer d'autres financements et permettre des économies d'échelle.
  - Une future étude de marché pour valider les hypothèses dérivées du scénario d'utilisation et un exercice portant sur l'ampleur de la demande (par exemple en comparant les AVS et la vaccination systématique ou la vaccination de proximité et la vaccination sur site fixe) doivent être envisagés.
- Observation générale:
  - L'efficacité des systèmes dans leur ensemble doit être prise en compte (par exemple moins de gaspillage, utilisation plus facile, économies sur les coûts de la délivrance par rapport à la disposition à payer) afin d'évaluer pleinement les compromis économiques concernant le lieu d'utilisation et la manière d'administrer les timbres à micro-aiguilles contenant le vaccin RR. Cela sera crucial pour passer d'un exercice directionnel de dimensionnement de la demande qui propose des fourchettes possibles à un modèle de prévision de la demande.
  - Il sera important de motiver les fabricants potentiels avec ces données supplémentaires afin d'encourager l'investissement dans le développement des timbres à micro-aiguilles, car beaucoup d'entre eux tirent actuellement profit des systèmes d'administration traditionnels (par exemple seringue avec aiguille).

## Session 5: RTS,S malaria vaccine

### Introduction

Data from the pilot evaluation of RTS,S malaria vaccine will probably be reviewed for policy considerations in late 2021. IVIR-AC previously recommended that an economic analysis with a sequential approach not be used to introduce individual malaria control interventions until a coverage threshold is reached, as this is not a real-world scenario on which to base policy.

The Committee was asked, in the context of the forthcoming policy review, for advice on use of WHO Choosing Interventions that are Cost-Effective (CHOICE)/Generalized Cost-Effectiveness Analyses (GCEA) to inform future economic analysis of the RTS,S vaccine as part of a package of malaria interventions (including currently recommended interventions).

### Recommendations

- GCEA should be considered with other approaches, e.g. incremental CEA and probabilistic uncertainty analysis, as well as other considerations in decision-making (e.g. equity, budget impact analysis, acceptability).
- Stand-alone incremental CEA with probabilistic uncertainty analysis and a societal perspective might also be required to assess the full value of vaccine.
- Human capital approach-based assessment may be adopted to measure the impact of RTS,S on broader outcomes such as school attendance and labour supply.
- The budget impact requires careful consideration, as the immunization programmes in many LMICs are funded from different national and/or international financing streams, in contrast to other malaria interventions.
- Careful attention should be paid to accounting for non-linear interactions of interventions (in dynamic models) to estimate incidence under the “null scenario” and to evaluate the iterative effects of adding interventions
- Generic malaria control interventions generally affect all vector-borne diseases and have broader outcomes.
- Details of the dynamic model used to predict the impact of interventions should be included and explained. Multiple models might be considered (e.g. sensitivity analysis of the dynamic structure).
- Model transparency and the reproducibility of results should be given preference over complexity.
- Communication of the results to decision-makers and other stakeholder will require careful consideration, given the GCEA perspective.
- In line with previous recommendations, IVIR-AC restates that additional models with a sequential design would not be helpful for public health deci-

## Session 5: Vaccin antipaludique RTS,S

### Introduction

Les données de l'évaluation pilote du vaccin antipaludique RTS,S seront probablement examinées à la fin de 2021 en vue de formuler des considérations stratégiques. L'IVIR-AC avait précédemment recommandé de ne pas utiliser une analyse économique avec approche séquentielle pour introduire des interventions individuelles de lutte contre le paludisme avant qu'un seuil de couverture ne soit atteint, car il ne s'agit pas d'un scénario réel sur lequel fonder la politique.

Il a été demandé au Comité, dans le contexte du prochain examen des politiques, de donner son avis sur l'utilisation des analyses de rentabilité des interventions WHO-CHOICE/Generalized Cost-Effectiveness Analyses (GCEA) pour éclairer l'analyse économique future du vaccin RTS,S dans le cadre d'un ensemble d'interventions contre le paludisme (y compris les interventions actuellement recommandées).

### Recommandations

- Les GCEA devraient être envisagées avec d'autres approches, par exemple l'analyse coût-efficacité différentielle et l'analyse probabiliste de l'incertitude, ainsi que d'autres considérations dans la prise de décisions (par exemple l'équité, l'analyse de l'impact budgétaire, l'acceptabilité).
- Une analyse coût-efficacité différentielle autonome avec une analyse probabiliste de l'incertitude et une perspective sociétale pourrait également être nécessaire pour évaluer la pleine valeur du vaccin.
- L'évaluation fondée sur l'approche du capital humain peut être adoptée pour mesurer l'impact du vaccin RTS,S sur des résultats plus larges tels que la fréquentation scolaire et l'offre de main-d'œuvre.
- L'impact budgétaire nécessite un examen attentif, car les programmes de vaccination dans de nombreux pays à revenu faible ou intermédiaire sont financés à partir de différentes sources de financement nationaux et/ou internationaux, contrairement à d'autres interventions contre le paludisme.
- Il convient d'accorder une attention particulière à la prise en compte des interactions non linéaires des interventions (dans les modèles dynamiques) afin d'estimer l'incidence dans le cadre du «scénario néant» et d'évaluer les effets itératifs de l'ajout d'interventions.
- Les interventions générales de lutte contre le paludisme affectent généralement toutes les maladies à transmission vectorielle et produisent des résultats plus étendus.
- Les détails du modèle dynamique utilisé pour prédire l'impact des interventions doivent être inclus et expliqués. Plusieurs modèles peuvent être envisagés (par exemple une analyse de sensibilité de la structure dynamique).
- La transparence des modèles et la reproductibilité des résultats doivent être privilégiées par rapport à la complexité.
- La communication des résultats aux décideurs et aux autres parties prenantes devra être soigneusement étudiée, compte tenu du point de vue des GCEA.
- Conformément aux recommandations précédentes, l'IVIR-AC réaffirme que d'autres modèles à conception séquentielle ne seraient pas utiles pour la prise de décisions en matière

sion-making, as they do not reflect implementation in the real world.

## Session 6: Vaccine costing

### Introduction

Methods for costing vaccine delivery are not currently standardized, which limits the clarity and reliability of the results, leading to misinterpretation. In March 2018, IVIR-AC recommended that the WHO guidance for estimating costs of new vaccines be updated, and a working group evaluated WHO and external guidelines. Multiple discrepancies in workstreams, definitions and guidelines demonstrated that a standardized costing approach should be developed and documented that included the input and agreement on terms and processes of all the groups that are currently working on methods or guidelines for costing vaccine delivery. This culminated in a “Vaccine Delivery Costing Consensus Statement”, which was acknowledged by the working group.

The Committee was asked to review the process that led to the final draft of the consensus statement and to suggest the next steps and lessons learnt from the process.

### Recommendations

- This is a beneficial, valuable process, with constructive and useful outputs, which strengthens the community of practice.
- Continuing collaboration among different organizations and institutions is encouraged to maintain the momentum for the next steps.
- Harmonization of the definitions and recommendations in different guidelines is recommended
- A WHO webpage should be set up to summarize this work, and new work on vaccine delivery costing should refer to the webpage and consensus statement.
- This is a good model for funders and stakeholders. The process and lessons learnt should be recorded for the information of other groups (not necessarily in the immunization area).

## Session 7: Immunization agenda 2030 (IA2030)

### Introduction

Estimates of vaccine impact should be updated to inform strategic priorities for 2021–2030 for IA2030. The indicator for vaccine impact, “2.5M lives saved annually”, is outdated, and its method has been little documented and is not transparent. To guide strategic priorities and track progress, modelled vaccine estimates should be updated to provide a baseline for monitoring and evaluation.

The analytical framework for estimating the numbers of future deaths averted was presented, with an over-

de santé publique, car ils ne reflètent pas la mise en œuvre dans le monde réel.

## Session 6: Etablissement des coûts des vaccins

### Introduction

Les méthodes d'établissement des coûts de la délivrance des vaccins ne sont pas standardisées à l'heure actuelle, ce qui limite la clarté et la fiabilité des résultats, entraînant une mauvaise interprétation. En mars 2018, l'IVIR-AC a recommandé que les orientations de l'OMS pour estimer les coûts des nouveaux vaccins soient mises à jour, et un groupe de travail a évalué les lignes directrices de l'OMS et d'autres lignes directrices extérieures. De multiples divergences dans les flux de travail, les définitions et les lignes directrices ont montré la nécessité d'élaborer et de documenter une approche standardisée de l'établissement des coûts, qui inclue les contributions et l'accord sur les termes et les processus de tous les groupes qui travaillent actuellement sur les méthodes ou les lignes directrices pour l'établissement des coûts de la délivrance des vaccins. Cela a abouti à une «déclaration consensuelle sur l'établissement des coûts de la délivrance des vaccins», qui a été reconnue par le groupe de travail.

Il a été demandé au Comité d'examiner le processus qui a mené à l'ébauche finale de la déclaration consensuelle et de suggérer les prochaines étapes et les leçons tirées de ce processus.

### Recommandations

- Il s'agit d'un processus bénéfique et précieux, avec des résultats constructifs et utiles, qui renforce la communauté de pratique.
- La poursuite de la collaboration entre les différents organismes et institutions est encouragée afin de maintenir l'élan pour les prochaines étapes.
- Il est recommandé d'harmoniser les définitions et les recommandations des différentes lignes directrices.
- Une page Web de l'OMS devra être mise en place pour résumer ces travaux, et les nouveaux travaux sur l'établissement des coûts de la délivrance des vaccins devront se référer à cette page Web et à la déclaration consensuelle.
- Il s'agit d'un bon modèle pour les bailleurs de fonds et les parties prenantes. Le processus et les leçons apprises devront être consignés pour informer d'autres groupes (pas nécessairement dans le domaine de la vaccination).

## Session 7: Programme de vaccination 2030 (IA2030)

### Introduction

Les estimations de l'impact des vaccins doivent être mises à jour afin d'éclairer les priorités stratégiques du programme de vaccination 2021-2030. L'indicateur de l'impact des vaccins, «2,5 millions de vies sauvées chaque année», est dépassé, et sa méthode a été peu documentée et n'est pas transparente. Afin de guider les priorités stratégiques et de suivre les progrès réalisés, les estimations modélisées pour les vaccins doivent être mises à jour afin de fournir une base de référence pour le suivi et l'évaluation.

Le cadre analytique pour l'estimation du nombre de décès futurs évités a été présenté, avec une vue d'ensemble des plans



view of plans to incorporate additional indicators. Several methodological questions were posed to IVIR-AC on competing risk and double-counting of deaths, uncertainty and short- and long-term analytical approaches to impact.

### Recommendations

- The demographic model proposed is a good start for providing a reasonable overall framework to avoid double-counting of deaths, because of its explicit inclusion of overall mortality.
- IVIR-AC recommends that the team elaborate on implementation of the impact estimates for individual vaccines into the demographic modelling approach to avoid double-counting, especially in areas where the burden of vaccine-preventable disease (VPDs) is large. For instance, at country level, technical advice will be required on how the summation of all VPD-related deaths is constrained by specific age-group mortality rates.
- The full estimation strategy and its specific analytical steps remain to be fully described. Thorough thinking will be required to develop statistical estimation of the currently proposed static regression model, which draws on the assembly of multiple independent and dependent variables that emerge from heterogeneous sources of modelled estimates.
- In order to include different sources of uncertainty, the model should fully reflect incorporation of both input uncertainty and structural modelling uncertainty.
- 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.
- In order to best compare health outcomes with a short- and a long-term impact (e.g. immediate mortality reduction conferred by measles vaccine versus long-term mortality reductions by human papillomavirus vaccines), IVIR-AC recommends reporting of both cohort- and period-specific impact. This will provide an appropriate starting point for comparison of short- and long-term impacts of vaccines.
- 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.
- The project team should consider contacting suitable members of IVIR-AC who could conduct more detailed reviews of methods and provide advice.

visant à intégrer des indicateurs supplémentaires. Plusieurs questions méthodologiques ont été posées à l'IVIR-AC sur les risques concurrents et le double comptage des décès, l'incertitude et les approches analytiques à court et à long terme de l'impact.

### Recommandations

- Le modèle démographique proposé est un bon début pour fournir un cadre global raisonnable permettant d'éviter le double comptage des décès, car il inclut explicitement la mortalité globale.
- L'IVIR-AC recommande à l'équipe de préciser la manière dont les estimations de l'impact de chaque vaccin sont intégrées à l'approche de modélisation démographique afin d'éviter le double comptage, en particulier dans les régions où la charge des maladies évitables par la vaccination est importante. Par exemple, au niveau des pays, des conseils techniques seront nécessaires sur l'effet des taux de mortalité spécifiques à chaque tranche d'âge sur la somme de tous les décès liés aux maladies évitables par la vaccination.
- La stratégie d'estimation complète et ses étapes analytiques spécifiques doivent encore être décrites en détail. Une réflexion approfondie sera nécessaire pour élaborer une estimation statistique du modèle de régression statique actuellement proposé, qui s'appuie sur l'assemblage de multiples variables indépendantes et dépendantes qui émergent de sources hétérogènes d'estimations modélisées.
- Afin d'inclure différentes sources d'incertitude, le modèle doit refléter pleinement l'incorporation de l'incertitude des données d'entrée et de l'incertitude de la modélisation structurelle.
- Étant donné que le programme est complexe et que le calendrier proposé est ambitieux, il convient d'établir des priorités en ce qui concerne le niveau d'incertitude attendu dans les nombreuses estimations d'impact différentes. Il a été suggéré de se concentrer initialement sur les estimations de la mortalité et sur les vaccins dont l'impact attendu est plus élevé et pour lesquels les données sont plus fiables.
- Afin de comparer au mieux les résultats sanitaires qui ont un impact à court et à long terme (par exemple la réduction immédiate de la mortalité conférée par le vaccin antirougeoleux par rapport à la réduction à long terme de la mortalité par les vaccins contre le papillomavirus humain), l'IVIR-AC recommande de rendre compte de l'impact spécifique à des cohortes et à des périodes données. Cela fournira un point de départ approprié pour comparer les impacts à court et à long terme des vaccins.
- Les scénarios d'utilisation des estimations doivent être soigneusement définis pour garantir que les résultats ne seront pas utilisés à mauvais escient. Par exemple, la disponibilité et l'utilisation des estimations au niveau des pays pourraient être réduites au minimum et les estimations mondiales et régionales prioritaires.
- L'équipe du projet doit envisager de communiquer avec des membres concernés de l'IVIR-AC qui pourraient examiner plus en détail les méthodes et fournir des conseils.

## Session 8: Country-led Assessment for Prioritization on Immunization

### Introduction

The aim of the Country-led Assessment for Prioritization on Immunization (CAPACITI) project is to strengthen the ability of LMICs to evaluate immunization choices according to their priorities and programmes, which will inform national decision-making and vaccine research and development. The project includes 3 frameworks, for decision support, country context and innovation. The Committee assessed the readiness of the decision-support tool for release in December 2020 and for review of the other 2 frameworks.

### Recommendations

IVIR-AC acknowledges the helpful modifications made to the decision support tool in response to previous IVIR-AC recommendations in September 2019.

#### Decision-support framework

- With the following caveats, the decision-support tool is ready to be made publicly available:
  - To ensure that CAPACITI strengthens decision-making, the tool should be complemented with training modules, such as for interpreting epidemiological data, economic evaluation and community engagement.
  - Implementation of the decision-support tool should be evaluated continuously after its release.
  - CAPACITI is comprehensive, but the trade-off is its length. It is worth considering a “light” version in the future, after early evaluation.
  - Caution should be maintained concerning its use for comparing vaccination strategies, as this has not yet been pilot-tested.

These caveats should be considered in medium-term work but need not delay the launch in December 2020.

#### Country-context framework

- This framework is potentially very useful, as it draws on the systematic approach to identifying barriers to immunization that is being prepared as guidance and a workbook for desk reviews of programme performance.
- The focus should be on simplicity and feasibility, given early feedback from pilot studies.
- As it is an expensive process in terms of human and financial resources, the framework should undergo formal evaluation – not just ad hoc feedback – and also before and after or between-country comparisons with

## Session 8: Évaluation menée par les pays pour déterminer les priorités de vaccination

### Introduction

Le but du projet d'évaluation menée par les pays pour déterminer les priorités de vaccination (*Country-led Assessment for Prioritization on Immunization* ou CAPACITI) est de renforcer la capacité des pays à revenu faible ou intermédiaire à évaluer les choix en matière de vaccination en fonction de leurs priorités et de leurs programmes, ce qui éclairera la prise de décisions nationales et la recherche et le développement de vaccins. Ce projet comprend 3 cadres pour l'aide à la décision, le contexte national et l'innovation. Le Comité a évalué l'état de préparation de l'outil d'aide à la décision en vue de sa publication en décembre 2020 et examiné les 2 autres cadres.

### Recommandations

L'IVIR-AC prend acte des modifications utiles apportées à l'outil d'aide à la décision en réponse à ses recommandations formulées en septembre 2019.

#### Cadre d'aide à la décision

- Avec les réserves suivantes, l'outil d'aide à la décision est prêt à être mis à la disposition du public:
  - Pour garantir que le projet CAPACITI renforce la prise de décisions, l'outil doit être complété par des modules de formation, par exemple pour l'interprétation des données épidémiologiques, l'évaluation économique et la mobilisation communautaire.
  - La mise en œuvre de l'outil d'aide à la décision devra être évaluée de manière continue après sa diffusion.
  - Le projet CAPACITI est complet, mais sa longueur est un inconvénient. Il vaut la peine d'envisager une version «allégée» à l'avenir, après une première évaluation.
  - Il convient de rester prudent quant à son utilisation pour comparer les stratégies de vaccination, car elle n'a pas encore mise à l'essai.

Ces réserves doivent être prises en compte dans les travaux à moyen terme mais ne doivent pas retarder le lancement prévu en décembre 2020.

#### Cadre contextuel propre à chaque pays

- Ce cadre est potentiellement très utile, car il s'appuie sur une approche systématique d'identification des obstacles à la vaccination en cours d'élaboration qui fournira des orientations et servira de manuel pratique pour l'examen des performances des programmes.
- L'accent devra être mis sur la simplicité et la faisabilité, compte tenu des premiers retours d'information des études pilotes.
- Comme il s'agit d'un processus coûteux en termes de ressources humaines et financières, ce cadre devra faire l'objet d'une évaluation formelle – et pas seulement d'un retour d'information ad hoc – et aussi de comparaisons avant et après sa diffusion ou entre pays à l'aide de

qualitative and quantitative methods. Evaluation requires both process (e.g. Have the issues identified been accurate and have they led to change?) and outcome indicators (e.g. Have coverage and equity improved after use of the tool?).

#### Innovation framework

- It is recommended that the innovation framework be applied when there is a short timeline for products coming to market.
- Two paradigms could be considered:
  1. Market intelligence: As the information is valuable to private manufacturers and expensive for countries to collect, it could be sold to manufacturers to generate revenue. The money earned could then be put into a fund to develop resources for vaccine data collection and decision-making in countries that take part in the process. A suitable model could be the pandemic influenza preparedness framework, which is funded by influenza vaccine manufacturers, who benefit from influenza surveillance.
  2. Advanced market commitments: Information from the framework could be placed in the context of more formal communications and eventually lead to binding commitments between suppliers and buyers of vaccines.
- To stimulate innovative thinking by country stakeholders about future needs, CAPACITI should consider using specialized facilitation techniques for improving creative thinking.
- The innovation framework should include interventions to increase coverage and equity that are not product-based.

## Session 9: Burden of enteric disease

### Introduction

The mortality estimates for the Enteric Burden of Disease Project are a follow-up to previous recommendations made by IVIR-AC in March 2019.<sup>5</sup> IVIR-AC was asked during the current meeting on whether the workstreams presented could affect the assessment of mortality due to pathogens and whether IVIR-AC agrees that the results of mortality workstreams be included in future enteric mortality modelling estimates. With regard to the morbidity workstream, IVIR-AC was asked to comment on the proposed scope of work to measure the impact of enteric pathogens on morbidity and to consider whether it is an appropriate next step for

méthodes qualitatives et quantitatives. Cette évaluation exige des indicateurs de processus (par exemple les problèmes ont-ils été précisément identifiés et cela a-t-il conduit à des changements?) et des indicateurs de résultats (par exemple la couverture et l'équité ont-elles progressé grâce à l'utilisation de cet outil?).

#### Cadre de l'innovation

- Il est recommandé d'appliquer le cadre de l'innovation lorsque le délai de mise sur le marché des produits est court.
- Deux paradigmes peuvent être envisagés:
  1. Informations sur le marché: comme les informations sont précieuses pour les fabricants privés et coûteuses à collecter pour les pays, elles pourraient être vendues aux fabricants pour générer des revenus. L'argent ainsi obtenu pourrait ensuite être versé dans un fonds destiné à développer les ressources pour la collecte de données sur les vaccins et la prise de décisions dans les pays qui participent au processus. Un modèle approprié pourrait être le cadre de préparation en cas de grippe pandémique, qui est financé par les fabricants de vaccins antigrippaux qui tirent parti de la surveillance de la grippe.
  2. Engagements commerciaux anticipés: les informations issues du cadre pourraient être placées dans le contexte de communications plus formelles et déboucher à terme sur des engagements contraignants entre les fournisseurs et les acheteurs de vaccins.
- Pour stimuler une réflexion innovante sur les besoins futurs de la part des parties prenantes dans les pays, le projet CAPACITI devrait envisager d'employer des techniques de facilitation spéciales pour améliorer la pensée créative.
- Le cadre de l'innovation devrait comprendre des interventions visant à accroître la couverture et l'équité qui ne sont pas basées sur des produits.

## Session 9: Charge des maladies entériques

### Introduction

Les estimations de la mortalité pour le projet sur la charge des maladies entériques font suite aux recommandations formulées par l'IVIR-AC en mars 2019.<sup>5</sup> Au cours de la présente réunion, il a été demandé à l'IVIR-AC si les axes de travail présentés pouvaient affecter l'évaluation de la mortalité due aux agents pathogènes et si l'IVIR-AC approuvait que les résultats des axes de travail sur la mortalité soient inclus dans les futures estimations issues de la modélisation de la mortalité entérique. En ce qui concerne l'axe de travail sur la morbidité, il a été demandé à l'IVIR-AC de formuler des observations sur la portée des travaux proposée pour mesurer l'impact des agents pathogènes entériques sur la morbidité et d'examiner s'il s'agit d'une

<sup>5</sup> See [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.htm](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.htm)

<sup>5</sup> Voir [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.htm](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.htm)

further evaluating the full burden, and ultimately the value, of enteric disease vaccines.

## Recommendations

### Mortality workstream

- IVIR-AC commends both the high-quality scientific work and the extensive exchanges and collaborations by all the researchers and institutions involved.
- The workstreams presented could affect assessment of mortality due to pathogens and therefore the relative value of vaccines against those pathogens. The results of the mortality workstreams should be included in future enteric mortality modelling estimates.
- The process, including the steps in comparisons of model estimates, should be documented. This is good practice and could serve as a model for future exercises that could benefit other disease areas in which multiple groups are estimating the burden of disease.
- Incorporation of the results could improve the robustness and credibility of mortality estimates. Convergence of independent estimates might be necessary, which might be achieved in this collaborative work with proposals of consensus definitions, harmonized protocols for data selection and use, using only the best available evidence as shown in the analyses and accounting for local context considerations.
- The proposed publications of the comparison exercise, workstreams and perspective of modellers could include how the exercise and exchange have strengthened collaboration among partners and whether it has led the modelling teams to review the selection criteria for data input and/or the methods.
- If feasible, an assessment of the quality of the studies should be included in the systematic reviews of odds ratios and case fatality rates. This inclusion could also facilitate assessment of whether low-quality studies influenced the strong heterogeneity observed in the results.
- Two significant findings are highly relevant: 1) Neither IHME nor the Maternal Child Epidemiology Estimation used a study to inform their estimates, and 2) the diagnostic adjustments incorporated by IHME were responsible for increasing their mortality estimates for *Shigella* and decreasing the mortality estimates for enterotoxigenic *Escherichia coli*. These results appear to contribute significantly to the discrepancies in the mortality estimates for the two organisms. Moreover, the possible impact on mortality estimates for other enteric pathogens is unknown.

prochaine étape appropriée pour évaluer plus avant la charge complète, et en fin de compte la valeur des vaccins contre les maladies entériques.

## Recommandations

### Axe de travail sur la mortalité

- L'IVIR-AC salue à la fois le travail scientifique de qualité et les nombreux échanges et collaborations de tous les chercheurs et de toutes les institutions impliqués.
- Les axes de travail présentés pourraient influencer sur l'évaluation de la mortalité due aux agents pathogènes et, par conséquent, sur la valeur relative des vaccins contre ces agents pathogènes. Les résultats des axes de travail sur la mortalité devraient être inclus dans les futures estimations de la modélisation de la mortalité entérique.
- Le processus, y compris les étapes de comparaison des estimations des modèles, devrait être documenté. Il s'agit d'une bonne pratique qui pourrait servir de modèle pour de futurs exercices susceptibles d'être bénéfiques à d'autres maladies pour lesquelles plusieurs groupes estiment la charge de morbidité.
- L'incorporation des résultats pourrait améliorer la robustesse et la crédibilité des estimations de mortalité. Une convergence des estimations indépendantes pourrait être nécessaire; cela pourrait être réalisé dans ce travail de collaboration avec des propositions de définitions consensuelles, de protocoles harmonisés pour la sélection et l'utilisation des données, en utilisant uniquement les meilleures preuves disponibles comme indiqué dans les analyses et en tenant compte des considérations liées au contexte local.
- Les publications proposées de cet exercice de comparaison, des axes de travail et de la perspective des modélisateurs pourraient inclure la manière dont l'exercice et l'échange ont renforcé la collaboration entre les partenaires et si cela a conduit les équipes de modélisation à revoir les critères de sélection des données l'entrée et/ou des méthodes.
- Si possible, une évaluation de la qualité des études devrait être incluse dans les examens systématiques des odds-ratios et des taux de létalité. Cela pourrait aider à comprendre si des études de mauvaise qualité ont influé sur la forte hétérogénéité observée dans les résultats.
- Deux résultats importants sont très pertinents: 1) ni l'Institute for Health Metrics and Evaluation (IHME) ni l'estimation de l'épidémiologie maternelle et infantile (Maternal Child Epidemiology Estimation) n'ont fondé leurs estimations sur une étude, et 2) les ajustements diagnostiques incorporés par l'IHME ont entraîné une augmentation de leurs estimations de la mortalité due à *Shigella* et une diminution des estimations de la mortalité due à *Escherichia coli* entérotogénique. Ces résultats semblent contribuer de façon significative aux écarts dans les estimations de la mortalité due à ces 2 organismes. En outre, l'impact possible sur les estimations de la mortalité due à d'autres agents pathogènes entériques n'est pas connu.



## Morbidity workstream

- IVIR-AC fully concurs with the importance of long-term morbidity outcomes, while also highlighting the importance of mortality and acute morbidity. Assessment of the full value of vaccines must include their impact on mortality and morbidity and possibly even broader population implications, once good-quality evidence of causality is available.
- IVIR-AC agrees with prioritization of a systematic review of evidence on the impact of enteric pathogens and diarrhoea on long-term morbidity, with an assessment of the quality and external validity of that evidence, particularly the strength of evidence for causality. This could be followed by meta-analyses, if the evidence is strong enough.
- IVIR-AC encourages the group to evaluate broader consequences of long-term morbidity on human capital, such as on school attendance and educational performance. In the vicious cycle of poverty, other consequences of impaired cognitive development may include loss of human capital and productivity. IVIR-AC suggests that these be evaluated for inclusion in both reviews and in the development of metrics of the potential full value of vaccines.
- IVIR-AC highlights the importance of the 2 longitudinal studies (GEMS<sup>6</sup> and MAL-ED<sup>7</sup>) for which results have begun to be published. Collaboration with the study teams should be maintained and strengthened in order to address long-term morbidity associated with enteric pathogens.
- The assessment of long-term morbidity is challenging, given the difficulties of establishing causality. High-quality evidence to support a causal association between diarrhoea, enteric pathogens and malnutrition (“the double burden”), and perhaps with chronic noncommunicable diseases (“the triple burden”), is encouraged. Accordingly, for the work to move forward, it is relevant to discuss, evaluate and, if appropriate, borrow from existing studies (ABCD,<sup>8</sup> CHAIN,<sup>9</sup> risk factors for Global Burden of Disease) to shed light on which long-term conditions should be included and how.
- Additionally, perhaps in collaboration within the 2 longitudinal studies, causal inference models might be included to assess causal pathways among multiple variables (i.e. exposures of interest and confounders). Proper analyses of the data with

## Axe de travail sur la morbidité

- L'IVIR-AC est entièrement d'accord avec l'importance des résultats à long terme en matière de morbidité, tout en soulignant l'importance de la mortalité et de la morbidité aiguë. L'évaluation de la pleine valeur des vaccins doit inclure leur impact sur la mortalité et la morbidité et éventuellement des implications plus larges pour la population, une fois que des données de bonne qualité sur la causalité seront disponibles.
- L'IVIR-AC approuve la priorité accordée à un examen systématique des données probantes sur l'impact des agents pathogènes entériques et de la diarrhée sur la morbidité à long terme, avec une évaluation de la qualité et de la validité externe de ces données, en particulier la force des preuves de causalité. Cela pourrait être suivi de méta-analyses, si les preuves sont suffisamment solides.
- L'IVIR-AC encourage le groupe à évaluer les conséquences plus larges de la morbidité à long terme sur le capital humain, comme la fréquentation et les résultats scolaires. Dans le cercle vicieux de la pauvreté, la perte de capital humain et de productivité peut être une autre des conséquences de l'altération du développement cognitif. L'IVIR-AC suggère que ces conséquences soient évaluées en vue d'être incluses dans ces examens et dans l'élaboration de mesures de la pleine valeur potentielle des vaccins.
- L'IVIR-AC souligne l'importance des 2 études longitudinales (GEMS<sup>6</sup> et MAL-ED<sup>7</sup>) dont les résultats commencent à être publiés. La collaboration avec les équipes des études doit être maintenue et renforcée afin de lutter contre la morbidité à long terme associée aux agents pathogènes entériques.
- L'évaluation de la morbidité à long terme est un défi en raison des difficultés à établir la causalité. La production de données probantes de qualité à l'appui d'un lien de causalité entre la diarrhée, les agents pathogènes entériques et la malnutrition («la double charge»), et peut-être avec les maladies chroniques non transmissibles («la triple charge»), est encouragée. Par conséquent, pour que les travaux avancent, il est pertinent de discuter, d'évaluer et, le cas échéant, d'emprunter à des études existantes (ABCD,<sup>8</sup> CHAIN,<sup>9</sup> facteurs de risque pour la charge mondiale des maladies) pour faire la lumière sur les maladies à long terme qui doivent être incluses et de quelle manière.
- De plus, dans le cadre d'une collaboration avec les équipes de ces 2 études longitudinales, des modèles d'inférence causale pourraient être inclus pour évaluer les voies de causalité des multiples variables (c'est-à-dire les expositions d'intérêt et les facteurs de confusion). Des analyses

<sup>6</sup> Global Enteric Multicenter Study (GEMS): [http://dx.doi.org/10.1016/S0140-6736\(13\)60844-2](http://dx.doi.org/10.1016/S0140-6736(13)60844-2)

<sup>7</sup> MAL-ED: The Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health: [http://dx.doi.org/10.1016/S2214-109X\(15\)00151-5](http://dx.doi.org/10.1016/S2214-109X(15)00151-5)

<sup>8</sup> Antibiotics for Children with Severe Diarrhoea.

<sup>9</sup> Childhood Acute Illness and Nutrition.

<sup>6</sup> Global Enteric Multicenter Study (GEMS): [http://dx.doi.org/10.1016/S0140-6736\(13\)60844-2](http://dx.doi.org/10.1016/S0140-6736(13)60844-2)

<sup>7</sup> MAL-ED: The Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health: [http://dx.doi.org/10.1016/S2214-109X\(15\)00151-5](http://dx.doi.org/10.1016/S2214-109X(15)00151-5)

<sup>8</sup> Antibiotics for Children with Severe Diarrhoea.

<sup>9</sup> Childhood Acute Illness and Nutrition.

directed acyclic graphs might allow adequate adjustment for covariates and inference of causal pathways by estimation of direct and indirect paths. This method allows the assessment of associations as causal paths, their significance and magnitude. ■

appropriées des données accompagnées de graphiques acycliques dirigés pourraient permettre un ajustement adéquat des covariables et de l'inférence causale par l'estimation des voies directes et indirectes de causalité. Cette méthode permet d'évaluer les associations comme des voies causales, leur importance et leur ampleur. ■

## WHO calls for reinvigorated action to fight malaria

30 November 2020

WHO is calling on countries and global health partners to step up the fight against malaria, a preventable and treatable disease that continues to claim hundreds of thousands of lives each year. A better targeting of interventions, new tools and increased funding are needed to change the global trajectory of the disease and reach internationally-agreed targets.

According to WHO's latest *World malaria report*,<sup>1</sup> progress against malaria continues to plateau, particularly in high burden countries in Africa. Gaps in access to life-saving tools are undermining global efforts to curb the disease, and the COVID-19 pandemic is expected to set back the fight even further.

"It is time for leaders across Africa – and the world – to rise once again to the challenge of malaria, just as they did when they laid the foundation for the progress made since the beginning of this century," said WHO Director-General Dr Tedros Adhanom Ghebreyesus. "Through joint action, and a commitment to leaving no one behind, we can achieve our shared vision of a world free of malaria."

In 2000, African leaders signed the landmark Abuja Declaration pledging to reduce malaria deaths on the continent by 50% over a 10-year period. Robust political commitment, together with innovations in new tools and a steep increase in funding, catalyzed an unprecedented period of success in global malaria control. According to the report, 1.5 billion malaria cases and 7.6 million deaths have been averted since 2000.

### A plateau in progress

In 2019, the global tally of malaria cases was 229 million, an annual estimate that has remained virtually unchanged over the last 4 years. The disease claimed some 409 000 lives in 2019 compared to 411 000 in 2018.

## L'OMS appelle à relancer la lutte contre le paludisme

30 novembre 2020

L'OMS appelle les pays et les partenaires mondiaux dans le domaine de la santé à intensifier la lutte contre le paludisme, une maladie qu'il est possible d'éviter et de traiter mais qui fait encore des centaines de milliers de morts chaque année. Il faut des interventions mieux ciblées, de nouveaux outils et un financement plus important pour changer le cours des choses au niveau mondial et atteindre les objectifs convenus à l'échelle internationale.

Selon le dernier *Rapport de l'OMS sur le paludisme dans le monde*,<sup>1</sup> les progrès réalisés dans la lutte contre le paludisme stagnent encore, en particulier dans les pays africains où la charge est élevée. Les difficultés d'accès aux outils vitaux sapent les efforts mondiaux visant à juguler la maladie, et la pandémie de COVID-19 devrait entraver encore davantage les efforts de lutte.

«Il est temps que les dirigeants en Afrique – et dans le monde – relèvent une fois encore le défi du paludisme, comme ils l'ont fait lorsqu'ils ont jeté les bases des progrès réalisés depuis le début du siècle», a déclaré le Directeur général de l'OMS, le Dr Tedros Adhanom Ghebreyesus. «En agissant ensemble et en nous engageant à ne laisser personne de côté, nous pouvons atteindre notre vision commune d'un monde sans paludisme», a-t-il ajouté.

En 2000, les dirigeants africains ont signé la Déclaration d'Abuja, un document historique dans lequel ils s'engagent à réduire de 50% en 10 ans le nombre de décès dus au paludisme sur le continent. Un engagement politique solide, la mise au point d'outils novateurs et une forte augmentation du financement ont permis de remporter des succès sans précédent en matière de lutte contre le paludisme dans le monde. Selon le rapport, 1,5 milliard de cas de paludisme et 7,6 millions de décès ont été évités depuis 2000.

### Stagnation des progrès

En 2019, 229 millions de cas de paludisme ont été enregistrés dans le monde. Ce chiffre n'a pratiquement pas varié depuis 4 ans. La maladie a fait quelque 409 000 morts en 2019 contre 411 000 en 2018.

<sup>1</sup> See <https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2020>.

<sup>1</sup> Voir <https://www.who.int/docs/default-source/malaria/world-malaria-reports/world-malaria-report-2020-briefing-kit-fre.pdf>

As in past years, the African Region shouldered more than 90% of the overall disease burden. Since 2000, the region has reduced its malaria death toll by 44%, from an estimated 680 000 to 384 000 annually. However, progress has slowed in recent years, particularly in countries with a high burden of the disease.

A funding shortfall at both the international and domestic levels poses a significant threat to future gains. In 2019, total funding reached US \$3 billion against a global target of \$5.6 billion. Funding shortages have led to critical gaps in access to proven malaria control tools.

## COVID-19 an added challenge

In 2020, COVID-19 emerged as an additional challenge to the provision of essential health services worldwide. According to the report, most malaria prevention campaigns were able to move forward this year without major delays. Ensuring access to malaria prevention – such as insecticide-treated nets and preventive medicines for children – has supported the COVID-19 response strategy by reducing the number of malaria infections and, in turn, easing the strain on health systems. WHO worked swiftly to provide countries with guidance to adapt their responses and ensure the safe delivery of malaria services during the pandemic.

However, WHO is concerned that even moderate disruptions in access to treatment could lead to a considerable loss of life. The report finds, for example, that a 10% disruption in access to effective antimalarial treatment in sub-Saharan Africa could lead to 19 000 additional deaths. Disruptions of 25% and 50% in the region could result in an additional 46 000 and 100 000 deaths, respectively.

“While Africa has shown the world what can be achieved if we stand together to end malaria as a public health threat, progress has stalled,” said Dr Matshidiso Moeti, WHO Regional Director for Africa. “COVID-19 threatens to further derail our efforts to overcome malaria, particularly treating people with the disease. Despite the devastating impact COVID-19 has had on African economies, international partners and countries need to do more to ensure that the resources are there to expand malaria programmes which are making such a difference in people’s lives.”

## WHO response

A key strategy to reignite progress is the *High burden to high impact*<sup>2</sup> (HBHI) response, catalyzed in 2018 by

Comme les années précédentes, la Région africaine a supporté plus de 90% de la charge de morbidité totale. Depuis 2000, le nombre de décès dus au paludisme dans la Région a diminué de 44%, passant de 680 000 à 384 000 par an, selon les estimations. Toutefois, les progrès ont ralenti ces dernières années, en particulier dans les pays où la charge de morbidité est élevée.

L’insuffisance du financement aux niveaux international et national est une menace importante pour les progrès futurs. En 2019, le financement total a atteint 3 milliards de dollars des États-Unis alors que l’objectif mondial était de 5,6 milliards de dollars. Les déficits de financement ont entraîné de graves difficultés d’accès à des outils de lutte contre le paludisme dont l’efficacité est prouvée.

## La COVID-19: un obstacle supplémentaire

En 2020, la COVID-19 a été un obstacle supplémentaire à la fourniture de services de santé essentiels partout dans le monde. Selon le rapport, la plupart des campagnes de prévention du paludisme ont pu se dérouler cette année sans retards importants. L’accès garanti aux moyens de prévention du paludisme – comme les moustiquaires imprégnées d’insecticide et les médicaments préventifs à usage pédiatrique – a facilité la mise en œuvre de la stratégie de riposte à la COVID-19 en réduisant le nombre d’infections palustres, ce qui a diminué la pression sur les systèmes de santé. L’OMS a agi rapidement pour fournir aux pays des orientations afin qu’ils adaptent leurs mesures de lutte et assurent la prestation de services contre le paludisme en toute sécurité pendant la pandémie.

Toutefois, l’OMS craint que même des perturbations modérées de l’accès au traitement n’entraînent un nombre considérable de décès. Ainsi, selon le rapport, une perturbation de 10% de l’accès à un traitement antipaludique efficace en Afrique subsaharienne pourrait entraîner 19 000 décès supplémentaires. Des perturbations de 25% et 50% dans la région pourraient entraîner 46 000 et 100 000 décès supplémentaires, respectivement.

«Alors que l’Afrique a montré au monde ce qu’il est possible de faire si nous sommes unis pour mettre fin au paludisme en tant que menace pour la santé publique, les progrès sont au point mort», a déclaré la D<sup>re</sup> Matshidiso Moeti, Directrice régionale de l’OMS pour l’Afrique. «La COVID-19 risque de compromettre davantage nos efforts de lutte pour vaincre le paludisme, en particulier le traitement des personnes atteintes de la maladie. Malgré l’impact dévastateur de la COVID-19 sur l’économie des pays africains, les partenaires internationaux et les pays doivent déployer davantage d’efforts pour que les ressources soient disponibles afin d’étendre les programmes de lutte contre le paludisme qui ont un réel impact sur la vie des gens», a-t-elle ajouté.

## L’action l’OMS

L’une des principales stratégies pour relancer le progrès est l’*Initiative pour une action à fort impact dans les pays à forte charge*,<sup>2</sup>

<sup>2</sup> Voir <https://apps.who.int/iris/bitstream/handle/10665/275868/WHO-CDS-GMP-2018.25-eng.pdf>

<sup>2</sup> Voir <https://apps.who.int/iris/bitstream/handle/10665/311506/WHO-CDS-GMP-2018.25-fre.pdf>

WHO and the RBM Partnership to End Malaria. The response is led by 11 countries – including 10 in sub-Saharan Africa – that account for approximately 70% of the world's malaria burden.

Over the last 2 years, HBHI countries have been moving away from a “one-size-fits all” approach to malaria control – opting, instead, for tailored responses based on local data and intelligence. A recent analysis from Nigeria, for example, found that through an optimized mix of interventions, the country could avert tens of millions of additional cases and thousands of additional deaths by the year 2023, compared to a business-as-usual approach.

While it is too early to measure the impact of the HBHI approach, the report finds that deaths in the 11 countries were reduced from 263 000 to 226 000 between 2018 and 2019. India continued to make impressive gains, with reductions in cases and deaths of 18% and 20%, respectively, over the last 2 years. There was, however, a slight increase in the total number of cases among HBHI countries, from an estimated 155 million in 2018 to 156 million in 2019.

## Meeting global malaria targets

This year's report highlights key milestones and events that helped shape the global response to the disease in recent decades. Beginning in the 1990s, leaders of malaria-affected countries, scientists and other partners laid the groundwork for a renewed malaria response that contributed to one of the biggest returns on investment in global health.

According to the report, 21 countries eliminated malaria over the last 2 decades; of these, 10 countries were officially certified as malaria-free by WHO. In the face of the ongoing threat of antimalarial drug resistance, the 6 countries of the Greater Mekong subregion continue to make major gains towards their goal of malaria elimination by 2030.

But many countries with a high burden of malaria have been losing ground. According to WHO global projections, the 2020 target for reductions in malaria case incidence will be missed by 37% and the mortality reduction target will be missed by 22%.

## Note to editors

WHO's work on malaria is guided by the *Global technical strategy for malaria 2016–2030 (GTS)*,<sup>3</sup> approved by the World Health Assembly in May 2015. The strategy includes 4 global targets for 2030, with milestones along

lancée en 2018 par l'OMS et le Partenariat RBM pour en finir avec le paludisme. Cette initiative est dirigée par 11 pays – dont 10 d'Afrique subsaharienne – qui supportent environ 70% de la charge mondiale de morbidité due au paludisme.

Au cours des 2 dernières années, ces pays ont abandonné une approche uniforme de la lutte contre le paludisme au profit de mesures adaptées en fonction des données et des informations locales. Ainsi, une analyse récente effectuée au Nigéria a montré que grâce à une gamme optimisée d'interventions, le pays pourrait éviter des dizaines de millions de cas et des milliers de décès supplémentaires d'ici à 2023, par rapport à la situation actuelle.

Bien qu'il soit trop tôt pour mesurer l'impact de l'approche de l'initiative pour une action à fort impact dans les pays à forte charge, le rapport indique que le nombre de décès dans les 11 pays concernés est passé de 263 000 à 226 000 entre 2018 et 2019. L'Inde a continué à progresser de façon spectaculaire. En effet, le nombre de cas et de décès y a reculé de 18% et de 20%, respectivement, au cours des 2 dernières années. Toutefois le nombre total de cas parmi les pays participant à l'initiative pour une action à fort impact dans les pays à forte charge a légèrement augmenté et est passé de 155 millions en 2018 à 156 millions en 2019, selon les estimations.

## Atteinte les objectifs mondiaux en matière de paludisme

Le rapport de cette année signale les principaux événements qui ont eu une influence sur la lutte contre la maladie au cours des dernières décennies. À partir des années 1990, les dirigeants des pays touchés par le paludisme, les scientifiques et d'autres partenaires ont jeté les bases d'un renouvellement de la lutte qui a contribué à l'un des plus grands retours sur investissement dans le domaine de la santé mondiale.

Selon le rapport, 21 pays ont éliminé le paludisme au cours des 2 dernières décennies, dont 10 ont été officiellement certifiés exempts de paludisme par l'OMS. Face à la menace permanente de la résistance aux médicaments antipaludiques, les 6 pays du bassin du Mékong continuent de progresser considérablement en vue d'éliminer le paludisme d'ici à 2030.

Mais de nombreux pays où la charge du paludisme est élevée ont perdu du terrain. Selon les projections mondiales de l'OMS, l'écart sera de 37% par rapport à l'objectif de réduction de l'incidence du paludisme pour 2020 et de 22% par rapport à l'objectif de réduction de la mortalité.

## Note à l'intention des rédacteurs

Les activités de l'OMS en matière de paludisme s'appuient sur la *Stratégie technique mondiale de lutte contre le paludisme 2016–2030*,<sup>3</sup> approuvée par l'Assemblée mondiale de la Santé en mai 2015. Cette stratégie comprend 4 buts mondiaux à atteindre

<sup>3</sup> Voir [https://apps.who.int/iris/bitstream/handle/10665/176712/9789241564991\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/176712/9789241564991_eng.pdf)

<sup>3</sup> Voir [https://apps.who.int/iris/bitstream/handle/10665/176720/9789242564990\\_fre.pdf](https://apps.who.int/iris/bitstream/handle/10665/176720/9789242564990_fre.pdf)



the way to track progress. The 2030 targets are: 1) reducing malaria case incidence by at least 90%; 2) reducing malaria mortality rates by at least 90%; 3) eliminating malaria in at least 35 countries; and 4) preventing a resurgence of malaria in all countries that are malaria-free.

Near-term GTS milestones for 2020 include global reductions in malaria case incidence and death rates of at least 40% and the elimination of malaria in at least 10 countries. According to the report, the 2020 milestones for malaria case incidence and mortality rates will be missed:

**Case incidence:** WHO projects that, in 2020, there were an estimated 56 malaria cases for every 1000 people at risk of the disease against a GTS target of 35 cases. The GTS milestone will be missed by an estimated 37%.

**Mortality rate:** the estimate for globally projected malaria deaths per 100 000 population at risk was 9.8 in 2020 against a GTS target of 7.2 deaths. The milestone will be missed by an estimated 22%.

## WHO African Region

Since 2014, the rate of progress in both cases and deaths in the region has slowed, attributed mainly to the stalling of progress in several countries with moderate or high transmission. In 2019, 6 African countries accounted for 50% of all malaria cases globally: Nigeria (23%), the Democratic Republic of the Congo (11%), United Republic of Tanzania (5%), Niger (4%), Mozambique (4%) and Burkina Faso (4%). In view of recent trends, the African Region will miss the GTS 2020 milestones for case incidence and mortality by 37% and 25%, respectively.

*High burden to high impact (HBHI)* – Launched in November 2018, HBHI builds on the principle that no one should die from a disease that is preventable and treatable. It is led by 11 countries that, together, accounted for approximately 70% of the world's malaria burden in 2017: Burkina Faso, Cameroon, Democratic Republic of the Congo, Ghana, India, Mali, Mozambique, Niger, Nigeria, Uganda and United Republic of Tanzania. Over the last 2 years, all 11 HBHI countries have implemented activities across 4 response elements: 1) political will to reduce the toll of malaria; 2) strategic information to drive impact; 3) better guidance, policies and strategies; and 4) a coordinated national malaria response

## Malaria elimination

Between 2000 and 2019, 10 countries received the official WHO certification of malaria elimination: United Arab Emirates (2007), Morocco (2010), Turkmenistan (2010), Armenia (2011), Kyrgyzstan (2016), Sri Lanka (2016), Uzbekistan (2018), Paraguay (2018), Argentina (2019)

d'ici à 2030, avec des objectifs intermédiaires pour suivre les progrès réalisés. Les buts à l'horizon 2030 sont les suivants: 1) réduire d'au moins 90% l'incidence du paludisme; 2) réduire d'au moins 90% les taux de mortalité palustre; 3) éliminer le paludisme dans 35 pays au moins; et 4) empêcher la réapparition du paludisme dans tous les pays exempts.

Les objectifs intermédiaires pour 2020 fixés dans la stratégie sont la réduction de l'incidence du paludisme et des taux de mortalité d'au moins 40%, au plan mondial, et l'élimination du paludisme dans au moins 10 pays. Selon le rapport, les objectifs intermédiaires pour 2020 concernant l'incidence du paludisme et les taux de mortalité ne seront pas atteints:

**Incidence:** selon les projections de l'OMS pour 2020, il y aura environ 56 cas de paludisme pour 1000 personnes risquant de contracter la maladie, contre un objectif de 35 cas. L'écart pour cet objectif intermédiaire est estimé à 37%.

**Taux de mortalité:** pour 2020, le nombre de décès dus au paludisme estimé à l'échelle mondiale pour 100 000 personnes à risque est de 9,8, contre un objectif de 7,2 décès selon la stratégie. L'écart pour cet objectif intermédiaire est estimé à 22%.

## Région africaine de l'OMS

Depuis 2014, le rythme des progrès concernant l'incidence et les décès dans la Région a ralenti, principalement en raison d'une stagnation dans plusieurs pays où la transmission est modérée ou élevée. En 2019, 6 pays de la Région africaine concentraient 50% des cas de paludisme dans le monde: le Nigéria (23%), la République démocratique du Congo (11%), la République-Unie de Tanzanie (5%), le Niger (4%), le Mozambique (4%) et le Burkina Faso (4%). Dans la Région africaine, compte tenu de l'évolution récente, l'écart par rapport aux objectifs intermédiaires fixés pour 2020 dans la stratégie sera de 37% pour l'incidence et de 25%, pour la mortalité.

L'initiative pour une action à fort impact dans les pays à forte charge, lancée en novembre 2018, s'appuie sur le principe selon lequel personne ne devrait mourir d'une maladie qu'il est possible d'éviter et de traiter. Elle est dirigée par 11 pays qui, ensemble, supportaient environ 70% de la charge mondiale de morbidité due au paludisme en 2017: le Burkina Faso, le Cameroun, le Ghana, l'Inde, le Mali, le Mozambique, le Niger, le Nigéria, l'Ouganda, la République démocratique du Congo et la République-Unie de Tanzanie. Au cours des 2 dernières années, ces 11 pays ont mis en œuvre des activités suivant 4 axes d'intervention: 1) la volonté politique de faire baisser le nombre de cas de paludisme; 2) l'information stratégique pour accroître l'impact; 3) l'amélioration des orientations, des politiques et des stratégies; et 4) la lutte coordonnée contre le paludisme au niveau national.

## Élimination du paludisme

Entre 2000 et 2019, l'élimination du paludisme a été officiellement certifiée par l'OMS dans 10 pays: les Émirats arabes unis (2007), le Maroc (2010), le Turkménistan (2010), l'Arménie (2011), le Kirghizistan (2016), Sri Lanka (2016), l'Ouzbékistan (2018), le Paraguay (2018), l'Argentine (2019) et l'Algérie (2019).

and Algeria (2019). In 2019, China reported zero indigenous cases of malaria for the third consecutive year; the country recently applied for the official WHO certification of malaria elimination. In 2020, El Salvador became the first country in Central America to apply for the WHO malaria-free certification

In the 6 countries of the Greater Mekong subregion – Cambodia, China (Yunnan Province), Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – the reported number of malaria cases fell by 90% from 2000 to 2019, while *Plasmodium falciparum* cases fell by 97% in the same time period. This accelerated decrease in *P. falciparum* malaria is notable in view of the threat posed by antimalarial drug resistance in the subregion.

### A call for innovation

Eliminating malaria in all countries, especially those with a high disease burden, will likely require tools that are not available today. In September 2019, the WHO Director-General issued a “malaria challenge,”<sup>4</sup> calling on the global health community to ramp up investment in the research and development of new malaria-fighting tools and approaches. This message was further reinforced in the April 2020 report<sup>5</sup> of the WHO Strategic advisory group on malaria eradication. ■

<sup>4</sup> See <https://www.who.int/director-general/speeches/detail/malaria-eradication>

<sup>5</sup> See <https://www.who.int/publications/i/item/9789240003675>

En 2019, la Chine n'a notifié aucun cas autochtone de paludisme pour la troisième année consécutive. Elle a récemment demandé que l'élimination du paludisme soit officiellement certifiée par l'OMS. En 2020, El Salvador est devenu le premier pays d'Amérique centrale à demander à l'OMS de certifier l'élimination du paludisme sur son territoire.

Dans les 6 pays du bassin du Mékong – Cambodge, Chine (province du Yunnan), République démocratique populaire lao, Myanmar, Thaïlande et Viet Nam – le nombre de cas de paludisme notifiés a baissé de 90% de 2000 à 2019 et le nombre de cas de paludisme à *P. falciparum* a chuté de 97% au cours de la même période. Cette diminution accélérée du paludisme à *P. falciparum* est remarquable compte tenu de la menace que représente la résistance aux médicaments antipaludiques dans le bassin du Mékong. ■

### Un appel à l'innovation

L'élimination du paludisme dans tous les pays, en particulier ceux où la charge de morbidité élevée, nécessitera probablement des outils qui ne sont pas disponibles aujourd'hui. En septembre 2019, le Directeur général de l'OMS a lancé un «défi de l'éradication du paludisme»,<sup>4</sup> appelant la communauté mondiale de la santé à investir davantage dans la recherche-développement de nouveaux outils et de nouvelles méthodes de lutte contre le paludisme. Ce message a été réaffirmé dans le rapport d'avril 2020<sup>5</sup> du Groupe. ■

<sup>4</sup> Voir <https://www.who.int/fr/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19--30-november-2020>

<sup>5</sup> Voir <https://www.who.int/publications/i/item/9789240003675>

#### 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@who.int](mailto: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: À 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@who.int](mailto: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](http://www.who.int/wer)**

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

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

## **Session background information**



## **Session 1: COVID 19 vaccine modelling**

# Update on vaccine impact modelling:

- 1) prioritization of populations for COVID-19 vaccination
- 2) additional modelling questions beyond prioritization

SAGE WORKING GROUP ON COVID-19 VACCINES  
IMPACT MODELLING SUBGROUP

# Vaccine impact modelling subgroup of SAGE COVID-19 vaccines WG



Requests for information (Rfi) and commissioning of work (RfP)



Ad hoc presentations from modelling groups (weekly)

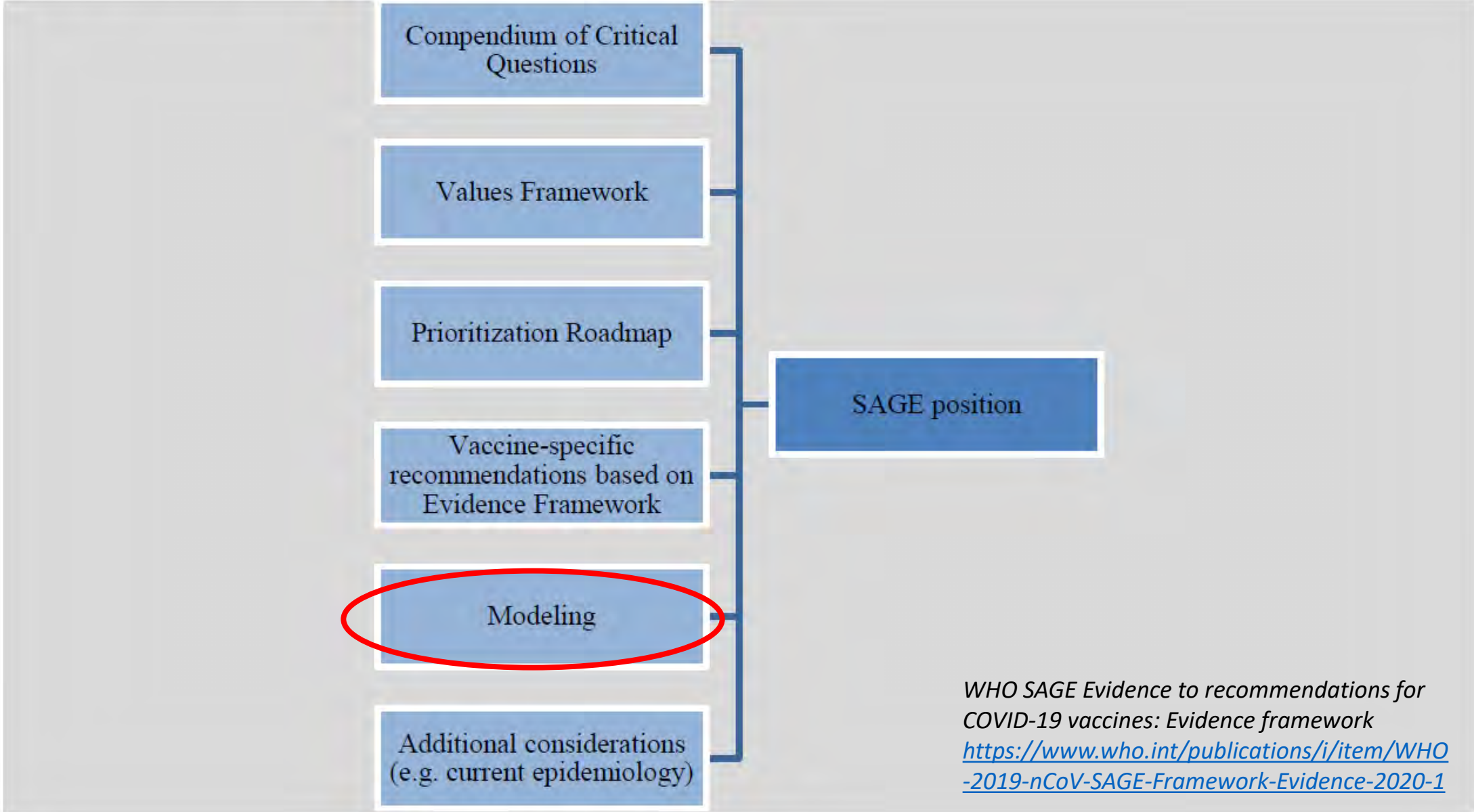


Summary of findings for SAGE/SAGE WG & systematic review of literature

## Presentations to modelling subgroup

Country modelled	# models presented
U.K. / EU	7
Global/multi-country	3
U.S.	5
Indonesia	1
Kenya	1 (no vaccination)
Mexico	1
Pakistan	1
Singapore	1
South Africa	1
Thailand	1
<b>TOTAL</b>	<b>22</b>

**Figure 1: Process for developing the draft SAGE position.**



# Outputs

## WHO SAGE ROADMAP FOR PRIORITIZING USES OF COVID-19 VACCINES IN THE CONTEXT OF LIMITED SUPPLY

*An approach to inform planning and subsequent recommendations based upon  
epidemiologic setting and vaccine supply scenarios*

*Version 1  
20 October 2020*



### **Background paper on Covid-19 disease and vaccines**

Prepared by the Strategic Advisory Group of Experts (SAGE) on Immunization Working Group on  
COVID-19 vaccines

*22 December 2020*

### **Interim recommendations for use of the Pfizer– BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing**

Interim guidance  
8 January 2021



Which questions in the July 2020 RfI have been addressed, which questions are still outstanding?

## Health and epidemiological impacts

Question	HIC	LMIC
1. What would be the impact of vaccinating each of the following target groups on SARS-CoV-2 infections, COVID-19 deaths, and COVID-19 years of life lost, for vaccines given during 2020-21 when vaccination is added to counterfactual scenarios of: (i) no interventions, or (ii) continued implementation of non-pharmaceutical interventions (NPIs)?		
a. older adults (50+, 65+ or 75+ years)	+++	++
b. younger adults (18-49 years)		
c. school-age children (5-17 years)		
d. those at high risk of severe disease because of their underlying health conditions (e.g., cardiovascular disease, kidney disease; see section III)	+	
e. key workers (e.g., workers in health and social care, teachers; see section III)	++	
f. groups at high risk of infection (e.g., dense urban slums/informal settlements, health workers; see section III)	+	+

+strength of evidence (0-3, none-high)

## Health and epidemiological impacts (contd.)

Question	HIC	LMIC
2. What are the optimal vaccination strategies in terms of target groups under different possible supply scenarios for COVID-19 vaccine during 2020-21 to achieve the maximum reduction in SARS-CoV-2 infections, COVID-19 deaths or years of life lost?	++	+
3. How would health impacts be distributed across country income groups (high, middle, low) and within countries across household wealth quintiles for the different vaccination targeting approaches described in Questions 1-2?	+ <i>(across countries)</i>	+ <i>(across countries)</i>

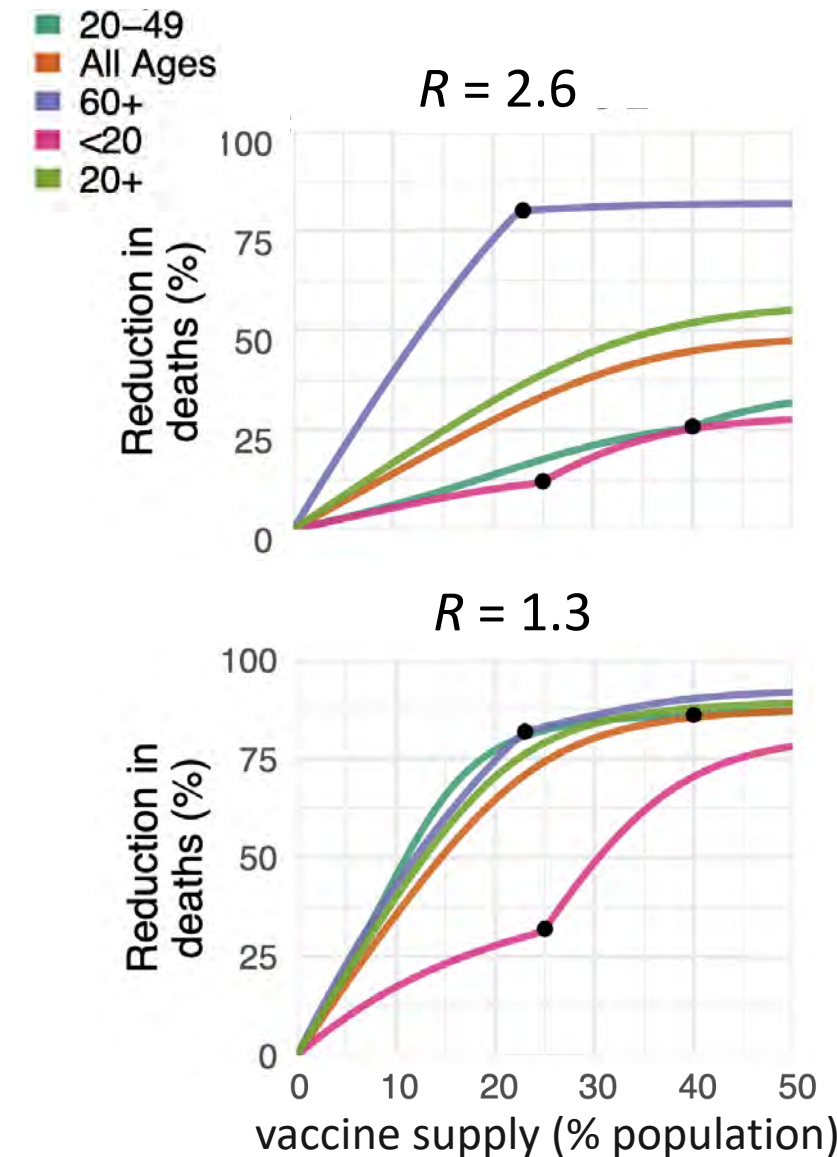
# Age-based vaccine prioritisation

## Key finding

- Across studies and countries, prioritising older adults over younger age-groups minimizes COVID-19 mortality and YLL/QALYs for initial limited supply, across age-dependent vaccine efficacy levels and for vaccines effective against infection or disease only

## Recent updates

- Robust to realistic supply dynamics, additional country-specific analyses and phase 3 results
- Robust to substantially lower efficacy in older adults
- For low  $R$ , prioritizing younger adults can minimize mortality (as well as infections) – however, the differences are small and depend on high VE against infection/ shedding (currently limited evidence)





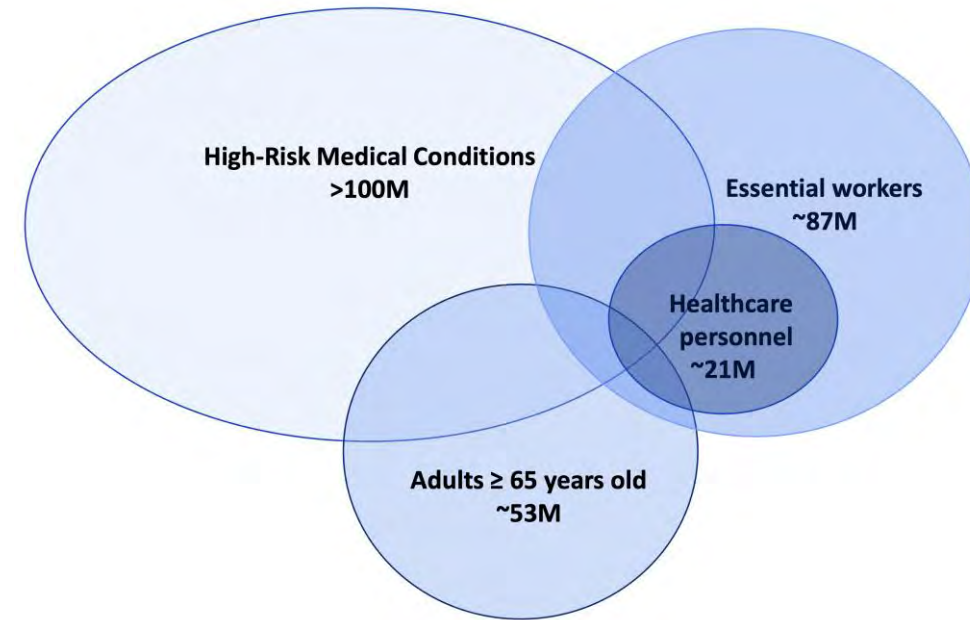
# Individuals with underlying health conditions

## Key finding

- Individuals with underlying health conditions at high-risk of severe COVID-19 should be prioritized, although the exact order of prioritisation relative to specific age-groups depends on the setting and VE against infection

## Recent updates

- Prioritisation depends on the specific comorbidity(ies)
- Prioritising oldest first is usually optimal because absolute risk of severe outcomes in younger age-groups is typically lower
- Other priority groups may have a high prevalence of comorbidities and high exposure (e.g., essential workers in the US)



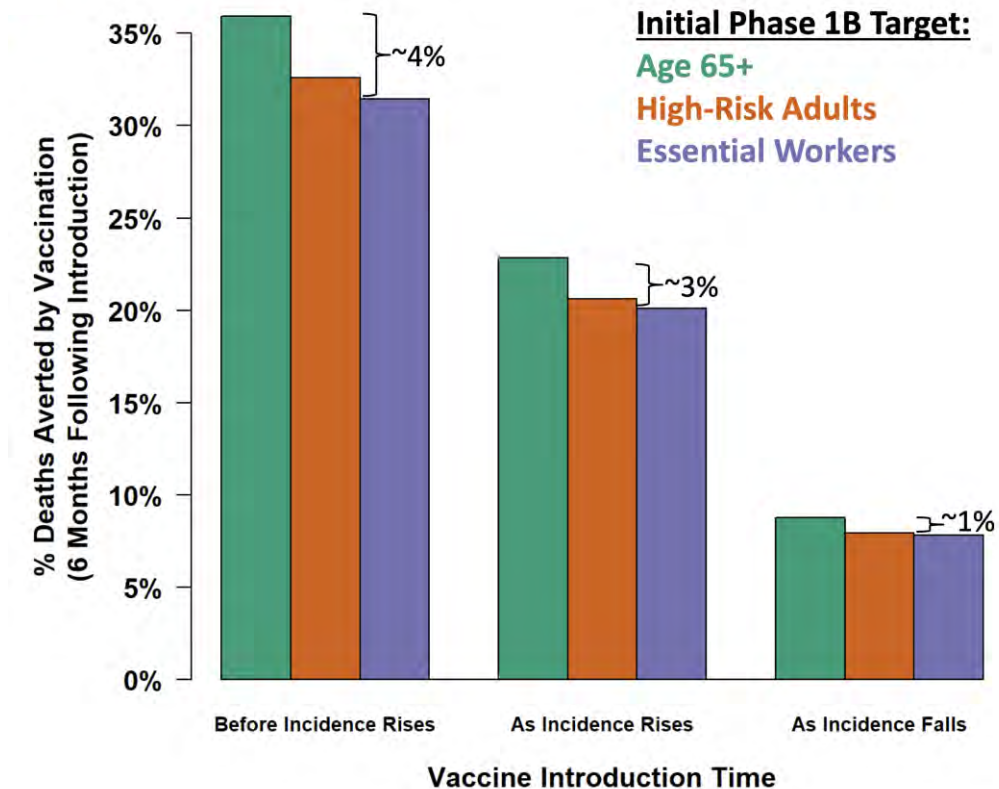
# Essential workers

## Key finding

- Health and social care workers should be prioritised to minimise mortality or infections, given their relatively high exposure and potential to transmit infection to vulnerable individuals

## Recent updates

- Impact of vaccinating all (health and non-health) essential workers (in the US) similar impact on mortality to strategies targeting high-risk (comorbid) or older adults if vaccine effective against infection
- Occupational exposure risk varies across essential worker occupational categories, and should be considered along with other factors (e.g., age)



Biggerstaff, M. (2020) ACIP presentation for vaccine prioritisation in the US 30 October 2020

# Optimal strategy

- Modelling broadly supports WHO roadmap on prioritized populations for COVID-19 vaccination
- Some national decisions may require country-specific models (e.g. identification of essential workers)
- Vaccine impact depends on counterfactual and policy decisions around NPIs
- Some gaps in modelling evidence to support roadmap (e.g. transmission prevention strategy targeting travellers and younger age groups in epidemiological setting of 'no cases'), some to be addressed by RfP commissioning work

## Prioritisation for settings with community transmission

### Stage 1 (1-10% coverage)

- High-risk health workers
- Older adults (age cut-off depends on setting)

### Stage 2 (11-20% coverage)

- Remaining older adults
- Groups with comorbidities
- Sociodemographic groups at high-risk of severe disease
- Health workers delivering immunisation
- High priority teachers & school staff

### Stage 3 (21-50% coverage)

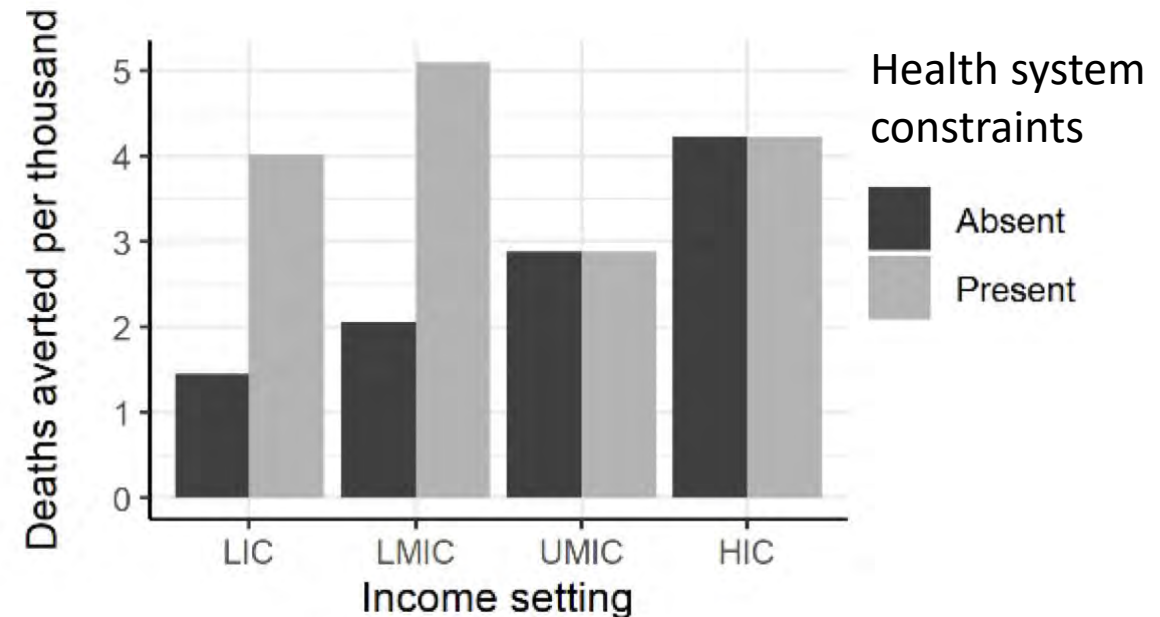
- Remaining teachers & school staff
- Other essential workers (non-health or education)
- Pregnant women
- Low and moderate risk health workers
- Personnel required for vaccine manufacture
- Social employment groups unable to physically distance

<https://www.who.int/publications/m/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply> (13 November 2020)

# Equity

- Limited work on distribution of COVID-19 vaccination health impact within or between countries
- Between countries “a strategy in which doses are allocated to countries in proportion to their population size is close to optimal in averting deaths.”
- More work to be reviewed and/or commissioned by modelling subgroup

Vaccine impact by income setting



Hogan, Winskill et al. 2020 Imperial College London report doi: [10.25561/82822](https://doi.org/10.25561/82822)

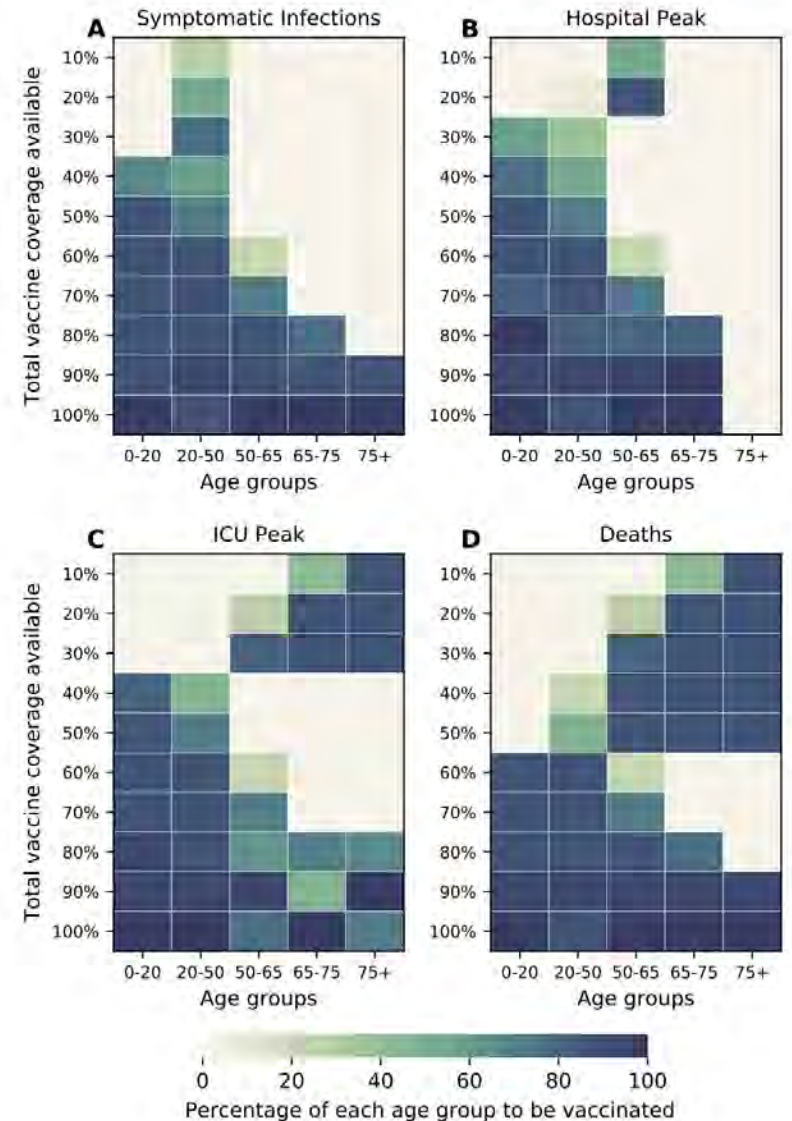
# Economic and social impacts

Question	HIC	LMIC
4. What would be the impact on protecting essential services (e.g., health and social care, education) of the different vaccination targeting approaches described in Questions 1-2?	+	
5. At what level of vaccine efficacy and vaccination coverage <u>for which target groups</u> could those NPIs that are most economically and societally disruptive (e.g., lockdowns, travel restrictions) be discontinued?	++	+
6. What would be the impacts in terms of economic welfare (e.g., as measured by GDP growth) and economic security (e.g., as measured by number of people living in poverty) <u>of different vaccination targeting approaches</u> (e.g., those in Questions 1-2) across country income groups (high, middle, low)?	+	+
7. From the societal perspective, what would be the cost-effectiveness per averted SARS-CoV-2 infection, COVID-19 death, and COVID-19 year of life lost <u>for the vaccination targeting approaches</u> described in Questions 1-2?	+	+
8. In monetary terms, what is the full public health and societal value of vaccination with a COVID-19 vaccine?	+	

# Protecting essential services

## Key finding

- With initial limited supply, vaccinating older adults (50-65) was optimal for keeping hospitalizations below peak capacity (thereby protecting health services)
- vaccinating the oldest adults (65+) was optimal to keep ICU use below peak capacity
- Sensitive to assumed VE against infection
- Work on schools commissioned as part of RfP



# Economic impacts, cost-effectiveness, and value of vaccination

## Key finding

- COVID-19 vaccine likely to be cost-effective from healthcare perspective in HICs using conventional thresholds (e.g., £20,000 per QALY), and to deliver net monetary benefits from averted GDP losses
- Full societal perspective analysis is challenging given pandemic's many indirect effects

## Recent updates

- Equitable global access to COVID-19 vaccines across country income groups could avert \$3.4 trillion (3.7%) in GDP losses annually in contact-intensive sectors alone.
- Ensuring access to COVID-19 vaccines in low-income countries has an estimated return on investment of \$4.8 in averted GDP losses for every \$1 invested.

# Model essential features

Feature	Questions for which most relevant
Differences in COVID-19 severity by age	Q1-2
Different vaccine profiles	All
Separate analyses for high-, middle- and low-income countries or country groups	All
Uncertainty and sensitivity analysis to model parameters	All
Counterfactual analysis	All



# Model desirable features – addressed in at least 1 analysis

Feature
Indirect (herd) effects of vaccination (including consideration of acquired immunity and its variation across countries) and age-dependent transmission risk
Differences in COVID-19 severity by comorbidities, ideally stratified by age
Additional health, social, and economic outcome measures, e.g., COVID-19 cases, hospitalisations, SARS-CoV-2 infection averted per dose; COVID-19 death averted per dose; COVID-19 YLL averted per dose
Health system capacity (ventilators, ICU beds) and available therapies and non-vaccine pharmaceutical interventions (e.g., therapeutics, monoclonal antibodies) that may affect the infection fatality rate (IFR)
Impact of vaccinating seropositives, and potential impact of pre-vaccination serological testing and exclusion of seropositives from vaccination
Cost-effectiveness analyses conducted from other perspectives (e.g., health system, government)
Detailed analysis of exemplar country(ies) that have good epidemiologic data
Implementation of models or model results in interactive software that can be used in countries by decision makers to explore scenarios
Distribution of impacts across social groups (rural/urban)

# Model desirable features – not yet addressed

Feature
Potential reduction in infectiousness of breakthrough infections among vaccinated individuals
Potential differences in vaccine efficacy against mild or severe/fatal COVID-19 disease
Risk/benefit analysis for vaccines with hypothetical risks of adverse outcomes (e.g., vaccine-associated enhanced disease) at different frequencies
Distribution of impacts across social groups (other dimensions such as gender, race/ethnicity)
Additional health, social, and economic outcome measures, e.g., cases with long-term sequelae, years lived with disability, DALYs, SEYLL; Excess deaths and years of life lost due to the COVID-19 pandemic generally; In GNI, poverty gap, GNI per capita, income inequality, employment
Impact of inclusion/exclusion of pregnant women from groups eligible for vaccination
Effect on coverage, cost, and cost-effectiveness of different programmatic delivery assumptions (e.g., delivery platforms such as facility-based, outreach, campaign; cold chain availability; human resource requirements) and how this may vary among countries
Effect on coverage of different vaccine acceptance and demand assumptions and how this may vary among countries
Scenarios exploring impacts of combinations of different COVID-19 vaccines with different characteristics
Effects of different combinations of NPIs for different vaccination scenarios and epidemiological and country settings
Sensitivity analysis of results to potential viral mutation and antigenic change

Pause for IVIR-AC feedback

# Outstanding priority modelling questions identified by SAGE WG (beyond just prioritization)

RfP\* issued on 8 Jan with 31 Jan deadline: 18 questions under 5 topics:

- **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

\*<https://www.ungm.org/Public/Notice/120376>

# Summary of RfP bids received

- 23 bids received, of which 19 met RfP eligibility criteria; total bids = \$1.5M
- Range of geographic settings proposed (global multi-country, individual country LMICs)

Topic	# Qs in topic	# bids with topic
Topic I: Vaccination strategies to <b>maximize in-person schooling</b> provision	6	5
Topic II: Vaccination strategies to <b>keep health system use below maximum capacity</b>	2	17
Topic III: Importation into <b>settings with no cases and outbreak response vaccination</b>	4	4
Topic IV. Extent to which vaccination can <b>allow non-pharmaceutical interventions to be lifted</b>	5	12
Topic V. Strategies to <b>maximize impact of available supply</b> of vaccines	5	8

- Current status: Initial evaluation of bids has been completed; clarifications and revised budget proposals received. Awards from WHO are pending.
- Timeline for initial results: 3-6 months, depending on scope of questions and countries

# Additional priority & emerging questions outside RfP

## Questions not yet fully addressed from RfI

- The distribution of health impacts within and between countries
- The full public health and societal value of vaccination with a COVID-19 vaccine (in monetary terms)
- Cost-effectiveness of vaccination

## Emerging questions not addressed in initial RfI or RfP

- Impact of variants on vaccine impact, prioritization, and potentially cross-country allocation\*
- Impact of vaccines on transmission
- Disease control scenarios if vaccines are/are not licensed for pediatric use

\*desired features in our initial RfI in July 2020 included “Sensitivity analysis of results to potential viral mutation and antigenic change” but we have not reviewed any modelling of multiple strains/antigenic change

# Questions for IVIR-AC

- What additional modelling questions should SAGE WG and SAGE consider related to COVID-19 vaccination impacts in the short, medium and longer term?
- What are the remaining critical evidence or quality gaps (methodological, data, model parameters, other) related to COVID-19 vaccination impact modelling, considering the models identified by the Working Group through literature review, Request for Information, and Request for Proposals? How can these gaps be addressed?
- How should modelling of vaccination in combination with other COVID-19 interventions beyond SAGE's remit be addressed?
- More generally, any recommendations on process of reviewing and summarizing modelling evidence and process of incorporating this into SAGE's Evidence to Recommendations process, particularly for vaccine-specific recommendations?

Additional slides (modelling  
scenarios, RfP questions)



# Modelling scenarios

July 2020

Counterfactual scenario	Vaccine characteristics scenario	Coverage scenario	Supply scenario	Analytic horizon
I. No intervention	A. Efficacy vs. disease and infection*, all ages	1. High (80%)	a. COVAX	i. Short term (end-2021)
II. Continued NPIs	B. Efficacy vs. disease, all ages	2. Mid (50%)	b. COVAX + direct	ii. Medium term (end-2022)
	C. Efficacy vs. disease, younger ages only	3. Low (20%)	c. COVAX + direct (shared)	iii. Long term (end-2030)

- Key areas to update:
  - VE central estimates based on trial results (already led by modellers)
  - Vaccine supply (COVAX projections shared with modellers)
  - Vaccine coverage
  - VE against infection
  - VE against severe disease/death
  - COVID-19 morbidity

# Topic I: Vaccination strategies to maximize in-person schooling provision

- **Health impacts on teachers/staff and students:** Vaccinating teachers/staff vs. students vs. other adults: what would be health impacts on teachers/school staff, students, households of teachers, staff, and students, broader community?
- **Impacts on use of school-based mitigation measures:** Would vaccinating teachers/staff vs. students vs. other adults permit reduction of any school-based mitigation measures while not increasing SARS-CoV-2 infections?
- **Economic impacts of use of remote learning:** If vaccinating teachers/staff vs. students vs. other adults would permit reduction of remote learning, what would be the economic impacts on parents and students?

## Topic II: Vaccination strategies to keep health system use below maximum capacity

- **Priority groups to vaccinate:** In which order should groups be prioritized for COVID-19 vaccination as vaccine supply increases so as to keep hospitalizations, and intensive care unit use (where available), due to COVID-19 and other background causes below maximum hospital capacity in the setting(s) modelled?
- **Vaccination and NPI combinations:** What would be the optimal vaccination strategy in combination with which non-pharmaceutical interventions to keep hospitalizations due to COVID-19 and other background causes below maximum hospital capacity in the settings modelled?

## Topic III: Importation into settings with no cases and outbreak response vaccination

- **Outbreak likelihood:** In settings with no COVID-19 cases with and without previous COVID-19 vaccination (per Prioritization Roadmap), what would be the estimated probability and timeline for an outbreak of SARS-CoV-2 due to importation in the absence of continued non-pharmaceutical interventions (e.g., travel restrictions)?
- **Outbreak control with vaccination:** In these settings, in the event of an outbreak due to SARS-CoV-2 importation, what level of vaccine efficacy, speed of vaccination and vaccination coverage targeting different groups would be needed to control the outbreak through (i) vaccination alone in the absence of non-pharmaceutical interventions, and (ii) vaccination in combination with non-pharmaceutical interventions?
- **Outbreak health impacts:** What would be the number of SARS-CoV-2 infections, hospitalizations, and deaths incurred before the outbreak is contained through (i) vaccination alone in the absence of non-pharmaceutical interventions, and (ii) vaccination in combination with non-pharmaceutical interventions? How would these health impacts be distributed across population subgroups?

## Topic IV. Extent to which vaccination can allow non-pharmaceutical interventions to be lifted

- **Health impacts of lifting NPIs under vaccination scenarios:** What would be the health impacts of lifting non-pharmaceutical interventions (e.g., business closures, school closures, travel restrictions, gathering size limits, mask wearing) at different levels of vaccine efficacy and vaccination coverage for different priority groups?
- **Vaccination in combination with NPIs to keep  $R_t < 1$ :** What combinations of vaccine efficacy and vaccination coverage in different priority groups as outlined in the SAGE Prioritization Roadmap together with which combinations of non-pharmaceutical interventions could keep  $R_t$  below 1?
- **Elimination potential and cost-benefit:** What is the probability and stability of local or regional elimination of SARS-CoV-2 transmission under different scenarios of (i) vaccine efficacy and vaccination coverage in different priority groups and (ii) different combinations of non-pharmaceutical interventions?
  - Net monetary benefits of elimination vs. high control

## Topic V. Strategies to maximize impact of available supply of vaccines

- **Coverage with different dose intervals:** For vaccines that require two doses, for a given vaccination rate, vaccine supply timeline, and analytic horizon, what 1<sup>st</sup> dose and 2<sup>nd</sup> dose coverage would be achieved for different intervals between doses?
- **Health impacts of different dose intervals:** For vaccines that require two doses, for what combinations of 1<sup>st</sup> and 2<sup>nd</sup> dose (i) vaccine efficacy, (ii) duration of vaccine-induced protection, (iii) interval between doses, and (iv) 2<sup>nd</sup> dose coverage would the health impacts be larger, faster, or of longer duration if available supply was used to vaccinate more individuals with a 1<sup>st</sup> dose more quickly by delaying the 2<sup>nd</sup> dose or allowing flexibility in the retention of supply sufficient to guarantee a second dose?
- **Optimal distribution of different vaccine products:** What would be the optimal distribution of different vaccine products (e.g., mRNA, viral-vectored) with different characteristics among priority groups within countries and between countries to maximize health impacts?

# Background information

RfI:

- <https://www.who.int/publications/m/item/prioritized-infectious-disease-and-economic-modelling-questions>

RfP:

- <https://www.ungm.org/Public/Notice/120376>

Background paper:

- <https://www.who.int/publications/i/item/background-paper-on-covid-19-disease-and-vaccines>

## **Session 2: Optimizing COVID-19 vaccine costing**



# IVIR-AC Meeting Session: Optimizing COVID-19 Vaccine Costing

March 1, 2021

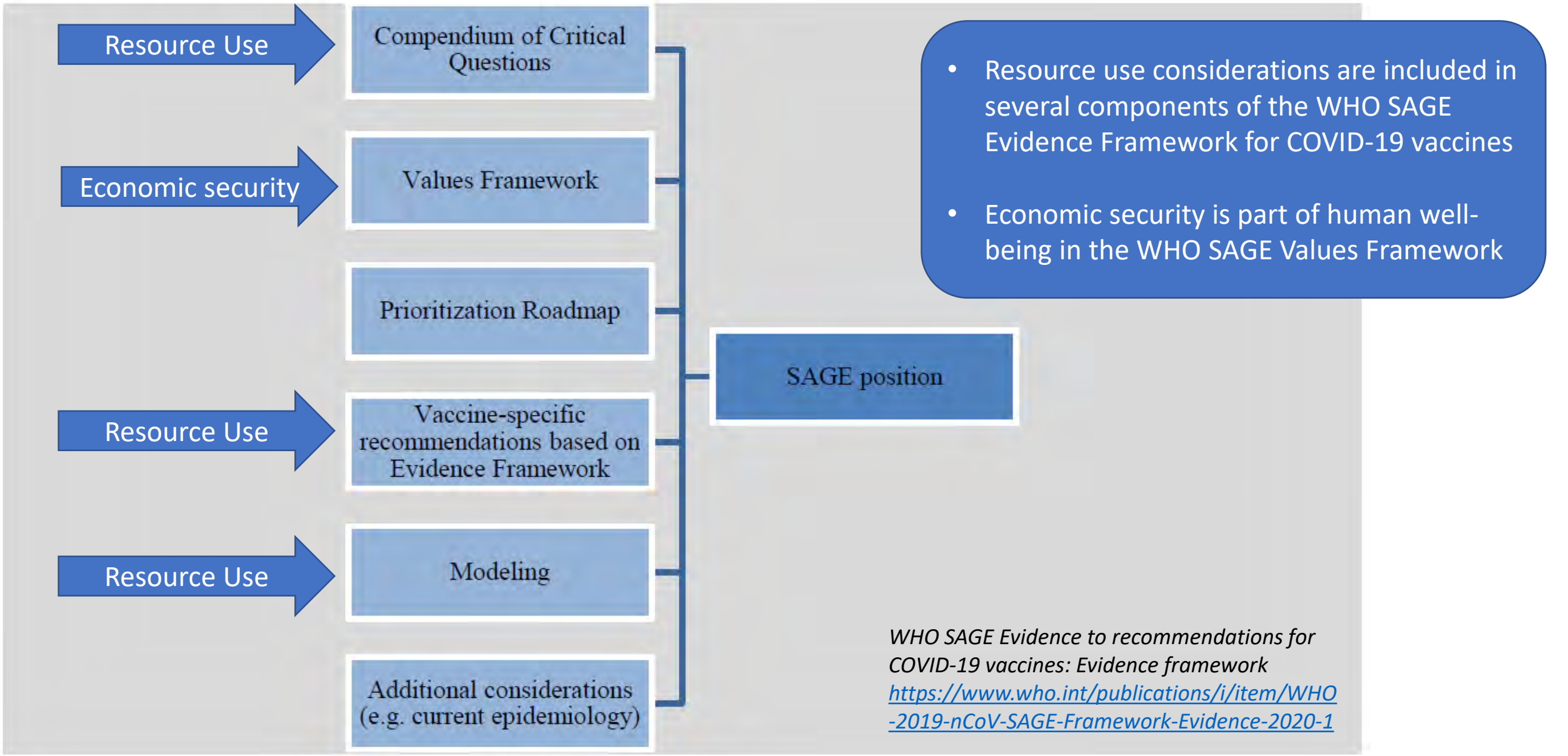
Disclaimer: The presenter is speaking as a member of the WHO SAGE Working Group on COVID-19 Vaccines. All Working Group members serve in their individual capacities. The views in this presentation are those of the presenter and do not necessarily reflect the views of the U.S. Centers for Disease Control and Prevention.

BACKGROUND

# Session overview and objectives

- This session serves to inform IVIR-AC of the SAGE Evidence to Recommendations (E2R) “Resource Use” criterion for the vaccine-specific recommendations, and the tools and approaches to estimating resource needs for COVID-19 vaccination identified to date.
  - E2R questions:
    - “Are the resources required small?”
    - “Cost effectiveness”
    - “Is vaccine X a reasonable and efficient use of resources?”
  - Considerations of perspective, intervention, and comparator (currently always placebo/no vaccination)

**Figure 1: Process for developing the draft SAGE position.**



# Evidence to Recommendations (EtR) Framework

Example: 5 Jan 2021  
SAGE meeting

EtR Domain	Question
Public Health Problem	<ul style="list-style-type: none"><li>• Is the problem of public health importance?</li></ul>
Benefits and Harms	<ul style="list-style-type: none"><li>• How substantial are the desirable anticipated effects?</li><li>• How substantial are the undesirable anticipated effects?</li><li>• Do the desirable effects outweigh the undesirable effects?</li></ul>
Values	<ul style="list-style-type: none"><li>• Does the target population feel the desirable effects are large relative to the undesirable effects?</li><li>• Is there important variability in how patients value the outcomes?</li></ul>
Acceptability	<ul style="list-style-type: none"><li>• Is the intervention acceptable to key stakeholders?</li></ul>
Feasibility	<ul style="list-style-type: none"><li>• Is the intervention feasible to implement?</li></ul>
Resource Use	<ul style="list-style-type: none"><li>• Is the intervention a reasonable and efficient allocation of resources?</li></ul>
Equity	<ul style="list-style-type: none"><li>• What would be the impact of the intervention on health equity?</li></ul>

**“The vaccine” or “The intervention” = Pfizer-BioNTech COVID-19 vaccine**  
**“The problem” = COVID-19 disease**



E2R	Question	SAGE WG Judgement
Public health problem	Is the COVID-19 pandemic of public health importance?	Yes
Benefits and Harms	How substantial are the desirable benefits of the intervention?	Substantial
	How substantial are the undesirable harms of the intervention?	Small
	Do the benefits outweigh the risk/harm?	Yes
	What is the overall certainty of the evidence for the outcomes?	High for prevention of symptomatic SARS-CoV-2 Low for hospitalizations and death Moderate for safety Absent for impact on transmission
Value	Do the target populations value the desirable benefit as large relative to the undesirable risks/harms?	Will vary within and between countries
Acceptability	Is BNT162b2 acceptable to key stakeholders?	Probably yes
Feasibility	Is BNT162b2 feasible to implement?	Very difficult but not impossible in many LMICs
Resource use	Is BNT162b2 a reasonable and efficient use of resources?	Will vary within and between countries
Equity	What would be the impact of the intervention on health equity within and between countries?	Risk of increasing inequity

# EVIDENCE ASSESSMENT: mRNA-1273 COVID-19 vaccine

Example: 21 Jan 2021 SAGE meeting

Key evidence to inform policy recommendations on the use of mRNA-1273 COVID-19 vaccine

[https://cdn.who.int/media/docs/default-source/immunization/sage/2021/january/3-evidence-assessment\\_covid19\\_moderna\\_revised\\_final.pdf?sfvrsn=61ab4400\\_8](https://cdn.who.int/media/docs/default-source/immunization/sage/2021/january/3-evidence-assessment_covid19_moderna_revised_final.pdf?sfvrsn=61ab4400_8)

## Population

- Adults (18-64 years)
- Older adults ( $\geq 65$  years)
- Individuals with comorbidities or health states that increase risk for severe COVID-19

## Intervention

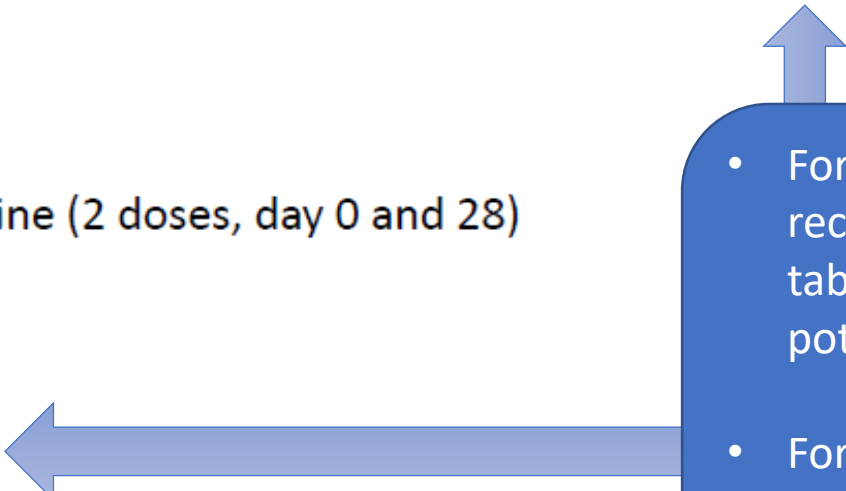
- mRNA-1273 COVID-19 vaccine (2 doses, day 0 and 28)

## Comparison

- Placebo/active control

## Outcomes

- Efficacy against (PCR confirmed) COVID-19 or severe COVID-19, any adverse event, serious adverse events, systemic and local adverse events

- 
- For each COVID-19 vaccine-specific recommendation, currently three E2R tables are completed for three potential priority populations.
  - For all E2R tables, the comparison is against placebo/active control, depending on Phase III trial design.

Key evidence to inform policy recommendations on the use of mRNA-1273 COVID-19 vaccine

[https://cdn.who.int/media/docs/default-source/immunization/sage/2021/january/3-evidence-assessment\\_covid19\\_moderna\\_revised\\_final.pdf?sfvrsn=61ab4400\\_8](https://cdn.who.int/media/docs/default-source/immunization/sage/2021/january/3-evidence-assessment_covid19_moderna_revised_final.pdf?sfvrsn=61ab4400_8)**Resource Use- is mRNA-1273 an efficient allocation of resources?*****Are the resources required small?***

- Considerable additional resources are required for procurement of vaccine and vaccination supplies, training, social mobilization and communication, delivery logistics, information systems, immunization safety surveillance, and planning and coordination, especially for vaccination of priority groups without existing robust immunization platforms and where surge resources will be needed to accelerate roll-out.

No	Uncertain	Yes	Varies
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

***Cost-effectiveness***

- Cost-effectiveness analyses and economic impact of vaccination will depend on: Cost of vaccine, COVID-19 burden, timing of vaccine roll-out (at time of rise of cases versus decline), vaccination coverage levels achieved, duration of vaccine protection, vaccination implementation costs, other mitigation measures used.

No	Uncertain	Yes	Varies
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>



# Questions to IVIR-AC

- How should the Resource Use criterion in the Evidence to Recommendations process be interpreted and applied for SAGE's COVID-19 vaccine-specific recommendations (e.g., perspective, intervention, counterfactual)?
- Which types of estimation approaches and tools are most appropriate for global- and country-level costing and decision making around COVID-19 vaccination resource use?

# RESOURCE USE ESTIMATES

# E2R tables: Resource Use criterion

Resource Use Criterion elements	WG Judgments to date for interim recommendations for Pfizer-BioNTech <sup>1</sup> , Moderna <sup>2</sup> , & AstraZeneca <sup>3</sup> COVID-19 vaccines			
E2R table: <b>Are the resources required small?</b>	No <input checked="" type="checkbox"/>	Uncertain	Yes	Varies
E2R table: <b>Cost-effectiveness</b>	No	Uncertain	Yes	Varies <input checked="" type="checkbox"/>
Summary E2R slides: <b>Is the intervention a reasonable and efficient allocation of resources?</b>	Will vary within and between countries			

- **What is the comparison and perspective?**
  - Small compared to what? For whom?
  - Cost-effective compared to what? For whom?
  - Reasonable and efficient compared to what alternative allocation? For whom?

*NB: WHO Economic Evaluation of Immunization Programmes guidance recommends societal perspective, but other perspectives may be appropriate depending on the policy question.*

1. [https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-\(pfizer-biontech\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-(pfizer-biontech)-against-covid-19)
2. [https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)
3. [https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1)

# E2R tables: Resource Use criterion

Resource Use criterion elements	WG Judgments to date for interim recommendations for Pfizer-BioNTech <sup>1</sup> , Moderna <sup>2</sup> , & AstraZeneca <sup>3</sup> COVID-19 vaccines			
E2R table: <b>Are the resources required small?</b>	No <input checked="" type="checkbox"/>	Uncertain	Yes	Varies
E2R table: <b>Cost-effectiveness</b>	No	Uncertain	Yes	Varies <input checked="" type="checkbox"/>
Summary E2R slides: <b>Is the intervention a reasonable and efficient allocation of resources?</b>	Will vary within and between countries			

- All EtR tables for vaccine-specific recommendations are framed in terms of the product vs. placebo/ no vaccination for the prevention of COVID-19 as the PICO question.
  - **Should “placebo/no vaccination” be understood as the prevailing non-pharmaceutical policy and behavioral responses (e.g., lockdowns, distancing, masks, hand hygiene) during the clinical trials as the comparator for resource use judgments?**
  - **Should SAGE comment on differences in resource use implications across vaccine products in the vaccine-specific recommendations (e.g., price differences, cold chain cost implications)?**
    - Should this be done for the resource use criterion alone if evidence is not yet systematically available to compare across other vaccine characteristics (e.g., efficacy, safety)?
    - If so, should this be done neutrally rather than comparatively (e.g., state vaccine price and cold chain requirements for the product, without stating if these are higher/lower vs. other products)?

1. [https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-\(pfizer-biontech\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-(pfizer-biontech)-against-covid-19)

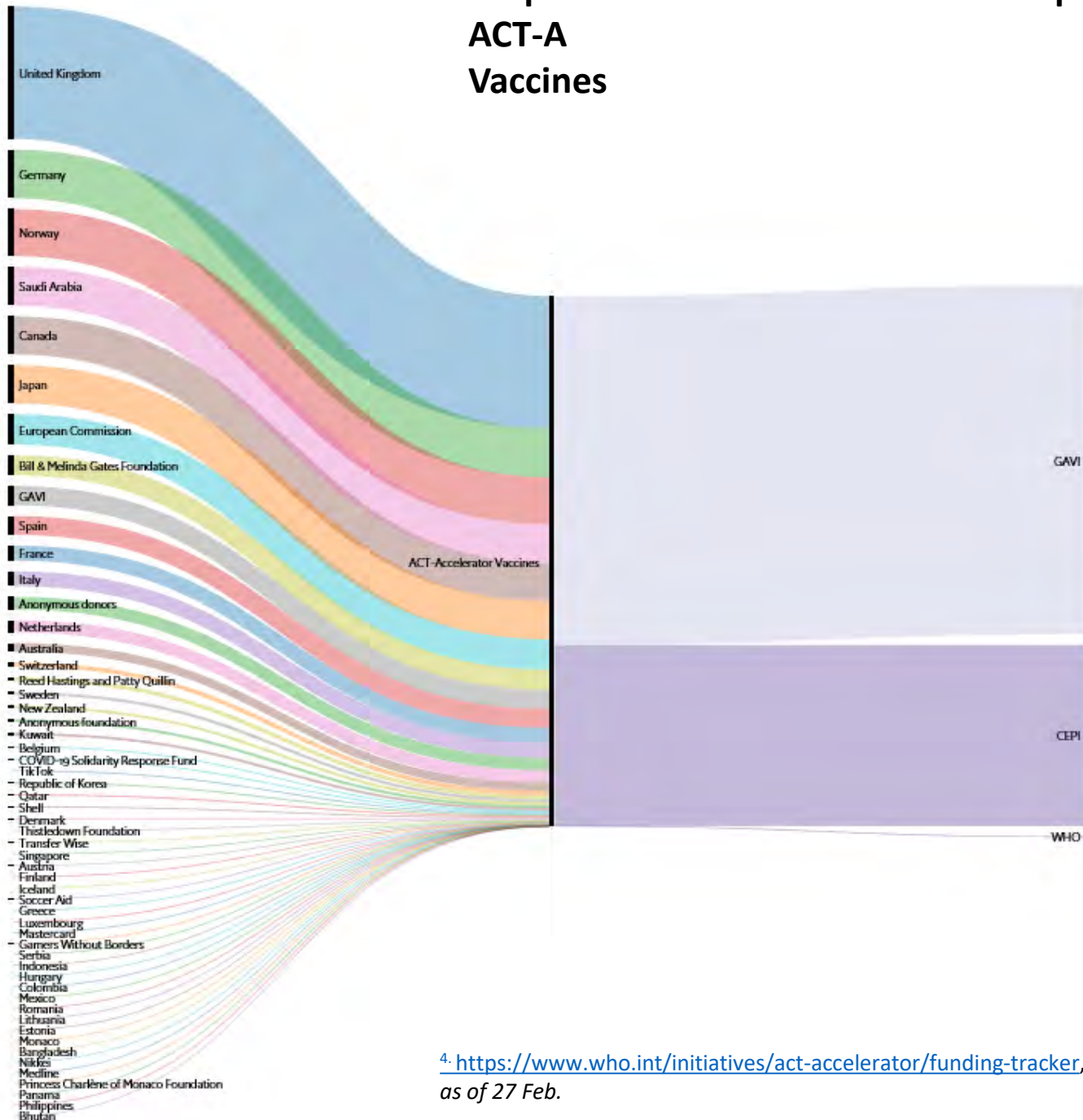
2. [https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)

3. [https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1)

# Source

## Purpose: ACT-A Vaccines

## Recipient



## Are the resources required small?

- **\$16.6B** in 2020-2021 resources required for ACT Accelerator Vaccines Pillar (COVAX)<sup>1,2,3</sup>
- **\$4.8B** in COVAX Facility costs financed by Self-Financing Participant economies<sup>2,3</sup>
- **\$4.1B** committed to date to ACT-A Vaccines pillar<sup>4</sup>
- *By comparison, \$8.8B for Gavi budget 2021-2025 for 18 VPDs<sup>5</sup>*

<sup>1</sup>. <https://www.who.int/docs/default-source/coronaviruse/act-accelerator/economic-investment-case-final-v2.pdf>

<sup>2</sup>. <https://www.who.int/docs/default-source/coronaviruse/act-accelerator/act-a-urgent-priorities-financing-requirements-final-single-11nov20.pdf>

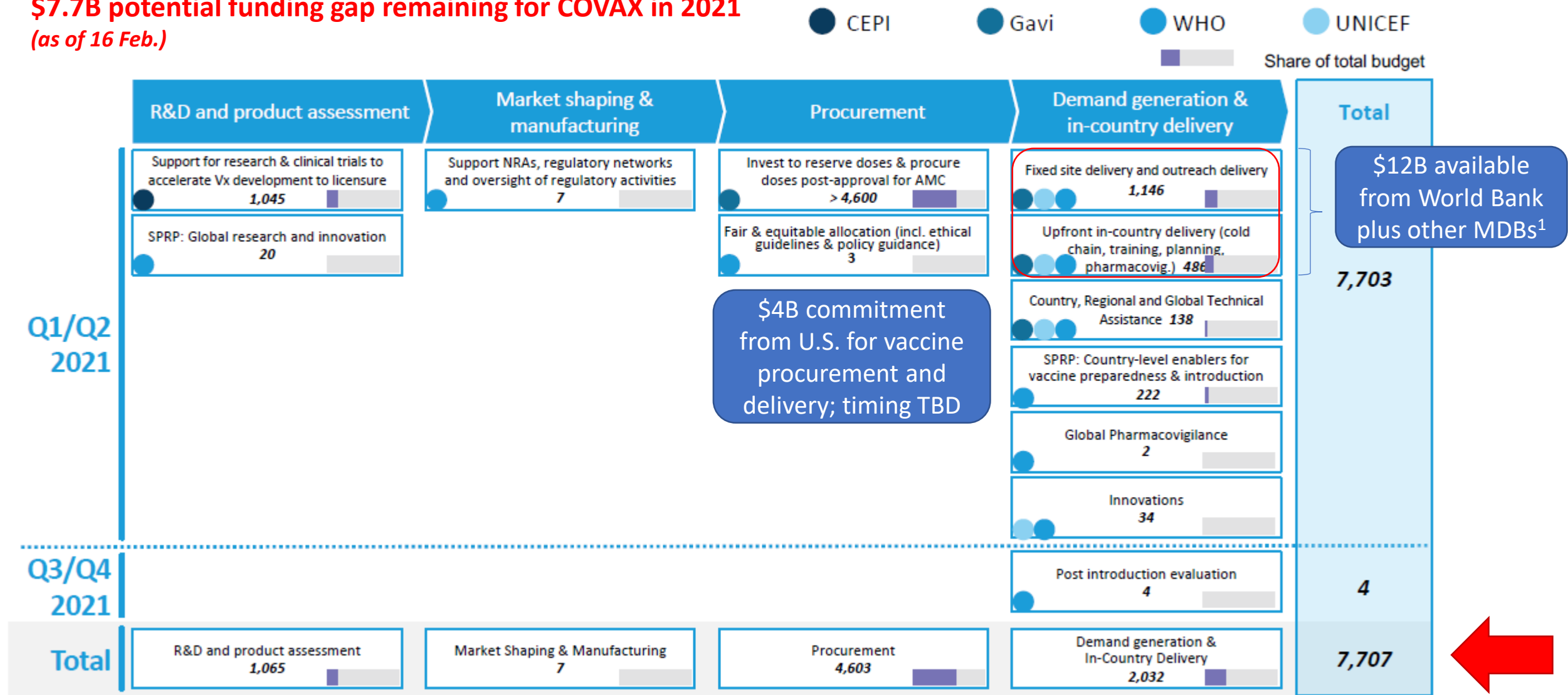
<sup>3</sup>. [https://www.who.int/docs/default-source/coronaviruse/act-accelerator/act-accelerator-strategy-report-2021-16\\_feb\\_2021-post-council-version.pdf?sfvrsn=3fad3d0\\_5](https://www.who.int/docs/default-source/coronaviruse/act-accelerator/act-accelerator-strategy-report-2021-16_feb_2021-post-council-version.pdf?sfvrsn=3fad3d0_5)

<sup>5</sup>. <https://www.gavi.org/sites/default/files/publications/2021-2025-Gavi-Investment-Opportunity.pdf>

<sup>4</sup>. <https://www.who.int/initiatives/act-accelerator/funding-tracker>, as of 27 Feb.

**Figure D.1 – Vaccines Pillar funding gap by period and deliverable packages – in US\$ million**

**\$7.7B potential funding gap remaining for COVAX in 2021**  
(as of 16 Feb.)



Notes: <sup>1</sup> Upfront in-country delivery already received a US\$ 90 million pledge, budget is US\$ 576 million. <sup>2</sup> Technical Assistance also received a US\$ 60 million pledge, budget is US\$ 198 million.

[https://www.who.int/docs/default-source/coronavirus/act-accelerator/act-accelerator-strategy-report-2021-16\\_feb\\_2021-post-council-version.pdf?sfvrsn=3fadb3d0\\_5](https://www.who.int/docs/default-source/coronavirus/act-accelerator/act-accelerator-strategy-report-2021-16_feb_2021-post-council-version.pdf?sfvrsn=3fadb3d0_5)

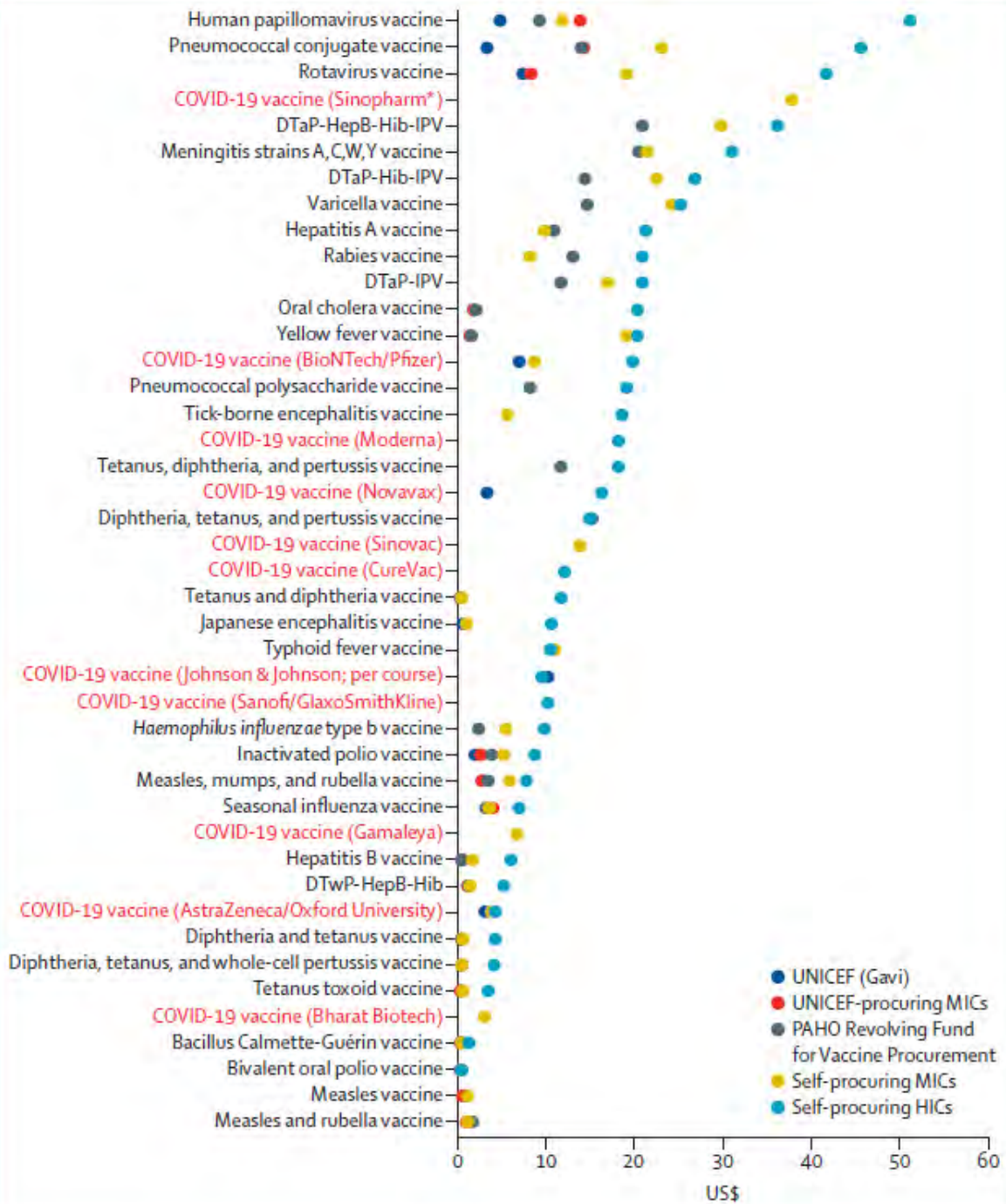
1. <https://www.worldbank.org/en/news/factsheet/2020/10/14/world-bank-covid-19-response>



## Median price per dose for COVID-19 vaccines by procurement mechanism and country income group

- Currently known COVID-19 vaccine prices range from \$2.50/dose (\$5/course) to \$44/dose (\$88/course)
- As with other vaccines, prices in self-procuring HICs and MICs are higher than in MICs using pooled procurement (UNICEF, PAHO RF) or Gavi-eligible LMICs
- COVAX AMC 92 countries may cost-share additional doses beyond 20% population at estimated \$7/dose (\$10.55/dose for SFP countries) based on supply availability, with potential for MDB financing

Wouters et al, 2021, *The Lancet*, [https://doi.org/10.1016/S0140-6736\(21\)00306-8](https://doi.org/10.1016/S0140-6736(21)00306-8)



# COVID-19 vaccine delivery costing in 92 AMC countries

**Table 9: In-country costs of delivering 1,219 million COVID-19 vaccine doses (US\$)**

Cost category	Upfront	Recurring		Total	Percent of total
		Facility	Outreach		
Planning and coordination	68,350,000			68,350,000	4%
Training	16,636,305			16,636,305	1%
Social mobilization	316,256,959			316,256,959	18%
Cold chain equipment (2-8°)	137,935,484			137,935,484	8%
Cold chain recurrent		3,154,155	8,991,480	12,145,636	1%
Pharmacovigilance	32,118,038			32,118,038	2%
Vaccination certificates		9,462,466	26,974,441	36,436,907	2%
PPE		22,079,088	98,906,283	120,985,371	7%
Hand hygiene	5,080,715	31,541,555	98,906,283	135,528,552	8%
Vaccine transport		6,926,325	16,329,953	23,256,279	1%
Waste management		13,878,284	39,562,513	53,440,797	3%
Per diem for outreach			567,465,884	567,465,884	33%
Transportation for outreach			200,041,930	200,041,930	12%
<b>Total</b>	<b>576,377,501</b>	<b>86,894,562</b>	<b>1,058,734,348</b>	<b>1,722,006,412</b>	<b>100%</b>
Percent of total	33%	5%	61%	100%	

- **\$1.7B in country-level costs for 2021**, not including vaccine procurement costs
- \$1.41 per dose supplied; \$3.15 per person vaccinated with 2 doses
- 17% of population in all countries except India (8.5%)
- 90% coverage of core HCWs + 80% coverage of 65+ + some coverage of <65
- Global-level estimates to inform fundraising → countries need to tailor to local context / strategies

COVAX Working Group on Delivery Costs. Costs of delivering COVID-19 vaccine in 92 AMC countries. 8 Feb. 2021.

<https://www.corecommitments.unicef.org/kp/costs-of-delivering-covid19-vaccine-in-92-amc-countries.url>



# Overview | The COVID-19 Vaccine Introduction & deployment Costing tool (CVIC)

The tool provides a **structured** and **comprehensive**, estimation of:

- Incremental **operational** and selected **capital costs** of introducing and deploying COVID-19 vaccines

It is used for **resource mobilization**, **budgeting**, requests for **external funding**, **strategy refinement**, e.g.,

- **NDVP<sup>1</sup> Budgeting and Costing**
- Refinement of strategy (**scenario analysis**)
- TA and funding resource requests through **WHO COVID-19 Partners Platform** (both AMC and self-financing countries)

In alignment with

- Guidance on developing a NDVP<sup>1</sup> for COVID-19 vaccines
- Guidance for prioritization and allocation: WHO SAGE values framework and prioritization roadmap
- Readiness assessment tool (VIRAT-VRAF-2.0)
- Gavi COVAX Readiness and Preparation TA Plan

## About the tool

Current version (1.0) available at:  
[www.who.int/publications/i/item/10665337553](http://www.who.int/publications/i/item/10665337553)

Version 2.0 will be available in February 2021 in all six working UN languages (Arabic, Chinese, English, French, Russian, Spanish) and Portuguese



# Inputs: What data is required to fill in the CVIC?

Note: the tool is prepopulated with data from national/international sources and updateable via internet each time the user logs on

## Population



- Demographic data **optional** – only if wish to override UN WPP

## Priorities



- NDVP / Sage Target Populations, incl. older adult age cutoff and those with comorbidities
- Geographic distribution of target population (access to health facilities)
- Prioritization plans

## Vaccines



- Vaccine Supply – Covax and non-Covax
- Vaccine prices and approximate delivery schedule
- Assumptions on vaccine wastage and expected uptake

## Distr./Admin.



- **Cold storage distribution points:** Regional stores, district stores
- **Service points:** Fixed sites with cold storage, fixed sites, outreach sites
- **HRH supply**
- **Unit prices** for HRH compensation, transportation/logistics, data management, demand generation. Optional: Unit prices for commodities
- **Unit prices** for central activities

## Output



- Relevant Country Partners
- Potential financing interest areas

# What is not included in these estimates?


- **Vaccination delivery costs in COVAX Self-Financing Participant economies and other high-income countries**
  - *Could potentially be estimated with CVIC tool customized to country*
- **Bilateral deals** by countries to procure vaccines (>\$20B globally)<sup>1</sup>
- **Prior R&D costs** for COVID-19 vaccines (public + non-profit R&D funding to date estimated >\$10B globally<sup>2</sup>)
- **Beneficiary costs** to access and receive vaccination

1. WHO, Gavi, CEPI, UNICEF. Media monitoring of vaccine deals. As of 10 Feb. 2021.

2. Wouters et al, 2021, *The Lancet*, [https://doi.org/10.1016/S0140-6736\(21\)00306-8](https://doi.org/10.1016/S0140-6736(21)00306-8)

*Note: (1) and (2) are underestimates based on available public information.*

# E2R tables: Resource Use criterion → Summary (1)



Resource Use Criterion elements	WG Judgments to date for interim recommendations for Pfizer-BioNTech <sup>1</sup> , Moderna <sup>2</sup> , & AstraZeneca <sup>3</sup> COVID-19 vaccines			
E2R table: <b>Are the resources required small?</b>	No <input checked="" type="checkbox"/>	Uncertain	Yes	Varies
E2R table: <b>Cost-effectiveness</b>	No	Uncertain	Yes	Varies <input checked="" type="checkbox"/>
Summary E2R slides: <b>Is the intervention a reasonable and efficient allocation of resources?</b>	Will vary within and between countries			

- Current WG judgment is that the resources required at country and global levels are not small compared to:
  - Existing EPI vaccines and vaccination programs in countries
  - Existing global immunization aid initiatives (e.g., Gavi annual budget)
- Even in HICs that may pay higher prices for certain routine vaccines than for COVID-19 vaccines, the larger population to be reached with COVID-19 vaccination and the delivery costs associated with rapid rollout under pandemic conditions likely offset any price difference.
- As each vaccine product is compared against placebo / no vaccination (i.e., as if it was the only vaccine available for use to prevent COVID-19), it is appropriate to use indicative costs at this stage of interim vaccine-specific recommendations. Empirical country-level cost evidence may be used once available.

1. [https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-\(pfizer-biontech\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-(pfizer-biontech)-against-covid-19)

2. [https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)

3. [https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1)



## COVID-19 vaccine products differ in price and other characteristics

- Cost-effectiveness analyses comparing different actual COVID-19 vaccine products not yet identified – important uncertainties remain (e.g., duration of protection)
- Price and other potential cost implications can be described in E2R table notes; however, not clear which perspective to use (global, country, payer) to judge cost-effectiveness

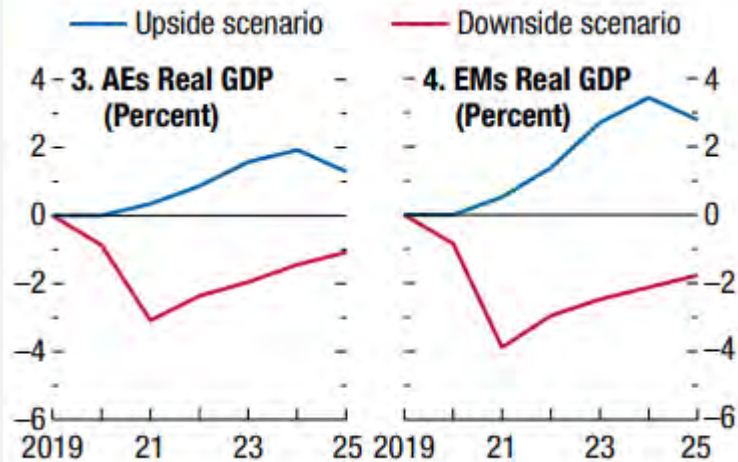
Wouters et al, 2021, *The Lancet*,  
[https://doi.org/10.1016/S0140-6736\(21\)00306-8](https://doi.org/10.1016/S0140-6736(21)00306-8)

	Development and production			Affordability	Allocation		Deployment	
	Authorised by a stringent regulatory body or WHO*	Efficacy in phase 3 trials†	Estimated production capacity for 2021	Lowest price offered (US\$ per course)‡	Percentage of doses pre-purchased by HICs for 2021 (based on known deals)	Supply agreement with COVAX§	Number of doses	Storage requirement during transport
AnGes with Osaka University	--	--	--	--	--	No	2	-70°C
Anhui Zhifei with CAMS	--	--	300 m	--	--	No	2 or 3	2-8°C
AstraZeneca with Oxford University	Yes	62%¶	3 bn	\$5	27%	Yes	2	2-8°C
Bharat Biotech	No	--	700 m	\$6	0%	No	2	2-8°C
Biological E	--	--	--	--	--	No	2	2-8°C
BioNTech with Pfizer	Yes	95%	2 bn	\$14	77%	Yes	2	-70°C
CAMS with IMB	--	--	--	--	--	No	2	2-8°C
CanSino	--	--	320 m	--	0%	No	1	2-8°C
Clover Pharmaceuticals with Dynavax	--	--	1 bn	--	--	No	2	2-8°C
Covax with Nebraska University	--	--	1 bn	--	0%	No	2	2-8°C
CureVac	--	--	300 m	\$24	100%	No	2	5°C
Gamaleya	Yes	92%	1 bn	\$6	0%**	No	2	-18°C
Inovio	--	--	100 m	--	--	No	2	2-8°C
Johnson & Johnson	--	66%††	1 bn	\$9	38%	Yes	1†‡	2-8°C
Medicago	--	--	80 m	--	100%	No	2	2-8°C
Moderna	Yes	94%	1 bn	\$31	97%	No	2	-20°C
Novavax	--	89%††§§	2 bn	\$6	31%	Yes	2	2-8°C
RIBSP	No	--	60 m	--	--	No	2	2-8°C
Sanofi with GlaxoSmithKline	--	--	--	\$19	73%	Yes	2	2-8°C
SII with Max Planck Institute	--	--	--	--	--	No	--	-50°C to -15°C
Sinopharm with Beijing Institute	Yes	79%††	1 bn	\$62	8%	No	2	2-8°C
Sinopharm with Wuhan Institute	No	--	600 m	\$62	8%	No	2	2-8°C
Sinovac	No	50-91%††¶¶	1 bn	\$21	18%	No	2	Room temperature
SK Biosciences	--	--	--	--	--	No	--	2-8°C
University of Hong Kong	--	--	--	--	--	No	--	-50°C to -15°C
Vector Institute	No	--	11 m	--	--	No	2	2-8°C

Figure 2: Key characteristics of leading vaccine candidates with traffic-light system signalling potential for achieving global vaccine immunity

# Equitable access to any COVID-19 vaccine has large economic benefits

**Scenario Figure 1. Alternative Evolutions in the Fight against the COVID-19 Virus**  
(Deviation from baseline)

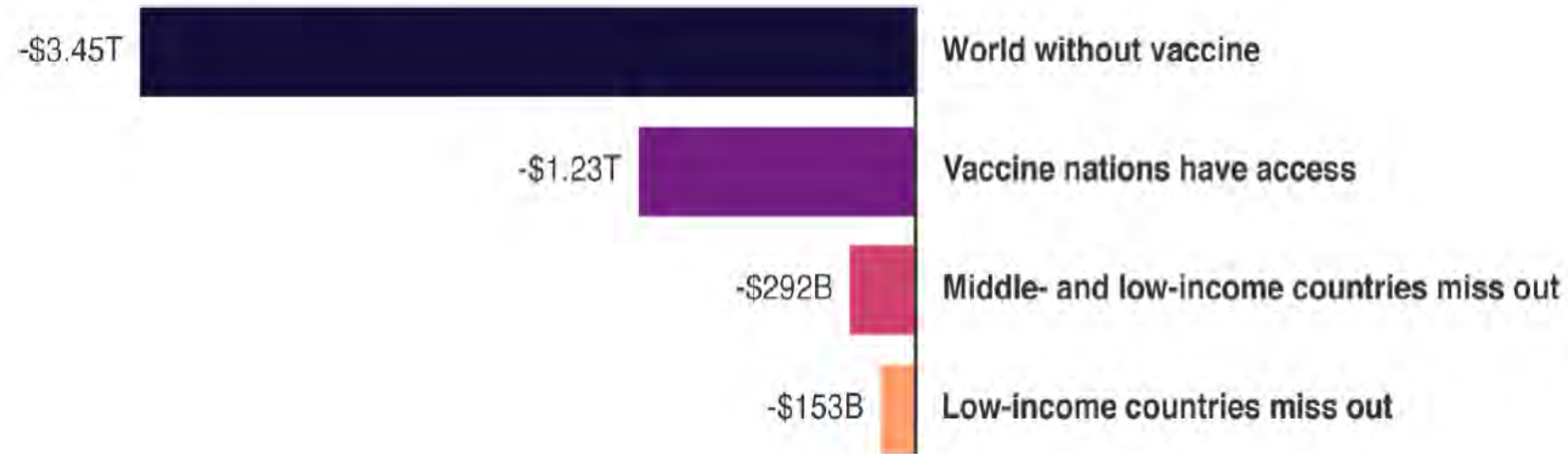


AE: Advanced Economies  
EM: Emerging Markets

IMF World Economic Outlook October 2020.  
<https://www.imf.org/en/Publications/WEO/Issues/2020/09/30/world-economic-outlook-october-2020>

Note: estimates are not specific to any COVID-19 vaccine product.

## Global GDP Change



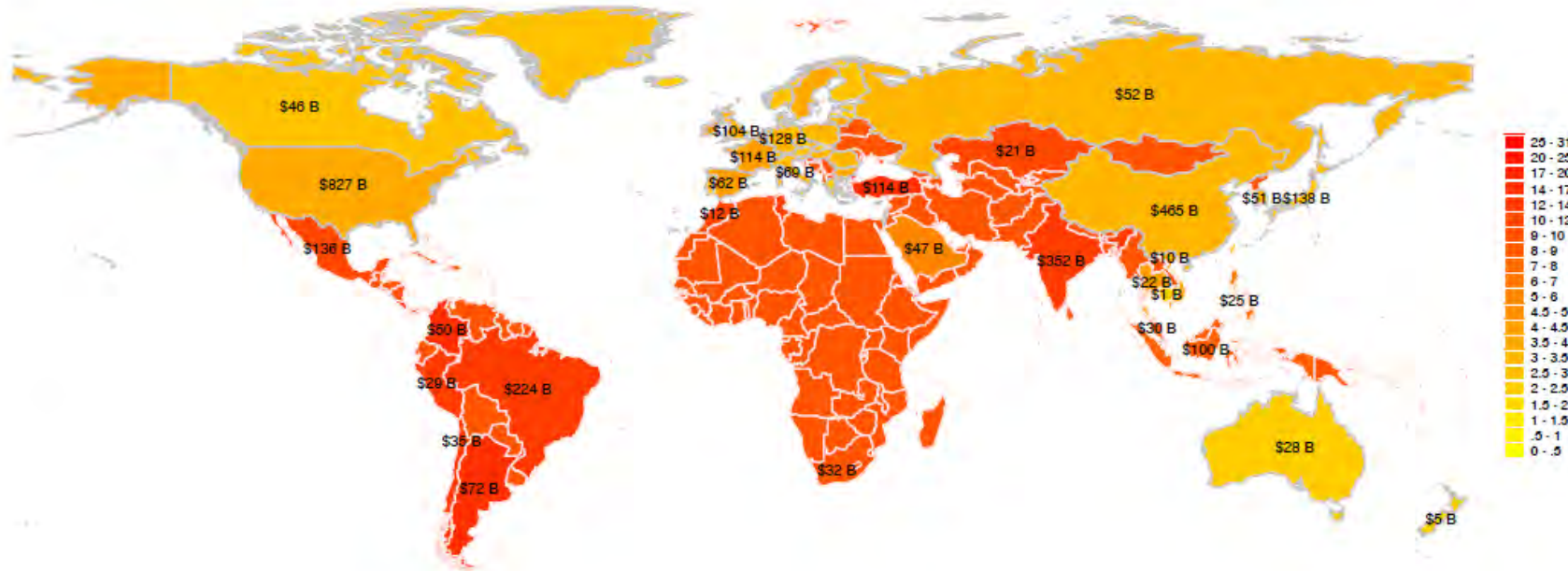
RAND Europe. 2020. COVID-19 and the cost of vaccine nationalism. [https://www.rand.org/pubs/research\\_reports/RRA769-1.html](https://www.rand.org/pubs/research_reports/RRA769-1.html)  
Considers only losses in 5 contact-intensive sectors (hospitality, recreation, retail and wholesale, transportation, health/social care)

- GDP is projected to recover faster if COVID-19 vaccination roll-out permits reduction in physical distancing, and travel and trade interruptions.
- Slower vaccination roll-out and inequitable vaccine access globally will result in greater GDP losses, including for high-income countries.



# More equitable COVID-19 vaccine access also benefits high-income countries economically

(c) Specification 3 – Country-Industry Level Intermediate Inputs

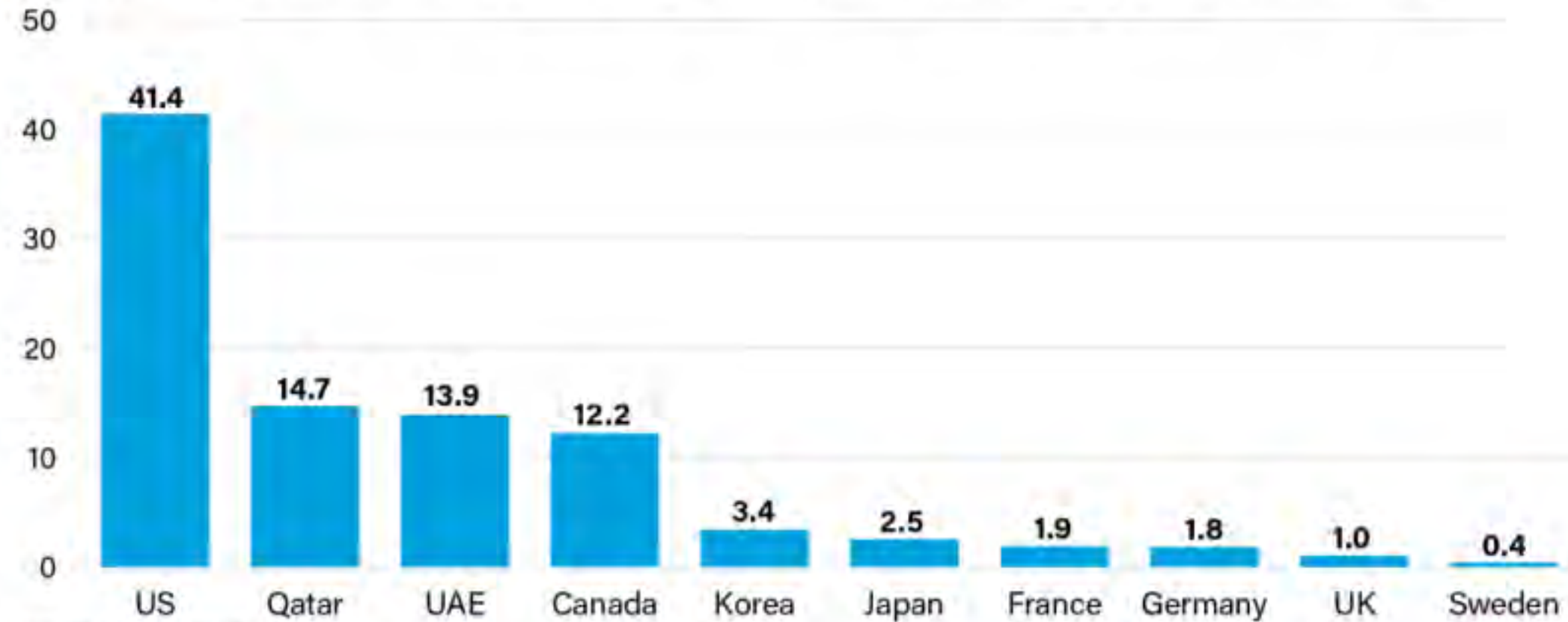


- **Additional \$4.7T in global GDP losses** if emerging markets and developing economies have no access to vaccine during 2021 but lockdown periodically to not overwhelm health system, vs. if these economies could vaccinate 50% of their susceptible populations over 12 months beginning in 2021.
- **\$2.1T in GDP losses would be in advanced economies,** mostly due to international trade and supply chain interruptions.

NOTES: This figure shows the reductions in relative GDP under Scenario 3, where we model the gradual vaccination. The shades of yellow correspond to relatively lower ratios and the shades of red correspond to higher relative losses. Vaccinated countries are highlighted with light gray borders. GDP loss numbers are typed on the map for the G-20 countries and a few selected countries.

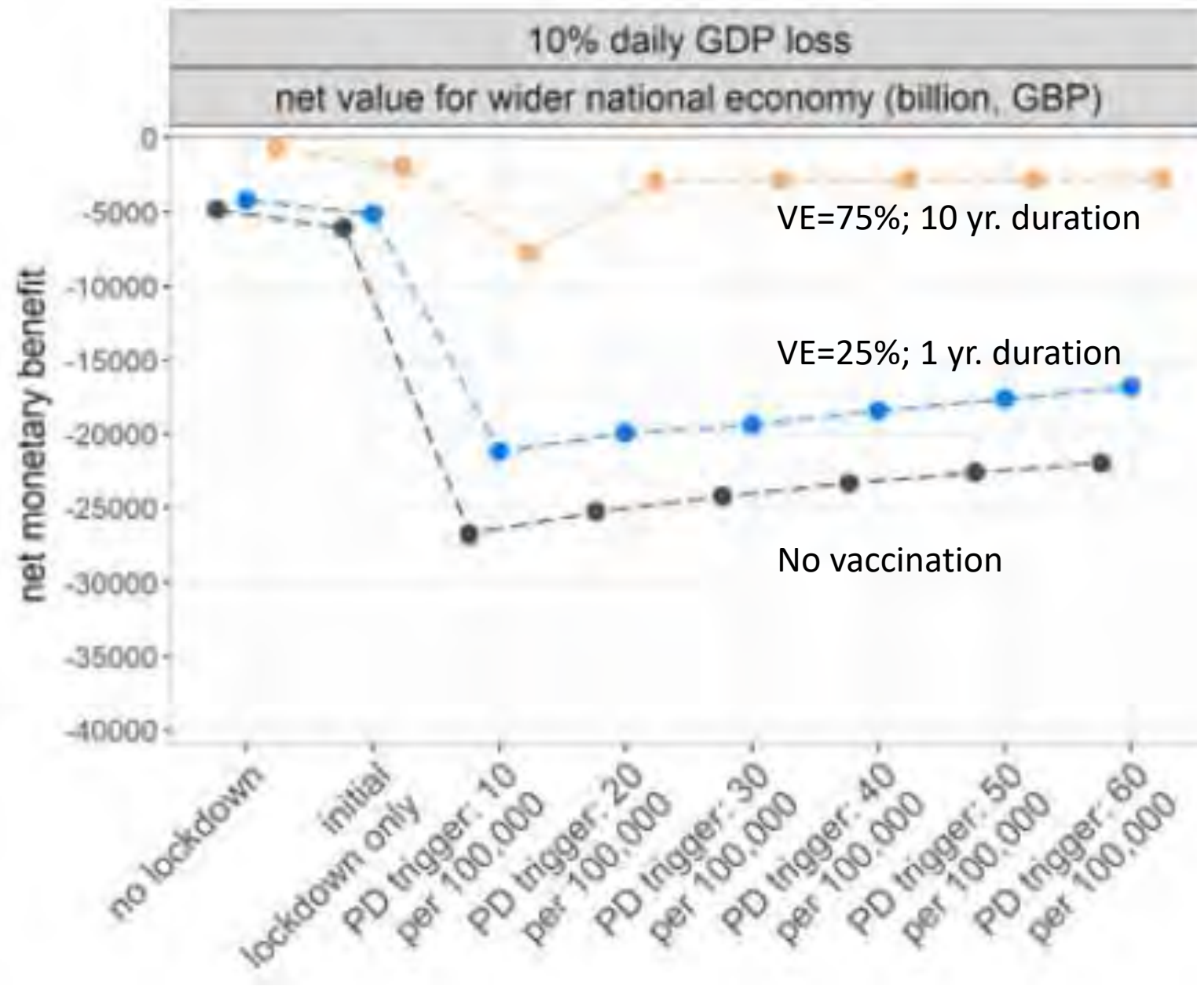
# More equitable COVID-19 vaccine access also benefits high-income countries economically

**Ratio of economic benefits (2020-25) to current \$5B funding gap for Covax-AMC**



Source: Eurasia Group analysis





Net present value over 10 years (discounted at 3.5%); monetary value per QALY at £20,000  
Daily GDP losses were assumed with 2% if not breaching PD incidence threshold rate but incidence > 1000 cases daily.

## Country-level wider economic benefits of COVID-19 vaccination (UK, over 10 years)

- Lower GDP losses with a hypothetical vaccine with higher VE and longer duration of protection that reduced need for physical distancing to control epidemic waves
- Even vaccine with lower VE/ shorter duration had economic benefits vs. no vaccination

Source: Sandmann et al, (2020) The potential health and economic value of SARS-CoV-2 vaccination alongside physical distancing in the UK: transmission model-based future scenario analysis and economic evaluation; <https://doi.org/10.1101/2020.09.24.20200857> 25

# CEA of COVID-19 vaccination in Sindh province, Pakistan


- Assumed CE threshold of \$500/DALY averted
- Vaccination is cost-saving under several scenarios, and cost-effective under most, from health system and partial societal perspectives
- However, when vaccine price is higher (\$10/dose) or VE is lower (30% protection against infection), a 1-year vaccination campaign would not be cost-effective at the assumed threshold
- Scenarios consider 1, 5, and 10-year vaccination programs, with immunity durations of 1, 2.5, 5 years, and lifelong, over 10-yr. analytic horizon

Pearson et al. (2021) "Health impact and cost-effectiveness of COVID-19 vaccination in Sindh Province, Pakistan"

<https://www.medrxiv.org/content/10.1101/2021.02.24.21252338v1>

No.	Description	Impact compared to no vaccination				
		Cases Averted (millions)	Deaths Averted (thousands)	Difference in Cost (USD millions)	DALYs Averted (thousands)	Cost per DALY Averted (USD)
Base case						
1	Vaccine base case	0.9 (0.9, 1.0)	7.3 (7.2, 7.4)	-0.4 (-3.7, 0.9 )	85.1 (84.6, 86.8)	dom (dom, 10.3)
Vaccination strategy						
2	Not age targeted (vaccinate everyone 15+ from outset)	0.9 (0.9, 1.0)	6.4 (6.3, 6.5)	0.4 ( -3.4, 1.6)	80.9 (80.3, 83.0)	5.1 (dom, 19.7)
3	5 year campaign	6.2 (6.1, 6.2)	39.1 (38.5, 39.7)	63.5 (62.8, 66.5)	504.9 (498.3, 506.9)	126.1 (124.4, 133.5)
4	10 year campaign	11.0 (11.0, 11.2)	65.3 (64.5, 66.4)	234.2 (227.8, 236.0)	861.6 (857.4, 872.4)	271.9 (261.1, 274.2)
Immunity characteristics						
5	1 year vaccine & natural immunity duration	1.0 (1.0, 1.0)	7.6 (7.5, 7.7)	-6.5 (-6.8, -6.2)	87.1 (86.4, 87.8)	dom (dom, dom)
6	5 year vaccine & 2.5 year natural immunity duration	1.8 (1.7, 1.9)	13.4 (13.3, 13.6)	-56.0 (-58.6, -54.2)	159.7 (159.5, 160.5)	dom (dom, dom)
Vaccine characteristics						
7	1 dose regimen (twice rate of people vaccinated)	1.7 (1.7, 1.8)	13.0 (12.9, 13.3)	10.2 (4.9, 11.4)	154.2 (153.2, 156.6)	65.9 (31.0, 74.3)
8	30% vaccine efficacy	0.4 (0.4, 0.4)	3.4 (3.3, 3.4)	34.5 (33.3, 35.3)	38.9 (38.6, 39.3)	887.5 (847.2, 914.8)
9	90% vaccine efficacy	1.2 (1.1, 1.3)	9.0 (9.0, 9.2)	-16.3 (-20.6, -15.2)	106.1 (105.5, 108.3)	dom (dom, dom)
10	\$10 price per dose	0.9 (0.9, 1.0)	7.3 (7.2, 7.4)	118.4 (115.0, 119.6)	85.1 (84.6, 86.8)	1391.1 (1325.2, 1411.5)
Economic methodology choices						
11	DALYs discounted at 3%	0.9 (0.9, 1.0)	7.3 (7.2, 7.4)	-0.4 (-3.7, 0.9)	59.5 (59.0, 61.0)	dom (dom, 14.8)
12	DALYs based on higher comorbidities	0.9 (0.9, 1.0)	7.3 (7.2, 7.4)	-0.4 (-3.7, 0.9)	65.6 (65.2, 67.0)	dom (dom, 13.3)
13	Societal perspective	0.9 (0.9, 1.0)	7.3 (7.2, 7.4)	-20.6 (-24.9, -19.0)	85.1 (84.6, 86.8)	dom (dom, dom)

# E2R tables: Resource Use criterion → Summary (2)



Resource Use Criterion elements	WG Judgments to date for interim recommendations for Pfizer-BioNTech <sup>1</sup> , Moderna <sup>2</sup> , & AstraZeneca <sup>3</sup> COVID-19 vaccines			
E2R table: <b>Are the resources required small?</b>	No <input checked="" type="checkbox"/>	Uncertain	Yes	Varies
E2R table: <b>Cost-effectiveness</b>	No	Uncertain	Yes	Varies <input checked="" type="checkbox"/>
Summary E2R slides: <b>Is the intervention a reasonable and efficient allocation of resources?</b>	Will vary within and between countries			

- At **global level**, the current WG judgment is that any COVID-19 vaccine product that meets WHO Target Product Profile specifications would be considered a reasonable and efficient allocation of resources compared to no vaccination, on the basis of its contribution to restoring global economic activity alone. Valuation of the averted costs of illness would likely make this judgment only more favorable.
- At **country level**, the current WG judgment is that whether a specific vaccine would be cost-effective will vary based on the COVID-19 burden, other mitigation measures in use, vaccine price and delivery costs, coverage achieved, vaccine efficacy against circulating virus strains, epidemic trajectory and degree of existing immunity in the population, duration of protection, analytic horizon, and willingness-to-pay threshold used, among other factors.

1. [https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-\(pfizer-biontech\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-(pfizer-biontech)-against-covid-19)

2. [https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)

3. [https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1)

# Questions to IVIR-AC

- How should the Resource Use criterion in the Evidence to Recommendations process be interpreted and applied for SAGE's COVID-19 vaccine-specific recommendations (e.g., perspective, intervention, counterfactual)?
- Which types of estimation approaches and tools are most appropriate for global- and country-level costing and decision making around COVID-19 vaccination resource use?

EXTRA SLIDES



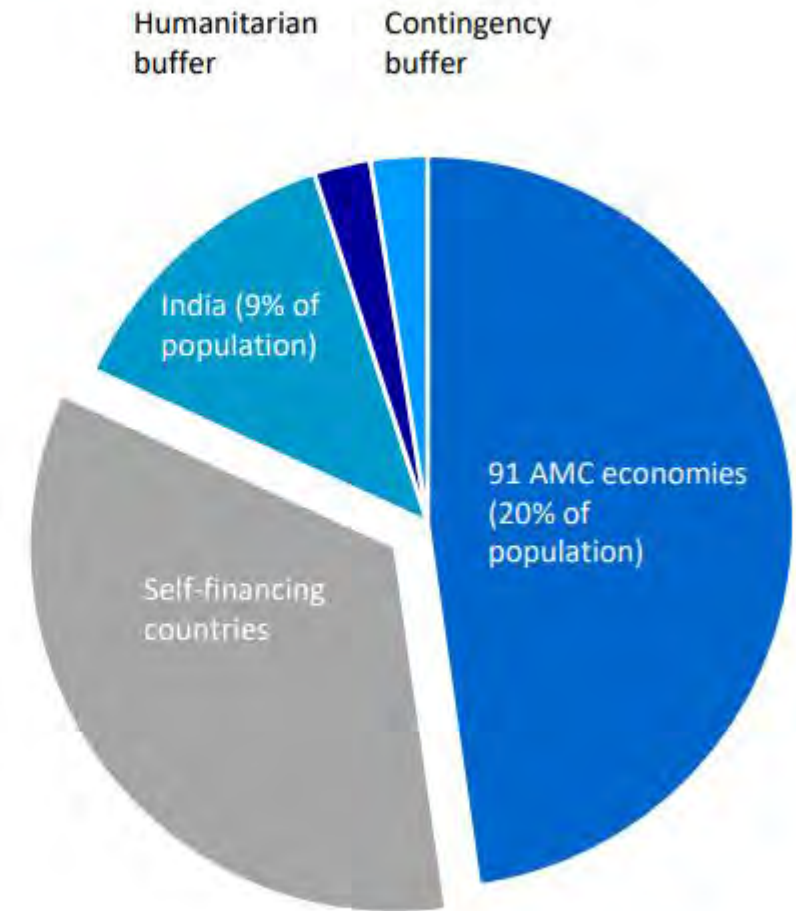
# Two billion COVID-19 vaccine doses expected for COVAX during 2021

## Allocation of 2 billion doses\*

• AMC91	955.2 million	} <b>1.219 billion doses</b>
• India	263.8 million	
• Humanitarian buffer	50 million	} Excluded from the delivery cost analysis
• Contingency buffer	50 million	
• Self-financing countries	681 million	

## Assumptions made for cost estimates:

- 2-dose schedule
- 10-dose vial
- 10% vaccine wastage
- 2-8°C cold chain storage
- Syringes and safety boxes bundled with COVID-19 vaccine and not included in delivery costs



COVID-19 Vaccine Delivery Costing Working Group. 8 Feb. 2021. "Costs of delivering COVID-19 vaccines in 92 Advance Market Commitment economies." <http://immunizationeconomics.org/recent-activity/2021/2/10/cost-of-delivering-covid-19-vaccines-in-92-covax-countries>

## Number of people predicted to be vaccinated in AMC92 during 2021 with the allocation of 1.219 billion doses (vaccination coverage)

**1** Core health workers through fixed site delivery

**2** 65+ years through outreach

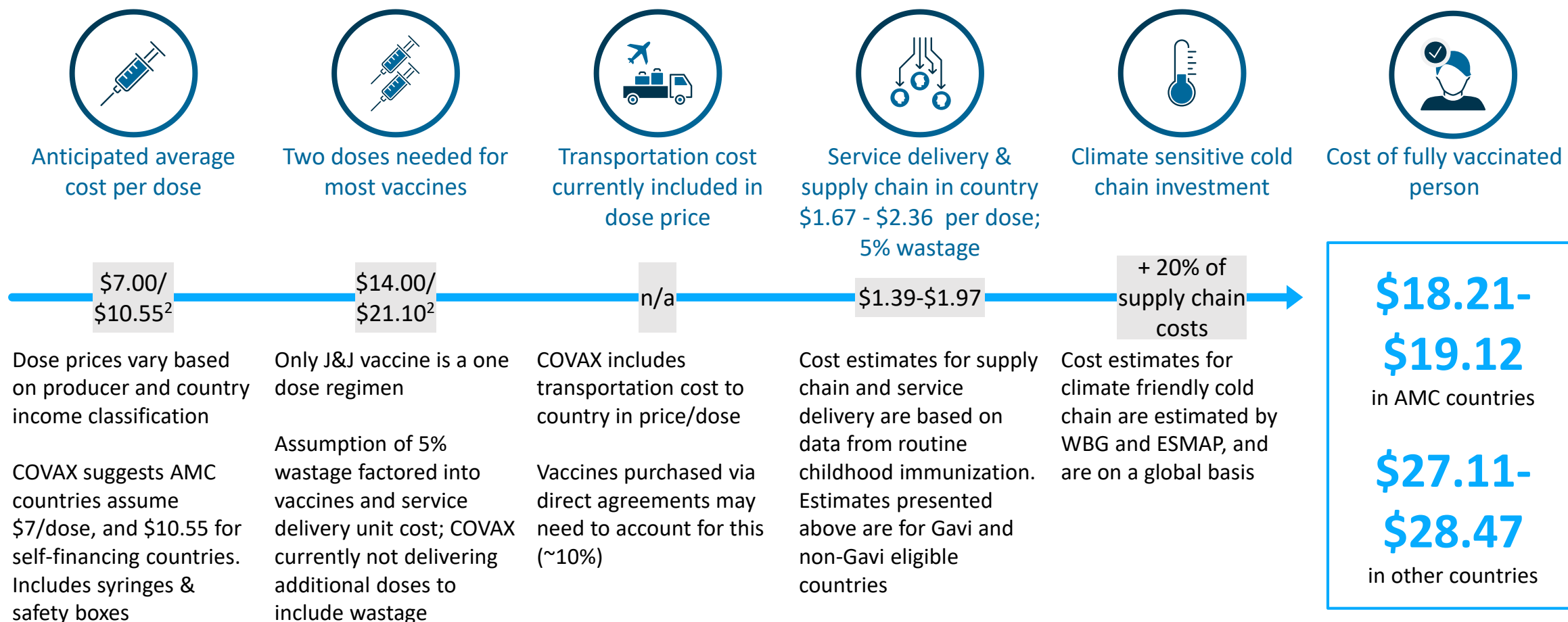
**3** 50-64 years through outreach

**4** Less than 50 years through outreach

	Core health workers	65+ year old	50-64 years old	Less than 50 years	Total
Gavi eligible (n=57)	4,137,445 (90%)	58,610,676 (80%)	125,013,809 (77%)	118,073,630 (7%)	305,835,560 (17%)
India (n=1)	5,981,983 (90%)	75,489,372 (80%)	37,238,646 (21%)	-	118,710,001 (8%)
Gavi transitioned (n=12)	1,682,149 (90%)	24,818,635 (80%)	37,024,751 (63%)	3,938,419 (1%)	67,463,954 (17%)
Non-Gavi (n=22)	1,587,903 (90%)	16,251,415 (80%)	29,896,964 (77%)	6,535,467 (2%)	54,271,749 (17%)
<b>Total (n=92)</b>	<b>13,389,480 (90%)</b>	<b>175,170,099 (80%)</b>	<b>229,174,171 (52%)</b>	<b>128,547,515 (4%)</b>	<b>546,281,265 (14%)</b>



# Estimated cost to vaccinate one person in MENA countries



*Costs assume existing system can be leveraged; only includes incremental financial cost; health worker salaries excluded*

1. (20% of service delivery and supply chain cost); 2. AMC / Other Source: Portnoy A, Vaughan K, Clarke-Deelder E, Suharlim C, Resch SC, Brenzel L, Menzies NA. Producing standardized country-level immunization delivery unit cost estimates. PharmacoEconomics. Sept 2020;38 (9):995-1005.



# Indicative costs for vaccine and delivery in MENA countries

Countries	AMC	Vaccine cost (\$M)			Service delivery, supply chain, incl. climate-friendly (\$M)			Total Cost of vaccination (\$M)		
		Coverage: 20%	Coverage: 50%	Coverage: 70%	Coverage: 20%	Coverage: 50%	Coverage: 70%	Coverage: 20%	Coverage: 50%	Coverage: 70%
Algeria	✓	31	209	341	42	107	149	73	316	490
Bahrain	✗	6	17	25	2	4	6	7	22	31
Djibouti	✓	1	5	8	1	2	2	1	6	10
Egypt	✓	73	489	797	98	250	349	171	740	1146
Iran	✗	280	837	1214	80	203	284	360	1040	1498
Iraq	✗	136	408	592	39	99	138	174	508	730
Jordan	✗	34	100	146	10	24	34	44	125	180
Kuwait	✗	14	43	62	4	10	14	18	53	76
Lebanon	✗	22	66	95	6	16	22	29	82	117
Libya	✗	23	68	99	7	17	23	29	85	122
Morocco	✓	26	174	284	35	89	125	61	264	409
Oman	✗	17	52	75	5	13	17	22	64	92
Qatar	✗	10	29	42	3	7	10	12	36	52
Saudi Arabia	✗	116	348	505	33	85	118	150	433	623
Tunisia	✓	8	56	91	11	29	40	20	84	131
UAE	✗	33	98	142	9	24	33	42	122	175
WB&Gaza	✓	4	25	40	5	13	18	9	37	58
Yemen	✓	21	143	234	20	52	72	42	195	306
Total		855	3167	4792	410	1044	1456	1266	4211	6248

# Public and non-profit funding for COVID-19 vaccine R&D

- Developers of advanced COVID-19 vaccine candidates have received **at least \$10B in total R&D funding** from governments and foundations.
- This is an underestimate due to data limitations.

	Technology	Known public and non-profit funding, US\$	Funders
Sanofi with GlaxoSmithKline	Protein subunit	\$2.1 billion	US Government
Novavax	Protein subunit	\$2.1 billion	Bill & Melinda Gates Foundation, CEPI, US Government
AstraZeneca with Oxford University	Non-replicating viral vector	\$1.7 billion	CEPI, UK Government, US Government
Johnson & Johnson	Non-replicating viral vector	\$1.5 billion	US Government
Moderna	mRNA	\$957 million	CEPI, Dolly Parton COVID-19 Research Fund, US Government
BioNTech with Pfizer	mRNA	\$445 million	German Government
Clover Pharmaceuticals with Dynavax	Protein subunit	\$430 million	Bill & Melinda Gates Foundation, CEPI
CureVac	mRNA	\$348 million	CEPI, German Government
Sinopharm with Wuhan Institute	Inactivated virus	\$142 million	Chinese Government
Medicago	Virus-like particle	\$137 million	Canadian Government
Inovio	DNA	\$107 million	Bill & Melinda Gates Foundation, CEPI, US Government
Covaxx with Nebraska University	Protein subunit	\$15 million	Taiwanese Government
SK Biosciences	Protein subunit	\$14 million	Bill & Melinda Gates Foundation, CEPI
Biological E	Protein subunit	\$9 million	Bill & Melinda Gates Foundation, CEPI, Indian Government
University of Hong Kong	Replicating viral vector	\$4 million	CEPI, Hong Kong Government
CAMS with IMB	Inactivated virus	\$3 million	Chinese Government, Jack Ma Foundation
AnGes with Osaka University	DNA	Unknown	Japanese Government
Anhui Zhifei with CAMS	Protein subunit	Unknown	Chinese Government
Bharat Biotech	Inactivated virus	Unknown	Indian Government
CanSino	Non-replicating viral vector	Unknown	Unknown
Gamaleya	Non-replicating viral vector	Unknown	Russian Government
RIBSP	Inactivated virus	Unknown	Kazakh Government
SII with Max Planck Institute	Live attenuated virus	Unknown	Unknown
Sinopharm with Beijing Institute	Inactivated virus	Unknown	Chinese Government
Sinovac	Inactivated virus	Unknown	Unknown
Vector Institute	Protein subunit	Unknown	Russian Government

Data are as of Feb 3, 2021. The sources and methodology are outlined in appendix 2, which also includes more information about the funding arrangements. In brief, for developers with COVID-19 vaccines that have been approved or authorised for human use in one or more countries, are in phase 3 clinical testing, or are under contract with CEPI or the COVAX Facility, we searched press releases from developers and funders, as well as financial reports filed by developers with regulators in various countries, for information on public and non-profit funding. We did not count funds provided to licensees that produce and distribute vaccines on behalf of lead developers or to contract development and manufacturing organisations, nor did we count loans (ie, debt financing) from international financial institutions (eg, European Investment Bank) or national governments. We included pre-purchase agreements between governments and companies where it appeared as though a substantial portion of the funding went towards late-stage development (ie, phase 1–3 trials) or scaling up production at risk before the completion of clinical testing. CAMS=Chinese Academy of Medical Sciences; CEPI=Coalition for Epidemic Preparedness Innovation; IMB=Institute of Medical Biology (China); RIBSP=Research Institute for Biological Safety Problems (Kazakhstan); SII=Serum Institute of India.

**Table: Public and non-profit funding for the research, development, and production of leading vaccine candidates**

Wouters et al, 2021, *The Lancet*  
[https://doi.org/10.1016/S0140-6736\(21\)00306-8](https://doi.org/10.1016/S0140-6736(21)00306-8)

# Background information

Latest ACT-A budget and financing framework:

- <https://www.who.int/publications/m/item/act-a-prioritized-strategy-and-budget-for-2021>
- <https://www.who.int/publications/m/item/a-financial-framework-for-act-accelerator>

Vaccine product-specific background papers:

- Pfizer: [https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-\(pfizer-biontech\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-mrna-vaccine-bnt162b2-(pfizer-biontech)-against-covid-19)
- Moderna: [https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-\(moderna\)-against-covid-19](https://www.who.int/publications-detail-redirect/background-document-on-the-mrna-1273-vaccine-(moderna)-against-covid-19)
- AZ: [https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1)

CVIC tool (will be mentioned though not reviewed in detail):

- <https://apps.who.int/iris/handle/10665/337553>

### **Session 3: Measles Case Fatality Ratio (CFR) estimation**

# Measles Case Fatality Ratios

Background

Katrina Kretsinger, MD, MA

IVIR-AC meeting, Geneva, Switzerland

March 2, 2021

# Problem statement

**Which case fatality ratio (CFR) values should WHO use in estimating measles deaths?**

- WHO relies on measles CFR values in estimations of annual global measles mortality and measles deaths averted
- Urgency of issue: proposal to start using new CFR estimates in annual measles mortality estimates in 2021 (for 2020 mortality estimates)

# Background – static age – and country-specific measles CFRs

- Estimated measles mortality and deaths averted depend upon estimated incidence and CFR values
- Published WHO measles incidence estimates through 2019, back-calculated to 2000, based on Simons 2012 model<sup>1</sup>
- Associated mortality estimates based on age- and country-specific CFRs used to estimate deaths in each age-country class
  - CFRs determined by expert opinion and informed by CFRs published by Wolfson and colleagues in 2009<sup>2</sup>

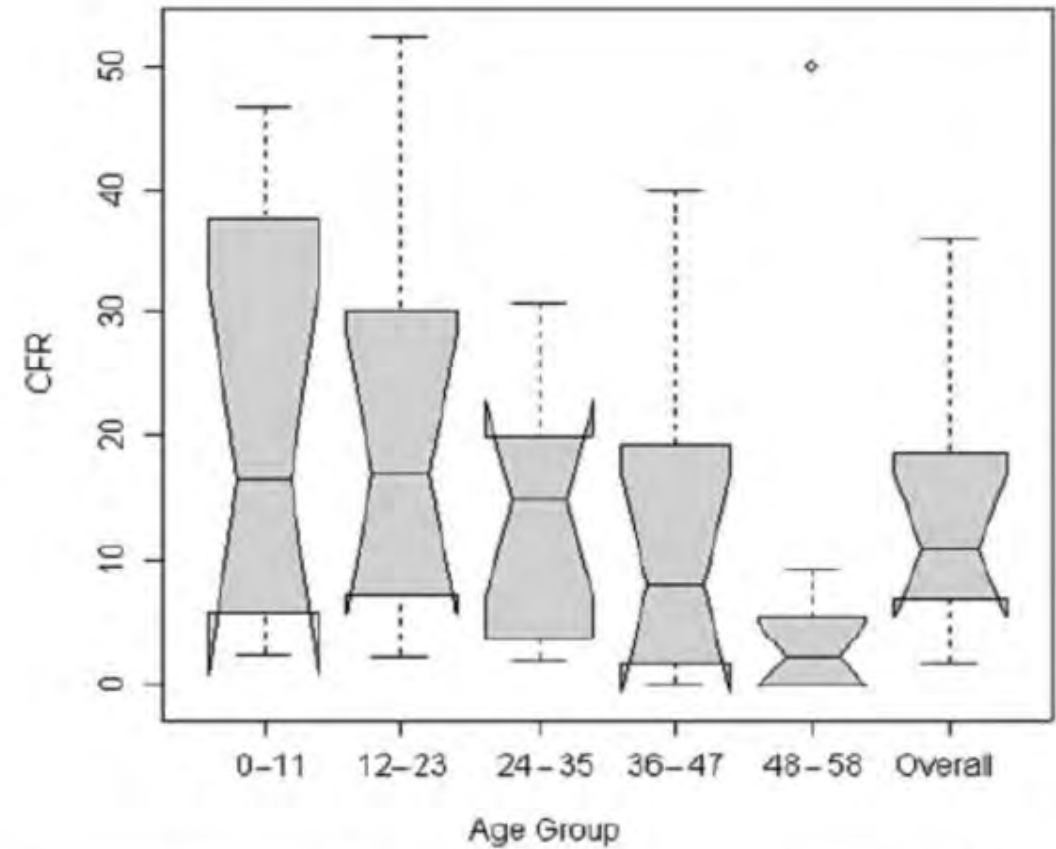
1. Simons E, Ferrari M, Fricks J, et al. Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data. *Lancet* 2012;379:2173–8. PMID:22534001 [https://doi.org/10.1016/S0140-6736\(12\)60522-4](https://doi.org/10.1016/S0140-6736(12)60522-4)
2. Wolfson, Grais, Luquero, Birmingham, Strebel. Estimates of measles cases fatality ratios: a comprehensive review of community-based studies. *Intl Journ of Epi*. 2009.18:192-205

# Wolfson et al 2009 measles CFR review

- Community-based studies published 1980-2008 w age-specific measles CFRs
  - Excluded hospital-based studies, refugee/IDP camps, industrialized countries:
- Kruskal-Wallis test to evaluate differences in CFR by categories
- 58 publications w 102 measles studies in 29 countries
  - India, Senegal, Guinea-Bissau overrepresented
- 117,336 cases w 3857 deaths (overall CFR = 3.29)
- Overall higher measles CFRs in outbreaks, in children under 5 years of age, in secondary cases, in cases w complications, in unvaccinated individuals
- Not reviewed by QUIVER



# Wolfson et al, cont'd. CFRs by year of age



**Figure 2** Notched box plot of CFR for studies with defined age groups. In a notched box plot, the notches represent a robust estimate of the uncertainty about the medians for box-to-box comparison. Boxes whose notches do not overlap indicate that the medians of the two groups differ at the 5% significance level. The median is represented by the horizontal line through each box

# Wolfson et al, cont'd: data limitations

- Inconsistent CFR measurements
  - Measles diagnosis: 37/102 studies used WHO case definition; 14/37 had laboratory confirmation on subset
  - Attribution of death quite variable: deaths 4-6 weeks after rash for most part; some required verbal autopsy or physician record of measles
  - Sample size (measles cases): mean 1150; median 328
- Literature not representative: most studies in sub-populations; only 29 countries in dataset; some countries w good access to care over-represented (India, Senegal, Guinea-Bissau)
- Need for more empirical data: authors advocated further studies and standard measurement and reporting
- Authors concluded that data were not sufficiently robust to derive country-specific estimates, leading to “implausible results”
  - Heterogeneity and sparseness of available data
  - Degree of variation in study results
- Expert group categorized countries by similarity of factors that influence CFRs to derive CFR ranges among children aged 1-4 years

# Wolfson et al 2009, cont'd: Proposed CFRs by country for children 1-4 years of age

Table 2 CFRS by region and level

CFR range (%)	AMR	EUR	WPR	SEAR	EMR	AFR
0.05	All	Developed economies	NZ, Australia, Japan			
0.1–0.5		Economies in transition	Malaysia, Rep Korea, Singapore, Brunei, China, Pacific Islands	DPRK, Thailand, Maldives	All others	Mauritius, Swaziland
0.5–1			Philippines, Mongolia	Bhutan, Sri Lanka	Jordan, Egypt, Iraq	
1–2				India, Bangladesh	Pakistan	
2–3			Cambodia, VietNam	Nepal, Indonesia, Timor-Leste	Djibouti, Yemen	Malawi, South Africa, Cape Verde, Algeria
3–4			Laos, PNG	Myanmar	Sudan	Angola, Ethiopia, Uganda, Kenya, Tanzania, Cameroon, Madagascar
4–5					Afghanistan, Somalia	Chad, Congo, Nigeria, Central African Republic, Equatorial Guinea, Gabon, Namibia, Sao Tome and Principe, Comoros, Mozambique, Côte d'Ivoire, Lesotho, Rwanda, Burundi, Zambia, Botswana, DR Congo, Niger, Senegal, Mali, Burkina Faso, Ghana, Eritrea
5–6						Sierra Leone, Guinea, Liberia, Togo, Guinea-Bissau, Mauritania, Benin, Zimbabwe, Gambia, Seychelles

AMR = American Region, EUR = European Region, WPR = Western Pacific Region, SEAR = South East Asian Region, EMR = Eastern Mediterranean Region, AFR = African Region.

# Simons et al 2012: Revised CFRs for children < 5 years of age by country

Relative to CFRs for children 1-4 years of age, CFRs for infants were assumed to be equal for infants, half for children 5-9 years of age, and zero for children 10 years of age and older

Revised to consider additional data from Nepal and India

CFR	Countries
<.002	All remaining countries
0.002-<.01	China, Cook Islands, Egypt, Fiji, Jordan, Kiribati, Marshall Islands, Micronesia, Nauru, Niue, Palau, Samoa, Solomon Islands, Swaziland, Tonga, Tuvalu, Vanuatu
.01-<.02	Bangladesh, Bhutan, India, Iraq, Mongolia, Pakistan, Philippines, Sri Lanka
.02-<.03	Algeria, Botswana, Cambodia, Cape Verde, Djibouti, Indonesia, Malawi, Namibia, Nepal, South Africa, Timor-Leste, Viet Nam, Yemen
.03-<.04	Angola, Cameroon, Ethiopia, Kenya, Lao People's Democratic Republic, Madagascar, Papua New Guinea, Sudan, Uganda, United Republic of Tanzania
.04-<.05	Burundi, Central African Republic , Chad, Comoros , Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Lesotho, Mozambique, Myanmar, Niger, Nigeria, Rwanda, Sao Tome and Principe, Zambia
0.06	Benin, Gambia, Guinea, Guinea-Bissau, Liberia, Mauritania, Sierra Leone, Togo, Zimbabwe

# Harvard University paper

- Prompted by concerns that additional CFR data had emerged
- Objectives:
  - Update on CFRs for community and hospital settings in LICs and MICs 1980-2016
  - Predictive model to estimate CFRs across heterogeneous groupings (country, region, year, age) from 1990-2015
  - Project future measles CFRs through 2030.
- Background literature
  - Extended literature search through 2016
  - Included hospital-based studies
  - Excluded refugee/IDP camps and HIC settings

*Portnoy, Jit, Ferrari, Hanson, Brenzel, Verguet. Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis. Lancet Glob Health 2019*



# Harvard University paper, cont'd

## Results: literature

- 124 journal articles
- Included all studies in Wolfson review
- 85 community-based studies (158 observations across 35 countries; 46% of observations in 5 countries: Ghana, Guinea-Bissau, India, Nigeria and Senegal)
- 39 hospital-based studies (68 observations across 23 countries)
- 65/226 observations in LICs; 161/226 in MICs
- Lab-confirmation: 29/158 community and 13/68 hospital observations
- Total number of measles cases: 523,885
- Sample size in studies (# measles cases): median 349 (range 8-124,865) in community studies and 357 in hospital-based studies (range 29-7447)
- Unweighted median CFR: community 3.0%; hospital 8.0%

# Harvard University paper, cont'd

## Prediction model:

- Studies were weighted by sample size but not adjusted by study quality
- Best-fit regression model selected (log-linear prediction)
- Overall, mean predicted 1990-2015 CFR = 2.2%
  - Communities = 1.5%; hospitals = 2.9%
  - <5 years = 3.3%;  $\geq$  5 years = 0.9%
  - CFR correlated <5 mortality and inversely w/ country income status
  - Excluding largest community-based studies accounting for 62% of cases\* increased CFR 1990-2015 from 2.2% to 2.5 %
- Projected overall CFR 2016-2030 = 1.3

\*China (2005 surveillance data with 125,000 cases – CFR 0.04%)

Democratic Republic of the Congo (2010 surveillance data with 77,000 cases – CFR 1.4%; outbreak investigation 2011 11,000 cases w CFR 3.75% - CFR 3.75%)

Malawi (2010 surveillance data [outbreak investigation] 110,000 case CFR <0.5%)

# New model for estimating measles incidence

- New model to be used beginning in 2021 for global measles incidence estimates
- Model reviewed by IVIR-AC 2017  
[https://www.who.int/immunization/research/committees/IVRACReport2017\\_19042017.pdf](https://www.who.int/immunization/research/committees/IVRACReport2017_19042017.pdf);  
[https://www.who.int/immunization/research/committees/WER9215\\_IVIR\\_Feb2017.pdf](https://www.who.int/immunization/research/committees/WER9215_IVIR_Feb2017.pdf)
- No explicit review of CFRs to be used in new model for mortality calculations
  - The assumption has been that CFR calculations based on recent work by Harvard University would replace prior static CFRs

Eilertson KE, Fricks J, Ferrari MJ. *Estimation and prediction for a mechanistic model of measles transmission using particle filtering and maximum likelihood estimation*. Statistics in Medicine. 2019; 38:4146-4158.



# Issues of concern

## Empirical literature

- Concerns about quality of literature noted
- Three countries (Malawi, China, DR Congo) represented 62% of all cases
- Lack of laboratory confirmation
- Methodologic inadequacies make direct comparisons difficult

## Equity: measles cases not randomly distributed

- Absence of patient-level data e.g., vaccination, nutrition, HIV status, case management
- Assumption of homogeneity across country-age groupings
- Measles cases are concentrated in excluded settings with high incidence and low coverage (e.g., low-resourced, marginalized communities)
- CFRs may be higher in isolated communities, famine and conflict-affected settings
  - CFR studies in IDP and refugee settings excluded from analyses

## Lower incidence may be associated with lower specificity of measles diagnoses

## Impact of COVID-19 on mortality?

- Decreasing MCV1 coverage, decreased access to care, possible associated malnutrition/vitamin A deficiency

# Questions for IVIR-AC

1. What are the trade-offs between utilizing fixed estimates vs. adapting a dynamic methodology that can incorporate new information to provide time-varying, updatable estimates?
2. What additional primary data are needed to refine the assessment of the effect measles vaccination programmes and other factors such as health care and nutritional status have on mortality in high-risk populations?
3. Which future approach would result in best outputs in terms of incorporating new primary data, and what considerations would need to be given in terms of hosting model updates and refinements?
4. In a concrete fashion, how to proceed with mortality estimates and IA2030 deaths averted in (i) 2020 (time-sensitive), and (ii) beyond (for possible future discussion)?

# Thank you

## Acknowledgments

Logan Brenzel

Natasha Crowcroft

Felicity Cutts

Matthew Ferrari

Jim Goodson

Raymond Hutubessy

Mark Jit

Kendall Krause

Philipp Lambach

Peter Strebel

Back-up slides

# Wolfson et al, cont'd

- Study type
  - Outbreak investigations (32%): CFR = 5.18 (2.26, 11.555)
  - Reviews (38%): CFR = 3.92 (1.39, 12.73)
  - Surveys (31%): CFR = 1.85 (1.17, 9.5)
- Study setting
  - Nationally representative (n=8): median CFR = 1
  - Rural (n=69): CFR = 5.06 (2.0, 12.57)
  - Urban (n = 25): CFR = 2.8 (1.0, 7.54)
- No fatalities
  - N = 10; median sample size 122.5; highly immunized, vaccine trial setting, or in India (n=7) where “adequate treatment available”
- Studies w high CFRs
  - 16 studies had CFRs>15% for all age groups
  - Median sample size 118.5 (range 12 – 961)
  - Mostly in isolated populations
  - One study w high malnutrition prevalence
  - Others w low or no measles vaccination

# A Model-based Approach for Updating Measles CFRs

IVIR-AC

2 March 2021

# An Operational CFR

**The Need:** an approach for quantifying the measles CFR for assessing the current burden of measles mortality, the benefit attributable to historical measles control efforts, and the value of future investments in measles control and/or elimination



# An Operational CFR

**The Need:** an approach for quantifying the measles CFR for assessing the current burden of measles mortality, the **benefit attributable** to **historical** measles control efforts, and the value of **future** investments in measles control and/or elimination

- Comparison of scenarios
- Change over time

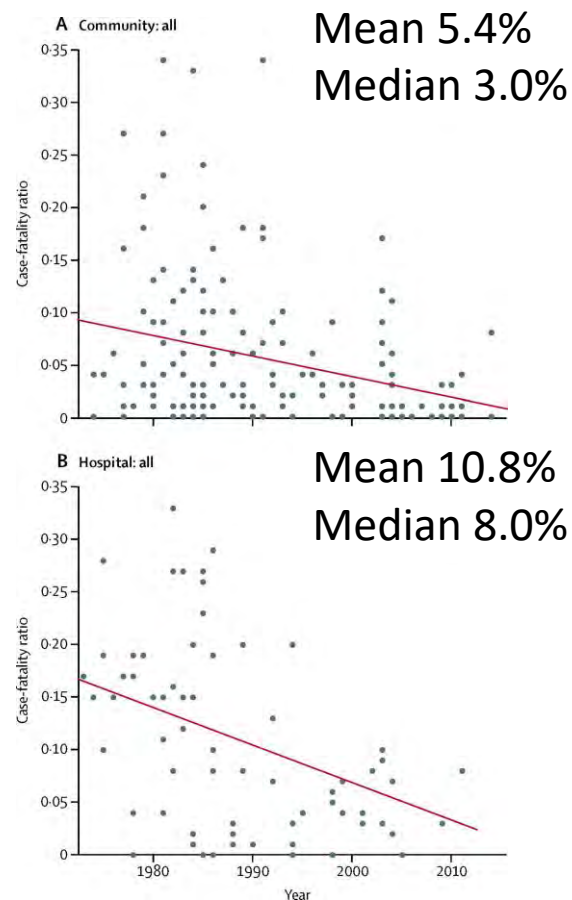
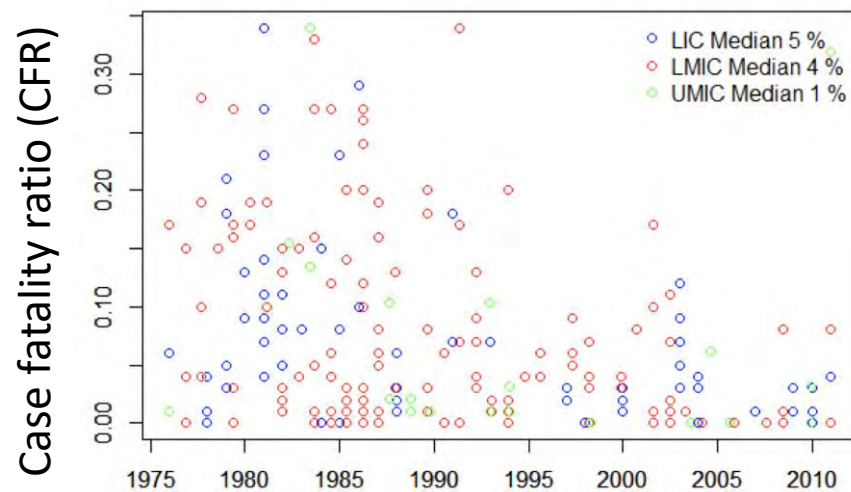
# CFR is context dependent

Measles CFR varies based on the context. The **current approach**, adapted from Wolfson et al 2009 uses **geography as a proxy** for underlying causes of CFR difference. Importantly, this assumes that CFR is **constant over time** – not responsive to improvements in health systems or measles incidence.

# Harvard Analysis

- Updated literature review to include studies through 2016
- Regression model of CFR as a function of:
  - Year of study
  - National MCV1 coverage (in year of study)
  - Indicator of whether study was done in a community-based setting
  - Age (was study limited to children <5yo)
  - Measles attack rate (est'd annual incidence/birth cohort in year of study)
  - National <5yo mortality (in year of study)
  - Population density (national in year of study)
  - Total fertility rate (in year of study)
  - Percentage urban (in year of study)
- Published as Portnoy et al (2019) The Lancet Global Health

# Raw CFR for Analysis



Wolfson et al 2009  
median

3.9%

Clear trends over:  
time,  
development level,  
and setting

# Harvard Analysis

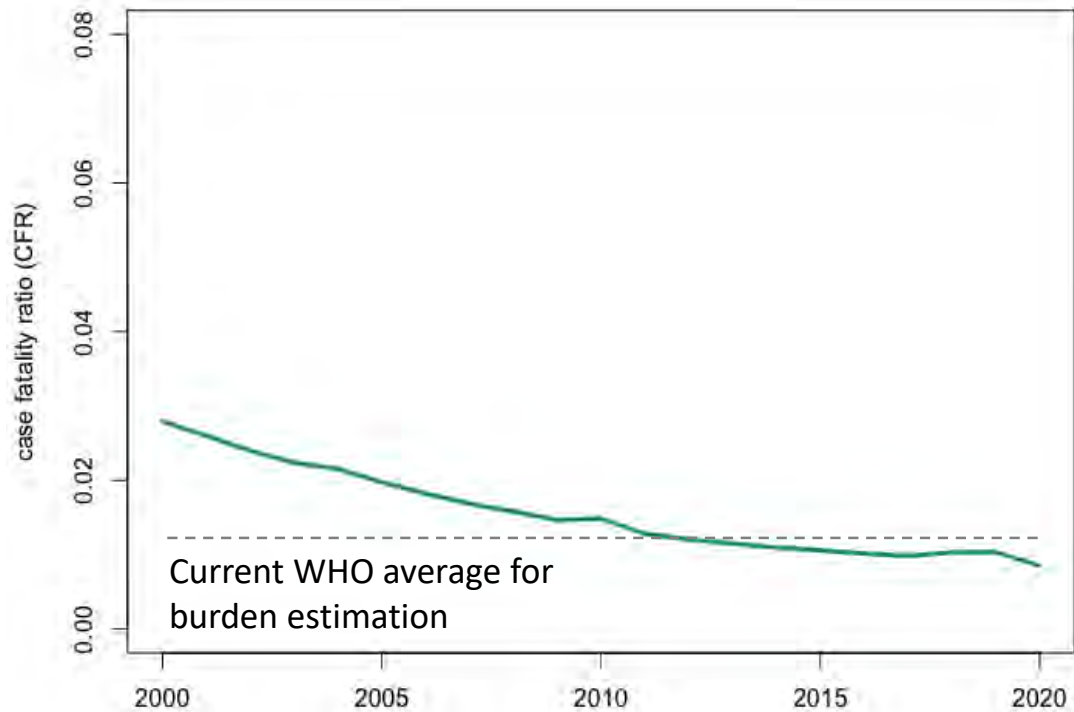
- Updated literature review to include studies through 2016
- Regression model of CFR as a function of:
  - Year of study
  - + National MCV1 coverage (in year of study)
  - Indicator of whether study was done in a community-based setting
  - Age (was study limited to children <5yo)
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# Change in CFR Over Time

The observed decrease in measles CFR over time may be attributable to the combined effects of **increased vaccine coverage** and **reduced total incidence** (fewer large outbreaks) and overall **improvements in health system performance and access**.

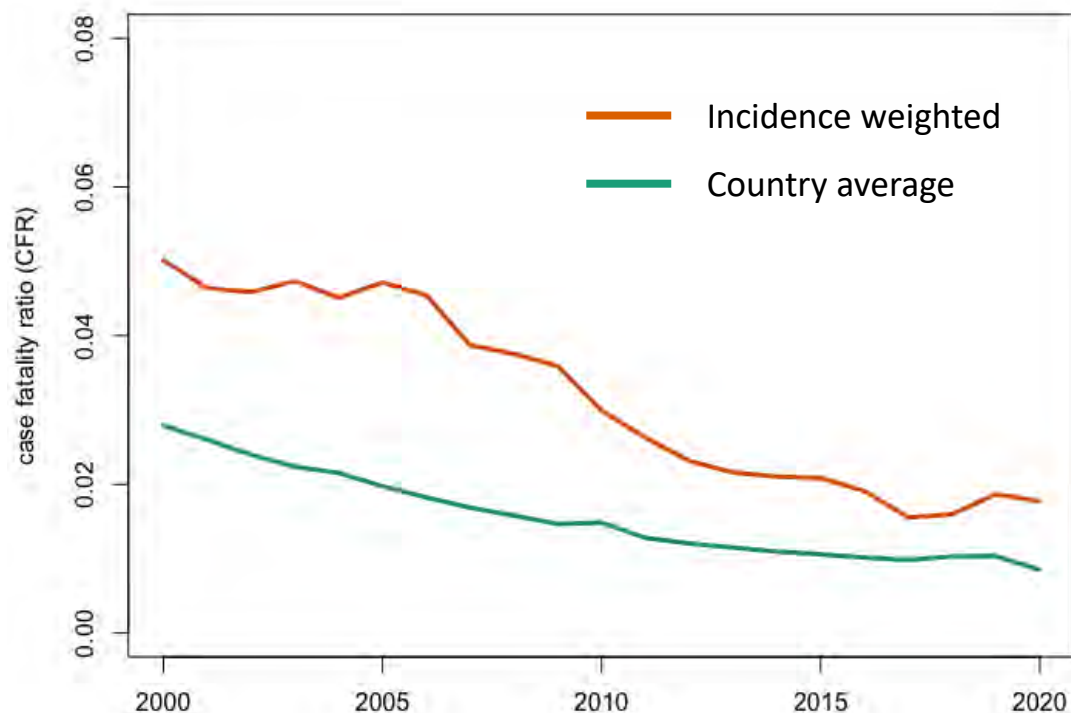
In country/years without studies, or simulation scenarios, the former can be included as **explicit co-variate** the latter relies on time/U5 mortality as a **proxy**.

# Two Interpretations of Mean CFR



Fitted CFR, averaged over all countries, is expected to decline over time.

# Two Interpretations of Mean CFR



Fitted CFR, averaged over all countries, is expected to decline over time.

However, the average child that gets measles will experience a higher CFR because measles persists in lower coverage, higher incidence settings



# Harvard Analysis

- Updated literature review to include studies through 2016
- Regression model of CFR as a function of:
  - Year of study
  - + National MCV1 coverage (in year of study)
  - Indicator of whether study was done in a community-based setting
  - Age (was study limited to children <5yo)
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  - + Percentage urban (in year of study)
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# Change in CFR Over Time

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In country/years without studies, or simulation scenarios, the former can be included as **explicit co-variate** the latter relies on time/U5 mortality as a **proxy**.

CFR must be recalculated conditional on incidence in any new scenario

# Modeled CFR Depends on Incidence

Define Scenario

# Modeled CFR Depends on Incidence

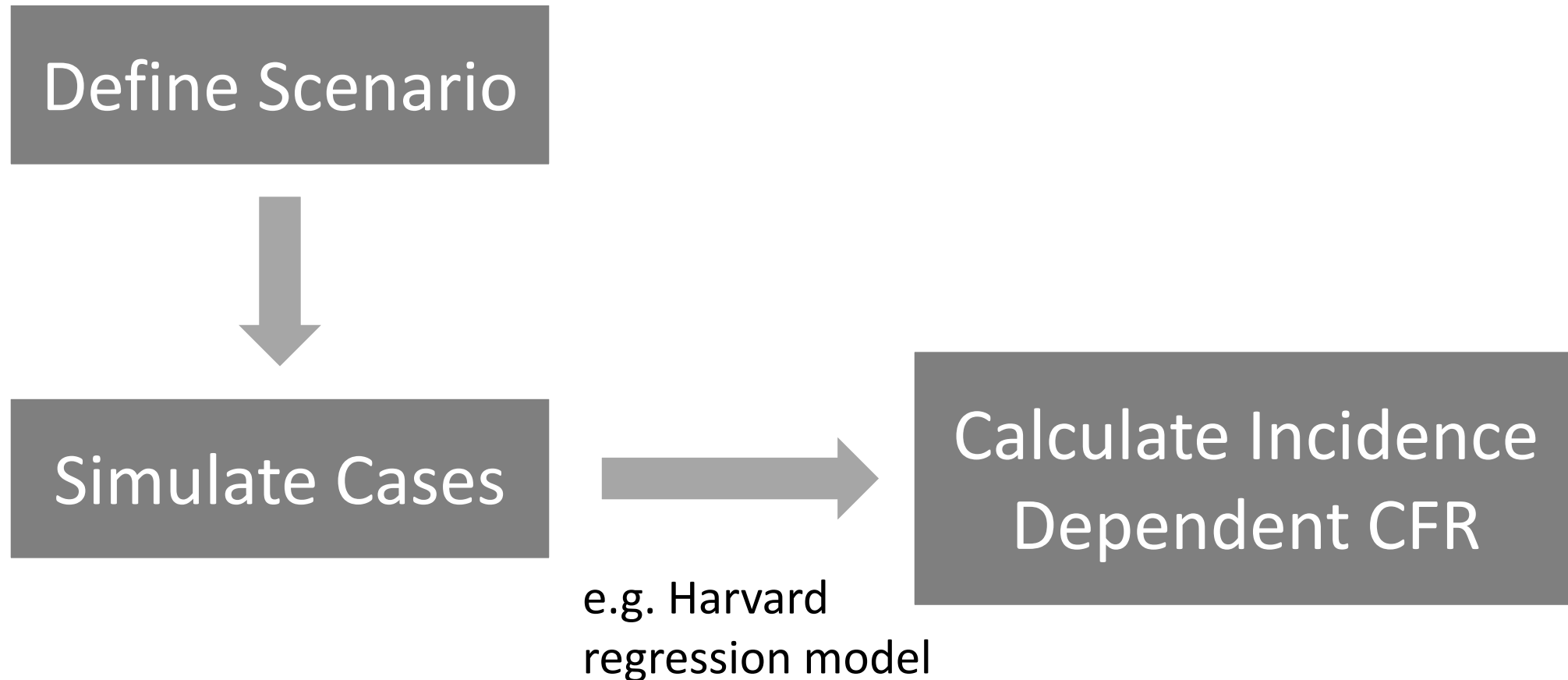
Define Scenario

e.g. VIMC  
models

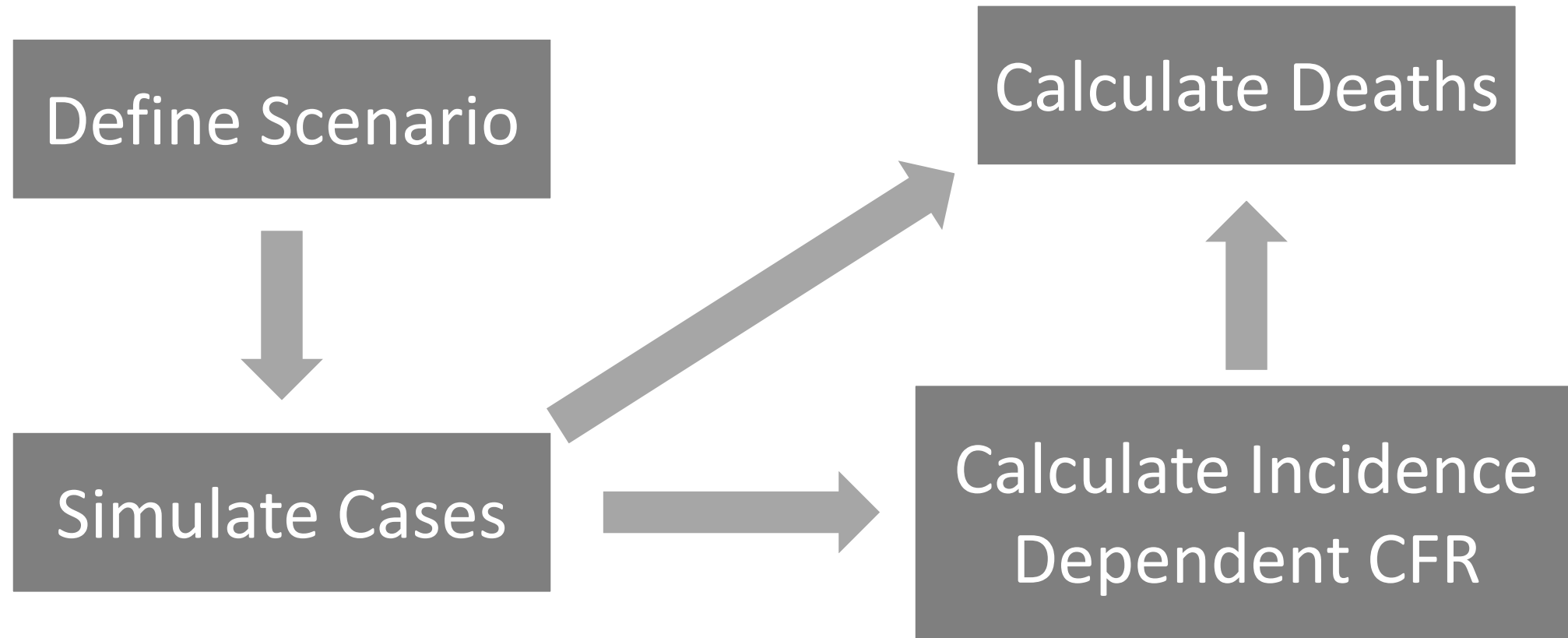


Simulate Cases

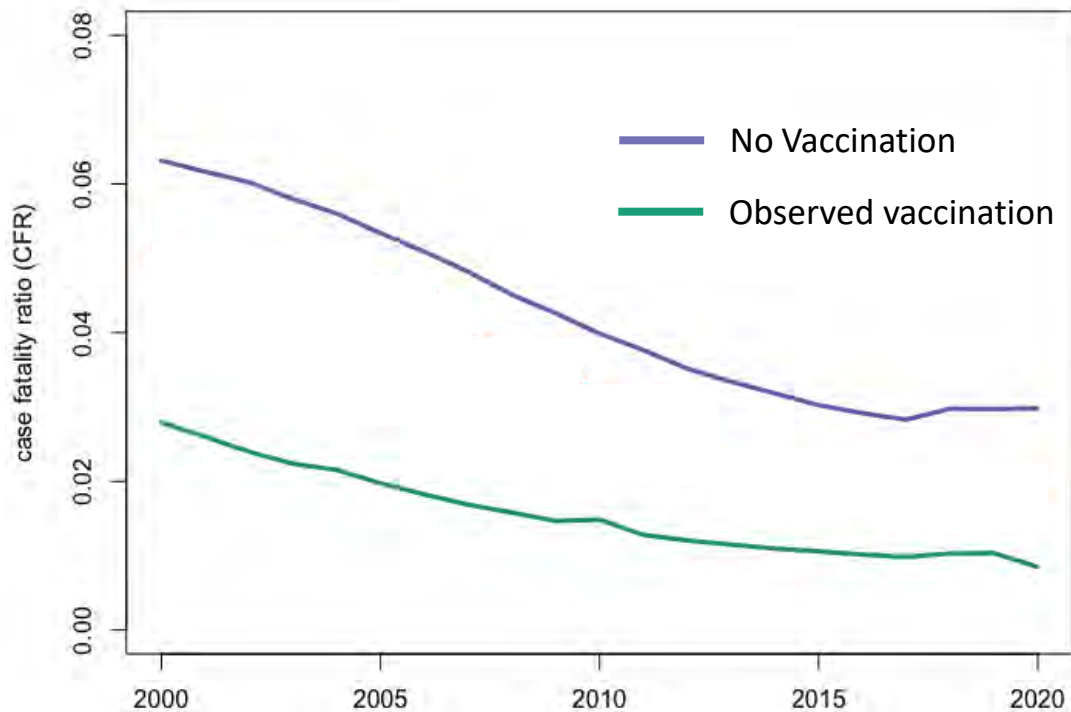
# Modeled CFR Depends on Incidence



# Modeled CFR Depends on Incidence



# Deaths Averted Depends on Counterfactual



To assess consequences of improved programs, should consider effect of counterfactual scenario on CFR. Higher incidence in counterfactual leads to higher predicted CFR.

Current method with static CFR does not do this.

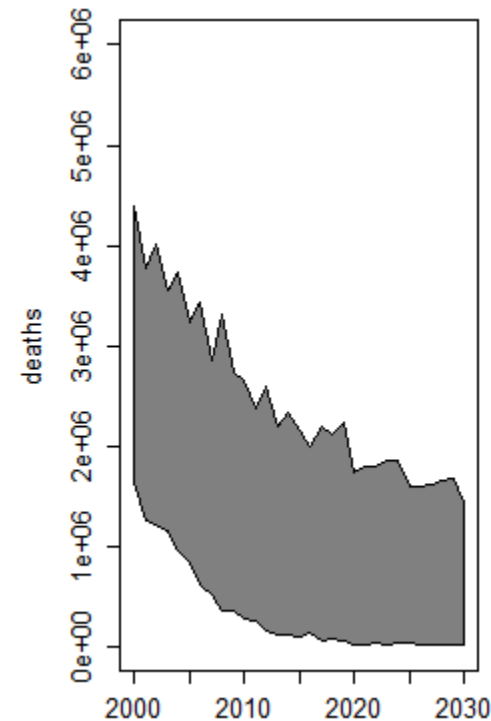
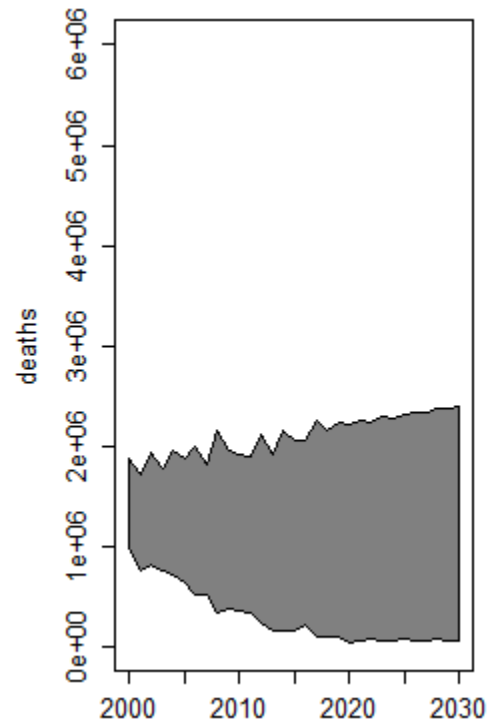
# Deaths Averted Depends on Counterfactual

Vaccination Scenario – As reported 2000-2018; 1% annual increase thereafter

Counterfactual Scenario – no vaccination

Total cases are the same in left and right panel

Assuming static CFR over time and same for both vaccination and counterfactual scenarios



CFR as predicted from Harvard model in both scenarios – CFR different in vaccination and no vaccination scenarios



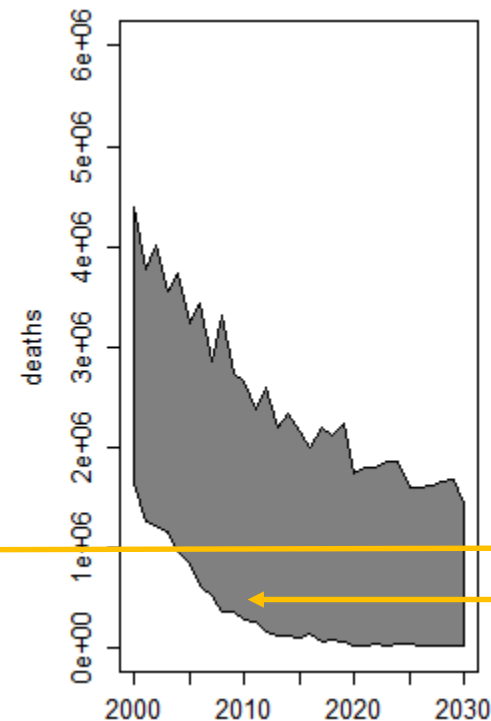
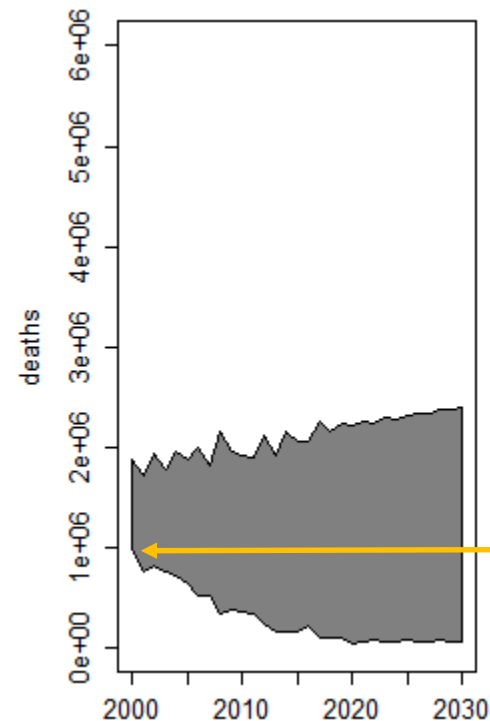
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Assuming static CFR over time and same for both vaccination and counterfactual scenarios



CFR as predicted from Harvard model in both scenarios – CFR different in vaccination and no vaccination scenarios

Steeper decline because of multiplicative effect of declining incidence AND CFR

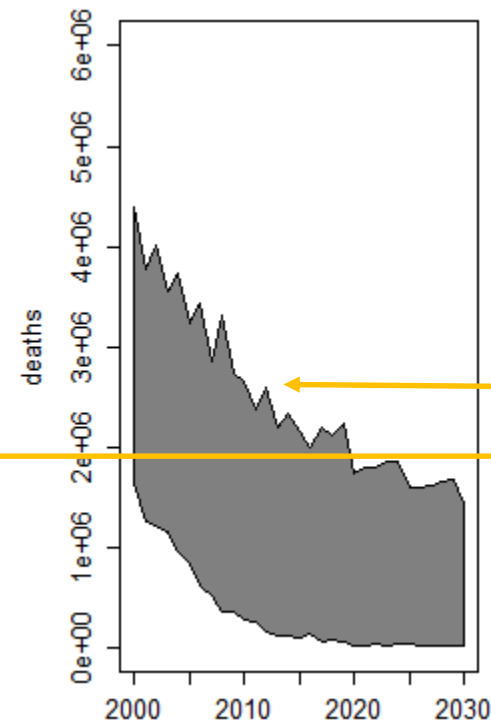
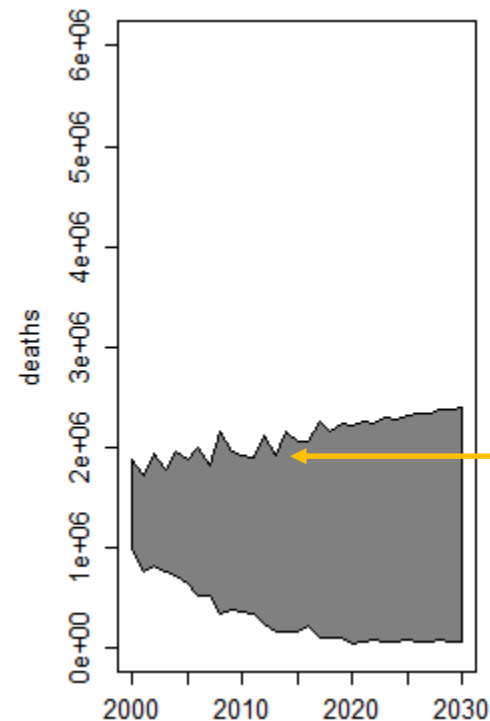
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Assuming static CFR over time and same for both vaccination and counterfactual scenarios



CFR as predicted from Harvard model in both scenarios – CFR different in vaccination and no vaccination scenarios

Counterfactual, no vaccination scenario reflects effect of **Higher incidence** AND decline in overall **under 5 mortality**

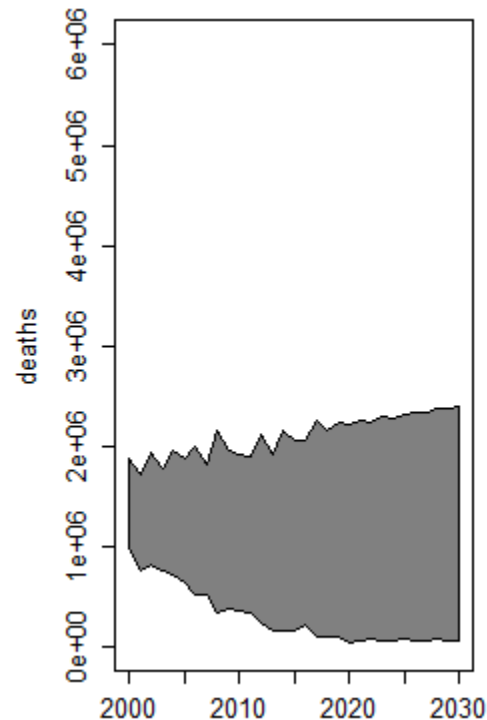
# Deaths Averted Depends on Counterfactual

Vaccination Scenario – As reported 2000-2018; 1% annual increase thereafter

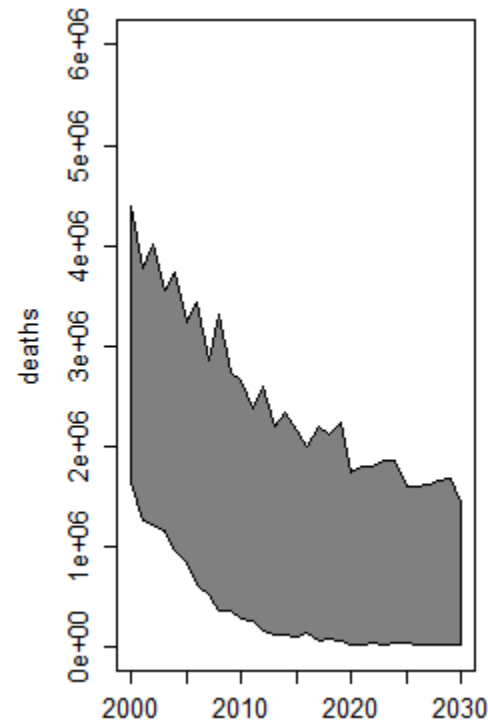
Counterfactual Scenario – no vaccination

Total cases are the same in left and right panel

Assuming static CFR over time and same for both vaccination and counterfactual scenarios



**56 million** deaths averted



CFR as predicted from Harvard model in both scenarios – CFR different in vaccination and no vaccination scenarios

**66 million** deaths averted

# Considerations Going Forward

- Measles CFR is context dependent
- Assuming static CFRs may overstate future mortality and underestimate current deaths averted
- We want method to BOTH:
  - estimate historical and current CFR, and
  - to project CFR for alternative scenarios (counterfactual, alternative investments)

# Considerations Going Forward

- Measles CFR is context dependent
- Assuming static CFRs may overstate future mortality and underestimate current deaths averted
- We want method to BOTH:
  - estimate true historical and current CFR, and
  - to project CFR for alternative scenarios (counterfactual, alternative investments)
- Regression approach proposed by the Harvard analysis is one way to achieve this
  - Allows updating of current CFR each year
  - Allows calculation of CFR for arbitrary scenarios (though requires input covariates)
  - Straightforward to update regression analysis with additional studies as they are done

Requires investment to be generally used and maintained

# Investment in a CFR Platform

Using Harvard regression method as an example:

1. Consolidation of regression method into a documented software package (e.g. R) that allows user to input coverage and incidence and output corresponding CFR  
e.g. VIMC currently requests ~10 future projection scenarios per year. I would generate each projection of incidence conditional on the coverage scenario, then use above to calculate corresponding CFR for each country and year for each scenario.  
**Contrast:** a single time series projection, or annual release, of updated CFRs would account for temporal change, but not be tailored to incidence in each scenario

# Investment in a CFR Platform

Using Harvard Regression method as an example:

1. Consolidation of regression method into a documented software package (e.g. R) that allows user to input coverage and incidence and output corresponding CFR
2. Update default coverage and demographic inputs each year, and release as package update

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2. Update default coverage and demographic inputs each year, and release as package update
3. Update studies included in regression method as new work is done and release as package update
4. Update methodology as new analyses are developed ... e.g. next presentation

# Investment in a CFR Platform

The current static CFRs are simple, but don't reflect context dependence that we expect

Any improvement upon the existing method should be dynamic in time, reactive to differences in scenarios, transparent, and produce reproducible estimates.

# Proposed work on Harvard CFR extension and spatial disaggregation

Alyssa Sbarra<sup>1,2</sup>, Jonathan Mosser<sup>2</sup>, Mark Jit<sup>1</sup>

<sup>1</sup>Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine

<sup>2</sup>Institute for Health Metrics and Evaluation (IHME), University of Washington

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



# Harvard CFR extension & spatial disaggregation

- Objectives: to update the Harvard CFR review and produce location, age, and year-specific spatially disaggregated estimates of measles CFR
- Data: Harvard review & any additional available data (including high-income locations) through December 30, 2020
  - High-income: 354 studies identified by search terms
  - Since 2017: 379 studies identified by search terms, 34 to be extracted
  - Additional 73 sources identified
- Covariates: National and subnational (as available) from Harvard review + other identified as significant
  - Vitamin A supplementation (a modeled surface)
  - Travel time to nearest health facility (Weiss et al<sup>1</sup>)

<sup>1</sup>Weiss, D.J., Nelson, A., Vargas-Ruiz, C.A. et al. Global maps of travel time to healthcare facilities. Nat Med 26, 1835–1838 (2020).  
<https://doi.org/10.1038/s41591-020-1059-1>

# Harvard CFR extension & spatial disaggregation

- Methods: Bayesian meta-regression platform<sup>1</sup>, publicly available code and online repository, with prediction using spatially disaggregated covariates
  - Methods similar to Harvard review, but with Bayesian methods and spatial disaggregation
  - Meta-regression platform to perform variable selection
- Expected output: Open access, location, age, year-specific estimates of CFR with spatial resolution
  - Ability to be updated in the future using publicly available code and data

<sup>1</sup>See <https://www.tandfonline.com/doi/ref/10.1080/10618600.2020.1868303?scroll=top> for methods and code (in Python).

# Background information

Estimates of measles case fatality ratios: a comprehensive review of community-based studies

- <https://pubmed.ncbi.nlm.nih.gov/19188207/>

Estimation and prediction for a mechanistic model of measles transmission using particle filtering and maximum likelihood estimation

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6771900/>

Estimates of case-fatality ratios of measles in low-income and middle-income countries: a systematic review and modelling analysis

- [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)

**Session 4: Overview of Vaccine Impact Modelling  
Consortium (VIMC)**

# Vaccine Impact Modelling Consortium (VIMC): Overview

**WHO Value of Vaccines, Economics and Modeling Team**

2 March 2021



# Agenda



1. Introduction to Vaccine Impact Modelling Consortium (VIMC)
2. Collaboration with WHO



# Vaccine Impact Modeling Consortium (VIMC)



- The Vaccine Impact Modelling Consortium (VIMC) coordinates the work of 18 modelling groups on 12 vaccine-preventable diseases and aims to deliver more sustainable, efficient and transparent approach to generating disease burden and vaccine impact estimates.
- VIMC was established in 2016 and is coordinated by secretariat based at Imperial College London.
- VIMC is funded by Gavi, the Vaccine Alliance and the Bill and Melinda Gates Foundation.

# Collaboration with WHO

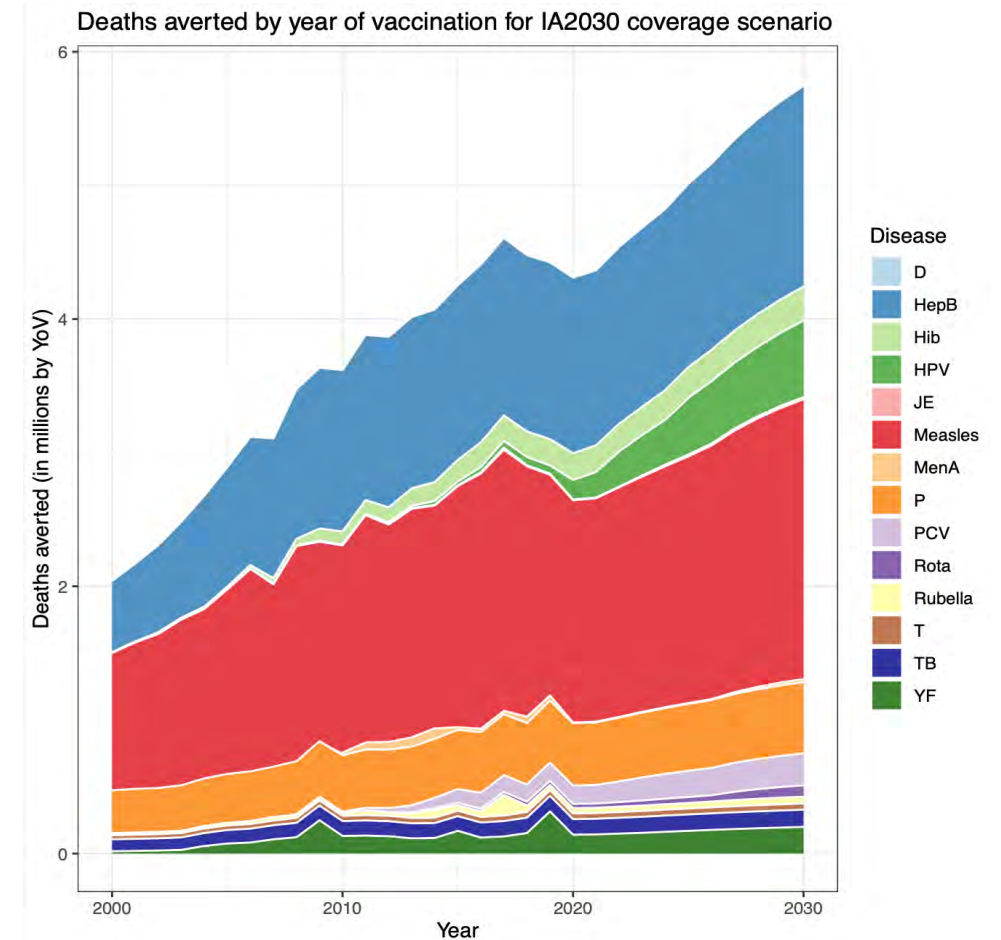


1. IA2030 vaccine impact estimates
2. Vaccine-preventable disease modeling in the context of COVID-19
3. Future collaboration
  - Country engagement for evidence-based strategies and policy decisions
  - WHO COVID-19 Essential Health Services modelling hub



# IA2030 vaccine impact estimates

- Project and method updates presented to IVIR-AC during the ad-hoc session in February 2021
- VIMC estimates for 10 pathogens and 112 countries as key inputs into IA2030 vaccine impact estimates
- Alignment with VIMC method and processes of capturing the long-term impact of vaccination (“Year of Vaccination method”)



# VPD modeling in the context of COVID-19

## VPD Modeling for COVID: Partnership approach

A partnership of vaccine modellers, international organisations and disease experts are investigating the potential impact of reduced RI and delayed/cancelled SIAs during the COVID-19 pandemic



Updated: 23 June 2020

- In April 2020, “Core Coordination Group” (WHO, Gavi, UNICEF, BMGF and VIMC) was formed to coordinate modeling analyses on the impact of reduction in RI coverage and postponement of SIA due to COVID-19
- Focus on measles, yellow fever and MenA, for select countries prioritized by disease and program experts

# Collaboration with WHO



1. IA2030 vaccine impact estimates
2. Vaccine-preventable disease modeling in the context of COVID-19
3. Future collaboration
  - Country engagement for evidence-based strategies and policy decisions
  - WHO COVID-19 Essential Health Services modelling hub



Vaccine Impact Modelling Consortium

# Overview of the consortium

March 2021



**Imperial College**  
**London**



**BILL & MELINDA**  
**GATES** *foundation*



# VIMC's goals

## 💧 Provide vaccine impact estimates to Gavi and BMGF

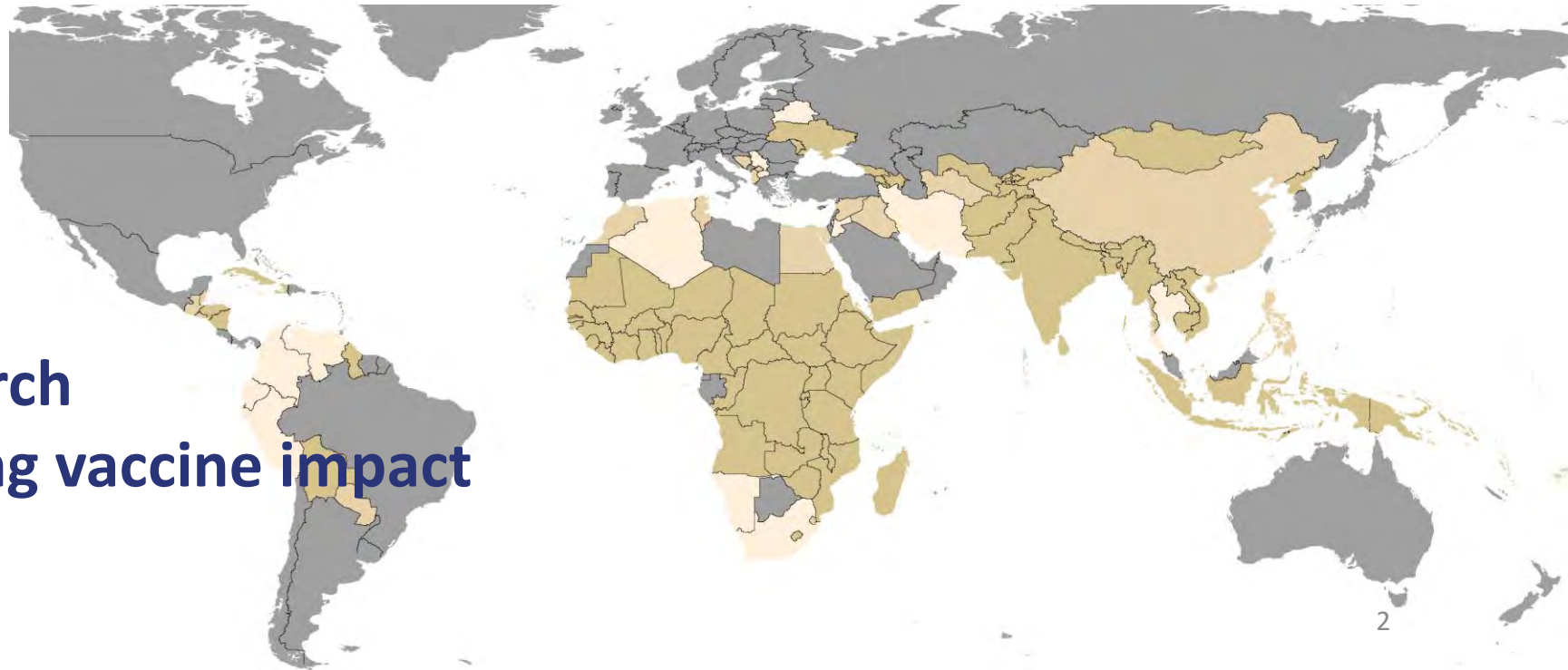
- 💧 12 diseases (cholera, hepatitis B, Hib, HPV, Japanese encephalitis, measles, meningitis A, pneumococcal disease, rotavirus, rubella, typhoid and yellow fever)
- 💧 112 countries (shown in light/dark beige on the map)

## 💧 Further analyses as required by the funders

## 💧 Focus on

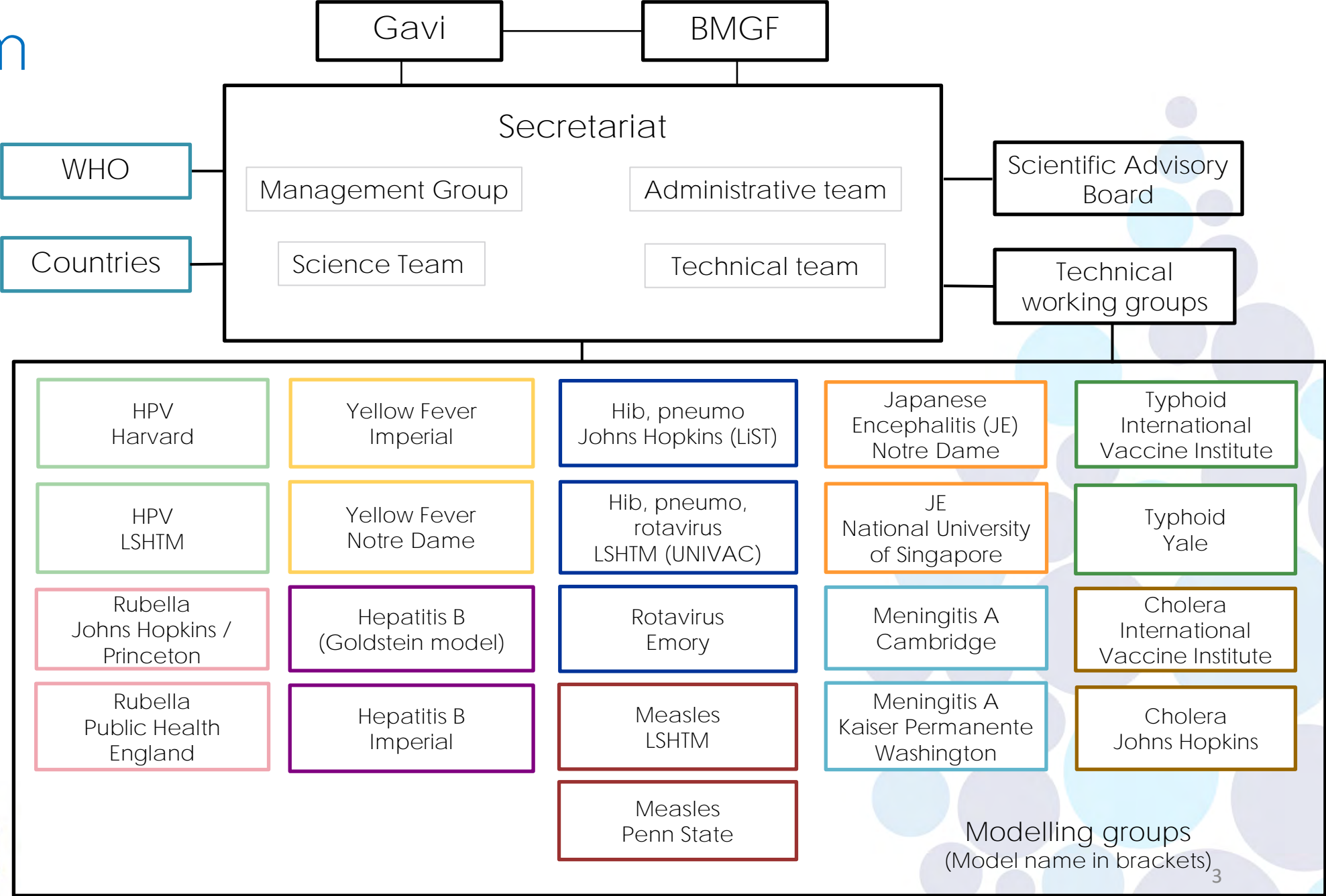
- 💧 Consistency
- 💧 Efficiency
- 💧 Quality

## 💧 Advance the research agenda in modelling vaccine impact





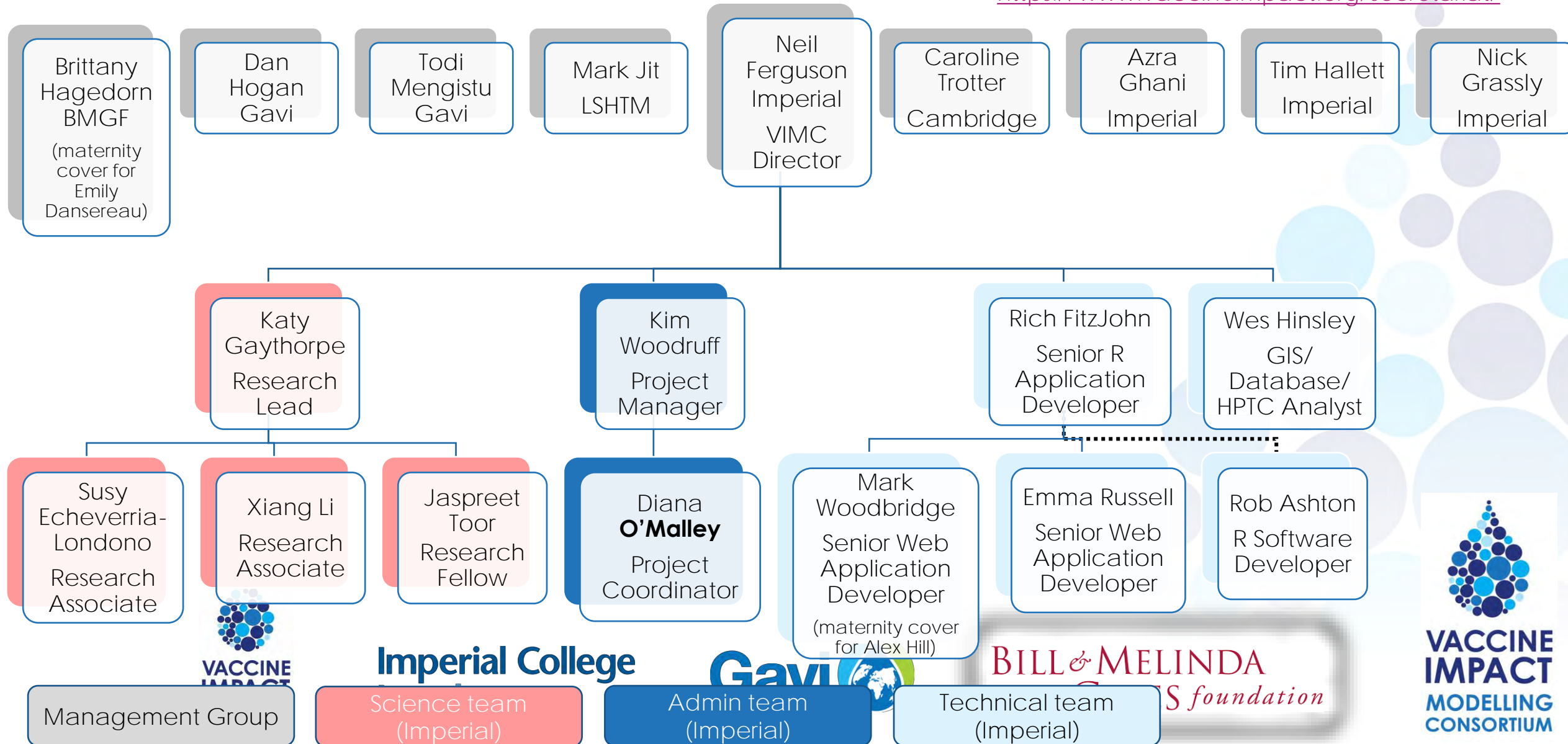
# Consortium structure



# Secretariat Organogram

Photos:

<https://www.vaccineimpact.org/secretariat/>



# Roles and expectations – Management Group and SAB

## 💧 Management Group (MG)

- 💧 Sets priorities and strategy, provides technical and operational oversight

## 💧 Scientific Advisory Board (SAB)

- 💧 Consulting body to MG and overall Consortium

## 💧 Secretariat

### 💧 Science team (with research lead Katy Gaythorpe)

- 💧 Calculates impact, prepares model inputs, performs consortium analysis

### 💧 Admin team (with project manager Kim Woodruff)

- 💧 Co-ordinates the consortium

### 💧 Tech team

- 💧 Develops infrastructure

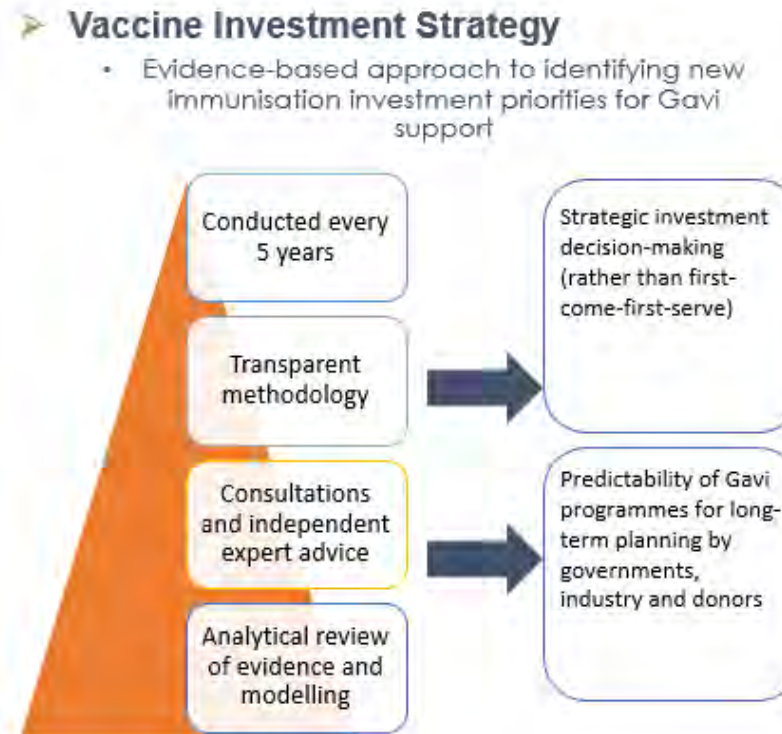
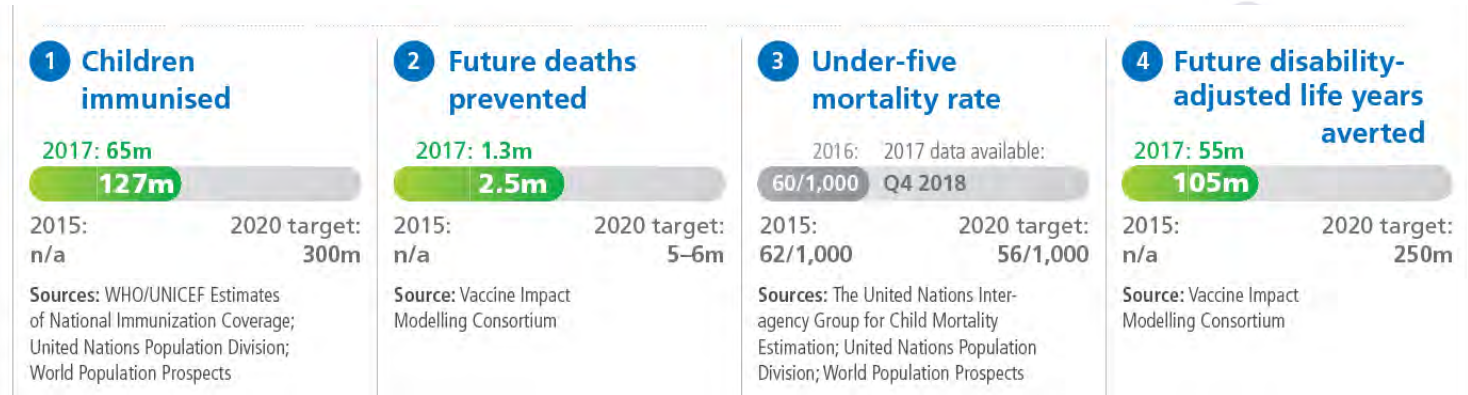
# Roles and expectations – Modellers

- 💧 Provide disease burden estimates
- 💧 Improve own models, focusing on VIMC quality standards
- 💧 Participate in annual model reviews
- 💧 Contribute to research and publications
- 💧 Lead specific research topics of interest
- 💧 Advise on presentation of estimates and disease-specific questions



# Main uses of VIMC impact estimates at Gavi

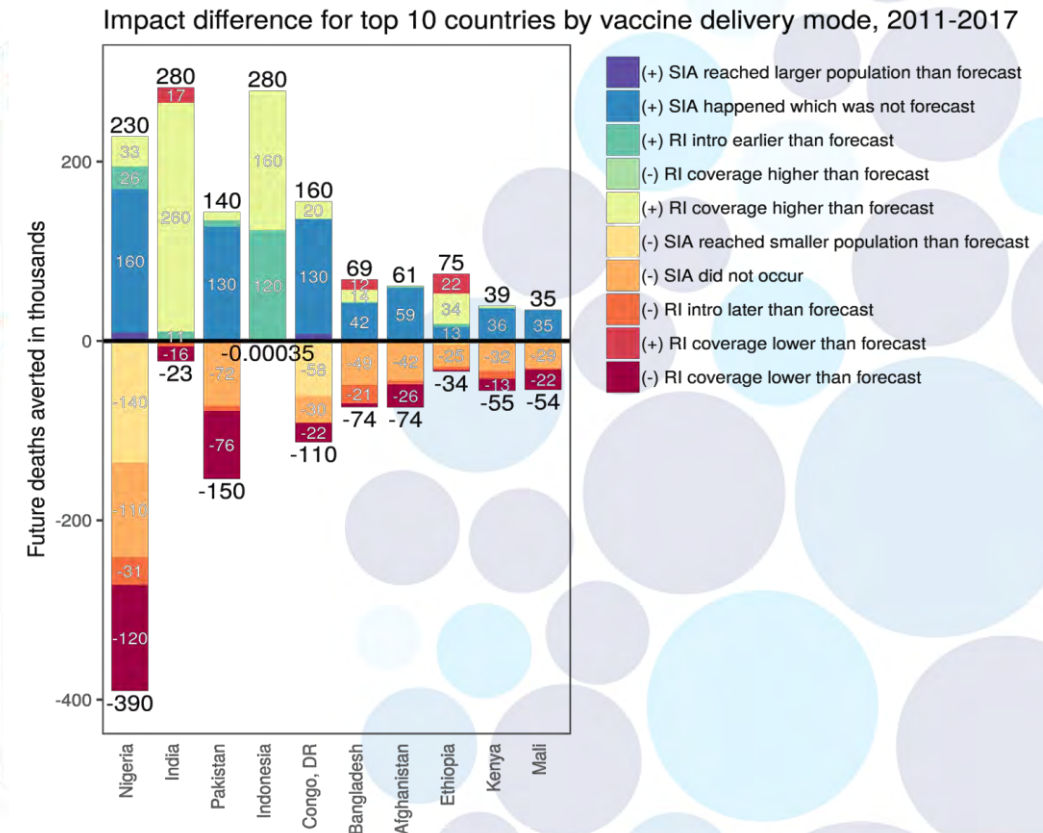
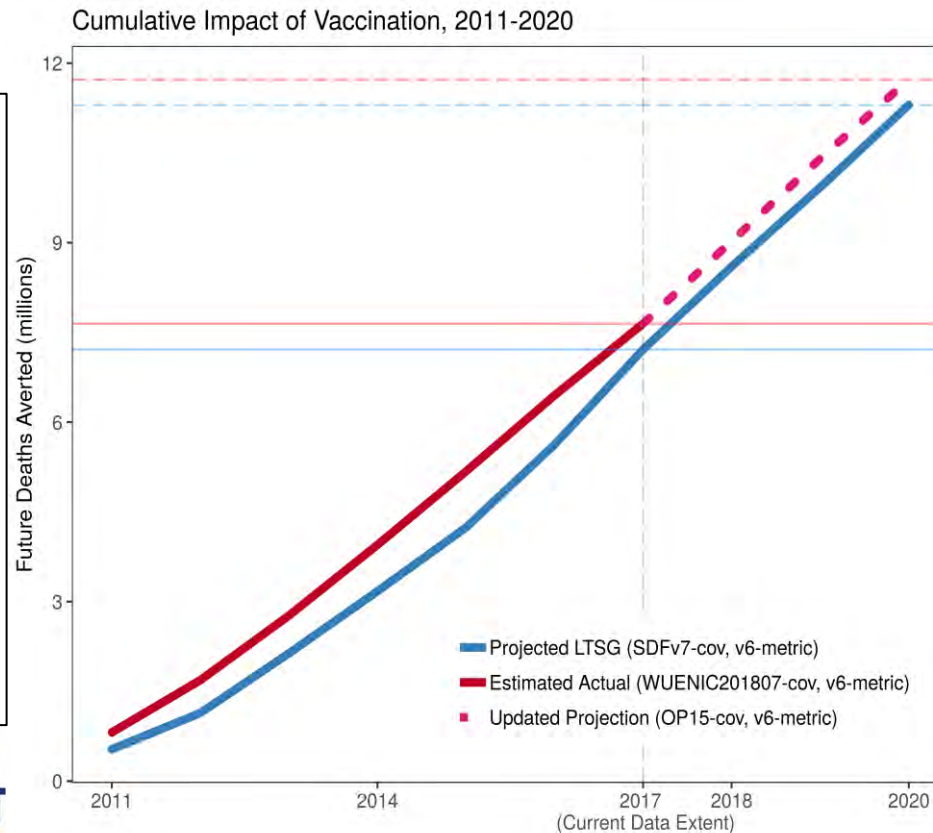
- Report on progress of current strategy
- Inform investment and policy decisions
  - Vaccine Investment Strategy
- Support resource mobilization (past impact, future targets, ROI)
- Inform advocacy and communication messages



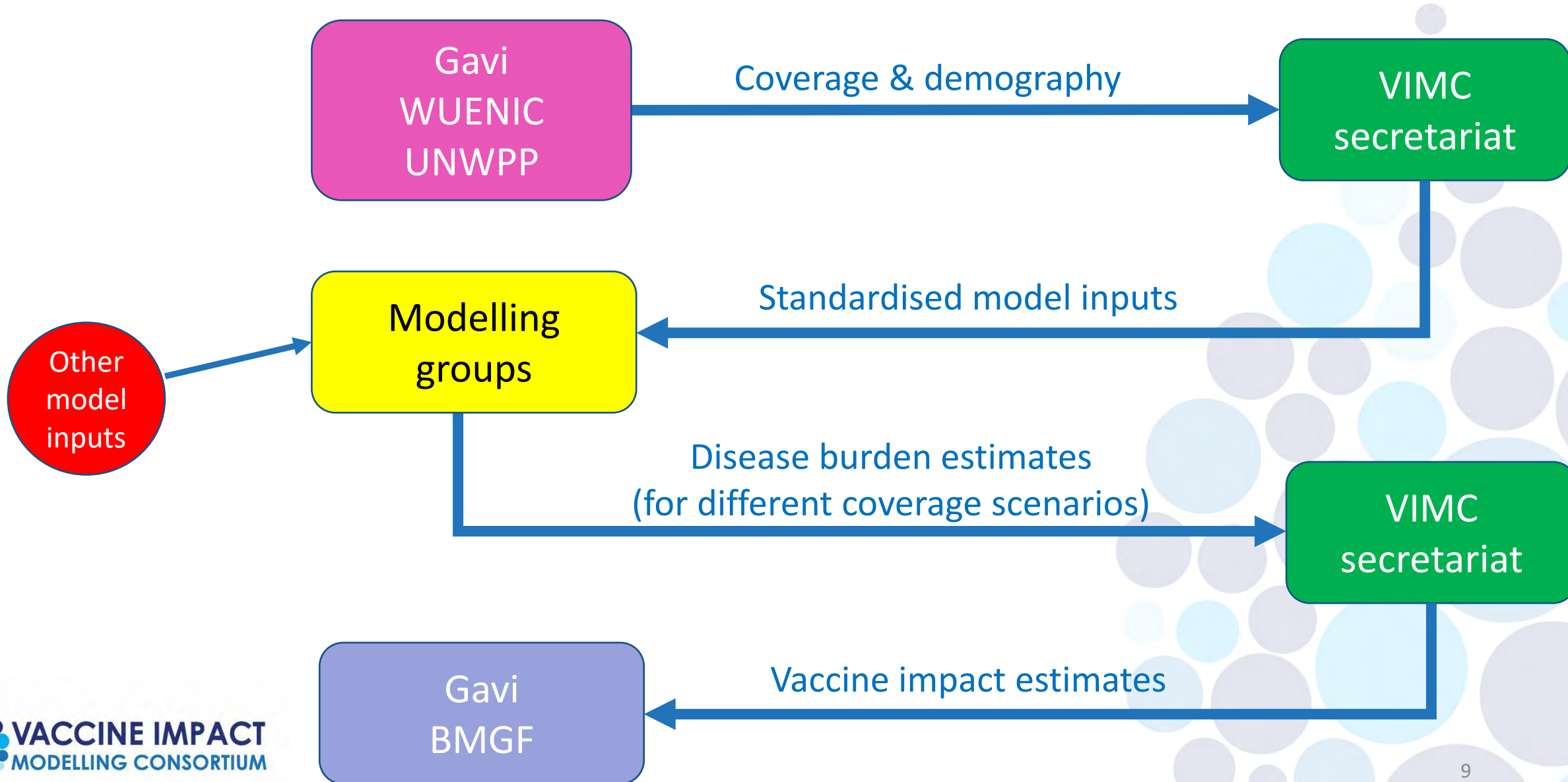
# Main uses of impact estimates at BMGF

- 💧 Setting and tracking progress against health impact targets (example below)
- 💧 Advocacy and resource mobilization
- 💧 Strategy development

- 1. Avert 11.3M future deaths
- 2. Coverage: 90% national; 80% in every district
- 3.0 polio cases



# VIMC workflow for full model runs





# Infrastructure: Montagu

- 💧 Infrastructure to support generation, storage and dissemination of impact estimates
- 💧 Substantial software development project

montagu.vaccineimpact.org

Logged in as kim.woodruff | Log out

**VACCINE IMPACT**  
MODELLING CONSORTIUM

**MONTAGU**

Montagu is the VIMC's digital delivery platform. Authorised users can access Montagu through user-facing portals, and programmatically through REST APIs.

Click [here](#) to view Montagu's privacy policy and terms.

Click [here](#) to return to VIMC home page.

### Portals

- Reporting portal
- Modellers' contribution portal
- Admin portal

Access reports and figures summarising results, as well as the underlying data.

Focused on modellers and modelling groups, this portal allows you to download coverage and demographic data, and to upload burden estimates.

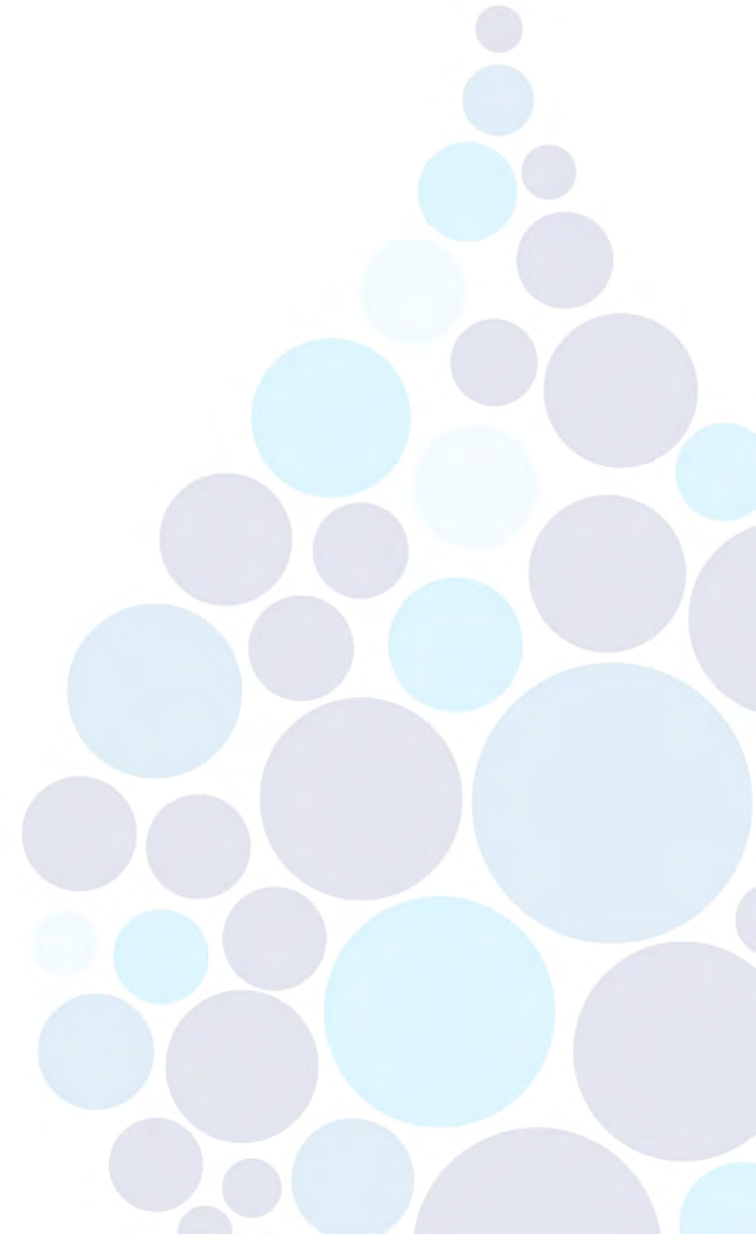
For internal use by the consortium admin staff.

### APIs

- Montagu API
- Reports API



Publications and preprints



# 1<sup>st</sup> VIMC-wide publication

## Estimating the health impact of vaccination against 10 pathogens in 98 low and middle income countries from 2000 to 2030

- 💧 Published in the [Lancet](#)
- 💧 [Data visualisation tool](#) available
- 💧 Documents the first round of VIMC model estimates presenting impact by calendar year and birth cohort
- 💧 “In terms of deaths averted by calendar year, 69 million (95% CrI 52–88) deaths were estimated to be averted between 2000 and 2030, of which 37 million (30–48) were averted between 2000 and 2019.”

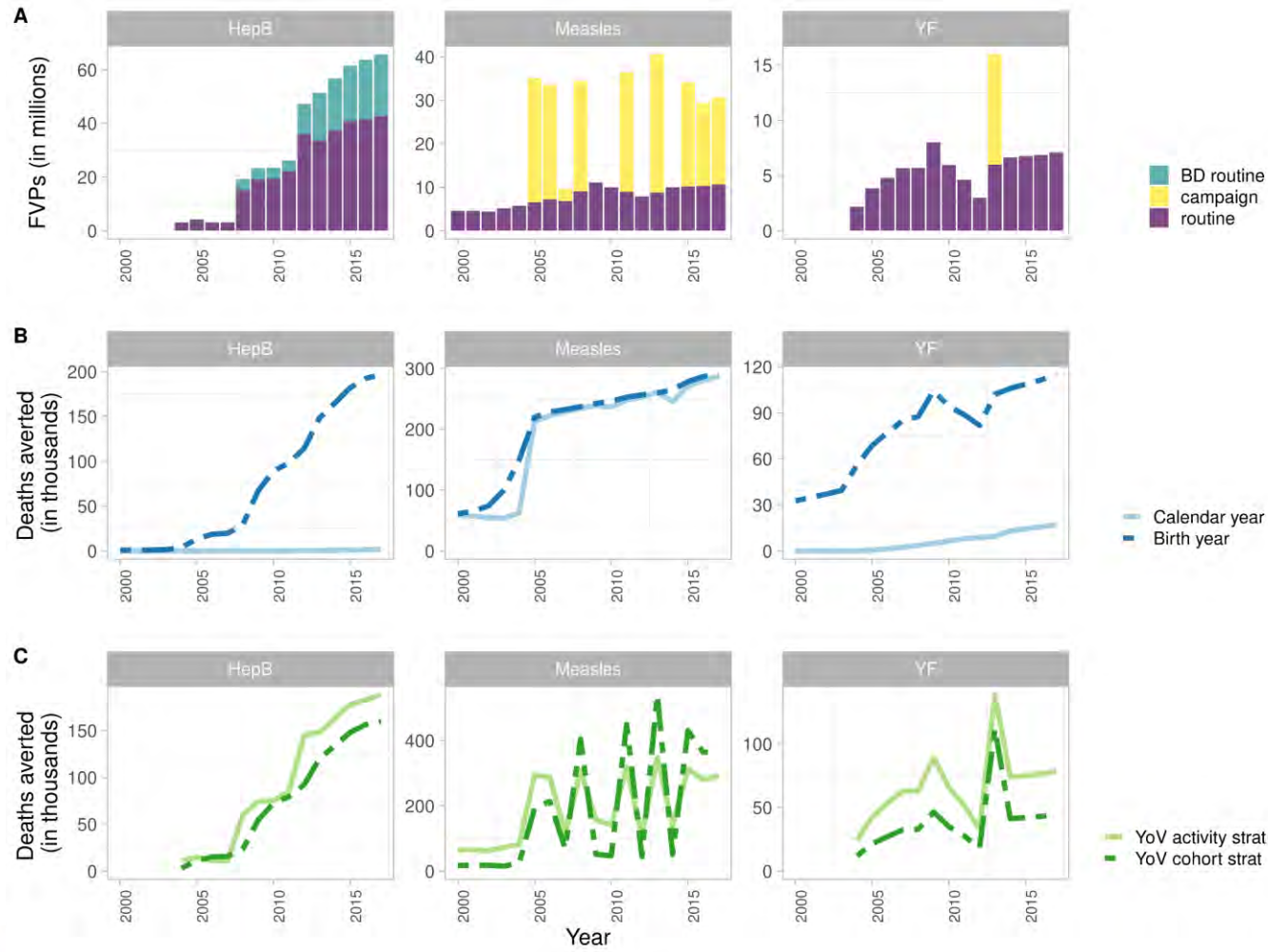
# Impact methodology

## How can the public health impact of vaccination be estimated?

Preprint available on [MedRxiv](#)

- 💧 We describe the methods to estimate impact by calendar year, birth year and year of vaccination (YoV)
- 💧 We use examples from measles, Hepatitis B and yellow fever to demonstrate the different impact methods
- 💧 We also illustrate the “interim update method”
  - 💧 allows us to approximate what the models would have predicted given new vaccination data
  - 💧 allows us to perform quick estimates of impact in between model runs

# Impact methodology



Fully vaccinated persons (FVPs) and mean estimates of deaths averted for Hepatitis B (HepB) in Country A, measles in Country B and yellow fever (YF) in Country C from 2000 to 2017. (A) FVPs for HepB birth dose (BD routine) and infant dose (routine) routine vaccination activities. FVPs for first routine dose of a measles containing vaccine and measles campaign activities. FVPs for YF routine and campaign activities. (B) Impact by calendar and birth year methods. (C) Impact by year of vaccination (YoV) with impact ratio stratified by activity type and birth cohort.

# The second consortium-wide paper

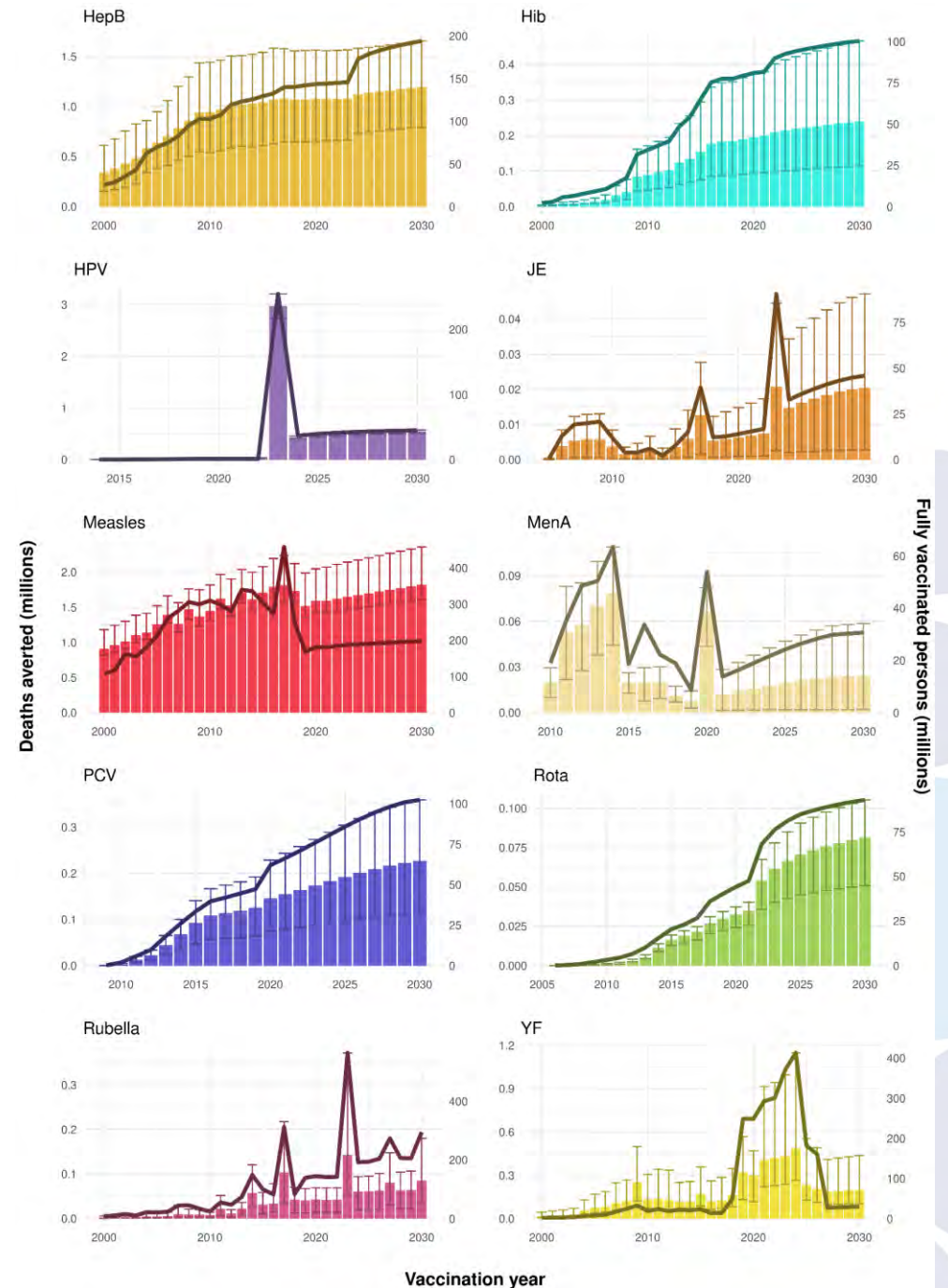
## Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world

- 💧 Coming later this year
- 💧 New [data visualisation tool](#) available
- 💧 Results inform IA2030 modelling
- 💧 Includes more countries, more modelling groups and more impact approaches



# The second consortium-wide paper

Deaths averted per year of vaccination for each pathogen. Height of bar is proportional to deaths averted per that vaccination year. Error bars indicate 95%CI. Line represents the FVPs of each year's vaccination activities calculated.



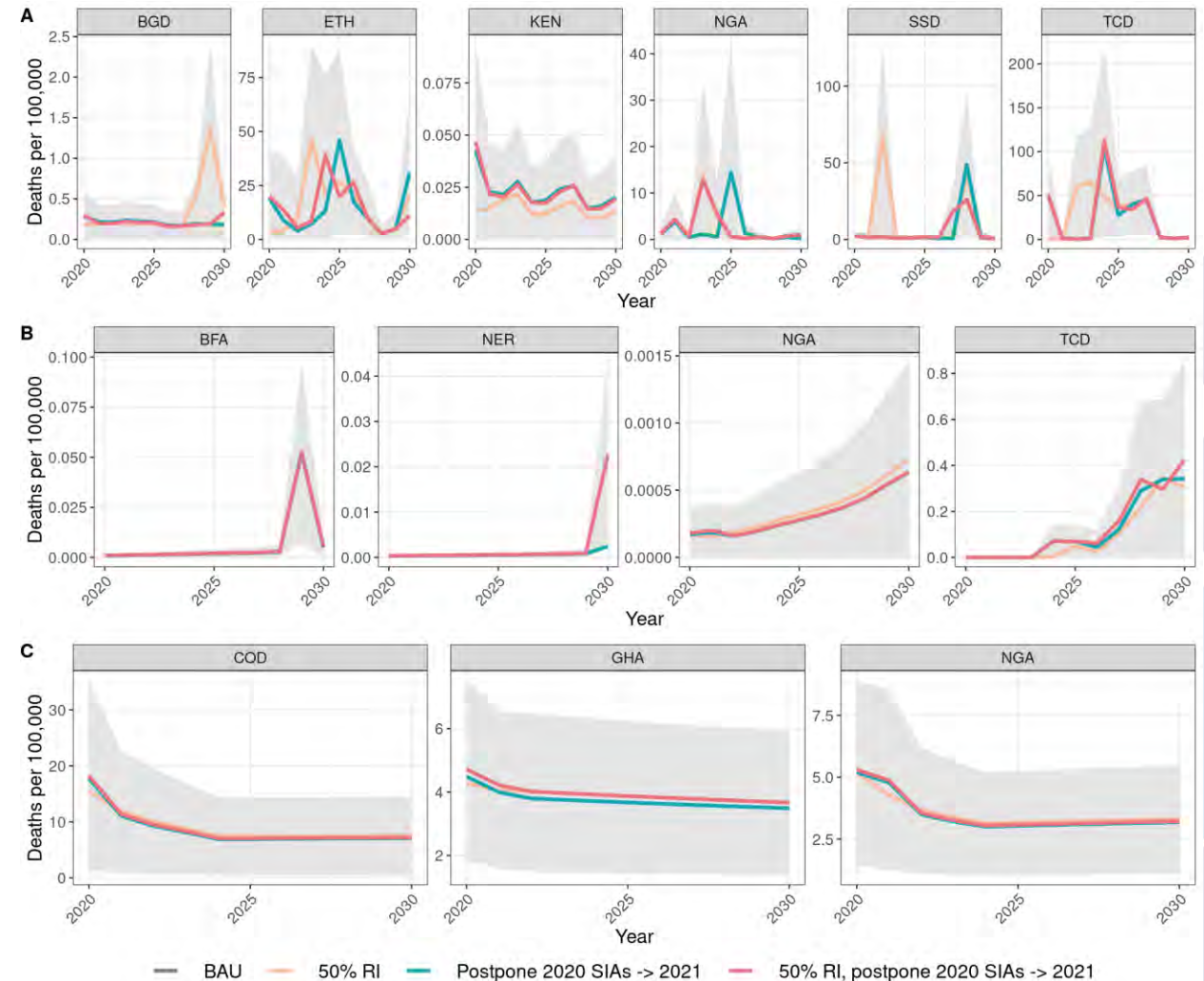
# The impact of COVID-19 disruption on VPDs

**Health impact of routine immunisation service disruptions and mass vaccination campaign suspensions caused by the COVID-19 pandemic: Multimodel comparative analysis of disruption scenarios for measles, meningococcal A, and yellow fever vaccination in 10 low- and lower middle-income countries**

- 💧 Examine disruption scenarios for measles, menA and yellow fever
- 💧 Preprint available on [MedRxiv](#)
- 💧 Quantified the change in burden due to disruption in 10 countries

# The impact of COVID-19 disruption on VPDs

Health impact of predicted total deaths for immunisation disruption scenarios and no disruption scenario for measles, meningococcal A, and yellow fever. The average model predicted total deaths per 100,000 population per year for routine and campaign immunisation disruption scenarios and no disruption scenario (BAU – business-as-usual scenario) for measles, meningococcal A, and yellow fever during 2020-2030. Grey ribbon indicates the most extreme (maximum and minimum) model projections for all scenarios; the thick line indicates mean model projection.





# Looking ahead to VIMC 2021-22

## Workstreams

- Demographic uncertainty
- Subnational heterogeneity
- Health inequity and vaccination
- Disruption due to COVID-19
- Clustering of vaccination
- Country engagement

## Deliverables

- The third round of VIMC model estimates covering 12 pathogens over 112 countries
- Informing IA2030 with latest estimates



# Thank you to all our members

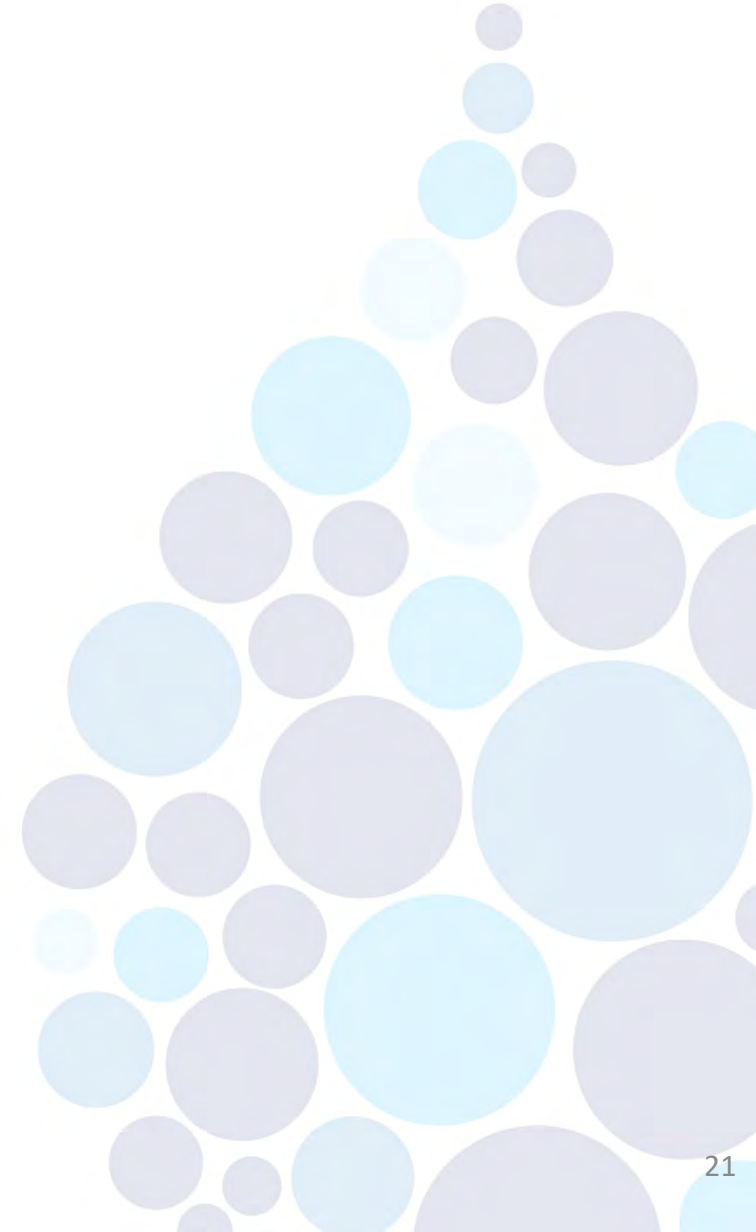


Imperial College  
London



BILL & MELINDA  
GATES *foundation*

# Discussion





# Background information

About VIMC:

- <https://www.vaccineimpact.org/>

Health impact of routine immunisation service disruptions and mass vaccination campaign suspensions caused by the COVID-19 pandemic: Multimodel comparative analysis of disruption scenarios for measles, meningococcal A, and yellow fever vaccination in 10 low- and lower middle-income countries:

- <https://www.medrxiv.org/content/10.1101/2021.01.25.21250489v1>

Estimating the health impact of vaccination against 10 pathogens in 98 low and middle income countries from 2000 to 2030: a modelling study

- [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)

How can the public health impact of vaccination be estimated?

- <https://www.medrxiv.org/content/10.1101/2021.01.08.21249378v1>

Link to VIMC's interactive data visualization tool

- <https://montagu.vaccineimpact.org/2020/visualisation/>

## **Session 5: Meta-analysis of Economic Evaluations**

**3rd Mar 2021**

Meta-analysis of global literature on  
economic evaluation studies:  
**Strengths and Criticisms**

**Ammarin Thakkinstian, PhD**

Faculty of Medicine Ramathibodi Hospital,  
Mahidol University, Thailand

**Nathorn Chaiyakunapruk PharmD, PhD**

College of Pharmacy, University of Utah, USA

# Outline

- Why MA of EE studies?
- How to pool studies?
- Examples of MA of EE studies
- Strengths and Criticisms
- Summary

# Why's MA of economic evaluation (EE) studies?

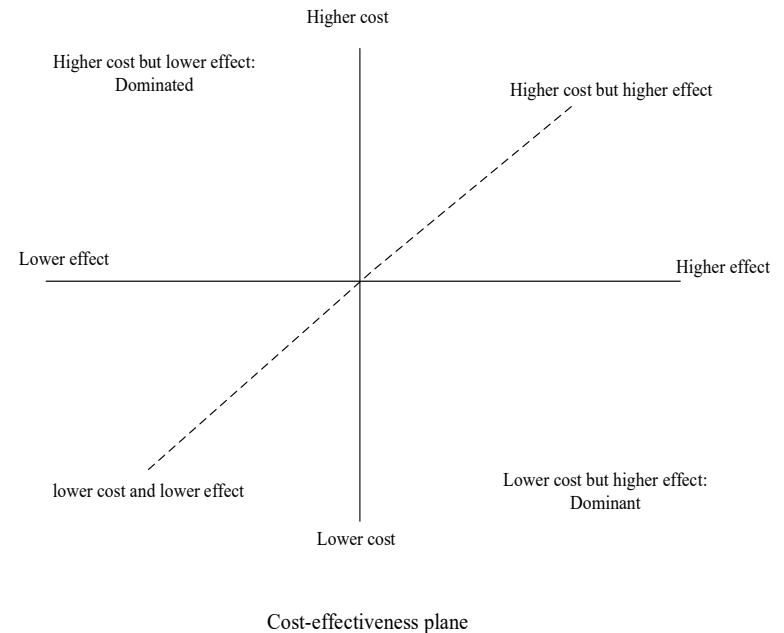
- EE studies are **important in providing** evidence for policy decisions in healthcare
- Systematic review (SR) of EE studies has been commonly reported in literature. Globally, WHO has commissioned several **SRs** of various vaccines as part of the Global Public Health Value Proposition Evidence Generation
- Most previous SRs of EE provided only *descriptive summary without quantitative evidence*
- Meta-analysis (**MA**) of EE studies has been developed and recently modified and applied in **vaccine and therapeutic areas**
- The benefit of MA of EE is that the evidence can *support policy decision making* as it provides an overall summary of evidence based on similar contexts



# EE studies

- Most EE studies apply an ICER for comparing cost and effectiveness
- Limitations
  - Not normal distribution and invalid estimation of its confidence interval
  - A negative ICER may indicate a lower cost with higher effectiveness or higher cost along with lower effectiveness of interventions, thus introducing ambiguity in interpretation

$$ICER = \frac{c_1 - c_2}{e_1 - e_2}$$



# Meta-analysis (MA) for EE studies

- Originally developed by Crespo et al 2014\*
- Known as COMparative Efficiency Research, COMER
- Purposed pooling incremental net benefit (INB)

$$ICER < K$$

$$\frac{(\hat{\mu}_{C1} - \hat{\mu}_{C2})}{(\hat{\mu}_{E1} - \hat{\mu}_{E2})} < K$$

$$K(\hat{\mu}_{E1} - \hat{\mu}_{E2}) - (\hat{\mu}_{C1} - \hat{\mu}_{C2}) > 0$$

$$INB = K(\hat{\mu}_{E1} - \hat{\mu}_{E2}) - (\hat{\mu}_{C1} - \hat{\mu}_{C2}) > 0$$

- Positive and negative INBs could directly indicate cost-effectiveness and non-cost-effectiveness of the treatments

# MA for EE studies: Data Harmonization and Methodological issues<sup>\*</sup>

## 1. Data harmonization

- *Currency conversions*
  - Standardize different money units (e.g, **US \$**, **€**, **£**, **¥**) and years by converting to purchasing power parity (PPP) adjusted to US\$ for the latest year of analysis

## 2. Estimation of INB and its variance

### ■ INB

$$INB = Kx\Delta E - \Delta C \text{-----} (1) \quad \text{or}$$

$$INB = \Delta E(K - ICER) \text{-----} (2)$$

### ■ Variance

$$Var(INB) = K^2\sigma_{\Delta E}^2 + \sigma_{\Delta C}^2 - 2K\sigma_{\Delta E\Delta C} \text{-----} (3) \quad \text{or}$$

$$Var(INB) = K^2\sigma_{\Delta E}^2 + \sigma_{ICER}^2 \text{-----} (4)$$

- K is the WTP,  $\Delta C$  and  $\Delta E$  are incremental cost and incremental effectiveness;
- $\sigma_{\Delta E\Delta C}$  are covariance of  $\Delta C$  and  $\Delta E$  and  $\sigma_{\Delta E}^2, \sigma_{\Delta C}^2$  are their variances,
- $\sigma_{ICER}^2$  is variance of ICER

# Five scenarios developed to obtain variance

- **Scenario-1:** EE studies ideally reports the point estimates & variances for every parameter required for calculation
- **Scenario-2:** The study reports the means and 95% CIs of incremental costs & outcomes, and ICER
- **Scenario-3:** The study reports means and 95% CI of costs/outcomes, or  $\Delta C$  &  $\Delta E$ , but not ICER or its variance.
  - Monte Carlo simulation with a gamma and normal distributions for  $\Delta C$  and  $\Delta E$  was performed to estimate covariance between  $\Delta C$  and  $\Delta E$ .

$$95\%CI \text{ of } \mu_{ICER} = \hat{\mu}_{ICER} \pm Z_{\alpha/2} x SE$$

$$UL_{ICER} = \hat{\mu}_{ICER} + Z_{\alpha/2} x SE$$

$$SE = \frac{UL_{ICER} - \hat{\mu}_{ICER}}{Z_{\alpha/2}}$$

$$\hat{\sigma}_{ICER}^2 = SE^2$$

$$UL_{ICER} = \text{Upper limit of ICER}$$

$$Z_{\alpha/2} = \text{Standardize normal} = 1.96$$

$$\hat{\mu}_{ICER} = \text{mean ICER}$$

# Five scenarios developed to obtain variance

- **Scenario-4:** The study does not report any dispersion, but does provide the CE plane graphs, in which data can be directly extracted from the CE plane using Web-Plot-Digitizer software.
  - The means of  $\Delta C$ ,  $\Delta E$ , and their variances and co-variance can be estimated accordingly. Finally, the INB and its variance can be estimated.
- **Scenario-5:** The study reports only the means (or point estimates) of costs, outcomes, and ICER.
  - The measures of dispersions can be borrowed from another similar study if they fulfil the following criteria:
  - They are in the same stratum of country income level, perspective, intervention, comparator, time period, country region, model type, and inputs (i.e., discounting, time horizon).
  - Their ICERs are not much different, e.g.,  $\pm 50\%$  to  $75\%$

### 3. Methods for pooling INB

- Fixed-effects Model

$$INB_p = \frac{\sum_{i=1}^S w_i INB_i}{\sum_{i=1}^S w_i}$$

$$w_i = \frac{1}{\text{var}(INB_i)}$$

$$= \frac{1}{K^2 \sigma_{\Delta E}^2 + \sigma_{\Delta C}^2 - 2K\rho_{CE} \sigma_{\Delta C} \sigma_{\Delta E}}$$

- Random-effects Model

$$INB_p = \frac{\sum_{i=1}^S w_i^* INB_i}{\sum_{i=1}^S w_i^*}$$

$$w_i^* = \frac{1}{\text{var}(INB_i) + \tau^2}$$

$$\tau^2 = \frac{Q - (S - 1)}{\sum w_i - \frac{\sum w_i^2}{\sum w_i}}$$

$$Q = 0 \text{ if } Q < S - 1$$

- Heterogeneity

$$Q = \sum_{i=1}^S w_i (\text{INB}_i - \text{INB}_P)^2$$

$$w_i = \frac{1}{\text{var}(\text{INB}_i)}$$

$$I^2 = \frac{[Q - S + 1] \times 100}{Q}$$

- Meta-regression

- Reporting bias

- Funnel plot
- Egger's test

- Analysis should be stratified by

- Level income's country
- Type of model
- Perspective
- Time horizon





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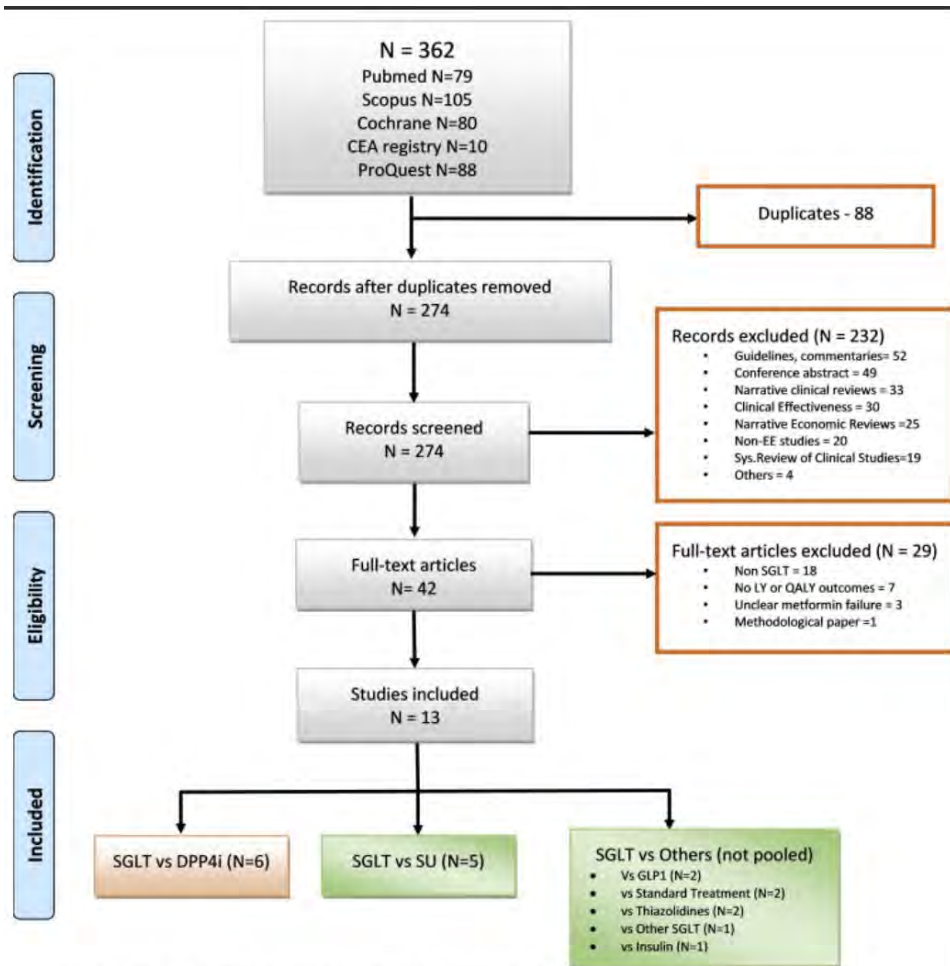
# Examples

Systematic Literature Review

# Cost Utility of Sodium-Glucose Cotransporter 2 Inhibitors in the Treatment of Metformin Monotherapy Failed Type 2 Diabetes Patients: A Systematic Review and Meta-Analysis

Bhavani Shankara Bagepally, MBBS, PhD,<sup>1,2</sup> Yogesh Krishnarao Gurav, MBBS, MD,<sup>1,3</sup> Thunyarat Anothaisintawee, MD, PhD,<sup>1,4</sup> Sitaporn Youngkong, PhD,<sup>1,5</sup> Usa Chaikledkaew, PhD,<sup>1,5</sup> Ammarin Thakkinstant, PhD<sup>1,6,\*</sup>

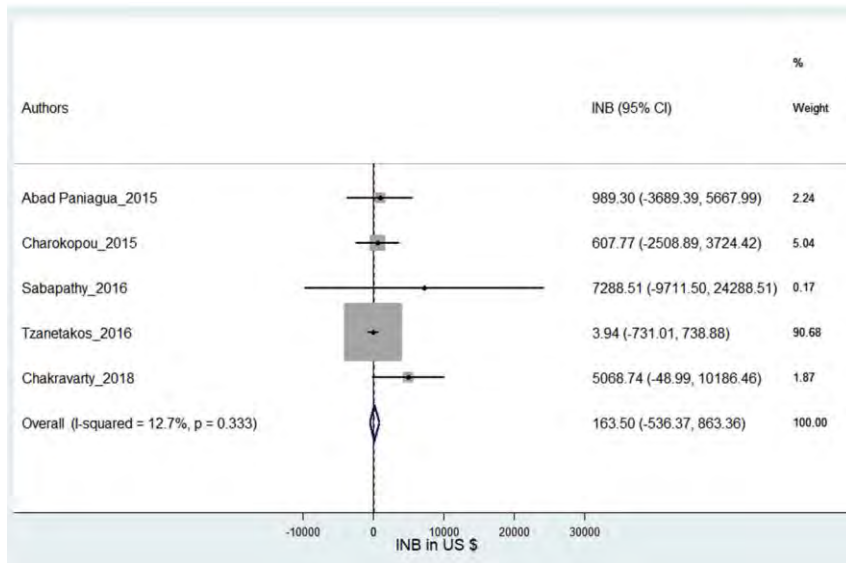
<sup>1</sup>Mahidol University Health Technology Assessment Graduate Program, Bangkok, Thailand; <sup>2</sup>ICMR–National Institute of Epidemiology, Chennai, India; <sup>3</sup>ICMR–National Institute of Virology, Pune, India; <sup>4</sup>Department of Family Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; <sup>5</sup>Department of Pharmacy, Mahidol University, Bangkok, Thailand; <sup>6</sup>Section for Clinical Epidemiology and Biostatistics, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.



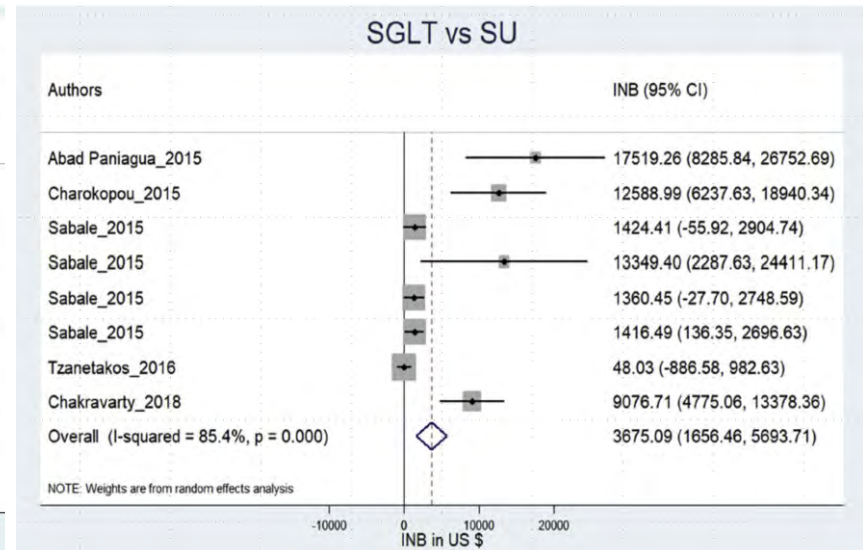
\* The last row indicates the comparison information from studies (number is >13 due to multiple comparison, details in the text)

# Pooling INB in High income countries

## SGLT2 vs DPP4



## SGLT2 vs SU

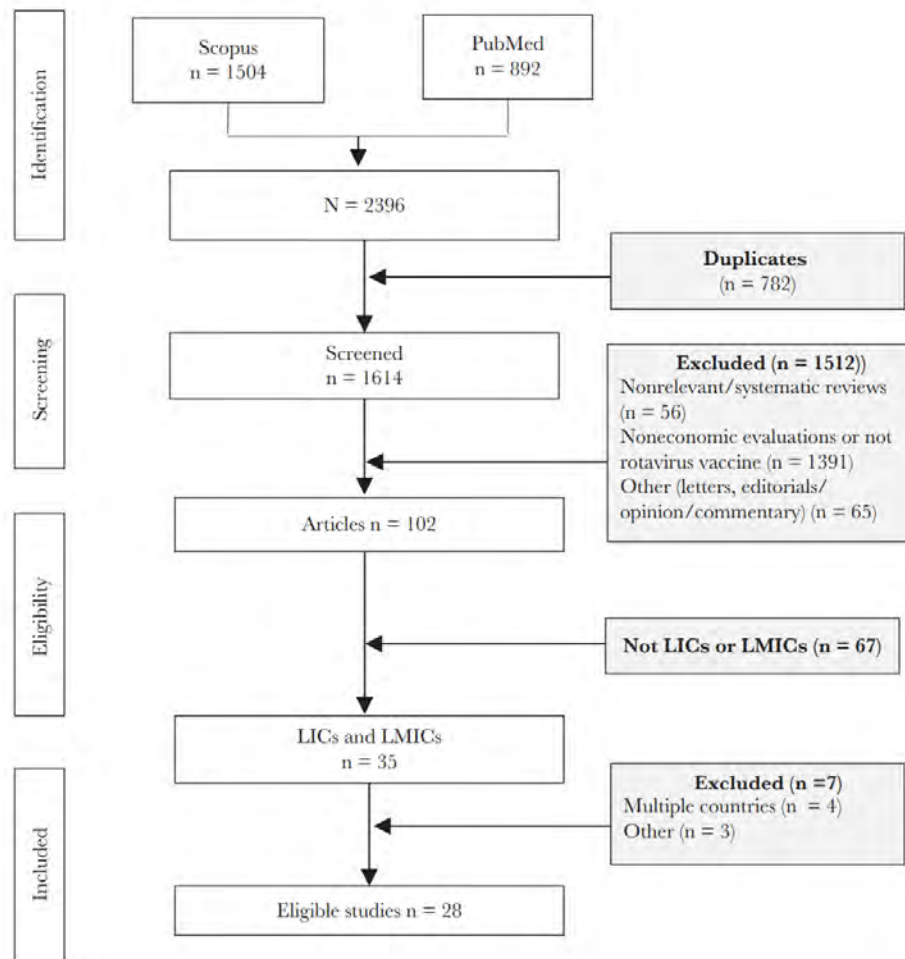


- INB of SGLT2 vs DPP4 was not significant, SGLT2 was not cost-effective relative to DPP4
- INB of SGLT2 compared to SU was significant, SGLT2 was cost-effective relative to SU

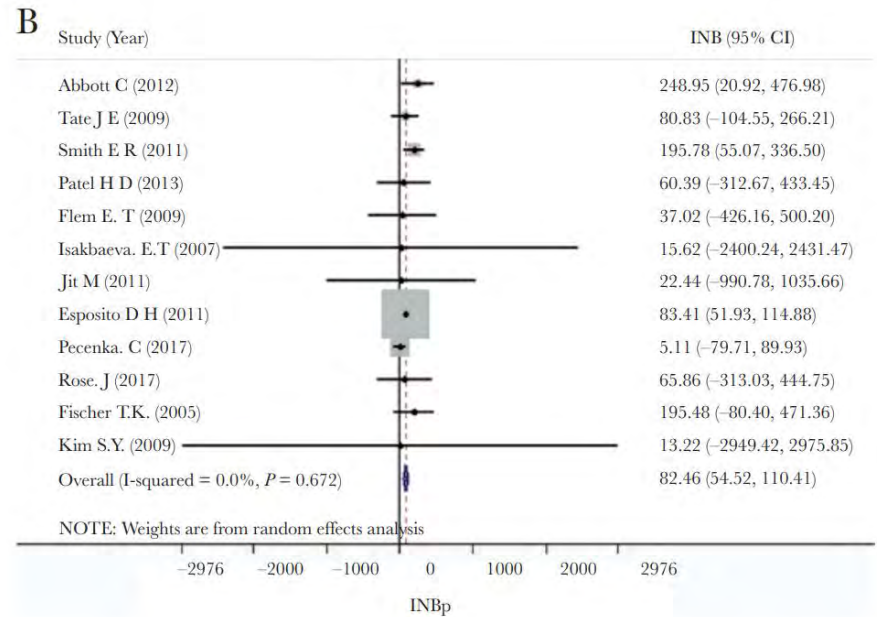
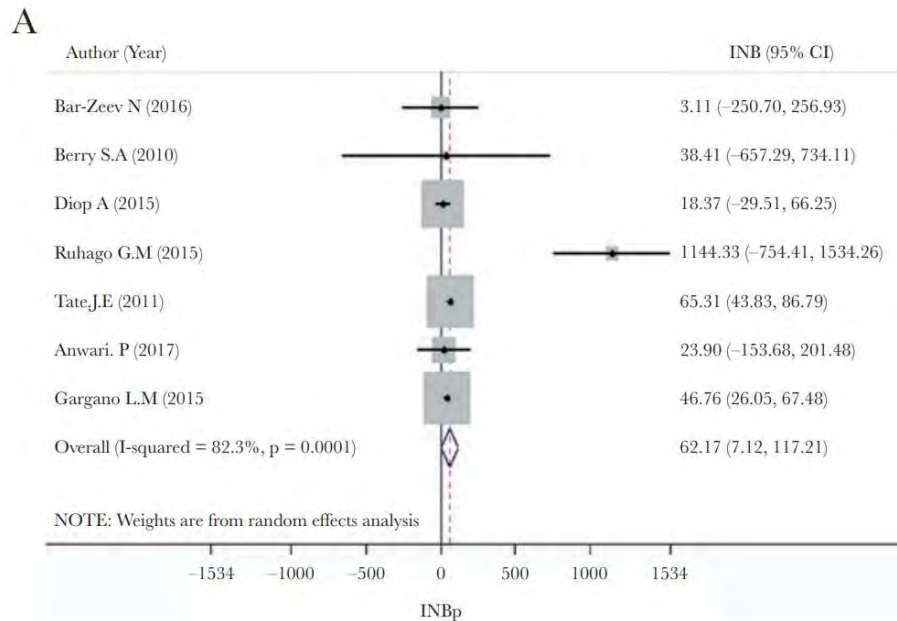
# Systematic Review and Meta-Analysis of Cost-effectiveness of Rotavirus Vaccine in Low-Income and Lower-Middle-Income Countries

Sabbir Haider,<sup>1,2</sup> Usa Chaikledkaew,<sup>1,3</sup> Montarat Thavorncharoensap,<sup>1,3</sup> Sitaporn Youngkong,<sup>1,3</sup> Md. Ashadul Islam,<sup>2</sup> and Ammarin Thakkinstant<sup>1,4</sup>

<sup>1</sup>Mahidol University Health Technology Assessment (MUHTA) Graduate Program, <sup>2</sup>Social and Administrative Pharmacy Excellence Research Unit, Department of Pharmacy, Faculty of Pharmacy, and <sup>3</sup>Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; <sup>4</sup>Health Economics Unit, Ministry of Health and Family Welfare, Bangladesh, Bangladesh



# Pooling INB of Rotavirus Vaccination in Low income (A) countries and LMIC (B)

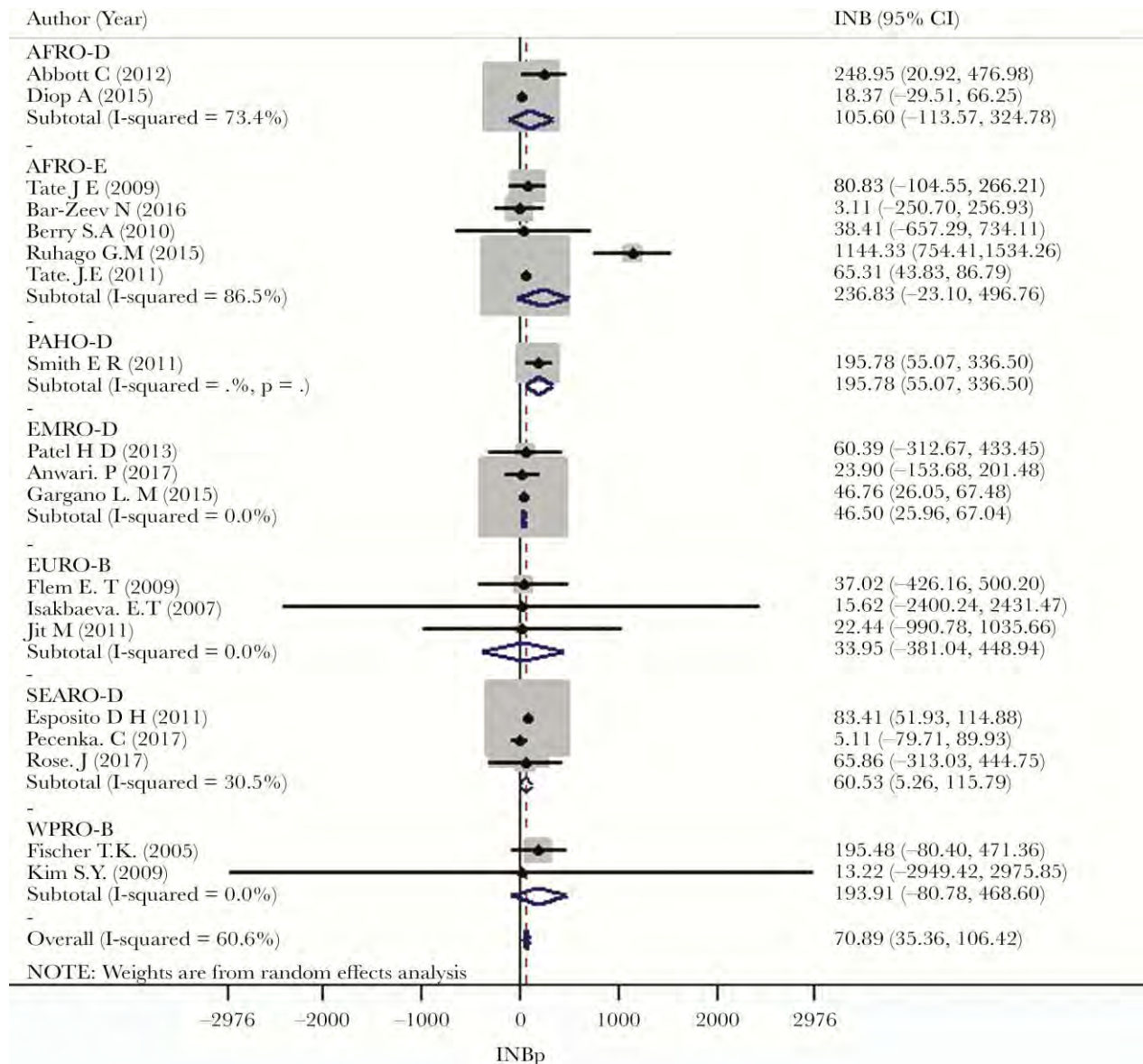


**Figure 3.** Pooled incremental net benefit (INB) of rotavirus vaccination by country's income level. *A*, Low-income countries. *B*, Lower-middle-income countries. Abbreviation: CI, confidence interval.





# Pooling INBs by WHO Epidemiological Subregions



# Other SR-MAs

- **Glucagon-like peptide 1 agonists** for treatment of patients with type 2 diabetes who fail metformin monotherapy: systematic review and meta-analysis of economic evaluation studies (BMJ Open Diabetes Res Care 2020 Jul;8(1))
- Evaluation of the cost utility of **phosphate binders** as a treatment option for hyperphosphatemia in **chronic kidney disease patients**: A systematic review and meta-analysis of the economic evaluations (EJHE in press Feb 2021)
- Economic evaluation of **Direct Oral Anticoagulants (DOACs) versus Vitamin K Antagonists (VKAs)** for stroke prevention in atrial fibrillation patients: a systematic review and meta-analysis (BMJ Evidence-Based Medicine submitted 2020)
- Ongoing projects:
  - Meta-analysis of economic evaluation studies of **influenza vaccine**
  - A network meta-analysis of economic evaluation studies
    - Which second line treatment of T2D is the most cost-effective: A network meta-analysis of economic evaluation studies
    - What treatment is the best among DOACs in prevention of stroke in AF patients

# Strengths

- MA of EE summarizes all economic evidence *quantitatively*
- MA of EE summarizes evidence stratified by income country level, methodology, and factors affecting EE findings, to provide specific evidence for each group with *less heterogeneity*
- It provides evidence to
  - *Global* decision makers from both resource-rich and resource-poor countries for supporting *overall evidence-informed recommendation*
  - *Local* decision makers to consider the pooled evidence based on similar contexts, given the challenges that not all countries may resources to have EE evidence generated for their own countries



# Criticisms

- Critique #1 MA of EE studies should **not** be performed b/c of differences in their context and settings.
  - Given the clear value of evidence summarized **quantitatively** to support policy decision making and **not all countries have EE evidence** for their own countries, it might be possible that country without such evidence *can possibly consider the pooled evidence based on similar contexts* during their local decision making process
  - **Examples of similar contexts include level of country's income, study perspective, time horizon, type of model, and possibly level of WTP which would reduce heterogeneity of EE findings within the stratum**

# Criticisms

- Critique #2: Quality of EE studies is varied
  - Sensitivity analysis excluding studies with poor quality should be performed.
- Critique #3: Lack of variance reported in EE studies
  - We developed 5 scenarios to guide how to obtain variance
  - Most data should be (70%) based on scenario 1-4
  - We performed sensitivity analysis excluding studies with scenario 5 to determine the robustness of our findings.
  - Importantly, we envision the value of data sharing which will possibly become a standard requirement in the field of HE to improve ability in performing MAs

# Summary

- MA of EE studies has been recently developed but not widely applied as MA of clinical outcomes (e.g. RCT)
- The step-by-step approach of data harmonization is demonstrated for facilitating the process of MA.
- Evidence of CE is context specific for each country, conducting such specific individual study is challenging due to various practical limitations and resources
- MA of EE studies is valuable and policy relevant since the pooled evidence could support policy decision making by providing an overall summary of evidence based on similar contexts

# Acknowledgement

- Mahidol University-Health Technology Assessment (MUHTA)
  - Bhavani Shankara Bagepally, MD, PhD
  - Sabbir Haider, MD, PhD candidate
  - Team
- Sariya Udayachalerm, BSP Pharm, PhD
- Lan my Le, PhD
- Piyameth Dilokthornsakul, PharmD, PhD



Mahidol University

Thank you

**Session 6: Full Public Health Value of Vaccines**  
**(FPHVV) - Influenza Vaccine**

# Full value of influenza vaccines assessment (FVIVA)

**WHO VOV Team**

3 March 2021

# Global impact of influenza




- **Seasonal influenza:** each year, across the globe, there are an estimated 1 billion cases
  - 3–5 million severe cases
  - 290 000–650 000 influenza-related respiratory deaths
  - In low-income countries in sub-Saharan Africa and Southeast Asia (particularly in elderly and children under 5 years) rates of illness and death from influenza are estimated to be even higher
- **Pandemic influenza:**
  - Influenza A viruses from animal reservoirs can spill over to human populations, posing a continuous threat of pandemic influenza
  - Vaccination is considered a key public health intervention to reduce both
    - burden of seasonal influenza
    - enhance preparedness for emergence of severe pandemic influenza





# Global efforts to strengthen pandemic influenza preparedness



- **1999:** WHO released its 1<sup>st</sup> Influenza Pandemic Plan outlining responsibilities of WHO and national authorities to prepare and plan for pandemic outbreaks
- **2005:** Prompted by H5N1 – WHA agrees on new set of *International Health Regulations* (WHA58.3) and *Influenza preparedness resolution* (WHO58.5)
- **2006:** *Global Action Plan* for Influenza developed to expand influenza vaccine access: increase in seasonal and pandemic influenza manufacturing capacity:
  - 500 million and 1.5 billion doses in 2006  1.5 billion and 6.2 billion in 2013

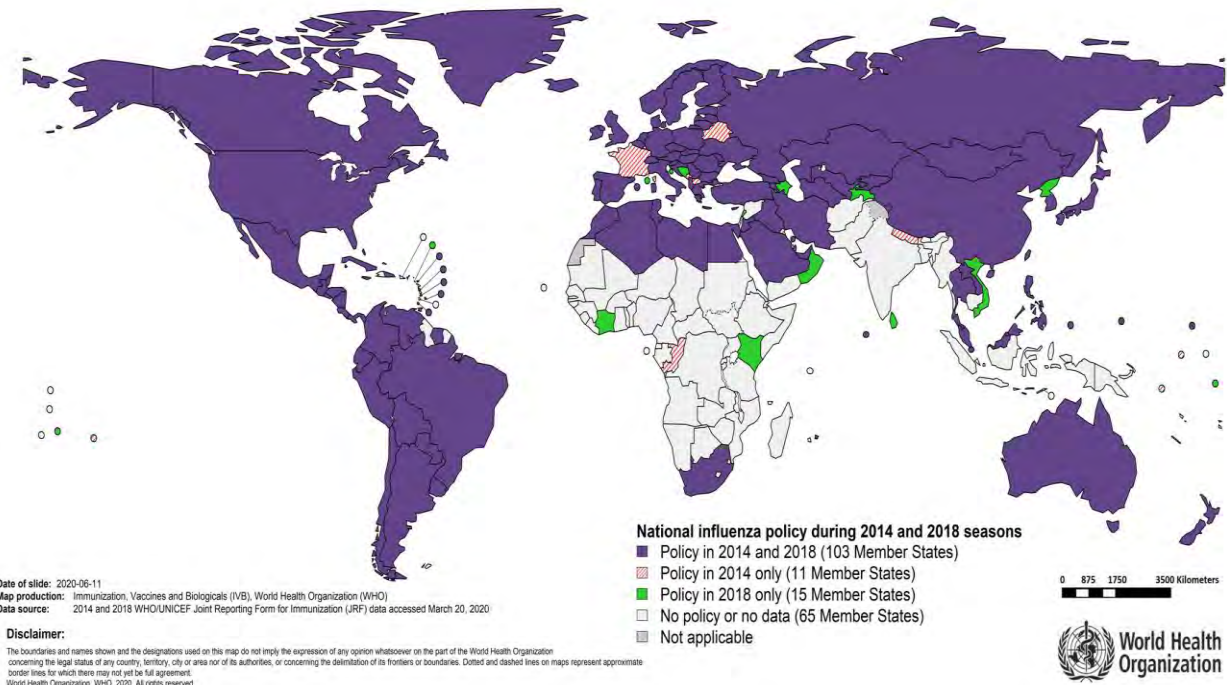


# Innovations needed to overcome shortcomings of current vaccines

Introduction/sustainability of seasonal influenza programs in LMICs challenged among others by profile of current vaccines:

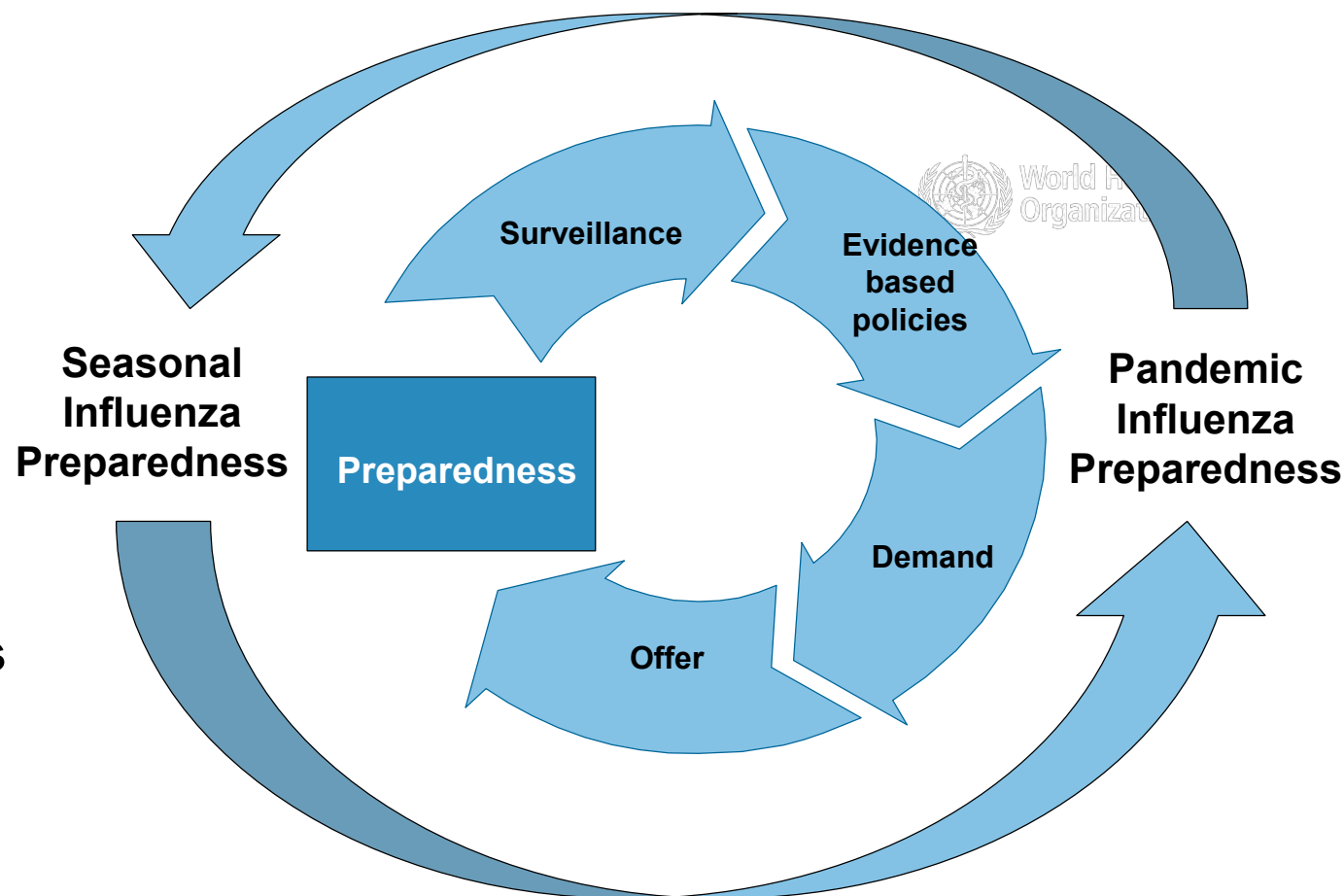
- moderate efficacy against ambulatory influenza illness
- need to be tailored each year to match circulating strains
- limited duration of protection

Existing seasonal influenza vaccines may not provide long-term solutions for LMICs as they challenge already strained vaccination programmes



# Supply Challenges: Unreliable demand prevents sustained pandemic production capacities

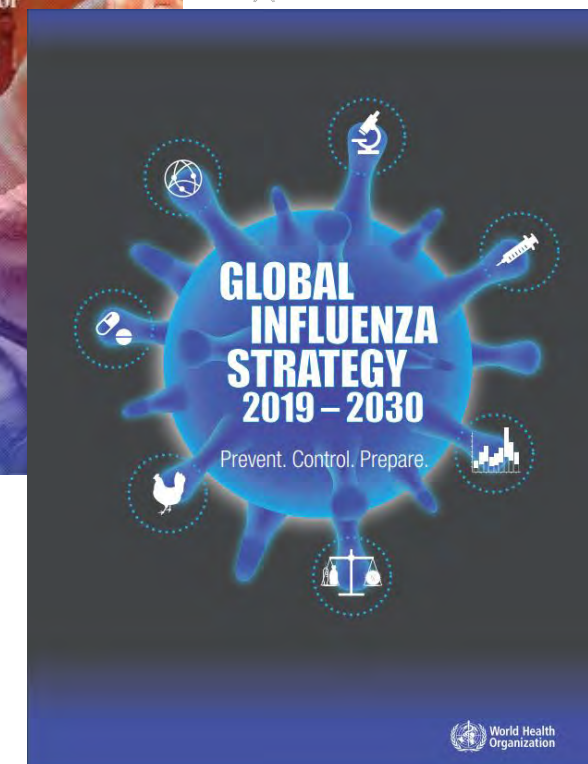
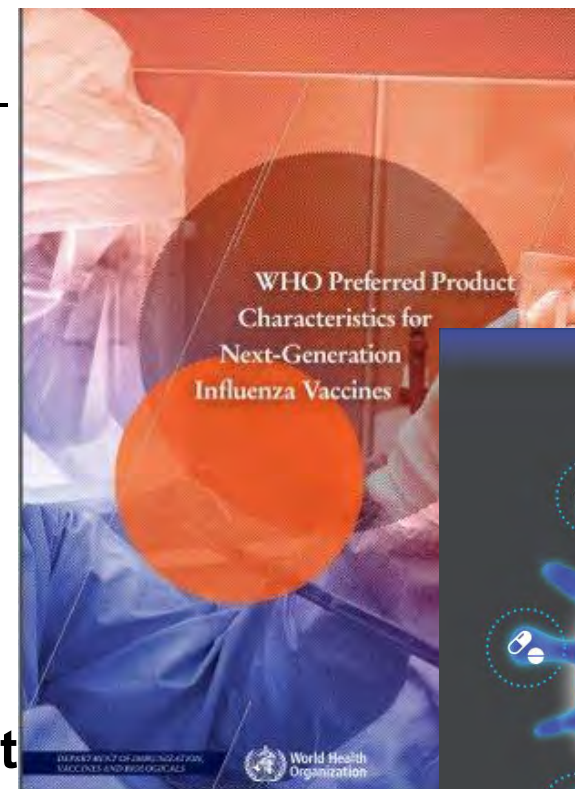
- Country decision makers hesitate to introduce vaccines due to financial constraints, competing priorities, and lack of evidence
- Pharmaceutical companies currently not tempted by market to continue to ramp up production of current vaccines to ensure pandemic preparedness
- **Vaccine development for next-generation seasonal influenza vaccines may help overcome challenges - but comes with uncertainties on how to best improve suitability of vaccines and increase uptake**



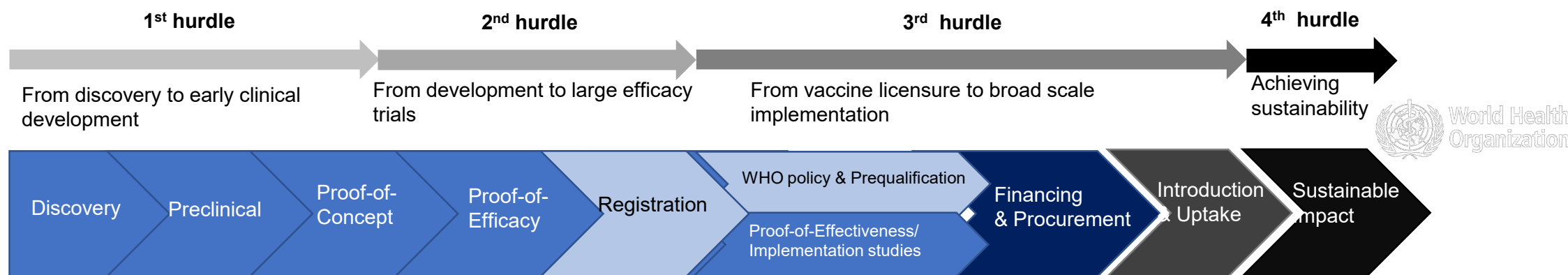
# Recent global policies/guidance supports next generation vaccine development



- **2017:** WHO Preferred Product Characteristics for Next – Generation Influenza Vaccines define preferences for parameters of vaccines shaped by “global unmet public health need in a WHO priority disease area”
- **2019:** WHO’s Global Influenza Strategy (GIS) 2019-30 stresses the need to develop new influenza vaccine technologies which improve the suitability of influenza vaccines for all countries
- **To complement the guidance an indepth assessment of the value of influenza vaccines is needed, both**
  - To inform global efforts to expand seasonal influenza programs as part of a larger pandemic readiness effort
  - To drive innovative research for next generation influenza vaccines for LMICs

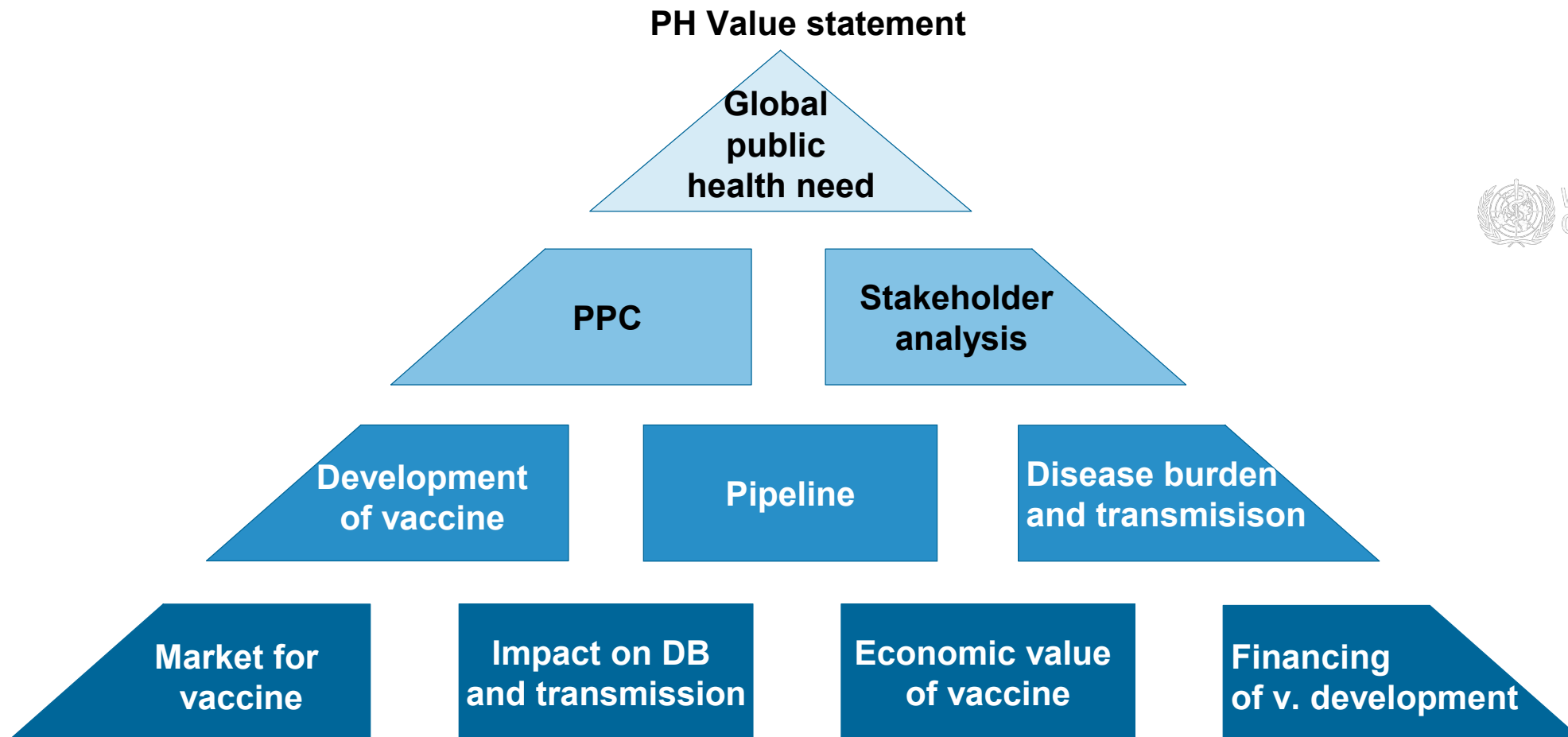


# Value proposition utilization at different levels of vaccine production



- **Vaccine development:** Vaccine manufacturers encouraged of further development/production of vaccines tailored to refined Preferred Product Characteristics
- **From development to implementation:** Funders, vaccine developers and implementers are provided with an improved understanding of influenza vaccine market conditions
- **Sustainability:** Country policy decision making informed of optimal ways of implementing seasonal influenza vaccines

# Key components of the catalogue of components of full value of vaccines assessment (FVVA)





# Currently planned components of the full value of influenza vaccines assessment (FVIVA)

## Draft influenza use cases\* and country archetypes

## Validation of use cases and country archetypes

## Market - supply and demand

## Vaccination strategies and supply/demand projections

## Value proposition

- Lessons learnt from delivery to specific influenza risk groups
  - Mapping of pros and cons of various delivery approaches in diff. settings
  - Review of factors affecting use cases of influenza vaccine (target population, delivery location, immunization provider, vaccine characteristics, cost reimbursement...)
  - Mapping of use cases and country archetypes
- Refinement of draft use cases and country archetypes through stakeholder surveys, interviews and workshops at global, regional and country level
- Seasonal influenza vaccine market analysis, relative supply projections
  - Estimated global demand for influenza vaccine
  - Estimated potential demand of each use case for existing and potential future influenza vaccines with supply projections
- Vaccination strategies / roadmaps and action plans for seasonal influenza vaccines in the different WHO regions
  - Scenarios for the definition and validation of use cases for potential next generation influenza vaccines
  - Supply and demand projections for potential next generation influenza vaccines

**\*Use case definition (as discussed with IVIR-AC in 2020): “A specific situation in which a product or a service could potentially be used to accomplish a defined goal”. This is different from scenarios, delivery strategies or product characteristics**



# DEFINITION OF USE CASES FOR SEASONAL INFLUENZA VACCINES

MMGH Consulting  
March 3, 2021

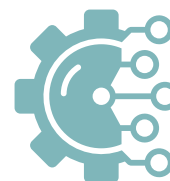


# Background and context

## Challenges to sustaining high production levels of influenza vaccines



Competing manufacturer priorities



Infrastructure challenges



Low public health priority

## WHO's efforts to increase availability and uptake of seasonal influenza vaccines

- Develop seasonal influenza value proposition to inform efforts to expand influenza programs as part of a larger pandemic readiness effort and to drive innovative research for next generation influenza vaccines for LMICs
- Provide improved understanding of influenza vaccine market conditions and support decision-making of country policy makers and vaccine manufacturers

### Focus for today's discussion:

*Definition of draft use cases and country archetypes which reflect the different settings, needs, challenges and opportunities of current seasonal influenza vaccination as part of the value proposition development*

# Use case and country archetype definitions

## Use case

A specific situation in which a product or a service could potentially be used to accomplish a defined goal

## Country archetype

A group of countries that behave similarly in terms of product use and delivery strategies

# Use cases help to identify the most appropriate design for products and interventions



## Product design

What are the most appropriate product features to address the targeted **persons'** unmet needs?



## Program design

How should the program be designed to maximize its reach and efficiency?



## Product and program critical success factors

What product or program features can contribute to the success or failure of the intervention?

# Seasonal influenza vaccine “Use Cases” definition

01

---

Identify  
relevant  
dimensions

02

---

Define generic  
use cases

03

---

Map country  
archetypes

# Screening and selection of dimensions potentially influencing the way seasonal influenza vaccines are used



## Burden of Disease & Target Population

Geography  
*Northern & Southern Hemisphere vs. Tropical Belt*  
Target populations



## Delivery methods

*Delivery strategy*  
Delivery location  
*Service provider*



## Vaccination program characteristics



*Seasonal vs. year-round vaccination*  
*Reimbursement<sup>1</sup> vs. out-of-pocket payment*

**Bold:** selected dimensions defining the use cases

*Italics:* dimensions that are relevant in the use cases description and country archetypes

1. Reimbursement also includes free vaccination

# Use case dimensions selected based on their role in how seasonal influenza vaccines are delivered

Use case dimension	Rationale
 Target population	<ul style="list-style-type: none"><li>• Each country, in line with WHO and other policy recommendations for seasonal influenza vaccine will target different risk groups (i.e., pregnant women, children 6-59mo, health workers, people w/chronic conditions, elderly) based on burden of disease, risk of severe outcomes and role in reaching program objectives</li><li>• Different delivery strategies (e.g., fixed site, outreach, etc.) will be needed to reach different target groups</li></ul>
 Location	<ul style="list-style-type: none"><li>• Location of seasonal influenza vaccine administration varies depending on country context, specific target populations and selected vaccination strategies</li></ul>

# Potential use cases for seasonal influenza vaccines: location-target population framework

Location	Target population				
	Priority populations				
	Pregnant women	Children (6-59mo)	Health workers	People w/chronic conditions	Elderly
	Health facility (hospital, health center, health post, private practice)	1. Vaccination in a health facility Delivery strategy: Fixed site <i>Service provider: Doctor, Nurse, Midwife, CHW</i>			
	Pharmacy (public or private)		2. Vaccination in a pharmacy Delivery strategy: Fixed site or outreach <i>Service provider: Pharmacist, Nurse</i>		
	Formal setting w/health services (e.g., school, nursing home)				3. Vaccination in formal setting w/health services Delivery strategy: Fixed site or outreach <i>Service provider: Doctor, Nurse, CHW</i>
	Setting w/out health service (e.g., school, workplace, religious institutions)				4. Vaccination in setting w/out health services Delivery strategy: Outreach / mobile <i>Service provider: Nurse, CHW</i>

# Potential use cases for seasonal influenza vaccines: location-target population framework (2)

		Target population						
		High priority					Medium-low priority	
		Pregnant women	Children (6-59mo)	Health workers	People w/chronic conditions	Elderly	Children / Adolescent (5-18yo)	Adult population Essential workers / service providers
Location	Health facility (hospital, health center, health post, private practice)	1. Vaccination in a health facility Delivery strategy: Fixed site <i>Service provider: Doctor, Nurse, Midwife, CHW</i>						
	Pharmacy (public or private)	2. Vaccination in a pharmacy Delivery strategy: Fixed site, outreach <i>Service provider: Pharmacist, Nurse</i>						
	Formal setting w/health services (e.g., school, childcare center, nursing home)		3. Vaccination in formal setting w/health services Delivery strategy: Fixed site, outreach <i>Service provider: Nurse, CHW</i>		3. Vaccination in formal setting w/health services Delivery strategy: Fixed site, outreach <i>Service provider: Nurse, CHW</i>			
	Setting w/out health service (e.g., workplace, mosque)		4. Vaccination in setting w/out health services Delivery strategy: Outreach, mobile <i>Service provider: Nurse, CHW</i>		4. Vaccination in setting w/out health services Delivery strategy: Outreach, mobile <i>Service provider: Nurse, CHW</i>			



# Country archetypes for seasonal influenza use cases

## Elements for country archetypes



World Bank  
income groups



Seasonal  
transmission



Year-round  
transmission



Out-of-pocket  
payments



## Country archetypes

- 1 Seasonal out-of-pocket
- 2 Seasonal reimbursed/free
- 3 Year-round out-of-pocket
- 4 Year-round reimbursed/free

Mapping the country archetypes against the use cases helps to determine which country archetypes are likely to use each UC

← USE CASES →

	UC1	UC2	UC3	UC4
COUNTRY ARCHETYPES ↑				
Seasonal out-of-pocket	X	X		
Seasonal reimbursed/free	X	X	X	X
Year-round out-of-pocket	X	X		
Year-round reimbursed/free	X	X	?	?
COUNTRY ARCHETYPES ↓				

### Use Cases

- ① Delivery in a health facility
- ② Delivery in a pharmacy

- ③ Delivery in formal setting w/health services
- ④ Delivery in setting w/out health services

# Country archetypes for seasonal influenza use cases

## Elements for country archetypes

 World Bank income groups<sup>1</sup>

 Seasonal transmission

 Year-round transmission

 Out-of-pocket payment



## Country archetypes

- 1 HIC/UMIC seasonal
- 2 LMIC/LIC seasonal
- 3 HIC/UMIC year-round
- 4 LMIC/LIC year-round

The following assumptions about out-of-pocket costs for seasonal influenza vaccines are made for countries classified by World Bank income group: HIC/UMIC: Reimbursed; LMIC/LIC: Out-of-pocket/not reimbursed

Mapping the country archetypes against the use cases helps to determine which country archetypes are likely to use each UC

← USE CASES →

	UC1	UC2	UC3	UC4
HIC/UMIC seasonal	X	X	X	X
LMIC/LIC seasonal	X	X	X	X
HIC/UMIC year-round	X	X	X	
LMIC/LIC year-round	X	X		

COUNTRY ARCHETYPES

### Use Cases

- 1 Delivery in a health facility
- 2 Delivery in a pharmacy

- 3 Delivery in formal setting w/health services
- 4 Delivery in setting w/out health services

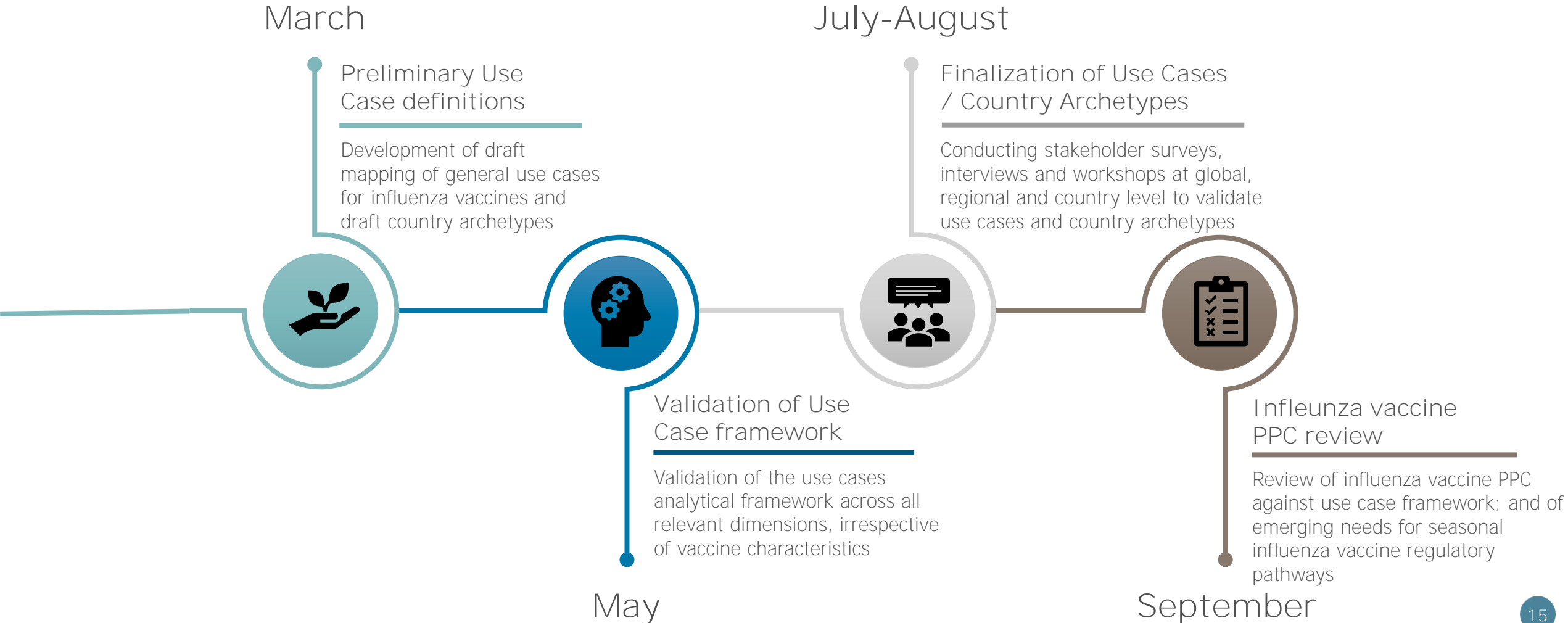
# Exploring relationship between country income level and health system reimbursement to inform use cases and country archetypes

World Bank Income Group	Health system reimbursement					
	Universal-Government funded	Universal-Public insurance	Universal-Public/Private insurance	Universal-Private insurance	Non-universal insurance	No data
Low-income countries	1	0	0	0	5	23
Lower-middle income countries	2	2	1	0	6	38
Upper-middle income countries	6	8	4	0	3	34
High-income countries	23	20	3	5	1	10
Total	32	30	8	5	15	105

Additional sources of data to explore include: cMYP, surveys, etc.

Sources: World Bank (country income groups), US Social Security Administration (health system reimbursement)

# Timelines for use case / country archetype development and validation





## Questions to IVIRAC for discussion

- Does IVIR-AC agree with the approach to defining use cases and country archetypes for seasonal influenza vaccination?
- Would IVIR-AC propose any changes to the draft use cases for seasonal influenza vaccines?
- Would IVIR-AC propose any changes to the draft country archetypes for seasonal influenza vaccines?
- Are there any key dimensions or considerations for the draft use cases/country archetypes not currently captured that IVIR-AC recommends are included?

# Background information

## WHO guidance

Preferred Product Characteristics for Next-Generation Influenza Vaccines

- [https://www.who.int/immunization/documents/ISBN\\_9789241515597/en/](https://www.who.int/immunization/documents/ISBN_9789241515597/en/)

How to implement seasonal influenza vaccination of health workers

- [https://www.who.int/immunization/documents/ISBN\\_9789241515597/en/](https://www.who.int/immunization/documents/ISBN_9789241515597/en/)

## Publications

Seasonal influenza vaccination in middle-income countries

- <https://www.sciencedirect.com/science/article/pii/S0264410X1931401X>



## **Session 7: IA 2030 Costing**

# IA2030 Costing Analysis

By WHO Value of Vaccines, Economics and Modeling team  
Presented to IVIR-AC

4 March 2021

# Agenda



1. Background & project objective
2. Costing exercises in the past
3. Scope
4. Project team & timeline



# Background

- In August 2020, the 73rd World Health Assembly endorsed **The Immunization Agenda 2030: A Global Strategy to Leave No One Behind (IA2030)** in resolution WHA 72/(90).
- Understanding the level of investment needed for the next decade is critical to mobilizing resources and developing effective strategies for IA2030.
- During the Executive Board meeting in 2021, several member states emphasized the need for articulating financial implications of IA2030 for resource mobilization.

## Project objective

- To this end, WHO IVB aims to collaborate with partners to generate cost estimates for IA2030, leveraging the latest developments and rigorous evidence to date in immunization economics.
- In collaboration with Economics & Finance team from International Vaccine Access Center (IVAC), we aims to generate global and regional level estimates of vaccine and immunization delivery costs from 2021-2030, for 194 WHO Member States.
- The estimates will be used primarily for advocacy.

# Costing exercises for global advocacy



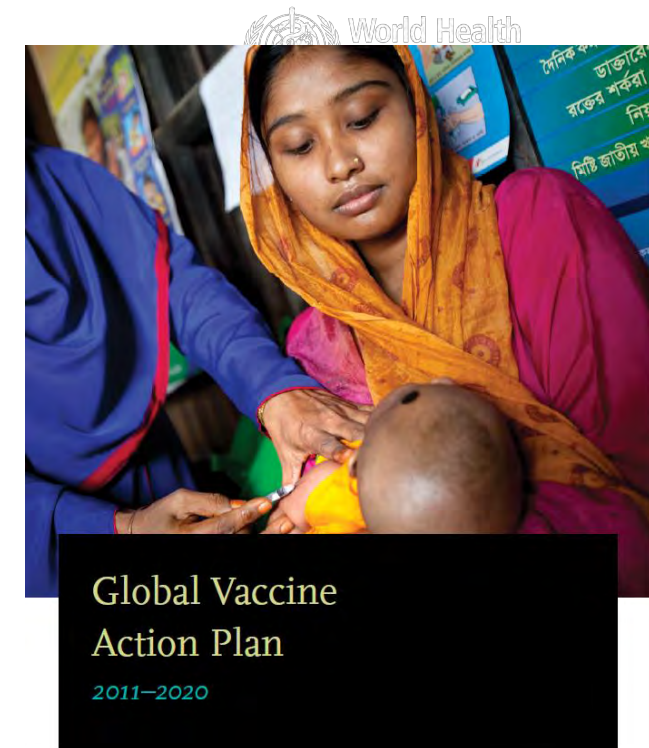
## Estimating the costs of achieving the WHO–UNICEF Global Immunization Vision and Strategy, 2006–2015

Lara J Wolfson,<sup>a</sup> François Gasse,<sup>b</sup> Shook-Pui Lee-Martin,<sup>c</sup> Patrick Lydon,<sup>d</sup> Ahmed Magan,<sup>b</sup> Abdelmajid Tibouti,<sup>b</sup> Benjamin Johns,<sup>e</sup> Raymond Hutubessy,<sup>a</sup> Peter Salama<sup>b</sup> & Jean-Marie Okwo-Bele<sup>d</sup>

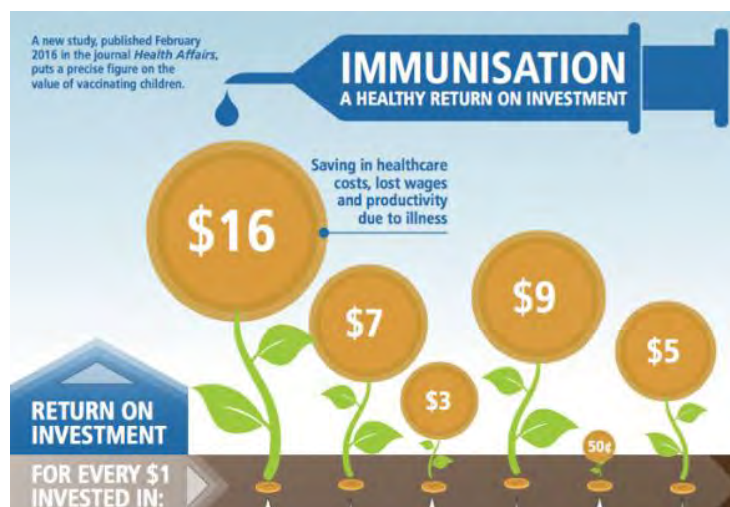
### Review

Projections of costs, financing, and additional resource requirements for low- and lower middle-income country immunization programs over the decade, 2011–2020

Gian Gandhi<sup>a,\*</sup>, Patrick Lydon<sup>b</sup>, Santiago Cornejo<sup>c</sup>, Logan Brenzel<sup>d</sup>, Sandra Wrobel<sup>e</sup>, Hugh Chang<sup>f</sup>



# Costing exercises for calculating ROI



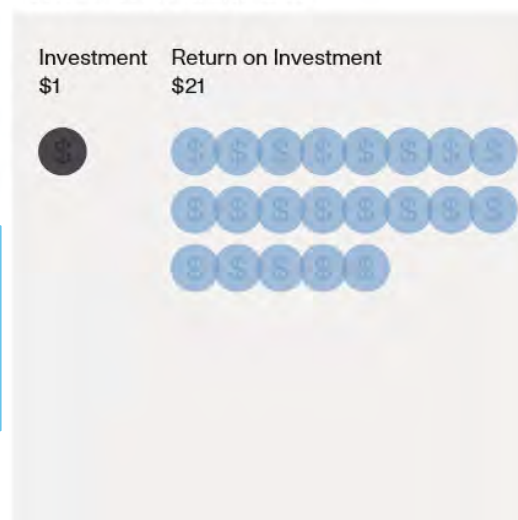
## Costs of vaccine programs across 94 low- and middle-income countries

Allison Portnoy<sup>a</sup>, Sachiko Ozawa<sup>a,\*</sup>, Simrun Grewal<sup>a</sup>, Bryan A. Norman<sup>b,1</sup>, Jayant Rajgopal<sup>c,1</sup>, Katrin M. Gorham<sup>a,d,1</sup>, Leila A. Haidari<sup>d,e,1</sup>, Shawn T. Brown<sup>e,1</sup>, Bruce Y. Lee<sup>a,d,1</sup>

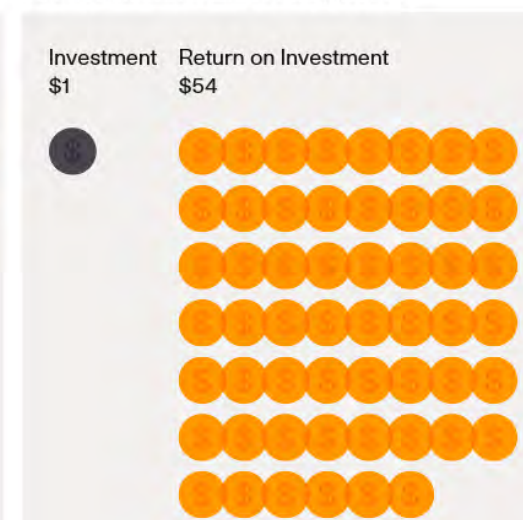
## Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle-Income Countries From 2011 to 2030

So Yoon Sim, MA, MSPH, Elizabeth Watts, MHS, Dagna Constenla, PhD, Shuoning Huang, MSPH, Logan Brenzel, PhD, Bryan N. Patenaude, ScD

### Cost of Illness (COI) approach<sup>□</sup>



### Value of Statistical Life (VSL) approach<sup>□</sup>





# Scope: IA2030 cost estimates



## **Perspective**

- Global immunization community

## **Time frame**

- Future projection for 2021-2030

## **Target countries**

- All 194 WHO Member States
- Reporting at the global and regional level

## **Pathogens**

- 14 pathogens (aligned with the first iteration of IA2030 vaccine impact estimates)

## **Cost category**

- Vaccine costs
- Immunization delivery costs



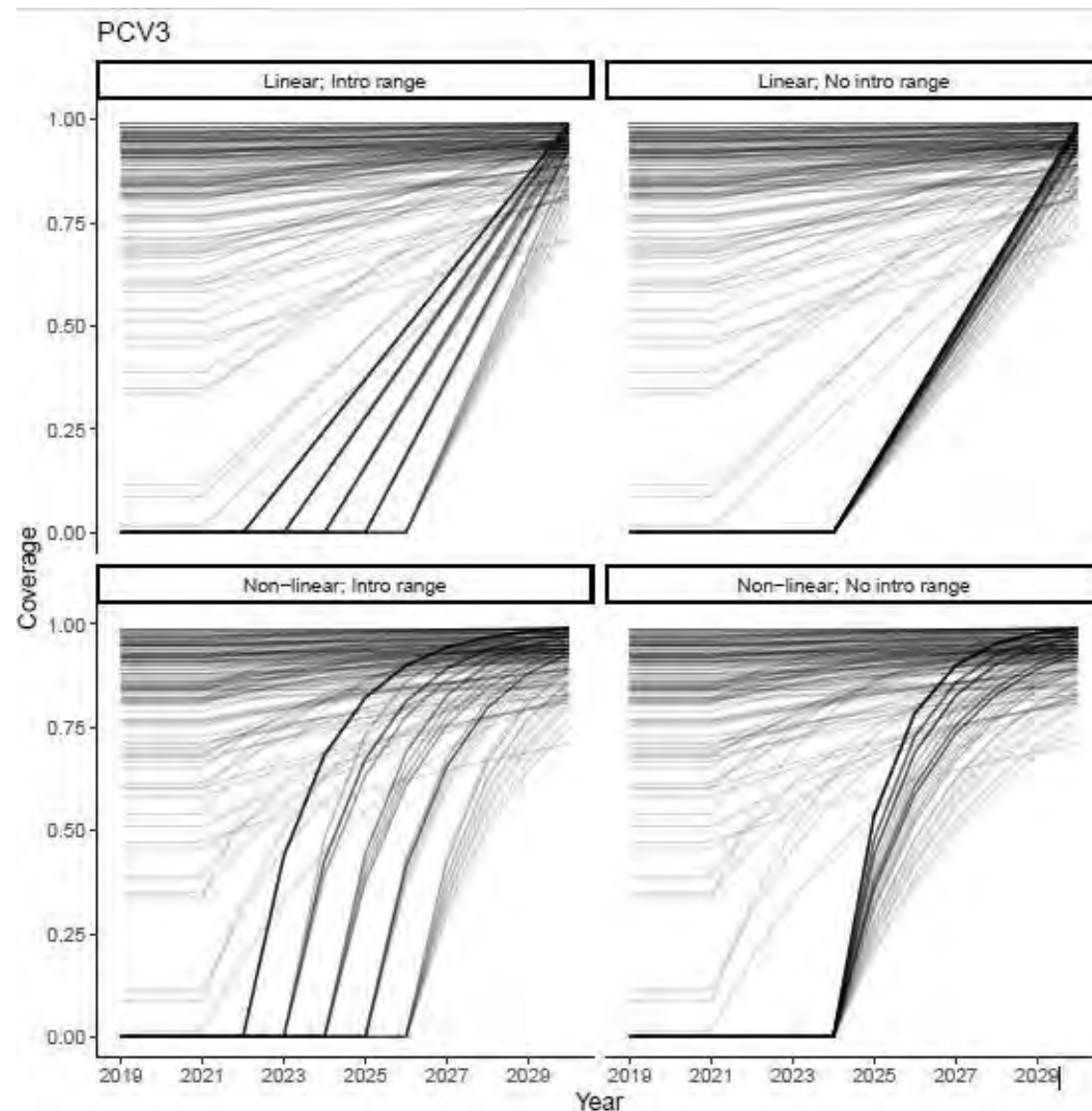


# IA2030 vaccine impact & cost estimates

IA2030	Vaccine impact estimates	Cost estimates
<b>Objective</b>	<ul style="list-style-type: none"> <li>Update modeled impact estimates and inform strategic priorities for IA2030 and GPW 13</li> </ul>	<ul style="list-style-type: none"> <li>Understand the level of investment needed for the next decade to mobilize resources and develop strategies for IA2030</li> </ul>
<b>Timeframe</b>	2021-2030	
<b>Target countries</b>	194 Member States (reporting at global and regional level)	
<b>Pathogens</b>	<p>Phased approach to generating estimates for additional pathogens:</p> <p><b>2021-2030:</b> VIMC 10 pathogens (hepatitis B, Hib, HPV, JE, measles, MenA, <i>Streptococcus pneumoniae</i>, rotavirus, rubella, yellow fever), diphtheria, tetanus, pertussis, TB (BCG)</p> <p><b>2022-2030:</b> Polio, typhoid, influenza, cholera, multivalent meningitis, COVID-19</p> <p><b>2023-2030:</b> Varicella, dengue, mumps, rabies, hepatitis A, hepatitis E, other new vaccines</p>	
<b>Use case (2021)</b>	<ul style="list-style-type: none"> <li>Impact Goal 1.1. (number of deaths from vaccine-preventable diseases averted) as part of IA2030 M&amp;E framework to be submitted to the 74<sup>th</sup> WHA</li> <li>Advocacy for IA2030 during World Immunization Week 2021, WHA and beyond</li> </ul>	<ul style="list-style-type: none"> <li>Advocacy for IA2030 during World Immunization Week 2021, WHA and beyond</li> </ul>
<b>Partnership</b>	<ul style="list-style-type: none"> <li>WHO IVB &amp; DDI (project team)</li> <li>VIMC, BMGF, CDC, Gavi, IHME, UNICEF</li> </ul>	<ul style="list-style-type: none"> <li>WHO IVB &amp; JHU IVAC (project team)</li> <li>BMGF, CDC, Gavi, UNICEF</li> </ul>

# IA2030 coverage scenario

- **The same coverage scenario will be used for IA2030 vaccine impact & cost estimates**
- Four options based on:
  - Common assumptions across pathogens about 2030 coverage targets (HPV as an exception) and disruptions due to COVID-19
  - Pathogen-specific introduction assumptions
  - Two variations for introduction and scale up
- Input from Stakeholder Committee and WHO disease focal points
- **In the costing analysis, coverage rates are used to calculate the number of doses.**



# Project team & timeline



## Project team

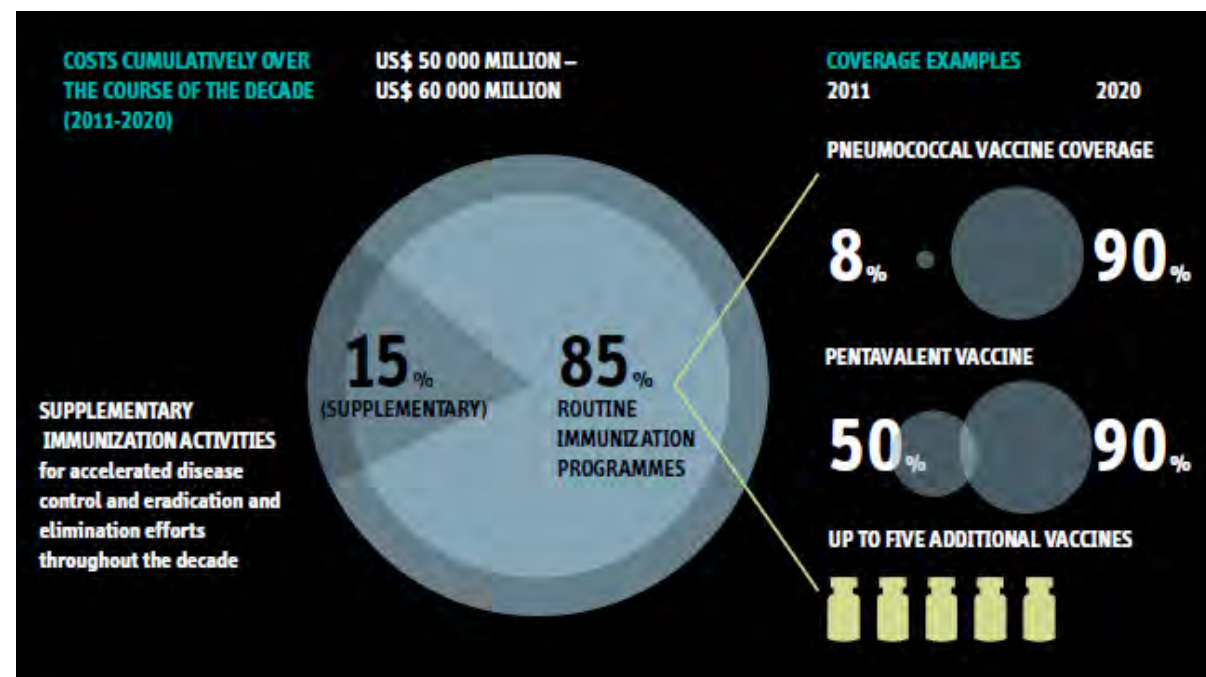
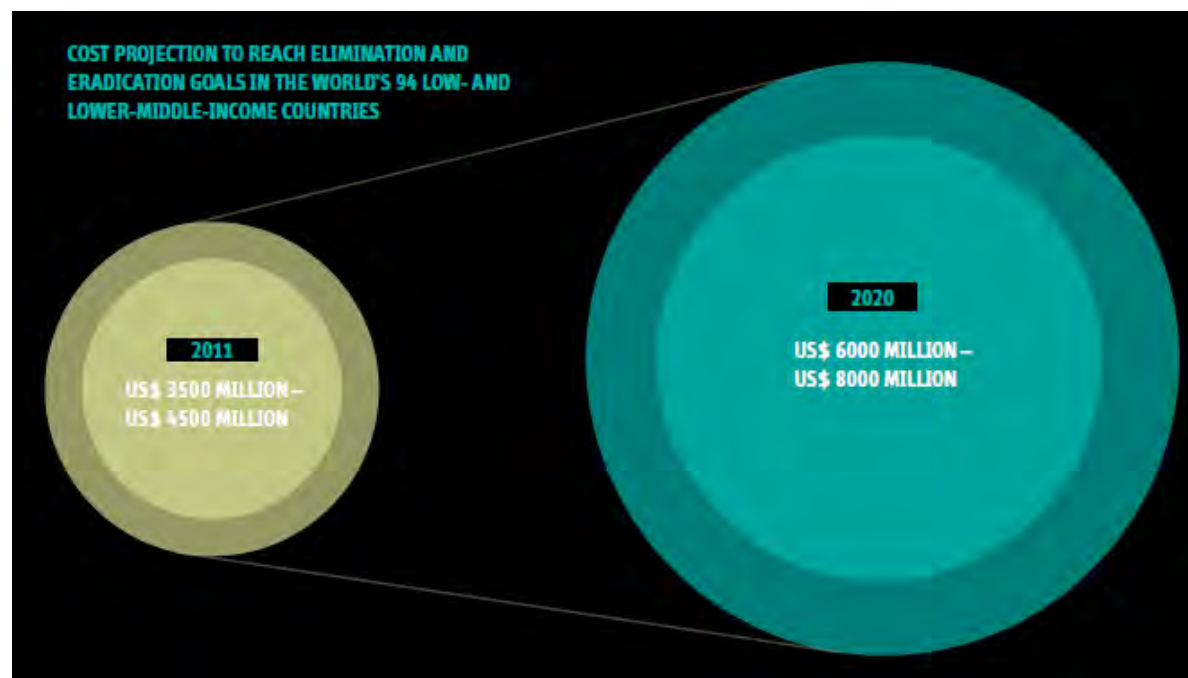
- **Johns Hopkins University- International Vaccine Access Center (IVAC)**
  - Salin Sriudomporn
  - Libby Watts
  - Bryan Patenaude (PI)
- **WHO IVB**
  - Yoonie Sim
  - Raymond Hutubessy

## Technical consultations

- Experts from BMGF, CDC, Gavi, UNICEF, WHO HQ

# Appendix

# Costing & funding gap analysis for GVAP report



# Scope: cost categories and data sources (for future projection)

	Cost categories	Data source
Wolfson et al. 2008	<ol style="list-style-type: none"> <li>1. Vaccine cost</li> <li>2. Systems cost</li> <li>3. Campaign cost</li> </ol>	<ol style="list-style-type: none"> <li>1. UNICEF</li> <li>2. Gavi, McKinsey, WHO-CHOICE</li> <li>3. Gavi Financial Sustainability Planning</li> </ol>
Gandhi et al. 2013	<ol style="list-style-type: none"> <li>1. Vaccine cost</li> <li>2. Delivery cost</li> </ol>	<ol style="list-style-type: none"> <li>1. Gavi, UNICEF, PAHO, expert opinions</li> <li>2. cMYP (routine); cMYP + published reports (SIA)</li> </ol>
Portnoy et al. 2016	<ol style="list-style-type: none"> <li>1. Vaccine cost</li> <li>2. Supply chain cost</li> <li>3. Service delivery cost (RI) /operational cost (SIA)</li> </ol>	<ol style="list-style-type: none"> <li>1. Gavi, PAHO, UNICEF</li> <li>2. HERMES simulation modeling and extrapolation</li> <li>3. cMYP</li> </ol>
Sim et al. 2020	<ol style="list-style-type: none"> <li>1. Vaccine cost</li> <li>2. Immunization delivery cost</li> </ol>	<ol style="list-style-type: none"> <li>1. Gavi, PAHO, UNICEF</li> <li>2. cMYP, Immunization Delivery Cost Catalogue (IDCC), other published studies, Gavi data, MI4A for scenario analyses</li> </ol>

# Immunization delivery cost

	Definition used	Cost components
Wolfson et al. 2008	Systems costs	Cold chain, waste management, transportation for outreach and vaccine distribution, training, supervision, M&IEC, social mobilization, monitoring, evaluation, surveillance, laboratory, service delivery
Gandhi et al. 2013	Delivery cost	Human resources, training, supply chain and logistics, program management, social mobilization, disease surveillance, other recurrent operating and maintenance costs
Portnoy et al. 2016	Supply chain cost	Transportation (immunization and shared), storage, equipment, maintenance, energy, labor
	Delivery cost	Personnel (immunization and shared), program management, training, social mobilization and other recurrent costs
Sim et al. 2020	Immunization delivery cost	Labor (personal, per diems, volunteer human resources), storage (cold chain equipment and maintenance) , transportation (vehicles), other capital (building, overheads, equipment) , program management, short-term training, IEC/social mobilization, disease surveillance, wastage management, other recurrent costs





4 March 2021

# **Cost Estimates for Immunization Agenda 2030 (IA2030)**

## **Methodology for costing IA2030**

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# Objective & Scope

**Goal:** Generate global, and regional estimates for the cost of Immunization Agenda (IA2030) from 2021-2030

**Scope:**

- 12 vaccines
- 194 WHO member states

Vaccines Included
Hepatitis B (Hep B)
Haemophilus influenzae type b (Hib)
Human papillomavirus (HPV)
Japanese Encephalitis (JE)
Measles
MenA conjugate (MenA)
Pneumococcal conjugate (PCV)
Rotavirus (RV)
Rubella
Yellow Fever (YF)
Diphtheria, Tetanus, Pertussis (DTP)
Bacillus Calmette-Guérin (BCG)



# Methods

- Building upon the methodology of the study developed by IVAC DOVE-IV/ VERSE team:

*“Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle-Income Countries From 2011 to 2030”*

\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010



# Methods for costing Routine Immunization (RI) and Supplemental Immunization Activities (SIA)

Total Cost (RI + SIA) = Vaccine Cost + Immunization Delivery Cost

*Vaccine costs<sub>ijk</sub>*

$$= \sum_{k=2021}^{2030} \sum_{j=1}^{194} \sum_{i=1}^{12} (\text{number of doses}_{ijk} \times \text{price per dose}_{ijk})$$

*k = year*  
*j = country*  
*i = vaccine*

$$\begin{aligned} \text{Number of doses}_{ijk} &= \text{Target population}_{ijk} \\ &\times \text{Coverage rate}_{ijk} \\ &\times \text{Number of recommended doses}_{ij} \\ &\times (1 + \text{Wastage rate}_{ij}) \\ &\times (1 + \text{Buffer stock rate}_i) \end{aligned}$$

*Immunization delivery costs<sub>ijk</sub>*

$$= \sum_{k=2021}^{2030} \sum_{j=1}^{194} \sum_{i=1}^{12} (\text{number of doses}_{ijk} \times \text{delivery cost per dose}_{ij})$$



# Data Sources – Vaccine Cost

- Data for vaccine price will be extracted from different sources depending on country income level and Gavi eligibility

Component	Source(s)
Vaccine Price	<ul style="list-style-type: none"><li>- Gavi countries: <b>Gavi pricing</b><sup>1</sup></li><li>- PAHO countries: <b>PAHO Revolving Fund price list</b><sup>2</sup></li><li>- All other low-income, lower-middle income and upper-middle income countries: <b>UNICEF vaccine price</b><sup>3</sup></li><li>- High-income countries: <b>Market Information for Access to Vaccines (MI4A)</b><sup>4</sup></li></ul>
Injection supplies and freight	<ul style="list-style-type: none"><li>- LIC, LMIC and UMICs: <b>Gavi Pricing for injection supplies and freight</b><sup>5</sup></li><li>- HICs: <b>WHO data</b><sup>6</sup> (TBC)</li></ul>
Wastage Rate	<b>Gavi's Vaccine specific wastage</b> <sup>7</sup> (all countries)
Buffer stock rate	<b>WHO data</b> <sup>8</sup> (all countries)



# Data Sources – Delivery Cost

Key data sources:

1. WHO-UNICEF Country Multi-year Plans (CMYP) <sup>9</sup>
2. Immunization Delivery Cost Catalogue (IDCC) <sup>10</sup>
3. Literature review by Gandhi et. al. (2013) <sup>11</sup>
4. EPIC Costing Study by Portnoy et. al. (2020) <sup>12</sup>

Cost Category	Cost Component	CMYP	IDCC	Gandhi et al. 2013 (Literature review)	EPIC Costing study
Labor	Personnel (paid human resources)	X	X	X	X
	Shared Personnel costs	X			
	Volunteer human resources		X		
	Per diem and travel allowances	X	X	X	
Storage	Cold chain equipment and their overheads (installation, energy, maintenance, repairs)	X	X	X	X
Transportation	Vehicles, transport and fuel	X	X	X	X
	Shared transportation costs	X		X	X
Other capital costs	Buildings, utilities, other overheads and/or shared costs	X	X	X	X
Recurrent costs	Program management	X	X	X	X
	Training and capacity building	X	X	X	X
	IEC/social mobilization and advocacy	X	X	X	X
	AEFI and disease surveillance	X	X	X	X
	Waste management		X	X	
	Other supplies and recurrent costs	X	X	X	
Other	Other	X	X	X	



# DOVE Costing Model - List of delivery cost predictors & sources

- Initial list of predictors were identified through a literature review
- K-Fold Cross Validation and Duan's Smearing Retransformation** were used to identify the most well performing model

No	Indicators	Source
1	Land area (sq. km)*	World Bank Open Data
2	Maternal mortality ratio (per 100,000 live births)	World Bank Open Data
3	Under 5 mortality rate (per 1000 live births)	UN World Population Prospects (VIMC)
4	Total number of births	UN World Population Prospects (VIMC)
5	Pregnant women receiving prenatal care*	World Bank Open Data
6	Population growth (annual %)	UN World Population Prospects (VIMC)
7	Total population	World Bank Open Data
8	Population density (people per sq.km of land area)	World Bank Open Data
9	Poverty headcount ratio at \$1.90 a day (2011 PPP) (%)*	World Bank Open Data
10	Urban population (% of total population)*	World Bank Open Data
11	GDP growth (annual %)	World Bank Open Data
12	Access to electricity (% of population)	World Bank Open Data
13	Investment in transport with private participation (current US\$)	World Bank Open Data
14	Electric power consumption (kWh per capita)	World Bank Open Data
15	GDP per capita*	World Bank Open Data
16	Domestic general government health expenditure as % GDP	WHO NHA database
17	DTP3 coverage rate (%)	UN World Population Prospects (VIMC)
18	Total number of DTP3 doses delivered*	DOVE team calculation based on VIMC data
19	Total number of doses*	DOVE team calculation based on VIMC data



# Delivery Cost Per Dose Prediction : MLR (1)

- Final Model for LIC and LMIC imputation contained four predictors:

$$\text{Cost per dose}_i = \text{Exp} [\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \sum_j \frac{e_j}{N}]$$

$X_1$  = Total number of DTP3 doses

$X_2$  = Urban population (% of total population)

$X_3$  = Under 5 mortality rate (per 1000 live births)

$X_4$  = Investment in transport with private participation (current US\$)

- Model used to impute costs for countries with missing data in the DOVE costing analysis (31 out of 94 LMICs in the study)
- This model was tested for all 194 countries, but the predictions were not comparable to existing studies for UMICs and HICs



# Delivery Cost Per Dose Prediction : MLR (2)

- LICs were excluded from the data (a combination of IDCC, cMYP and EPIC data), to identify the most well performed model among middle- and high-income countries
- Final Model for UMIC and HIC imputation contained eight predictors:

$$\text{Cost per dose}_i = \text{Exp} [\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + \sum_j \frac{e_j}{N}]$$

$X_1$  = *Population growth (annual %)*

$X_2$  = *Total number of DTP3 doses delivered*

$X_3$  = *GDP per capita*

$X_4$  = *Poverty headcount ratio at \$1.90 a day (2011 PPP) (%)*

$X_5$  = *Total number of births*

$X_6$  = *DTP3 coverage rate (%)*

$X_7$  = *Electric power consumption (kWh per capita)*

$X_8$  = *Domestic general government health expenditure as % GDP*





# Modeled Cost per Dose estimates from DOVE and EPIC models

- DOVE regression results were used to impute delivery costs for previous costing analysis (comparable to EPIC estimates)
- DOVE regression exclude LICs model will be used to impute delivery costs among UMICs and HICs for IA2030 (comparable to EPIC estimates)

Income level	DOVE Model I (92 LIC, LMIC, UMICs)	EPIC Model (134 LIC-HICs)	DOVE Model II (165 LMIC, UMIC, HICs)
LIC	\$1.41	\$1.64	NA
LMIC	\$2.94	\$3.28	\$1.99
UMIC	\$2.85	\$5.65	\$5.99
HIC	NA	\$11.49	\$17.11



## Regional and Income level average delivery cost per dose

- DOVE Model II produced more reasonable estimates for delivery costs in UMICs and HICs than DOVE Model I
- Imputed estimates will be validated from literature review

		DOVE Model I (92 LIC, LMIC, UMICs)	EPIC Model (134 LIC-HICs)	DOVE Model II (165 LMIC, UMIC, HICs)
AFRO	LIC	\$1.39	\$1.73	-
	LMIC	\$2.21	\$3.18	\$2.26
	UMIC	-	\$3.67	\$5.20
	HIC	-	\$9.06*	\$6.71
EMRO	LIC	\$1.37	\$0.97	-
	LMIC	\$2.70	\$2.92	\$2.41
	UMIC	\$2.19	\$3.85	\$4.73
	HIC	-	-	\$18.12
AMRO	LIC	\$1.50	\$1.04	-
	LMIC	\$3.57	\$3.19	\$3.16
	UMIC	\$3.35	\$6.52	\$5.90
	HIC	-	\$5.94*	\$11.75
SEARO	LIC	\$3.04	\$2.56	-
	LMIC	\$3.51	\$3.14	\$1.65
	UMIC	\$0.62	\$5.52	\$4.10
	HIC	-	-	-
WPRO	LIC	-	-	-
	LMIC	\$4.02	\$3.94	\$1.39
	UMIC	\$3.77	\$7.17	\$9.26
	HIC	-	\$27.17*	\$16.42
EURO	LIC	\$0.37	\$2.89	-
	LMIC	\$2.13	\$2.82	\$1.17
	UMIC	\$1.80	\$5.01	\$5.40
	HIC	-	\$3.78*	\$19.27

\*n=1 (AFRO = Mauritius, AMRO = Panama, WPRO = Palau, and EURO = Romania)



# Literature search strategy for HICs

- This search strategy is adapted from Immunization Costing Action Network (ICAN)
- Limited to most recent 10 years
- IVAC team will screen for studies, literature reviews and meta-analyses specific to HICs
- Data from literature will be compared with estimates from DOVE Model II

Categories	Query	Results
Cost	"Costs and Cost Analysis"[mh] OR costs[tiab] OR cost effective*[tiab] OR costing[tiab] OR cost-benefit[tiab] OR costutility[tiab] OR "Immunization Programs/economics"[mh] OR "Vaccination/economics"[mh] OR "Mass Vaccination/economics"[mh]	476,004
Immunization	immuniz*[tiab] OR immunis*[tiab] OR vaccin*[tiab]	408,802
Delivery	delivery[tiab] OR campaign*[tiab] OR incremental[tiab] OR strategy[tiab] OR strategies[tiab] OR "cold chain"[tiab] OR logistic*[tiab] OR equipment[tiab] OR personnel[tiab] OR overhead[tiab] OR operational[tiab] OR transport*[tiab] OR distribut*[tiab] OR "non-vaccine"[tiab] OR "per dose"[tiab] OR "per capita"[tiab] OR "per child"[tiab] OR "per person"[tiab] OR "per fully immunized child"[tiab] OR "per fully immunised child"[tiab] OR "per FIC"[tiab] OR universal[tiab] OR "disabilityadjusted"[tiab] OR DALY[tiab] OR extrapolat*[tiab]	3,742,259
Countries	Andorra [tiab] OR Antigua and Barbuda [tiab] OR Australia [tiab] OR Austria [tiab] OR Bahamas [tiab] OR Bahrain [tiab] OR Barbados [tiab] OR Belgium [tiab] OR Brunei Darussalam [tiab] OR Canada [tiab] OR Chile [tiab] OR Croatia [tiab] OR Cyprus [tiab] OR Czech Republic [tiab] OR Denmark [tiab] OR Estonia [tiab] OR Finland [tiab] OR France [tiab] OR Germany [tiab] OR Greece [tiab] OR Hungary [tiab] OR Iceland [tiab] OR Ireland [tiab] OR Israel [tiab] OR Italy [tiab] OR Japan [tiab] OR Kuwait [tiab] OR Latvia [tiab] OR Lithuania [tiab] OR Luxembourg [tiab] OR Malta [tiab] OR Monaco [tiab] OR Nauru [tiab] OR Netherlands [tiab] OR New Zealand [tiab] OR Norway [tiab] OR Oman [tiab] OR Poland [tiab] OR Portugal [tiab] OR Qatar [tiab] OR Saint Kitts and Nevis [tiab] OR San Marino [tiab] OR Saudi Arabia [tiab] OR Seychelles [tiab] OR Singapore [tiab] OR Slovakia [tiab] OR Slovenia [tiab] OR South Korea [tiab] OR Spain [tiab] OR Sweden [tiab] OR Switzerland [tiab] OR Trinidad and Tobago [tiab] OR United Arab Emirates [tiab] OR United Kingdom [tiab] OR United States [tiab] OR Uruguay [tiab] OR Cook Islands [tiab] OR Niue [tiab] OR OECD [tiab] OR "High Income"[mh] OR High-Income[tiab]	1,270,964
Timeline	(y_10[Filter]))	



# IA2030 Methods & Data Sources – Delivery Cost

## Delivery costs in previous costing analyses:

DOVE Costing Model	EPIC Costing Model
Data available: 63 countries <b>Imputed using DOVE Model I for LMICs:</b> 31 countries LIC: 29 countries LMIC: 47 countries UMIC: 16 countries	Data available: 136 countries LIC: 29 countries LMIC: 49 countries UMIC: 54 countries HIC: 4 countries – (Mauritius, Palau, Panama, Romania)

## Delivery costs for 194 countries for IA2030

### Data prioritization for routine immunization:

1. IDCC and CMYP data will be used for all countries with available estimates (n=63)
2. EPIC modeled data will be used for remaining countries with no IDCC or CMYP data (n=71)
3. For remaining countries, the updated DOVE Model II will be used to impute the estimates and will be cross validated with estimates derived from published literature (n=55)
4. For countries without EPIC estimates or insufficient data to impute, income and regional averages will be used (n=5)

### SIA:

- Simple average of the vaccine specific SIA delivery cost per dose from IDCC and published literature



# References

1. Gavi the Vaccine Alliance. Gavi V16. Public Price Forecast.; 2018
2. Pan American Health Organization. PAHO Revolving Fund.  
[https://www.paho.org/hq/index.php?option=com\\_content&view=article&id=1864:paho-revolving-fund&Itemid=4135&lang=en](https://www.paho.org/hq/index.php?option=com_content&view=article&id=1864:paho-revolving-fund&Itemid=4135&lang=en) .  
Published 2018
3. UNICEF. Supplies and Logistics: Vaccine Price Data.
4. World Health Organization. Market Information 4 Access to Vaccines (MI4A): Vaccine Purchase Data.  
[https://www.who.int/immunization/programmes\\_systems/procurement/mi4a/platform/module1/en/](https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module1/en/). Published 2019
5. Personal communication with Gavi
6. Personal communication with WHO
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[https://apps.who.int/iris/bitstream/handle/10665/100618/WHO\\_IVB\\_14.01\\_eng.pdf?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/100618/WHO_IVB_14.01_eng.pdf?sequence=1).
10. Immunization Costing Action Network (ICAN). Immunization Delivery Cost Catalogue. <http://immunizationeconomics.org/ican-idcc>.  
Published 2019. Accessed April 9, 2019.
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12. Portnoy, A., Vaughan, K., Clarke-Deelder, E. et al. Producing Standardized Country-Level Immunization Delivery Unit Cost Estimates. *PharmacoEconomics* 38, 995–1005 (2020). <https://doi.org/10.1007/s40273-020-00930-6>

# Appendix

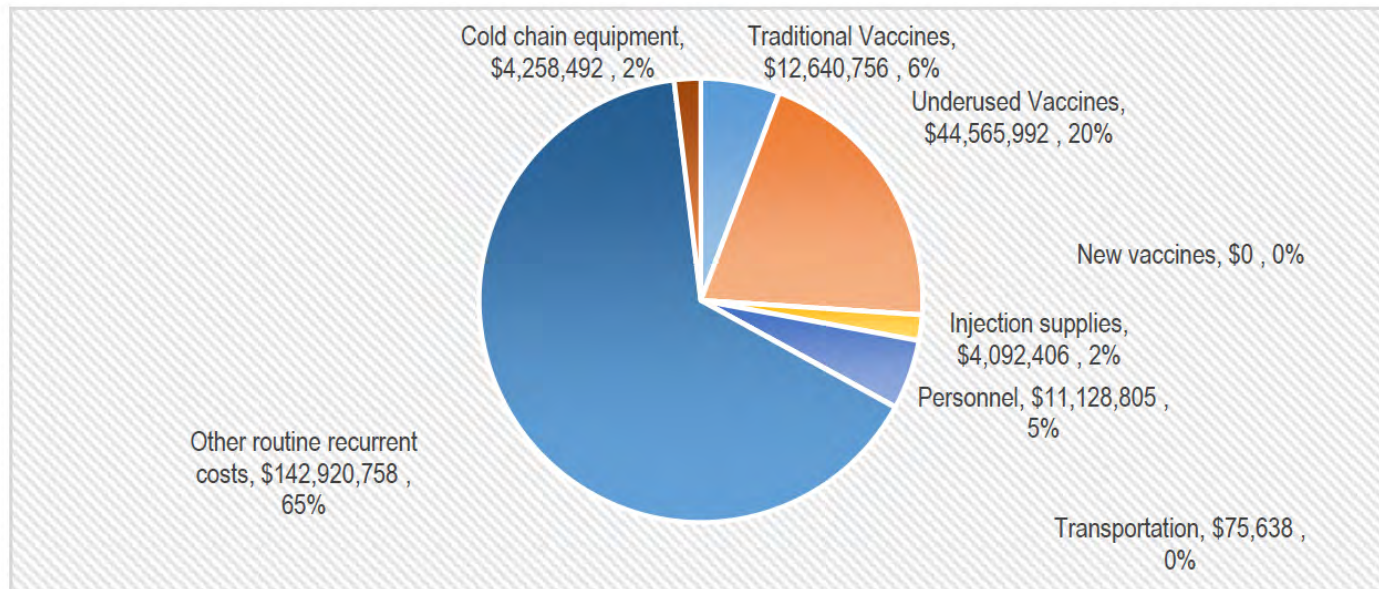




# Appendix – cMYP and personnel cost

## Ex: Nigeria Comprehensive EPI Multi-Year Plan 2016 - 2020

- Baseline Cost Profile for Routine Immunization in 2013



The analysis of the baseline cost profiles (2013) shows that USD 11,128,805 million was incurred on personnel cost which constituted to 5.1% of the total expenditure on Routine Immunization Program.



# Appendix II

- Select Results from:

\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010





**Table 1.** Summary table for immunization delivery cost per dose estimates (USD 2018).

Category	Type	n <sup>‡</sup>	Average (SD)	Median	Range
Routine immunization*	Total immunization delivery cost per dose	94	2.47 (1.96)	2.30	0.18-11.31
	Incremental cost per dose for introducing HPV <sup>§</sup>	42	3.90 (3.30)	2.86	0.52-13.44
	Incremental cost per dose for introducing PCV	21	1.20 (1.00)	1.06	0.15-3.50
	Incremental cost per dose for introducing Rotavirus vaccine	12	1.04 (0.64)	0.85	0.10-2.31
SIA <sup>†</sup>	Measles	17	0.95 (0.88)	0.70	0.04-3.63
	MR/MMR	13	0.88 (0.20)	0.84	0.69-1.46
	JE	2	0.69(0.01)	0.69	0.68-0.70
	MenA	15	0.51(0.39)	0.65	0.00-1.44
	Yellow Fever	4	0.65 (0.19)	0.69	0.42-0.81
	HPV SIA (Multi-age cohort)	1	0.53	0.53	0.53-0.53

\*Ten vaccines for routine immunization: Pentavalent, human papilloma virus, Japanese encephalitis, measles, measles-rubella, measles-mumps-rubella, meningococcal group A conjugate, pneumococcal conjugate, rotavirus, and yellow fever vaccines.

<sup>†</sup>Seven vaccines for SIA: Human papilloma virus, Japanese encephalitis, measles, measles-rubella, measles-mumps-rubella, meningococcal group A conjugate, and yellow fever vaccines.

<sup>‡</sup>Number of estimates in the model.

<sup>§</sup>No distinction was made to HPV cost estimates from routine delivery via health facility and school delivery given uncertainty about country decisions regarding delivery strategies.

\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010



**Table 2.** Cost of immunization programs for 10 vaccines by decade, 94 low- and middle-income countries (base case scenario).

	2011-2020	2021-2030	Total
By strategy			
Routine, total	\$22.9 billion (18.4-29.5)	\$39.0 billion (30.7-53.3)	\$61.9 billion (49.2-82.3)
<i>Vaccine</i>	\$12.4 billion (11.3-13.5)	\$21.3 billion (19.5-23.0)	\$33.7 billion (30.9-36.3)
<i>Delivery</i>	\$10.5 billion (7.1-16.0)	\$17.7 billion (11.2-30.4)	\$28.2 billion (18.2-46.0)
SIA, total	\$5.2 billion (3.3-9.5)	\$3.2 billion (2.3-5.0)	\$8.5 billion (5.7-14.5)
<i>Vaccine</i>	\$2.2 billion (2.0-2.4)	\$1.6 billion (1.5-1.7)	\$3.8 billion (3.5-4.0)
<i>Delivery</i>	\$3.1 billion (1.3-7.2)	\$1.6 billion (0.9-3.3)	\$4.7 billion (2.2-10.5)
Stockpile, total	\$0.20 billion (0.17-0.24)	\$0.22 billion (0.19-0.25)	\$0.42 billion (0.36-0.49)
By component			
Immunization program, total	28.4 billion (22.7-36.3)	\$42.4 billion (33.8-57.1)	\$70.8 billion (56.5-93.4)
<i>Vaccine, total</i>	\$14.6 billion (13.4-15.8)	\$22.8 billion (21.1-24.60)	\$37.4 billion (34.4-40.3)
<i>Delivery, total</i>	\$13.6 billion (9.2-20.3)	\$19.4 billion (12.5-32.3)	\$32.9 billion (21.7-52.5)
<i>Stockpile, total</i>	\$0.20 billion (0.17-0.24)	\$0.22 billion (0.19-0.25)	\$0.42 billion (0.36-0.49)

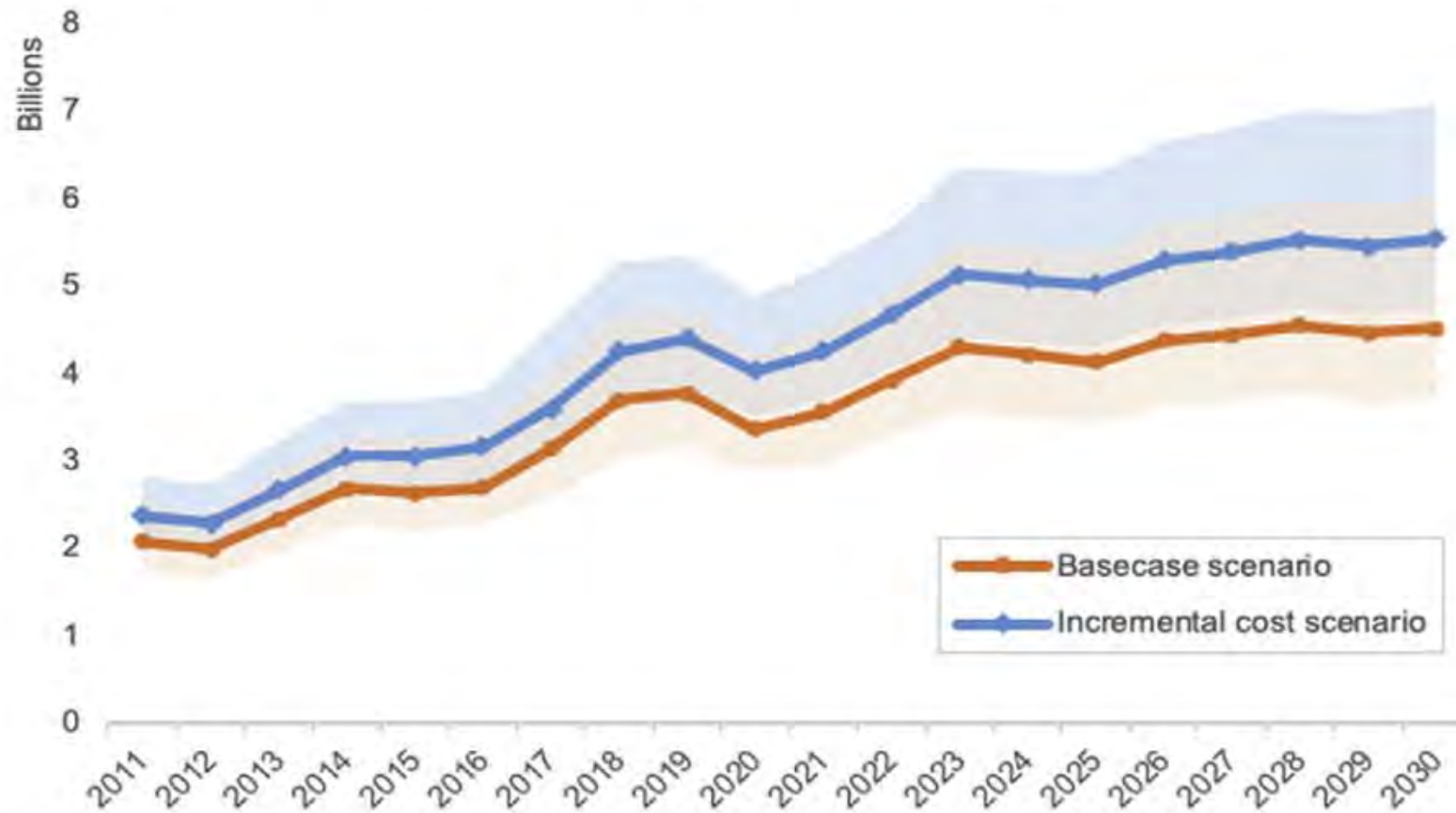
Note. All cost in USD 2018.

\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010





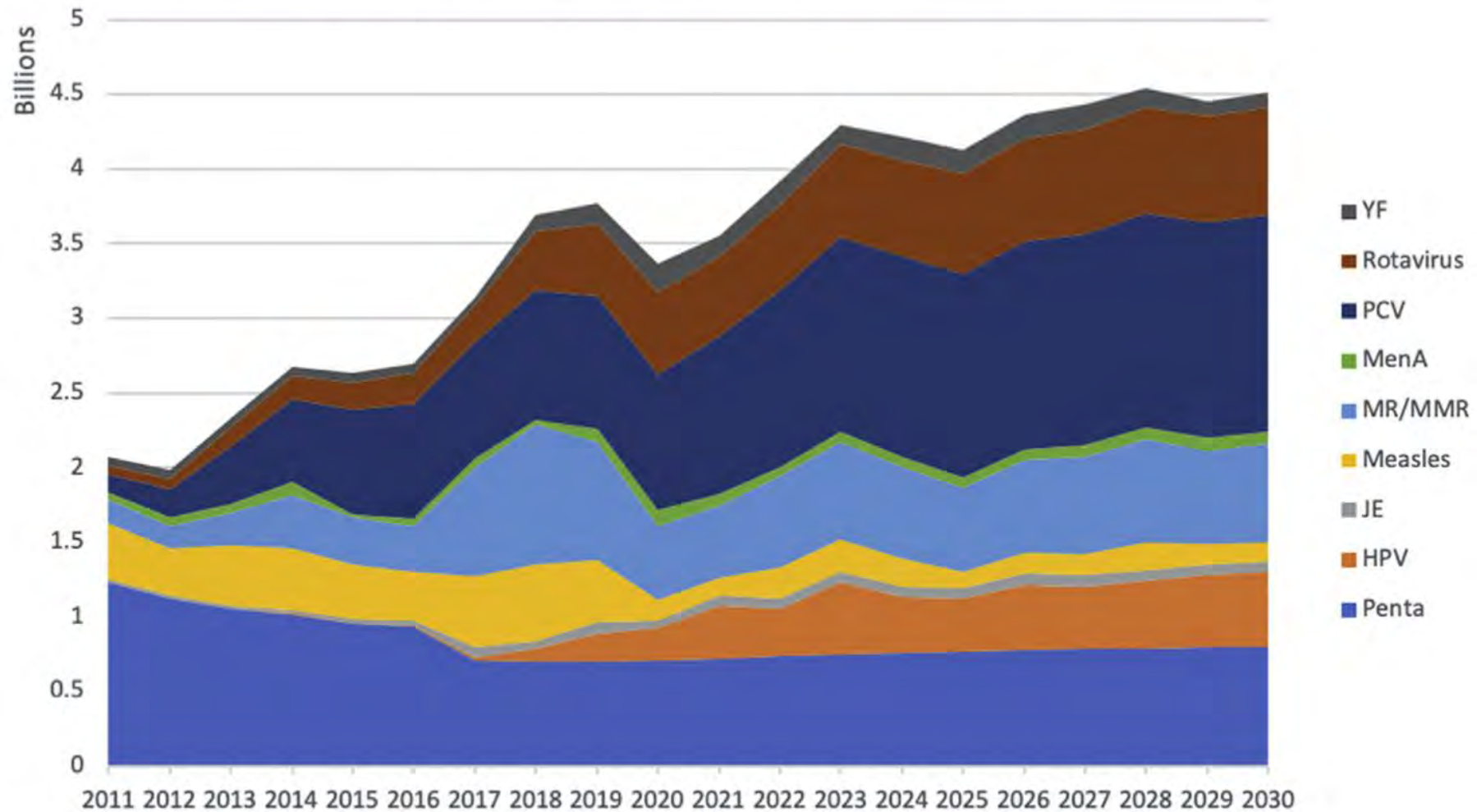
**Figure 1.** Total immunization program costs for 10 vaccines over time (base case scenario vs incremental delivery cost scenario).



\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010



## Total immunization program cost by vaccine for 94 countries from 2011 to 2030.



\*Sim SY, Watts E, Constenla D, Huang S, Brenzel L, Patenaude BN. Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle Income Countries From 2011 to 2030. Value in Health. 2020. doi:10.1016/j.jval.2020.07.010

# Background information

Costs of Immunization Programs for 10 Vaccines in 94 Low- and Middle-Income Countries From 2011 to 2030

- <https://www.sciencedirect.com/science/article/pii/S109830152034393X>

Return on Investment From Immunization Against 10 Pathogens In 94 Low- And Middle-Income Countries, 2011–30

- <https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00103>

**Ad hoc session (February 2015):**  
**IA 2030 vaccine impact estimates**

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

**Microsoft Teams - Virtual Meeting**

**WHO Headquarters, Geneva, Switzerland**

**15 Feb 2021**

**Draft list of participants**

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

Microsoft Teams - Virtual Meeting  
WHO Headquarters, Geneva, Switzerland  
15 February 2021

**Background reading materials available at:** [https://worldhealthorg.sharepoint.com/sites/ws-VaccinesResearch/IVIR-AC/ivirac\\_sept20/SitePages/Welcome.aspx](https://worldhealthorg.sharepoint.com/sites/ws-VaccinesResearch/IVIR-AC/ivirac_sept20/SitePages/Welcome.aspx)

**Chair:** Walt Orenstein

15 February				
Duration	Title	Content and key questions to IVIRAC	Purpose	Proposed speaker
1200 – 1205 5’	Opening of Meeting	<ul style="list-style-type: none"><li>Reason for ad hoc session</li></ul>	For information	R Hutubessy
1205-1215 10’	Introduction/ Objectives of the meeting	<ul style="list-style-type: none"><li>Administrative issues</li></ul>		P Lambach W Orenstein
IA 2030 vaccine impact estimates				
1215 - 1220 5’	Background	<ul style="list-style-type: none"><li>Project updates related to IVIR-AC recommendations (September 2020)<ul style="list-style-type: none"><li>Prioritization of vaccines</li><li>IA2030 coverage scenario</li></ul></li></ul>	For information	Y Sim
1220 – 1245 25’	Technical presentation	<ul style="list-style-type: none"><li>Method updates<ul style="list-style-type: none"><li>Have the latest developments sufficiently incorporated your recommendations from the last meeting (September 2020)?</li><li>What are the limitations of the current approach to generating vaccine impact estimates for 194 Member States?</li></ul></li><li>Preliminary results for the first iteration of estimates</li></ul>		William Msemburi and Austin Carter

1245-1315 30'	Q&A and Discussion	<ul style="list-style-type: none"> <li>IVIR-AC is asked to take stock of progress made, review the preliminary results available, and make practical recommendations to inform the forthcoming discussions at the upcoming WHA</li> </ul>		S Verguet and J Wu
1315-1325 10'	Wrap up	<ul style="list-style-type: none"> <li>Summarize day's findings and request any follow up from WHO Secretariat/IVIR-AC FPs for closed session</li> </ul>	For information	W. Orenstein, Chair

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

**WHO IVB&DDI Project Team**

15 February 2021

# Agenda

1. Project updates related to IVIR-AC recommendations (September 2020)
2. Method updates
3. Preliminary estimates
4. Questions for IVIR-AC

# Project objectives



WHO IVB and DDI aim to:

- Update the modeled **vaccine impact estimates**
- Document the **methodology** in a transparent manner
- Inform **strategic priorities** for:
  - Immunization Agenda 2030
  - Triple Billion target for the Thirteenth General Programme of Work (GPW 13)
- Provide **baseline estimates** for IA2030 Impact Goal 1.



# Timeline until WHA

## Project timeline



## IA2030 M&E timeline

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

74<sup>th</sup> World Health Assembly



# **Project updates related to IVIR-AC Recommendations (September 2020)**



**World Health  
Organization**

**Organisation mondiale de la Santé**

# Weekly epidemiological record Relevé épidémiologique hebdomadaire

4 DECEMBER 2020, 95th YEAR / 4 DÉCEMBRE 2020, 95<sup>e</sup> ANNÉE

No 49, 2020, 95, 609–628

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

## Contents

- 609 Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC)
- 623 WHO calls for reinvigorated action to fight malaria

## Sommaire

- 609 Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC)
- 623 L'OMS appelle à relancer la lutte contre le paludisme

## Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC)

### Summary and recommendations, September 2020

The IVIR-AC recommendations reported below are based on deliberations held during a virtual meeting on 21–25 September 2020. A detailed version of these recommendations and the session background and discussions can be found at: [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.html](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.html)

## Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC)

### Résumé et recommandations, septembre 2020

Les recommandations de l'IVIR-AC présentées ci-dessous sont fondées sur les délibérations qui se sont tenues lors d'une réunion virtuelle du 21 au 25 septembre 2020. Une version détaillée de ces recommandations ainsi que le contexte et les discussions de la session peuvent être consultés à l'adresse [https://www.who.int/immunization/research/committees/ivir\\_ac/en/index4.html](https://www.who.int/immunization/research/committees/ivir_ac/en/index4.html)

# 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

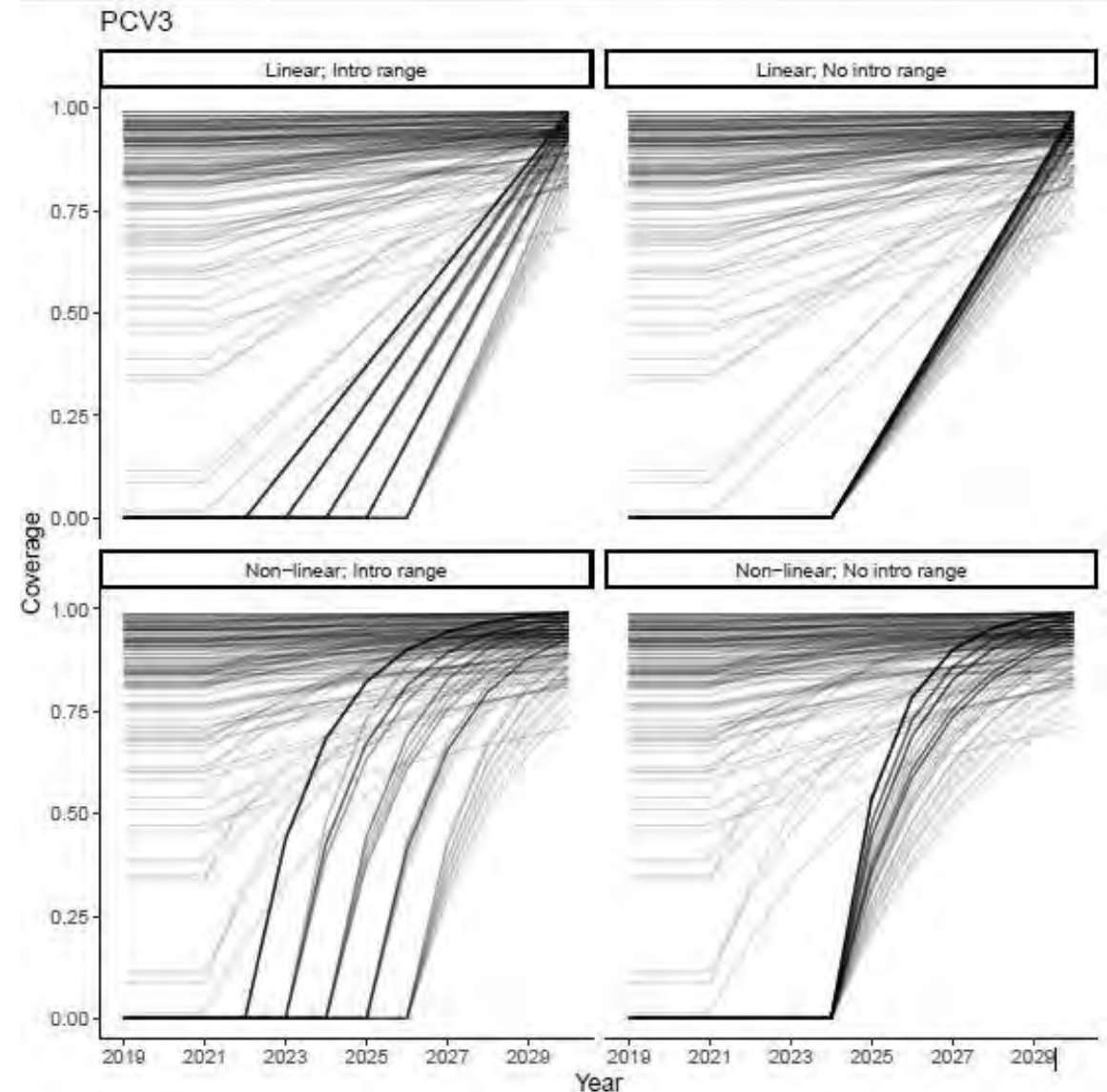
Impact Goals	Proposed Indicators		Proposed Targets
1 Disease	Save lives	1.1 Number of deaths from vaccine-preventable diseases averted	<b>TBD</b> (based on coverage targets & ongoing modelling)
	Control, eliminate & eradicate VPDs	1.2 Number of countries that have achieved global or regional VPD control, elimination and eradication targets	<b>TBD</b> (based on updates of regional & global commitments)
	Reduce VPD outbreaks	1.3 Number of large outbreaks of vaccine-preventable diseases	<b>Annual improvement</b>
2 Equity	Leave no child behind	2.1 Number of zero dose children	<b>Reduce by 50%</b>
	Deliver across the life course	2.2 Coverage of vaccines included in national immunization schedules (DTP3, MCV2, HPVc, PCV3)	<b>Global target:</b> 90% <b>Country target:</b> 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	<b>TBD</b> (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)

# IA2030 coverage scenario

- We developed four options based on:
  - Common assumptions across pathogens about coverage targets and disruptions due to COVID-19
  - Pathogen-specific introduction assumptions
  - Variations for introduction and scale up
- Input from Stakeholder Committee and WHO disease focal points
- *Stakeholder Committee will deliberate upon the final IA2030 coverage scenario later this week.*



# Methodology updates

# IVIR-AC recommendations on methodology (1)

- The demographic model proposed is a good start for providing a reasonable overall framework to avoid double-counting of deaths, because of its explicit inclusion of overall mortality.
- IVIR-AC recommends that the team elaborate on implementation of the impact estimates for individual vaccines into the demographic modelling approach to avoid double-counting, especially in areas where the burden of vaccine-preventable disease (VPDs is) large. For instance, at country level, technical advice will be required on how the summation of all VPD-related deaths is constrained by specific age-group mortality rates.
- The full estimation strategy and its specific analytical steps remain to be fully described. Thorough thinking will be required to develop statistical estimation of the currently proposed static regression model, which draws on the assembly of multiple independent and dependent variables that emerge from heterogeneous sources of modelled estimates.
- In order to include different sources of uncertainty, the model should fully reflect incorporation of both input uncertainty and structural modelling uncertainty.



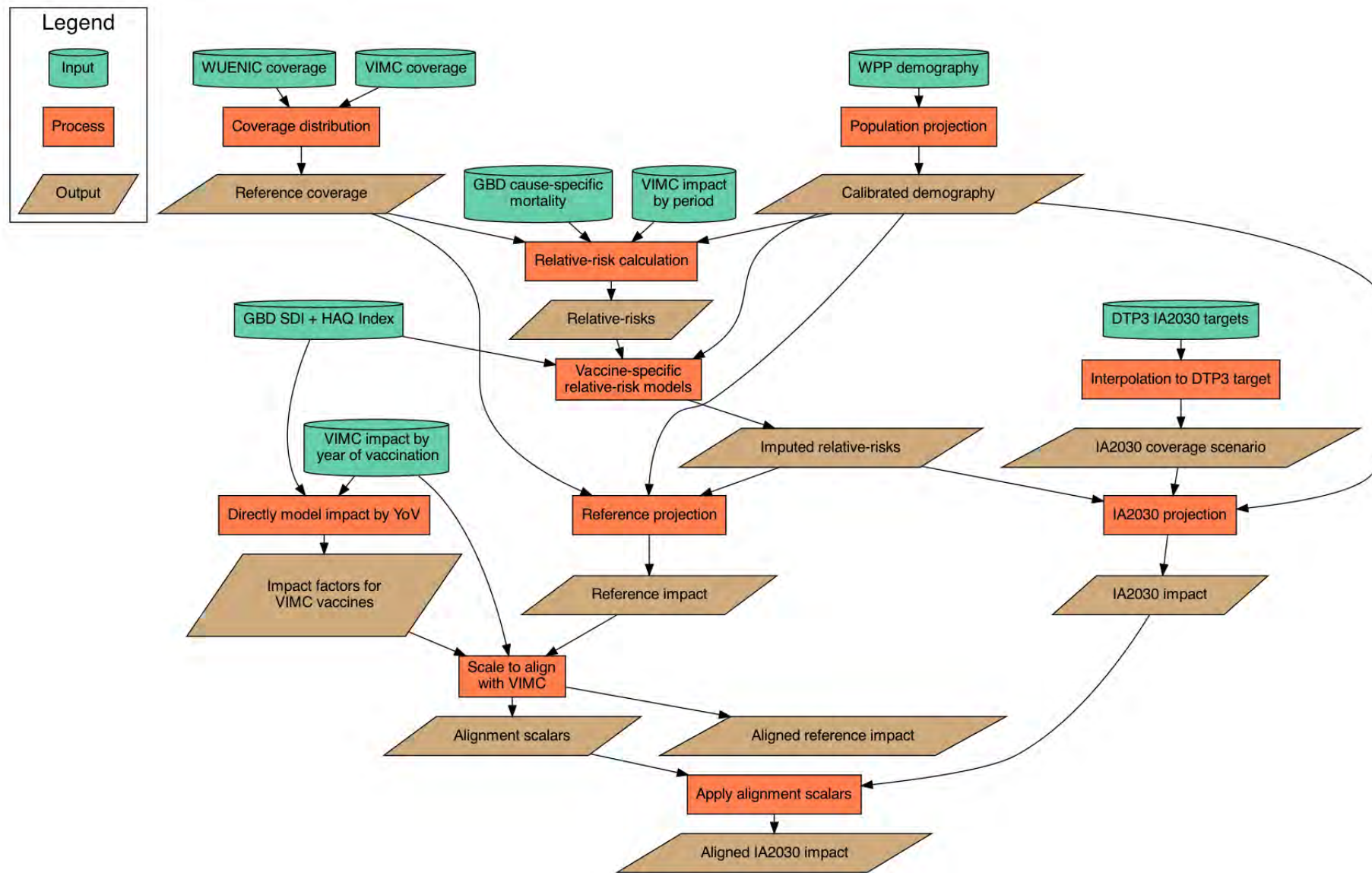
## IVIR-AC recommendations on methodology (2)

- In order to best compare health outcomes with a short- and a long-term impact (e.g. immediate mortality reduction conferred by measles vaccine versus long-term mortality reductions by human papillomavirus vaccines), IVIR-AC recommends reporting of both cohort- and period-specific impact. This will provide an appropriate starting point for comparison of short- and long-term impacts of vaccines.
- The project team should consider contacting suitable members of IVIR-AC who could conduct more detailed reviews of methods and provide advice.

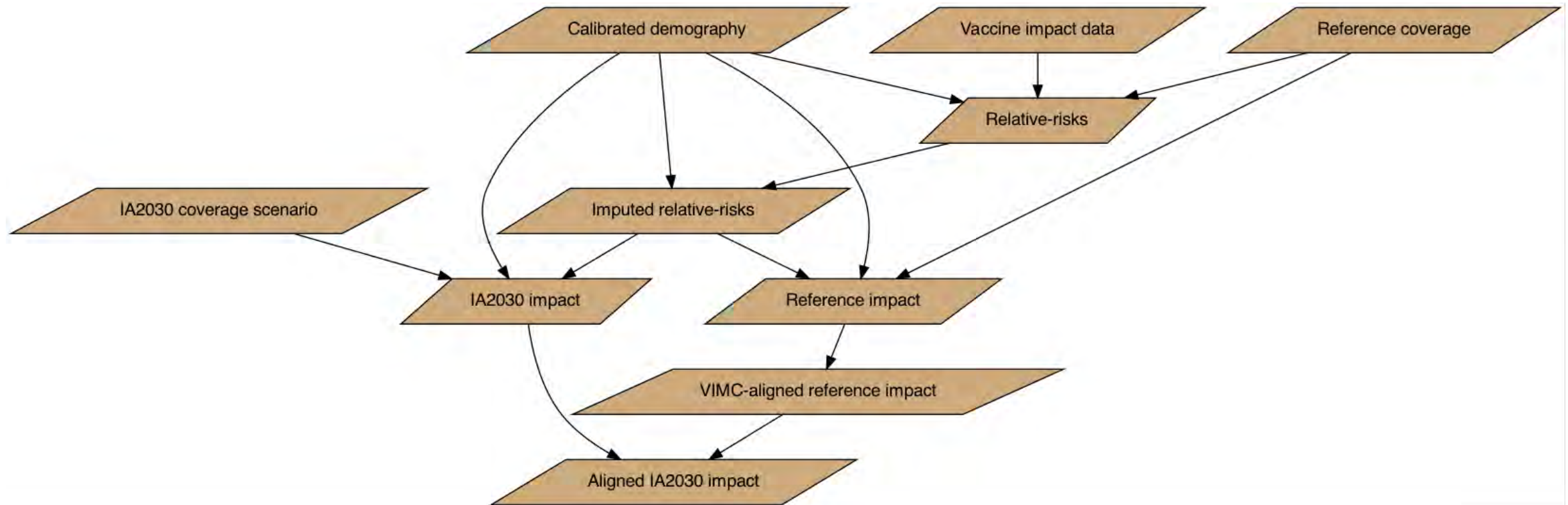
# Methods overview

1. **Input data:** Compile data on demographic rates, vaccine coverage, deaths averted (by calendar year and year of vaccination for Vaccine Impact Modeling Consortium locations and VPDs), deaths observed (for non-VIMC VPDs), and potential covariates
2. **Relative-risk calculation and model:** Convert observed and averted deaths, given observed coverage levels, into a single measure of relative-risk of death conditional on vaccine coverage levels. Model location-, age-, vaccine-specific relative-risk as a function of covariates.
3. **Predict and calibrate:** Predict deaths averted in all locations and VPDs using the relative-risk model and calibrate to VIMC estimates of deaths averted per fully vaccinated persons.
4. **IA2030 target scenario:** Develop IA2030 future coverage scenario and estimate associated deaths averted with the calibrated model and population projection

# Detailed process flowchart



# High-level process flowchart

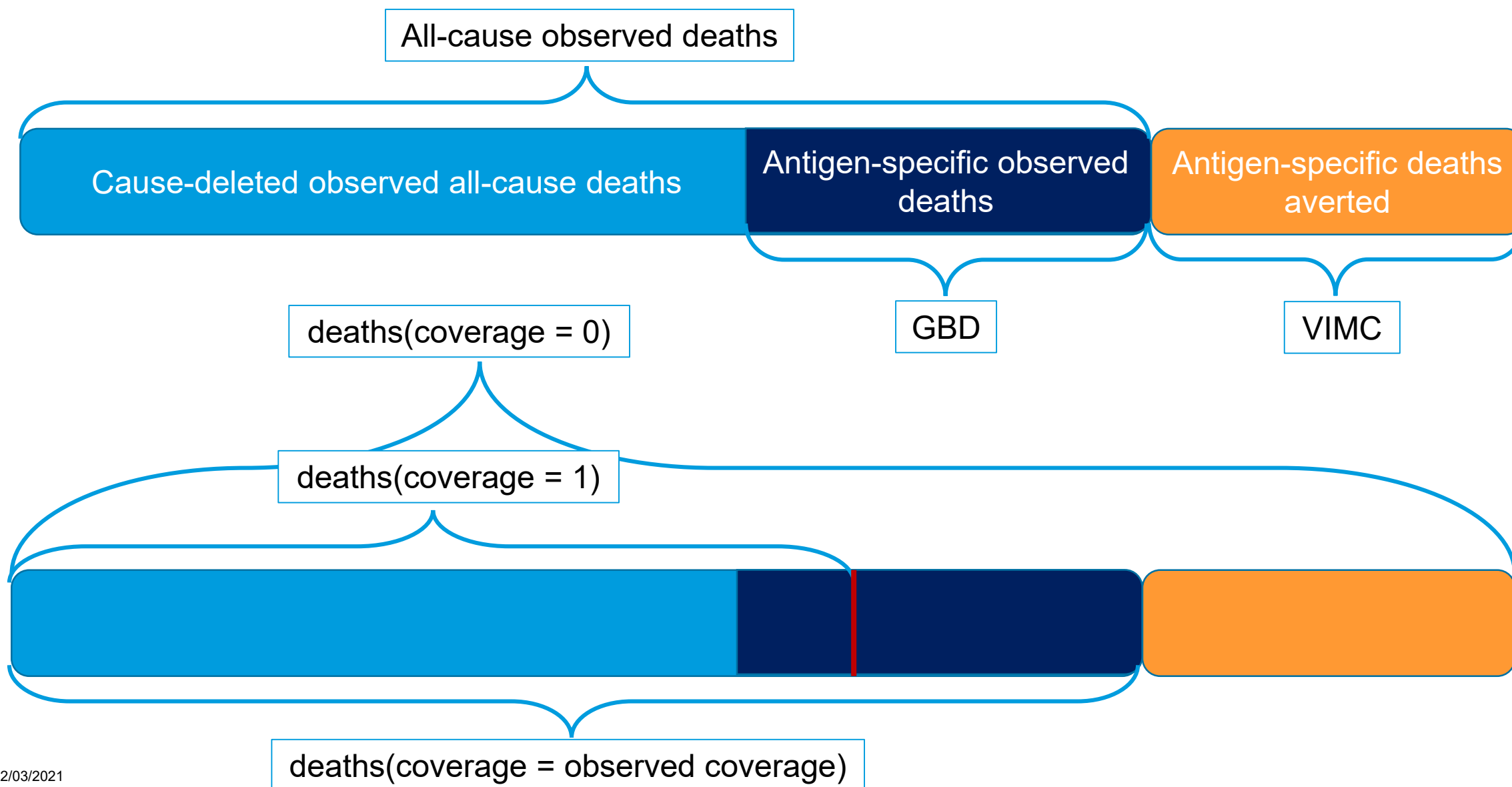


# Input data

Input	Source(s)	Stratification	Locations
Demographic rates	World Population Prospects	Five-year age groups and projection steps	All but a small subset of island nations
Vaccine coverage	WUENIC; VIMC	Annual by vaccine and activity type	All locations
Deaths averted	VIMC	Calendar year / Year of vaccination	VIMC locations
Deaths observed	Global burden of disease	Annual by five-year age groups	All locations
Covariates	Global burden of disease	Annual by five-year age groups	All locations

Health  
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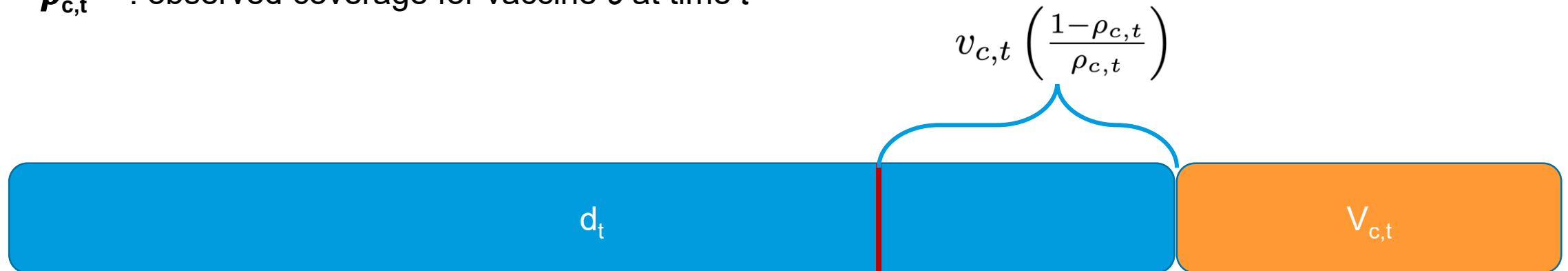
# Relative-risk calculation



# Relative-risk calculation (VIMC)

$$\widehat{RR}_{c,t} = \frac{d(\rho_c = 1)}{d(\rho_c = 0)} = \frac{d_t - v_{c,t} \left( \frac{1 - \rho_{c,t}}{\rho_{c,t}} \right)}{d_t + v_{c,t}}$$

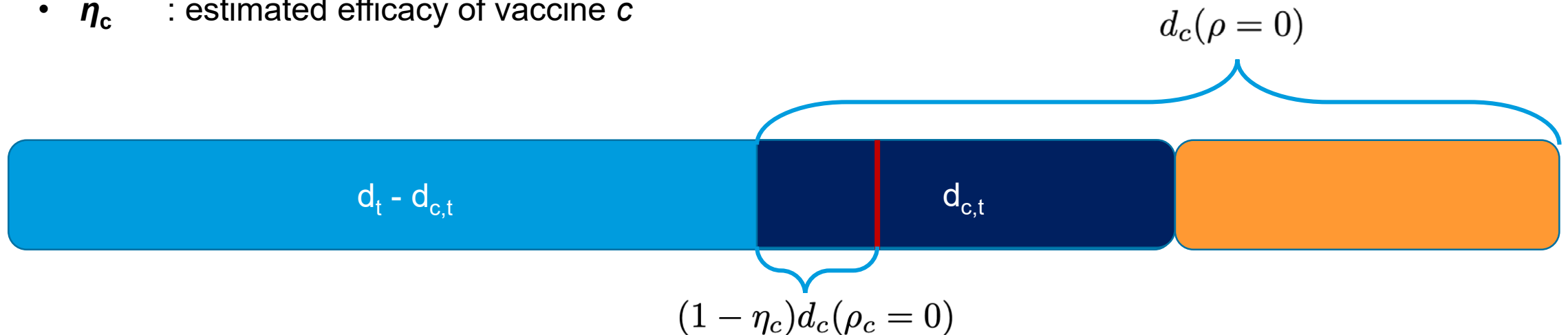
- $\widehat{RR}_{c,t}$  : all-cause relative-risk for vaccine  $c$  at time  $t$
- $d_t$  : all-cause observed deaths at time  $t$
- $v_{c,t}$  : VIMC estimated deaths averted by vaccine  $c$  at time  $t$
- $\rho_{c,t}$  : observed coverage for vaccine  $c$  at time  $t$



# Relative-risk calculation (GBD)

$$\widehat{RR}_{c,t} = \frac{d(\rho_c = 1)}{d(\rho_c = 0)} = \frac{d_t - d_{c,t} + (1 - \eta_c) \frac{d_{c,t}}{1 - \eta_c \rho_{c,t}}}{d_t - d_{c,t} + \frac{d_{c,t}}{1 - \eta_c \rho_{c,t}}}$$

- $RR_{c,t}$  : all-cause relative-risk for vaccine  $c$  at time  $t$
- $d_t$  : all-cause observed deaths at time  $t$
- $d_{c,t}$  : GBD estimated antigen-specific deaths vaccine  $c$  at time  $t$
- $\rho_{c,t}$  : observed coverage for vaccine  $c$  at time  $t$
- $\eta_c$  : estimated efficacy of vaccine  $c$

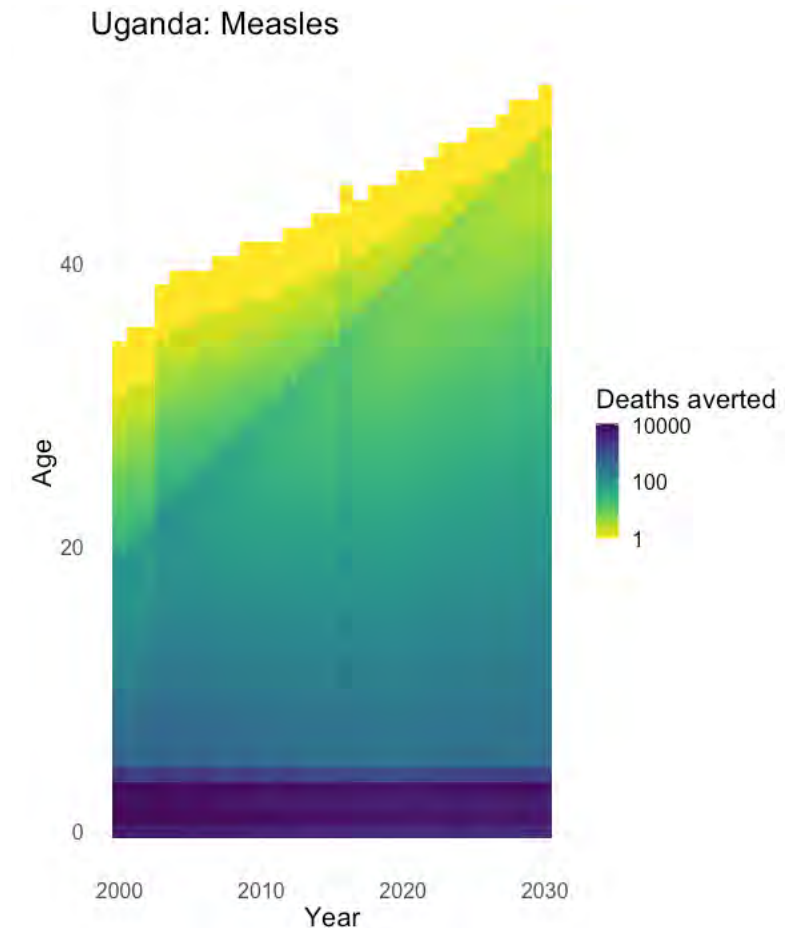




# Relative-risk model

$$\text{logit}(RR_{c,t,a}) = \beta_0 + \beta_1 \text{HAQI}_{c,t} + \beta_2 \text{SDI}_{c,t} + \beta_3 t + \sum_i \alpha_i B_{i,n}(a) + \epsilon$$

- **Vaccine / activity-type relative-risk varies by country (c), time (t), and age (a)**
- **Predict with covariates from the GBD**
  - Healthcare access and quality index (HAQi)
  - Socio-demographic index (SDI)
- **Spline on age to capture variation across ages**
- **Considering including all-cause mortality as a covariate**
- **We found improvements when including all-cause mortality as a covariate and after incorporating a non-linear relationship between coverage and deaths averted**



VIMC average deaths averted by age and year

# Predict and calibrate

After predicting deaths averted with the relative-risk model, we:

1. Convert the deaths averted from measured by calendar year to measured by year of vaccination
2. Calculate the ratio of observed deaths averted per fully vaccinated persons to the predicted rate in VIMC locations and VPDs.
3. Scale non-VIMC locations by the vaccine / activity-type specific median ratio
4. Scale non-VIMC vaccines by the median routine vaccination ratio

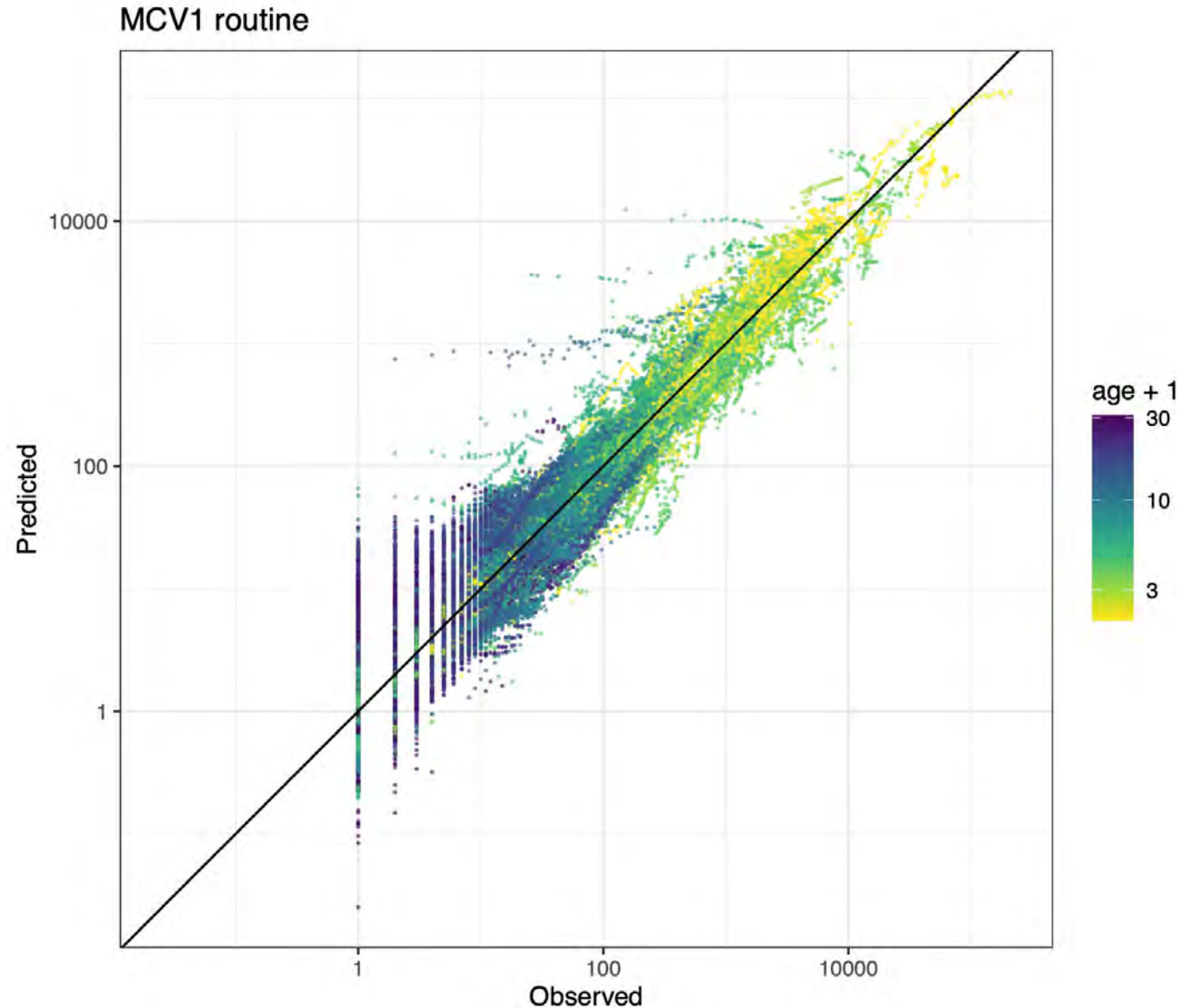
This calibration ensures that our results match the VIMC within VIMC VPDs and locations, while adjusting the non-VIMC VPDs and locations according to the median error of the relative-risk models

# Plans for validation

- DTP/BCG:
  - Expand on technical expert advisory group for DTP and BCG to validate the initial estimates
- HIC:
  - Use non-VIMC estimates from some of VIMC participating disease models for validation (short-term)
  - Collect data directly from HIC and literature search
- Approaches:
  - Apply DTP/BCG approach to vaccines we are extrapolating from VIMC and see what it looks like
  - Apply GBD method for VIMC countries to see what potential bias coming from the method
- Uncertainty:
  - Robust methods to incorporate uncertainty especially when we look at forecasting

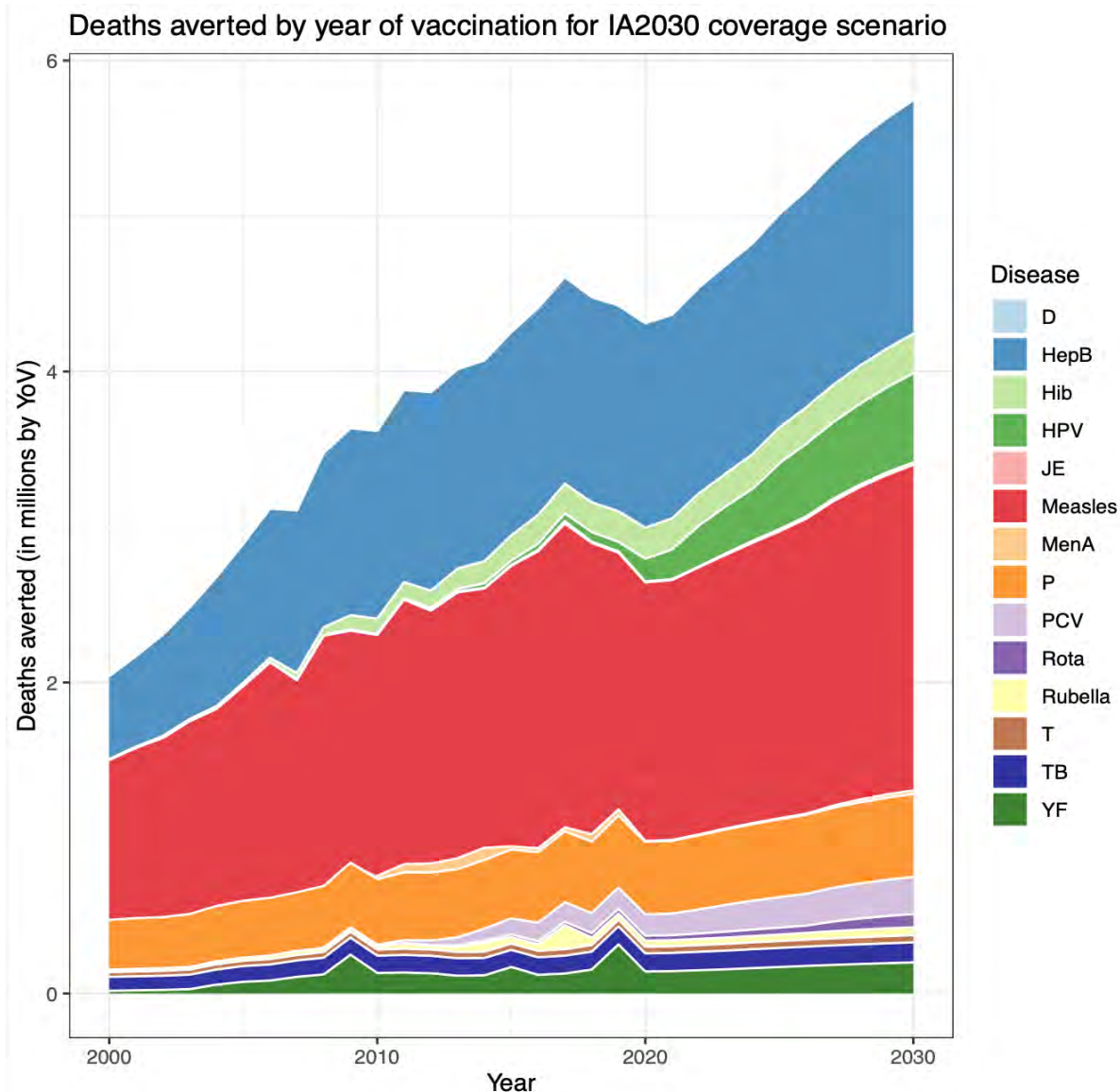
# Preliminary estimates

# Vaccine/activity-type model fit



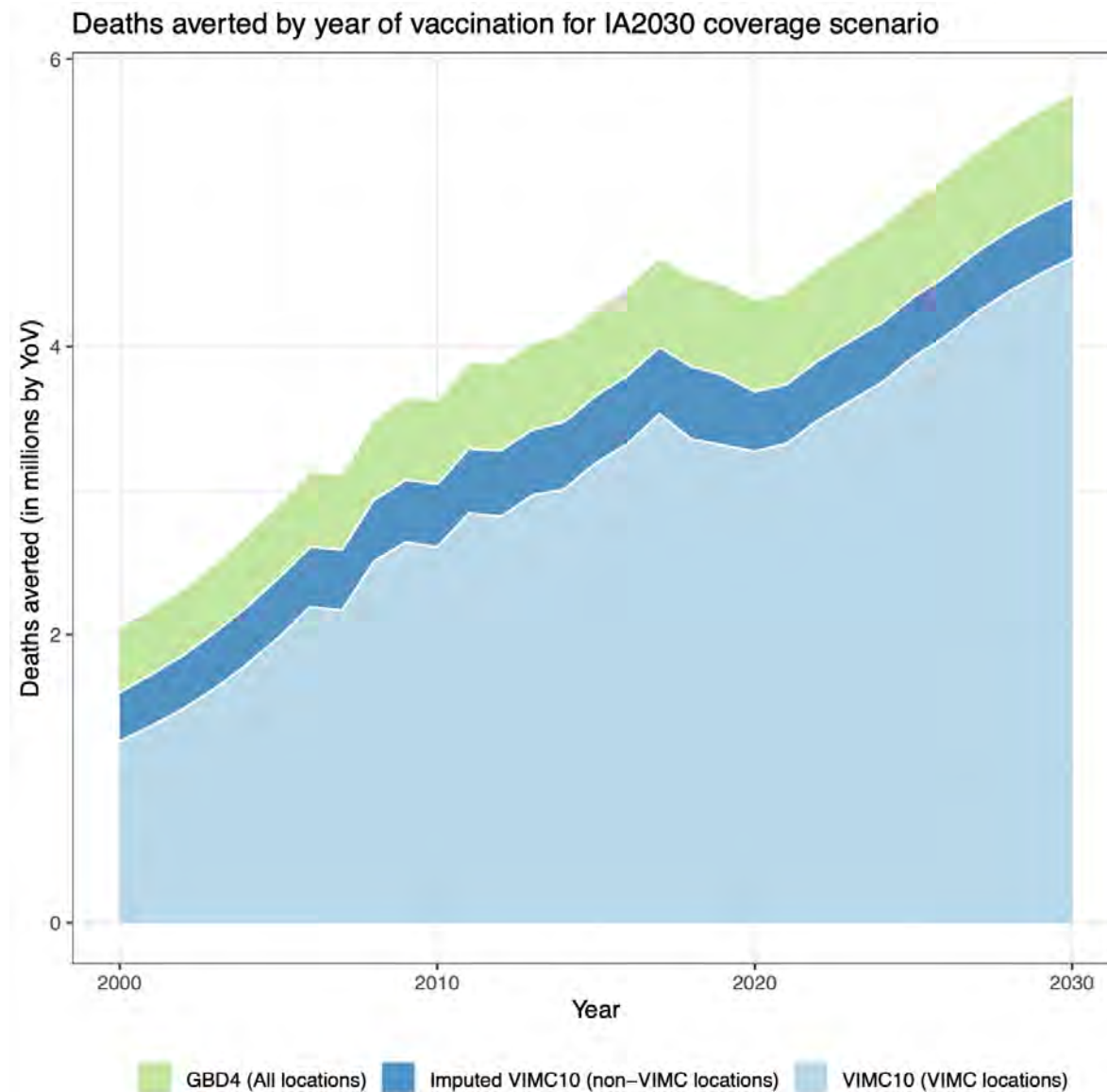
- Observed deaths averted from the VIMC compared to predicted deaths from our relative-risk based model
- Color varies of points varies by age
- Improved model fit (hopefully) translates to better out-of-sample prediction
- Validation of imputed results will be focus moving forward

# Global deaths averted by vaccine preventable disease



- Vaccine and activity-type specific results aggregated to the disease level
- Future lives saved according to current IA2030 coverage targets
- Deaths averted by year of vaccination means that the lifetime effects of vaccination are aggregated for the year the vaccines are delivered

# Global deaths averted by imputation category



Three groups:

1. Four non-VIMC vaccines for all locations
  2. VIMC vaccines for non-VIMC locations
  3. VIMC vaccines in VIMC locations
- Majority of deaths averted are captured in VIMC vaccines and VIMC locations
  - Growth in deaths averted is concentrated in VIMC vaccines and locations as well

# Questions for IVIR-AC



# Questions

- What aspects of the updated methodology should be further clarified?
- Does reporting deaths by year of vaccination satisfy the recommendation to capture both the short- and far-term impacts of vaccination?
- What are the limitations of the current approach to achieve the project objective of summarizing the impact of past and future vaccination?
  - Still need to propagate uncertainty through the estimation process

# Appendix

# Stakeholder Committee & Project team

## Stakeholder Committee

- **BMGF:** Emily Dansereau/Brittany Hagedorn
- **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**)
- **WHO IVIR-AC:** Walt Orenstein
- **WHO DDI:** Somnath Chatterji
- **WHO IVB:** Ann Lindstrand, Raymond Hutubessy

\*VIMC: Vaccine Impact Modelling Consortium

## Project team

- **Supervision:** Raymond Hutubessy
- **Analytics:** William Msemburi, Austin Carter
- **Project management:** Yoonie Sim
- **M&E focal point:** Jan Grevendonk
- **VIMC focal point:** Katy Gaythorpe (VIMC)

Acknowledgement: Olivia Bullock (IVB)

# Background information

IVIR-AC Sep 2020 WER report

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

Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study:

- [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)

How can the public health impact of vaccination be estimated?

- <https://www.medrxiv.org/content/10.1101/2021.01.08.21249378v1>