World Health Organization

Department of Immunization, Vaccines and Biologicals (IVB)

IVIR-AC – September 2025

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

MICROSOFT TEAMS - VIRTUAL MEETING

WHO HEADQUARTERS, GENEVA, SWITZERLAND

1 September 2025 – 5 September 2025

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)
1 September 2025 – 5 September 2025

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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Participating IVIR-AC Members

Sheetal Silal, Modelling and Simulation Hub, Africa (MASHA), University of Cape Town, Cape Town, **South Africa**
Rakesh Aggarwal, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, **India**
Habib Hasan Farooqui, Additional Professor, Public Health Foundation of India, Delhi, **India**
Stefan Flasche, Professor for Infectious Disease Dynamics and Global Health at Charité – Universitätsmedizin Berlin , **Germany** Professor for London School of Hygiene & Tropical Medicine, London, **United Kingdom of Great Britain and Northern Ireland**
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Kathy Leung, School of Public Health, The University of Hong Kong, **Hong Kong SAR, China**

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William Moss, International Vaccine Access Center Johns Hopkins Bloomberg School of Public Health, **USA**
Allison Portnoy, Department of Global Health of the Boston University School of Public Health, Boston, **USA**
Meru Sheel, School of Public Health, the University of Sydney, Sydney, **Australia**
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IVIR-AC Terms of References

The IVIR-AC Terms of References
can be accessed at the following link:
https://www.who.int/publications/m/item/terms-of-reference-for-the-immunization-and-vaccines-related-implementation-research-advisory-committee-(ivir-ac)

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DOI and Confidentiality undertakings

DECLARATION OF INTERESTS FOR WHO EXPERTS

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

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

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

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

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

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

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

Name: Institution: Email:

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

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

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

EMPLOYMENT AND CONSULTING

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

1a Employment — Yes ☐ No ☐

1b Consulting, including service as a technical or other advisor — Yes ☐ No ☐

RESEARCH SUPPORT

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

2a Research support, including grants, collaborations, sponsorships, and other funding — Yes ☐ No ☐

2b Non-monetary support valued at more than US $1000 overall (include equipment, facilities, research assistants, paid travel to meetings, etc.) — Yes ☐ No ☐

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

INVESTMENT INTERESTS

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

3a Stocks, bonds, stock options, other securities (e.g., short sales) — Yes ☐ No ☐

3b Commercial business interests (e.g., proprietorships, partnerships, joint ventures, board memberships, controlling interest in a company) — Yes ☐ No ☐

INTELLECTUAL PROPERTY

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

4a Patents, trademarks, or copyrights (including pending applications) — Yes ☐ No ☐

4b Proprietary know-how in a substance, technology or process — Yes ☐ No ☐

PUBLIC STATEMENTS AND POSITIONS (during the past 3 years)

5a As part of a regulatory, legislative or judicial process, have you provided an expert opinion or testimony, related to the subject of the meeting or work, for a commercial entity or other organization? — Yes ☐ No ☐

5b Have you held an office or other position, paid or unpaid, where you represented interests or defended a position related to the subject of the meeting or work? — Yes ☐ No ☐

ADDITIONAL INFORMATION

6a If not already disclosed above, have you worked for the competitor of a product that is the subject of the meeting or work, or will your participation in the meeting or work enable you to obtain access to a competitor's confidential proprietary information, or create for you a personal, professional, financial or business competitive advantage? — Yes ☐ No ☐

6b To your knowledge, would the outcome of the meeting or work benefit or adversely affect interests of others with whom you have substantial common personal, professional, financial or business interests (such as your adult children or siblings, close professional colleagues, administrative unit or department)? — Yes ☐ No ☐

6c Excluding WHO, has any person or entity paid or contributed towards your travel costs in connection with this WHO meeting or work? — Yes ☐ No ☐

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

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

7. **TOBACCO OR TOBACCO PRODUCTS** *(answer without regard to relevance to the subject of the meeting or work)*
Within the past 4 years, have you had employment or received research support or other funding from, or had any other professional relationship with, an entity directly involved in the production, manufacture, distribution or sale of tobacco or tobacco products or representing the interests of any such entity? Yes ☐ No ☐

EXPLANATION OF "YES" RESPONSES: If the answer to any of the above questions is **"yes", check above and briefly describe the circumstances on this page. <u>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.</u>**

Nos. 1 - 4: **Type of interest, question number and category (e.g., Intellectual Property 4.a copyrights) <u>and</u> 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				

<u>CONSENT TO DISCLOSURE</u>. 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.

<u>DECLARATION</u>. 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: _____ Signature: _____
Dr Philipp Lambach
Medical officer
Initiative for Vaccine Research

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)

World Health Organization

Agenda and List of Participants

World Health Organization

Meeting of the Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC)
1 September – 5 September 2025
Virtual Meeting
WHO HQ
Agenda

Day 1: Monday, 01 September 2025 (CEST)

Time CEST	Session	Purpose of session, target outcomes and questions for IVIR-AC	Duration
12:00	**Welcome** K O'Brien	Update on global strategies and issues of relevance to WHO	**10 min**
12:10	**Introduction** P Lambach S Silal, Chair	Welcome, Objectives, Administrative information	**10 min**
12:20	**Session 1: Immunization implementation Research in WHO African region** Background summary. *10 min.* L. Rey, R. Hutubessy Technical Presentation. *10 min.* A. Adamu Discussion. *20 min.* IVIR-AC FPs: R Aggarwal, **B Moss**, H Hasan SAGE/ SAGE WG FP: Y Berhane	•Does IVIR-AC consider the DRIVE framework suitable for conducting case studies in immunization programmes to document implementation strategies that worked or "did not work"? How would the DRIVE framework provide the highest utility for immunization programmes in Africa? •What recommendations can IVIR-AC propose to immunization programme managers and researchers to promote the use of the DRIVE framework? •Beyond the DRIVE framework, what additional strategic role can IVIR-AC play to provide methodological guidance in implementation research for the African region to promote faster uptake and integration of evidence-based innovations in immunization programmes?	**40 min**
13:00	**Break**		**10 min**
13:10	**Session 2: IA2030 Impact Modelling** Background summary. *10 min.* Y Sim Technical Presentation. 20 *min.* P Klepac Discussion. 25 *min.* IVIR-AC FPs: A Hogan, S Silal, **SY Kim** SAGE/ SAGE WG FP: G Leung	· Feedback and additional comments with regards to implementation of the vaccination impact estimation methods · IVIR-AC recommendations on effective communication of updated target estimates	**55 min**
14:05	**Wrap-up** S Silal, Chair	Summary of the day's findings and request any follow-up from WHO Secretariat/IVIR-AC FPs for a closed session	**5 min**
14:10	**Closed sessions**	Closed session discussion/finalization of recommendations among IVIR-AC focal points of the day's sessions	**60 min**
15:10	**End of day**		

Day 2: Tuesday, 02 September 2025 (CEST)

Time	Session	Purpose of session, target outcomes and questions for IVIR-AC	Duration
12:00	**Recap** S Silal, Chair	Recap of the previous day and objectives for the day	**10 min**
12:10	**Session 3: Immunization coverage estimates - subnational estimates for priority countries and cohort monitoring** Background summary. *10 min.* C Danovaro Technical Presentation. *10 min.* TBD Discussion. *20 min.* IVIR-AC FPs: **A Portnoy**, B Moss, M Sheel, XY Wang	1. Considering the ongoing data triangulation exercises, and the initial experience with DRC data, notably limited contextual information for each province at the global level and no mechanisms to collect such data: a. Does IVIR-AC support the proposed plan to identify and evaluate criteria necessary to estimate subnational vaccine coverage at the administration 1 level, including estimates of uncertainty? b. What potential risks does IVIR-AC foresee? c. Would criteria need to be set for stopping admin1 estimates? 2. After reviewing initial data from the electronic Joint Reporting Form for immunization (eJRF) on delayed vaccination and examples of cohort monitoring: a. Does IVIR-AC support the proposed plan to identify and evaluate approaches to monitor vaccination coverage and timeliness in cohorts of children, including the data requirements and analytical methods?	**40 min**
12:50	**Break**		**10 min**
13:00	**Session 4: Modelling Pertussis Burden & Vaccination Strategies** Background summary. *10 min.* M Marti, S Shendale Technical Presentation- "DTP Boost Vaccination Strategy Tool", modelling the health and economic impact of introducing DTP-containing vaccine booster doses. *20 min.* R Hounsell, S Silal Discussion. *20 min.* IVIR-AC FPs: S Flasche, A Hogan, R Aggarwal SAGE/ SAGE WG FP: A Scott	• Question 1: DTP Boost Use & Dissemination - Provide feedback on the scope and methodology of the DTP Boost tool, and recommendations for onward use and dissemination of the tool, including integration into the WHOL vaccine evidence compendium. • Question 2: Calibration & Burden - How to overcome challenges with calibration where reliable estimates of burden or reported incidence are not available or not in line with country experience? Should functionality be added for user-uploaded seroprevalence data to help a country with calibration? • Question 3: Estimating Impact - With the growing interest in diphtheria, how to put a value on increased population protection as a measure (ie potential to avert or reduce an outbreak) when there are no endemic cases to get an immediate benefit measure?	**70 min**
13:50	**Wrap-up**	Summary of the day's findings and request any follow-up from WHO Secretariat/IVIR-AC FPs for a closed session	**10 min**
14:00	**Closed sessions**	Closed session, discussion/finalization of recommendations among IVIR-AC focal points of the day's sessions	**60 min**
15:00	**End of day**		

Day 3: Wednesday, 03 September 2025 (CEST)

Time	Session	Purpose of session, target outcomes and questions for IVIR-AC	Duration
12:00	**Recap** S Silal, Chair	Recap of the previous day and objectives for the day	**10 min**
12:10	**Session 5: WHO guidance to translate modeling to support evidence-informed decision making for immunization** Background summary. *10 min.* Y Sim, P Lambach Technical Presentation. 20 min. A Sbarra Discussion. *25 min.* IVIR-AC FPs: M Sheel, H Habib, XY Wang	• Question 1: As the document is intended to be a resource to decision-makers, is the content, perspective, and tone of the writing appropriate (i.e., not too technical, while still being informative)? • Question 2: Given the document's intended perspective and audience, would the technical chapter on modeling process (currently Chapter 3) be better suited as a separate online resource? If it should remain in the main document, how might we restructure it to better address the needs of decision makers • Question 3: Is the current format of the document, including plans for an online appendix, appropriate? • Question 4: How can individual resources (i.e., guidance document, online web appendix, executive summary) as part of the overall package of material be most synergistic with one another?	**55 min**
13:05	**Break**		**5 min**
13:10	**Session 6: WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS)** Background summary. *10 min.* R Hutubessy, J. Van Holten Technical Presentation. *10 min.* S. Omer, G Pitzer/C Wenger Discussion. *20 min.* IVIR-AC FPs: K Leung, A Portnoy, SY Kim SAGE/ SAGE WG FP: Saad Omer	Feedback from IVIR-AC on draft final results of MMC-TAS in the context of SAGE deliberations, specifically on: • the implementation of the IVIR-AC February 2025 recommendations • the harmonization of the data including the interpretation of potential outliers from the different models • how to interpret and translate the multi-model results including uncertainty for deliberations of the SAGE WG to support their policy recommendations	**40 min**
13:50	**Break**		**10 min**
14:00	**Session 7: Novel matrix for valuing combination vaccines.** Background summary. *10 min.* M Hasso-Agoposowicz Technical Presentation. 10 min. TBD Discussion. *25 min.* IVIR-AC FPs: S Flasche, H Habib, M Sheel	• Does the IVIR-AC agree that the current value drivers and metrics to assess the value of novel combination vaccines are not sufficiently comprehensive? • Would the benefits/risks, value drivers or metrics proposed by the PATH/WHO framework help mitigate this challenge? • How should we encourage the use of prioritized value drivers and associated metrics by analysts and decision makers to enhance the comprehensiveness of combination vaccine evaluation?	**45 min**
14:45	**Wrap-up**	Summary of the day's findings and request any follow-up from WHO Secretariat/IVIR-AC FPs for a closed session	**5 min**
14:50	**Closed sessions**	Closed session, discussion/finalization of recommendations among IVIR-AC focal points of the day's sessions	**90 min**
16:20	**End of day**		

Day 4: Thursday, 04 September 2025 (CEST)

Time	Session	Purpose of session, target outcomes and questions for IVIR-AC	Duration
12:00	**Recap** S Silal, Chair	Recap of the previous day and objectives for the day	**10 min**
12:10	**Session 8: Stockpiling and vaccination strategies for Ebola response: insights from Integrated epidemiological and epidemic modelling** Background summary. *10 min.* A Costa Technical Presentation. *10 min.* Imperial College Discussion. *20 min.* IVIR-AC FPs: K Leung, **A Hogan**, R Aggarwal SAGE/ SAGE WG FP: R Grais	IVIR-AC discusses presentation, clarifies on content and acknowledges main issues Key input sought by the Imperial College team includes: 1) Are there any aspects of the mathematical or economic model structure that you think are not appropriate to address the questions of interest? 2) Are the epidemiological and economic parameter ranges we are considering appropriate (and if not, what should we use)? In particular are we considering too extreme scenarios? Or not extreme enough? 3) How should we measure whether a given stockpile strategy is successful? E.g. is "having enough doses to respond to demand" sufficient? What other endpoints should we consider? And what level of risk should we consider acceptable in designing the stockpile, i.e. what fraction of scenarios do we want to be covered for? E.g. 95%? 99%? 4) inputs on effective strategies for communicating the work, both the technical details of our approach and the results	**40 min**
12:50	**Break**		**10 min**
13:00	**Session 9: Malaria multi-model comparison of prioritized interventions (M3CPI)** Background summary. *10 min.* V Moorthy, R Hutubessy Technical Presentation. *10 min.* M. Golumbeanu Discussion. *20 min.* IVIR-AC FPs: S Flasche, K Leung, B Moss SAGE/ SAGE WG FP: K Neuzil, K Mullholland	Feedback from IVIR-AC on the multi-model comparison methodology, result communication in the context of MPAG/SAGE deliberations, translation into policy guidance, and future project directions	**40 min**
13:40	**Wrap-up**	Summary of the day's findings and request any follow-up from WHO Secretariat/IVIR-AC FPs for a closed session	**10 min**
13:50	**Closed sessions**	Closed session, discussion/finalization of recommendations among IVIR-AC focal points of the day's sessions	**60 min**
14:50	**End of day**		

Day 5: Friday, 05 September 2025 (CEST)

Time CEST	Session	Purpose of session, target outcomes and questions for IVIR-AC	Duration
12:00	**Introduction** S Silal, Chair	Recap of the previous day and objectives for the day	**10 min**
12:10	**Closed Session**	Closed session with all IVIR-AC members	**1h 50 min**
14:00	**End of day**		

World Health Organization

Meeting of the Advisory Committee on Immunization and Vaccines-Related Implementation Research (IVIR-AC)
Microsoft Teams
1 to 5 September 2025

List of participants

Participating Advisory Committee Members

Rakesh Aggarwal, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, **India**

Habib Hasan Farooqui, College of Medicine, Qatar University, Doha, **Qatar** (invited as ad hoc expert)

Stefan Flasche, Centre for Mathematical Modelling of Infectious Diseases (CMMID), London School of Hygiene & Tropical Medicine, London, **UK**

Alexandra Hogan, School of Population Health, University of New South Wales, Sydney, **Australia**

Sun-Young Kim, Global Health, School of Public Health, Seoul National University, Seoul, **Republic of Korea**

Kathy Leung, University of Hong Kong, Hong Kong, **People's Republic of China**

William Moss, International Vaccine Access Center, Johns Hopkins Bloomberg School of Public Health, Baltimore**, USA**

Allison Portnoy, Boston University School of Public Health, Boston, **USA**

Meru Sheel, University of Sydney, Sydney, **Australia**

Sheetal Silal, Modelling and Simulation Hub, Africa (MASHA), University of Cape Town, Cape Town, **South Africa**

Xuan-Yi Wang, Shanghai Medical College, Fudan University, Shanghai*,* **People's Republic of China** (invited as ad hoc expert)

SAGE WG Focal Points

Yemane Berhane, Addis Continental Institute of Public Health (ACIPH), Addis Ababa, **Ethiopia**

Rebecca Grais, Pasteur Network, Paris, **France**

Gabriel Leung, University of Hong Kong, Hong Kong, **People's Republic of China**

Kim Mullholland, Murdoch Children's Research Institute, Victoria, **Australia**

Kathleen Neuzil, Independent Consultant, Atlanta, **USA**

Hanna M. Nohynek, National Institute for Health and Welfare THL, Helsinki, **Finland**

Saad Omer, Peter O'Donnell Jr. School of Public Health, Dallas, **USA**

Anthony Scott, KEMRI-Wellcome Trust Research Programme in Kilifi, **Kenya**

Presenters/participants

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Anne Cori, Imperial College London, London, **UK**

Frédéric Debellut, PATH, Geneva, **Switzerland**

Monica Golumbeanu, Swiss Tropical and Public Health Institute, **Switzerland**

Katharina Hauck, Imperial College London, London, **UK**

Rachel Hounsell, Green Templeton College, University of Oxford, Oxford, **UK**

Maria Knoll, Johns Hopkins Bloomberg School of Public Health, Baltimore**, USA**

Gemma Nedjati, Imperial College London, London, **UK**

Clint Pecenka, PATH, Seattle, **USA**

Virginia Pitzer, Yale School of Public Health, New Haven, **USA**

Emilie Pothin, Swiss Tropical and Public Health Institute, **Switzerland**

Alyssa Sbarra, Johns Hopkins Bloomberg School of Public Health, Baltimore**, USA (Presenter, Rapporteur)**

Janetta Skarp, Imperial College London, London, **UK**

Brian Wahl, Yale University, New Haven, **USA**

Peter Winskill, Imperial College London, London, **UK**

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Roy Burnstein, Bill and Melinda Gates Foundation (BMGF), Seattle, **USA**

Long-Sheng Chen, Centers for Disease Control, Taiwan, **China**

Somyoung Cho, International Vaccine Institute**, Republic of Korea**

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Anna-lea Kahn, Immunization, Vaccines & Biologicals, World Health Organization, **Switzerland**

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Mitsuki Koh, Immunization, Vaccines & Biologicals, World Health Organization, **Switzerland**

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World Health Organization

Last IVIR-AC Report

World Health Organization

Last IVIR-AC Report can be found below:

Lambach, P., Silal, S., Sbarra, A. N., Koh, M., Aggarwal, R., Farooqui, H. H., Flasche, S., Hogan, A. B., Kim, S. Y., Leung, K., Moss, W. J., Portnoy, A., Sheel, M., & Wang, X. Y. (2025). Report from the World Health Organization's immunization and vaccines-related implementation research advisory committee (IVIR-AC) meeting, virtual gathering, 17-21 February 2025. *Vaccine*, *61*, 127384. https://doi.org/10.1016/j.vaccine.2025.127384

World Health Organization

Background information to the sessions

World Health Organization

Session 1: Immunization implementation Research in WHO African region

IVIR-AC Pre-briefing meeting – WHO African Region

IVIR-AC Meeting 2025

- For the September 2025 IVIR-AC, WHO AFRO has proposed two presentations:
  A. A proposed framework for Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE)
  B. IA2030 SP7 Scoping project for Vaccine and Immunization Implementation Research Strategy and Prioritization

A

A proposed framework for Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE)

A Proposed Framework for Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE)

There is an urgent need to transform immunization programmes in the African Region into agile learning systems where implementation strategies of vaccination efforts are systematically and rapidly incorporated into policies and practice within and across contexts to drive performance improvement.

Implementation strategies are those ‘methods, practices, innovations, or techniques’ that are deliberately and purposively used to enhance the implementation outcomes of vaccination efforts.

Implementation strategies are important because they represent the “how to” of promoting/integrating evidence-based innovations in routine practice settings.

A Proposed Framework for Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE)

- Systematically documenting the implementation strategies of vaccination efforts can aid in their dissemination across various contexts.
- DRIVE is a framework to guide the documentation and reporting of vaccination efforts.
- It is developed by adapting existing frameworks for the immunization context.
- This framework elicits granular details of the core elements of the implementation strategies to facilitate optimal replication.
- It relies on co-creation with stakeholders.

DRIVE framework has eight sections

Adamu, A. A., Petu, A., Masresha, B. G., Bathondoli, B., Jalo, R. I., Ndwandwe, D., & Wiysonge, C. S. (2025). Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE) framework for fostering systems learning to enhance cross-context replication in immunization programmes. *Discover Public Health*, *22*(1), 1-8.

- The name of the implementation strategy
- The implementation problem
- The context
- Strategy definition
- The mechanism of action of the implementation strategy
- The implementation strategy specifications and results
- Facilitators and barriers of successful implementation of the strategy
- Additional information

Questions for IVIR-AC (updated 02.07.2025)

- Does IVIR-AC consider the DRIVE framework suitable for conducting case studies in immunization programmes to document implementation strategies that worked or “did not work”? How would the DRIVE framework provide the highest utility for immunization programmes in Africa?
- What recommendations can IVIR-AC propose to immunization programme managers and researchers to promote the use of the DRIVE framework?
- Beyond the DRIVE framework, what additional strategic role can play to provide methodological guidance in implementation research for AFRO to promote faster uptake and integration of evidence-based innovations?

B

IA2030 SP7 Scoping project for Vaccine and Immunization Implementation Research Strategy and Prioritization

IA2030 SP7 Scoping project for Vaccine and Immunization Implementation Research Strategy and Prioritization

There is need for more responsive research on vaccine/programme implementation and innovation ecosystem for immunization program decision-makers at regional and national levels.

3 phased multi-year project discussed with Wellcome Trust to enable innovation and strengthen research on implementation for immunization, in context of IA2030 SP7 objectives on Research & Innovation.

Phase 1 = **Scoping project** aiming to examine and characterize the current immunization research ecosystem and how implementation research fits within it, utilizing an innovative immunization intervention as a test case.

Phase 2 = prioritization, agenda setting, and capacity building.

Phase 3 = Evidence generation & translation.

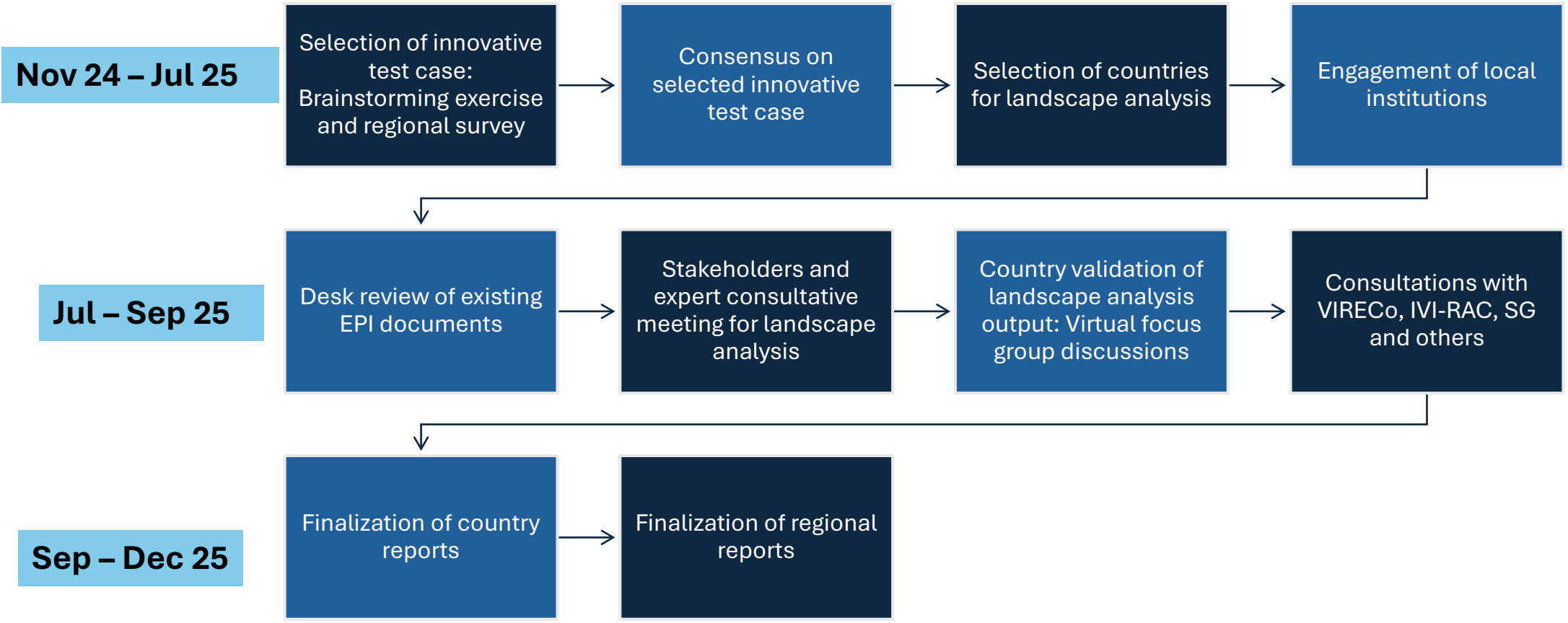
Workstreams of the IA2030 SP7 Scoping Project

Workstream 1: To undertake a **taxonomy exercise** to enable classification of vaccine-related research and associated stakeholders. This will include defining nomenclature, types of evidence for different lines of inquiry for different outcomes, use cases and varying stakeholder needs. (SEARO).

Workstream 2: To conduct a **multi-country landscape analysis** examining challenges in evidence-based decision-making and existing processes which can determine the implementation research needed to inform policy and practice. (AFRO)

Workstream 3: To implement **regional-level consultations,** followed by a **final validation workshop,** allowing broader expert input and perspective to inform the above two workstreams, while building momentum for regional partnership. (AFRO)

Road map: Workstream 2 of the scoping project



Questions for IVIR-AC (1/2)

Does IVIR-AC agree with the proposed methodologies for the prioritized implementation research questions addressing country-level gaps and needs regarding the reference innovative test case?

Are there alternative methodologies that IVIR-AC would like to propose for consideration?

What advice can IVIR-AC provide to ensure quality assurance, use of an appropriate analytical framework, and ethical consideration for the proposed methodologies?

Questions for IVIR-AC (2/2)

What kind of partnership models can national immunization programmes leverage to address the implementation research questions using the proposed methodologies?

Does IVIR-AC consider the likely outputs of these research questions and methodologies to be specific to a single country's context or is there a potential value beyond the implementing country such as for policy and practice recommendations in other countries or to inform global level product development (i.e., preferred product characteristics)?

What criteria does IVIR-AC recommend to determine which country-level implementation research question should be included in a regional-level research agenda for optimal coordination of funding, dissemination, and knowledge translation?

Thank you

Overview of WHO-led Immunization Implementation Research Activities in the African Region

IVIR-AC Session

1 September 2025

Agenda

01	Introduction
02	IA2030 SP7 Scoping Project
03	Mainstream Project
04	Summary of key messages

Immunization programs in the African region continue to face complex challenges.

The current realities

Immunization coverage (for multiple antigens) continues to lag across many countries.

Immunization schedules continue to expand (covering adolescents and adults).

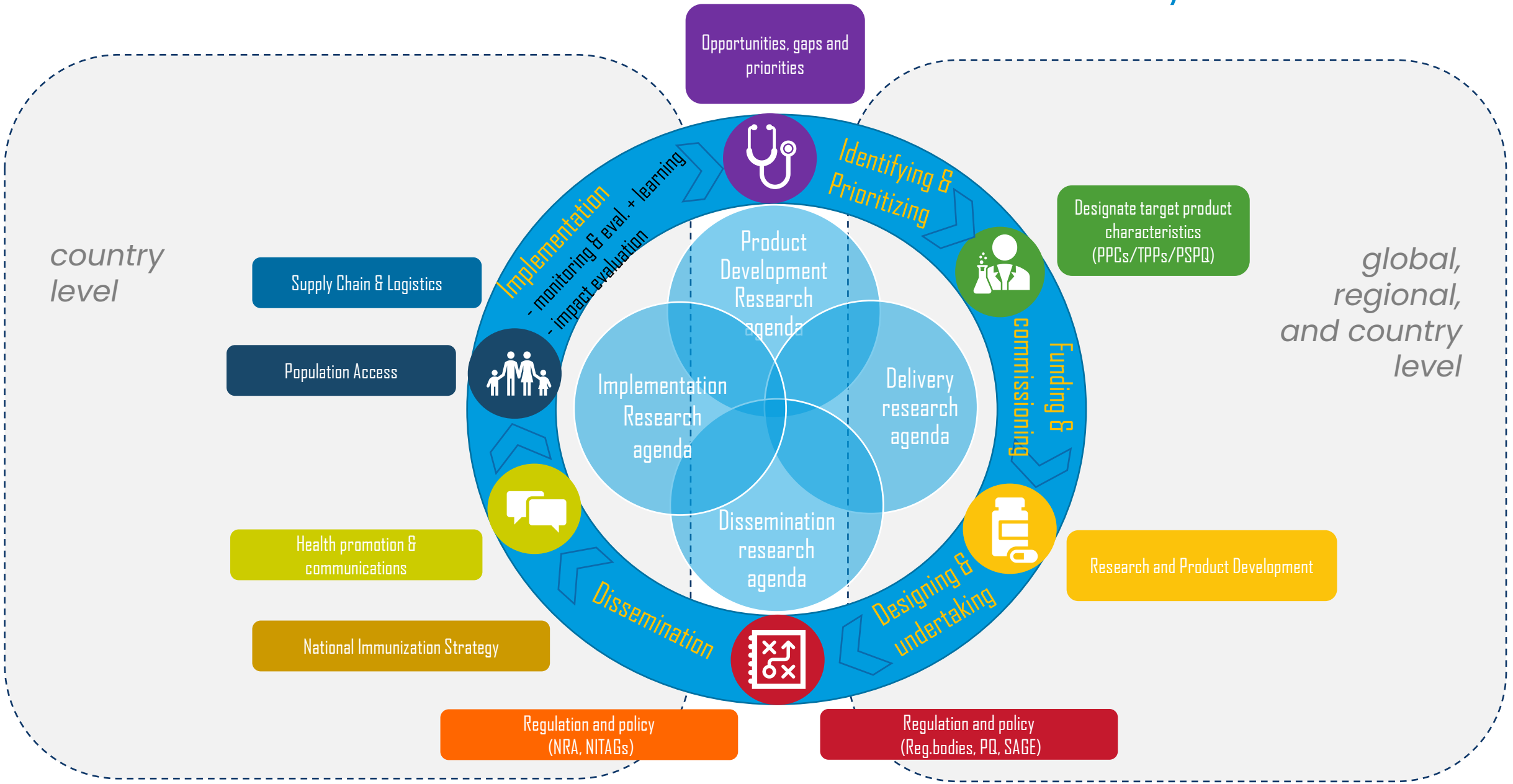
Global health funding is dwindling due to policy shifts.

The problem

- '**One size fits all**' or "**trial and error**" strategies for delivering vaccination services across communities.
- Less attention to **local evidence** undermines the effective implementation of immunization strategies.
- Inadequate focus on **innovative programme adaptation** to build resilience in this era of dwindling global health financing.

context

There is an urgent need to pay closer attention to implementation research in the broader immunization research ecosystem



Implementation Research in a resource-constrained global health context: *five new opportunities*

Strengthen informed **decision-making** using implementation evidence.	More targeted, efficient and impactful policies, practices, and products
Enhance country-driven (bottom-up) **research agendas** coordinated at regional level.	Most critical evidence is generated and used where & when needed most
Ensure optimal and equitable **use of resources** for research in prioritization processes.	Greater sensitivity to cost concerns and efficient use of resources
Enhance **local investment** and **country capacity** to conduct research.	Rapid, tailored, "home grown" responses with greater sustainability & ownership
Improve **cost effectiveness** and **program efficiency**	Strategic use of resources for greater returns on investment

Ongoing WHO-led immunization implementation research activities in the African region

The SP7 Scoping Project

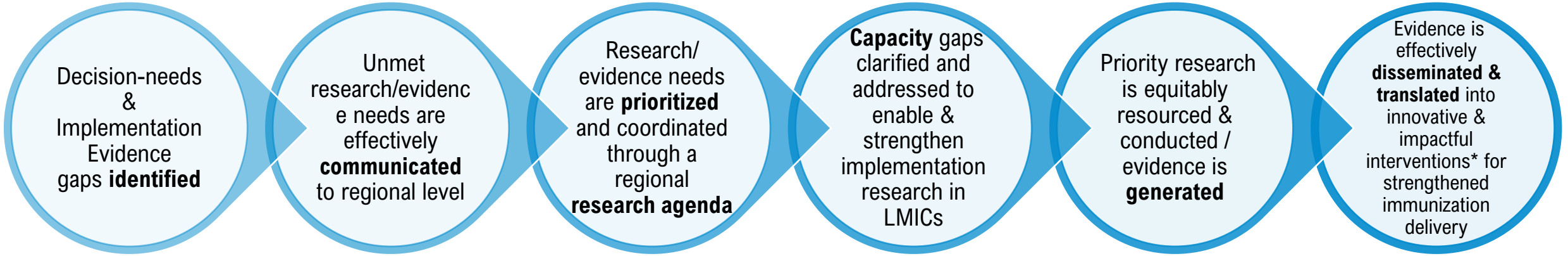
1. To undertake a **taxonomy exercise** to classify different types of vaccine-related research
2. To conduct a **multi-country landscape analysis** assessing decision-making processes using a reference test case.
3. To initiate and leverage a dynamic **community of immunization research experts.**

The mainstream project

1. Assess knowledge gaps and priorities regarding immunization coverage and equity.
2. Enable the integration of learning through embedded implementation research.
3. Scale up learning through embedded implementation research.
4. Improve the use of evidence to guide policy development and implementation of programmes.

objectives

Initiate regional pilot to demonstrate & strengthen implementation evidence pathway: enhance country capacity to confront existing and emerging challenges.



Phase 1
2025

SCOPING NEED

Examine & characterize the vaccine / immunization research ecosystem:

1. Taxonomy & stakeholders (SEARO)
2. Landscape analysis of strengths & weaknesses at beginning of pathway (AFRO) + Test case to assess types of evidence needed & capacity gaps (AFRO)
3. Community of experts (GLOBAL)

Phase 2
2026-2028

BUILDING INFRASTRUCTURE

Develop/enhance processes for regional vaccine evidence prioritization and research agenda setting + capacity building

Pilot in African region

Phase 3
2028-2030

DRIVING IMPACT

Generate, disseminate and translate needed evidence into impactful policies, practices, and products

Pilot in African region

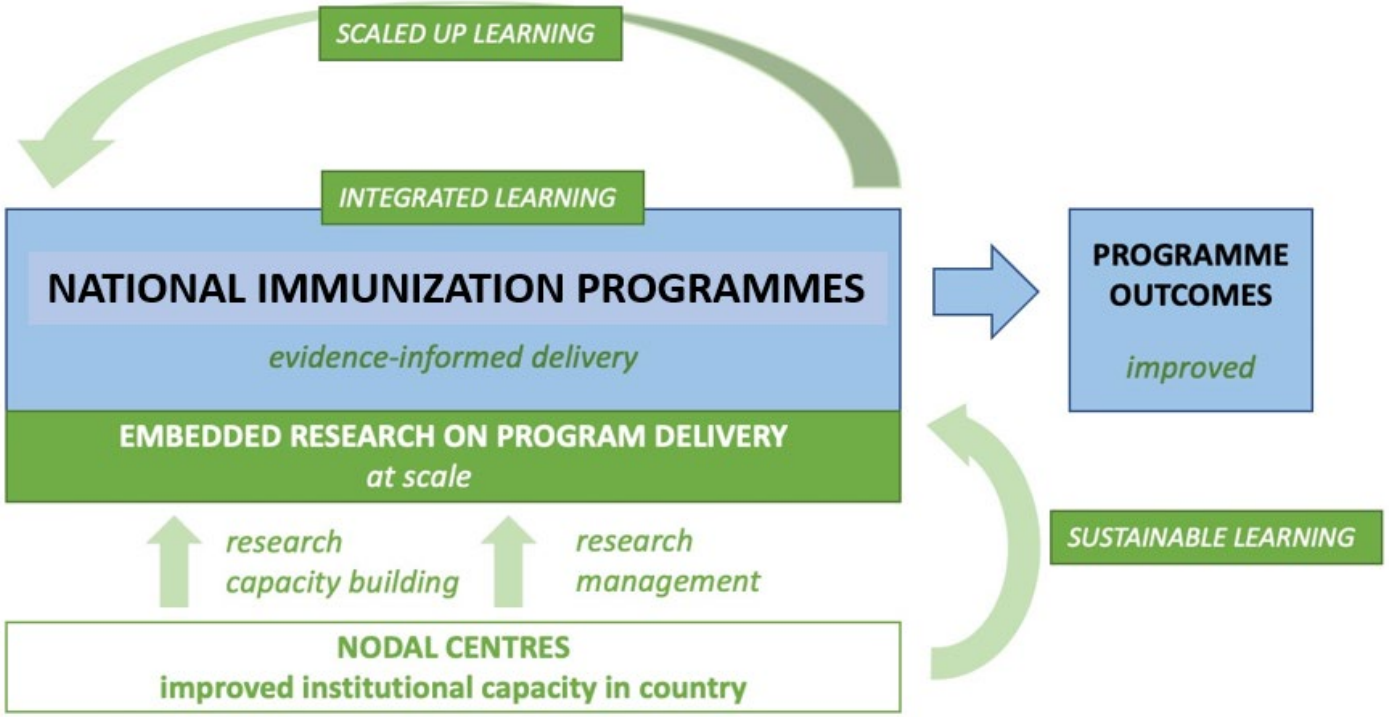
The MAINSTREAM initiative (2023-2025)

Overview

AHPSR / IVB / Gavi collaboration as part of Gavi 5.0 Zero Dose SFA

Goal:

- Support and improve the delivery of GAVI country programmes by institutionalizing learning by mainstreaming embedded implementation research in country immunization programmes



The MAINSTREAM initiative (2023-2025)

Process

Mentor institute convening and mentorship role

Prioritization

- Evidence review
- Immunization stakeholder prioritization workshop

What is preventing our achievement in immunization coverage and equity?

IR projects

- Open call for IR teams to tackle research priorities
- IR teams selected by mentor institutes + others

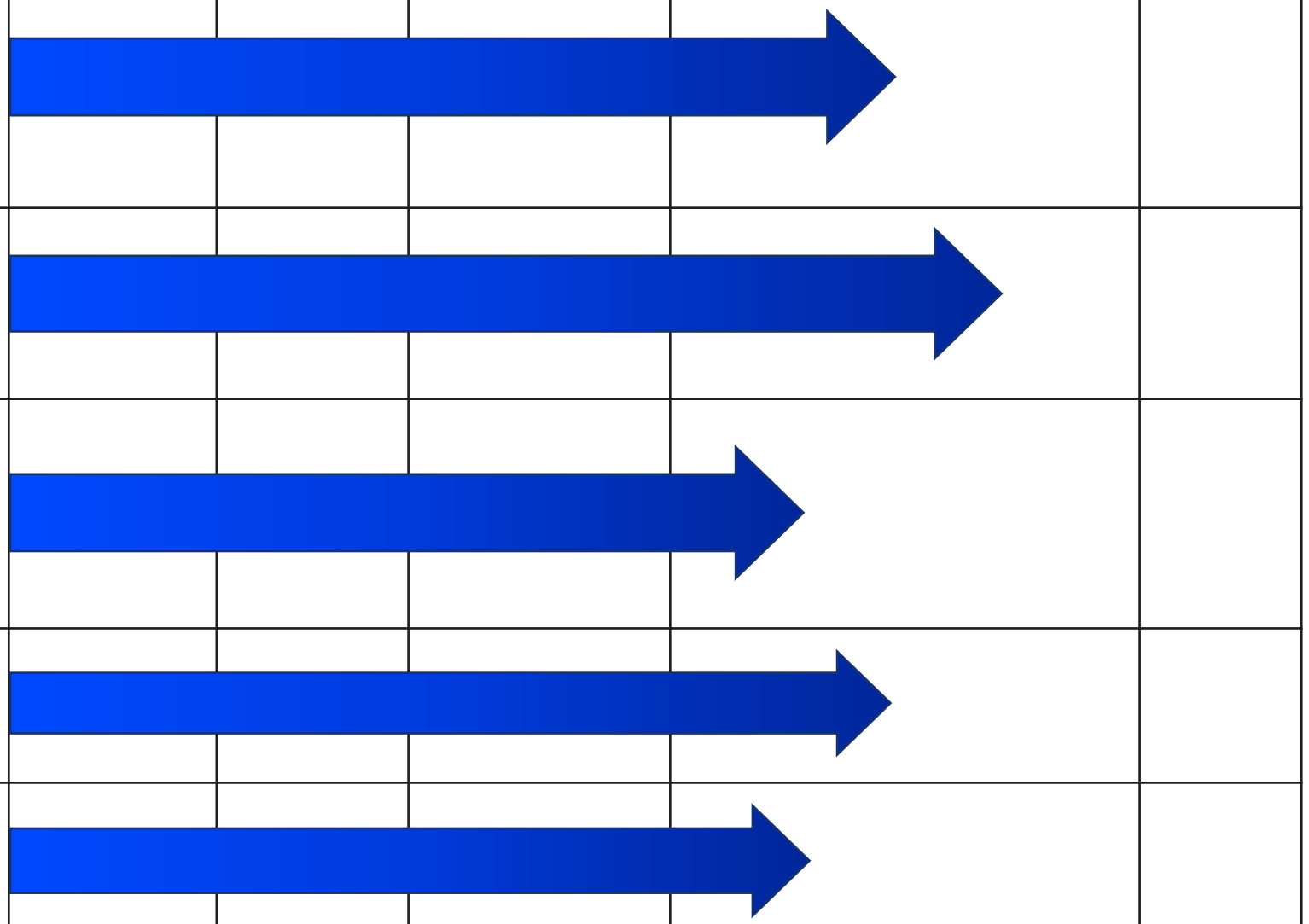
IR implementation and support

- Protocol development workshop with IR teams
- Mentorship and supervision from mentor institute

Plan of action

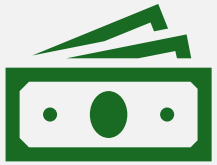
- Review emergent findings with local stakeholders
- Dissemination, communication and action plan jointly between mentor institutes, IR teams + others

Mentor Institute	Priority setting workshop	Call local IR teams selected	Protocol development workshop	IR projects implemented	Plan of action
CAMEROON - Centre for Development of Best Practices in Health (Centre pour le Développement des Bonnes Pratiques en Santé)					
GHANA - Center for Health Policy and Implementation Research, University of Health and Allied Sciences					
MADAGASCAR - National Institute for Public and Community Health (Institut National de Santé Publique et Communautaire)					
MALAWI - Blantyre Institute for Community Outreach					
MOZAMBIQUE - National Institute of Health (Institute Nacional de Saúde)					



Regional challenges with institutionalizing implementation research in immunization

INSUFFICIENT HUMAN RESOURCES

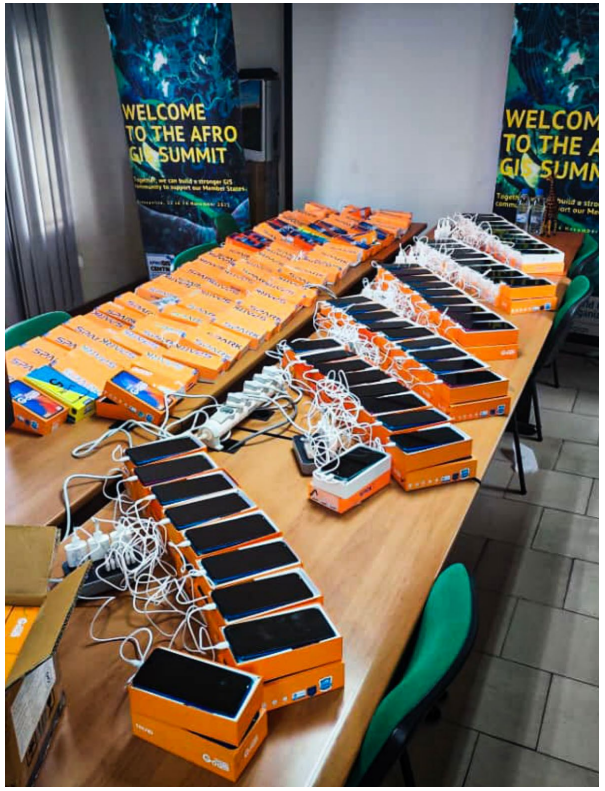


INADEQUATE FUNDING

INADEQUATE TECHNICAL RESOURCES

Summary of key messages

- The field of implementation science emerged specifically in response to **know-do gaps** in healthcare settings and offers tools that can be used to **strengthen systems learning and decision-making** in immunization programs, **making vaccines more impactful**.
- Enhancing knowledge and skills in implementation science among immunization stakeholders will enable immunization programs to take advantage of implementation research better. This can be achieved through:
  - ✓ Stronger collaboration with IVIR-AC can improve the use of appropriate and standardized methodological processes for implementation research. Tools development and **upskilling immunization programme implementers are** essential.
  - ✓ WHO AFRO needs to play a stronger **coordination role**, especially in vaccine implementation, research agenda setting, prioritization, and mobilization of resources from new avenues to address **evidence needs and gaps**.



A Framework for documenting and reporting implementation strategies of vaccination efforts

Technical presentation during the IVIR-AC Meeting

1 September 2025

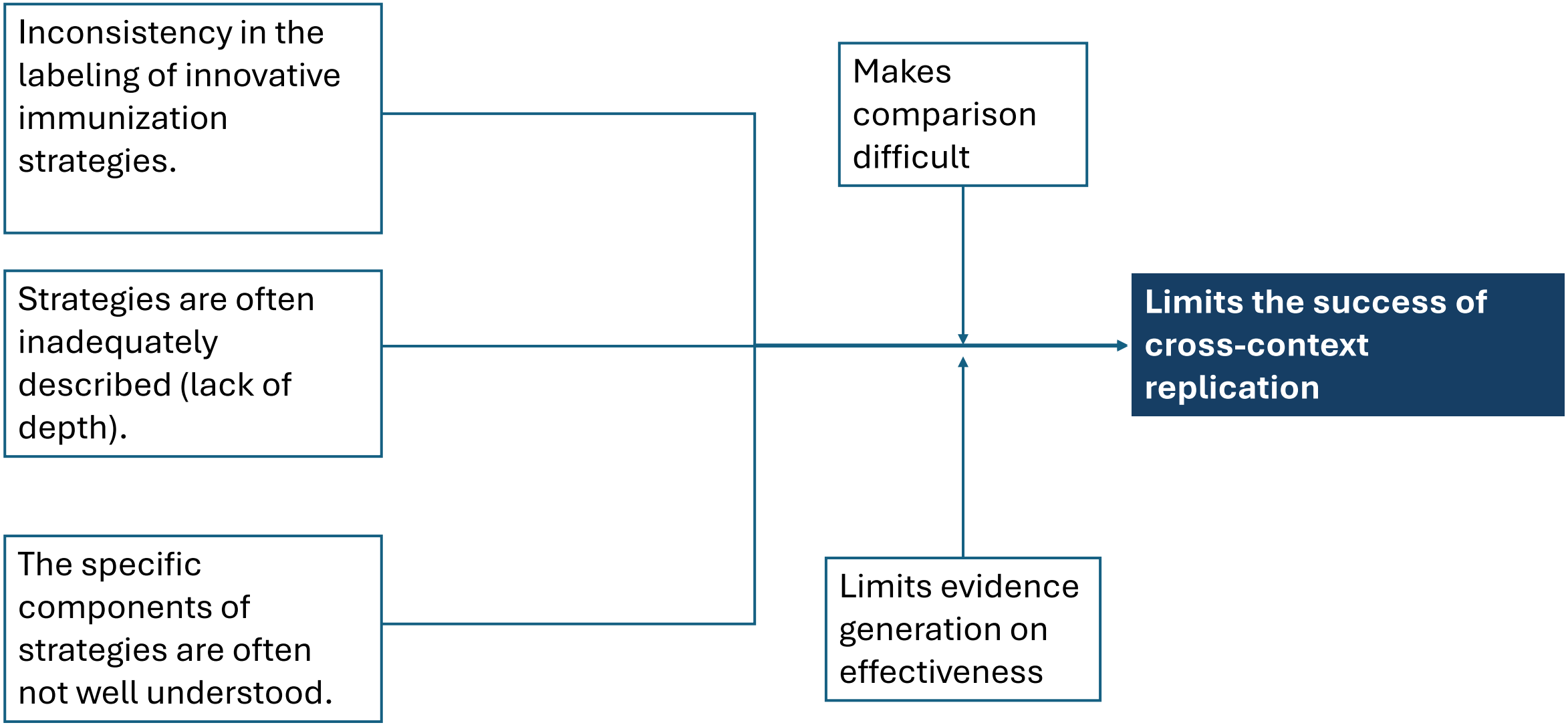
Routine vaccination has substantial public health benefits.

- Vaccines are one of the most impactful evidence-based interventions in public health.
- Between 1974 and 2024, the Expanded Program on Immunization (EPI) is estimated to have averted 49 million deaths among children under five in the African region, contributing to a 52% reduction in child mortality.
- Immunization programs are evolving within the IA2030 framework to meet broader needs, extending beyond infancy.

Countries are developing and sharing several innovative strategies to strengthen immunization programs and improve routine vaccination coverage.

- Several countries are innovating best practices and techniques to improve vaccination along the life course in their local settings, which can be beneficial to others. These innovations are often shared during peer learning engagements.
- Peer learning is critical for strengthening immunization, facilitating cross-context knowledge exchange.
- Peer learning in immunization does occur between countries, between subnational entities, and even between health facilities.
- Several learning platforms have emerged (e.g., Gavi's ZDLH. An example of a cross-country peer learning platform is the EPI managers' meeting.

There are limitations in how innovative practices from countries are shared, which can impact their effective replication in other settings.



There is a need for a common framework for documenting and reporting innovative practices from countries during peer learning.

- Countries make substantial investments to develop and roll out various kinds of innovative practices to improve vaccination efforts.
- In this era of funding shortages in global health, dissemination deserves closer attention to minimize wastage.
- There is a need to develop a comprehensive framework that is specific to vaccination efforts in immunization programs, leveraging an implementation science lens.
- Implementation strategies are those ‘methods, practices, innovations, or techniques’ that are deliberately and purposively used to enhance the implementation outcomes of vaccination efforts.
- Proctor et al in 2013 proposed some recommendations for specifying and reporting implementation strategies.

Developing the **Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE) framework** for immunization programmes

A PubMed search was conducted to find any relevant frameworks.

Google Scholar and a free-text Google search were also conducted.

“Guide for Documenting and Sharing Best Practices in Health Programmes” was identified. This guide was developed in 2008.

Proctor et al’s recommendations were adapted to develop the DRIVE framework.

The DRIVE Framework has eight main sections

S/No	Sections	Descriptions
1	The name of the implementation strategy	Unambiguous and should be able to imply whether its discrete or multicomponent.
2	The implementation problem	Issue(s) that the strategy intends to address
3	The context	Areas or settings of implementation
4	Strategy definition	general sense of what the implementation strategy entails
5	The mechanism of action of the implementation strategy	How the strategy works
6	The implementation strategy specifications and results	Granular details of the strategy
7	Facilitators and barriers of successful implementation of the strategy	Factors that contributed to the success or failure
8	Additional information	Any details that do not fit within earlier sections but relevant to the implementation strategy

Adamu, A. A., Petu, A., Masresha, B. G., Bathondoli, B., Jalo, R. I., Ndwandwe, D., & Wiysonge, C. S. (2025). Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE) framework for fostering systems learning to enhance cross-context replication in immunization programmes. *Discover Public Health*, *22*(1), 1-8.

Conclusion

- It is essential to strengthen the granularity of documentation of implementation strategies of vaccination efforts to enhance learning and replication in immunization programs.
- Adequate documentation of implementation strategies of vaccination efforts can foster rapid spread across settings and be sustainably integrated into policies and practices.

Questions for IVIR-AC

Does IVIR-AC consider the DRIVE framework suitable for conducting case studies in immunization programmes to document implementation strategies that worked or “did not work”? How would the DRIVE framework provide the highest utility for immunization programmes in Africa?

What recommendations can IVIR-AC propose to immunization programme managers and researchers to promote the use of the DRIVE framework?

Beyond the DRIVE framework, what additional strategic role can IVIR-AC play to provide methodological guidance in implementation research for the African region to promote faster uptake and integration of evidence-based innovations in immunization programmes?

Session 1: Immunization Implementation Research in the WHO African Region

Dr Lynda Rey, PhD.
Coordinator, Essential Program in Immunization and PHC

Leveraging implementation research to address immunization programs' complex challenges in the African region: *a realist approach*

Problem statement

Immunization coverage (for multiple antigens) continues to lag across many countries

"The glass ceiling for coverage"

Immunization schedules and targets continue to expand (life-course vaccination)

Global health funding is dwindling due to policy shifts.

Key implementation issues in immunization delivery

- **"Over-reliance on "one-size-fits-all"** approaches limits effectiveness in diverse community settings
- **Insufficient use of context-specific data** weakens strategy design and reduces impact on immunization outcomes
- **Limited innovation and adaptation** in response to changing needs and funding constraints undermine system resilience
- **Delayed translation of research into practice** creates a gap that hinders timely improvements in immunization delivery, reducing opportunities to respond effectively to emerging challenges.

Two technical presentations by WHO-AFRO Vaccine Preventable Disease Programme

A. An overview of WHO-led immunization implementation research activities in the African region

B. A proposed framework for Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE)

Questions to IVIR-AC

Does IVIR-AC consider the DRIVE framework suitable for conducting case studies in immunization programmes to document implementation strategies that worked or “did not work”? How would the DRIVE framework provide the highest utility for immunization programmes in Africa?

What recommendations can IVIR-AC propose to immunization programme managers and researchers to promote the use of the DRIVE framework?

Beyond the DRIVE framework, what additional strategic role can IVIR-AC play to provide methodological guidance in implementation research for the African region to promote faster uptake and integration of evidence-based innovations in immunization programmes?

Thank you

Published background documents for this session

Adamu, A.A., Petu, A., Masresha, B.G. *et al.* Documenting and Reporting Implementation Strategies of Vaccination Efforts (DRIVE) framework for fostering systems learning to enhance cross-context replication in immunization programmes. *Discov Public Health* **22**, 34 (2025). https://doi.org/10.1186/s12982-025-00417-9

World Health Organization

Session 2: IA2030 Impact Modelling

Background materials for the IVIR-AC session, Sept 2025

Dr Petra Klepac, So Yoon (Yoonie) Sim, Dr Austin Carter, and
Dr Raymond Hutubessy

Summary: A key part of vaccine impact estimates methodology is imputing the vaccine impact in WHO Member States for which modelling results are not available. Following the recommendations from the previous IVIR-AC meeting we validate the methodology for the estimates going forward. This document contains descriptions of the two analyses used so far in IA2030 vaccine impact estimates, their validation using the measles simulated data, and a proposal for modelling vaccine estimates going forward.

1. Recommendations from the Feb meeting

- ✓ IVIR-AC supports the vaccine impact calculations using the **year-of-vaccination method**
- ✓ Given different methodologies, purposes, audiences, and timeframes, IVIR-AC **recommends adopting only relevant and appropriate methodologies from the EPI@50 exercise** to improve IA2030 estimates going forward.
- ✓ IVIR-AC recommends that methodologic updates **balance improved accuracy in estimates versus the practicality** of interpretation.
- ✓ IVIR-AC recommends examination of **the impact that changing methods will have on communication** of methods and results to stakeholders.
- ✓ To reduce overfitting and improve understanding of drivers of vaccine impact, IVIR-AC recommends **limiting the suite of potential statistical models** via expert-guided predictor selection.
- ✓ IVIR-AC supports **region- and income-specific model selection** and suggests that it may be possible to reduce the total number of combinations analyzed.
- ❑ IVIR -AC suggests that **additional validation exercises could include sub-setting VIMC results** for diseases with delayed expected reductions in burden, such as HPV, or quantifying sensitivity to variation in impact estimates from both VIMC measles models.
- ✓ IVIR-AC supports exploring the **use of SDI as a predictor** in statistical models.

Implementation

We have implemented the Year-of-Vaccination calculation, by first calculating the **impact ratio**, defined as the number of deaths averted per fully vaccinated persons over their lifetime, using the **Year-Of-Vaccination** methodology (Echeveria-Londono et al 2021, see Appendix A).

Following the IVIR-AC advice we consider a simpler set of models that consider YoV-impact in the extrapolation to non-VIMC countries. We consider the following models:

simple = cov0 + cov1 + cov2 + gini,
moderate = cov0 + cov1 + cov2 + cov3 + **sdi** + gini,
complex = cov0 + cov1 + cov2 + cov3 + gini + stunt + mat,
complex_sdi = cov0 + cov1 + cov2 + cov3 + **sdi** + gini + stunt + mat,
full_epi50 = cov0 + cov1 + cov2 + cov3 + gini + stunt + mat + water + phs

where the **impact predictors** are as defined in Table 1.

Table 1 Vaccine impact predictors most used in regression, their descriptions and sources.

Predictor	**Description**
cov0	log(coverage in the current year)
cov1	log(coverage with 1-year lag)
cov2	log(coverage with 2-year lag)
cov3	log(coverage with 3-year lag)
mat	Maternal mortality – maternal deaths from pregnancy or childbirth per 100,000 as reported by UNICEF
gini	Gini coefficient from Gapminder Foundation that measures income inequality within a nation and ranges from 0 (perfect equality) to 1 (perfect inequality, e.g. one person owes everything)
stunt	Stunting – proportion in under-5 yo with severe and moderate-to-severe growth stunting as reported by UNICEF
phs	Private health spending – private share of the total health spending as reported by Gapminder Foundation
water	Proportion of the population with access to at least a basic water source as reported by Gapminder Foundation
sdi	Composite index of development status provided by IHME defined as the geometric mean of: (i) total fertility under 25, (ii) mean education level for those aged 15 and over, and (iii) lag distributed income. SDI = 1 is the maximum.

Validation of extrapolation methods

As before, we use repeated cross-validation to validate the models.

The benefit of **K-fold cross-validation** is that we can split existing data into training and testing set. The model is estimated using the training set, and then its performance is evaluated using the testing set. In order to evaluate the model multiple times, the data is split into *k* groups; if *k* = 5, the data is split into 5 groups. The advantage of this particular method is that it generally results in less biased results than other methods.

The general algorithm of the procedure we are using here:

(i) Randomly shuffle the data set
(ii) Split the data into *k* groups
(iii) For each unique group:
   a. Take a group as a test data set
   b. Take other groups as training set
   c. Fit the model on the training set and evaluate it on the testing set
   d. Keep predicted and observed values, and performance metrics (RMSE, MAE, and R^2)

In repeated k-fold cross-validation these steps are repeated *n* times, where data is shuffled before each repetition in order to get a different split of the sample and get estimates of the prediction error and accuracy of the model.

Performance metrics

To assess the quality of the models used to geographically extrapolate vaccine impact we look at the following metrics: Root Mean Square Error (RMSE), Bayesian Information Criterion (BIC), Mean Absolute Error (MAE) and the coefficient of determination (R^2).

RMSE is the quadratic mean of the differences between observed and predicted values, or the standard deviation of the residuals. A value of 0 means that the predicted values perfectly match the observed values. Generally, RMSE values below 0.5 show reasonably good accuracy.

BIC is the model selection criterion that balances fit against complexity, and is useful for time-series analysis where overfitting is a concern. BIC = -2*log(L) + k + log(n) where L is the maximised likelihood, k is the number of the parameters and n is the sample size.

MAE is the average magnitude of absolute errors between predicted and observed values (it gives same weight to all errors and is less sensitive to outliers). MAE equal to 0 would mean a perfect prediction, and values below 0.2 are considered good. Values above 0.5 suggest the model is wrong over half of the times.

R^2 is the proportion of the variation in the dependent variable that is predicted by the

independent variable. It is defined as $R^2 = 1 - \frac{SS_{res}}{SS_{tot}}$ where SS_{res} and SS_{tot} are residual and total sum of squares, respectively. A perfect model will result in $R^2 = 1$, where a baseline model that always predicts the mean of the observed data would result in $R^2 = 0$. In general, an R^2 value of x% would imply that x% of the variability of the dependent variable is explained by the model (and that (100-x)% of the variability is still unaccounted for).

Results

Figure 1 shows the balance between parsimony and precision for the 5 considered models, using full measles simulations for EPI50 model and YoV-impact as the response variable (target) for the regression. The best model overall is the complex_sdi model with 8 predictors (including SDI), while the full_epi50 with 9 predictors (but no SDI) is the second-best performing model.

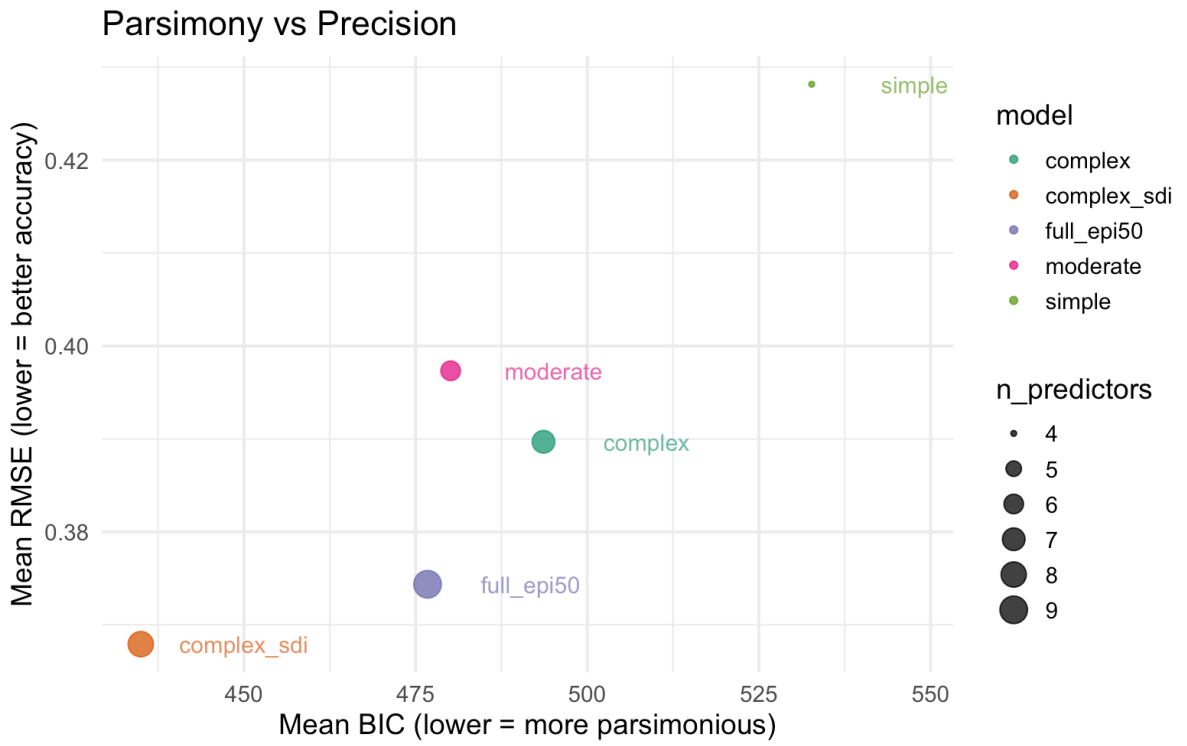


Figure 1 Mean RMSE vs mean BIC plot for the 5 models evaluated by the repeated k-fold cross validation. The size of the point indicates the number of predictors, ranging from 4 in the simple model to 9 in the full_epi50 model. Best performing model has 8 predictors (including SDI).

Figure 2 focuses on the top 3 performing models (complex model with SDI (8 predictors), full_epi50 model (9 predictors, no SDI) and complex model (7 predictors, no SDI) shows the standardised residuals and observed vs predicted values.

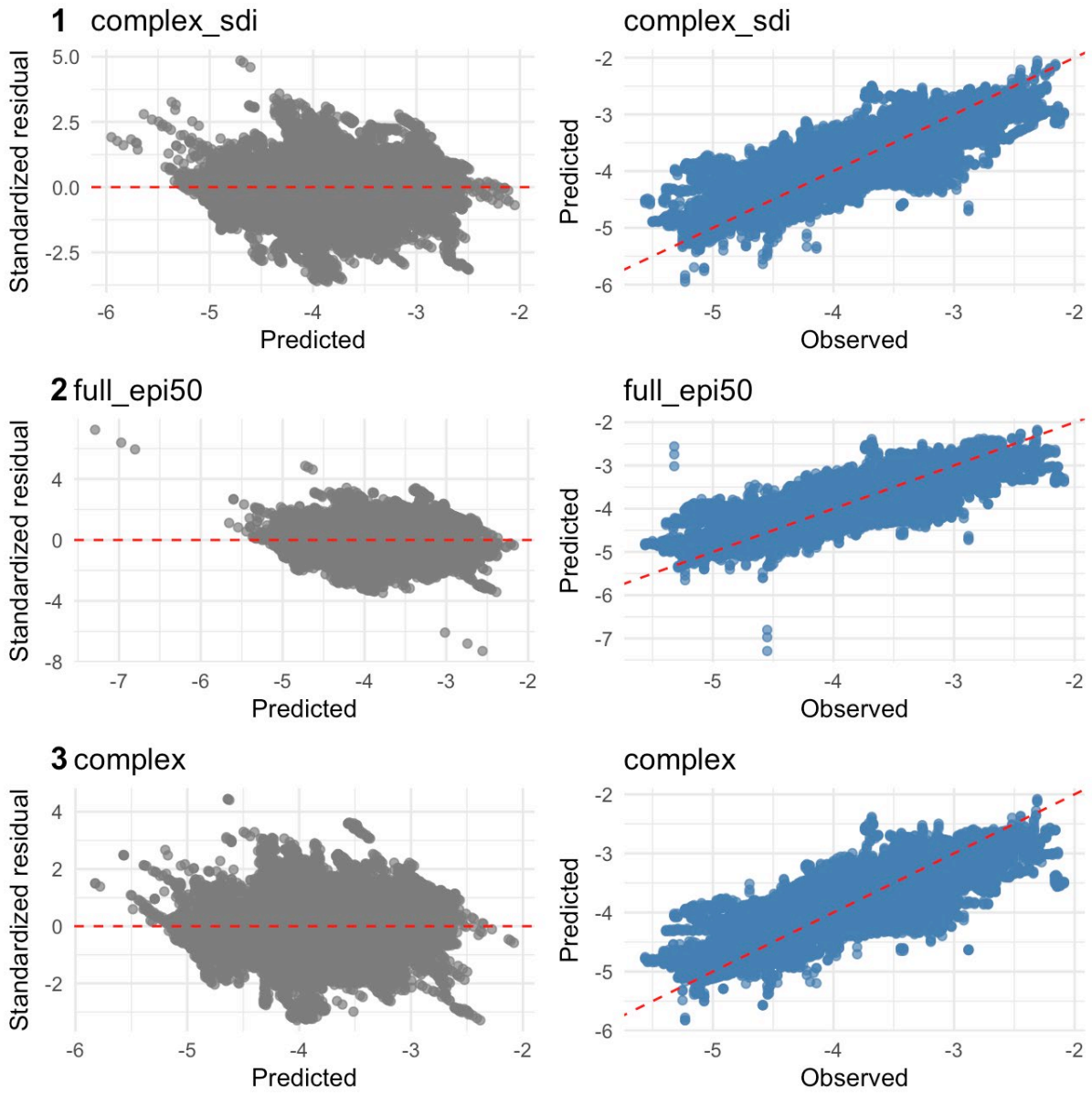


Figure 2 Standardised residuals (in gray on the left) and predicted vs observed (in blue on the right) for the 3 top performing models.

References

Carter, A., Msemburi, W., Sim, S. Y., Gaythorpe, K. A. M., Lambach, P., Lindstrand, A., & Hutubessy, R. (2024). Modeling the impact of vaccination for the immunization Agenda 2030: Deaths averted due to vaccination against 14 pathogens in 194 countries from 2021 to 2030. *Vaccine*, *42*, S28–S37. https://doi.org/10.1016/j.vaccine.2023.07.033

Echeverria-Londono, S., Li, X., Toor, J., de Villiers, M. J., Nayagam, S., Hallett, T. B., Abbas, K., Jit, M., Klepac, P., Jean, K., Garske, T., Ferguson, N. M., & Gaythorpe, K. A. M. (2021). How can the public health impact of vaccination be estimated? *BMC Public Health*, *21*(1). https://doi.org/10.1186/s12889-021-12040-9

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Shattock, A. J., Johnson, H. C., Sim, S. Y., Carter, A., Lambach, P., Hutubessy, R. C. W., Thompson, K. M., Badizadegan, K., Lambert, B., Ferrari, M. J., Jit, M., Fu, H., Silal, S. P., Hounsell, R. A., White, R. G., Mosser, J. F., Gaythorpe, K. A. M., Trotter, C. L., Lindstrand, A., … Bar-Zeev, N. (2024). Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization. *The Lancet*, *403*(10441), 2307–2316. https://doi.org/10.1016/S0140-6736(24)00850-X

APPENDIX A. Overview of different estimates of vaccine impact – impact by calendar year (cross-sectional impact), impact by birth year (life-time impact), and impact by year of vaccination from Echeverria-Londono et al (2021).

Impact by calendar year (cross-sectional impact) is the most intuitive method and calculates the impact accrued over all ages for a specific year. This is frequently used for calculating impact of vaccination from baseline and focal scenarios and performs well for childhood infections where the cases and deaths are averted soon after vaccination. The disadvantage of this method is that it does not account for the future burden averted through current vaccinations, so it will underestimate impact for diseases like HPV where burden averted can occur decades after vaccination.

Impact by birth year (lifetime impact) calculates the long-term impact of vaccination for a particular birth-cohort over their lifetime. In order to account for averted burden later in life (as it can be the case with HPV and HepB) the modelling needs to have long-enough future time-scale to account for the cohorts lifespan. If the modelling doesn't last long enough in the future, it will not account for the burden averted in older age groups of certain cohorts. This method accounts for direct effects only (impact on a given cohort from vaccinating a different cohort via herd protection is not accounted for).

Impact by year of vaccination calculates long-term impact of vaccination activities carried out in a given year. This method is based on determining impact ratio, ρ, as the impact or burden averted per fully vaccinated person (FVP), where FVP = coverage x cohort size over the modelled time period. The year-of-vaccination impact for a given country *c* in year y is then *D(c,y)* = ρ(c) x FVP(c,y).

Appendix B. Original IA2030 methodology (Carter at al Vaccine, 2024)

This approach brings together demographic modelling, vaccine coverage data and estimates of vaccine impact by the Vaccine Impact Modelling Consortium (VIMC) in a relative-risk calculation framework. This methodology quantifies relative risk attributable to different vaccine preventable diseases *c* in at time *t* to determine the deaths averted due to vaccination in terms of excess of the deaths observed in the baseline scenario of historical and projected mortality according to the WPP2019 data. For a given age *a* deaths averted per capita is given by:

$$\lambda_{a,c,t} = \mu_{a,t}\left(\frac{1}{RR_{a,c,t}} - 1\right) \quad (1)$$

For countries *i* not modelled by VIMC, a logistic regression model is used to extrapolate the relative risk using the Socio-Demographic Index (SDI) and Healthcare Access and Quality index (HAQI) as covariates.

$$logit\left(RR_{a,c,t,i}\right) = \beta_0 + \beta_1 \mathrm{SDI}_{t,i} + \beta_2 \mathrm{HAQI}_{t,i} + \beta_3 \mu_{a,t,i} + \beta_4 t + \sum_j \alpha_j B_j(a) + \epsilon_{a,c,t,i} \quad (2)$$

where β_0 is an intercept, β_k, k = 1,2,3,4 are respective fixed effects on SDI, HAQI, all-cause mortality μ and year t. $\sum_j \alpha_j B_j(a)$ is a b-spline on age, and ε is an error term.

The key summary measure in this methodology is the **impact ratio**, defined as the number of deaths averted per fully vaccinated persons over their lifetime, using the **Year-Of-Vaccination** methodology (Echeveria-Londono et al 2021, see Appendix A).

Impact predictors used

SDI (provided by IHME and the Global Burden of Disease study) is the composite index of development status strongly correlated with healthcare outcomes and is defined as the geometric mean of: (i) total fertility under 25, (ii) mean education level for those aged 15 and over, and (iii) lag distributed income. SDI equal to 0 is the theoretical minimum of development related to health, while SDI = 1 is the maximum.

HAQI (provided by IHME and the Global Burden of Disease study) is the arithmetic mean of scaled mortality-to-incidence ratios and risk-standardised death rates for 32 causes of death that should not occur in the presence of timely, quality healthcare and theoretically ranges from 0 (lowest quality) to 100 (highest quality).

Appendix C. Modified methodology for the EPI50 analysis (Shattock et at, Lancet ID, 2024)

Determining the vaccine impact of the 50 years of the Expanded Programme on Immunization required both the geographical imputation to countries not included in VIMC modelling and the temporal extrapolation to estimate the historic impact for the

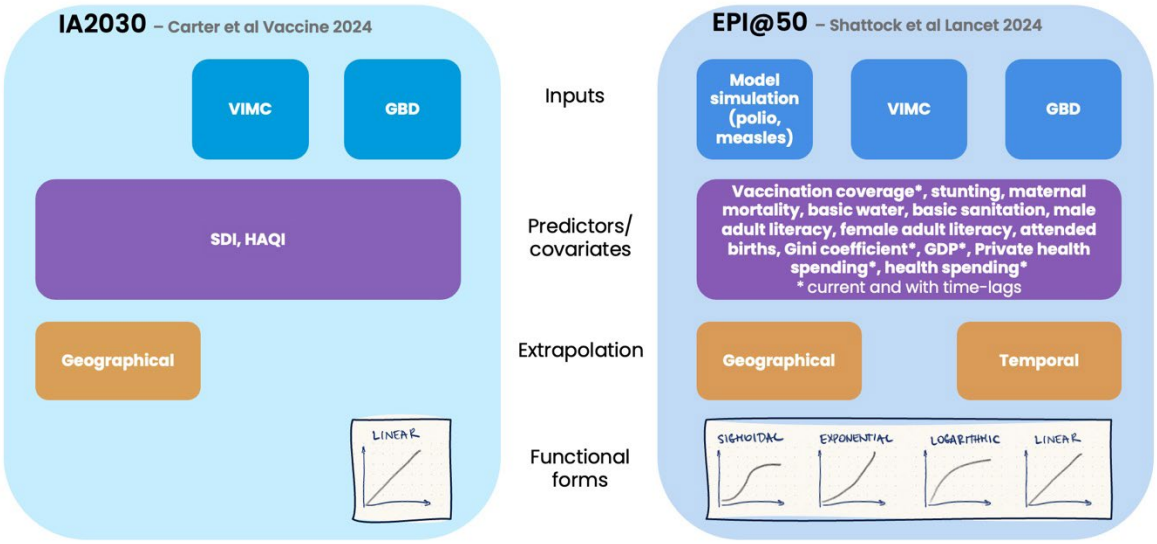


Figure 3 Overview of the two methods uses for estimating vaccine impact in IA2030, their similarities and differences.

years that were not modelled. This framework is more comprehensive and uses a corrected Akaike Information Criterion model selection approach in fitting time series regression models to vaccine impact and predictor data.

A number of regression models are considered here with different combinations of covariates:

- Coverage metrics (current and lagged up to 4 years)
- Socioeconomic indicators (e.g. Gini coefficient)
- Health indicators (maternal mortality, stunting, private health spending, basic water access).

In case where covariates were not available, they were interpolated to obtain missing data while accounting for time-series trends.

This framework consists of several steps: (i) evaluate multiple model specifications accounting for a different set of covariates, (ii) perform model selection based on AICc criterion, (iii) group countries by region and income status and assume high-income countries have the same vaccine impact predictors as upper middle-income countries, (iv) use regional best models to impute missing vaccine impact for countries not modelled by VIMC.

For time-periods not directly modelled by VIMC, the vaccine impact was extrapolated by fitting different functional forms between model-estimated cumulative impact and cumulative number of fully vaccinated people. Four functional forms were fitted for each disease in each country: (i) linear, (ii) logarithmic, (iii) exponential, and (iv) sigmoidal form (functional forms illustrated in Figure 1).

In this case, the impact is expressed in terms of years of life gained for each calendar year (rather than over the lifetime of a fully vaccinated person), also referred to as **impact by calendar year** (Escheverria-Londono, 2021, see Appendix A).

The main differences in two approaches: geographical and temporal extrapolation with four different functional forms (linear, exponential, logistic, sigmoidal) rather than just linear; model selection between multiple determinants of vaccine impact to be used as covariates for geographical extrapolation rather than the use of SDI and HAQI; impact calculated for calendar years rather than over the life-time of vaccinated individuals. (Note that impact per calendar year underestimates vaccine impact for pathogens like HPV where vaccination prevents morbidity and mortality years or decades after vaccination).

Immunization Agenda 2030 (IA2030)
Vaccine impact modeling

IVIR-AC session

Yoonie Sim & Petra Klepac

1 September 2025

Background

IA2030 Impact Goal indicator 1.1 “Number of future deaths averted through immunization”

1. Scientific analysis: modeling study (LINK)

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Modeling the impact of vaccination for the immunization Agenda 2030: Deaths averted due to vaccination against 14 pathogens in 194 countries from 2021 to 2030

Austin Carter [a,c,*], William Msemburi [b], So Yoon Sim [c,*], Katy A.M. Gaythorpe [d], Philipp Lambach [c], Ann Lindstrand [c], Raymond Hutubessy [c]

[a] University of Washington, Seattle, WA, USA
[b] World Health Organization, Division of Data, Analytics and Delivery for Impact (DDI), Geneva, Switzerland
[c] World Health Organization, Department of Immunization, Vaccines and Biologicals (IVB), Geneva, Switzerland
[d] Imperial College London, London, United Kingdom

2. Advocacy

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

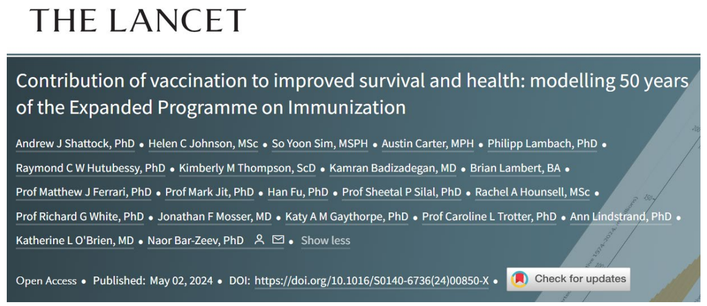
© UNICEF/Jannatul Mawa | A young boy is vaccinated against measles and rubella during a national vaccination campaign in Bangladesh.

3. Global Monitoring & Evaluation

Table 1. IA2030 Impact Goal Indicators and Targets

Impact Goal		Indicator	2030 Target
1 Prevent Disease	Save lives	**1.1** Number of future deaths averted through immunization[i]	**50 million future deaths averted globally**
	Control, eliminate & eradicate VPDs	**1.2** Number and % of countries achieving endorsed regional or global VPD control, elimination and eradication targets[ii]	**All countries achieve the endorsed regional or global VPD control, elimination and eradication targets**
	Reduce VPD outbreaks	**1.3** Number of large or disruptive VPD outbreaks[iii]	**All selected VPDs[iii] have a declining trend in the global annual number of large or disruptive outbreaks**
2 Promote Equity	Leave no one behind	**2.1** Number of zero dose children	**50% reduction in the number of zero dose children at country, regional, and global levels**
	Provide access to all vaccines	**2.2** Introduction of new or under-utilized vaccines[iv] in low and middle income countries	**500 vaccine introductions**
3 Build strong immunization programmes	Deliver across the life course	**3.1** Vaccination coverage across the life course (DTP3, MCV2, PCV3, HPVc)[v]	**90% global coverage for DTP3, MCV2, PCV3, and HPVc**
	Contribute to PHC/UHC	**3.2** UHC Index of Service Coverage	**Improve UHC Index of Service Coverage at country, regional, and global levels**

What are we updating at the midpoint of IA2030?


THE LANCET

Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization

Andrew J Shattock, PhD • Helen C Johnson, MSc • So Yoon Sim, MSPH • Austin Carter, MPH • Philipp Lambach, PhD • Raymond C W Hutubessy, PhD • Kimberly M Thompson, ScD • Kamran Badizadegan, MD • Brian Lambert, BA • Prof Matthew J Ferrari, PhD • Prof Mark Jit, PhD • Han Fu, PhD • Prof Sheetal P Silal, PhD • Rachel A Hounsell, MSc • Prof Richard G White, PhD • Jonathan F Mosser, MD • Katy A M Gaythorpe, PhD • Prof Caroline L Trotter, PhD • Ann Lindstrand, PhD • Katherine L O'Brien, MD • Naor Bar-Zeev, PhD • Show less

Open Access • Published: May 02, 2024 • DOI: https://doi.org/10.1016/S0140-6736(24)00850-X • Check for updates

Updating the target estimates in 2025

- More pathogens (**Polio and influenza**)
- New model runs from VIMC (including **COVID-19, Malaria, Cholera, and Typhoid**)
- Mortality and morbidity impact
- RI and non-routine immunization data
- Updated methods and models

EPI@50 impact modeling analysis

- Leveraging IA2030 analytical framework

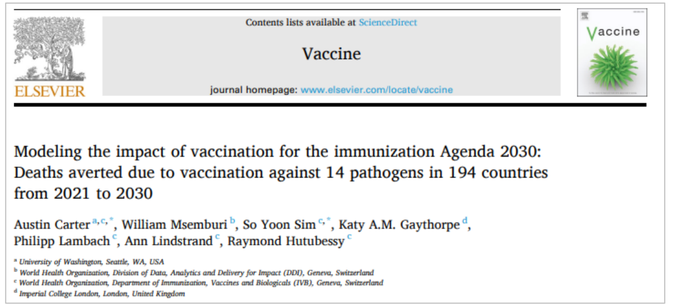
2021 2022 2023 2024 2025 2026 2027 2028 2029 2030

Annual reporting using 2021 model

Annual reporting using 2025 model

First round of target setting in 2021

- 14 pathogens (HepB, Hib, HPV, JE, measles, MenA, PCV, rota, rubella, yellow fever, diphtheria, tetanus, pertussis, TB)
- Mortality impact (deaths averted)
- Routine immunization data


Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Modeling the impact of vaccination for the immunization Agenda 2030: Deaths averted due to vaccination against 14 pathogens in 194 countries from 2021 to 2030

Austin Carter [a,c,*], William Msemburi [b], So Yoon Sim [c,*], Katy A.M. Gaythorpe [d], Philipp Lambach [c], Ann Lindstrand [c], Raymond Hutubessy [c]

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[d] Imperial College London, London, United Kingdom

Overview of IA2030 and EPI50 methods

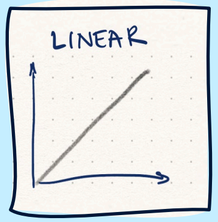
IA2030 – Carter et al Vaccine 2024

Inputs: VIMC; GBD

Predictors/ covariates: SDI, HAQI

Extrapolation: Geographical

Functional forms:



Vaccine impact: Impact by Year-Of-Vaccination

EPI50 – Shattock et al Lancet 2024

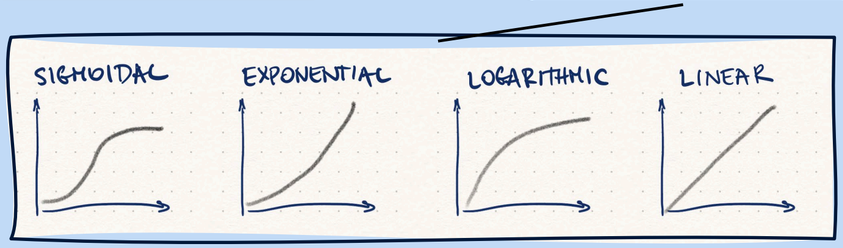
Inputs: Model simulation (polio, measles); VIMC; GBD

Predictors/ covariates: Vaccination coverage*, stunting, maternal mortality, basic water, basic sanitation, male adult literacy, female adult literacy, attended births, Gini coefficient*, GDP*, Private health spending*, health spending*

* current and with time-lags

Extrapolation: Geographical; Temporal

Functional forms:



Vaccine impact: Impact by calendar year

Feb 2025: problem statement & questions for IVIR-AC

We are trying to consolidate two methods used in IA2030 and EPI@50 modeling analyses to estimate vaccine impact that have very different levels of complexity and transparency.

*What is **the optimal level of complexity** to balance the **clarity, usability and transparency of a parsimonious method** to estimate vaccine impact against the underlying availability of data and multiple determinants of vaccine impact in demographically and epidemiologically varied locations?*

Presentation:

- Description of different methods used for IA2030 and EPI at 50
- Proposed method for cross validation and model selection

Request for IVIR-AC feedback:

- Validation exercise using results from measles transmission modelling
- Optimal level of complexity in the methodology for future estimates
- Potential additional validation exercises

IVIR-AC recommendations (Feb 2025) 1/2

- Given different methodologies, purposes, audiences, and timeframes, IVIR-AC recommends **adopting only relevant and appropriate methodologies from the EPI@50 exercise to improve IA2030 estimates** going forward. IVIR-AC recommends that methodologic updates balance **improved accuracy** in estimates versus the **practicality of interpretation**. IVIR-AC recommends examination of the impact that changing methods will have on **communication of methods and results** to stakeholders.

- Validation exercises using VIMC outputs, including measles impact estimates, found low root mean squared error and mean absolute error but moderate R2 (coefficient of determination), indicating output variability. IVIR-AC suggests that **additional validation exercises** could include **subsetting VIMC results for diseases with delayed expected reductions in burden**, such as HPV, and **quantifying sensitivity to variation in impact estimates from both VIMC measles models.**

- Further model selection via Akaike's Information Criterion (AIC) identified key predictors, including vaccine coverage, maternal mortality, and Gini coefficients, with stunting as an additional predictor for measles models. To reduce model overfitting and improve understanding of drivers of vaccine impact, IVIR-AC recommends **limiting the suite of potential statistical models via expert-guided predictor selection**. Additionally, IVIR-AC supports **region- and income-specific model selection** and suggests that it may be possible to **reduce the total number of combinations** analyzed.

IVIR-AC recommendations (Feb 2025)2/2

- Future steps include refining models by **year-of-vaccination**, simplifying frameworks for transparency, and incorporating the **Socio-demographic index(SDI) as a universal predictor**. These refinements aim to enhance the clarity, usability, and accuracy of vaccine impact estimates across diverse epidemiological settings. IVIR-AC supports the vaccine impact calculations using the year-of-vaccination method to better capture impact across different diseases and promote methodological consistency and comparability in future IA2030 updates. IVIRAC supports exploring the use of SDI as a predictor in statistical models.

Questions to IVIR-AC

- Question 1: IVIR-AC feedback on implementation of their recommendations (Feb 2025) for geographical imputation of VIMC-based estimates

- Question 2: IVIR-AC feedback on incorporating influenza impact estimates into IA2030 analytical framework

- Question 3: IVIR-AC feedback on switching calendar year-based approach to Year-of-Vaccination based approach for polio

- *Additionally, we would like to request IVIR-AC guidance on how to effectively communicate underlying changes made to the methodology and input data*

Technical presentation

IVIR-AC recommendations

- ✓ IVIR-AC supports the vaccine impact calculations using the **year-of-vaccination method**
- ✓ Given different methodologies, purposes, audiences, and timeframes, IVIR-AC **recommends adopting only relevant and appropriate methodologies from the EPI@50 exercise** to improve IA2030 estimates going forward.
- ✓ IVIR-AC recommends that methodologic updates **balance improved accuracy in estimates versus the practicality** of interpretation.
- ✓ IVIR-AC recommends examination of **the impact that changing methods will have on communication** of methods and results to stakeholders.
- ✓ To reduce overfitting and improve understanding of drivers of vaccine impact, IVIR-AC recommends **limiting the suite of potential statistical models** via expert-guided predictor selection.
- ✓ IVIR-AC supports **region- and income-specific model selection** and suggests that it may be possible to reduce the total number of combinations analyzed.
- ✓ IVIR -AC suggests that **additional validation exercises could include sub-setting VIMC results** for diseases with delayed expected reductions in burden, such as HPV, or quantifying sensitivity to variation in impact estimates from both VIMC measles models.
- ✓ IVIR-AC supports exploring the **use of SDI as a predictor** in statistical models.

Quick overview

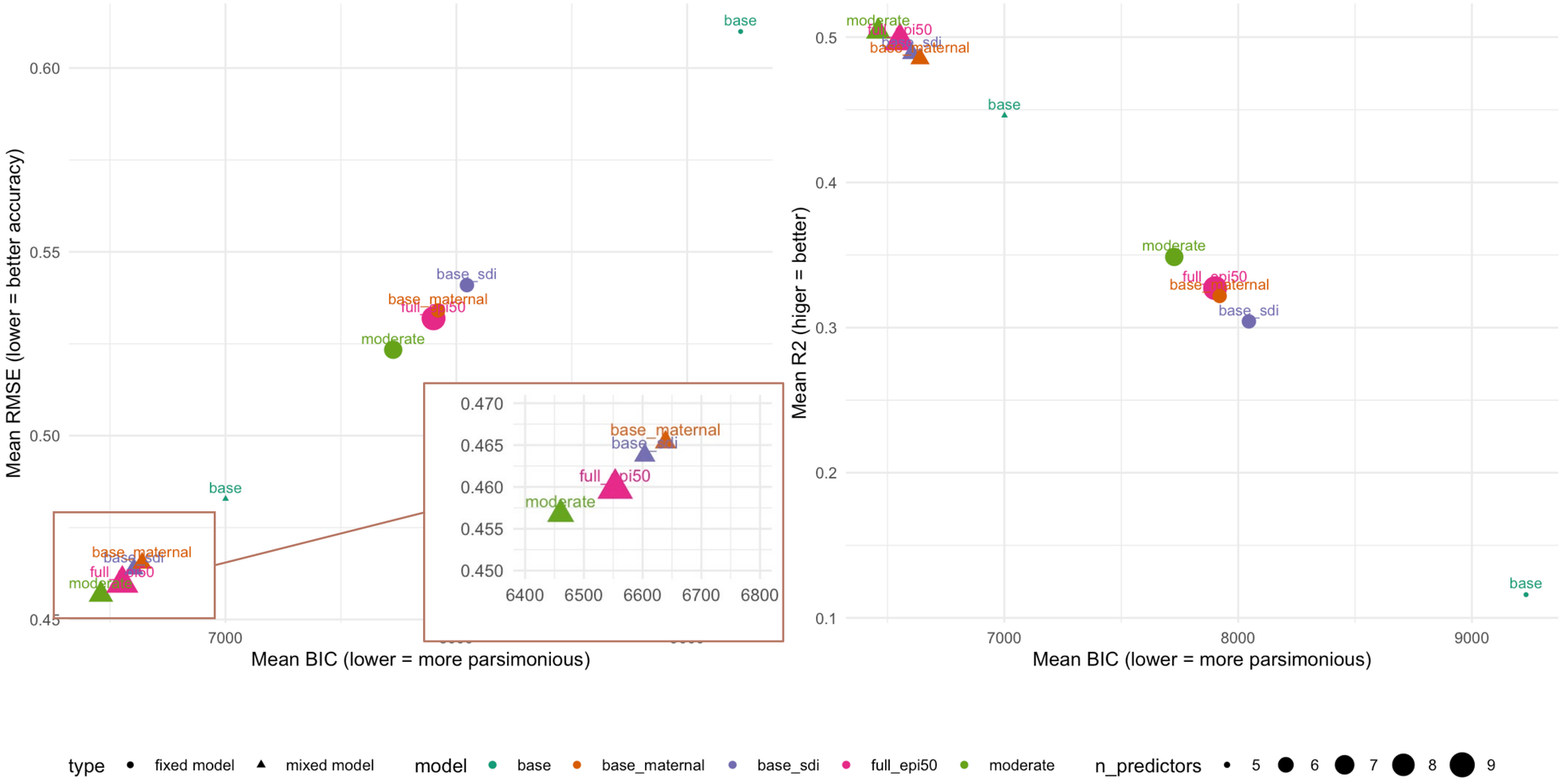
- Implemented year-of-vaccination impact calculation
- Reduced the number of potential statistical models and included SDI as a predictor
- Importance of region and income level is best captured with mixed effects models (otherwise the size of the subgroups can be too small for fitting)
  - Including random effects for WHO region and income level improves models
- Additional validation using HepB as an example of a disease with delayed vaccine impact:
  - Strong effect of geographic and economic context on HepB vaccine impact
  - Including random effects for WHO region and income level significantly improves explanatory and predictive performance of impact models compared to fixed-effects models (regardless of the number of fixed-effect predictors)

Modelling framework

- Base ~ cov0 + cov1 + cov2 + cov3 + gini
- Base_sdi ~ base + SDI
- Base_maternal ~ base + maternal_mortality
- Moderate ~ base + maternal_mortality + SDI
- Full_EPI50 ~ base + maternal_modtality + stunting + basic_water + public_health_spending

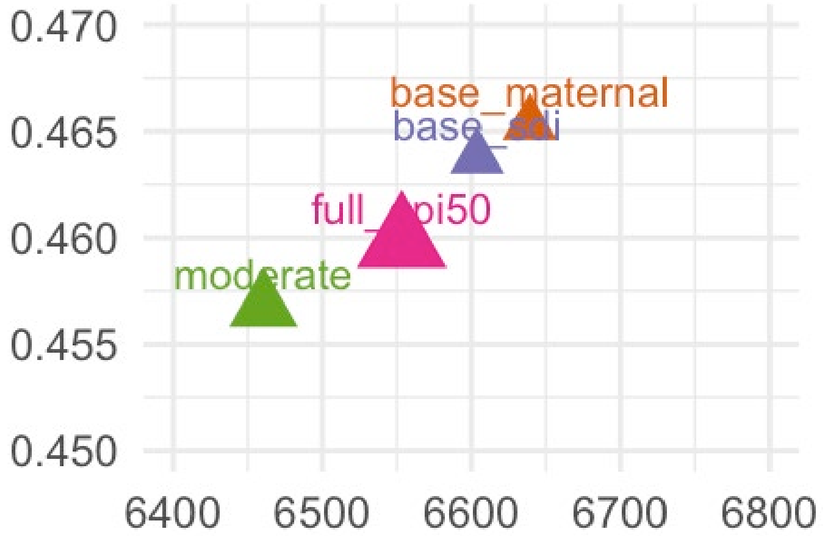
- All models are considered in **fixed** form (lm function in R) and with added **mixed effects** for WHO region and income group (lmer function in R)

Parsimony vs precision



- Grouping into **WHO region and income level** are important, but sometimes resulting subgroups are too small for fitting
- mixed-effects/hierarchical models offer a statistically coherent approach
- **Mixed-effects models** perform better than fixed models (triangles vs circles)
- Best performing model has **7** predictors, compared to **9** in the EPI50 model
    - Selected predictors: Coverage (4 predictors), SDI, gini, maternal mortality

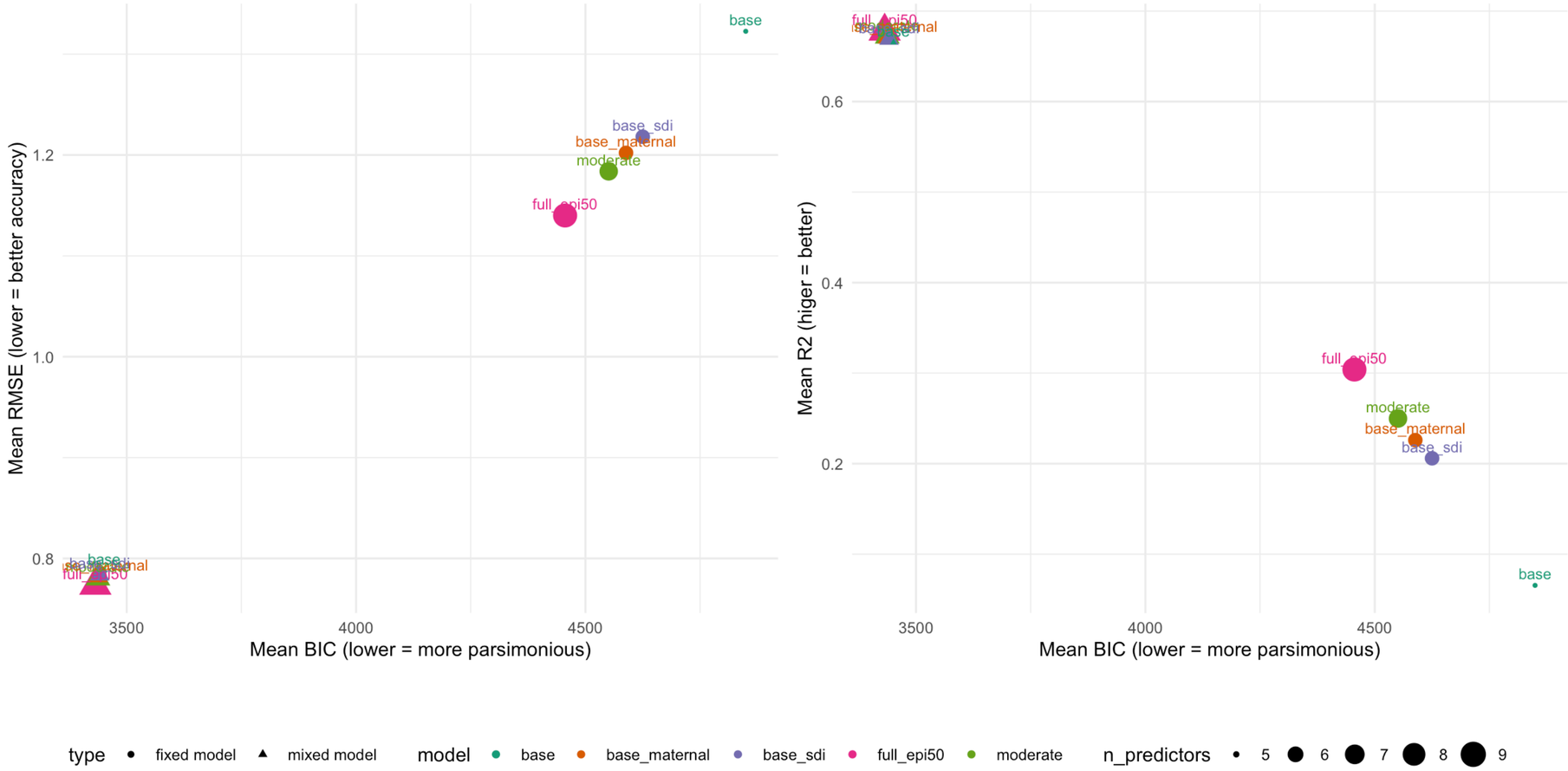
Top 3 models



1. **Moderate**: log(impact) ~ cov0 + cov1 + cov2 + cov3 + gini + mat_mortality + SDI
2. **Full_EPI50**: log(impact) ~ cov0 + cov1 + cov2 + cov3 + gini + mat_mortality + stunting + private_health_spending + basic_water
3. **Base_SDI**: log(impact) ~ cov0 + cov1 + cov2 + cov3 + gini + SDI

cov*X* = log(coverage(t-*X*))

HepB example of disease with delayed impact



- **mixed-effects for income group and region**—mixed models all cluster together
  - Strong influence on predictive performance (lower RMSE, higher R^2)
- **geographical and economic context** accounts for a substantial proportion of the observed variation in HepB vaccine impact—**much more so than the choice or number of fixed covariates alone**.

Validation conclusions

- **importance of contextual (income/group) factors** that capture unmeasured group-level heterogeneity
  - Mixed-effects models consistently outperform fixed-effects models across all metrics for both HepB and measles
- SDI captures key source of variation in measles vaccine impact

Influenza process

- LSHTM group have shared simulation results for **186 countries** by year and age group for their **current vaccines** and **no vaccine** scenarios (Goodfellow et al, PLOS Med 2025)
  - Median values, 95% uncertainty, 100 stochastic runs
- We focus on mean **averted annual outcomes** for **current vaccines**
  - Need to convert the impact to Year-of-Vaccination impact

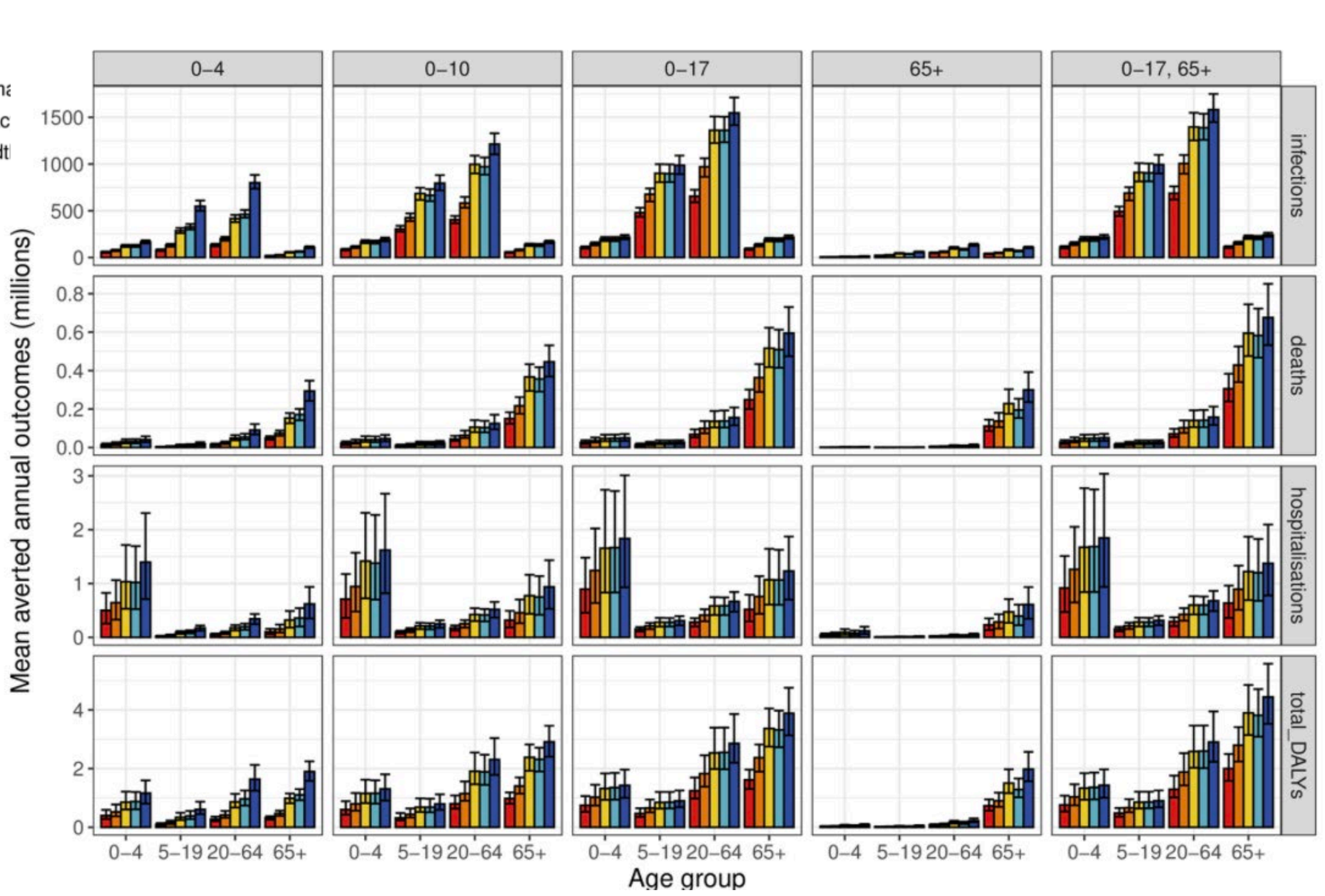
<u>Impact estimation steps and challenges</u>:

- Simulation period mismatch – 2025-2054 (no results for the first half of IA2030 period)
  - Requires **temporal extrapolation** for 2020-2024
- assumed that vaccination coverage reached **50% in each age group** (ages 0–4, 0–10, 0–17, 65 + , and 0–17 combined with 65 +) targeted by vaccination programmes
  - Requires back-calculation of the modelled number of FVPs (coverage x cohort) to calculate **impact ratios** ($\rho(c)$)
  - Impact Extrapolation from Echeverria-Londono et al using realised influenza coverage data (FVP*) where available

$$D^*(c) = \rho(c) \times FVP^*(c)$$

https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1004655

Influenza global outcomes



https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1004655

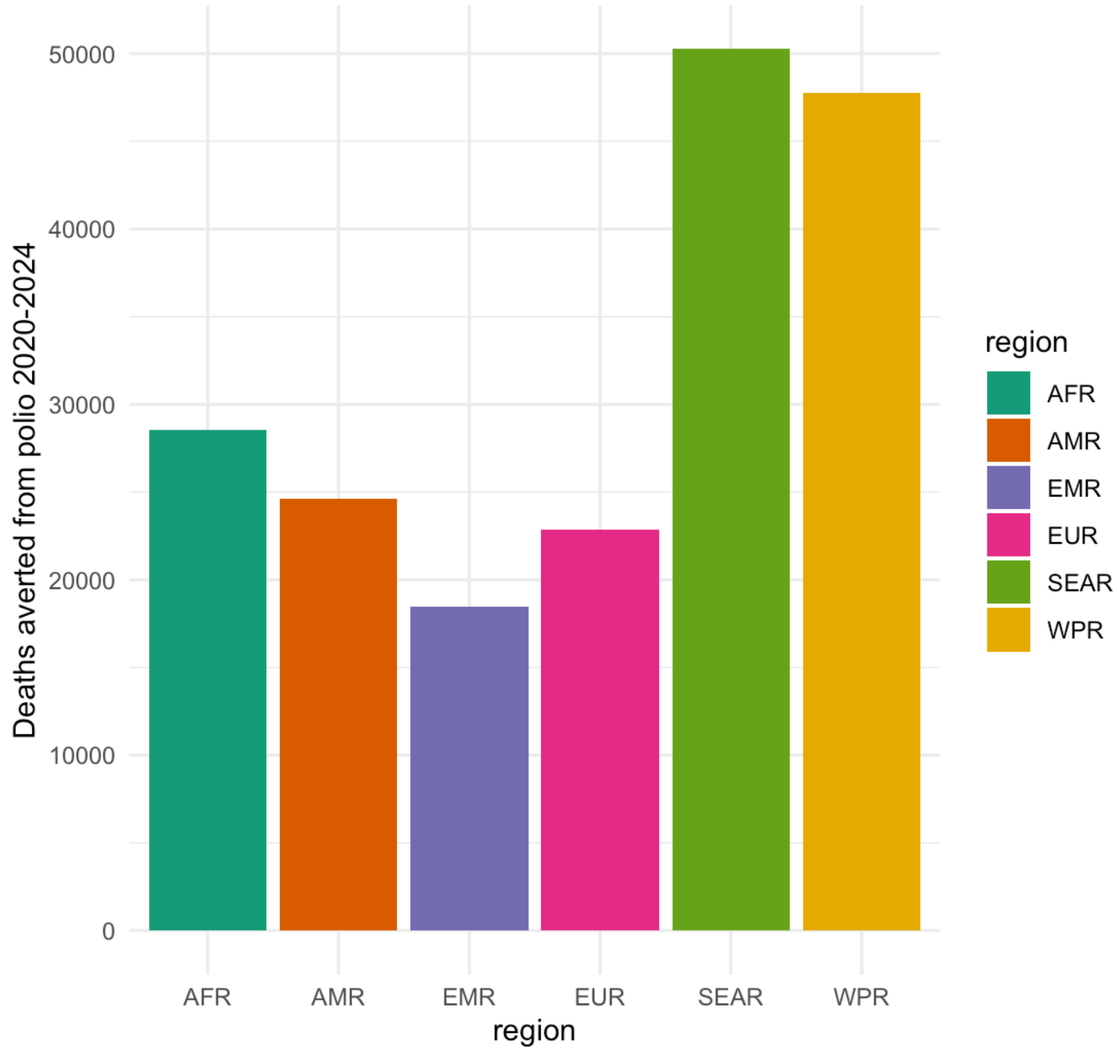
Polio process

- Polio EPI50 external runs:
  - Simulation period 1974 – 2023
  - 6 WHO regions
  - 6 age groups
  - Paralytic cases, deaths and dalys in no vaccination and vaccination scenario

Impact estimation steps and challenges:

- Disaggregate regional data by age and country according to the population size and structure in different countries (as in EPI50 framework)
- Use coverage data (OPV and IPV) from EPI50 to calculate FVPs and **impact ratios** over existing time-period
- Temporal extrapolation for period 2024-2030 – two options:
  - Impact Extrapolation from Echeverria-Londono et al and coverage data using impact ratios above
  - Using the cohort model (developed to look at population level immunity from vaccination) to propagate immunity and capture longer-term/future effects

Polio process



Thank you

World Health Organization

Session 3: Immunization coverage estimates - subnational estimates for priority countries and cohort monitoring

Concept Note - Session 3: Immunization coverage estimates - subnational estimates for priority countries and cohort monitoring

This session will cover two topics:

1. WHO/UNICEF Estimates of **Sub-national (Admin1)** Coverage (WUESNIC)[1] for selected countries
2. Approaches to monitor age-cohort vaccination coverage

1. WUESNIC for selected countries

Problem statement

Desire for independent WUENIC-like subnational estimates for five high-impact countries (Democratic Republic of the Congo (DRC), Ethiopia, India, Nigeria and Pakistan) primarily for partners and donors to be able to identify areas for more targeted support and monitor subnational progress. Ideally to be released annually alongside the WHO/UNICEF estimates of national immunization coverage (WUENIC)[i].

Background

- Current WUENIC rule-based approach has desirable properties (e.g., uses country statistics in as much as possible, incorporates contextual information and it is often considered more understandable and transparent than mathematical models) and is GATHER compliant[ii].
- However, there are limitations:
    - The quality of underlying data (admin data, surveys) affects the quality of WUENIC
    - There is no gold standard to allow benchmarking. This was highlighted by IVIR-AC in 2019[iii] (annex 1)
- In the last couple of years, partners have expressed interest in having independent WUENIC-like subnational estimates to be able to identify areas for more targeted support and monitor subnational progress.
- In 2024, the WUENIC working group[2] inputted data for the 26 provinces of DRC into the WHO Immunization Information System (WIISE), set up the WUENIC system, and fine-tuned code to produce sub-national estimates using the WUENIC rule-based approach.
    - DRC was selected as a pilot country given recent engagement in supporting the country in a data triangulation exercise to produce admin1/province-level coverage estimates – "ESNIC" –through a workshop in 2022 and continued production of "ESNIC" in the country in subsequent years

[1] WUESNIC is related to, but different from, "ESNIC" – estimates of sub-national immunization coverage – i.e., exercises conducted by countries to derive their own vaccination coverage figures.

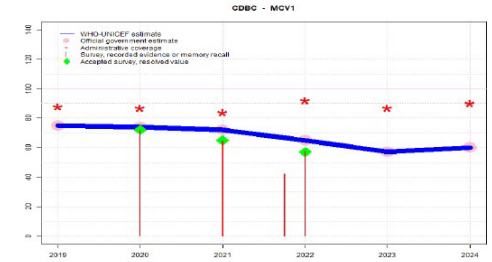
[2] The "WUENIC working group" in this note refers to WHO (3 people) and UNICEF (2 people) HQ staff that produces WUENIC. HPV estimates are currently produced separately and by a different team, though in 2025 one WHO member of the WUENIC WG was also engaged with the HPV coverage estimates.

- Data used included:
    - Admin coverage data for first and third dose of DTP-containing vaccine (DTP1, DTP3); third dose of pneumococcal conjugate vaccine (PCV3); first dose of inactivated polio vaccine (IPV1), and first dose of measles-containing vaccine (MCV1). *These data are collected annually through the eJRF and are in WIISE*
    - Official coverage data (DTP1 and 3, PCV3, IPV1 and MCV1) produced following triangulation exercises done in country since 2022. *These data are not routinely collected and there is no standard format to do so.*
        - Ongoing proposal circulating for collecting official sub-national estimates in eJRF exercise
    - Survey data from three Vaccination Coverage Surveys (ECV in French) and the Key Indicator report from the 2023 Demographic and Health Survey (DHS)
        - Sample sizes for DHS at admin1 not always >300, which is the WUENIC criteria of inclusion
    - Population estimates at admin1 by from WorldPop were used as an independent denominator to recalculate coverage and evaluate consistency.
        - This was needed to derive a Grade of Confidence (GoC)[iv], as done in WUENIC.
        - The UN Pop data on surviving infants used for WUENIC GoC is not available for subnational levels.
    - Contextual information, including vaccine-preventable disease outbreaks, campaigns, stock-outs, strikes, natural disasters, were not available
- In July 2025, draft WUESNIC estimates were produced for DTP1 and 3, PCV3, IPV1 and MCV1 for all 26 provinces of DRC for the period 2019-2024.
    - There is no precedent of WHO sub-national level estimates for other health indicators or a defined process
    - The draft estimates were sent to DRC in late July for a 6-week country consultation as required for WHO to publish national estimates of health indicators

The figure below illustrates a draft WUESNIC page for one DRC province.

For a summary of challenges refer to annex 2.

Province X - MCV1 - DRAFT



	2019	2020	2021	2022	2023	2024
Estimate	75	74	72	65	57	60
Estimate GoC	●●●	●	●	●	●	●
Official	75	74	72	65	57	60
Administrative	88	87	84	92	87	90
Survey	-	72	65	*	-	-

The WHO and UNICEF estimates of subnational (ADMIN-1 level) vaccination coverage are based on data and information that are of varying, and, in some instances, unknown quality. The grade of confidence (GoC) reflects the confidence or trust we have in these estimates. As there is no underlying probability model upon which the estimates are based, we are unable to present classical uncertainty measures, e.g., confidence intervals. Moreover, we have chosen not to make subjective estimates of plausibility/certainty ranges around the coverage. The GoC reflects the degree of empirical support upon which the estimates are based. It is not a judgment of the quality of data submitted by reporting authorities.

●●● Estimate is supported by reported data [R+], coverage recalculated with an independent denominator (D+), and at least one supporting survey within 2 years [S+]. While well supported, the estimate still carries a risk of being wrong.

●● Estimate is supported by at least one data source; [R+], [S+], or [D+]; and no data source, [R-], [D-], or [S-], challenges the estimate.

Description:

2024: [R:] Estimate informed by reported data. Estimate challenged by: D-
2023: [R:] Estimate informed by reported data. Estimate informed by official coverage data supported by prior year survey result. Current year DHS result, which is being interpreted cautiously, suggests lower coverage than reported. Regardless, available information supports need for programmatic improvements. Estimate challenged by: D-
2022: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 57 percent based on 1 survey(s). Democratic Republic of the Congo Demographic and Health Survey, Kongo Central, 2023-24 results ignored. Sample size 183 less than 300.Given a modest survey sample size at the provincial level and low levels of available documented evidence of vaccination history, cautious interpretation of DHS results at provincial level is encouraged. Result suggests coverage that is lower than that indicated by EPI coverage surveys. Estimate challenged by: D-
2021: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 65 percent based on 1 survey(s). Estimate challenged by: S-
2020: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 72 percent based on 1 survey(s). Estimate challenged by: S-
2019: [R:] Estimate informed by reported data. GoC=R+ S+ D+

- Since 2015, WHO and UNICEF have offered support to countries to produce WUENIC-like estimates of coverage at admin1 level using a WUENIC-like approach
    - Countries supported that were able produce such estimates include India (2015)[v], Pakistan (2018), Ethiopia (2018)[vi], DRC (2022), Cameroon (2024).
    - Indonesia (2017) and Cote d'Ivoire (2018) were supported, but WUENIC-like estimates at admin1 could not be produced mainly due to unavailability/ inaccessibility of survey data at that level at the time of the exercises
    - Country's interest has been somewhat limited, as admin1 not a programmatic unit in many countries
- Related to doing WUESNIC, Ethiopia, Nigeria and Pakistan had expressed interest in data triangulation workshops in 2025, but setting dates has not been possible due to competing priorities.
- In 2025, an IVIR-AC subgroup was established to provide advice on vaccination coverage estimation (terms of reference can be found here). This group provided feedback to the questions being posed to IVIR-AC in Sept 2025.

Proposal of next steps for IVIR-AC review

- Engage with priority countries to support data triangulation exercises leading to official coverage estimates for admin1
- Finish WUESNIC for at least 3 priority countries
- Work with the IVIR-AC subgroup on vaccination coverage estimation to:
    - Evaluate discrepancies in trends and levels between WUESNIC and country data, and with modeled estimates
    - Evaluate relaxing rules for survey inclusion
    - Explore GoC alternatives

2. Approaches to monitor age-cohort vaccination coverage

Problem statement

Current WUENIC estimates monitor coverage for the eligible cohort, e.g., surviving infants for vaccines recommended for infants. While this gives a good overview of routine program performance to reach target population for vaccination, it does not allow monitoring late or catch-up vaccination. This became more evident during the Covid pandemic and with global catch-up initiatives, notably the Big Catch-up[3].

Background

- Increase attention to catch-up vaccination
    - Guidance developed by the IA2030 Data Strengthening and Use WG for monitoring catch-up[vii]
    - Important data issues have been observed
- eJRF 2016-2022 included questions on system allowing monitoring by age groups and delayed MCV1[viii]
    - Analysis showed that roughly two thirds of countries reported having an information system to allow to separate by age groups, but variations by region and income
    - Limited reporting on delayed MCV1 doses and plenty of data quality issues.
    - PAHO has longer history and for more vaccines, still important data quality issues
- Tally sheet analysis done (for 2023)[ix], and planned for tally sheets shared for the year 2024
- eJRF questions 2023-2024 added delayed DTP3, analysis ongoing
- Questions have been received from countries and partners
    - Examples DPR Korea, Mozambique, Tanzania, Uganda (*to be mentioned in presentation*)
- Cohort monitoring being used by countries with Electronic Immunization Registries (EIRs) – Latin America, Egypt
- Surveys allow for cohort monitoring, but limited by age targeted and availability of vaccination data
    - Some examples exist from monitoring "catch-up" using surveys[x,xi]

[3] The Big Catch-up (BCU) was launched in 2023 as a coordinated effort by WHO, UNICEF, and Gavi, the Vaccine Alliance, along with the Immunization Agenda 2030 (IA2030) Partnership, to support countries to plan and implement intensified efforts to bolster immunization programmes.

- HPV estimates include “programmatic coverage” and one by age 15[xii]
- Supplementary Immunization Activities (SIA) may help “catch-up” children who missed doses at the target age, but SIA usually do not record doses in home-based records or (paper) registries. Thus, SIA doses are unlikely to be “counted” when monitoring coverage by age cohorts

Proposal of next steps for IVIR-AC review

- Revise eJRF
    - Add questions on info system, notably availability of EIR
    - Add DTP1
    - Change format of questions
- Finish analysis of information system and delayed dose 2023-2024 and tally sheets 2024
- Document issues seen in Big-catch-up countries
- Document issues with HPV coverage by age 15
- Work with the IVIR-AC subgroup on vaccination coverage estimation to:
    - Analyze more surveys to determine contribution of delayed vaccination to coverage
    - Test “coverage by age 2” for selected countries
        - Criteria for data availability and consistency

Annexes

Annex 1. Recommendations from IVIR-AC 2019 and *updates of what was done*

• Given the time constraints before any new methods can be adopted we should continue to rely on the current WUENIC methods in the near future.

WUENIC has continued being produced annually

• In the meantime, we should evaluate the strengths and weaknesses of alternative methods including the IHME [Institute for Health Metrics and Evaluation] model and what comes out of the three Expression of Interest letters.

IHME continues to produce estimates and they are included in the WUENIC trends app to facilitate comparison. Collaboration with IHME has been strengthened.

• Having high quality data for estimating coverage is critical for evaluating programme performance and stimulating improvements where and when needed.

IA2030 includes a companion document Data Action Framework and there is a Data Strengthening and Use Working Group

• A problem in estimating coverage is there is no gold standard against which different methods can be compared therefore there will still be need for human judgement. However, if finances allow, sites, in which there is comprehensive and accurate data available to determine true immunization coverage, should be set up to assess the feasibility and accuracy of various data collection methods to better refine vaccine coverage estimates.

This has not been feasible

• The Committee noted that refinements to country immunization coverage reports such as use of coverage surveys also involve subjective judgement as to how to use the supplementary information to adjust coverage estimates.

A survey checklist was developed, and it is being used. Country profiles were improved to include an interactive platform https://worldhealthorg.shinyapps.io/wuenic-trends

• Uncertainties in the methods should be described (e.g., when using alternative data such as surveys to adjust the estimates based on administrative methods). Some ranking of the quality of data used for adjustments should also be described.

• While coverage is important, it is no substitute for actual measurement of disease reduction as a result of immunization. Thus, disease surveillance would be the best indicator of programme performance but given the difficulties in establishing comprehensive systems capable of detecting all vaccine-preventable diseases it is difficult at this point; hence, we have to rely on coverage as the primary outcome measure for most immunization programmes.

Annex 2. Summary of key challenges and proposed mitigation

Challenge	Description	Proposed mitigation
Data availability	Not all countries have survey data at admin1 Not all countries have official estimates at admin1 Official coverage data not collected	Promote surveys that can provide representative and more precise estimates at admin1 Support countries with data triangulation (for example ESNIC exercises) eJRF to pilot collecting admin1 official data in a standardized format
Data quality	Unclear quality of admin and survey data at admin1 and no gold standard for comparing estimates	Continue implementing DQ recs from SAGE 2019
Methodological issues	WUENIC criteria to include survey data includes N>=300 GoC may need revisions as a GoC of 3 may not represent same confidence as for country-level	Evaluate pros and cons of "relaxing" sample size criteria Evaluate alternatives to GoC or alternative criteria
Human resources in current context and timelines	Each admin1 unit is like a country, so it takes time to run and review Small WUENIC WG team and HPV estimates with more involvement of WUENIC WG	
Country consultation process not established	No established process for country consultation or in-country process to have subnational level consultation	To be determined (TBD) as per DRC and other experiences

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IVIR-AC session
WUENIC Immunization coverage estimates - subnational estimates for priority countries and cohort monitoring

Dr. Carolina Danovaro (on behalf of the WHO/UNICEF Estimates of National Immunization Coverage [WUENIC] working group)

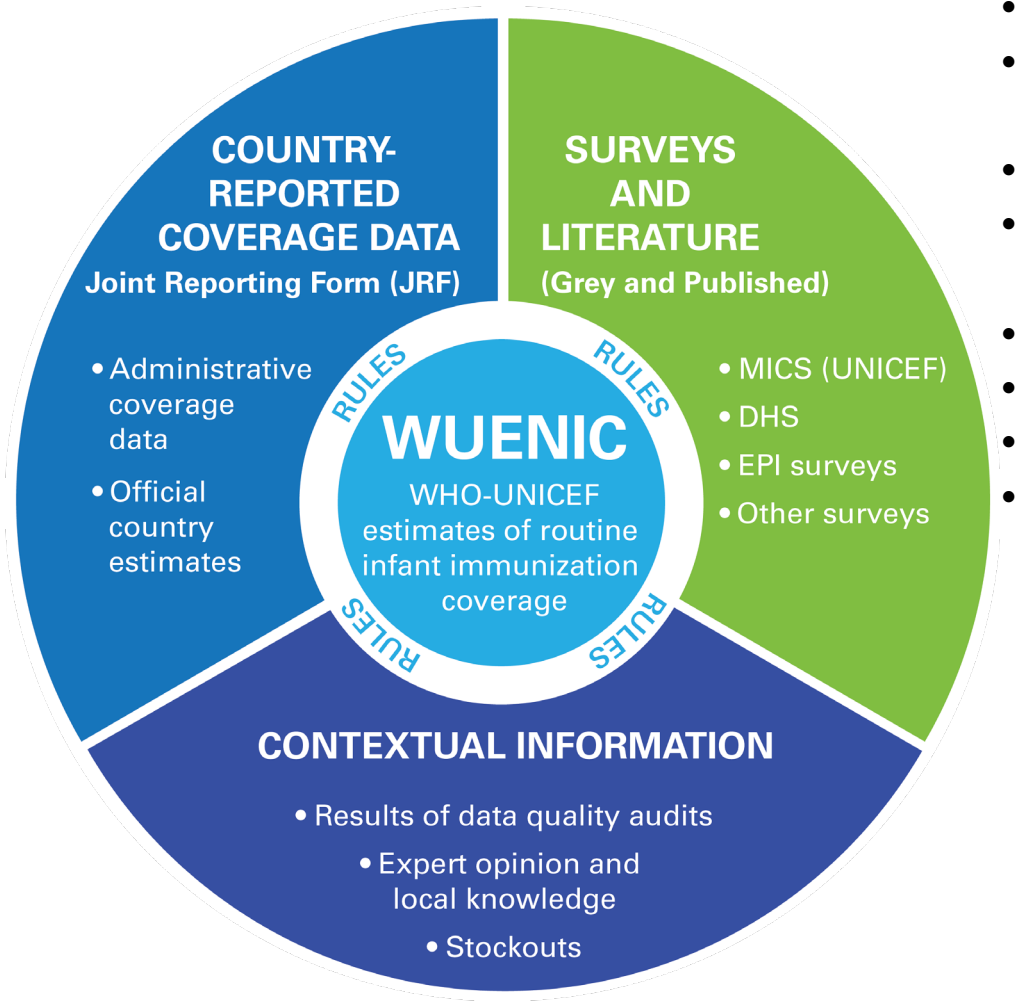
Dr. Franck Mboussou, WHO DRC Country Office

September 2, 2025

Problem Statement on WHO/UNICEF Estimates of sub-national (admin1) Immunization Coverage

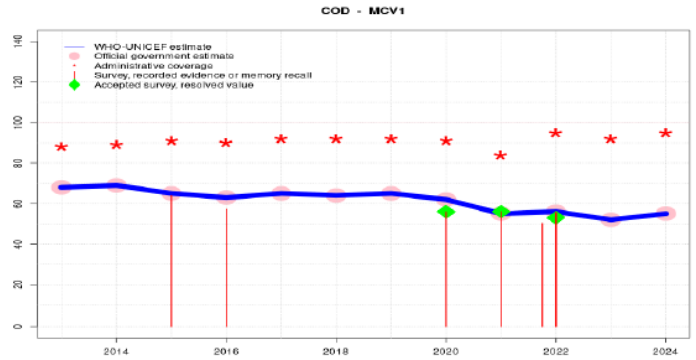
Desire for independent WUENIC-like subnational estimates for five high-impact countries (Democratic Republic of the Congo (DRC), Ethiopia, India, Nigeria and Pakistan) primarily for partners and donors to be able to identify areas for more targeted support and monitor subnational progress. Ideally to be released annually alongside the WHO/UNICEF estimates of national immunization coverage (WUENIC).

Background –WUENIC – Rule-based approach



- Rule-based data triangulation exercise undertaken by WHO and UNICEF
- Estimates produced for 16 childhood vaccine doses including three SDG and IA2030 indicator vaccines
- Includes Grade of Confidence (GoC)
- Routine immunization for single year cohorts (catch-up doses not included)
- 6-week country consultation with draft estimates sent to countries
- Annual release (mid-July)
- Immunization coverage trends since 1980 to previous year
- Revision of entire time series

Democratic Republic of the Congo - MCV1



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Estimate	68	69	65	63	65	64	65	62	55	56	52	55
Estimate GoC	•	•	•	•	•	•	•	•	•	•	•	•
Official	68	69	65	63	65	64	65	62	55	56	52	55
Administrative	88	89	91	90	92	92	92	91	84	95	92	95
Survey	-	-	64	57	-	-	-	56	56	*	-	-

Description:

2024: Estimate informed by reported data. Programme reported 1 month vaccine stockout at the national and subnational levels. Estimate challenged by: D-

2023: Estimate informed by reported data. Country reports strikes of nurses and other healthcare workers in the second half of 2023. WHO and UNICEF encourage continued improvement of data quality and use. Programme reports 5.2 months vaccine stockout at the national and subnational levels. Estimate challenged by: D-

2022: Estimate informed by reported data supported by survey.Survey evidence of 53 percent based on 2 survey(s). Official coverage estimates are based on a data triangulation exercise using the results of the 2022-2023 VCS. Official estimates do not appear to account for increases in reported number of doses administered for some vaccines in 2022, seen after declines in vaccination in the second half of 2021 due to a strike of health workers. Further survey analyses by month of birth may improve understanding of the impact of the 2021 strikes and subsequent recovery. Estimate challenged by: D-

2021: Estimate informed by reported data supported by survey.Survey evidence of 56 percent based on 1 survey(s). The official estimates from 2009 through 2021 for the Democratic Republic of Congo were determined through an exercise conducted in April 2022 with technical assistance from WHO and UNICEF in consultation with provinces using locally available survey data, administrative reports and data quality assessment results. Immunization services were disrupted during the second half of 2021 in several provinces due to a strike of health workers. Programme reports a 3.2-month vaccine stockout. Estimate challenged by: D-

2020: Estimate informed by reported data supported by survey.Survey evidence of 56 percent based on 1 survey(s). Estimate challenged by: D-

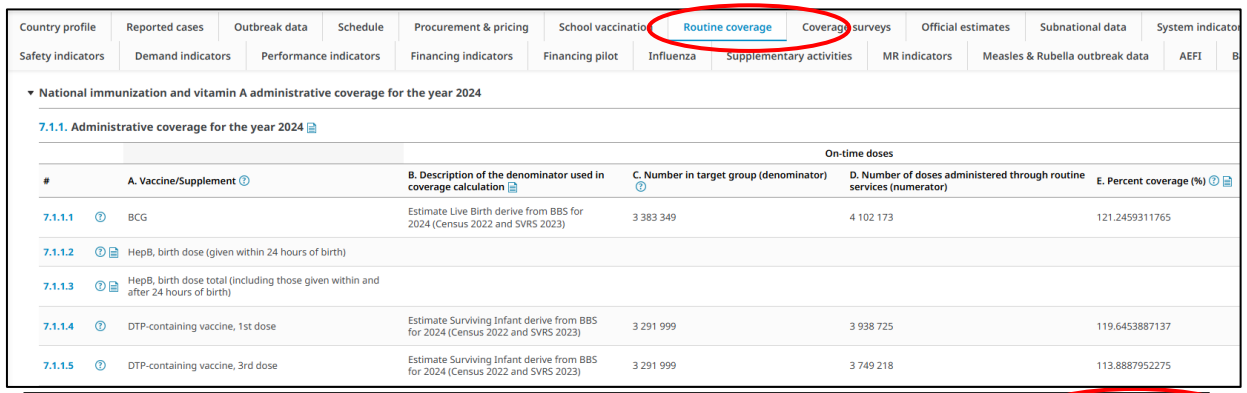
Background on coverage estimates

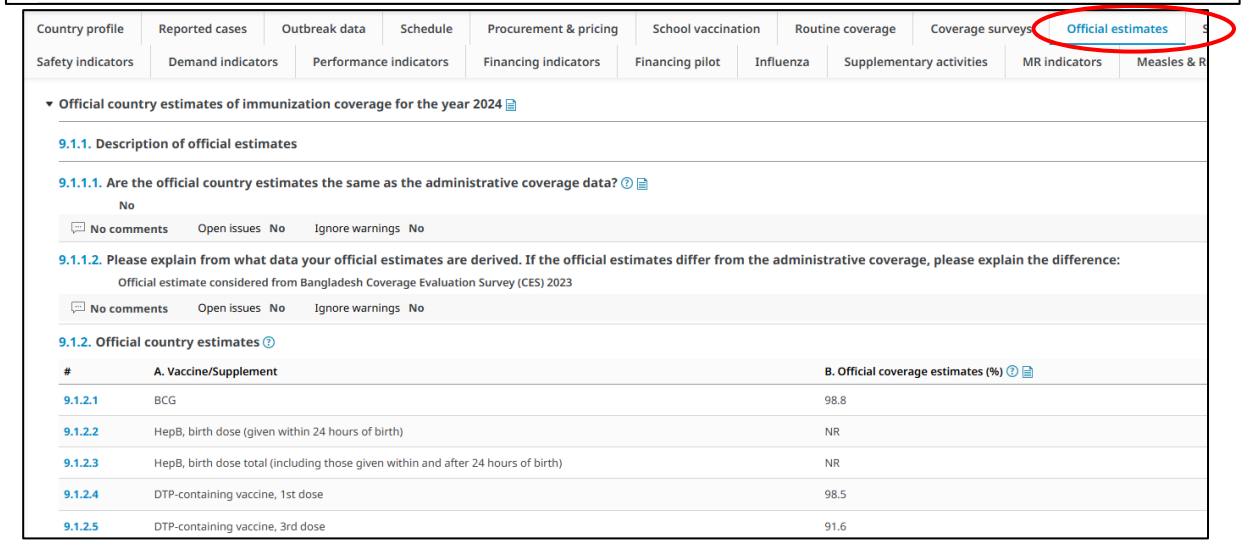
- **ESNIC –** national exercise to estimate Admin1 level (province/state) coverage trends, usually then aggregated and reported as **official coverage**
- **WUENIC** - independent review by WHO and UNICEF and **shared for country consultation with MoH**, for time series up to previous year, published every year on15 July
- **Subnational – WUESNIC** a WUENIC-like exercise - WHO and UNICEF reviews available data and provides subnational estimates (piloting in DRC)

Related initiatives

- AHEAD (Actionable health analytics for local decision-making) - UNICEF supported HF level data triangulation
- The Institute for Health Metrics and Evaluation (IHME) provides model based national and subnational estimates
- *Countdown* supports review of subnational and national coverage data for 26 African countries

Important terminology: admin coverage, official coverage, ESNIC, WUESNIC and WUENIC

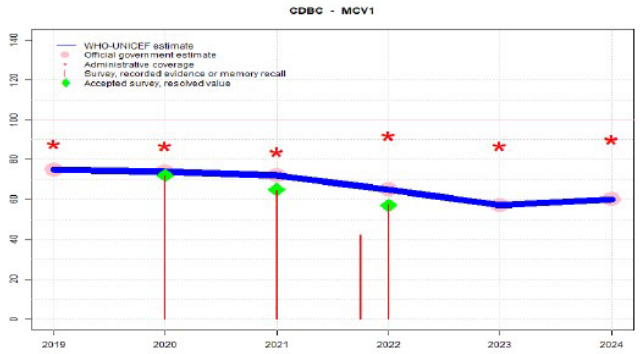




Background on WUESNIC – WUENIC-like sub-national estimates , DRC pilot

- Pilot WUESNIC exercise for the Democratic Republic of Congo (DRC) at admin 1 level
- Time period: 2019 –2024
- Antigens: DTP1, DTP3, PCV3,IPV1, MCV1
- Draft estimates completed up to 2024, undergoing country consultation
- Data available
  - Vaccination Coverage Surveys (ECV)
  - 2023 DHS Key Indicator report (no separate data by card and by recall, small sample size at admin 1)
  - Official estimates
- Not available: contextual info

Province X - MCV1 - DRAFT



	2019	2020	2021	2022	2023	2024
Estimate	75	74	72	65	57	60
Estimate GoC	●●●	●	●	●	●	●
Official	75	74	72	65	57	60
Administrative	88	87	84	92	87	90
Survey	-	72	65	*	-	-

The WHO and UNICEF estimates of subnational (ADMIN-1 level) vaccination coverage are based on data and information that are of varying, and, in some instances, unknown quality. The grade of confidence (GoC) reflects the confidence or trust we have in these estimates. As there is no underlying probability model upon which the estimates are based, we are unable to present classical uncertainty measures, e.g., confidence intervals. Moreover, we have chosen not to make subjective estimates of plausibility/certainty ranges around the coverage. The GoC reflects the degree of empirical support upon which the estimates are based. It is not a judgment of the quality of data submitted by reporting authorities.

●●● Estimate is supported by reported data [R+], coverage recalculated with an independent denominator (D+), and at least one supporting survey within 2 years [S+]. While well supported, the estimate still carries a risk of being wrong.

●● Estimate is supported by at least one data source; [R+], [S+], or [D+]; and no data source, [R-], [D-], or [S-], challenges the estimate.

Description:

2024: [R:] Estimate informed by reported data. Estimate challenged by: D-
2023: [R:] Estimate informed by reported data. Estimate informed by official coverage data supported by prior year survey result. Current year DHS result, which is being interpreted cautiously, suggests lower coverage than reported. Regardless, available information supports need for programmatic improvements. Estimate challenged by: D-
2022: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 57 percent based on 1 survey(s). Democratic Republic of the Congo Demographic and Health Survey, Kongo Central, 2023-24 results ignored. Sample size 183 less than 300.Given a modest survey sample size at the provincial level and low levels of available documented evidence of vaccination history, cautious interpretation of DHS results at provincial level is encouraged. Result suggests coverage that is lower than that indicated by EPI coverage surveys. Estimate challenged by: D-
2021: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 65 percent based on 1 survey(s). Estimate challenged by: S-
2020: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 72 percent based on 1 survey(s). Estimate challenged by: S-
2019: [R:] Estimate informed by reported data. GoC=R+ S+ D+

"ESNIC" in DRC - 2022

- **Estimates of Sub-National Immunization Coverage ("ESNIC") done upon request from country**
- **Collaborative workshop with representation from EPI, provinces, in-country partners, Bureau of Stats**
- **Long preparation period (remote + in-person)**
- **Data reviews/validation lasted a few weeks after workshop**

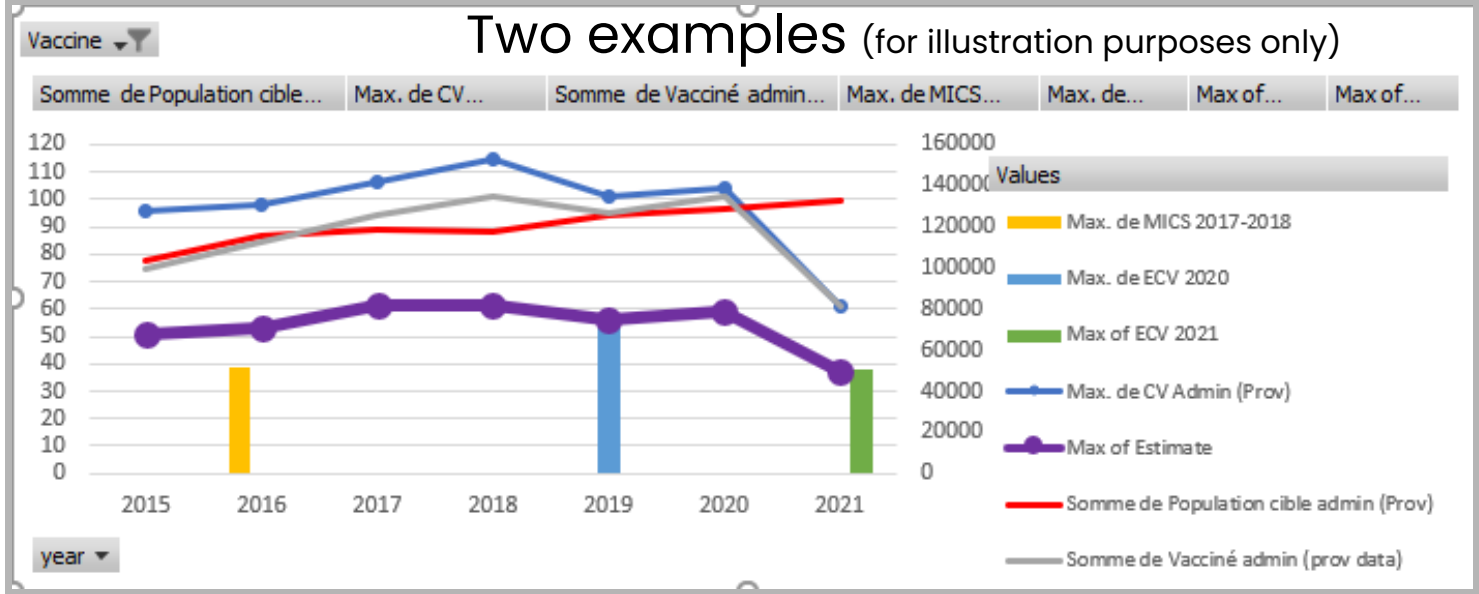
Reviewed data for all 26 provinces (11 till 2014) between 2009 and 2021

Enormous variations between provinces

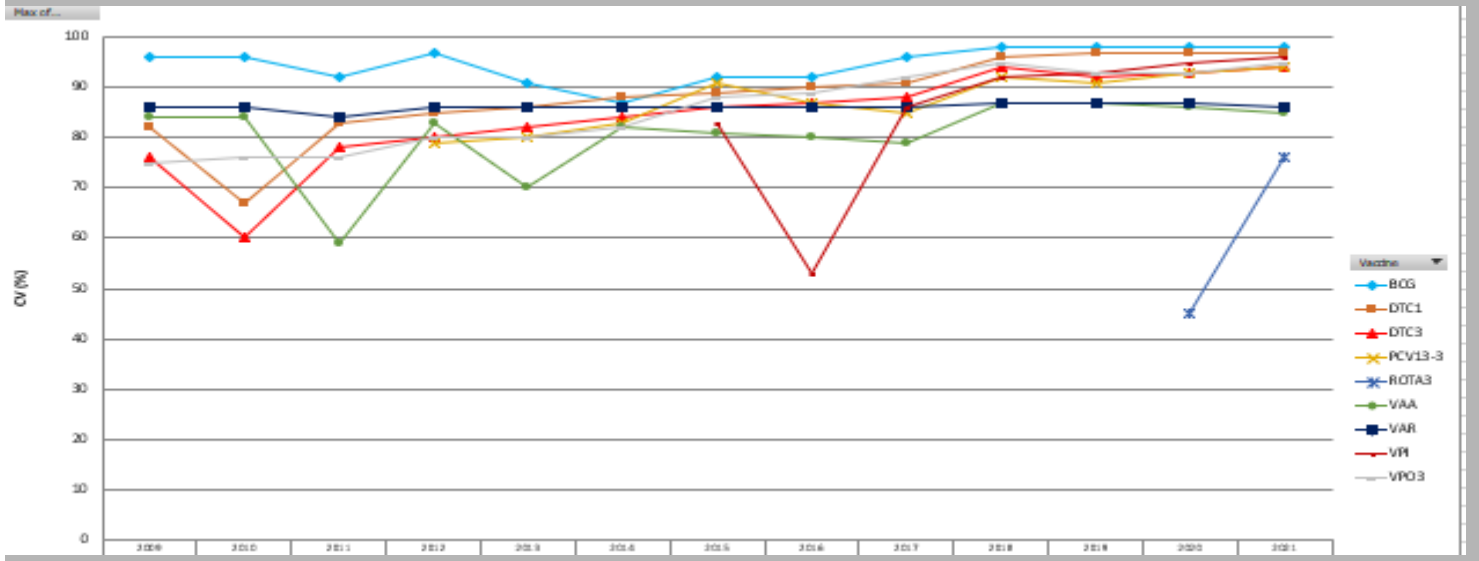
Over 12,000 data points:

- 9 vaccine-dose: BCG, Penta 1, Penta 3, OPV3, IPV, PCV3, Rota3, MCV1, YF
- Numerators/Denominators, Admin
- Multiple surveys (MICS, DHS, VCS/ECV)
- Tried - IHME & Imperial College London estimates, WorldPop <1 pop

Two examples (for illustration purposes only)



Province Y, DTP1 num/denom (lines) and coverage estimates: surveys as bars (with <20% card seen), admin cov. (blue) and "ESNIC" (purple)



Province X, Lines are estimates for each vaccine-dose: high access, high drop-out, supply issues overtime

Findings – starting with data quality review

Numerators

1. Unknown reliability, but they seemed to capture trends in vaccinated infants
2. 2021 data non-comparable to previous years
3. Stock-outs seen in the data
4. High drop-out

Denominators

1. Likely underestimated
2. Break in the time series in 2016 and then in 2020 and 2021
3. Same growth and implied infant mortality rate (IMR) used for all provinces
4. Implied IMR too high and has not varied in the entire time series

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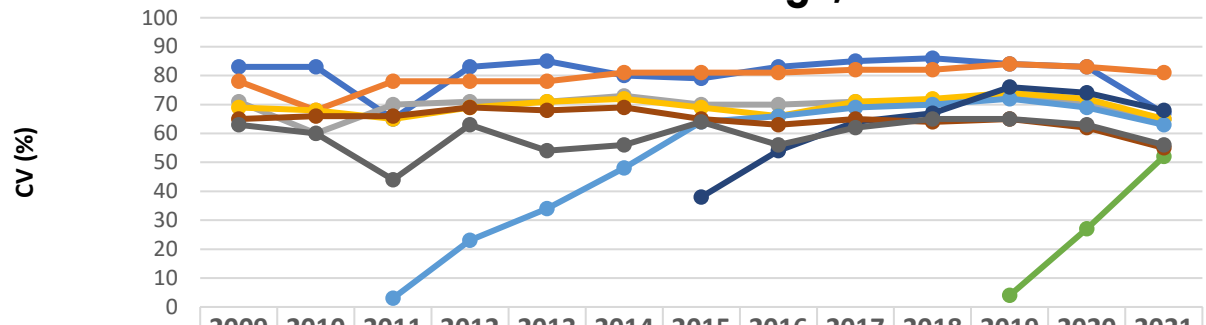
5. Non-usable

Surveys

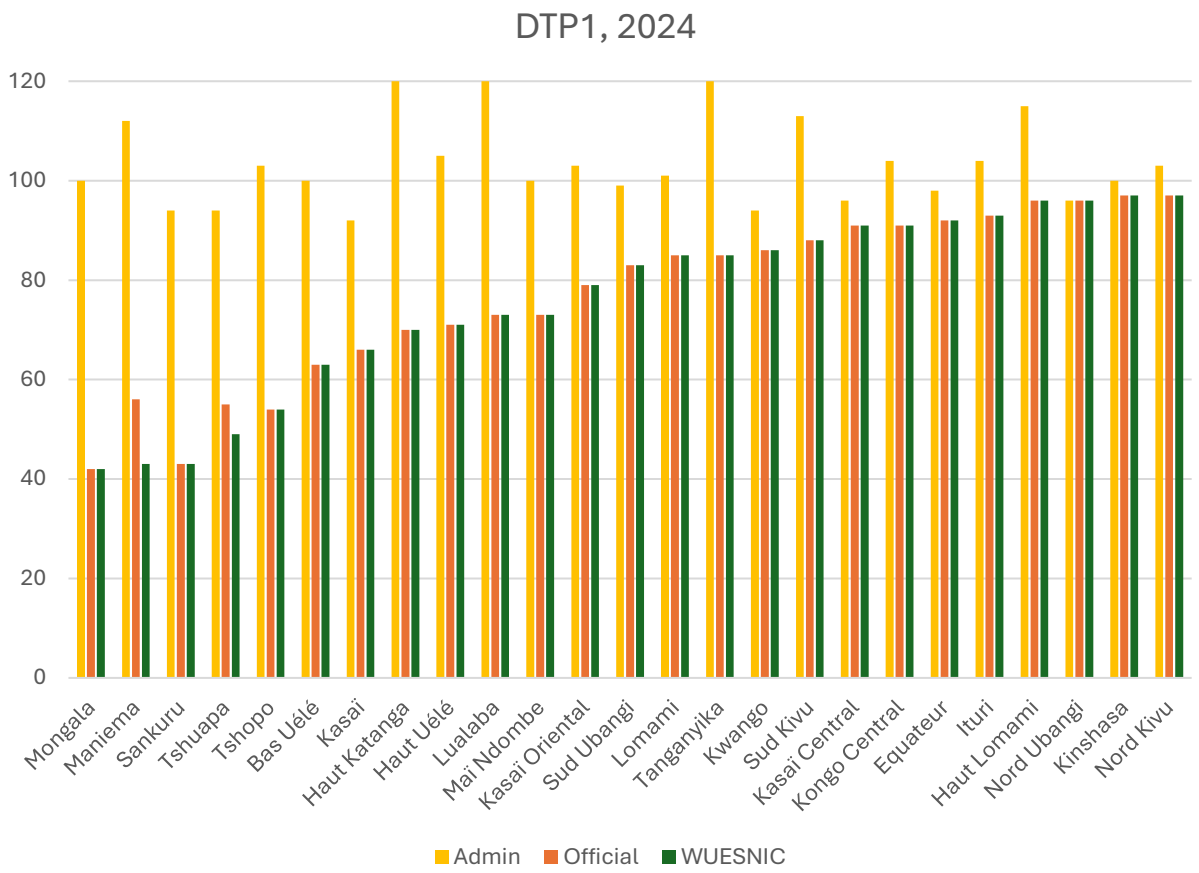
1. Variable details provided
2. Issues with card availability
3. MICS 2017-2018 too low compared to everything else – excluded
4. High drop-out

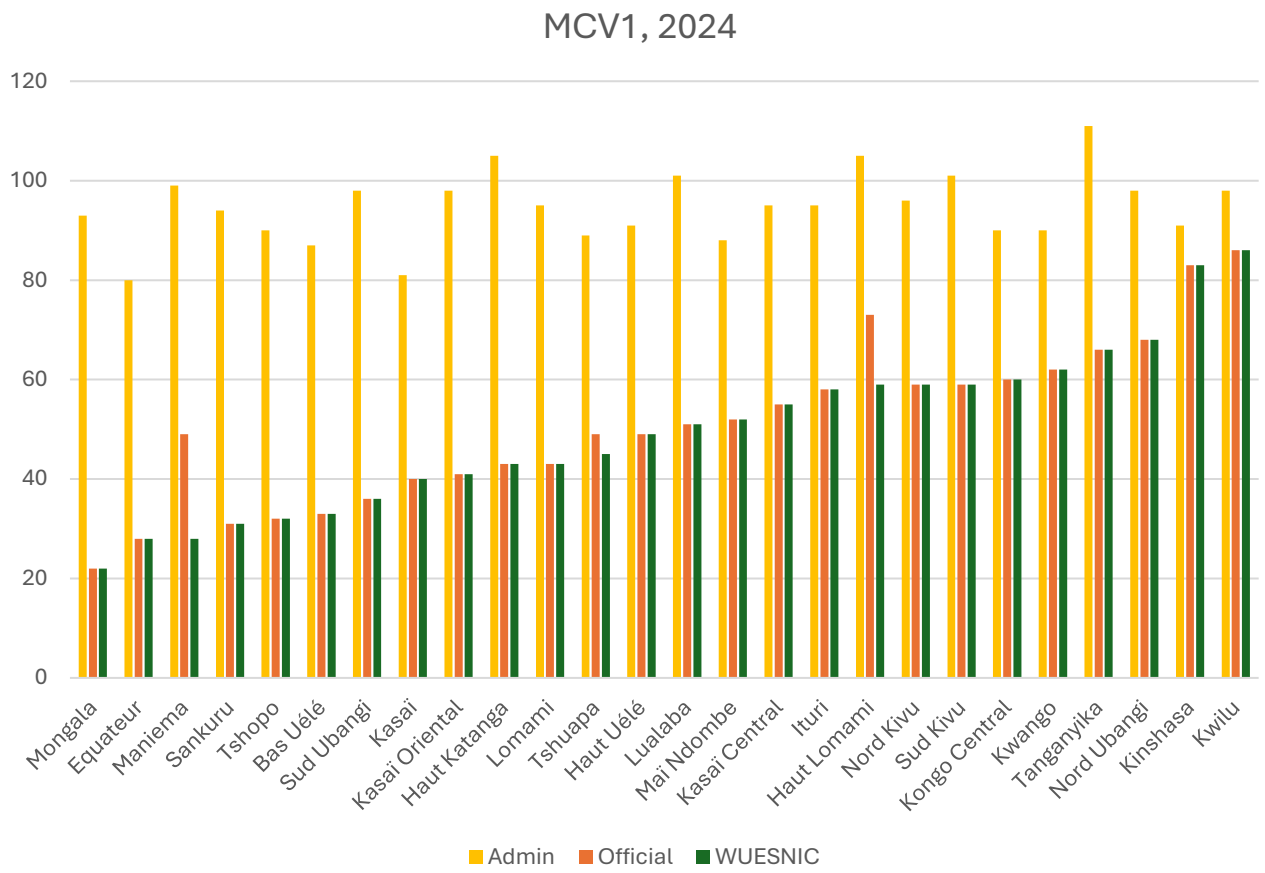
DRC Official vaccination Coverage, 2022 revision



	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
BCG	83	83	65	83	85	80	79	83	85	86	84	83	67
DTC1	78	68	78	78	78	81	81	81	82	82	84	83	81
DTC3	71	60	70	71	71	73	70	70	71	71	73	70	65
VPO3	69	68	65	69	71	72	69	66	71	72	74	72	65
PCV13-3			3	23	34	48	64	66	69	70	72	69	63
ROTA3											4	27	52
VPI							38	54	64	67	76	74	68
VAR	65	66	66	69	68	69	65	63	65	64	65	62	55
VAA	63	60	44	63	54	56	64	56	62	65	65	63	56

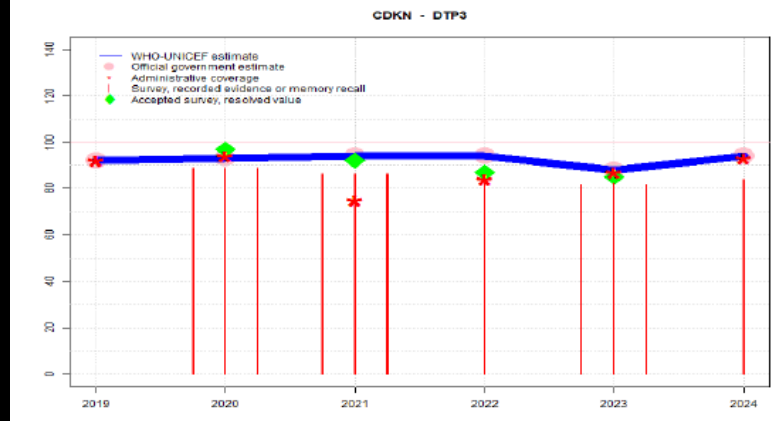
Coverage for DTP1 and MCV1 by province and by source, 2024 - Unreliable administrative data for almost all provinces





Summary of point differences between admin, official and S-WUENIC coverages

	WUESNIC – Official	Official - Admin	WUESNIC -Admin
2019	-3.5	-25.8	-29.2
2020	-2.9	-26.7	-29.6
2021	-1.0	-23.0	-24.0
2022	-1.1	-35.6	-36.7
2023	-0.8	-34.5	-35.3
2024	-2.0	-36.8	-38.8
Total	**-1.9**	**-30.4**	**-32.3**



	2019	2020	2021	2022	2023	2024
Estimate	92	93	94	94	88	94
Estimate GoC	•	•	•	•	•••	•••
Official	92	93	94	94	88	94
Administrative	92	94	75	84	87	93
Survey	-	*	*	*	*	-

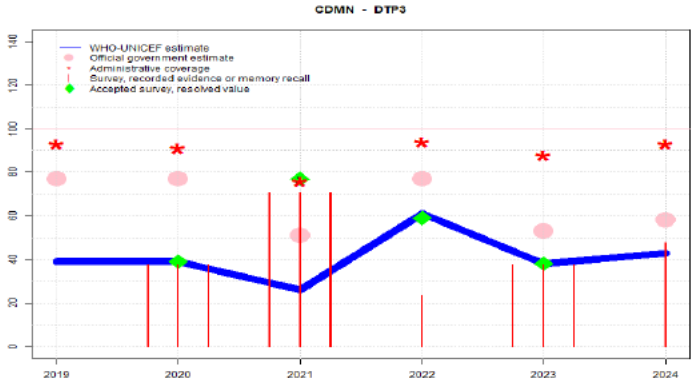
Description:

2024: [R:] Estimate informed by reported data. GoC=R+ S+ D+

2023: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 85 percent based on 1 survey(s). Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Kinshasa, 2023 record or recall results of 82 percent modified for recall bias to 85 percent based on 1st dose record or recall coverage of 96 percent, 1st dose record only coverage of 60 percent and 3rd dose record only coverage of 53 percent. GoC=R+ S+ D+

2022: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 87 percent based on 3 survey(s). Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Kinshasa, 2022 record or recall results of 89 percent modified for recall bias to 92 percent based on 1st dose record or recall coverage of 98 percent, 1st dose record only coverage of 64 percent and 3rd dose record only coverage of 60 percent.Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Kinshasa, 2023 record or recall results of 84 percent modified for recall bias to 87 percent based on 1st dose record or recall coverage of 97 percent, 1st dose record only coverage of 40 percent and 3rd dose record only coverage of 36 percent.Given a modest survey sample size at the provincial level and low levels of available documented evidence of vaccination history, cautious interpretation of DHS results at provincial level is encouraged. DHS result suggests lower coverage than that indicated by EPI survey results. Estimate challenged by: D-

2021: [R: AP] Estimate informed by reported data supported by survey.Survey evidence of 92 percent based on 1 survey(s). Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Kinshasa, 2022 record or recall results of 86 percent modified for recall bias to 92 percent based on 1st dose record or recall



	2019	2020	2021	2022	2023	2024
Estimate	39	39	26	61	38	43
Estimate GoC	•	•	•	•	•	•
Official	77	77	51	77	53	58
Administrative	93	91	76	94	88	93
Survey	-	*	*	*	*	-

Description:

2024: [C:] Reported data calibrated to 2023 levels. Estimate challenged by: D-R-S-

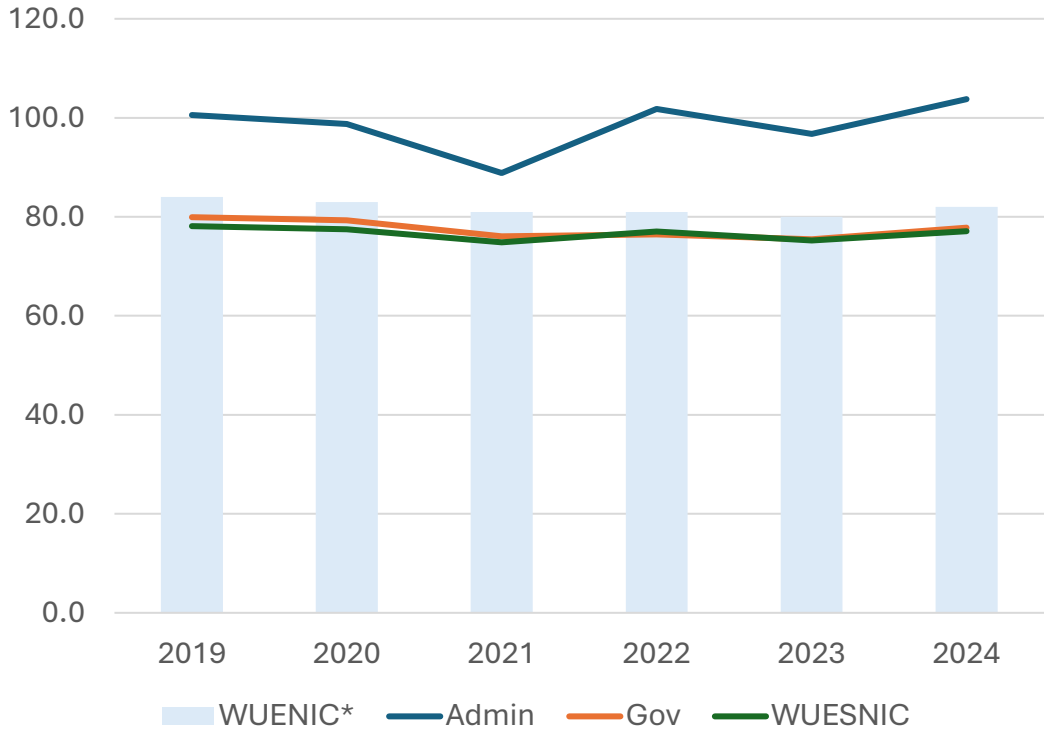
2023: [S: AP] Survey evidence does not support reported data. Estimate based on survey result. Survey evidence of 38 percent based on 1 survey(s). Estimate challenged by: D-R-S-

2022: [R: AP] Estimate informed by interpolation between reported data supported by survey.Survey evidence of 59 percent based on 2 survey(s). Democratic Republic of the Congo Demographic and Health Survey, Mai Ndombe, 2023-24 results ignored. Sample size 54 less than 300.Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Mai Ndombe, 2022 record or recall results of 55 percent modified for recall bias to 63 percent based on 1st dose record or recall coverage of 71 percent, 1st dose record only coverage of 36 percent and 3rd dose record only coverage of 32 percent.Vaccination coverage survey among children aged 6-23 months in the Democratic Republic of Congo, Mai Ndombe, 2023 record or recall results of 48 percent modified for recall bias to 54 percent based on 1st dose record or recall coverage of 67 percent, 1st dose record only coverage of 25 percent and 3rd dose record only coverage of 20 percent.Reported data excluded due to an increase from 51 percent to 77 percent with decrease to 53 percent.Given a modest survey sample size at the provincial level and low levels of available documented evidence of vaccination history, cautious interpretation of DHS results at provincial level is encouraged. DHS result suggests lower coverage than that indicated by EPI survey results. Estimate challenged by: D-S-

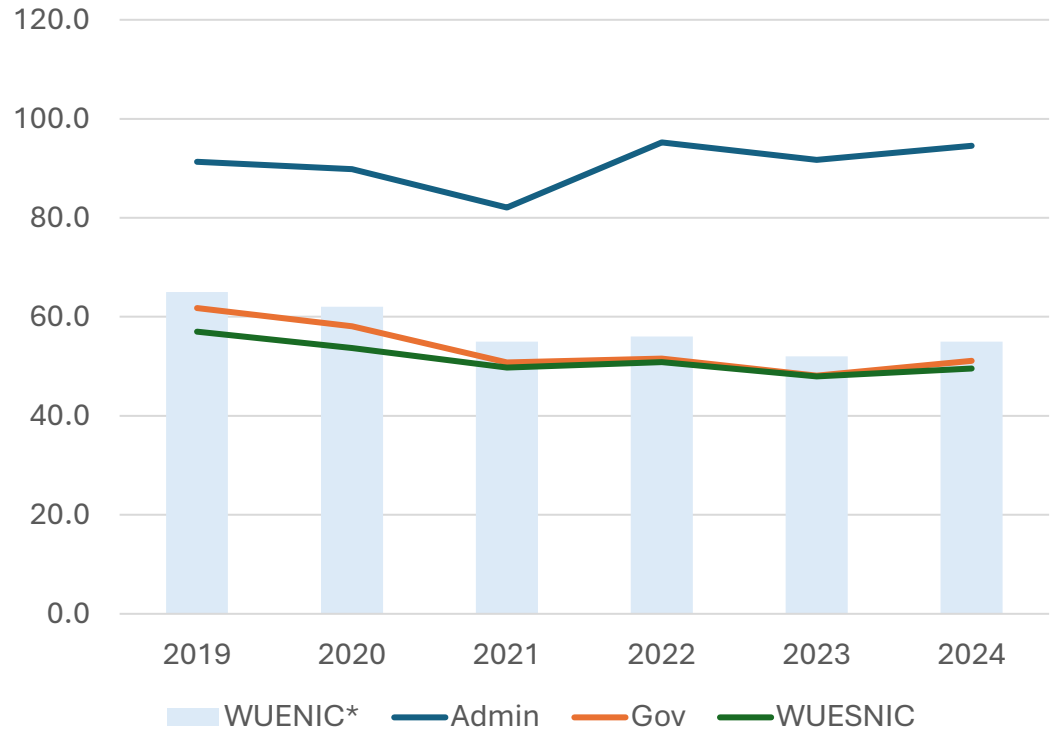
2021: [W:] Estimate informed by the relative difference between official and estimated coverage observed in the prior year applied to current year official coverage. Official coverage supported by prior year survey result, however, trend in reported data suggests a decline in coverage occurred from 2020 to 2021. Survey result suggests a trend that is inconsistent with other data. Vaccination coverage survey among children aged 6-23 months in the

Average DTP1 and MCV1 coverage by source, 2019-2024

DTP1



MCV1



- WUENIC was the same as official estimate between 2019-2024. It represents a weighted average by surviving infants.
- Admin, Gov and WUESNIC are the non-weighted averages of 26 provinces.

Challenges

- Subnational data from many countries are of variable and unknown quality
- Only one country done
- Outside of WUENIC cycle
- Heavy workload in a context of reduced resources
- No established process for country consultation
- Other priority countries don’t have official admin1 data from data triangulation exercises
- Official coverage data at admin1 not requested in eJRF

Adaptation of WUENIC Rules

- **Not all countries have survey data at admin1**
- **WUENIC criteria to include survey data includes N>=300**
- **Grade of confidence (GoC) approach may need revisions as a GoC of 3 may not represent same confidence as for WUENIC**
- **Average of admin1 WUESNIC may differ somewhat from WUENIC**
- **Ultimately, no gold standard for comparing estimates produced**

Proposed Next Steps

- To have WUESNIC ideally informed by annual country-level ESNICs
  - Engage with priority countries to support data triangulation exercises leading to official coverage estimates for admin1
  - Guidance and support to countries to promote independent estimation exercises
  - Institutionalizing regular data reviews at national and subnational level
    - MoH owned process,
    - Linked to National Immunization Strategy M&E frameworks, and
    - With coordinated partner support
- Finish WUESNIC for at least 3 priority countries in the next 6 months
- Work with the IVIR-AC technical subgroup on vaccination coverage estimation to:
  - Evaluate discrepancies in trends and levels between WUESNIC and country data, and with modeled estimates
  - Evaluate relaxing rules for survey inclusion
  - Explore GoC alternatives
  - Ultimately defining criteria on when is possible to do WUESNIC (data requirements, other factors)

Problem Statement on approaches to monitor age-cohort vaccination coverage

Current WUENIC estimates monitor coverage for the eligible cohort, e.g., surviving infants for vaccines recommended for infants. While this gives a good overview of routine program performance to reach target population for vaccination, it does not allow monitoring late or catch-up vaccination. This became more evident during the Covid pandemic and with global catch-up initiatives, notably the Big Catch-up.

Key concepts

Cohort coverage monitoring

- By age: children <12 months, 12-23 m, etc
- By year of birth: born in 2025, 2024, 2023, etc
- By a certain age (e.g., vaccinated by age 5 years)

Delayed/late vaccination

No globally accepted definition, but in general refers to vaccines given after the recommended age

- Most authors and PAHO guidance use 4 weeks (28 days, 1 month)
- Others use it for doses given the year after they are recommended (e.g. DTP3 in 2YL and later, MCV2 in 3YL+)

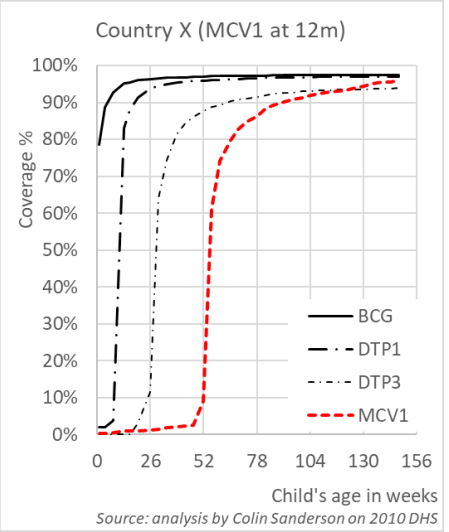
• Catch-up vaccination

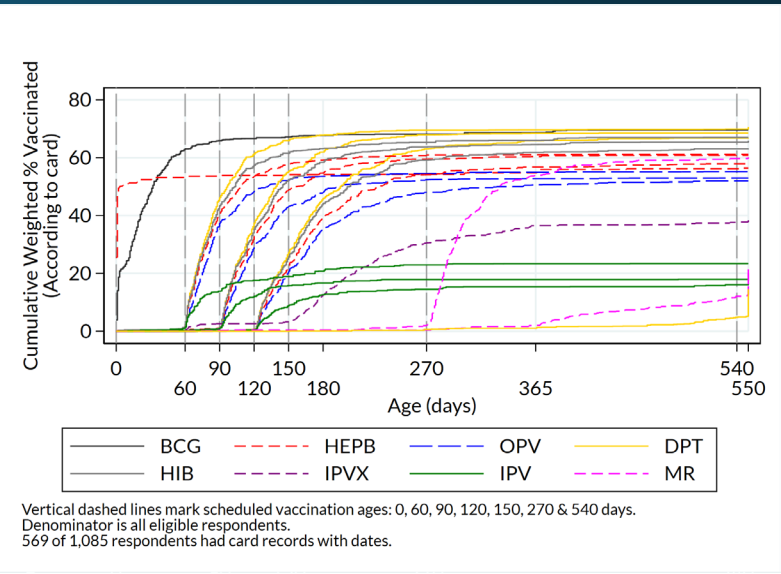
- Vaccinating children missed at the age the vaccine is recommended (e.g. children >=12 m receiving DTP1-3)

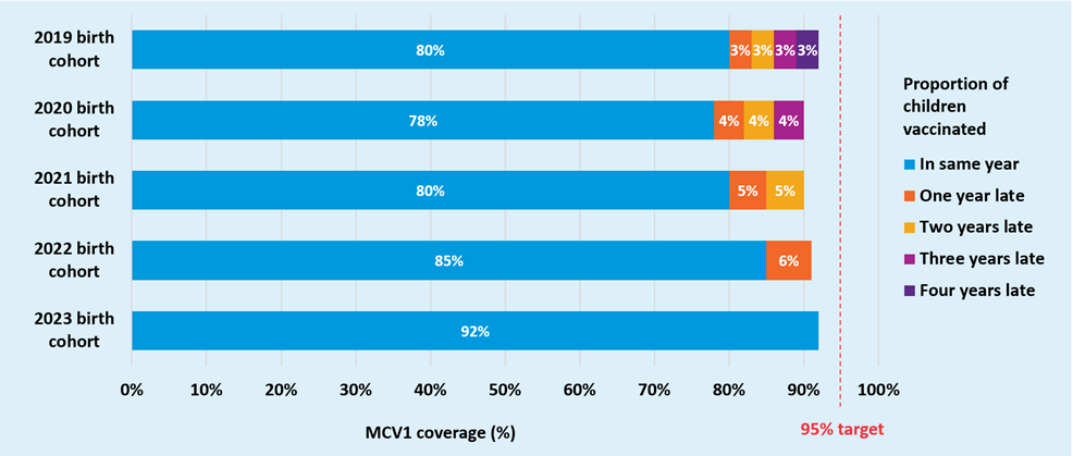
For example, catch-up MCV1 coverage for the 2021 birth cohort would be calculated as:

$$P_{\substack{catch-up\ MCV1\ coverage \\ for\ 2021\ birth\ cohort}} = \frac{Number\ of\ MCV1\ catch-up\ doses\ administered\ to\ 2021\ birth\ cohort}{Estimated\ number\ of\ MCV1\ missed\ children\ in\ 2021\ birth\ cohort} \times 100$$

- The above require that the age at vaccination be known and doses given recorded separately by age group



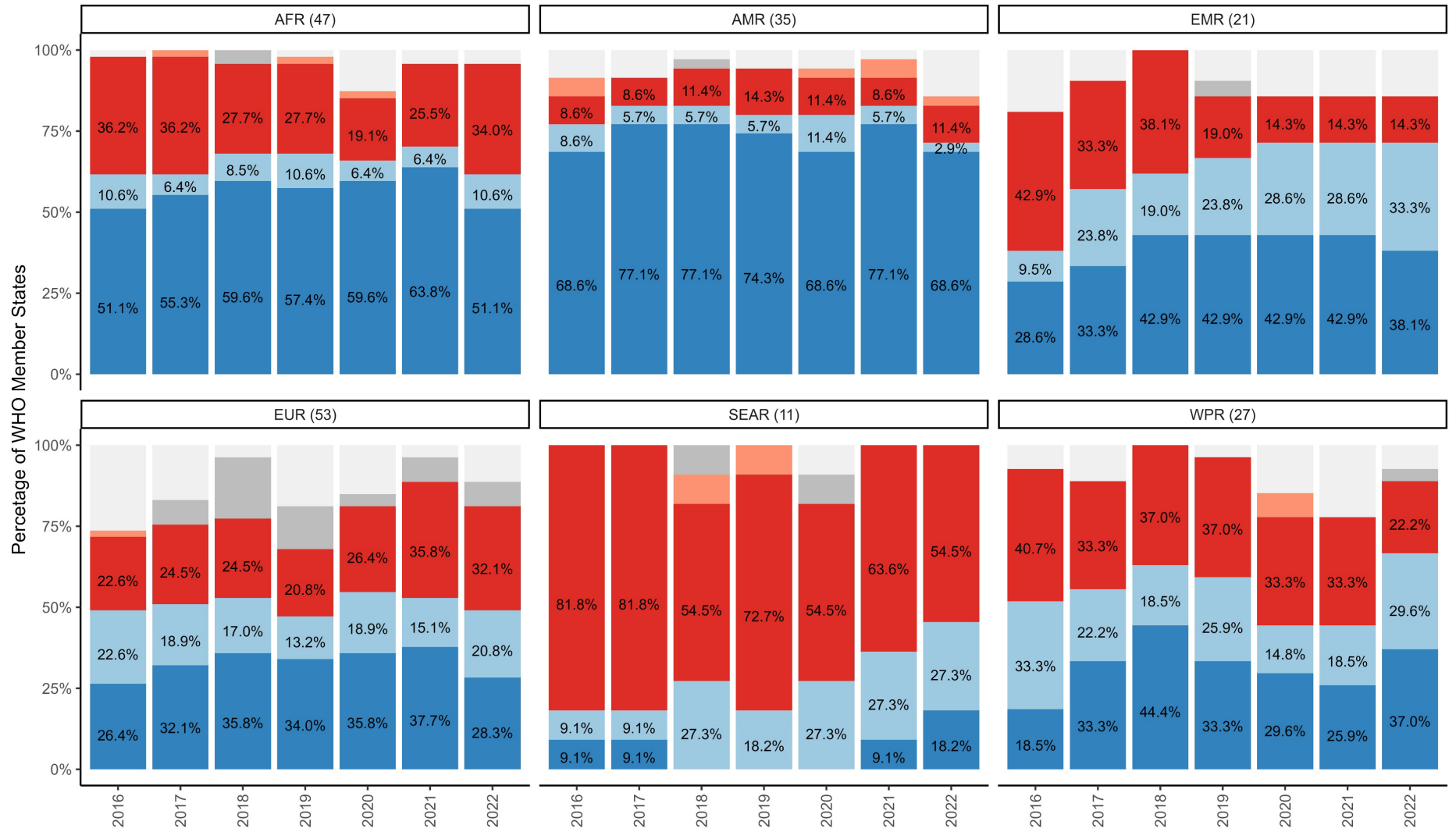




Background on catch-up and cohort monitoring

- At the global level, **childhood vaccination coverage** monitoring as focused on **coverage for one cohort**
  - For vaccines recommended in infancy (<12 months), numerator is infants vaccinated, and denominator is surviving infants (live births for vax recommended at birth)
  - For vaccines recommended in the second-year of life numerator is children aged 12-23 months vaccinated, and denominator is surviving infants from previous year (though many countries use same target as surviving infants)
  - Data collection is limited – **eJRF** is annual and since 2016 collecting only MCV1 by age group (<12 m, 12-23m; (or ≥24m)) . From 2023, also DTP3
- **WUENIC** is not designed to monitor catch-up
- **Survey data** (for people with cards/documented evidence of vaccination) can give an idea of timely vaccination and catch-up, but most surveys 12-36 months
- Cohort coverage monitoring is straightforward when an electronic immunization registry (**EIR**) is available
- **Very challenging with aggregated admin data**
  - **Data tools and systems** in many countries not set up to capture catch-up doses by separating age groups: <12 m; 12-23 m, 24-59m.
  - **Administrative data** at risk of being "contaminated", i.e., mixing doses given to infants with doses to children ≥12 months (or ≥24months)

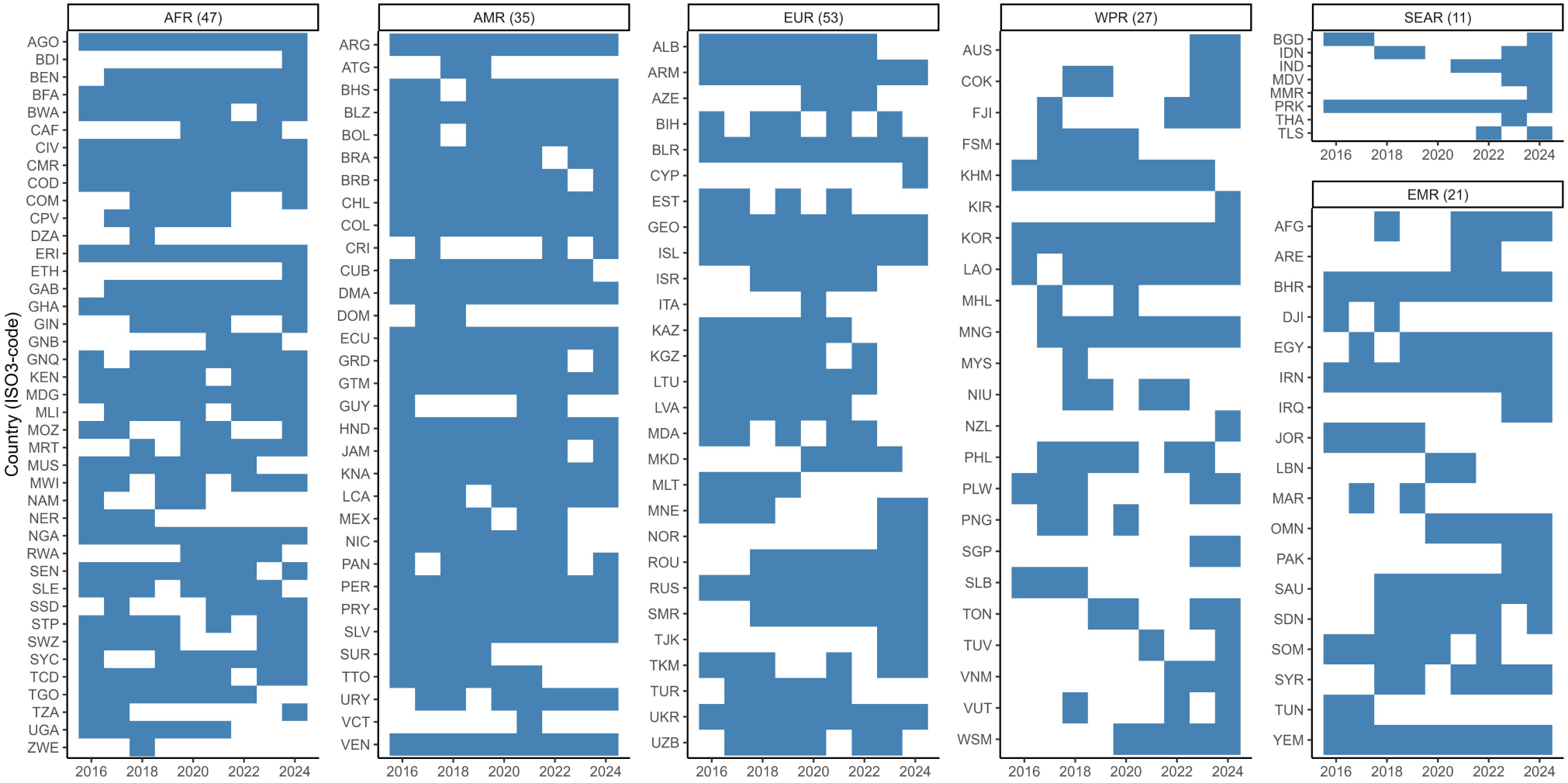
Responses to the question “ *Does your recording system allow for capture of data, at the national level, on the number of delayed or late doses administered?*”, Member States by WHO Region, 2016-2022



From 106 countries in 2016 to 119 (61%) in 2022

https://verixiv.org/articles/2-123

WHO Member States reporting delayed MCV1 doses, by WHO Region, 2016-2024



Between 2016-2022* the median proportion of delayed MCV1 vaccinations was 4.4% (interquartile range 1.2%-13.8%). Excluding suspected errors, the median was 3.9% (interquartile range 1.1%-9.5%).

https://verixiv.org/articles/2-123

Data 2023-2024 being cleaned up

Example of monitoring by cohort: Example from HPV

Programme coverage: vaccination coverage according to girls/boys reached in the programme as per eligibility criteria in each calendar year

By 15

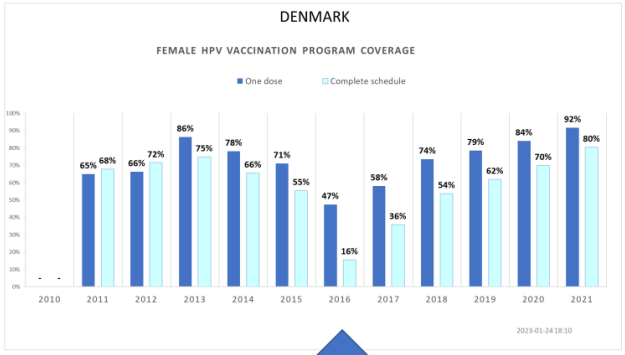
Coverage by age 15: proportion of girls/boys turning 15 in the reporting year that received HPV vaccine between ages 9 to 14 at any time during previous years

Complementarity of the two indicators

Example from Denmark

Denmark Programme design:
- **HPV delivered through Health Facility (GP)**
- **Invitation sent to each 12 yr old Girl and Boy + catch-up opportunities until 18 yr**

PROGRAMME COVERAGE

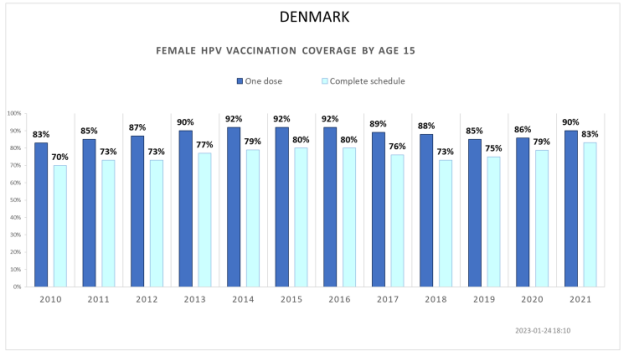


Coverage at age 12

recovery

Confidence crisis based on potential adverse events following immunization AEFI (POTS)

BY 15 COVERAGE



Primary cohort vaccination + catch-up strategies

Catch-up allowed to minimize the impact

Main challenges:

- by 15 indicator will only have additional value if countries report in JRF any doses delivered in cohorts beyond routine age cohort consistently over time
- Does not represent performance in the reporting year but accumulates data from several years back (up to 6 years) -> TIME LAG

Proposed Next Steps

- Revise eJRF
  - Add questions on info system, notably availability of EIRs
  - Add DTP1
  - Change format of questions
- Finish analysis of information system and delayed dose 2023-2024 and tally sheets 2024
- Document issues seen in Big-catch-up countries
- Document issues with HPV coverage by age 15
- Work with the IVIR-AC subgroup on vaccination coverage estimation to:
  - Analyze more surveys to determine contribution of delayed vaccination to coverage
  - Test “coverage by age 2” for selected countries and define criteria for data availability and consistency needed to do this

Questions for IVIR-AC

1. Considering the ongoing data triangulation exercises, and the initial experience with DRC data, notably limited contextual information for each province at the global level and no mechanisms to collect such data:
   a. Does IVIR-AC support the proposed next steps to identify and evaluate criteria necessary to estimate subnational vaccine coverage at the administration 1 level, including estimates of uncertainty?
   b. What potential risks does IVIR-AC foresee?
   c. Would criteria need to be set for stopping admin1 estimates (for a country, for some admin1 levels, for some years)?
2. After reviewing initial data from the electronic Joint Reporting Form for immunization (eJRF) on delayed vaccination and examples of cohort monitoring:
   a. Does IVIR-AC support the proposed next steps to identify and evaluate approaches to monitor vaccination coverage and timeliness in cohorts of children, including the data requirements and analytical methods?

EXTRA SLIDES

TOR IVIR-AC Sub-group

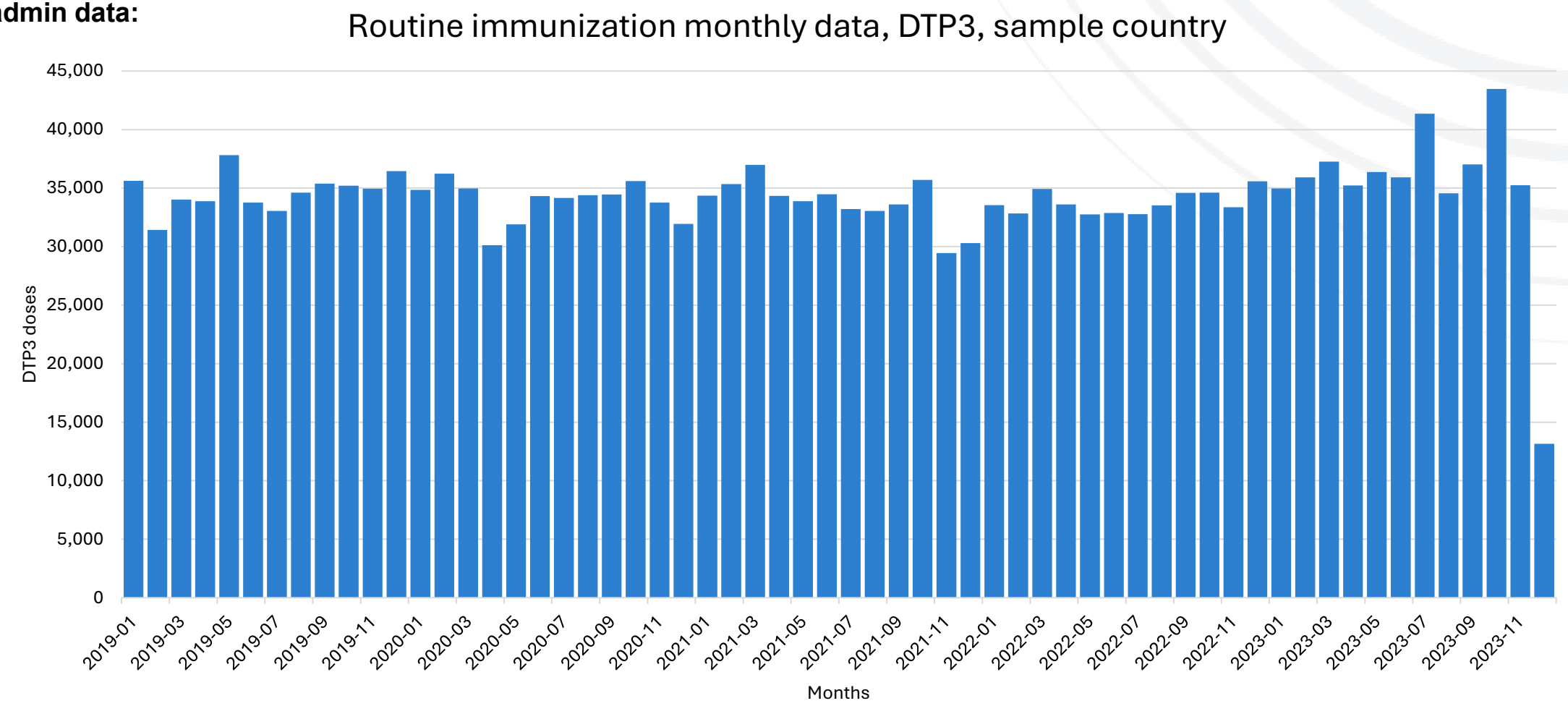
Main objective: To provide **independent technical advice** on coverage and related data analysis and quality to improve global vaccination coverage estimates.

Functions (summary)

- Provide **independent technical guidance to vaccination coverage measurements and estimation methodologies for global monitoring**, including data collection and compilation, analytic strategies, and related technical issues.
  - **Advise on effective visualization, dissemination and use of estimates**
  - **Provide guidance to WHO and UNICEF for the production of estimates of subnational data at admin level 1 for selected countries**
    - This may include providing inputs to develop guidance and tools to countries on conducting sub-national estimation exercises and help prioritize such exercises.
- Other possible functions:
  - Support the prioritization of vaccine-doses to monitor
  - Advise on linkages with related work
  - Provide inputs to the development of a research agenda to address measurement challenges and estimation strategies

How to monitor catch-up vaccination?

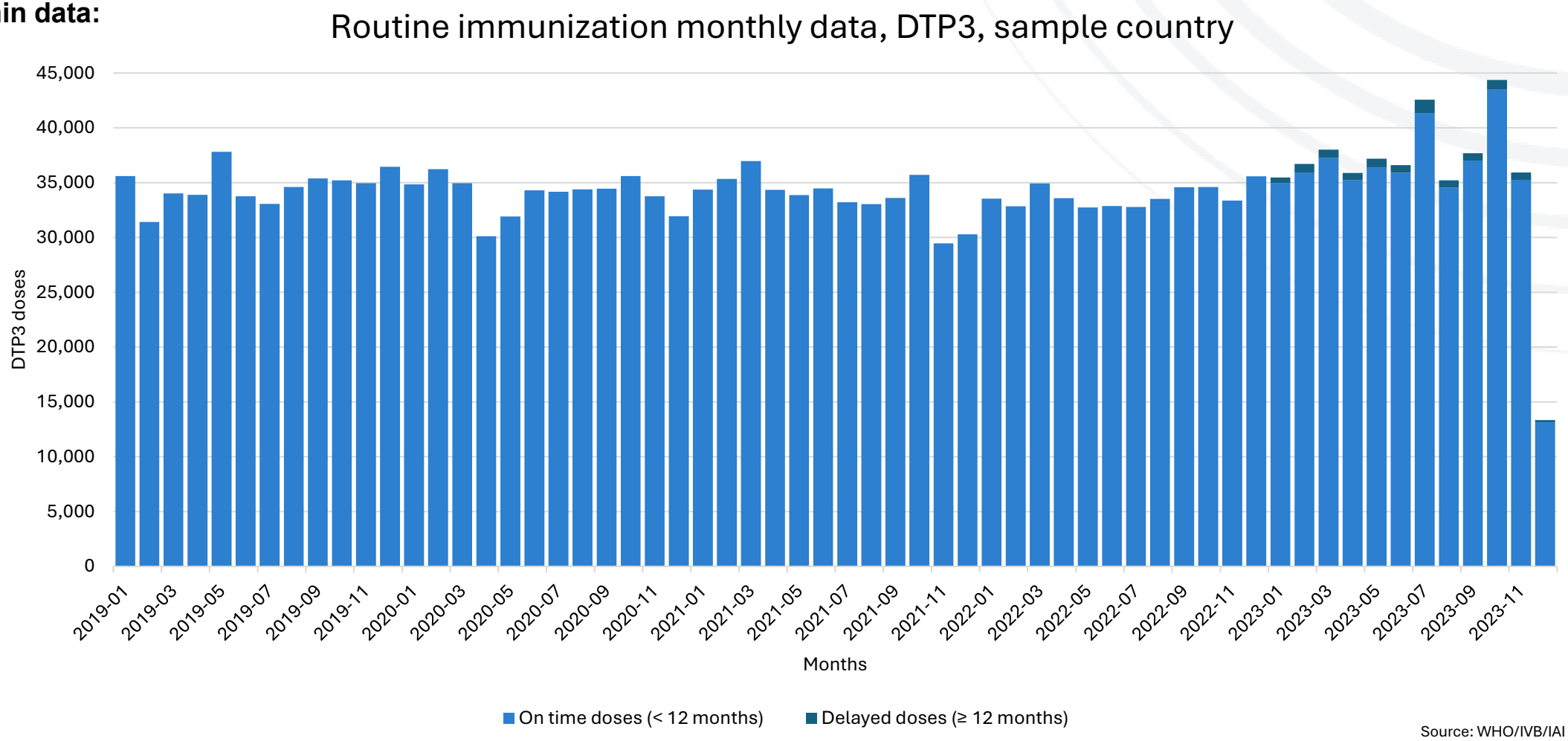
Monthly admin data:



Source: WHO/IVB/IAI

How to monitor catch-up vaccination?

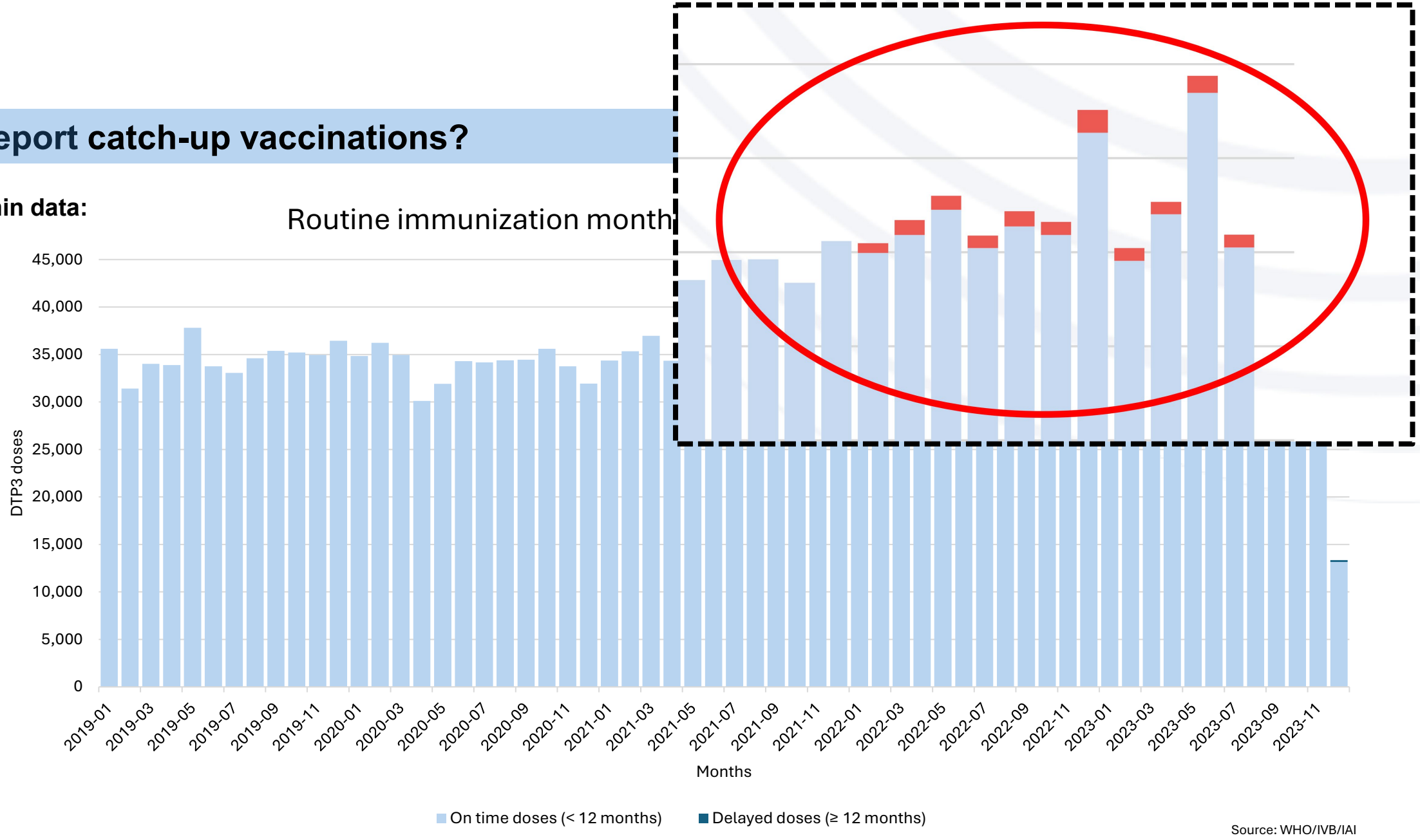
Monthly admin data:



Source: WHO/IVB/IAI

How to report catch-up vaccinations?

Monthly admin data:



Source: WHO/IVB/IAI

How to document catch-up vaccinations?

A **25-month-old boy without prior vaccinations** is brought to your health facility.

Where do you document the catch-up OPV vaccination?

Tally sheet:

ANTIGENS/ ITEMS	0-11 MONTHS	TOTAL	12-23 MONTHS	TOTAL
BCG	𝍸 𝍸 𝍸 𝍸 𝍸		𝍸 𝍸 𝍸 𝍸 𝍸	
Hep B BD	𝍸 𝍸 𝍸 𝍸 𝍸			
OPV 0	𝍸 𝍸 𝍸 𝍸 𝍸			
OPV 1	𝍸 𝍸 𝍸 𝍸 𝍸		𝍸 𝍸 𝍸 𝍸 𝍸	
OPV 2	𝍸 𝍸 𝍸 𝍸 𝍸		𝍸 𝍸 𝍸 𝍸 𝍸	
OPV 3	𝍸 𝍸 𝍸 𝍸 𝍸		𝍸 𝍸 𝍸 𝍸 𝍸	

?

Source: https://www.who.int/publications/i/item/9789240016514

Big Catch-up: Illustrative challenges observed (and still being gathered)

National & subnational

- Parallel data systems created for catch-up doses administered (since adding data elements to existing system takes time & urgency to roll-out)
  - More issues for MCV2, as some info systems only separate <12 months and 12-59 months
  - In some countries, different systems for delivery modalities (i.e. catch-up doses administered through intensification collected campaign-style, and catch-up doses administered at fixed site through a separate system)
- Capacity building for use of tools – unclear how systematically and thoroughly rolled out
- Reporting delays and data backlogs affecting completeness across levels (new and additional data elements and reporting requirements)

Illustration of how mixing on-time and catch-up doses affects coverage and comparability in trends

Service delivery level

- Inconsistent recording and reporting practices at the service delivery level for different reasons (may not have updated tools, training, supportive supervision) affecting data quality
- Additional recording and reporting tasks and forms to complete and verify with same number of health facility staff (in some facilities already short-staffed)
- Variable and low retention of home-based records to assess dose eligibility among children aged 12-59 months

HPV Cohort measurement and registering late vaccination (catch-up) to develop @15 yr coverage

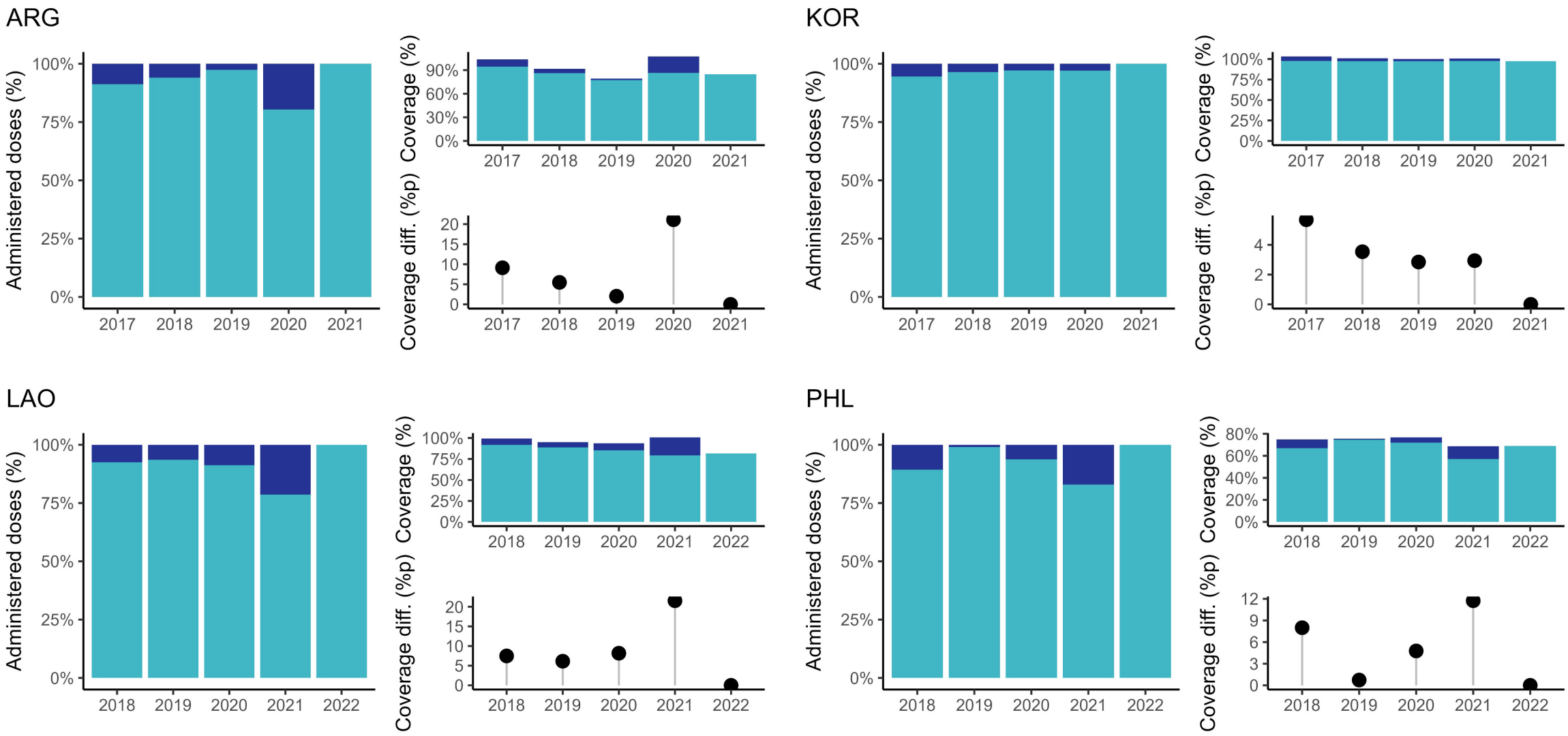
Example from country reporting doses delivered by age in each calendar year

Year	9	10	11	12	13	14	15+/15 (since 2020)	16+ (since 2020)	Missing	TOTAL DOSES CUM AT AGE 15- FINAL NUMERATOR	DOSES REPORTED AT AGE 15	PREVIOUS EDITION NUMERATOR	FINAL DENOMINATOR (DEFAULT NumMAC)	Calc by15 with UN denom
2006														
2007														
2008														
2009														
2010				22,000										
2011				23,500										
2012				22,790	1,115	98	96				96			
2013				24,091	1,232	107	184			22,098	184	*22,098*	22,098	71.3%
2014				24,905	862	164	341			24,722	341	*24,722*	24,722	79.9%
2015				25,597	647	131	587			24,186	587	*24,186*	24,186	77.5%
2016				26,844	759	250	2,670			25,084	2,670	*25,084*	25,084	81.4%
2017				27,176	656	295	3,722			25,802	3,722	*25,802*	25,802	85.5%
2018				28,098	995	366	5,596			26,651	5,596	*26,651*	26,651	88.0%
2019				28,231	817	215	1,192			27,866	1,192	*27,866*	27,866	90.7%
2020				29,064	808	154	238			28,386	238	*28,386*	28,386	91.8%
2021				28,490	839	160	198	219		29,069	198	*29,069*	29,069	92.8%
2022				29,251	1,787	210	258			29,199	258	*29,199*	29,199	91.8%
2023				28,581	926	311	303			30,113	30	*30,113*	30,113	92.9%
2024				28,648	903	333	374	340		=IF(SUM(H30,G29,F28,E27,D26,C25)=0,"",SUM(H30,G29,F28,E27,D26,C25))				
2025										30,510			30,510	91.7%
2026										29,484			29,484	90.6%
2027										28,648			28,648	89.7%

30,588

30,588

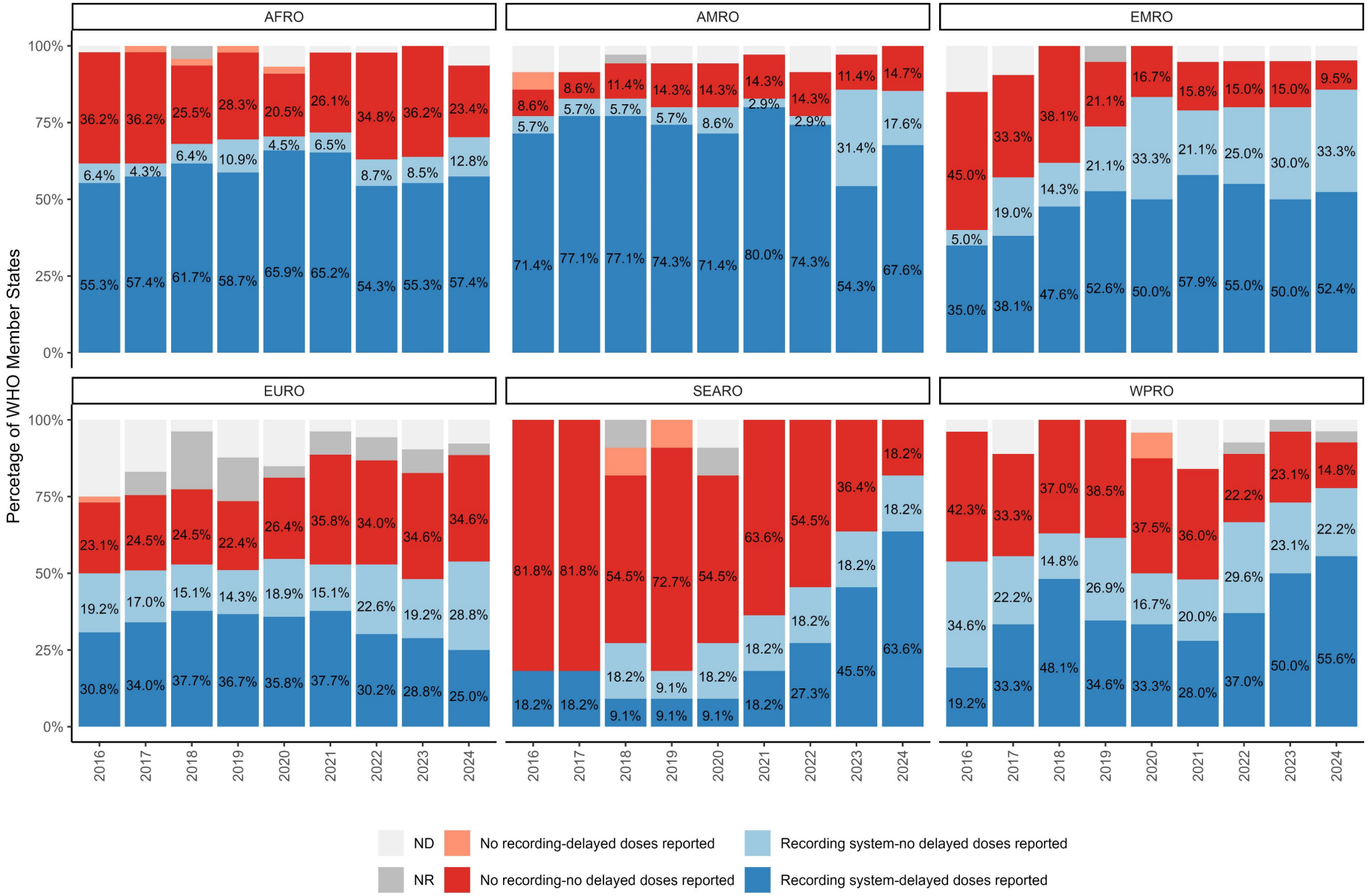
MCV1 doses administered and coverage, on-time and delayed, by birth cohort in selected countries (ARG, KOR, LAO, PHL), birth cohorts 2017-2021 for countries recommending



https://verixiv.org/articles/2-123

MCV1 in the second year of life and 2018-2022 for those recommending MCV1 in infancy.

Responses to the question “ *Does your recording system allow for capture of data, at the national level, on the number of delayed or late doses administered?*”, Member States by WHO Region, 2016-2024



Published background documents for this session

Bhatnagar, P., Gupta, S., Kumar, R., Haldar, P., Sethi, R., & Bahl, S. (2016). Estimation of child vaccination coverage at state and national levels in India. *Bulletin of the World Health Organization*, *94*(10), 728–734. https://doi.org/10.2471/BLT.15.167593

Danovaro-Holliday MC, Castro-Aguirre I, Koh M et al. Leave no one behind: Global Analysis on monitoring childhood vaccination timeliness and catch-up using data from the WHO/UNICEF joint reporting form on Immunization [version 2; peer review: 1 approved, 1 approved with reservations]. VeriXiv 2025, 2:123 (https://doi.org/10.12688/verixiv.1081.2)

World Health Organization

Session 4: Modelling Pertussis Burden & Vaccination Strategies

IVIR-AC 2 September 2025 | Session 4 - For DECISION

DTP Boost Vaccination Strategy Tool: Modelling the health and economic impact of introducing DTP-containing vaccine booster doses

WHO Focal Point: Stephanie Shendale
Presenters: Rachel Hounsell and Sheetal Silal

00_DTPBoost_background_materials_walkthrough_document

Context

Routine infant vaccination has contributed to considerable reduction of cases and deaths from diphtheria, tetanus, and pertussis globally. However, these diseases continue to pose serious health risks. To increase duration of protection, the WHO recommends three DTPCV booster doses be offered in early childhood, childhood, and adolescence. Evidence to inform country-level decision-making about the introduction of DTPCV booster doses is needed, especially considering the availability of support for Gavi-eligible countries.

DTP Boost is an interactive web-based tool to inform country-level decision making about the introduction and routine delivery of DTPCV booster doses. The tool allows users to design vaccination strategies to explore the health impact, budget impact, and cost-effectiveness of introducing DTPCV booster doses in a selected country. *The tool should be applied in collaboration between modellers and country partners.* DTP Boost is powered by an integrated epidemiological and health economic model, tailored to the selected country, accounting for differences in existing vaccination schedule, current burden of disease, health systems characteristics, costs of illness and vaccination. Multiple vaccination strategies can be designed, allowing a detailed and interactive exploration of the relative costs and benefits of different numbers of DTPCV booster doses, vaccination coverage levels, introduction approaches (e.g., simultaneous, phased), vaccine formulations and vaccination delivery platforms (e.g., health facility, outreach site, school-based).

DTP Boost was developed by the Modelling and Simulation Hub, Africa (MASHA) at the University of Cape Town in collaboration with the African Field Epidemiology Network (AFENET) and United States Centers for Disease Control and Prevention (U.S. CDC) with guidance from an expert steering committee. The tool has been piloted in Uganda, in partnership with the Ugandan National Program on Immunization (UNEPI).

Requests & questions to IVIR-AC focal points

The MASHA tool (DTP Boost) is one of very few dynamic transmission models focusing on DTP booster vaccination (integrating all three diseases + economic evaluation) and the only integrated decision-making tool (we are aware of) to inform country-level decision making about DTP booster dose introduction. The model is already available as a web-based tool but requires technical assistance for optimal use; some countries are already using this tool with their own data input for country level decision making.

Now that Gavi has launched a DTP booster programme, there is an accelerated need to include DTP boosters in the ongoing WHO work on developing decision making support tools for countries and NITAGs. We are seeking IVIR-AC's review and feedback on whether the model is fit for this purpose and how to best integrate this tool and/or outputs from this tool into the WHO vaccine evidence compendium (Compendium | NITAG RESOURCE CENTER).
Specific requests and questions to the IVIR-AC focal points are:

1) Use & Dissemination

- Provide feedback on the scope and methodology of the tool
- Provide recommendations for onward use and dissemination of the tool

2) Calibration & Burden

- How to overcome challenges with calibration where reliable estimates of burden or reported incidence are not available or not in line with country experience?
- Should functionality be added for user-uploaded seroprevalence data to help a country with calibration?

3) Estimating impact

- With the growing interest in diphtheria, how to put a value on increased population protection as a measure (i.e. potential to avert or reduce an outbreak) when there are no endemic cases to get an immediate benefit measure?

Background materials

The background reading materials are presented in three parts 1) DTP Boost tool; 2) First use-case in Uganda; and 3) Methodology report. These materials are of equal importance, but the most relevant component of each document is highlighted.

Background Document Set 1: 01_DTPBoost_tool_and_project_overview

This document provides an overview of the DTP Boost tool and project, including the following components:

- 01_A_DTPBoost_tool_and_project_overview: Background of the DTP Boost project and team; with details for accessing the tool and the GitHub repository
- 01_B_DTPBoost_tool_visual_tour: Visual tour slide deck of DTP Boost screenshots
- 01_C_DTPBoost_tool_demo_user_guide: User guide for the demo version of the DTP Boost tool (this version has pre-run scenarios to enable easy exploration of key features without running the models live)

01_A is the most important document, with priority to be given to Section 3, which provides instructions and links for accessing the DTP Boost tool (full and demo versions).

Background Document 2: 02_DTPBoost_uganda_pilot_policy_report_CONFIDENTIAL

This is the policy report for the pilot of the DTP Boost tool in Uganda, exploring the health and economic impact of introducing DTPCV booster doses. It presents the application of the tool, the methods for tailoring the tool to the Ugandan context, the scenarios, findings, and considerations for implementation.

The policy report includes an executive summary, which provides an overview of the application methods and the key messages. The executive summary (pages 6–10) and the summary of the findings (29–32) contain the most important information.

Background Document Set 3: 03_DTPBoost_model_methods_CONFIDENTIAL

This document provides methodological details for the development and validation of an integrated, multi-disease epidemiological-economic model for the transmission and vaccination of diphtheria, tetanus and pertussis. It includes:

- 03_A_DTPBoost_model_methods_CONFIDENTIAL. Overview of the **integrated multi-disease epidemiological-economic model** and participatory approach for its application (prioritising Sections 2 and 3)
- 03_B_DTPBoost_methods_tetanus_model_CONFIDENTIAL: Methodology for the development and validation of a new model for **tetanus** transmission and vaccination (prioritising Section 2. Model development)

- 03_C_DTPBoost_methods_diphtheria_model_CONFIDENTIAL: Methodology for the development and validation of a new model for **diphtheria** transmission and vaccination (prioritising Section 2. Model development)
- 03_D_DTPBoost_methods_pertussis_model_CONFIDENTIAL: Methodology for the development and validation of a new model for **pertussis** transmission and vaccination (prioritising Section 2. Model development)

IVIR-AC 2 September 2025 | Session 4 - For DECISION

DTP Boost Vaccination Strategy Tool: Modelling the health and economic impact of introducing DTP-containing vaccine booster doses

WHO Focal Point: Stephanie Shendale
Presenters: Rachel Hounsell and Sheetal Silal

01_A_DTPBoost_tool_and_project_overview

1. Background

DTP Boost is an interactive web-based tool to inform country-level decision making about the introduction and routine delivery of diphtheria-tetanus-pertussis-containing vaccines (DTPCV) booster doses. The tool allows users to design vaccination strategies to explore the health impact, budget impact, and cost-effectiveness of introducing DTPCV booster doses in a selected country.

This project was a collaboration between the Modelling and Simulation Hub, Africa (MASHA) at the University of Cape Town (UCT), the African Field Epidemiology Network (AFENET), and the United States Centers for Disease Control and Prevention (CDC), with guidance from an expert technical advisory group and partnership with the Ugandan EPI Programme (UNEPI).

The project was first conceived at an immunisation partners meeting held in Uganda in 2015, with representation from UNEPI, WHO, United Nations Children's Fund (UNICEF), CDC, AFENET, JSI, CHAI, and PATH. A need was identified based on the lack of any available integrated tools to inform country-level decision-making about DTPCV booster dose introduction and routine delivery. In 2021, the project was launched with the aim to develop the first interactive web-based decision-making tool (DTP Boost) allowing users to design vaccination strategies to explore the health impact, budget impact, and cost-effectiveness of introducing DTPCV booster doses in a selected country, focusing primarily on use for low- and middle-income country settings that had not yet introduced DTPCV boosters. The tool enables multiple different vaccination strategies to be designed, allowing a detailed and interactive exploration of the relative costs and benefits of introducing and routinely delivering different numbers of DTPCV booster doses, vaccination coverage levels, introduction approaches (e.g. simultaneous, phased), vaccine formulations and vaccination delivery platforms (e.g. health facility, outreach site, school-based).

2. DTP Boost Tool Overview

The DTP Boost tool was developed to facilitate a participatory modelling process and support country-level decision making. DTP Boost is a web-based decision-support tool that enables users to engage in the modelling process in an explicit, visual, and interactive way. The tool allows users to explore the health impact, budget impact, and cost-effectiveness of introducing DTPCV booster doses in a selected country.

DTP Boost is built in RShiny and powered by the integrated epidemiological-economic model for diphtheria, tetanus and pertussis; with cases, deaths, and immunity estimated for each disease over 15 years. The tool is prepopulated with default inputs from published literature and global datasets (e.g. WHO and United Nations), which users can amend. DTP Boost allows comparison of the relative costs and benefits of different combinations of DTPCV booster doses, target coverage levels, approaches to introduction, vaccine formulations, and delivery platforms.

The full disease models for diphtheria, tetanus and pertussis run live in the background, with users following a four-step process to tailor the application to the unique country context. During the first step, users establish a baseline country profile by specifying the disease burden; existing vaccination schedule and delivery locations; vaccination coverage; health system characteristics such as treatment seeking, diagnosis and reporting; costs of routine vaccine; cost of treatment; and co-financing arrangements. In the second step, users calibrate the model to the country setting by fitting to the reported or estimated disease burden. These two steps combine to form a realistic approximation of the country context up to the present. Steps three and four allow the user to explore potential future scenarios by designing vaccination strategies (Step 3) and reviewing the projected health and economic impact of the chosen strategies (Step 4). Figure 6.8 shows a series of screenshots from each of the four steps of the DTP Boost tool.

3. Accessing the DTP Boost tool

3.1 Accessing the full tool

The tool is designed to be used in collaboration between modellers and country partners. It requires data and contextual understanding to tailor it to the selected country. The multi-disease model runs live in the background of the app. Each run takes 5-8min.

Access to the code repository on GitHub: https://github.com/uct-masha/DTPBoost

Links to access the full DTP Boost tool:

- https://masha-app.shinyapps.io/DTPBoost-WHO-IVIR-AC
- https://masha-app.shinyapps.io/DTPBoost-WHO-AH
- https://masha-app.shinyapps.io/DTPBoost-WHO-SF
- https://masha-app.shinyapps.io/DTPBoost-WHO-RA

Note: The DTP Boost tool is designed to have a single instance of the application running per user. We have created a link for each of the IVIR-AC focal points (with initials) and a general IVIR-AC link.

For a visual tour of the tool, see the slide deck in **01_B_DTPBoost_tool_visual_tour**. There is instruction text throughout the tool, as well as info popups with more detail. However, please refer to the DTP Boost Demo tool user guide for further information.

DTP Boost suggested citation: Hounsell, R., Norman, J., Monyake, R., & Silal, S., (2025). DTP Boost (Version 2.0) [Computer software]. https://github.com/uct-masha/DTPBoost

3.2 Accessing the demo version

The full DTP Boost tool uses a live-running model and requires local data to tailor the projections to the selected country. To enable easy exploration of the tool and its key features, a demo version was developed with simplified optionality, default data, and a set of pre-run scenarios.

This link provides access to the DTP Boost Demo and can be used by multiple people simultaneously:

https://masha-app.shinyapps.io/DTPBoostDemo/

A user guide for the Demo tool is provided in document
01_C_DTPBoost_tool_demo_user_guide.

Note: DTP Boost Demo does not provide the full functionality of the main tool and is purely intended for demo purposes only.

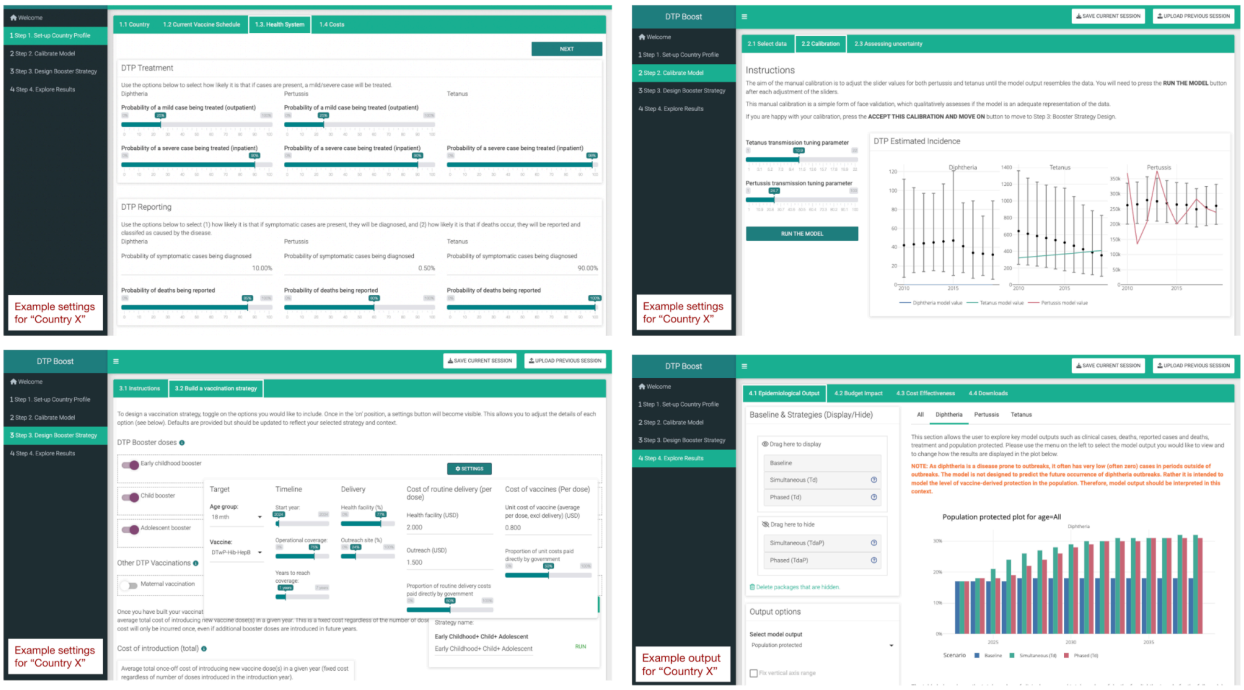


Figure 1. Example screenshots from the DTP Boost decision-support tool

4. DTP Boost Project Team

Modelling and Simulation Hub, Africa (MASHA)

The MASHA team was responsible for the development of the epidemiological and economic models, and the development of the interactive web-based tool. The MASHA team includes Prof Sheetal Silal, Ms Rachel Hounsell, Mr Jared Norman, Prof Rudzani Muloiwa and Mr Retselisitosoe Monyake.

U.S. Centers for Disease Control and Prevention

The U.S. Centers for Disease Control and Prevention's Global Immunization Division (CDC/GID) conceptualized the project, convened the Technical Expert Group, provided technical assistance to the development of the models and tool, and funded development of the models and web-based tool. CDC/GID team members included Dr. Kirsten Ward, Dr. Nishant Kishore, Dr. Sarah Pallas, Dr. Rania Tohme, and Dr. Aaron Wallace. The models and tool reflect the views of the individual team members and do not represent the official position of the U.S. Centers for Disease Control and Prevention.

African Field Epidemiology Network (AFENET)

The African Field Epidemiological Network (AFENET) provided technical assistance and financial support to the development of the epidemiological and economic models, and development of

the web-based tool. The AFENET team included Mr. Joseph Magoola, under the supervision of Dr. Nicholas Ayebazibwe.

Technical Expert Group

The role of the TEG was to advise on the model development, epidemiology and immunology of disease, DTP Boost application features and dissemination. The parameter values were established with input and review from the TEG.

- Dr Ampeire Immaculate, Ugandan National Immunization Program, Ministry of Health, Government of Uganda.
- Dr Anna Acosta, Meningitis and Vaccine Preventable Diseases Branch at U.S. Centers for Disease Control and Prevention (CDC)
- Dr Annet Kisakye, Expanded Program on Immunization, World Health Organization, Uganda
- Prof Paula Mendes Luz, Instituto Nacional de Infectologia Evandro Chagas (INI)
- Dr Todi Mengistu, Measurement, Evaluation and Learning (MEL) team at Gavi, the Vaccine Alliance
- Dr Helen Quinn, National Centre for Immunisation Research and Surveillance (NCIRS); University of Sydney Children's Hospital Westmead Clinical School.
- So Yoon Sim, Value of Vaccines, Modeling & Economics (VoV) team, Immunization Analysis & Insights (IAI) unit, Department of Immunization, Vaccines and Biologicals (IVB), World Health Organization
- Dr Rania Tohme, Hepatitis B and Tetanus Team in the Global Immunization Division at the U.S. Centers for Disease Control and Prevention (CDC)

DTP Boost: An Interactive Tool for Modelling the Health and Economic Impact of Introducing DTPCV Booster Doses

IVIR-AC 2 September 2025 - Session 4

Visual tour of DTP Boost tool

Background reading material: **01_B_DTPBoost_tool_visual_tour**

Contacts

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Rachel Hounsell | Presenter MASHA UCT (rachel.hounsell@uct.ac.za)

Sheetal Silal | Presenter MASHA UCT (sheetal.silal@uct.ac.za)

Session 4 - FOR DECISION

DTP Boost Vaccination Strategy Tool: Modelling the health and economic impact of introducing DTP-containing vaccine booster doses

WHO Focal Point: Stephanie Shendale
Presenters: Rachel Hounsell and Sheetal Silal

2 September 2025

Background document: 01_B_DTPBoost_tool_visual_tour

DTP Boost suggested citation: Hounsell, R., Norman, J., Monyake, R., & Silal, S., (2025). DTP Boost (Version 2.0) [Computer software]. https://github.com/uct-masha/DTPBoost

DTP Boost | Modelling tool to inform decision making

Gap

- No available integrated model to estimate health and economic effects of diphtheria tetanus pertussis containing vaccines (DTPCV) booster dose introduction and routine delivery – key for vaccine introduction decisions

Approach

- Interactive web-based decision-making tool - making modelling accessible
- Single integrated mathematical (3 diseases) and economic evaluation models
- Allows exploration and comparison of unlimited number of approaches to introduction and routine delivery, and sensitivity analysis
- Collaborative & multidisciplinary process involving end-users
- Collaboration between MASHA, CDC, AFENET and UNEPI with guidance from global TEG
- Piloted in Uganda (UNEPI & NITAG)

The team composed of CDC, MASHA, AFENET and UNEPI-MoH staff discussing the parameters and scenarios to use when working with the DTP booster App

Group photo of participants and trainers, left to right Joseph Magoola (AFENET,. Kirsten Ward (CDC), Rachel Hounsell (MASHA Group), Biroma Godfrey (MoH-UNEPI), Besigye Albert (MoH-UNEPI) and Dr. Nishant Kishore (CDC)

Acknowledgements

CORE Team

The **MASHA** team

- Prof Sheetal Silal
- Ms Rachel Hounsell
- Mr Jared Norman
- Prof Rudzani Muloiwa
- Mr Retselisitsoe Monyake

The U.S. Centers for Disease Control and Prevention (**CDC**) team includes

- Ms Kirsten Ward
- Dr Sarah Pallas
- Dr Nishant Kishore
- Dr Aaron Wallace

The **AFENET** team

- Mr Joseph Magoola
- Mr Michael Nkanika

Expert reference group

- Dr Ampeire Immaculate (UNEPI)
- Dr Anna Acosta (US CDC)
- Dr Annet Kisakye (WHO Uganda)
- Prof Paula Mendes Luz (INI, Brazil)
- Dr Todi Mengistu (Gavi)
- Dr Helen Quinn (NCIRS, Australia)
- So Yoon Sim (WHO HQ)
- Dr Rania Tohme (US CDC)

Ugandan National Expanded Program on Immunization

- Mr Albert Besigye (M&E unit, UNEPI)
- Mr Godfrey Biroma (M&E unit, UNEPI)
- Dr Ampeire Immaculate (UNEPI)

DTP Boost | Process

STEP 1. SET BASELINE COUNTRY PROFILE

STEP 2. CALIBRATE MODEL

REALISTIC PAST

STEP 3. DESIGN STRATEGIES

STEP 4. EXPLORE RESULTS

POTENTIAL FUTURE

Step 1. Country Profile

Setting up the baseline

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

About | The Project | The Model | The Team | Contact

DTP Booster Strategy Tool

Welcome to the DTP Booster Strategy Tool. DTP Boost is a tool that allows users to design vaccination strategies to explore the health impact and cost-effectiveness of introducing diphtheria, tetanus and pertussis booster doses in a selected country.

The tool uses a combination of epidemiological and economic models to generate projections. Multiple vaccination strategies can be designed, allowing a detailed and interactive exploration of the relative costs and benefits of each. The projections are tailored to the selected country, accounting for differences in existing vaccination strategy, current burden of disease, and health systems characteristics. Click on the tabs above to learn more about the tool and models used.

To begin, please click the 'Get Started' button or follow the steps outlined in the menu on the left.

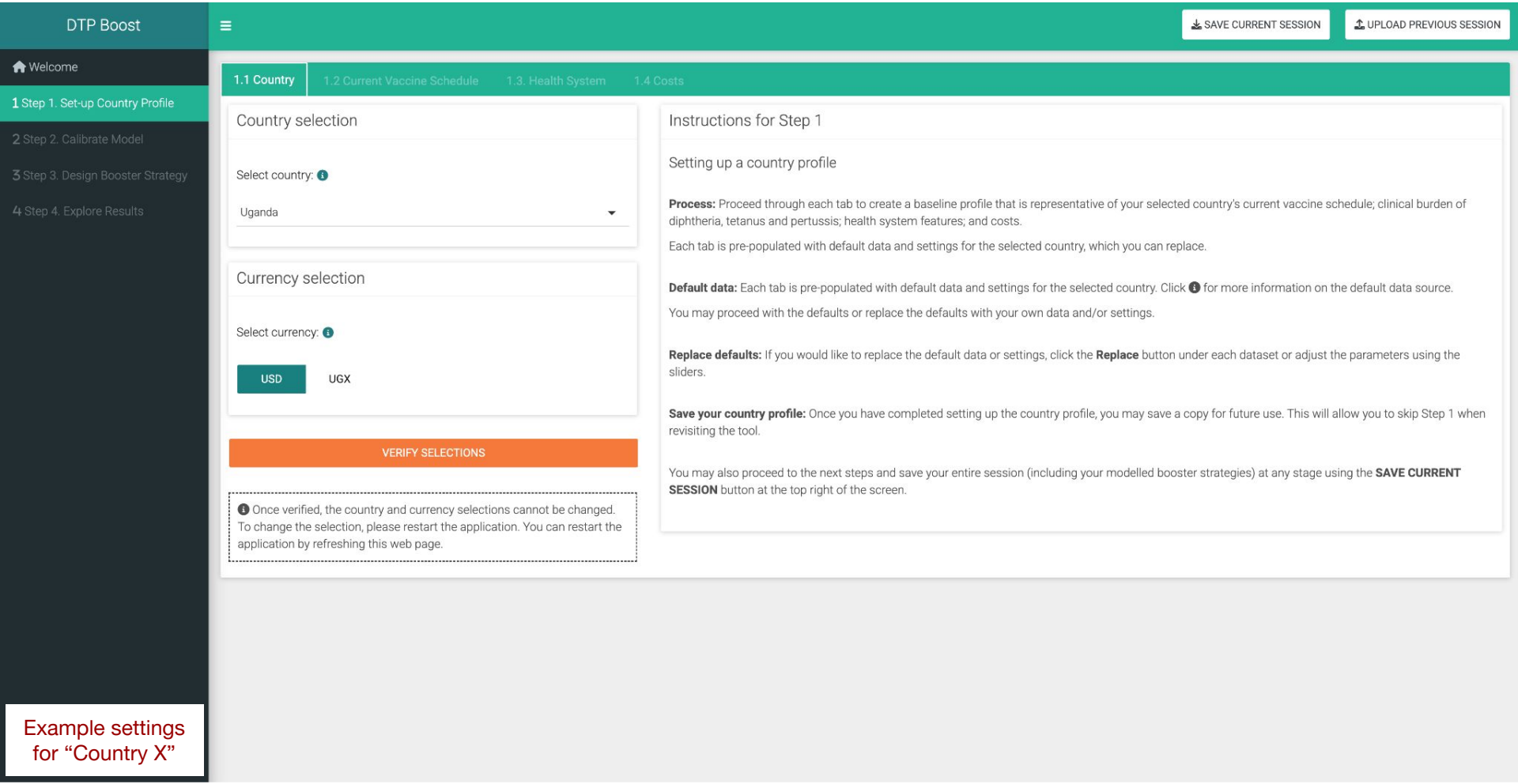
Alternatively, click the 'Load AFENET Session' button to load the session used in the Uganda first-use in May 2023.

This work was supported by funding from the U.S. Centers for Disease Control and Prevention under a Cooperative Agreement with the African Field Epidemiology Network (AFENET). By continuing to use this tool, you accept that the tool is as is and that the partners involved in development are not responsible for the results, interpretation, or decisions made based on the tool. They do not represent the official position of the U.S. Centers for Disease Control and Prevention, AFENET, or MASHA.

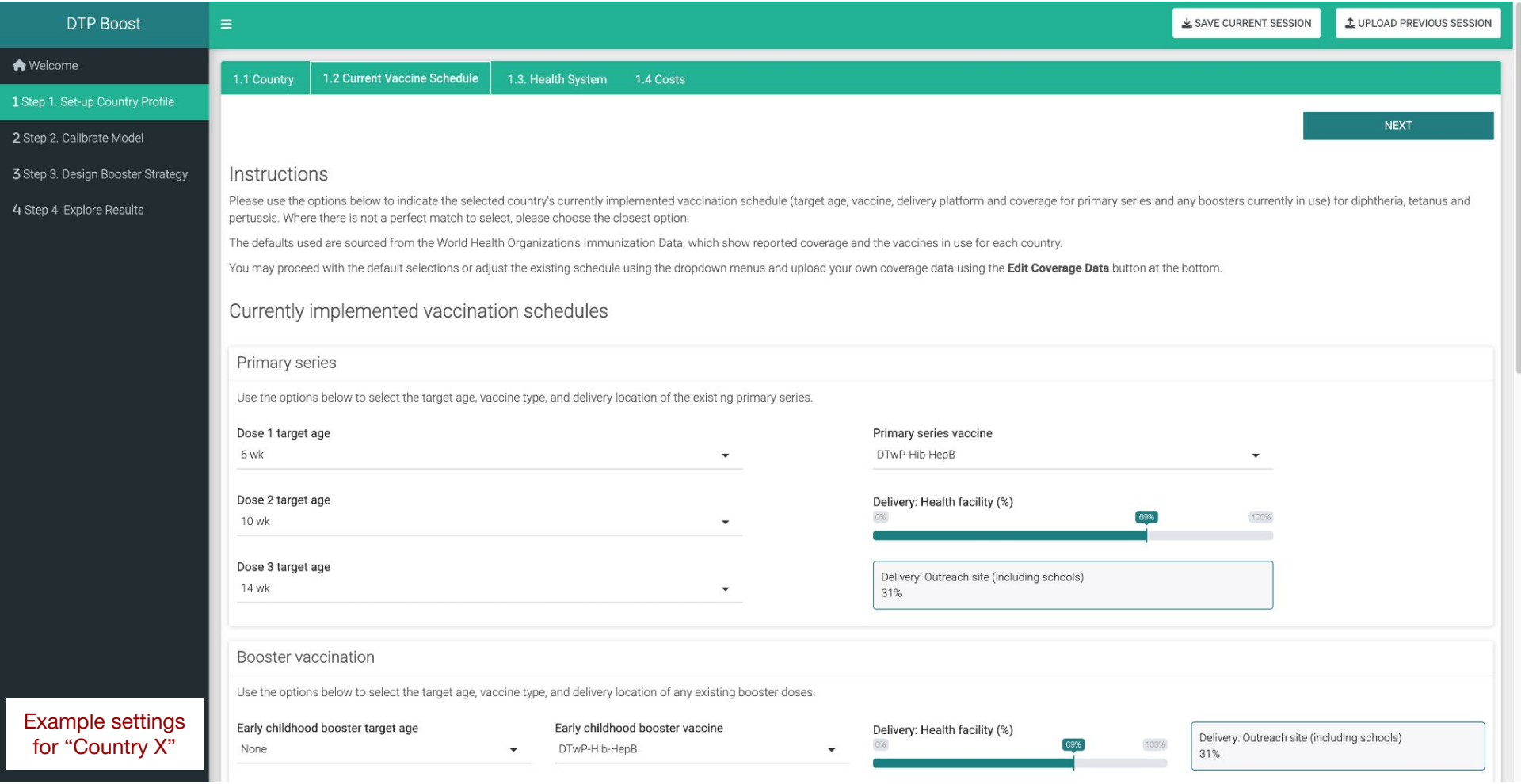
Citation for use of the tool: DTP Boost Strategy Tool, version 1.0 (18 July 2023).

GET STARTED | LOAD AFENET SESSION

Example settings for “Country X”



Example settings for "Country X"


DTP Boost
SAVE CURRENT SESSION
UPLOAD PREVIOUS SESSION
Welcome
1 Step 1. Set-up Country Profile
2 Step 2. Calibrate Model
3 Step 3. Design Booster Strategy
4 Step 4. Explore Results
1.1 Country
1.2 Current Vaccine Schedule
1.3. Health System
1.4 Costs
NEXT
Instructions
Please use the options below to indicate the selected country's currently implemented vaccination schedule (target age, vaccine, delivery platform and coverage for primary series and any boosters currently in use) for diphtheria, tetanus and pertussis. Where there is not a perfect match to select, please choose the closest option.
The defaults used are sourced from the World Health Organization's Immunization Data, which show reported coverage and the vaccines in use for each country.
You may proceed with the default selections or adjust the existing schedule using the dropdown menus and upload your own coverage data using the Edit Coverage Data button at the bottom.
Currently implemented vaccination schedules
Primary series
Use the options below to select the target age, vaccine type, and delivery location of the existing primary series.
Dose 1 target age
6 wk
Dose 2 target age
10 wk
Dose 3 target age
14 wk
Primary series vaccine
DTwP-Hib-HepB
Delivery: Health facility (%)
0%
69%
100%
Delivery: Outreach site (including schools)
31%
Booster vaccination
Use the options below to select the target age, vaccine type, and delivery location of any existing booster doses.
Early childhood booster target age
None
Early childhood booster vaccine
DTwP-Hib-HepB
Delivery: Health facility (%)
0%
69%
100%
Delivery: Outreach site (including schools)
31%
Example settings for "Country X"

None

DTwP-Hib-HepB

31%

Child booster target age

None

Child booster vaccine

Td

Delivery: Health facility (%)

0% 10% 100%

Delivery: Outreach site (including schools)
90%

Adolescent booster target age

None

Adolescent booster vaccine

Td

Delivery: Health facility (%)

0% 10% 100%

Delivery: Outreach site (including schools)
90%

Maternal vaccination (via ANC)

Td

Delivery: Health facility (%)

0% 69% 100%

Delivery: Outreach site (including schools)
31%

Coverage

Please review coverage data in the table below. Either proceed with the default values or use the EDIT COVERAGE DATA button to replace the values in the table.

Year	Dose 1	Dose 2	Dose 3	Early childhood booster	Child booster	Adolescent booster	ANC*	TTCV2
2022	94.0%	91.5%	89.0%	0.0%	0.0%	0.0%	77.2%	59.2%
2021	97.0%	94.0%	91.0%	0.0%	0.0%	0.0%	79.9%	64.7%
2020	94.0%	91.5%	89.0%	0.0%	0.0%	0.0%	79.9%	64.7%
2019	96.0%	94.5%	93.0%	0.0%	0.0%	0.0%	80.1%	65.0%
2018	97.0%	95.0%	93.0%	0.0%	0.0%	0.0%	80.4%	65.6%
2017	00.0%	96.5%	94.0%	0.0%	0.0%	0.0%	75.7%	54.0%

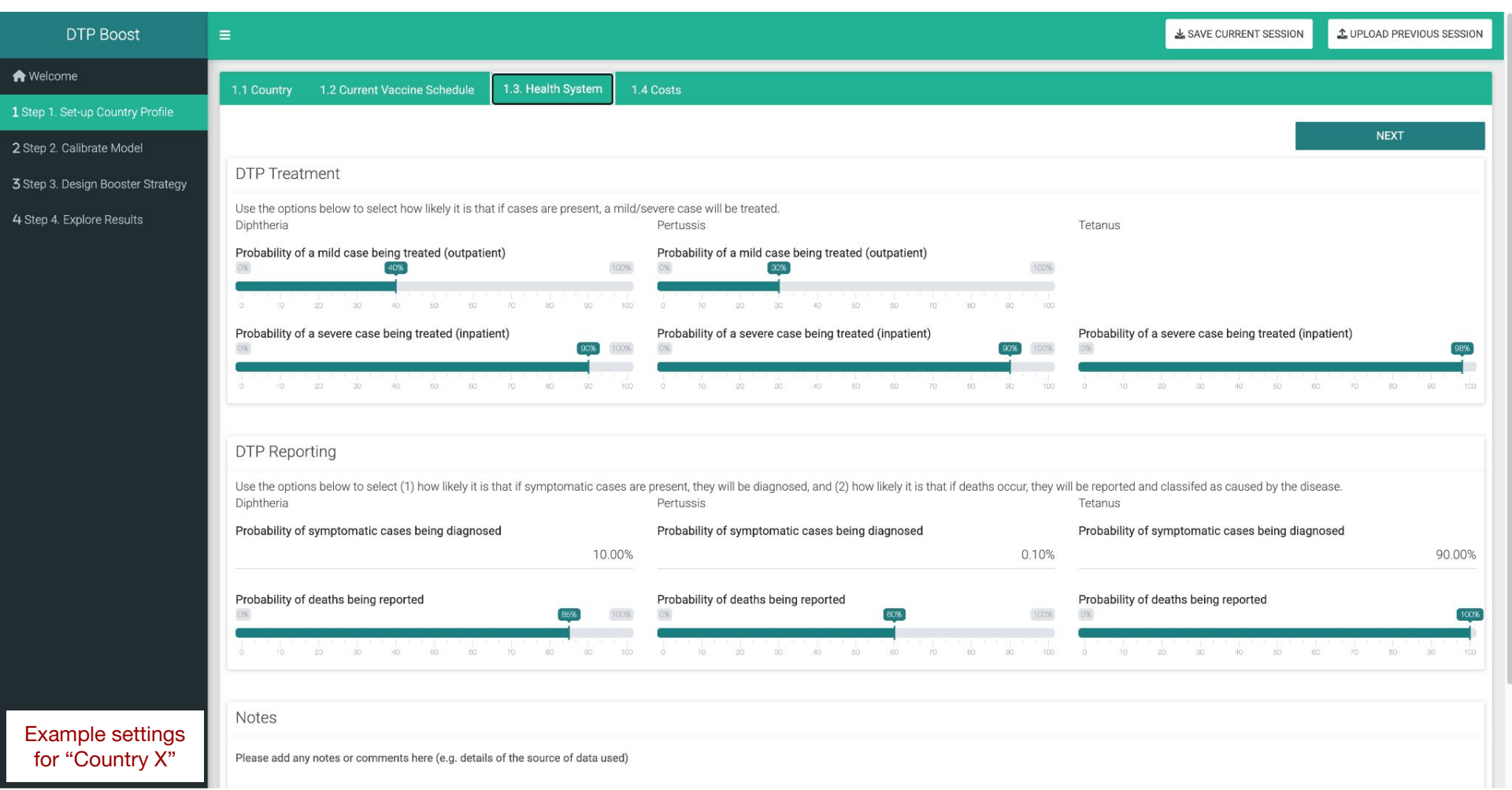
* If maternal vaccination is currently implemented, default vaccination coverage for the first dose will be 'Antenatal care coverage - at least 1 visit' based on WHO Global Health Observatory data. For dose 2 and above, TTCV2 data will be used.

EDIT COVERAGE DATA

Notes

Please add any notes or comments here (e.g. details of the source of data used)

Example settings for "Country X"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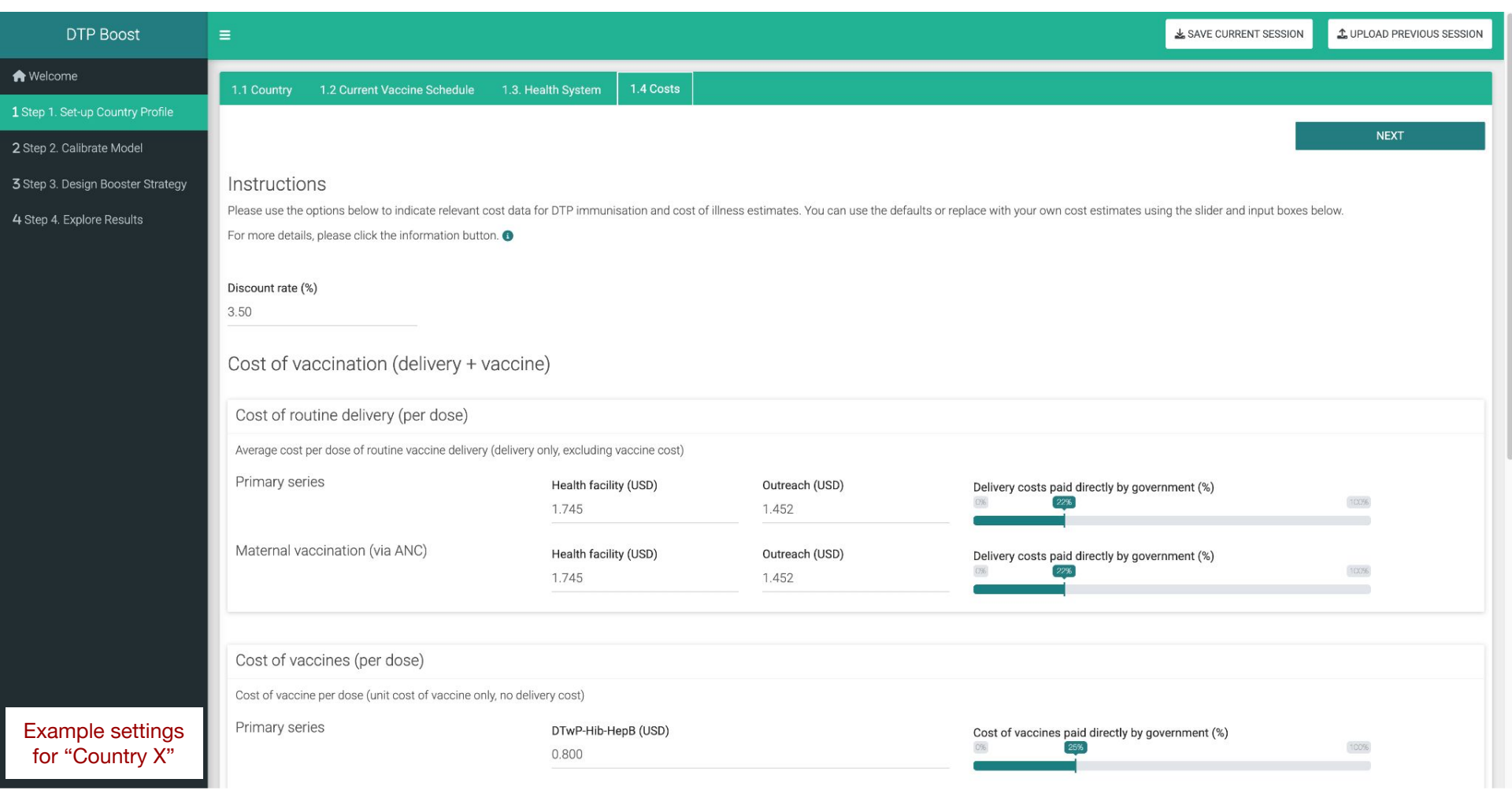
1.3. Health System
1.4 Costs
NEXT
DTP Treatment
Use the options below to select how likely it is that if cases are present, a mild/severe case will be treated.
Diphtheria
Pertussis
Tetanus
Probability of a mild case being treated (outpatient)
40%
30%
Probability of a severe case being treated (inpatient)
90%
90%
98%
DTP Reporting
Use the options below to select (1) how likely it is that if symptomatic cases are present, they will be diagnosed, and (2) how likely it is that if deaths occur, they will be reported and classifed as caused by the disease.
Diphtheria
Pertussis
Tetanus
Probability of symptomatic cases being diagnosed
10.00%
0.10%
90.00%
Probability of deaths being reported
85%
80%
100%
Notes
Please add any notes or comments here (e.g. details of the source of data used)
Example settings for “Country X”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4 Step 4. Explore Results
1.1 Country
1.2 Current Vaccine Schedule
1.3. Health System
1.4 Costs
NEXT
Instructions
Please use the options below to indicate relevant cost data for DTP immunisation and cost of illness estimates. You can use the defaults or replace with your own cost estimates using the slider and input boxes below.
For more details, please click the information button.
Discount rate (%)
3.50
Cost of vaccination (delivery + vaccine)
Cost of routine delivery (per dose)
Average cost per dose of routine vaccine delivery (delivery only, excluding vaccine cost)
Primary series
Health facility (USD)
1.745
Outreach (USD)
1.452
Delivery costs paid directly by government (%)
0%
22%
100%
Maternal vaccination (via ANC)
Health facility (USD)
1.745
Outreach (USD)
1.452
Delivery costs paid directly by government (%)
0%
22%
100%
Cost of vaccines (per dose)
Cost of vaccine per dose (unit cost of vaccine only, no delivery cost)
Primary series
DTwP-Hib-HepB (USD)
0.800
Cost of vaccines paid directly by government (%)
0%
25%
100%
Example settings for “Country X”

1.745

1.452

0% 22% 100%

Maternal vaccination (via ANC)

Health facility (USD)

1.745

Outreach (USD)

1.452

Delivery costs paid directly by government (%)

0% 22% 100%

Cost of vaccines (per dose)

Cost of vaccine per dose (unit cost of vaccine only, no delivery cost)

Primary series

DTwP-Hib-HepB (USD)

0.800

Cost of vaccines paid directly by government (%)

0% 25% 100%

Maternal vaccination

Td (USD)

0.110

Cost of vaccines paid directly by government (%)

0% 100%

Cost of illness

Diphtheria

Cost per outpatient case (USD)

30.000

Cost per inpatient case (USD)

800.000

Pertussis

Cost per outpatient case (USD)

25.000

Cost per inpatient case (USD)

500.000

Tetanus

Cost per outpatient case (USD)

50.000

Cost per inpatient case (USD)

2,000.000

Notes

Please add any notes or comments here (e.g. details of the source of data used)

Example settings for “Country X”

Step 2. Calibration

Calibrate model to different data sources

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

2.1 Select data | 2.2 Calibration | 2.3 Assessing uncertainty

Instructions

Please use the options below to select the incidence dataset to be used for model fitting. Model fitting is conducted to validate that the transmission model produces estimates that are similar to observed data. A fitted model adds validity to predictions of the impact of vaccination. The reporting rate specified in the Health System section will be used to correct for under-reporting of diagnosed cases.

Two data options are available: 1) WHO observed incidence data and 2) Global Burden of Disease incidence estimates. If you prefer to upload your own incidence data, you may do so in the 'Upload your data' box below.

Given that unpredictable external drivers often seed diphtheria outbreaks, calibration is applied to pertussis and tetanus only. It is important to interrogate the datasets to determine if data are valid given local experience *for both pertussis and tetanus* to fit the model.

Choose a dataset for calibration

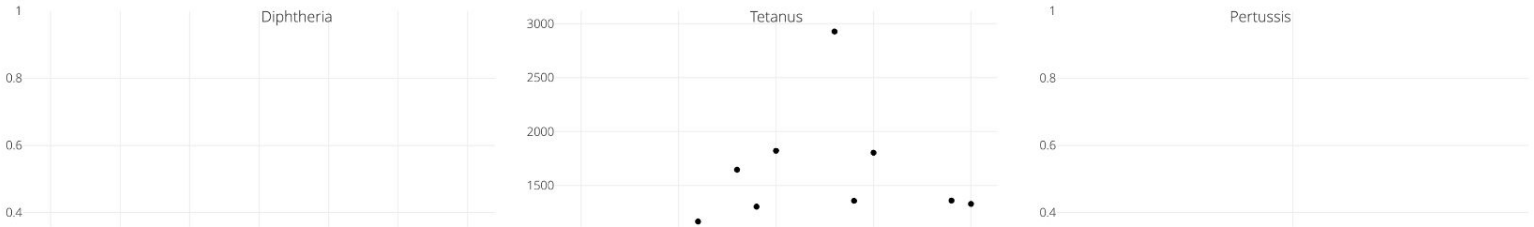
Use the buttons to select a dataset for calibration that best fits your country's profile.

- ○ WHO
- ◉ GBD
- ○ OWN DATA

GO TO CALIBRATION

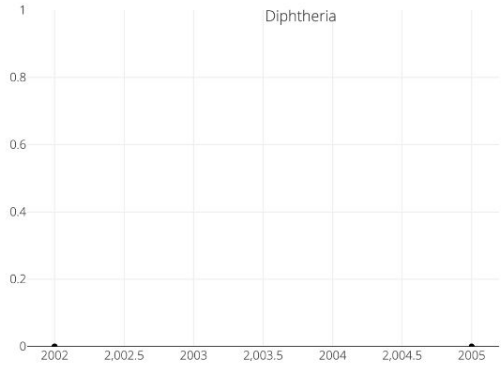
The plots below display the **WHO data** and **GBD estimates** to help you select the best approach. The option to upload your own data is shown under the heading **Upload your data.**

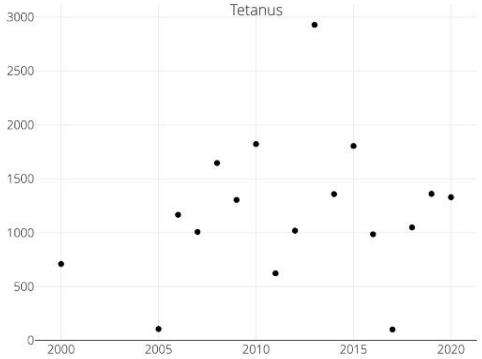
WHO data: Global Health Observatory annual reported incidence

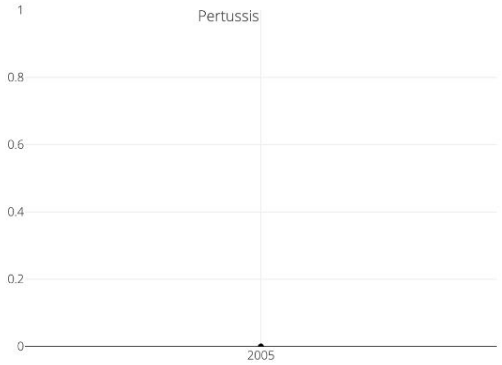


Example settings for "Country X"

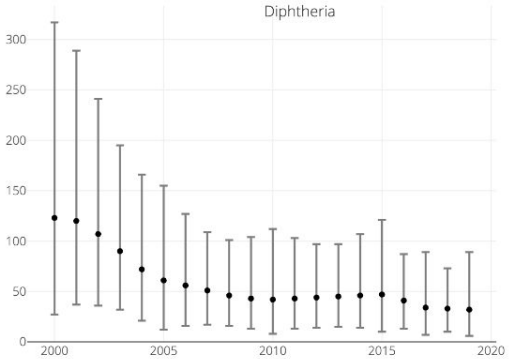
WHO data: Global Health Observatory annual reported incidence

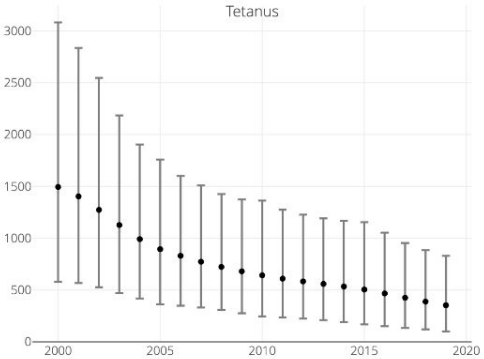


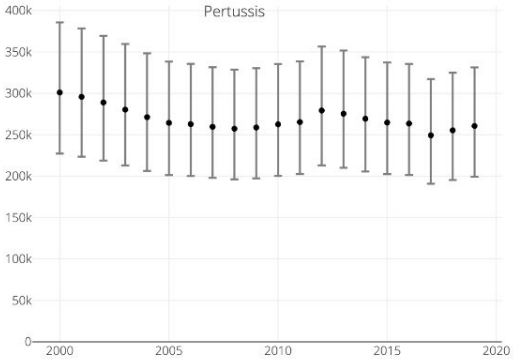




GBD estimates: Global Burden of Disease estimates of annual clinical incidence

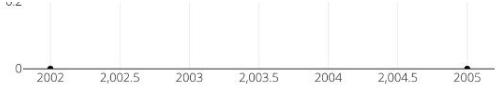


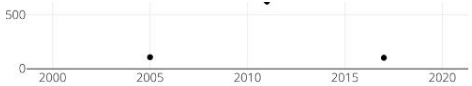


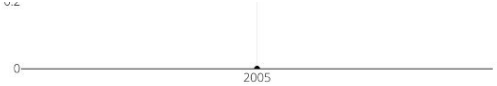


Upload your data

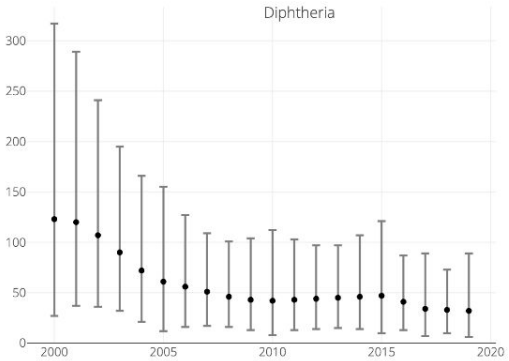
Example settings for “Country X”

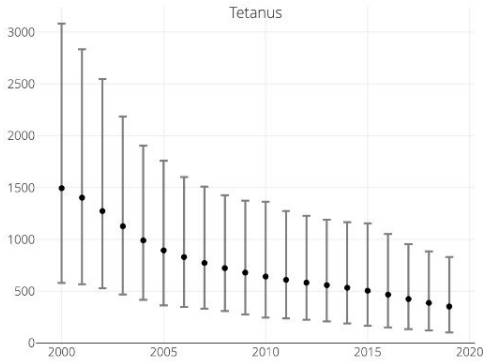


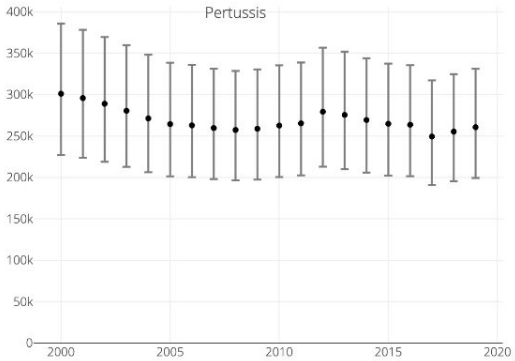




GBD estimates: Global Burden of Disease estimates of annual clinical incidence







Upload your data

To replace the default data, please download the template by clicking the **DOWNLOAD TEMPLATE** button on the right, make your changes on the downloaded template, and upload this file using the **BROWSE** option. Add notes on the source of your data or any other relevant details.

Once you have uploaded your own data, return to the top, make sure **OWN DATA** is selected and click **GO TO CALIBRATION** to continue.

Add notes

1. Download template

DOWNLOAD

2. Upload changes

BROWSE No file selected

Example settings for “Country X”

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

2.1 Select data | 2.2 Calibration | 2.3 Assessing uncertainty

Instructions

The aim of the manual calibration is to adjust the slider values for both pertussis and tetanus until the model output resembles the data. You will need to press the **RUN THE MODEL** button after each adjustment of the sliders.

This manual calibration is a simple form of face validation, which qualitatively assesses if the model is an adequate representation of the data.

If you are happy with your calibration, press the **ACCEPT THIS CALIBRATION AND MOVE ON** button to move to Step 3: Booster Strategy Design.

Tetanus transmission tuning parameter

1 12 22

1 3.1 5.2 7.3 9.4 11.5 13.6 15.7 17.8 19.9 22

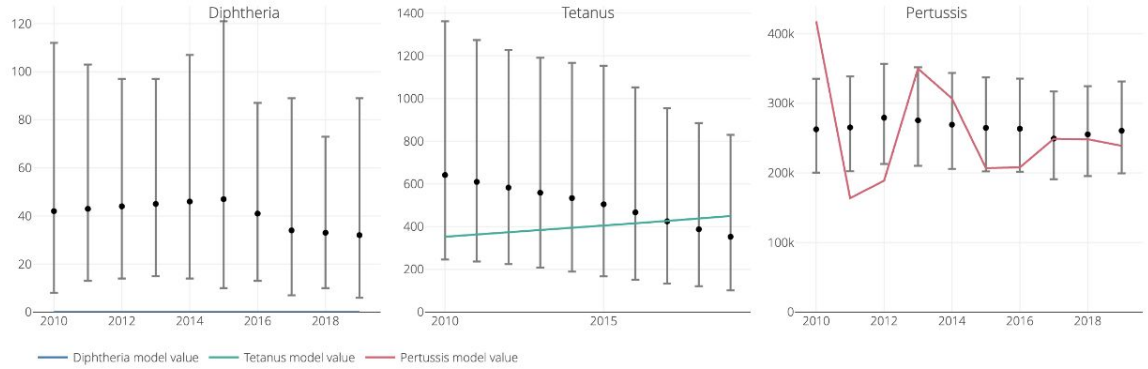
Pertussis transmission tuning parameter

1 24.1 100

1 10.9 20.8 30.7 40.6 50.5 60.4 70.3 80.2 90.1 100

RUN THE MODEL

DTP Estimated Incidence



ACCEPT THIS CALIBRATION AND MOVE ON

Example settings for “Country X”

DTP Boost

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Tetanus transmission tuning parameter

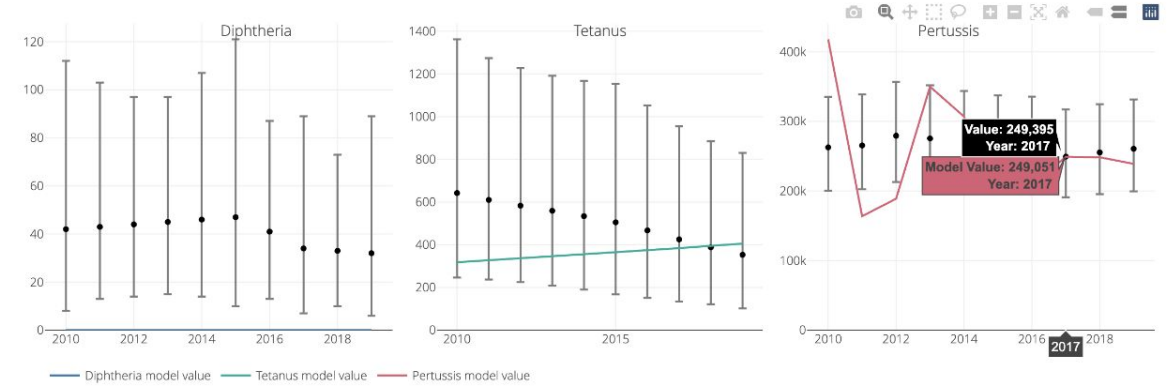
1 — 10.8 — 22

Pertussis transmission tuning parameter

1 — 24.1 — 100

RUN THE MODEL

DTP Estimated Incidence



ACCEPT THIS CALIBRATION AND MOVE ON

Example settings for “Country X”

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

2.1 Select data | **2.2 Calibration** | 2.3 Assessing uncertainty

Instructions

The aim of the manual calibration is to adjust the slider values for both pertussis and tetanus until the model output resembles the data. You will need to press the **RUN THE MODEL** button after each adjustment of the sliders.

This manual calibration is a simple form of face validation, which qualitatively assesses if the model is an adequate representation of the data.

If you are happy with your calibration, press the **ACCEPT THIS CALIBRATION AND MOVE ON** button to move to Step 3: Booster Strategy Design.

Tetanus transmission tuning parameter

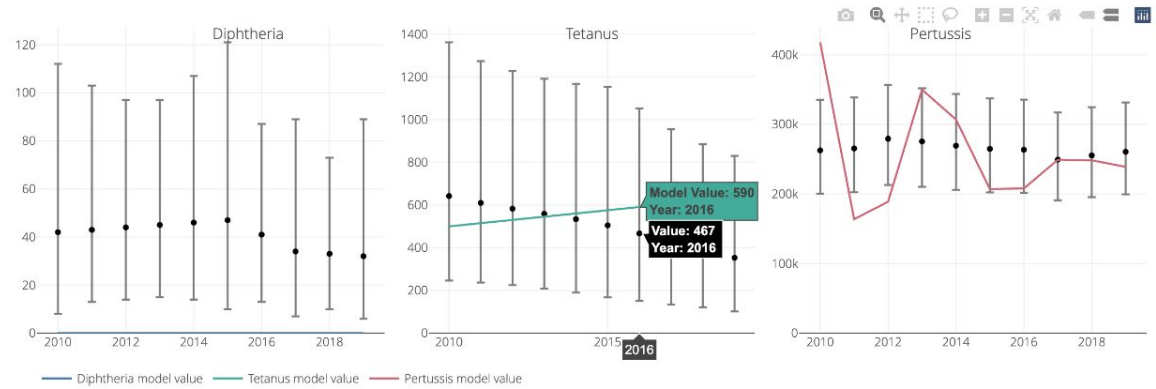
1 | 17 | 22

Pertussis transmission tuning parameter

1 | 24.1 | 100

RUN THE MODEL

DTP Estimated Incidence



ACCEPT THIS CALIBRATION AND MOVE ON

Example settings for “Country X”

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

2.1 Select data | 2.2 Calibration | 2.3 Assessing uncertainty

NEXT

Instructions

As models are simplifications of the real world, it is important to assess the variability of the model predictions in relation to the decision you wish to inform from model evidence. Guidance has been provided below on how to use the DTP Boost tool to test the robustness of model predictions.

Many sources of uncertainty

Uncertainty exists in many forms in modelling including:

- Uncertainty in the model inputs such as the those entered into the sliders and information boxes.
- Uncertainty in the case incidence data that is used to tune the model in the calibration process to create the baseline scenario.
- Uncertainty in the reduction of effectiveness of the vaccine booster strategies due to operational implementation.
- Uncertainty in the estimates of cost and cost effectiveness of the vaccine booster strategies.

Using the DTP Boost tool

Consider the example of using the DTP Boost tool to determine if the country should introduce a new adolescent booster dose.

The baseline scenario is important to establish correctly as it sets the foundation against which new strategies are explored and measured.

To develop a robust baseline scenario:

- Vary the input values such as annual vaccine coverage and health system characteristics to see how the baseline changes.
- Place emphasis on varying those input values you are most uncertain about. See how the baseline changes for a range of plausible values.

The value of the calibration is to position the baseline scenario in line with observed/estimated cases. It is important to choose the dataset for calibration carefully as this dataset should best describe the incidence in the population for both pertussis and tetanus.

- Where data does not exist, provide insight by uploading plausible expert-informed pseudo-data using the 'Upload your data' feature. Try to capture different trends and patterns in incidence.
- Fit the model to multiple datasets to define several baselines. You can use the 'Save your session' feature at the top right of the page to save your different baseline scenarios. You can then upload each session separately and test out the intended adolescent booster strategy.

To develop a robust booster scenario:

- Because there can be a decrease in vaccine impact due to operational challenges during implementation, you should test the booster scenario for a range of coverage values.
- Consider different target age groups if the intended age group may be difficult to reach or characterise.
- As potential implementation and vaccine costs are not always known in advance, run the scenario several times varying the input cost values. Note the impact that changing input costs has on the total cost and cost effectiveness.

Example settings for “Country X”

Step 3. Strategy design

Develop different scenarios to run

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

3.1 Instructions | 3.2 Build a vaccination strategy

NEXT

Designing a booster vaccination strategy

You may design, save and simulate as many strategies as you would like to compare and explore in the results section (Step 4).

Build package: To design a vaccination strategy, toggle on the options you would like to include. Once in the 'on' position, a settings button will become visible. This allows you to adjust the details of each option (see below). Defaults are provided but should be updated to reflect your selected strategy and context.

Vaccination options: You may build a vaccination strategy using any number of the following options. Click ⓘ in the next section for more information on each.

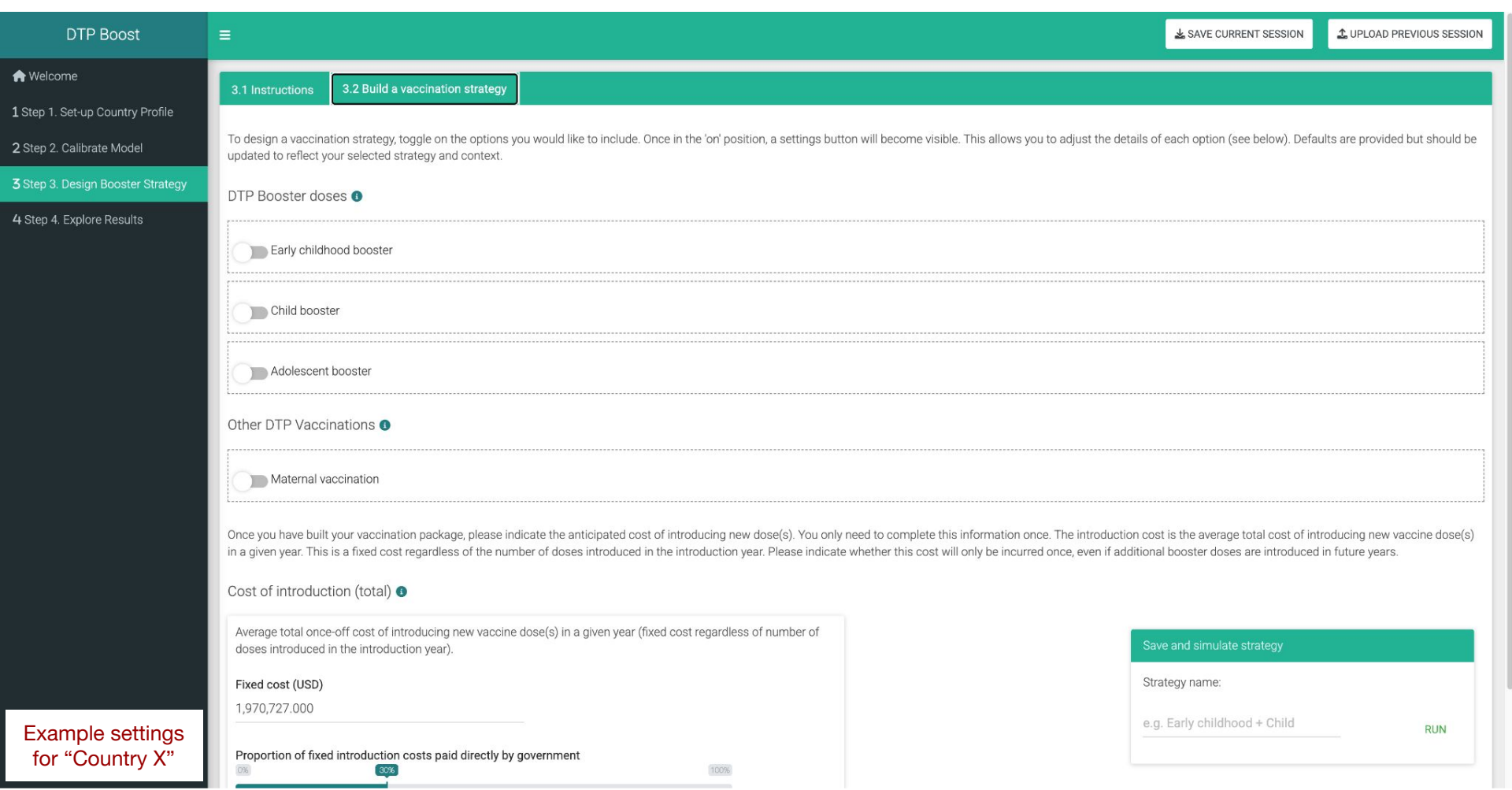
- Early childhood booster: recommended dose given between 12 - 23 months old
- Child booster: recommended dose given between 4 - 7 years old
- Adolescent booster: recommended dose given between 9 - 15 years old
- Maternal vaccinaton: dose(s) given to women during antenatal care (ANC) visits

Vaccination settings: You may define the following settings for each vaccination option you include in your strategy. Click ⓘ in the next section for more information on each.

- Target age
- Vaccine
- Year of introduction
- Coverage in year of introduction
- Target operational coverage
- Years to reach target coverage
- Average cost per dose
- Proportion paid directly by government
- Delivery platform (Health facility or Outreach site)

Save & simulate: Once you have completed designing a strategy, name it in the box (bottom right) and click **Run.** This strategy will be visible in the results section. If you **SAVE CURRENT SESSION** any time after setting vaccination strategies to simulate, these will be stored as part of your saved session.

Example settings for “Country X”


DTP Boost
SAVE CURRENT SESSION
UPLOAD PREVIOUS SESSION
Welcome
1 Step 1. Set-up Country Profile
2 Step 2. Calibrate Model
3 Step 3. Design Booster Strategy
4 Step 4. Explore Results
3.1 Instructions
3.2 Build a vaccination strategy
To design a vaccination strategy, toggle on the options you would like to include. Once in the 'on' position, a settings button will become visible. This allows you to adjust the details of each option (see below). Defaults are provided but should be updated to reflect your selected strategy and context.
DTP Booster doses
Early childhood booster
Child booster
Adolescent booster
Other DTP Vaccinations
Maternal vaccination
Once you have built your vaccination package, please indicate the anticipated cost of introducing new dose(s). You only need to complete this information once. The introduction cost is the average total cost of introducing new vaccine dose(s) in a given year. This is a fixed cost regardless of the number of doses introduced in the introduction year. Please indicate whether this cost will only be incurred once, even if additional booster doses are introduced in future years.
Cost of introduction (total)
Average total once-off cost of introducing new vaccine dose(s) in a given year (fixed cost regardless of number of doses introduced in the introduction year).
Fixed cost (USD)
1,970,727.000
Proportion of fixed introduction costs paid directly by government
0%
30%
100%
Save and simulate strategy
Strategy name:
e.g. Early childhood + Child
RUN
Example settings for “Country X”

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

3.1 Instructions | 3.2 Build a vaccination strategy

To design a vaccination strategy, toggle on the options you would like to include. Once in the 'on' position, a settings button will become visible. This allows you to adjust the details of each option (see below). Defaults are provided but should be updated to reflect your selected strategy and context.

DTP Booster doses

Early childhood booster — SETTINGS

Child booster

Adolescent booster

Other DTP Vaccinations

Maternal vaccination

Once you have built your vaccination package, please indicate the anticipated cost of intr
in a given year. This is a fixed cost regardless of the number of doses introduced in the in

Cost of introduction (total)

Average total once-off cost of introducing new vaccine dose(s) in a given year (fixed cos
doses introduced in the introduction year).

Fixed cost (USD)
1,970,727.000

Proportion of fixed introduction costs paid directly by government
0% 30%

Schedule

Age group: 18 mth

Vaccine: DTwP-Hib-HepB

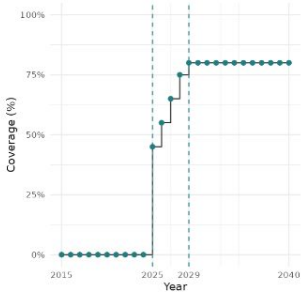
Year of introduction: 2026 (2034)

Coverage

Coverage in year of introduction: 0% 40% 100%

Target operational coverage: 0% 80% 100%

Years to reach target coverage: 0 years 4 years 7 years



Delivery

Health facility (%): 0% 69% 100%

Outreach site (%): 0% 31% 100%

Cost of routine delivery (per dose)

Health facility (USD): 1.745

Outreach (USD): 1.452

Proportion of routine delivery costs paid directly by government: 0% 22% 100%

Cost of vaccines (Per dose)

Unit cost of vaccine (average per dose, excl delivery) (USD): 0.800

Proportion of unit costs paid directly by government: 0% 25% 100%

Example settings for "Country X"

2 Step 2. Calibrate Model

3 Step 3. Design Booster Strategy

4 Step 4. Explore Results

To design a vaccination strategy, toggle on the options you would like to include. Once in the 'on' position, a settings button will become visible. This allows you to adjust the details of each option (see below). Defaults are provided but should be updated to reflect your selected strategy and context.

DTP Booster doses

Early childhood booster — SETTINGS

Child booster — SETTINGS

Adolescent booster

Other DTP Vaccinations

Maternal vaccination

Once you have built your vaccination package, please indicate the anticipated cost of intr
in a given year. This is a fixed cost regardless of the number of doses introduced in the in

Cost of introduction (total)

Average total once-off cost of introducing new vaccine dose(s) in a given year (fixed cos
doses introduced in the introduction year).

Fixed cost (USD)

1,970,727.000

Proportion of fixed introduction costs paid directly by government

0% 30%

Select if the introduction cost will only be incurred once

Schedule

Age group: 6 yr

Vaccine: Td

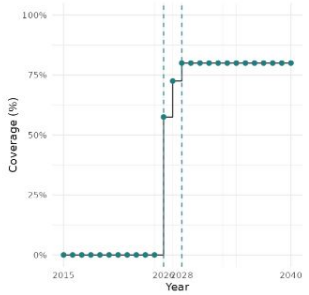
Year of introduction: 2024 2026 2034

Coverage

Coverage in year of introduction: 0% 50% 100%

Target operational coverage: 0% 80% 100%

Years to reach target coverage: 0 years 2 years 7 years



Delivery

Health facility (%): 0% 10% 100%

Outreach site (%): 0% 90%

Cost of routine delivery (per dose)

Health facility (USD): 1.745

Outreach (USD): 1.452

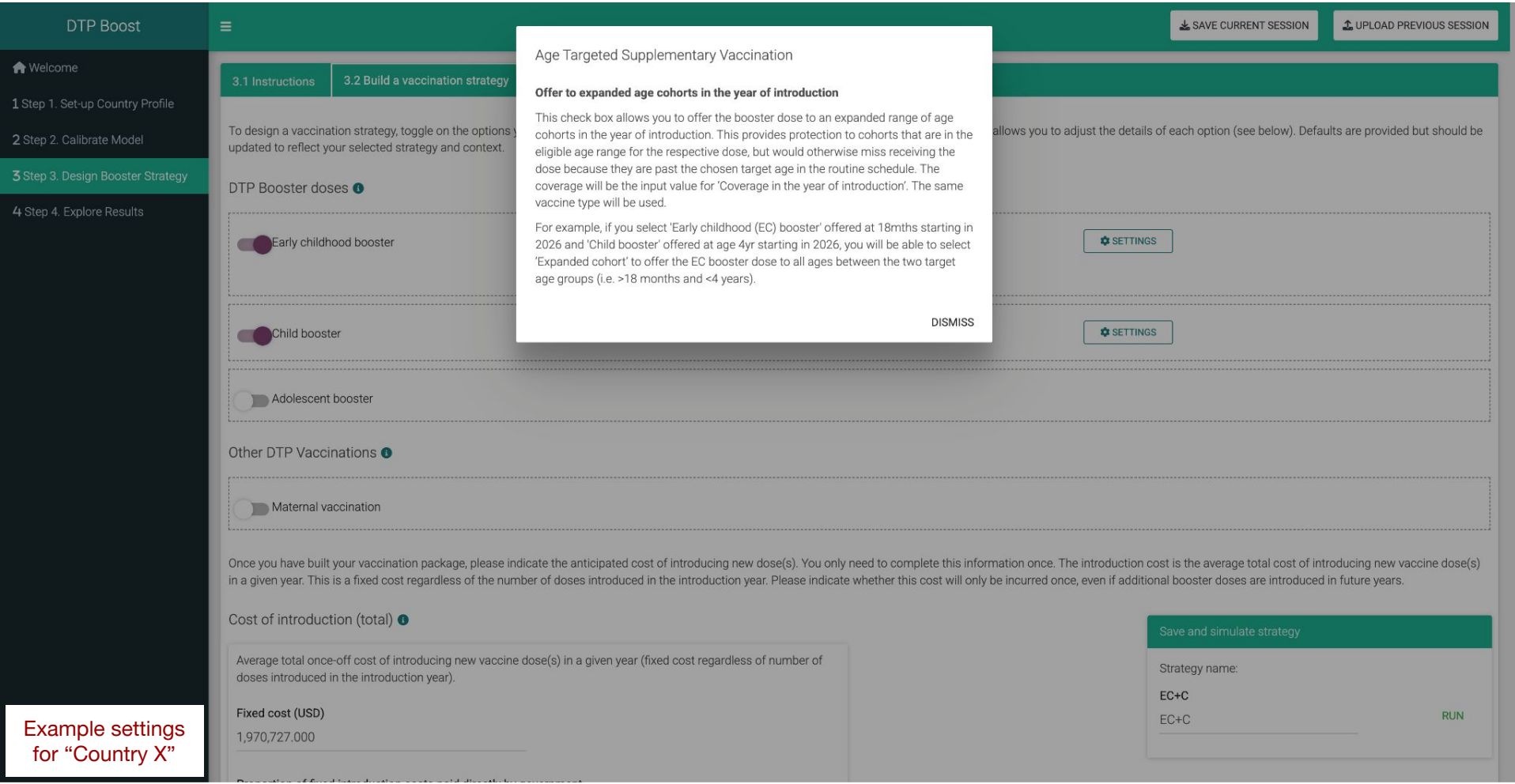
Proportion of routine delivery costs paid directly by government: 0% 22% 100%

Cost of vaccines (per dose)

Unit cost of vaccine (average per dose, excl delivery) (USD): 0.110

Proportion of unit costs paid directly by government: 0% 100%

Example settings for “Country X”


DTP Boost
Welcome
1 Step 1. Set-up Country Profile
2 Step 2. Calibrate Model
3 Step 3. Design Booster Strategy
4 Step 4. Explore Results
SAVE CURRENT SESSION
UPLOAD PREVIOUS SESSION
3.1 Instructions
3.2 Build a vaccination strategy
To design a vaccination strategy, toggle on the options y
allows you to adjust the details of each option (see below). Defaults are provided but should be updated to reflect your selected strategy and context.
DTP Booster doses
Early childhood booster
SETTINGS
Child booster
SETTINGS
Adolescent booster
Other DTP Vaccinations
Maternal vaccination
Age Targeted Supplementary Vaccination
Offer to expanded age cohorts in the year of introduction
This check box allows you to offer the booster dose to an expanded range of age cohorts in the year of introduction. This provides protection to cohorts that are in the eligible age range for the respective dose, but would otherwise miss receiving the dose because they are past the chosen target age in the routine schedule. The coverage will be the input value for 'Coverage in the year of introduction'. The same vaccine type will be used.
For example, if you select 'Early childhood (EC) booster' offered at 18mths starting in 2026 and 'Child booster' offered at age 4yr starting in 2026, you will be able to select 'Expanded cohort' to offer the EC booster dose to all ages between the two target age groups (i.e. >18 months and <4 years).
DISMISS
Once you have built your vaccination package, please indicate the anticipated cost of introducing new dose(s). You only need to complete this information once. The introduction cost is the average total cost of introducing new vaccine dose(s) in a given year. This is a fixed cost regardless of the number of doses introduced in the introduction year. Please indicate whether this cost will only be incurred once, even if additional booster doses are introduced in future years.
Cost of introduction (total)
Average total once-off cost of introducing new vaccine dose(s) in a given year (fixed cost regardless of number of doses introduced in the introduction year).
Fixed cost (USD)
1,970,727.000
Save and simulate strategy
Strategy name:
EC+C
EC+C
RUN
Example settings for "Country X"

3 Step 3. Design Booster Strategy

4 Step 4. Explore Results

updated to reflect your selected strategy and context.

DTP Booster doses

Early childhood booster

Expanded cohort

SETTINGS

Child booster

SETTINGS

Adolescent booster

Other DTP Vaccinations

Maternal vaccination

Once you have built your vaccination package, please indicate the anticipated cost of introducing new dose(s). You only need to complete this information once. The introduction cost is the average total cost of introducing new vaccine dose(s) in a given year. This is a fixed cost regardless of the number of doses introduced in the introduction year. Please indicate whether this cost will only be incurred once, even if additional booster doses are introduced in future years.

Cost of introduction (total)

Average total once-off cost of introducing new vaccine dose(s) in a given year (fixed cost regardless of number of doses introduced in the introduction year).

Fixed cost (USD)

1,970,727.000

Proportion of fixed introduction costs paid directly by government

0% 30% 100%

Select if the introduction cost will only be incurred once

Save and simulate strategy

Strategy name:

EC+C

EC+C

RUN

Example settings for “Country X”

Step 4. Results

Explore epidemiological and economic model outputs

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

4.1 Epidemiological Output | 4.2 Budget Impact | 4.3 Cost Effectiveness | 4.4 Downloads

Baseline & Strategies (Display/Hide)

Drag here to display

- Baseline
- Simultaneous (Td)
- Phased (Td)

Drag here to hide

- Simultaneous (TdaP)
- Phased (TdaP)

Delete packages that are hidden.

Output options

Select model output

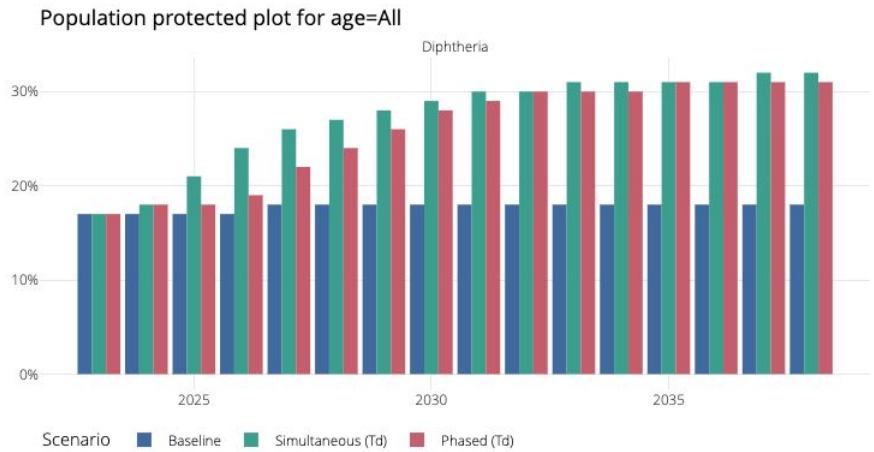
Population protected

Fix vertical axis range

All | Diphtheria | Pertussis | Tetanus

This section allows the user to explore key model outputs such as clinical cases, deaths, reported cases and deaths, treatment and population protected. Please use the menu on the left to select the model output you would like to view and to change how the results are displayed in the plot below.

NOTE: As diphtheria is a disease prone to outbreaks, it often has very low (often zero) cases in periods outside of outbreaks. The model is not designed to predict the future occurrence of diphtheria outbreaks. Rather it is intended to model the level of vaccine-derived protection in the population. Therefore, model output should be interpreted in this context.



Example output for “Country X”

1 Step 1. Set-up Country Profile

2 Step 2. Calibrate Model

3 Step 3. Design Booster Strategy

4 Step 4. Explore Results

Example output for “Country X”

Output options

Select model output

Clinical cases

Fix vertical axis range

View output as

COUNT | PER 100,000

Age groups

All

Plot time window

2020 2023 2038

2020 2022 2024 2026 2028 2030 2032 2034 2036 2038

Baseline & Strategies (Display/Hide)

Drag here to display

- Baseline
- Simultaneous (Td)
- Simultaneous (TdaP)
- Phased (TdaP)

Drag here to hide

- Phased (Td)

Delete packages that are hidden.

Output options

Select model output

Clinical cases

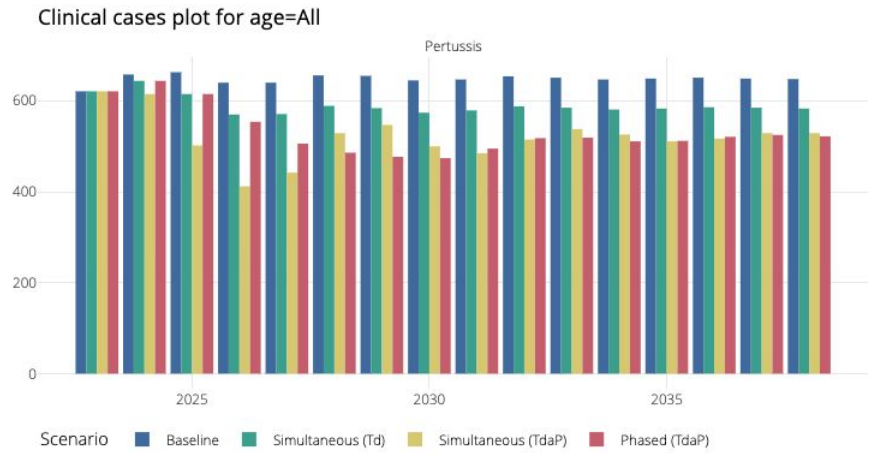
Fix vertical axis range

View output as

COUNT | PER 100,000

All | Diphtheria | Pertussis | Tetanus

This section allows the user to explore key model outputs such as clinical cases, deaths, reported cases and deaths, treatment and population protected. Please use the menu on the left to select the model output you would like to view and to change how the results are displayed in the plot below.



The table below shows the total number of clinical cases and total number of deaths for pertussis only, combined for the full model time frame (15 years). The baseline (existing schedule with no new doses added) and user-defined strategies are presented. Cases and deaths averted compare each strategy to the baseline.

Model outputs (pertussis)*

Scenario	Clinical cases (Total)	Deaths (Total)	Averted clinical cases**	Averted deaths**
Baseline	5,994,067	7,380	-	-

DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

4.1 Epidemiological Output | 4.2 Budget Impact | 4.3 Cost Effectiveness | 4.4 Downloads

Baseline & Strategies (Display/Hide)

Drag here to display

- Baseline
- Simultaneous (Td)
- Simultaneous (TdaP)
- Phased (Td)
- Phased (TdaP)

Drag here to hide

Output options

Model horizon
15 years

Costing approach
Proportion paid by government

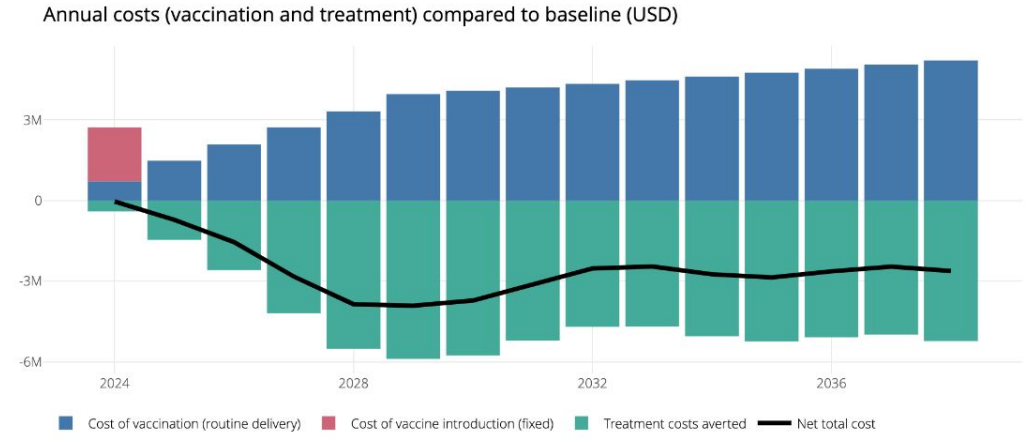
Discounting
Undiscounted costs and benefits

Example output for “Country X”

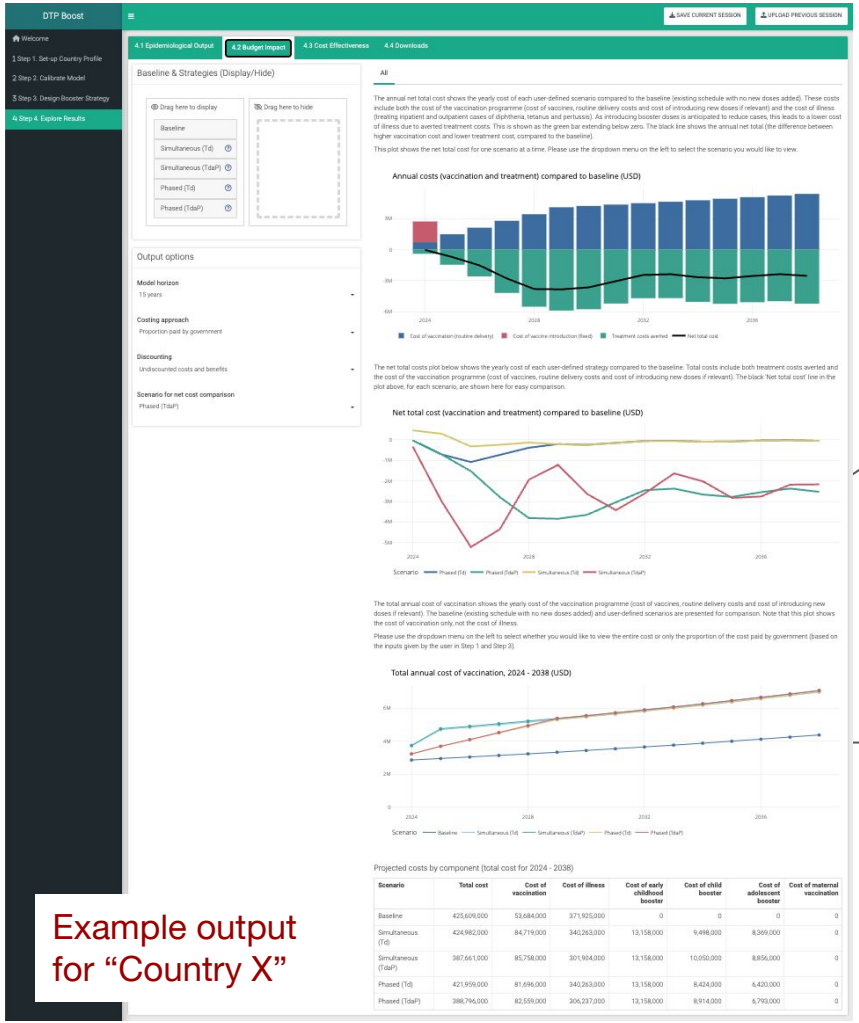
All

The annual net total cost shows the yearly cost of each user-defined scenario compared to the baseline (existing schedule with no new doses added). These costs include both the cost of the vaccination programme (cost of vaccines, routine delivery costs and cost of introducing new doses if relevant) and the cost of illness (treating inpatient and outpatient cases of diphtheria, tetanus and pertussis). As introducing booster doses is anticipated to reduce cases, this leads to a lower cost of illness due to averted treatment costs. This is shown as the green bar extending below zero. The black line shows the annual net total (the difference between higher vaccination cost and lower treatment cost, compared to the baseline).

This plot shows the net total cost for one scenario at a time. Please use the dropdown menu on the left to select the scenario you would like to view.

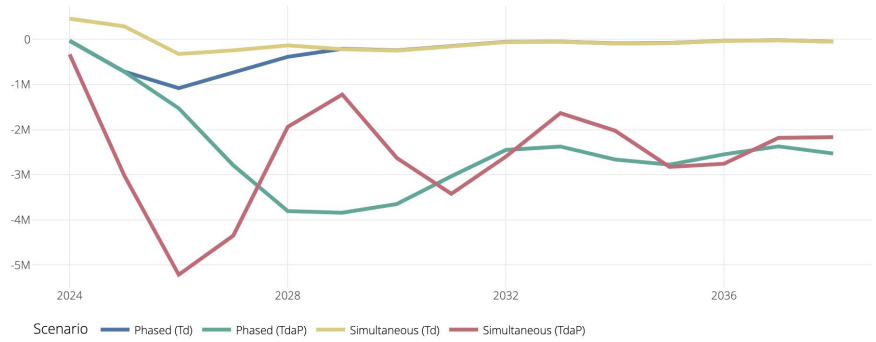


The net total costs plot below shows the yearly cost of each user-defined strategy compared to the baseline. Total costs include both treatment costs averted and the cost of the vaccination programme (cost of vaccines, routine delivery costs and cost of introducing new doses if relevant). The black 'Net total cost' line in the plot above, for each scenario, are shown here for easy comparison.

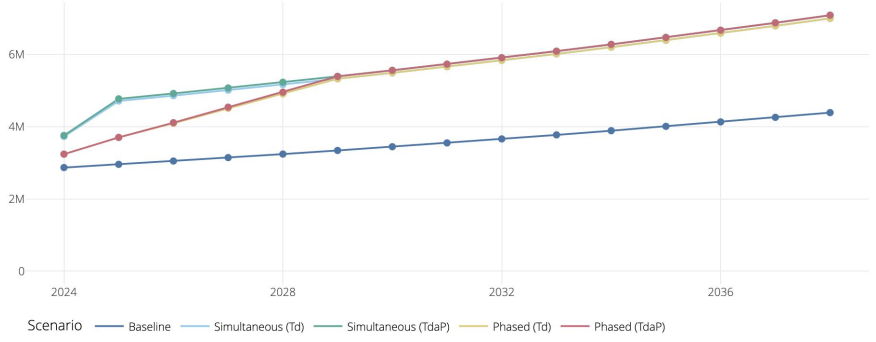


Example output for “Country X”

Net total cost (vaccination and treatment) compared to baseline (USD)



Total annual cost of vaccination, 2024 - 2038 (USD)



DTP Boost

SAVE CURRENT SESSION | UPLOAD PREVIOUS SESSION

- Welcome
- 1 Step 1. Set-up Country Profile
- 2 Step 2. Calibrate Model
- 3 Step 3. Design Booster Strategy
- 4 Step 4. Explore Results

Example output for "Country X"

4.1 Epidemiological Output | 4.2 Budget Impact | 4.3 Cost Effectiveness | 4.4 Downloads

Baseline & Strategies (Display/Hide)

Drag here to display

- Baseline
- Simultaneous (Td)
- Simultaneous (TdaP)
- Phased (Td)
- Phased (TdaP)

Drag here to hide

Output options

Select model output (cost effectiveness)
Clinical cases

Model horizon
15 years

Costing approach
Full cost (donor and government)

Discounting
Discounted costs and benefits

Output options

Select model output (cost effectiveness)
Clinical cases

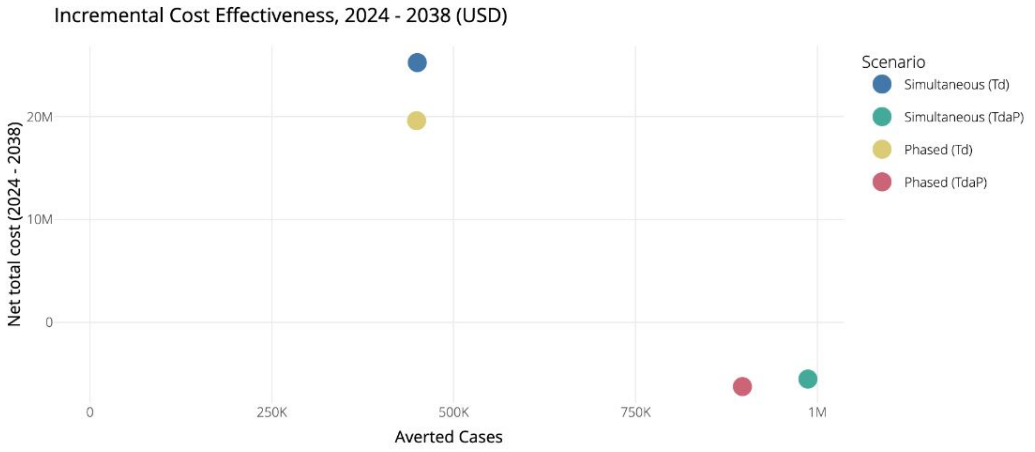
Model horizon
15 years

Costing approach
Full cost (donor and government)

All | Diphtheria | Pertussis | Tetanus

These results show the cost-effectiveness of the vaccination programme in terms of cost per clinical case averted and cost per death averted, for each user-defined strategy compared to baseline (existing schedule with no new doses added). The total cost includes both the cost of the vaccination programme (cost of vaccines, routine delivery costs and cost of introducing new doses if relevant) and the cost of illness (treating inpatient and outpatient cases of diphtheria, tetanus and pertussis). Clinical cases and deaths are counted for diphtheria, tetanus and pertussis combined.

Please use the dropdown menu on the left to select whether you would like to view the cost-effectiveness based on the entire cost or only the proportion of the cost paid by government (based on the inputs given by the user in Step 1 and Step 3).



Note: If the net total cost (plot above) or the cost per clinical case averted/cost per death averted (table below) is negative, the strategy is cost-saving. This happens when the amount saved through averted treatment costs is greater than the amount spent implementing the new vaccination strategy.

Phased (Td)

Phased (TdaP)

Drag here to hide

Output options

Select model output (cost effectiveness)

Clinical cases

Model horizon

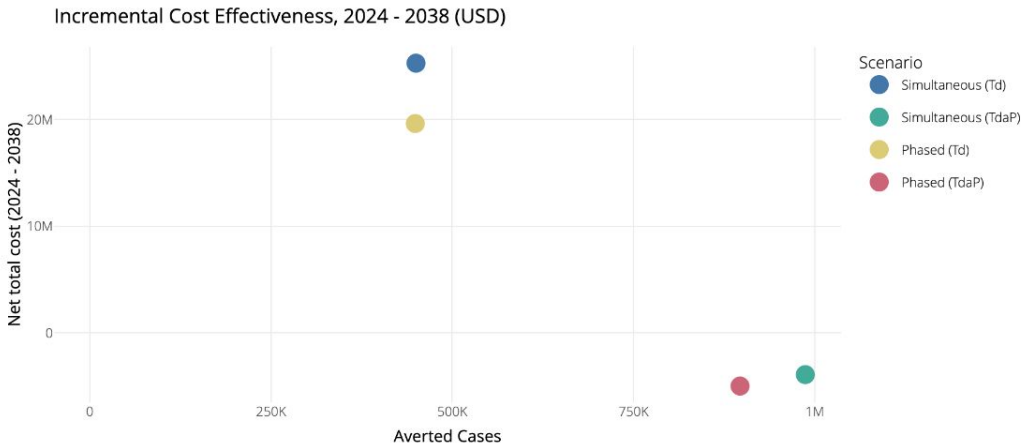
15 years

Costing approach

Full cost (donor and government)

Discounting

Discounted costs and benefits



Note: If the net total cost (plot above) or the cost per clinical case averted/cost per death averted (table below) is negative, the strategy is cost-saving. This happens when the amount saved through averted treatment costs is greater than the amount spent implementing the new vaccination strategy.

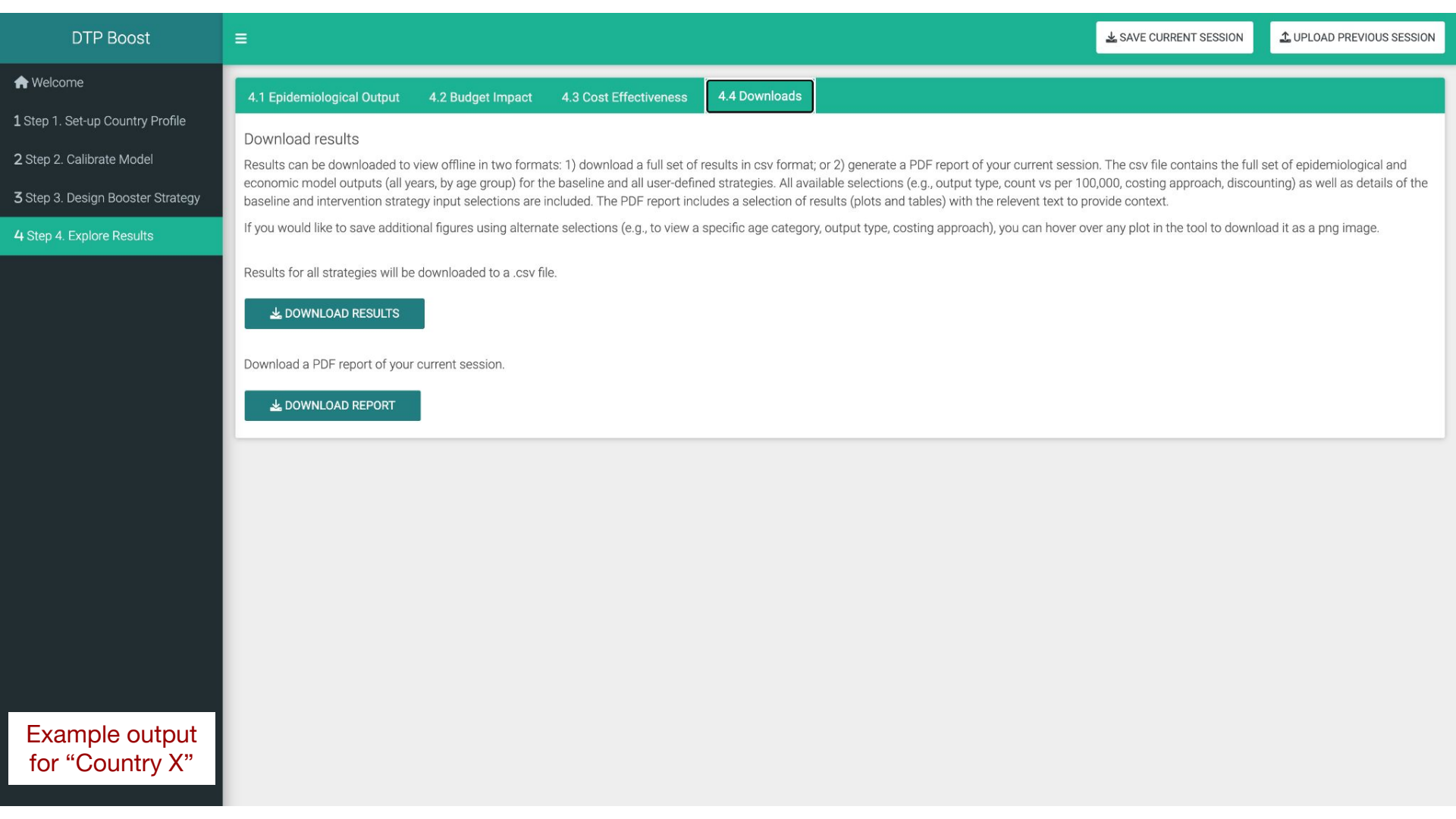
Effectiveness outputs (diphtheria, tetanus and pertussis)*

Scenario	Total cost	Cost of vaccination	Cost of illness	Clinical cases (Total)	Deaths (Total)	Cost per clinical case averted**	Cost per death averted**
Baseline	374,932,000	83,681,000	291,251,000	4,680,000	6,500	-	-
Simultaneous (Td)	400,209,000	133,660,000	266,549,000	4,231,000	5,920	843	651,000
Simultaneous (TdaP)	371,028,000	135,266,000	235,761,000	3,693,000	5,390	-59	-52,900
Phased (Td)	394,558,000	127,950,000	266,609,000	4,231,000	5,950	655	535,000
Phased (TdaP)	369,967,000	129,224,000	240,743,000	3,783,000	5,500	-83	-74,600

* Outputs are shown as the total for the full model timeframe

** Compared to Baseline

Example output for “Country X”


DTP Boost
SAVE CURRENT SESSION
UPLOAD PREVIOUS SESSION
Welcome
1 Step 1. Set-up Country Profile
2 Step 2. Calibrate Model
3 Step 3. Design Booster Strategy
4 Step 4. Explore Results
4.1 Epidemiological Output
4.2 Budget Impact
4.3 Cost Effectiveness
4.4 Downloads
Download results
Results can be downloaded to view offline in two formats: 1) download a full set of results in csv format; or 2) generate a PDF report of your current session. The csv file contains the full set of epidemiological and economic model outputs (all years, by age group) for the baseline and all user-defined strategies. All available selections (e.g., output type, count vs per 100,000, costing approach, discounting) as well as details of the baseline and intervention strategy input selections are included. The PDF report includes a selection of results (plots and tables) with the relevent text to provide context.
If you would like to save additional figures using alternate selections (e.g., to view a specific age category, output type, costing approach), you can hover over any plot in the tool to download it as a png image.
Results for all strategies will be downloaded to a .csv file.
DOWNLOAD RESULTS
Download a PDF report of your current session.
DOWNLOAD REPORT
Example output for “Country X”

DTP BOOST
DEMO GUIDE

VACCINATION STRATEGY TOOL

MODELLING THE HEALTH & ECONOMIC
IMPACT OF INTRODUCING DTPCV
BOOSTER DOSES

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DTP Boost

DTP Boost is an interactive web-based tool to inform country-level decision making about the introduction and routine delivery of diphtheria-tetanus-pertussis-containing vaccines (DTPCV) booster doses. The tool allows users to design vaccination strategies to explore the health impact, budget impact, and cost-effectiveness of introducing DTPCV booster doses in a selected country.

DTP Boost is powered by an integrated epidemiological and health economic model, tailored to the selected country, accounting for differences in existing vaccination schedule, current burden of disease, health systems characteristics, costs of illness and vaccination. Multiple vaccination strategies can be designed, allowing a detailed and interactive exploration of the relative costs and benefits of different numbers of DTPCV booster doses, vaccination coverage levels, introduction approaches (e.g., simultaneous, phased), vaccine formulations and vaccination delivery platforms (e.g., health facility, outreach site, school-based).

DTP Boost was developed by the Modelling and Simulation Hub, Africa (MASHA) at the University of Cape Town in collaboration with the African Field Epidemiology Network (AFENET) and United States Centers for Disease Control and Prevention (U.S. CDC) with guidance from an expert steering committee. The tool has been piloted in Uganda, in partnership with the Ugandan National Program on Immunization (UNEPI).

Using the Demo tool

The full DTP Boost tool uses a live-running model and requires local data to tailor the projections to the selected country. To enable easy exploration of the tool and its key features, a demo version was developed with simplified optionality, default data and a set of pre-run scenarios.

This guide is intended to show the process of using the app with sample scenarios and data. Additional resources are provided in later sections.

Four steps need to be followed to use the app:

1. Set up country profile
2. Calibrate model
3. Design booster strategy
4. Explore and download results

Access and citation

The DTP Boost Demo Tool is available through the link below. **Access to the full tool, as well as support for using it, is available on request.**

https://masha-app.shinyapps.io/DTPBoostDemo/

The demo model and application code is available on Github (uct-masha/DTPBoost-Demo)

Suggested citation: Hounsell, RA., Norman, JM., Monyake, R., Silal, SP (2025) DTPBoost-Demo. (Version 1.0.0). Available at: https://github.com/uct-masha/DTPBoost-Demo/releases/tag/1.0.0

Contact us

For more information DTP Boost, or to access the full tool, please contact:
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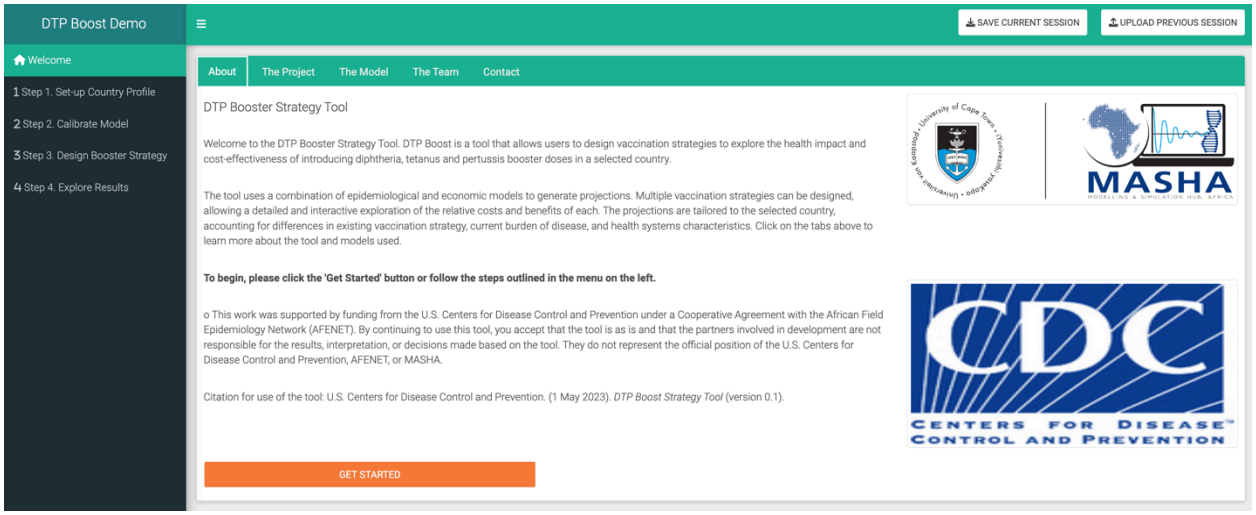
Modelling and Simulation Hub, Africa (MASHA),
University of Cape Town

Welcome – Landing page

Upon loading the DTP Booster Demo, the welcome screen provides information about the application, including details about the start of the project, the epidemiological and economic model being used, and team details with contact information. This can be accessed on their respective tabs at the top of the page.

On the left of the screen is the application menu detailing the different steps for using the DTP Boost App.

In the upper right corner of the application are two buttons, which allow users to save the current session or upload a previous session. These buttons are always displayed and, in the full version, allow users to resume or review a previously saved session.



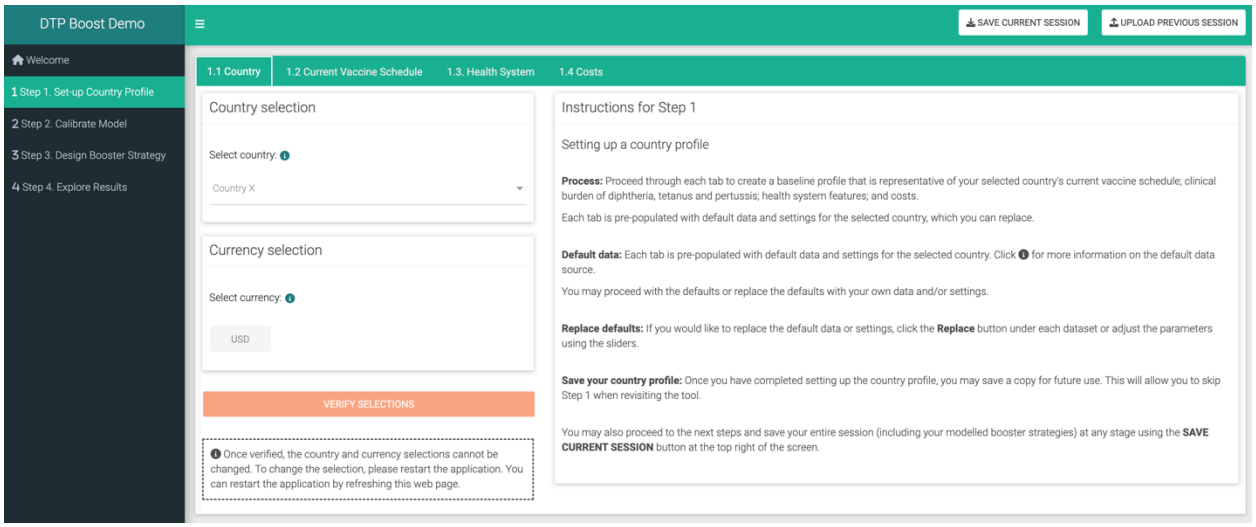
To begin using the demo click the **GET STARTED** button at the bottom of the **Welcome** page on the **About** tab. This will lead to **Step 1. Set-up Country Profile**.

Step 1. Set-up Country Profile

In this section, information provided by the user is used to create a baseline profile that represents the selected country's current vaccine schedule, health system features, and the clinical burden and cost of diphtheria, tetanus, and pertussis.

1.1 Country Selection

For this demo, **Country Selection** and **Currency selection** have been set as Country X and USD respectively. The full use of the application allows for selecting a country of interest and setting the currency to USD or the national currency.



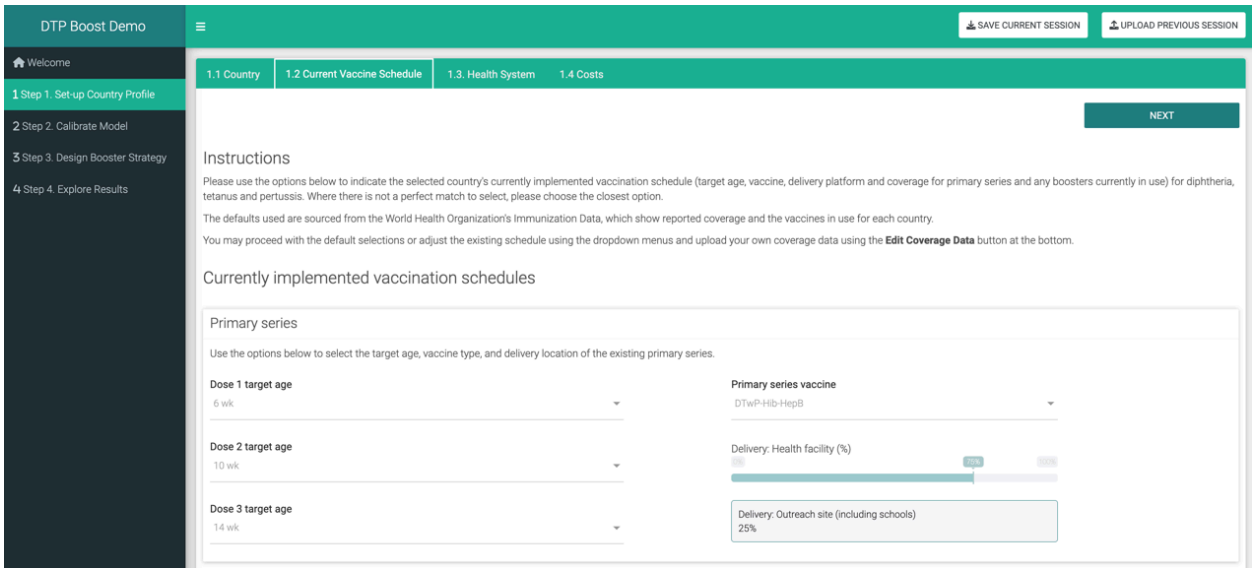
Click on the **VERIFY SELECTIONS** button to proceed to **1.2 Current Vaccine Schedule**.

1.2 Current Vaccine Schedule

This page provides the options to describe the selected country's currently implemented vaccination schedule for diphtheria, tetanus, and pertussis. This includes the primary series and any boosters in current use.

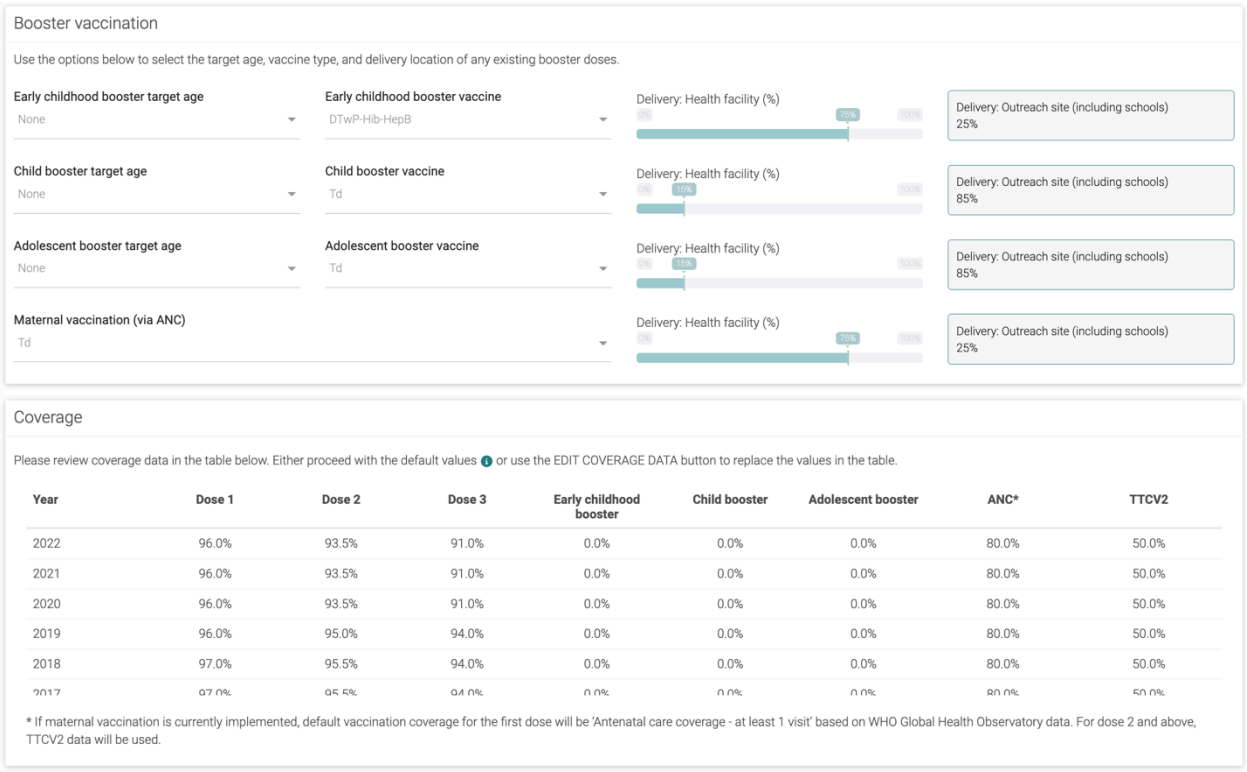
Primary Series

For Country X, the primary series is given as the DTwP-Hib-HepB (pentavalent) vaccine at 6, 10, and 14 weeks. The delivery location of the primary series is set at 75% at the health facility, and the remaining 25% is delivered through outreach sites, which includes schools. In this example, no existing booster vaccination is present and is specified to be 'none'. Maternal tetanus and diphtheria vaccination as part of antenatal care (ANC) is specified to be as Td and delivered via health facilities at 75%.



Coverage

Sample vaccine coverage data for Country X is provided in the Coverage section. Default values are taken from the WHO Global Health Observatory database for the coverage of the primary series, booster doses, tetanus toxoid-containing vaccine with at least two doses in reproductive-age women (TTCV2), and antenatal care coverage with at least one visit. Users can edit coverage data to replace values in the full application.

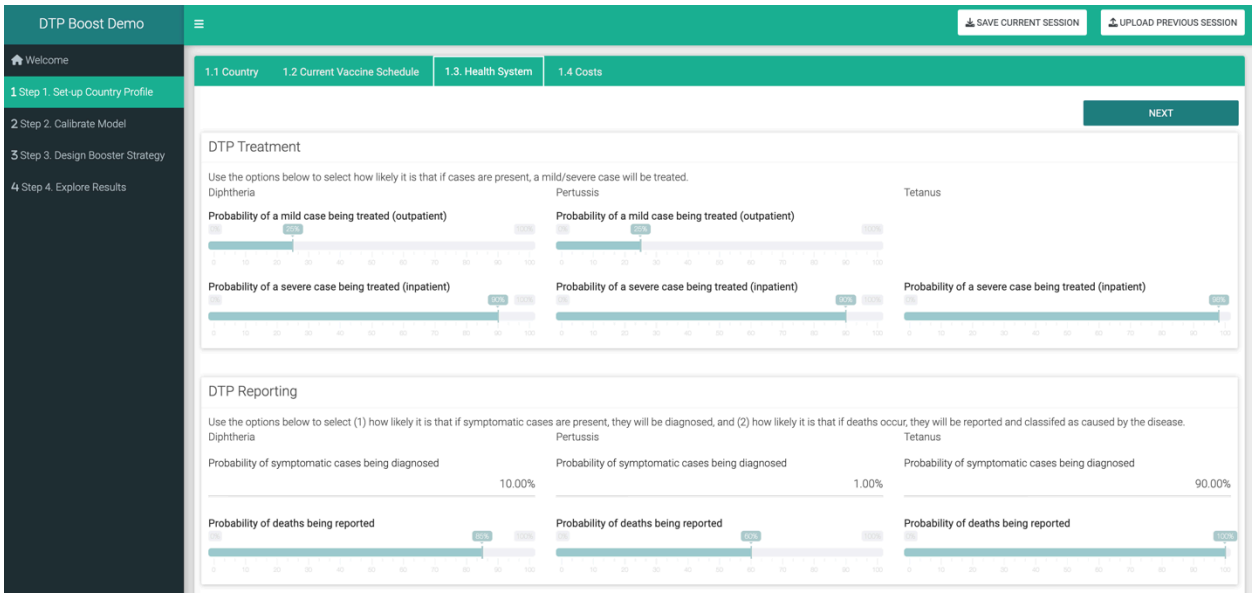


Click the **NEXT** button at the upper right corner to proceed to **1.3 Health System**.

1.3 Health System

In this section, the user can set values for the probabilities of the treatment and reporting of diphtheria, tetanus, and pertussis. Users can slide and adjust each value according to each disease. For the demo tool, the values have been predetermined and set accordingly. Under **DTP Treatment**, the probability of cases being treated in the outpatient or inpatient setting reflects how the population in the country seeks and accesses medical care. Under **DTP Reporting**, the probability of symptomatic cases being diagnosed and reported approximate disease reporting systems and surveillance reports in the country.

Please note: The probabilities for cases being recognised or diagnosed and treatment in the respective setting may require estimation and expert input. It is assumed that tetanus results in severe cases only. The notes section may be used to add notes on sources and any other relevant details.

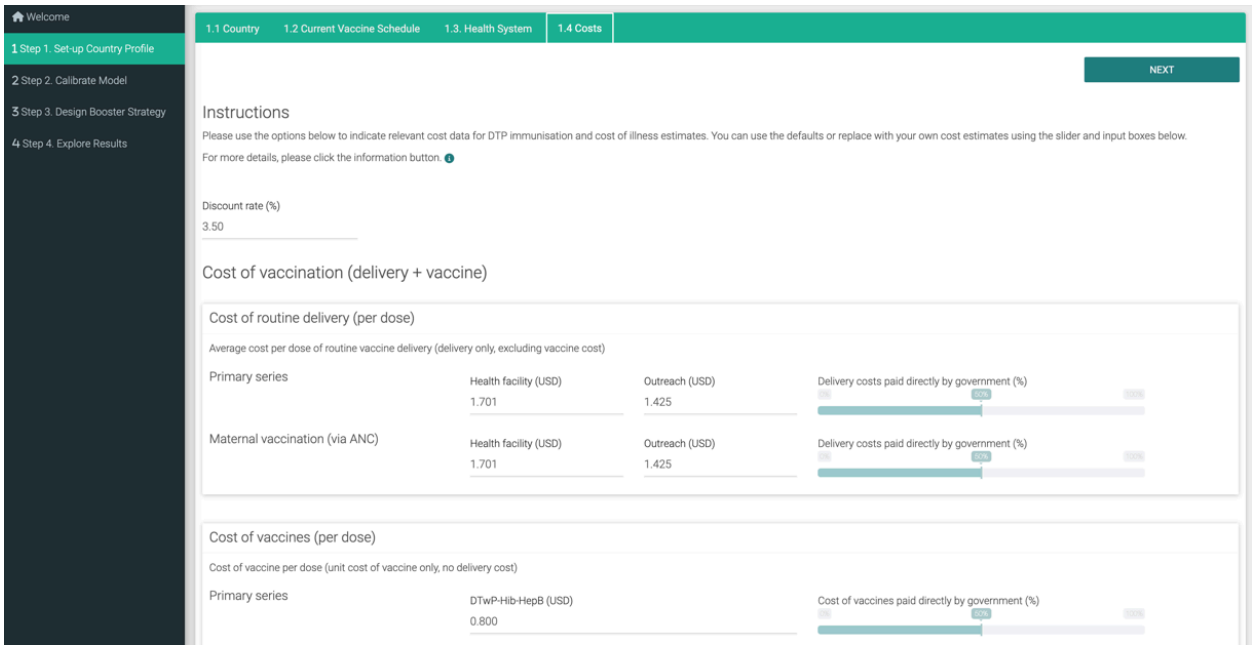


Click the **NEXT** button to proceed to **1.4 Cost**.

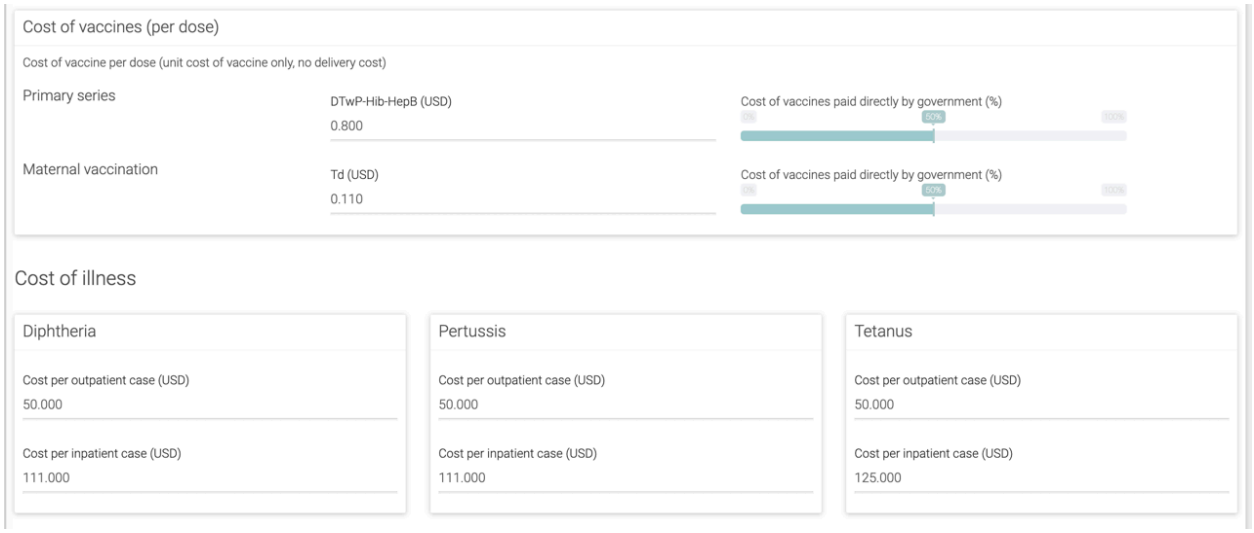
1.4 Cost

The cost page provides the user with options to indicate cost data for DTP vaccination and cost of illness estimates. The default discount rate used is 3.5%. The user can change this value. The provider (government) perspective is used. No societal costs are included.

The **Cost of Vaccination** is further separated into the cost of routine vaccination delivery by dose and the unit cost of the vaccine by dose. The costs for vaccine delivery location are further split by delivery location, either at a health facility or outreach site (including schools). It is assumed that the unit cost of these vaccines will be constant given the history of UNICEF prices for these vaccines. Costs are incremental.



Under **Cost of illness**, the indicated costs include the average cost per inpatient case and the average cost per outpatient case. The cost is shown from the provider's perspective (the government) and includes direct costs only.



The default values provided in this demonstration for Country X are sample values only. Users may draw from costing studies, published literature, databases, or official documents to source cost data. If no data are available, estimates from a similar context or illness may be used as a proxy.

This completes **Step 1. Set-up Country Profile**.

Click the **NEXT** button to proceed to **Step 2. Calibrate Model**.

Step 2. Calibrate Model

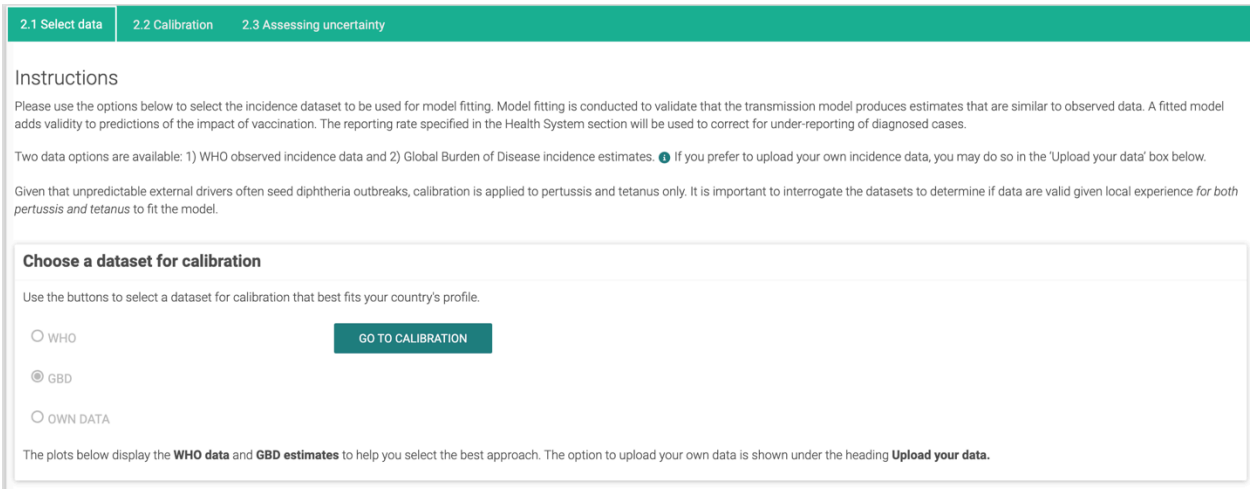
This section allows the user to calibrate the model to the chosen setting. Model fitting is conducted to validate that the transmission model produces estimates that are similar to observed data. A fitted model adds validity to predictions of the impact of vaccination. The reporting rate specified in the **Health System** section will be used to correct for under-reporting of diagnosed cases.

2.1 Select data

In this section, the next step is to select a dataset for calibration. The two main data options are the WHO observed incidence data or the Global Burden of Disease incidence estimates. Due to the nature of diphtheria occurring in outbreaks, the calibration is applied only to pertussis and tetanus. Users must check if the datasets are sufficient and plausible for both pertussis and tetanus to fit the model. Users may hover the cursor over the figures for additional information on the values per year.

In the full tool, users may upload their own data to replace the default data using a template and by selecting **OWN DATA** in the **Choose a dataset for calibration** section of the page.

For this demo the GBD estimates have been selected for the dataset to be used.

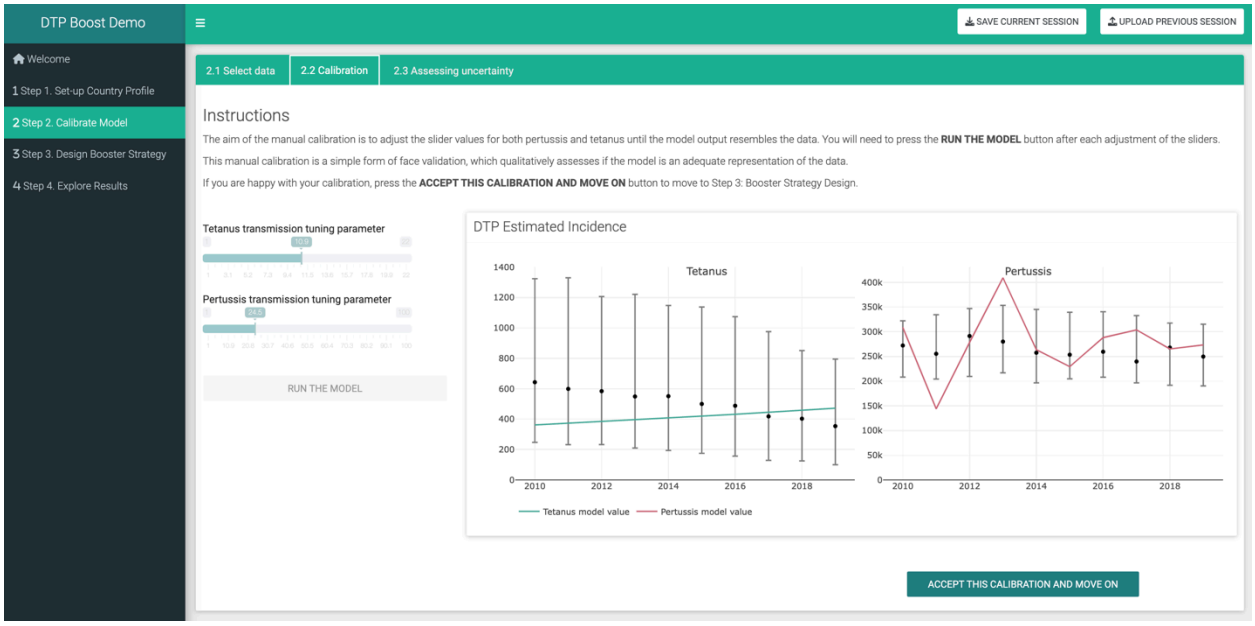


Click on **GO TO CALIBRATION** to proceed to **Step 2.2 Calibration**.

2.2 Calibration

The aim of the manual calibration is to adjust the slider values for both pertussis and tetanus until the model output resembles the data. The **RUN THE MODEL** button must be clicked after each adjustment of the sliders.

This manual calibration is a simple form of face validation, which qualitatively assesses if the model is an adequate representation of the data.



Once calibration is satisfactory, click on the **ACCEPT THIS CALIBRATION AND MOVE ON** button to proceed to **Step 3. Design Booster Strategy.**

Information is provided in **2.3 Assessing uncertainty** for factors that users may need to consider in using the app.

Step 3. Design Booster Strategy

3.1 Instructions

The list of vaccination options and settings are summarised to aid in designing a booster strategy. Users may design, save, and simulate as many strategies as they would like to compare and explore in the results section (Step 4).

Click on the **NEXT** button to proceed to section **3.2 Build a vaccination strategy**.

3.2 Build a vaccination strategy

Build package

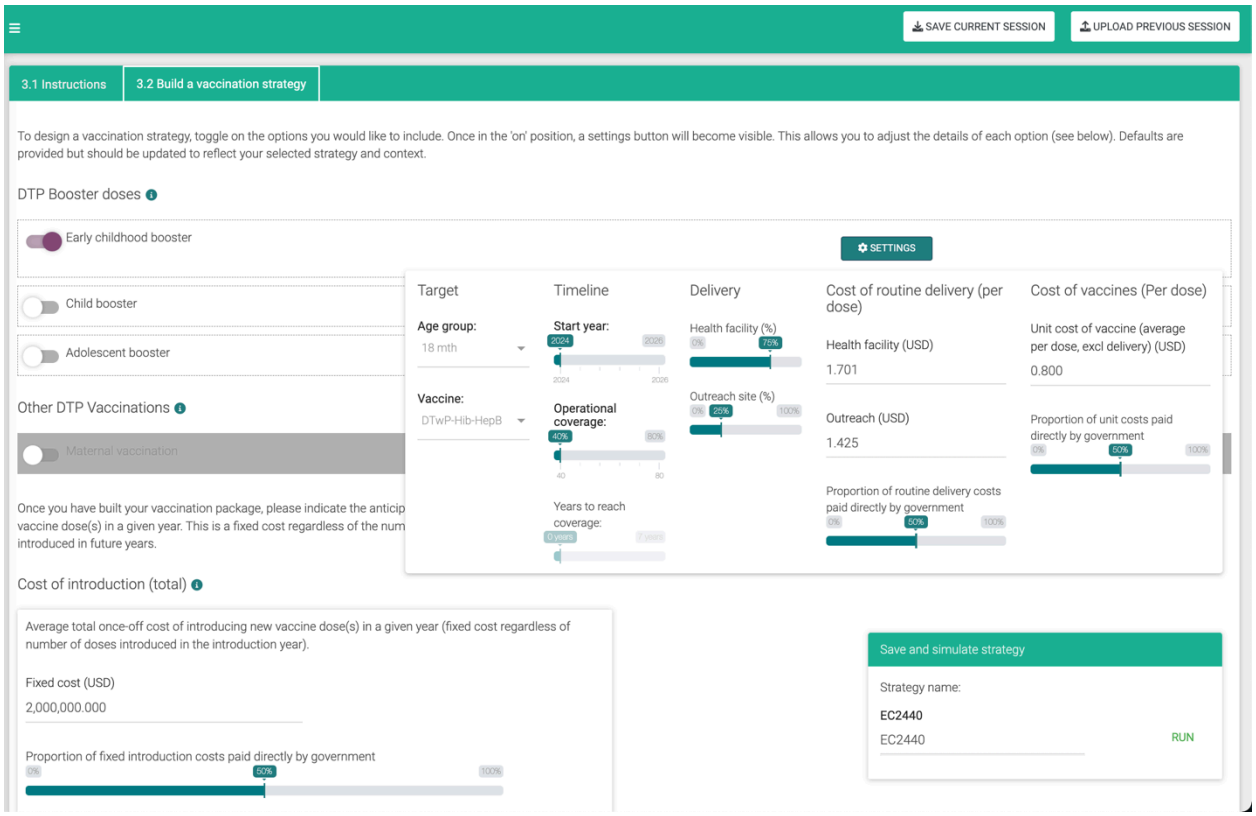
To design a vaccination strategy, users can toggle the options to be included. Once in the 'on' position, a settings button will become visible. This allows adjustment of the details of each option. Defaults and a limited set of options are provided for this demo. In the full use application, all details should reflect your selected strategy and context.

Cost of introduction

Once the desired vaccination package has been built, the anticipated cost of introducing new dose(s) must be indicated. This detail only needs to be entered once. The introduction cost is the average total cost of introducing new vaccine dose(s) in a given year. This is a fixed cost regardless of the number of doses introduced in the introduction year. Users have the option to indicate whether this cost will only be incurred once, even if additional booster doses are introduced in future years.

Save & simulate

Once done with designing a strategy, users can name it in the box located at the bottom right. For this demo strategy, names have been set for ease of use.



Click the **Run** button. This will direct the user to **Step 4. Explore results**. The strategy will be visible in the results section.

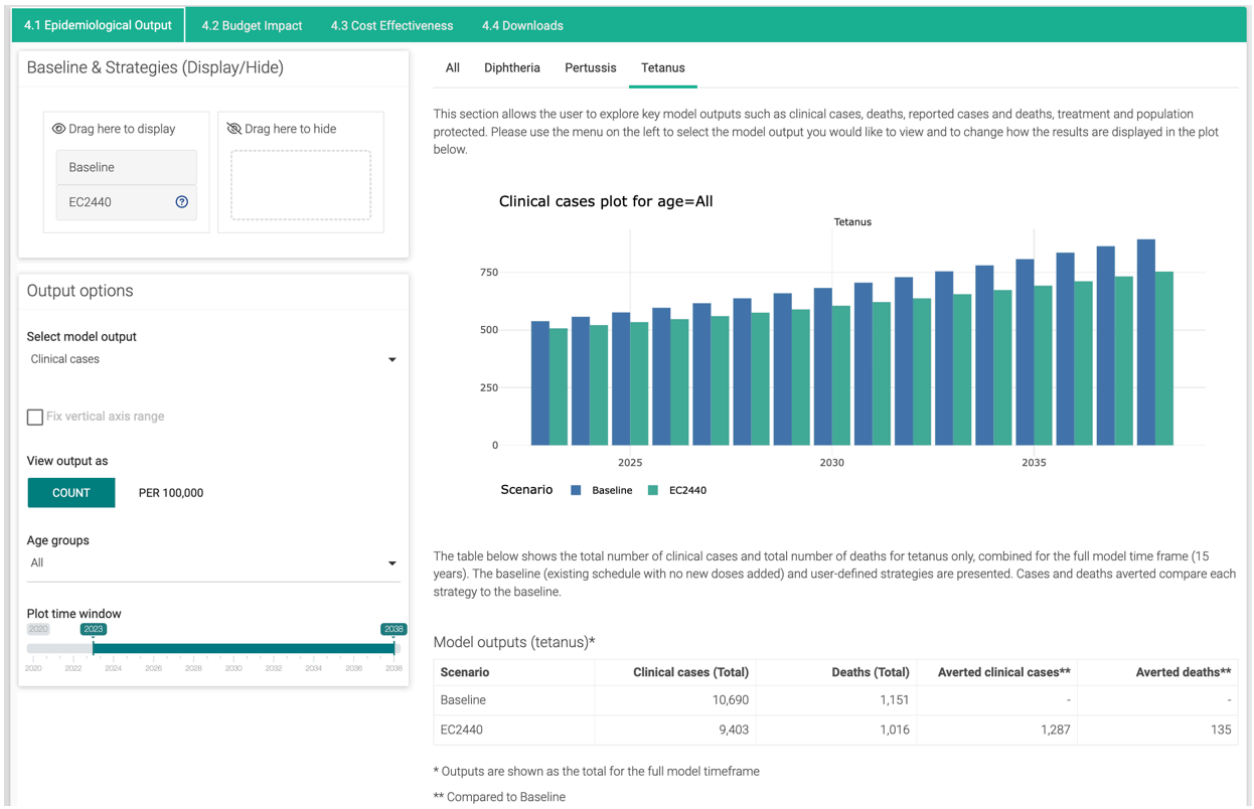
Users may repeat this several times to design and run multiple strategies. To return to Step 3, click on **Step 3. Design Booster Strategy** in the menu on the left side of the screen.

Step 4. Explore Results

4.1 Epidemiological Output

The controls on the left displaying the **Baseline & Strategies** can be used to filter the results. The **Output options** allow the selection of model output such as population protected, clinical cases, and deaths. Other options include the preferred output measure, age groups and time window to be displayed. Epidemiological results for all diseases, and for each specific disease, can be viewed by clicking on the tabs on the upper right side of the page. A table of projected epidemiologic results is shown at the bottom right of the page. Users can hover over the figures for additional details and to save the figures as png for offline use.

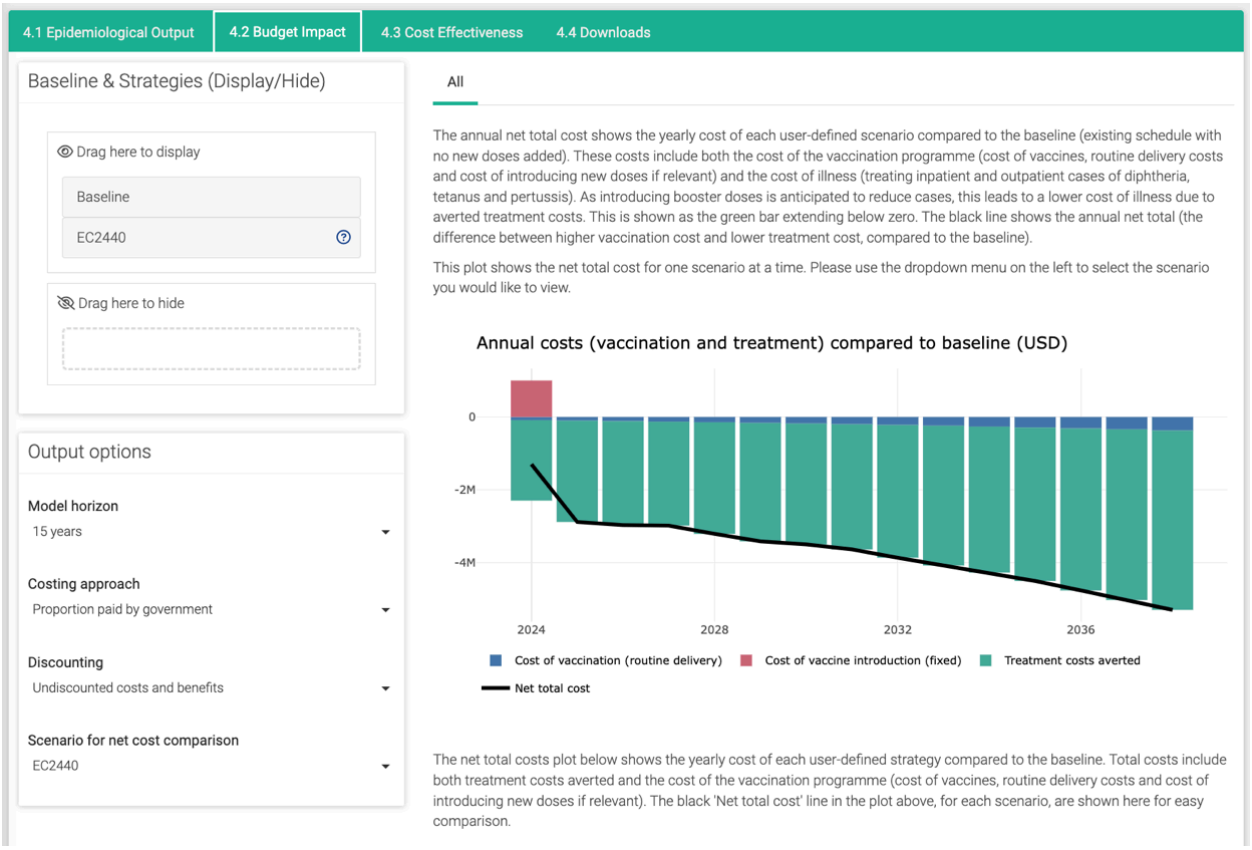
The full version of the tool has additional output options, such as reported cases, reported deaths, number of inpatient cases, and number of outpatient cases. There are also more aggregate age categories available for exploring the outputs (e.g. <1 year olds, <15 year olds, and all 5-year age bands).



4.2 Budget Impact

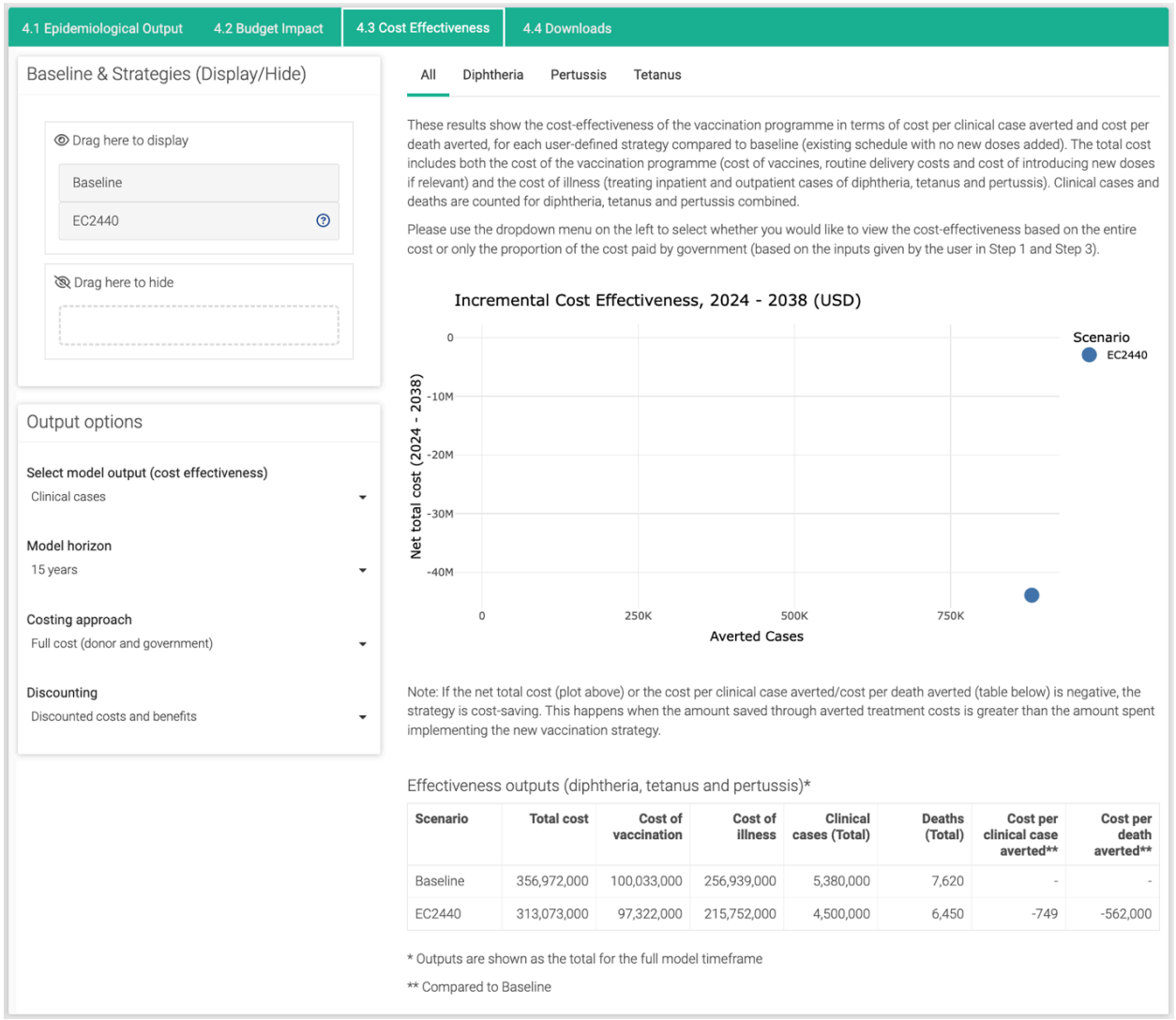
The budget impact tab shows three plots (Annual costs compared to the baseline, Net total cost compared to the baseline, Total annual cost of vaccination), a table of projected costs and the output option controls. Details of what each presents is captured in the tool.

Output can be viewed for a 10 year or 15 year time horizon; and either for the full cost or only the proportion paid by the government.



4.3 Cost Effectiveness

The cost effectiveness tab shows one plot (Incremental cost effectiveness) and a table of effectiveness outputs. Users have the option of viewing the results for all diseases or for a specific disease individually by clicking on the tabs. Options to adjust for the model output, model horizon, costing approach, and discounting is available in the **Output options** section on the left of the screen.



4.4 Downloads

Results can be downloaded for use offline as a PDF or in csv format for further analysis.

To save additional figures in various sections or selections, such as specific output, costing approach or age category, hover over any plot in the tool to download it as a png image.

Resources

Use the tables below as a guide in collecting the required data inputs for the full use of the app. Consider multiple sources and higher or lower values for comparison.

Table 1. Data Needs – Country Profile

Parameter	Point Estimate	Lower Limit	Higher limit	Sources
Existing Primary Series				
Primary series dose schedule & ages given				
Vaccine type/components				
Health Facility Delivery (%)				
Outreach site (%)				
Existing Booster Vaccination				
Booster: Early Childhood coverage				
Delivery: Health Facility (%)				
Delivery: Outreach site (%)				
Vaccine type/components				
Booster: Child booster coverage				
Delivery: Health Facility (%)				
Delivery: Outreach site (%)				
Booster: Adolescent				
Delivery: Health Facility (%)				
Delivery: Outreach site (%)				
Maternal vaccination: Td / Tetanus toxoid				
Delivery: Health Facility (%)				
Delivery: Outreach site (%)				
Vaccine Coverage (1985 to current year)				
Primary Series (Dose 1, 2, 3)				
Early Childhood booster				
Child booster				
Adolescent booster				
Antenatal care coverage – at least 1 visit (ANC)				
Tetanus toxoid containing vaccine ≥ 2 doses				
DTP Treatment				
Diphtheria				
Probability mild case treated OPD				
Probability severe case treated (inpatient)				
Pertussis				
Probability mild case treated OPD				
Probability severe case treated (inpatient)				
Tetanus				
Probability severe case treated (inpatient)				
DTP Reporting				

Diphtheria				
Probability symptomatic cases being diagnosed				
Probability deaths being reported				
Pertussis				
Probability symptomatic cases being diagnosed				
Probability deaths being reported				
Tetanus				
Probability symptomatic cases being diagnosed				
Probability deaths being reported				

Table 2. Data needs - Costs

Parameter	Point Estimate	Lower Limit	Higher limit	Sources
COSTS				
Discount rate (%)				
Cost paid by government (%)				
Primary series cost (USD)				
Health facility				
Outreach				
Maternal vaccination via ANC				
Health facility				
Outreach				
Cost of vaccine per dose				
Primary series				
Maternal vaccination (Td)				
Other DTP containing vaccines				
COST OF ILLNESS (USD)				
Diphtheria				
Cost per outpatient case				
Cost per inpatient case				
Pertussis				
Cost per outpatient case				
Cost per inpatient case				
Tetanus				
Cost per outpatient case				
Cost per inpatient case				
Cost of introduction				
Fixed cost (USD)				

Links to databases and relevant resources

WHO Immunization Data Portal
Provides country level vaccine schedules, vaccine coverage data, and disease incidence.

Immunization Delivery Cost Catalogue
This resource provided by the Immunization Costing Action Network (ICAN) and ThinkWell, includes cost information on routine immunization and immunization campaign costing studies from various contexts. Other links and resources are available on the Immunizationeconomics.org website such as cost of illness studies.

Market Information for Access to Vaccines (MI4A)
The MI4A vaccine purchase database includes information on vaccine prices as reported by 150 countries through the WHO/UNICEF Joint Reporting Form, and is updated yearly.

UNICEF Vaccines Pricing Data
Database of vaccine prices procured by UNICEF according to vaccine and as awarded price per dose in US Dollars. Includes data from previous years with consultation from UNICEF suppliers.

WHO Position Papers
These provide the basis for primary and booster doses in diphtheria, tetanus, and pertussis.

Modelling Diphtheria-Tetanus-and-Pertussis (DTP) burden and vaccination strategies to support country decision-making

Session introduction slides

IVIR-AC Meeting

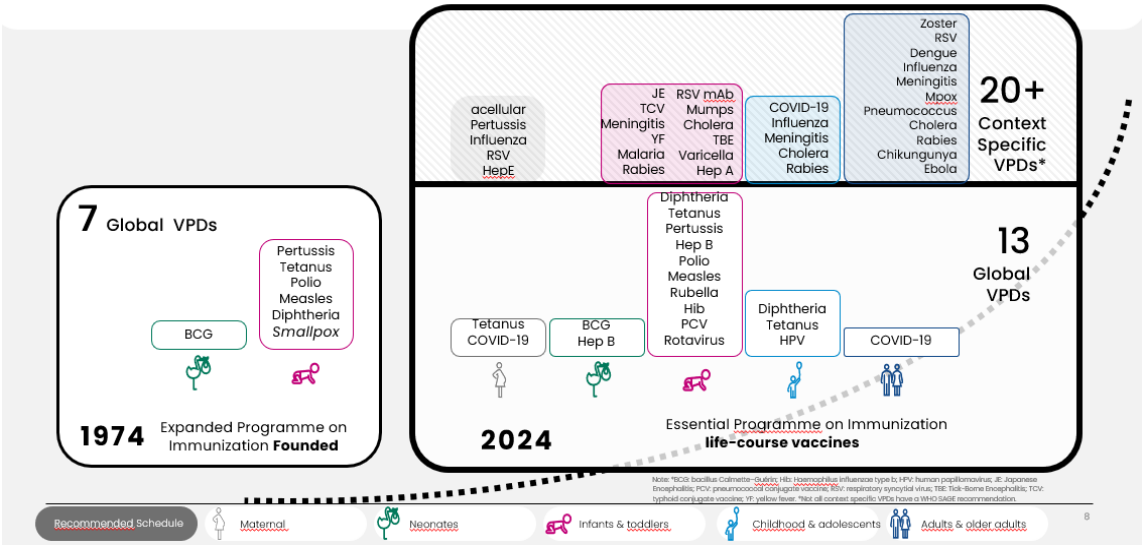
2 September 2025

World Health Organization | IVB

Increased interest in vaccine prioritisation and optimisation

- In a context of reduced external donor support and limited predictability on future funding, there is increased expectation for countries to prioritize interventions including new vaccines introductions.
- Yet country **decision making on new vaccine introductions is increasingly complex**

The number of new vaccines to consider is increasing



At the same time, current programmes continue to evolve with new products, new presentations, policy recommendations …

Between 2022 and 2024 only:

- Nearly 20 vaccines received WHO prequalification*
- WHO published 10 new or revised position papers**
- Gavi has opened 6 new vaccine programmes and the 2024 Vaccine Investment Strategy recommended potential 5 new programmes***

** WHO Prequalification webpage - excluding Covid 19 and influenza*
***Marti, M.; Nohynek, H.; Duclos, P.; O'Brien, K.L.; Hombach, J. The Strategic Advisory Group of Experts (SAGE) on Immunization—Past, Present and Future. Vaccines 2024, 12, 1402.*
**** Gavi website*

*1 Ozisik, L. The New Era of Pneumococcal Vaccination in Adults: What Is Next? Vaccines **2025**, 13, 498. https://doi.org/10.3390/vaccines13050498*

World Health Organization

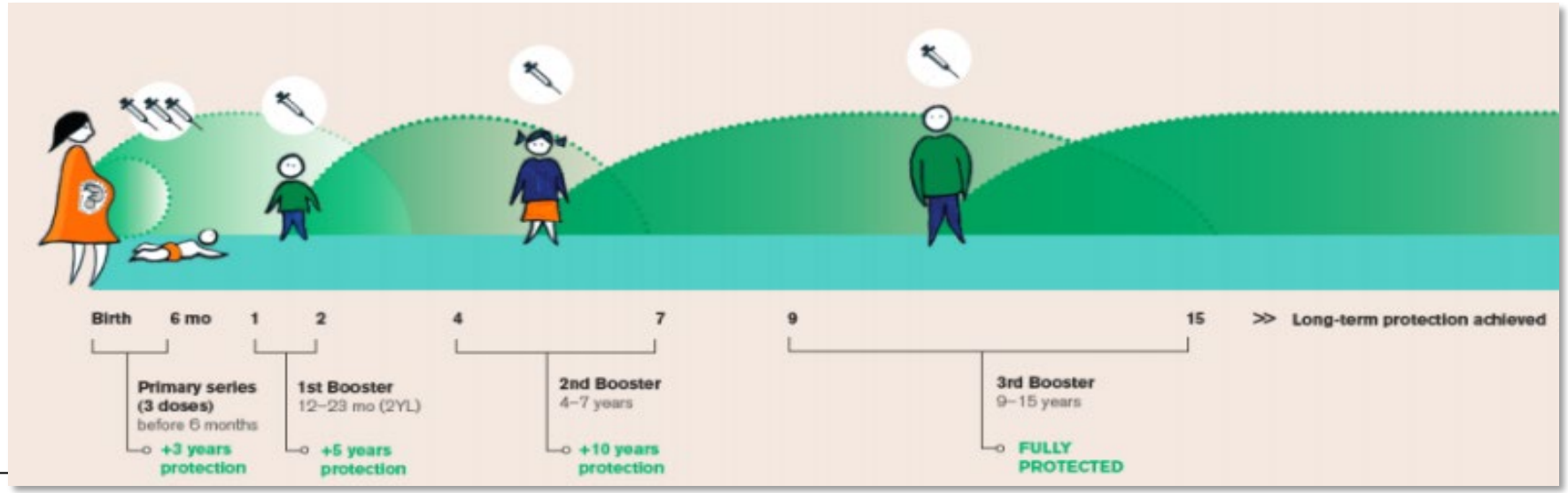
Vaccine Evidence Compendium

- A **one-stop shop** for vaccine evidence to strengthen country priority-setting and evidence-based decision-making.
- The Vaccine Evidence Compendium is available on the [NITAG resource centre]
- Target audience: NITAG secretariats and members, EPI managers, WHO and UNICEF Country Offices
- Launched on 21 July 2025 – 4 pilot vaccines to start

https://www.nitag-resource.org/compendium

Diphtheria-Tetanus-Pertussis (DTP)-containing vaccines

- Primary series vaccination against **diphtheria, tetanus, and pertussis (DTP)** is **highly effective** however, protective immunity **wanes over time**
- To maintain **long-term protection** against diphtheria, tetanus, and pertussis, **booster doses are needed** beyond the primary infant series
- WHO recommends **three diphtheria and tetanus boosters** and at least **one pertussis booster** during childhood and adolescence, given as combination vaccines.
- Each booster provides opportunities for integration and programme synergies with its delivery platform: **2YL, school-entry, HPV/adolescent health**.



WHO recommended DTP-cv schedule (6 doses)

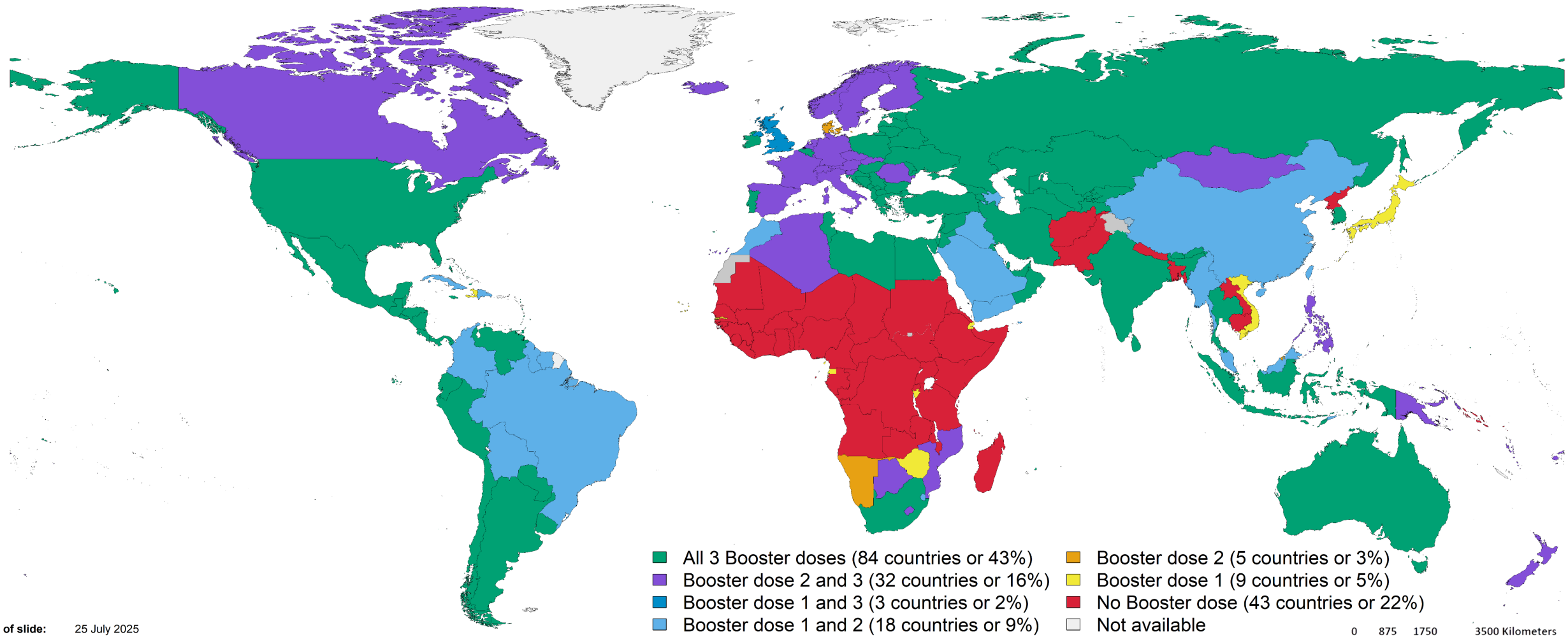
	Primary Series	Booster 1	Booster 2	Booster 3
Recommended Age[1]	**3 doses (from 6w-)**	**2YL (12-23 months)**	**4-7 years**	**9-15 years**
Recommended vaccine[2]	**3 doses of DTP-containing vaccine**	**DTP-containing vaccine**	**DT/Td- containing vaccine (with or without pertussis)**	**Td-containing-vaccine (with or without pertussis)**
Product options[3]	• DTwP or DTaP • Quadravalent combos • **Pentavalent (DTP-Hib-HepB**, DTP-Hib-IPV) • **Hexavalent (DTP-Hib-HepB-IPV)**	• **DTwP** or DTaP • Quadravalent combos • **Pentavalent (DTP-Hib-HepB**, DTP-Hib-IPV) • Hexavalent (DTP-Hib-HepB-IPV)	• Td (from ≥4yrs) or DT (if <7yrs) • DTP, TdaP	• Td • TdaP

Indicates a Gavi-supported option

1. Depending on local epidemiology; For WHO recommended schedules see: www.who.int/teams/immunization-vaccines-and-biologicals/policies/who-recommendations-for-routine-immunization---summary-tables
2. WHO recommends a tetanus-diphtheria-pertussis-containing combination vaccine for the 2YL booster, plus 2 additional tetanus-diphtheria-containing boosters
3. Countries currently using whole-cell pertussis vaccine (wP) for the primary series should continue to do so.

For up-to-date product information prequalified by WHO always check: https://extranet.who.int/prequal/vaccines/prequalified-vaccines .
For up-to-date information on UNICEF Supply Division vaccine prices see: https://www.unicef.org/supply/index_57476.html .

Globally, LMICs (particularly in the African Region) are lagging behind in DTP booster introductions



Date of slide: 25 July 2025
Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization (WHO)
Data source: IVB database as at 25 July 2025

Disclaimer:

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area nor of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

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World Health Organization

Gavi opened a funding window for DTP-cv boosters in Dec 2023

- Countries eligible for Gavi support can apply to introduce **each booster** under Gavi Product Menu **either individually** OR **any combination** of boosters together.

Gavi support	2YL booster (12m – 23m)	Childhood booster (4y – 7y)	Adolescent booster (9y – 15y)
Vaccine	DTwP or Pentavalent	(no vaccine support) – countries to self-finance vaccine	
Co-financing	Vaccine dose procurement and supplies, under current co-financing principles, for the **2YL booster only** (DTwP or Penta)	Vaccine financing support will **not** be provided for Td as long as the price remains equal to or below US$0.20 per dose (the minimum co-financing based on the current Gavi policy)	
Vaccine introduction grant (VIG)	For Gavi-eligible countries introducing DTP-containing vaccine boosters, Gavi will provide a **one-time VIG** for each new booster contact		

https://www.gavi.org/sites/default/files/support/guidelines-2024/GAVI-Vaccine-Funding-Guidelines-aug2024.pdf

Some of the documents related to this session are currently confidential and not available for public access.

World Health Organization

Session 5: WHO guidance to translate modeling to support evidence-informed decision making for immunization

IVIR-AC Sub-Group for translation of vaccine impact modelling into immunization strategy, policy and program decisions (2023-25)

Yoonie Sim & Philipp Lambach

3 September 2023

Agenda for today’s session

- **Background information** - Yoonie Sim & Philipp Lambach (WHO IVB)
- **WHO draft guidance document** - Alyssa Sbarra (on behalf of IVIR-AC sub-group)
- **Q&A and discussion** - with IVIR-AC members

Background information

At WHA 78 countries back resolution EB156(14) from the Executive Board's 156th session (24 May 2025)

- Aims to boost science-driven health policy & implementation and strengthen national capacities for developing public health guidance based on high-quality evidence
- Addresses gaps in data generation, use, and scale—barriers to equitable health outcomes
- Urges governments to invest in:
  - Regulatory frameworks
  - Digital tools
  - Local research
- Calls on WHO to:
  - Maintain highest standards in normative products
  - Support adaptation & implementation at country level
- Mandates creation of global framework & action plan for cross-border collaboration and regional science capacity

IVIR-AC's engagement to strengthen modelling expertise, improve local data availability, and enhance modeler–policymaker collaboration particularly in low resource settings promises to make use of the full potential of models to inform effective, context-specific policy.

WHO support to immunization policy development informed by modeling evidence

- **Review of Modelling Work**
  - Convene regular global expert review through **IVIR-AC** of immunization modeling studies to ensure scientific rigor, comparability, and policy relevance.
- **Technical Assistance to Countries**
  - Regional engagement via RITAGs and Regional Offices to leverage synergies among countries, and optimize use of modelling evidence
  - Build capacity to interpret and apply model outputs for immunization policy and program planning
- **Normative Guidance Development**
  - Incorporate robust modeling evidence into WHO immunization norms and recommendations SAGE
  - ***Provide national policy makers with guidance to optimize translation of modelling evidence into immunization policy decision making***

IVIR-AC Actions to Improve Use of Modelling in Immunization Policy (March 2023)

- Formation of dedicated **subgroup** to
  - Help bridge the gap between vaccine impact modelling outputs and immunization policy needs
  - Advise on communication strategies so modelling results are understandable, transparent about uncertainties, and relevant to diverse audiences
  - Engage with relevant modelling and immunization experts to ensure outputs are formatted and framed in ways that support timely, evidence-based immunization strategies and programmes
  - Develop clear, practical guidance for policy-makers to interpret, assess, and apply modelling evidence in decision-making

2023, 98, 127–144 No 13

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

31 MARCH 2023, 97th YEAR / 31 MARS 2023, 97e ANNÉE
No 13, 2023, 98, 127–144
http://www.who.int/wer

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Meeting of the Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC), February 2023

The IVIR-AC recommendations are based on technical discussions during a virtual meeting of the IVIR-AC, held 13–16 February 2023.[1] Eight groups sought technical feedback from IVIR-AC on topics that included COVID-19 vaccine impact modelling to inform vaccine prioritization and strategy, optimization of maternal and neonatal tetanus elimination (MNTE) assessments in conflict-prone areas, and vaccine value assessments[2] to capture vaccine impact on antimicrobial resistance (AMR) and antibiotic use.

The IVIR-AC secretariat began the meeting by sharing the results of a review of declarations of interests from all meeting contributors by an internal WHO panel. Contributing IVIR-AC members included: Rakesh Aggarwal, Habib Hasan Farooqui, Alexandra Hogan, Stefan Flasche, Sun-young Kim, Julie Leask, Paula M. Luz, Dafrossa C. Lyimo, William Moss, Walter Orenstein, Virginia Pitzer, Sheetal Silal, Xuan-yi Wang, Joseph Wu. The IVIR-AC members have not received funding specifically for this meeting. IVIR-AC recommendations were made through consensus of IVIR-AC members, following discussions in open and closed sessions of the drafts that were prepared by designated IVIR-AC member focal points.

[1] Meeting of the Advisory Committee on Immunization and Vaccines-related Implementation Research (IVIR-AC), Geneva: World Health Organization, 2023 (https://terranceu.who.int/mediacentre/data/sage/IVIR-AC_Pink%20Book%20Feb2023.pdf, accessed February 2023).

[2] Full value of vaccine assessments (FVVA). Geneva: World Health Organization, 2022 (https://www.who.int/teams/immunization-vaccines-and-biologicals/product-and-delivery-research/full-vaccine-value-assessments, accessed February 2023).

Réunion du Comité consultatif sur la vaccination et la recherche sur la mise en œuvre des vaccins (IVIR-AC), février 2023

Les recommandations de l'IVIR-AC présentées ici sont basées sur les discussions techniques qui ont eu lieu lors d'une réunion virtuelle du Comité qui s'est tenue du 13 au 16 février 2023.[1] Huit groupes ont sollicité des commentaires techniques de l'IVIR-AC sur des sujets tels que la modélisation de l'impact des vaccins contre la COVID-19 pour déterminer les priorités et la stratégie vaccinales, l'optimisation de l'évaluation de l'élimination du tétanos maternel et néonatal (TMN) dans les zones sujettes aux conflits et l'évaluation de la valeur des vaccins[2] pour déterminer leur impact sur la résistance aux antimicrobiens (RAM) et l'usage des antibiotiques.

Le secrétariat de l'IVIR-AC a commencé la réunion en présentant les résultats d'un examen des déclarations d'intérêts de tous les participants à la réunion par un groupe interne de l'OMS. Les membres contributeurs de l'IVIR-AC étaient les suivants: Rakesh Aggarwal, Habib Hasan Farooqui, Alexandra Hogan, Stefan Flasche, Sun-young Kim, Julie Leask, Paula M. Luz, Dafrossa C. Lyimo, William Moss, Walter Orenstein, Virginia Pitzer, Sheetal Silal, Xuan-yi Wang, Joseph Wu. Aucun n'a reçu de financement spécifique pour cette réunion. Les recommandations de l'IVIR-AC ont été formulées par consensus des membres à la suite de discussions en sessions ouvertes et fermées sur les projets de recommandations préparés par des membres référents désignés.

[1] Meeting of the Advisory Committee on Immunization and Vaccines-related Implementation Research (IVIR-AC), Genève, Organisation mondiale de la Santé, 2023 (https://terranceu.who.int/mediacentre/data/sage/IVIR-AC_Pink%20Book%20Feb2023.pdf, consulté en février 2023).

[2] Full value of vaccine assessments (FVVA). Genève, Organisation mondiale de la Santé, 2022 (https://www.who.int/teams/immunization-vaccines-and-biologicals/product-and-delivery-research/full-vaccine-value-assessments, consulté en février 2023).

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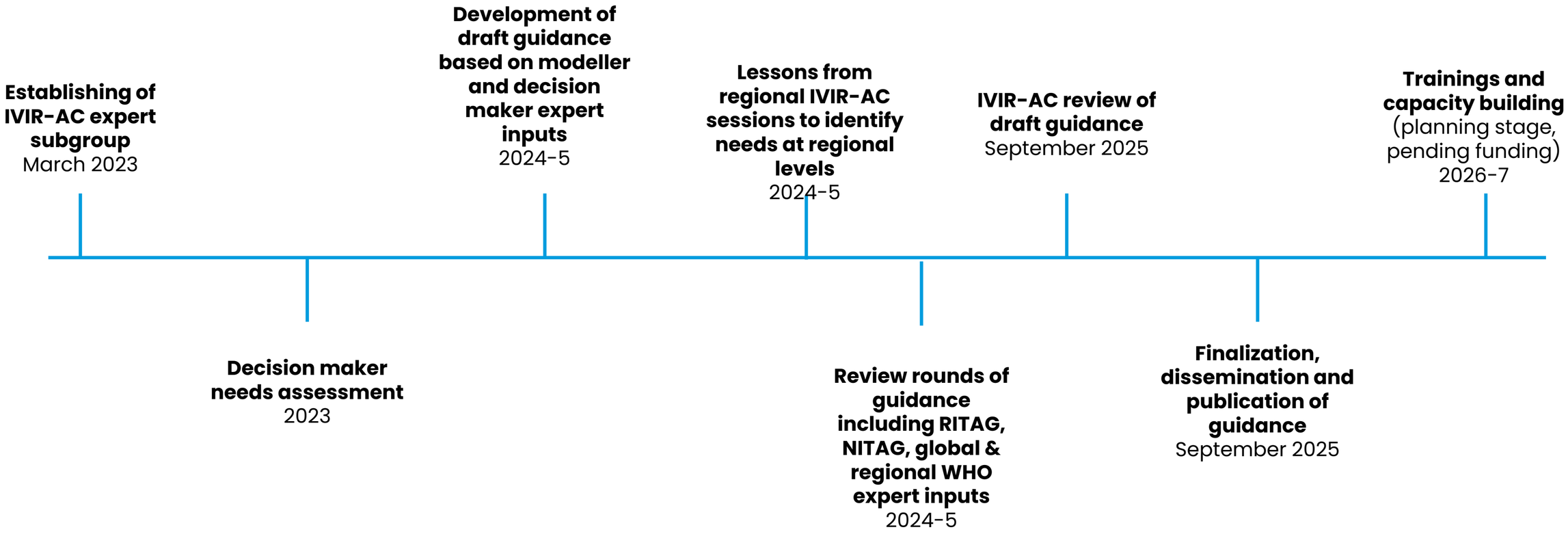
Weekly Epidemiological Record, 31 March 2023, No 13, 2023, 98, 127-144
https://www.who.int/publications/i/item/who-wer9813-127-144

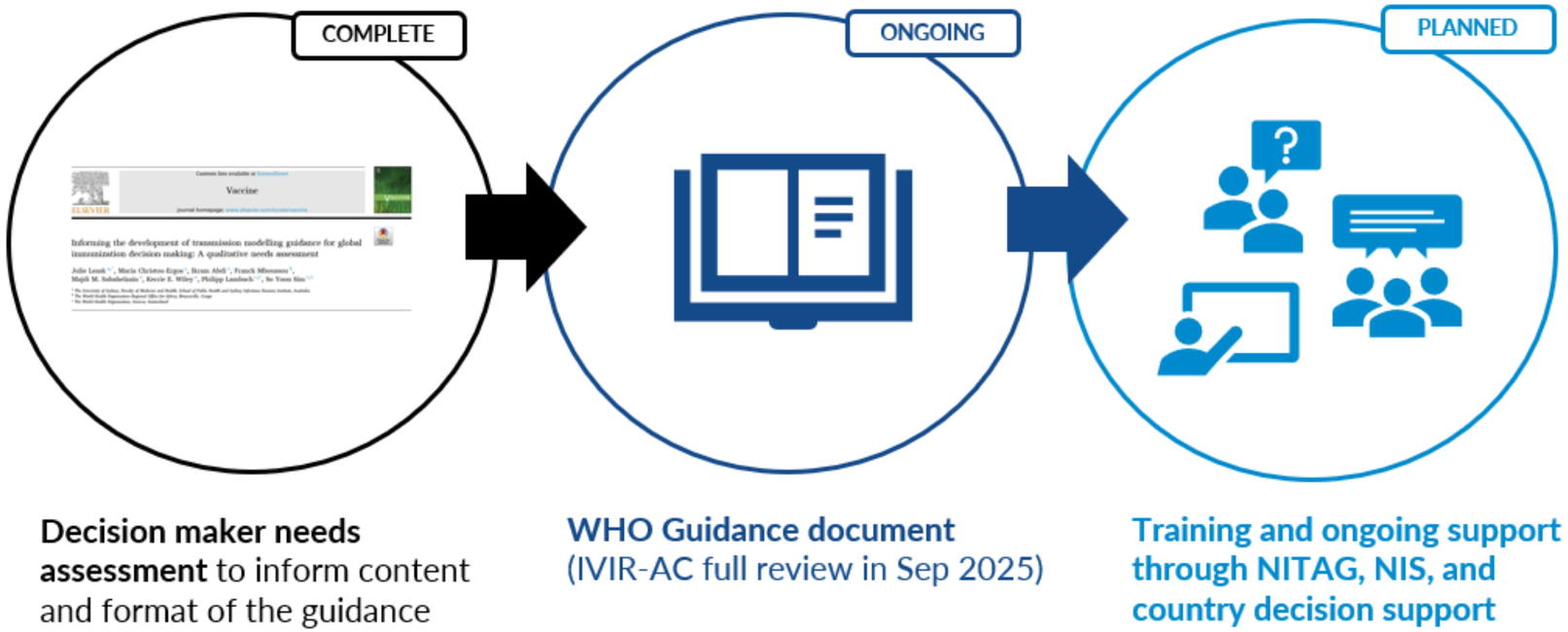
IVIR-AC Subgroup activity timeline to facilitate use of modeling evidence by immunization policy developers



WHO Guidance for developing and using modeling for evidence-informed immunization decision-making

The target audience

- NITAG/RITAG members
- EPI programme managers
- Immunization technical working group members
- Technical partners who support immunization policy decision-making



*The project has been funded by Ministry of Health and Welfare Republic of Korea and Gates Foundation

IVIR-AC recommendations from September 2023

- To reformulate the definition of modelling to be specific to **the role of modelling in immunization** and distinguished from other types of modelling (e.g., economic, statistical).
- To increase the relevance of the guidance, the content of the guidance should discuss **problem formulation**, **data contextualization**, **factors affecting generalizability** and **uncertainty of modelling results**, and acknowledge limitations and assumptions.
- To **demystify model complexity**, the guidance should provide **simple definitions** with explanations of common **modelling concepts**, including highlighting the importance of knowledge exchange.
- To exemplify the guidance delivered, **examples** could be used, in addition to **historical use cases**.
- To reduce the risk of inappropriate use of modelled evidence, the guidance should be **clear on limitations**, including but not limited to model structure, inherent uncertainties in the modelling results due to erroneous models or assumptions, biological systems that are not fully understood, and a need for reliable local data for parameters that are or can be influential to model results

Source: Report from the World Health Organization's immunization and vaccines related implementation research advisory committee (IVIR-AC) meeting, Geneva, 11–13 September 2023

Decision makers needs assessment

Informing the development of transmission modelling guidance for global immunization decision-making: A qualitative needs assessment

Julie Leask [a,*], Maria Christou-Ergos [a], Ikram Abdi [a], Franck Mboussou [b], Majdi M. Sabahelzain [a], Kerrie E. Wiley [a], Philipp Lambach [c,1], So Yoon Sim [c,1]

[a] The University of Sydney, Faculty of Medicine and Health, School of Public Health and Sydney Infectious Diseases Institute, Australia
[b] The World Health Organization Regional Office for Africa, Brazzaville, Congo
[c] The World Health Organization, Geneva, Switzerland

- **A qualitative needs assessment** based on in-depth interviews with national immunization decision makers from all WHO six regions
- Methodology reviewed by IVIR-AC in September 2023

Key findings

- Varying use of modeling
  - **Local context** regarding resources, capacity, and data
- Proposed content for guidance
  - Need for **nuanced understanding** of what modeling can and cannot achieve
  - **Assessment, validation, and communication** of models and results
  - **Localized application** of modeling
- Proposed formats
  - Interventions for **behavioral change**
  - Guidance document accompanied by **interactive training and community of practice**
- Key elements
  - Importance of **trust** between modelers and decision makers
  - **Co-creation and stronger local ownership** of the modeling process

For more information: Leask et al 2025. Informing the development of transmission modelling guidance for global immunization decision-making: A qualitative needs assessment

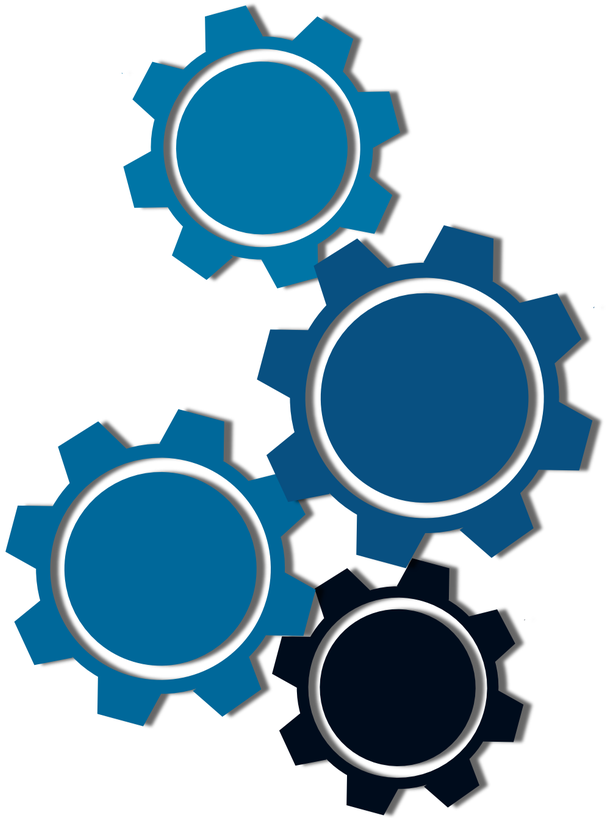
WHO guidance document: process overview

Year	Month	Activities	Stakeholders
2023	*March*	IVIR-AC sub-group established	IVIR-AC subgroup
	May	Meeting with WHO Regional Offices	IVIR-AC subgroup, WHO ROs
	June	Needs Assessment study commenced	U Sydney, country stakeholders, WHO HQ & ROs
	Sep	IVIR-AC session on the needs assessment	IVIR-AC subgroup and full committee
	Nov	Stakeholder feedback for WHO guidance (Epidemics9)	External experts
2024	*Jul-Aug*	Needs assessment finalized and pre-print published	U Sydney, WHO HQ
	Sep	IVIR-AC session on the Lancet Commission on Strengthening the Use of Epidemiological Modeling	IVIR-AC full committee
	Jul-Dec	Dissemination of needs assessment findings including: • Global NITAG Network • Annual Vaccinology Course for NITAGs (AVCN) • Infectious Diseases Modelling Conference 2024	NITAG members, external experts
	Dec 2023 – June 2024	Guidance document development • Writing team regular check-in • Four meetings and virtual exchange with IVIR-AC subgroup	Writing team, IVIR-AC subgroup
2025	*Jun-Aug*	Review of draft guidance document & stakeholder feedback	NITAG members (GNN), external experts, WHO HQ& ROs, WHO Collaboratory
	Aug	IVIR-AC sub-group review	IVIR-AC subgroup
	Sep	IVIR-AC session on the guidance document	IVIR-AC subgroup and full committee
	Sep-Dec	Additional feedback & revision	IVIR-AC, NITAG members, external experts, WHO HQ& ROs
	Dec	Finalized guidance document	WHO HQ
	Jul 2024 – Ongoing	Country implementation plan	WHO HQ & relevant stakeholders

Best use of the guidance: next steps

Partnership with local institutions across six WHO regions

Community of practice
- Knowledge sharing, Peer-to-peer learning, and collaboration



NITAG technical capacity strengthening
- Training, mentorship, and ongoing support

Feedback loop
- Continuous improvement and re-assessment of user needs

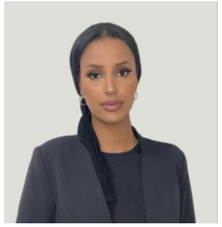
Acknowledgement: IVIR-AC sub-group members

IVIR-AC Sub-Group
Writing group
External experts & Qualitative research team
WHO Regional Offices
WHO Secretariat

Qualitative research team led team led by Prof Julie Leask, University of Sydney

Ms Maria Christou-Ergos

Dr Kerrie Wiley


Dr Ikram Abdi

IVIR-AC Sub-Group members and WHO Secretariat

Prof Sheetal Silal
Sub-Group Chair

Prof Julie Leask

Prof. Walt Orenstein

Dr Wirichada Pan-Ngum

Prof Stefan Flasche

Dr Dafrossa Lyimo

Prof. William Moss

Dr Jacquie Oliwa

Prof Rakesh Aggarwal

Dr Alyssa Sbarra

Dr Philipp Lambach

Ms Yoonie Sim

Main presentation

Alyssa Sbarra

Guidance document overview

- What are models and how can they help us?
- How can policy makers work together with modelers?
- How are models made?
- How should modeled results be interpreted and evaluated?

What are models and how can they help us?

Key messages:

- Mathematical models are tools that can simplify real-world systems and help us better understand disease trajectory and impact of different vaccination strategies under various scenarios, such as how well different vaccination plans might work depending on when and how vaccines are given.
- Health decision-makers can use these models to support their choices about vaccines and vaccine use policies.
- These models can provide important information, such as how many illnesses and deaths a vaccine could prevent, the threshold of herd protection, and the costs and economic benefits from an immunization strategy or program.
- Models complement, but do not replace, local evidence. However, local results may not be available. In either case, decision makers should use modeling results alongside other types of reliable evidence as well as operational realities to inform decisions.
- Modeling evidence may be presented in different formats from a variety of settings (e.g., epidemiologic setting, urban or rural, geographic area).

- Overview of what are mathematical models models and how can they help us
- Who uses mathematical models, and how are they used in the immunization decision-making process

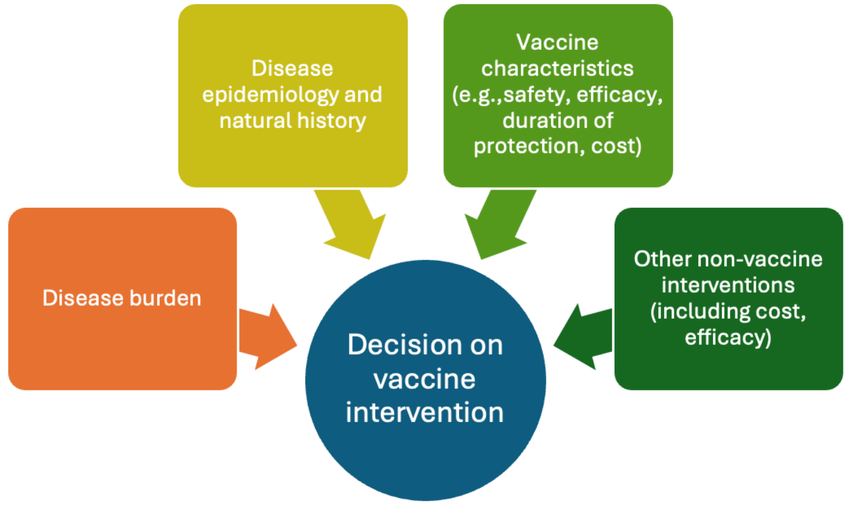
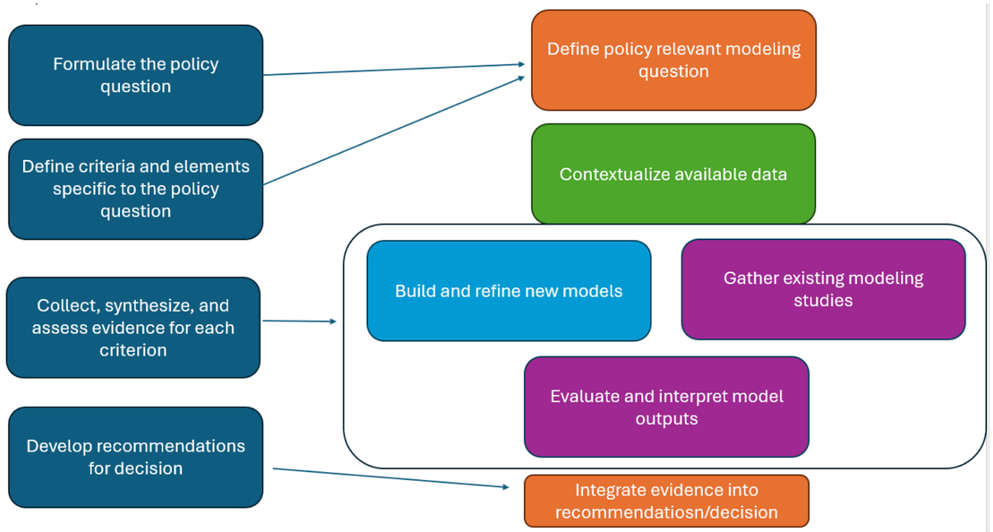


Figure 1. *Considerations made when deciding on a vaccine intervention*

What are models and how can they help us?

Immunization decision-making process

- Overview of how policy recommendations are made at global levels (via SAGE), at regional levels (via RITAGs), and at country levels (via NITAGs, with input from EPI managers)
- Consideration of Evidence to Recommendation process, which guides decision makers through an assessment and appraisal of evidence
- Modeled evidence may be commissioned or identified via other means
- Modeled evidence is often integrated with other complementary analyses, including economic evaluations



How can policy makers work together with modelers?

Key messages:

- Many diverse backgrounds and roles make up a successful modeling project team. Defining roles and responsibilities for each stage of the project at the onset will help facilitate a successful collaboration.
- Establishing internal communication and plans for wider dissemination help make possible clear expectations and respect among project team members.
- Respect in the engagement is critical to the success of the modeling project and should be prioritized.
- There are multiple tools that modeling project teams can use to help facilitate successful projects and guide long-standing collaborations.

Project stage	Task	Decision makers	Modelers	Advisory bodies	Public health officials	Disease specialists	Vaccine manufacturers	Implementers	General public
Problem formulation	Advise on priorities for research and modeling	■		■	■				■
	Define decision problems	■		■	■				■
	Translate policy question into quantifiable modeling questions	■	■						
	Advise on feasibility assessment	■							
	Synthesize knowledge on disease and vaccine/clinical trials					■			■

Overview roles and responsibilities at each project stage

How can policy makers work together with modelers?

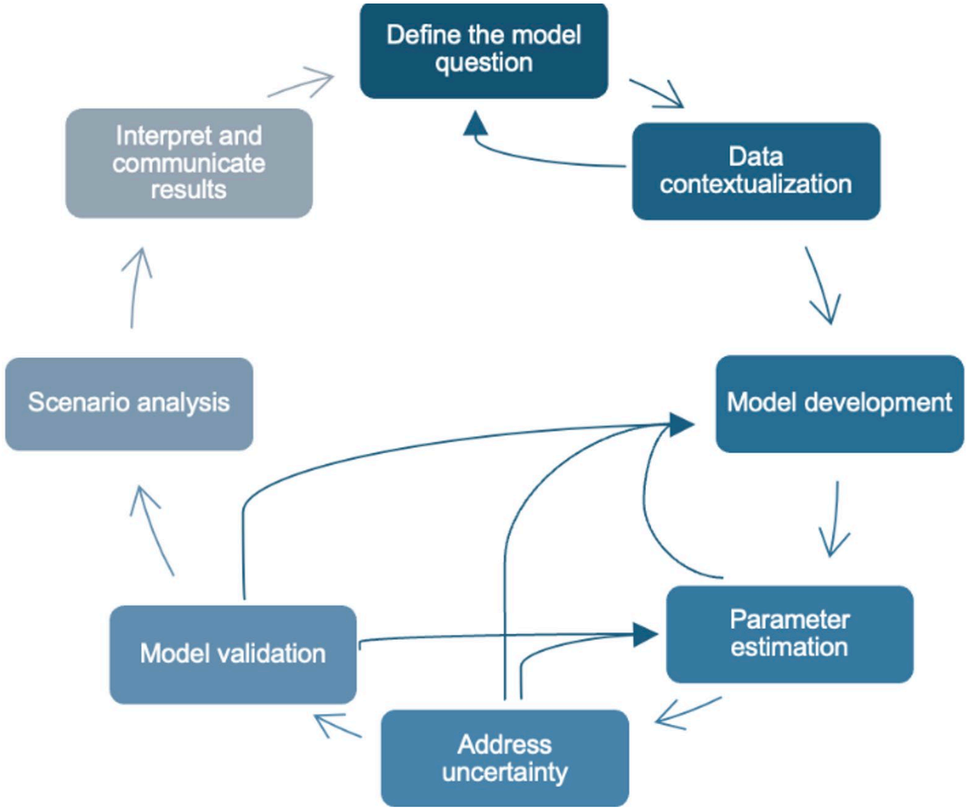
- Communication, including:
  - Open access data and code repositories, as appropriate
  - Developing dissemination plans
  - Setting up channels for contact and regular meetings
- Respect in the engagement
  - Importance of developing structural procedures, including roles and responsibilities
  - Ethical considerations, including data and results ownership and capacity building
  - Dissemination of model results and creating a feedback loop to share how model results were used in decision-making process

- Examples of useful tools for facilitating successful engagements: Lancet Commission SPOTT tool, Memorandums of Agreement, WHO Collaboratory, progress monitoring via key meetings

How are models made?

Key messages:

- The main phases in the modeling process are defining the modeling question, contextualizing the data, developing the model, estimating parameters, addressing uncertainty, validating the model, constructing scenario analyses, and interpreting and communicating results.
- The modeling process is iterative and requires input from many partners, including local experts, modelers, policy makers, epidemiologists and statisticians.



How are models made?

Defining modeling question

Key questions for consideration:
- What is the decision/policy question of interest?
- What modeling question does the study try to address? Does it match the policy question?

Key steps to defining modeling question:
1. Clarify the objective of the modeling exercise
2. Review existing data and information
3. Identify outcomes to measure

Illustrative example: A NITAG is required to provide a recommendation on whether the country should introduce HPV immunization program , and if so among which targeted age groups (i.e., 9- to 10-year-olds, 11- to 12-year-olds) and using one versus two doses.
- Policy question might be: “Should my country vaccinate against HPV?”
- Framing of this question for modeling : “What will be the health and economic impact of implementing an immunization program for one versus two doses for boys and girls specific targeted age groups in our country?”

How are models made?

Data contextualization

Key questions for consideration:
- What data was used? Are they representative of the population of interest?
- Where did the data come from?
- How were data gaps addressed?
- Was a quality assessment conducted?

- Review data types (i.e., case notifications, outbreak reports, vaccination coverage, demographic data, serological data, scientific publications)
- Overview data generalizability and transferability across geographic locations

How are models made?

Model development

Key questions for consideration:

- Is the type of model appropriate for the policy question of interest?
- How well does the model fit the data, and does it make an epidemiological sense?
- Is the outcome measure appropriate for the policy question of interest?
- What are the main sources of uncertainty in the models?
- Does the model correctly incorporated key mechanisms of disease epidemiology, dynamics and progression, transmission patterns, population behavior, immunity and vaccine introduction?
- Are these mechanisms and assumptions in the model in agreement with available data and evidence?
- On what basis were the assumptions chosen? How realistic they may be?
- What are the key assumptions and mechanisms driving the main modeled evidence?
- Are there concerns related to dose dependencies in the model structure?

Main modeling steps outlined, including:

How should modeled results be interpreted and evaluated?

Key messages:

- There is rarely a single 'correct' model for all questions and different models make different assumptions. Assess whether the modeled outcomes answer your specific policy questions.
- Recognize that all models have limitations and that their outcomes are inherently estimations. Model outputs having varying degrees of uncertainty and, thus, possibly inaccurately capturing future realities. However, you will need to assess whether it is qualitatively informative.
- Given the iterative nature of relating results to the original question and assumptions, continue asking and aligning questions to ensure informed decision-making. Consider the model's purpose, methods, assumptions, data inputs, and uncertainties.

Key questions for consideration:

- What can be learned about our policy question from interpreting outcomes and scenarios?
- What are the most important findings? how might they provide evidence for your decision?
- Are results from sensitivity analyses consistent? If not, what is driving discrepancy? What additional sensitivity or scenario analyses are needed to support a policy option?
- How will uncertainty affect my decision?
- For what period of time were impacts measured?
- What assumptions were tested across a range of scenarios?
- How sensitive are the results to changes in key parameters or assumptions?

How should modeled results be interpreted and evaluated?

Evaluating models

#1 : Example: Remember our overarching question: A NITAG is required to provide a recommendation on whether the country should introduce HPV immunization program , and if so among which targeted age groups (i.e., 9- to 10-year-olds, 11- to 12-year-olds) and using one versus two doses.

- We have identified a model in the literature that estimates the number of cervical cancer deaths averted from introduction of HPV vaccine.

2: Example: This identified model explores scenarios of HPV vaccine introduction at health facilities among girls aged 9 to 12 years and estimates subsequent cervical cancer deaths averted. Scenarios include coverage at different levels, and various age ranges targeted for vaccination delivery. This model is implemented using data from a neighboring country with similar demography.
Exploring the impact of different HPV coverage levels on deaths averted and target age of vaccination are both relevant to the policy question that we are interested in.
While the scenarios explored policy relevance of the scenarios and the underlying demography are relevant to our setting, we note the difference that this model considers vaccination of only girls, which is different than our policy question. We note that results should be interpreted in light of this difference.

How should modeled results be interpreted and evaluated?

Evaluating models

1. What methodology did the model use, and what assumptions did the model make?

Example: HPV vaccines prevent infection with vaccine-type HPV serotypes, which can progress into cervical lesions. Over time, these cervical lesions can develop into cancer. We are interested in evaluating how the model tracks that process and how people develop cases of cervical cancer, considering the target population, health system and demography.

- We may not know how modeling assumptions were chosen, so we can only assess how realistic they are given your expert knowledge and your specific setting context. If possible, discuss how any assumptions were chosen and implemented with the modeling team.
- The following key areas should be evaluated:
  - What type of model was used, and is it appropriate;
  - Which HPV serotypes are included in vaccine versus modeled;
  - Risk of HPV infection, lesions, and cancer by serotype;
  - Vaccine efficacy by serotype, including cross-protection, and if the model is built such that the vaccine prevents infection (instead of transmission);
  - How the probability of sexual interaction between age groups and sexual behavior; and
  - How long is the time window to accumulate impact; and
  - Any necessary biologic or behavioral considerations (e.g., vaccine efficacy, serotype prevalence, sexual behavior) that differ across girls and boys.

How should modeled results be interpreted and evaluated?

Evaluating models

1. What methodology did the model use, and what assumptions did the model make?

2. What is the quality of data used and its relevance to the setting?

Since our outcome of interest is cervical cancer cases, we need to consider what the source of incidence data. We need to ask the following questions:

- What reporting system was used to capture cases?
- What was considered a case of cervical cancer?
- If there was no direct evidence on cases, what other was used or assumed? What evidence was available for cervical cancer deaths or case fatality ratios (CFR)?

The data available captured cervical cancer deaths and CFR. Therefore, the model needed to compute backwards to get HPV incidence. CFR was assumed from results of a systematic review and meta-analysis of cervical cancer CFR by serotype. Deaths were captured from a cancer registry database. No quality assessment of the death data was performed, so decision makers may need to proceed with caution.

How should modeled results be interpreted and evaluated?

Evaluating models

1. What methodology did the model use, and what assumptions did the model make?
2. What is the quality of data used and its relevance to the setting?
3. What does the output uncertainty represent and what insight is it providing?

We have a deterministic model with no uncertainty included from data sources. The only uncertainty captured in the model outputs are from the model fitting process. This suggests that not much of the uncertainty in the process was captured and results should likely be interpreted cautiously.

A sensitivity analysis was conducted to test whether different estimates of vaccine effectiveness (within a reasonably plausible range) changed the overall prioritization across different scenarios. Another sensitivity analysis was conducted to assess whether adjusting the rate at which cervical lesions develop into cervical cancer among vaccinated persons changed the overall output across different modeled scenarios. In both sensitivity analyses, relative rankings of scenarios by the number of cases averted did not change. Therefore, we can be more confident in our model compared to if these rankings had changed.

How should modeled results be interpreted and evaluated?

Evaluating models

1. What methodology did the model use, and what assumptions did the model make?
2. What is the quality of data used and its relevance to the setting?
3. What does the output uncertainty represent and what insight is it providing?
4. What can be learned about our policy question from interpreting outcomes and scenarios?

How should modeled results be interpreted and evaluated?

Evaluating models

You identified an HPV model published in the literature for a similar demographic and epidemiologic setting to your country.

- Model outputs: what would be the health and economic impact of an HPV vaccination introduction among 9- to 10-year-old and 11- to 12-year-old children and using one versus two doses in your country?
- The model estimates number of cervical cases averted over the next 100 years
- You determine that the model uses an appropriate model structure and assumptions:
  - It is deterministic and does not include uncertainty from input data sources.
  - It fits to cervical cancer incidence data.
  - It assumes vaccination only among girls, which is different than our interest of all children.
  - Additional assumptions also reviewed (contact patterns, sexual behavior, serotype specific transmission, and serotype specific vaccine effectiveness)

All scenarios confidently estimate an increase in cases averted (i.e., a reduction in cases), the confidence interval for the scenario with introduction among children aged 9- to 10-years-old with one dose reaching 80% coverage does not overlapping with the confidence interval for any other scenario after 100 years.

Therefore, you are mildly confident that if your country is able to implement an HPV vaccine introduction among children aged 9- to 10-years-old that reaches 90% coverage you may maximize vaccine impact and minimize future health burden. You will then discuss this with implementers in your country to discuss feasibility of this introduction.

How should modeled results be interpreted and evaluated?

Evaluating the translation process

- **Evaluating the translation process itself (e.g., how well communication was facilitated) and the outcome of this process (including both direct and indirect implications) after the project concludes is critical**
  - Possible outcomes: direct recommendation of policy options, indirect impact policy and decision-making (e.g., identifying data gaps)
  - Outcomes and model results should be evaluated in short-term (i.e., to determine if translated adequately, to review how or what policy options were formed) and long-term (i.e., to re-examine as new evidence becomes available) time horizons
- **Suggested example: workshop with modelers and model users to:**
  - work through the policy recommendations and relate back to the model, data, and operational strengths and weaknesses; and
  - discuss key points of uncertainty and move from the model results to actionable recommendations.

Review process

- 62 reviewers invited
  - 21 from NITAG, 26 from WHO IVB and regional offices, 15 from other institutions (e.g., VIMC, LSHTM, HITAP, CEPI, Gates Foundation)
- 26 invited reviewers provided feedback

- Feedback collected via Google Form (9 respondents) and directly via document comments (over 300 comments made)

Themes of reviewer feedback

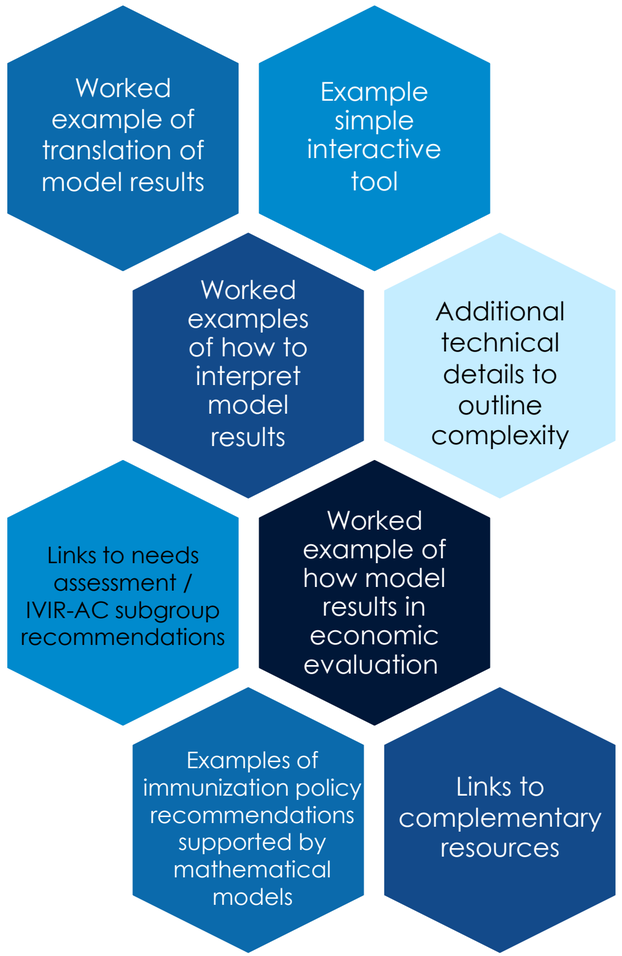
1. More useful / expanded glossary
2. Content with too much detail to move to supplementary material
3. Additional examples to highlight
4. Restructuring of content / chapters for better flow and readability

Remaining key considerations

1. How best to structure of document from decision-maker perspective?
   - How best to separate model development from model evaluation and/or use?
     - And how detailed should description of modeling process be in main document (versus appendix)?
   - How best to separate model evaluation regarding model itself (e.g., assumptions, structure) versus modeled results (e.g., interpreting scenarios)?

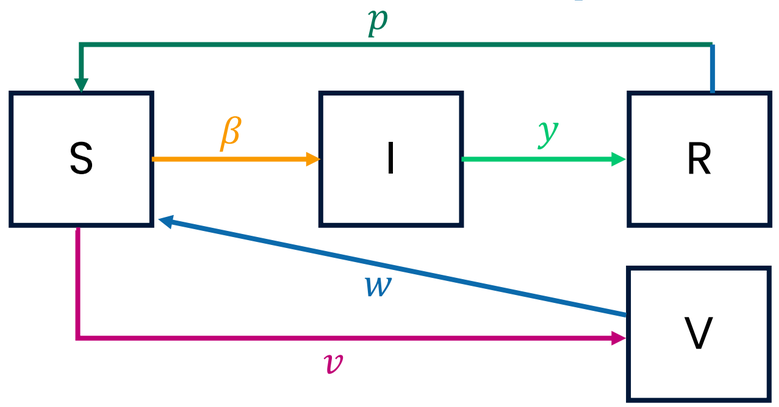
2. How best to balance providing gold standard guidance versus guidance tailored to local realities?
   - E.g., Co-creation of models with modelers and decision-makers versus decision-makers appraising existing modeling studies

Online Web Appendix



Example simple SIR-type model with vaccination, including demonstrated through with dialogue boxes, equations, graphical and tabular outputs, assumptions, etc.

Example SIR model



Rate of vaccination: should be informed by empiric data or assumptions about vaccination coverage

Rate of vaccine-induced immunity waning: should be informed by empiric data or assumptions about duration of vaccine protection

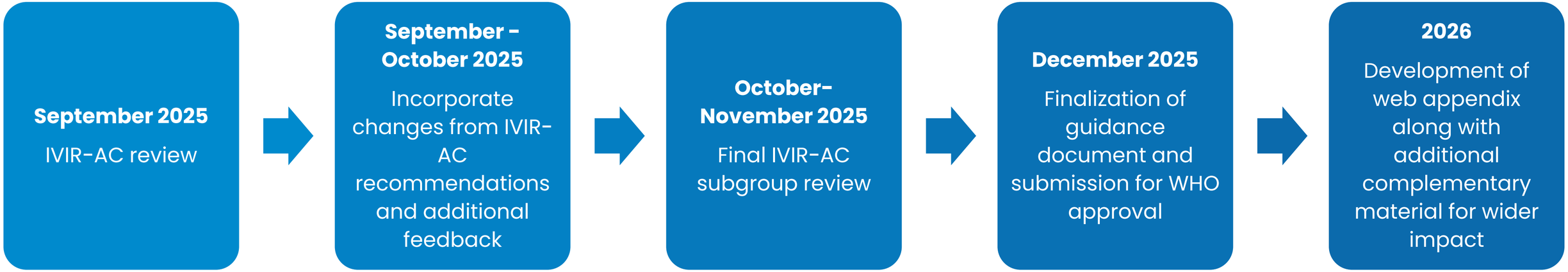
$$\frac{dS}{dt} = -\beta SI - vS + wV + pR$$

$$\frac{dI}{dt} = \beta SI - yI$$

$$\frac{dR}{dt} = yI - pR$$

$$\frac{dV}{dt} = vS - wV$$

Ongoing next steps & possible future directions



Opportunities for wider impact:

- To support a greater uptake of the guidance to result in an increased global consumption of modeled evidence in the future, an accompanying training toolkit (i.e., curriculum built on principles outlined in guidance document) could be developed to be used to train users of this guidance.
- Leveraging RITAG/NITAG engagements to deliver training on guidance document via workshops for members

Questions to the IVIR-AC (Sep 2025)

- As the document is intended to be a resource to decision-makers, is the content, perspective, and tone of the writing appropriate (i.e., not too technical, while still being informative)?
- Given the document's intended perspective and audience, would the technical chapter on modeling process (currently Chapter 3) be better suited as a separate online resource? If it should remain in the main document, how might we restructure it to better address the needs of decision makers?
- Is the current format of the document, including plans for an online appendix, appropriate?
- How can individual resources (i.e., guidance document, online web appendix, executive summary) as part of the overall package of material be most synergistic with one another?

Thank you

Some of the documents related to this session are currently confidential and not available for public access.

World Health Organization

Session 6: WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS)

Multi-model comparison of typhoid conjugate vaccine adequate schedules (MMC-TAS)

Summary of documents for IVIR-AC (in order of priority)

1. ***01_full_model_results.pdf:*** Slides showing figures summarizing all of the results of the four models for the predicted impact and cost-effectiveness of TCV delivery strategies.

2. ***02_ivirac_recommendations_response_15Aug25.docx*****:** Word document with the recommendations from IVIR-AC following the April special session (in which preliminary results were presented) and our responses to the previous recommendations.

3. ***03_SAGEwg_May2025.pdf:*** Preliminary results of the model comparison presented to the WHO SAGE typhoid working group in May 2025.

4. ***04_TCV_waning_ZP_June2025_DIC.pdf:*** Slides summarizing the statistical models used to estimate vaccine efficacy parameters for the "fast" (Bangladesh) and "slow" (Malawi) waning scenarios.

5. ***05_MMC-TAS_model_descriptions.pdf:*** Short descriptions of each of the four models included in the multi-model comparison. (These were previously shared for the February 2025 meeting.)

WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS)

Ginny Pitzer (on behalf of the modeling teams)

WHO IVIR-AC meeting

3 September 2025

Yale SCHOOL OF PUBLIC HEALTH

Vaccine Impact Results

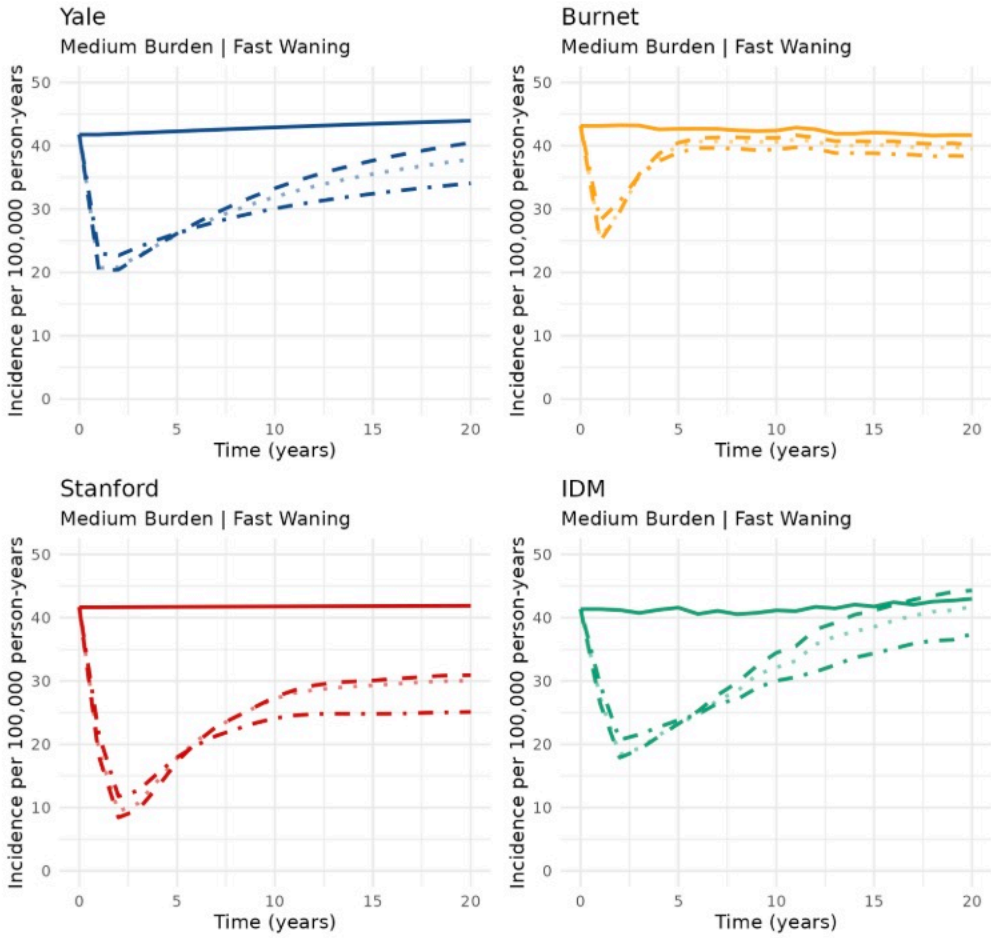
Time Series*

20 year time horizon

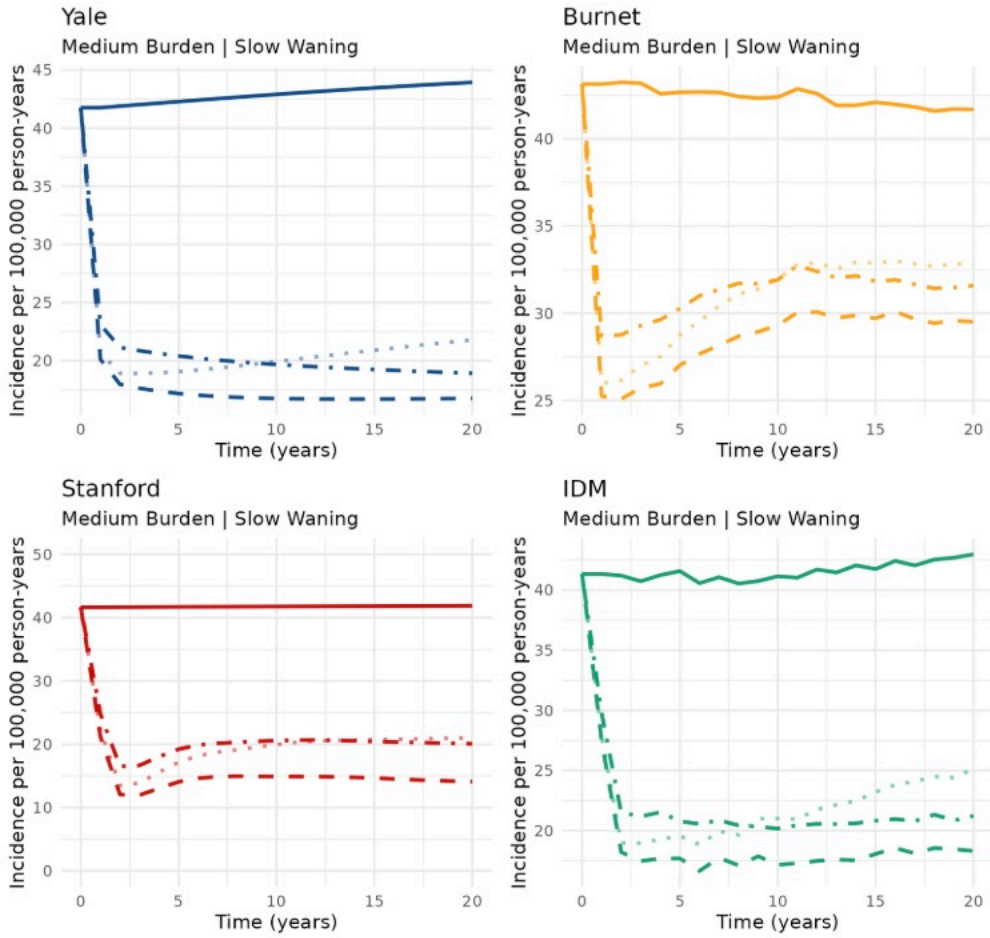
*Results do not differ by geographical region

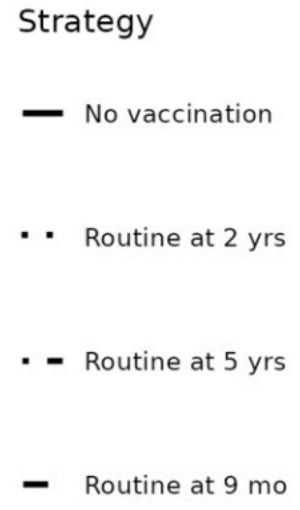
Routine strategies - Medium burden

Slow waning



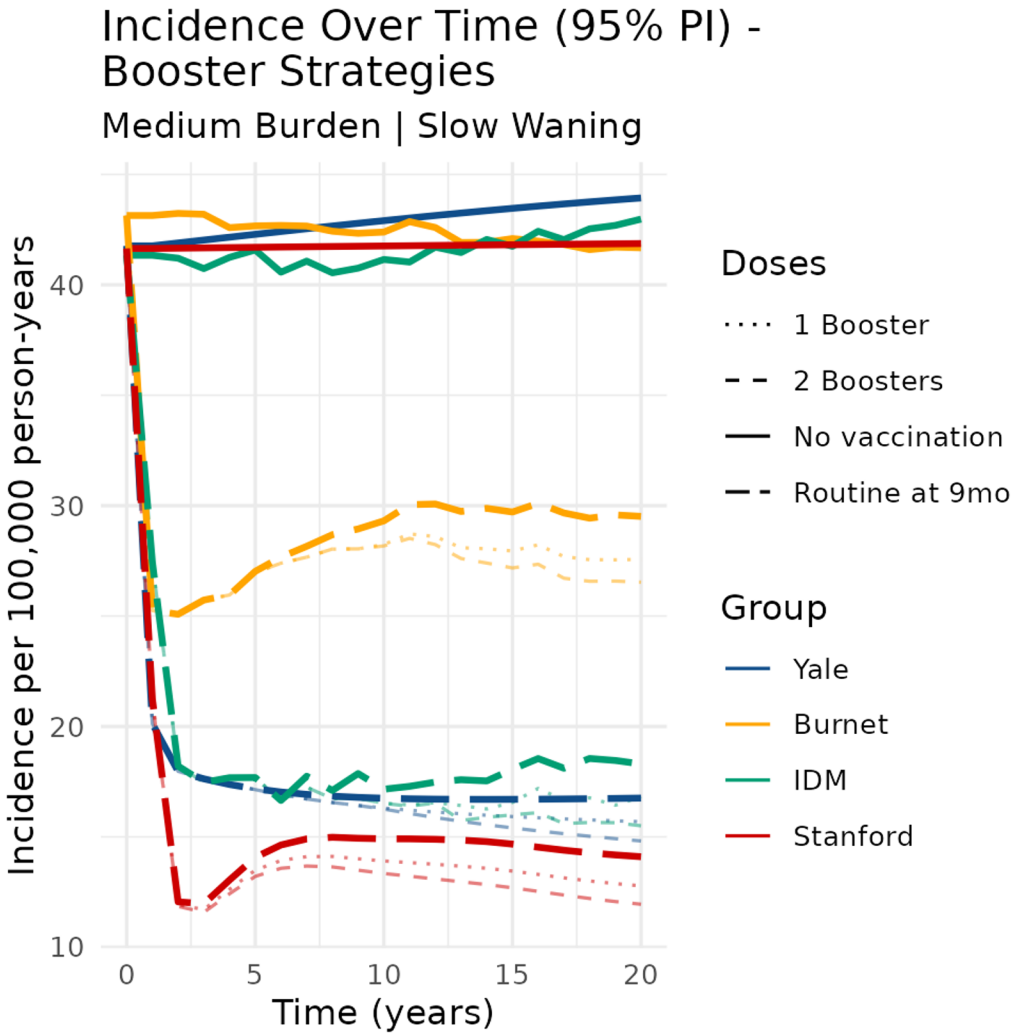
Fast waning



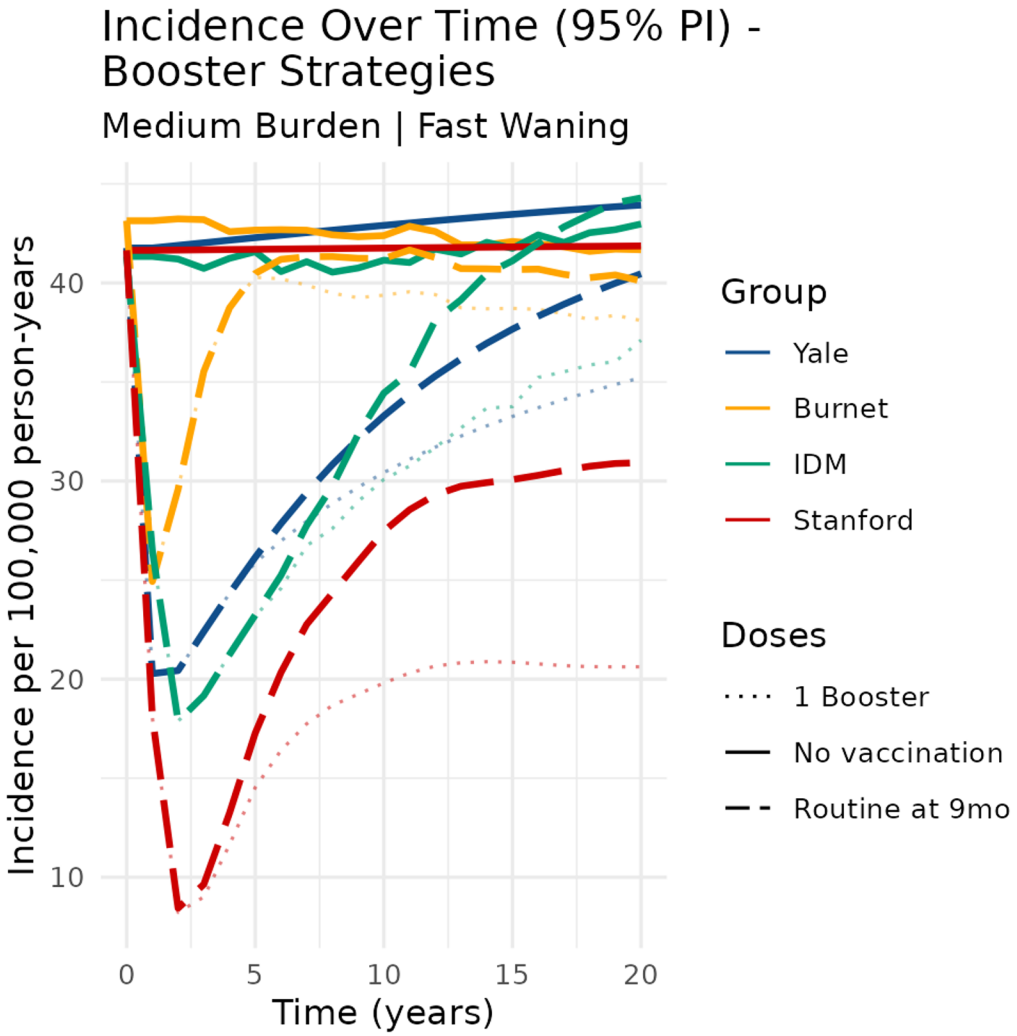


Booster strategies - Medium burden

Slow waning

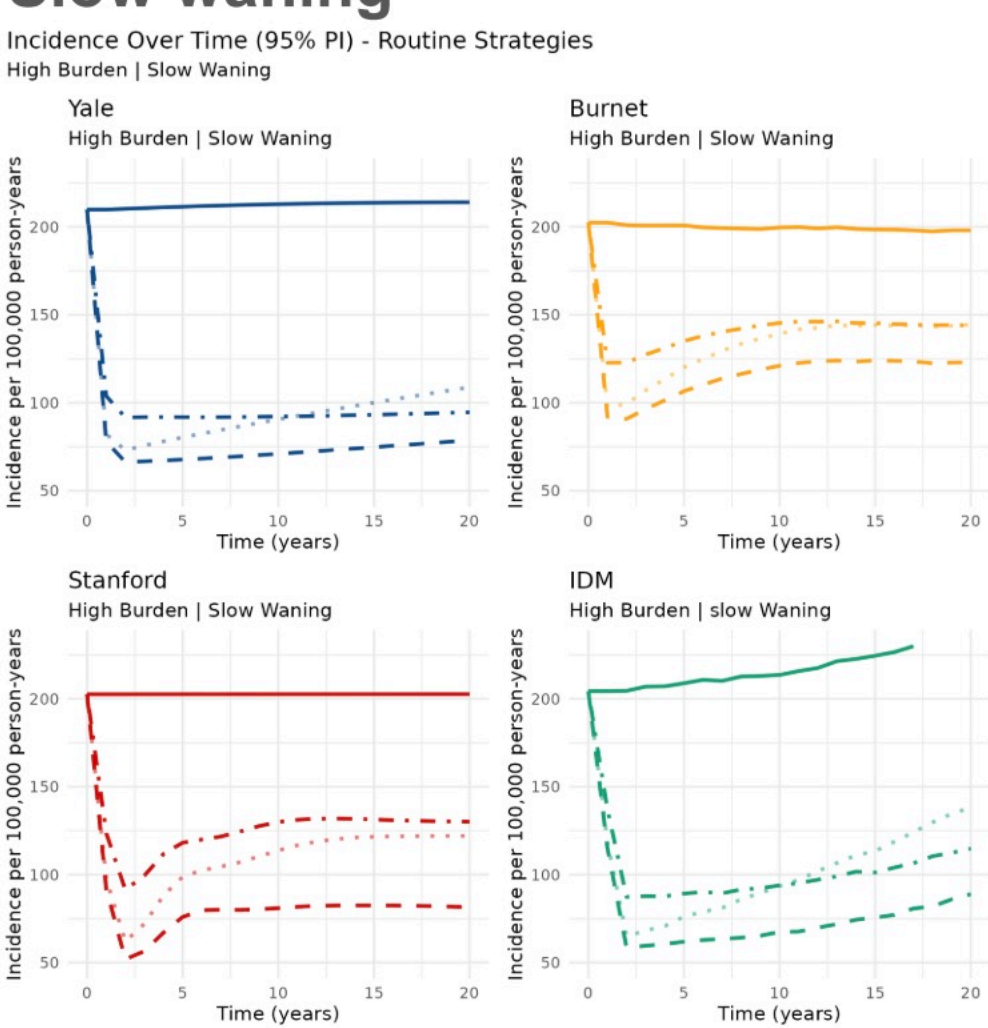


Fast waning

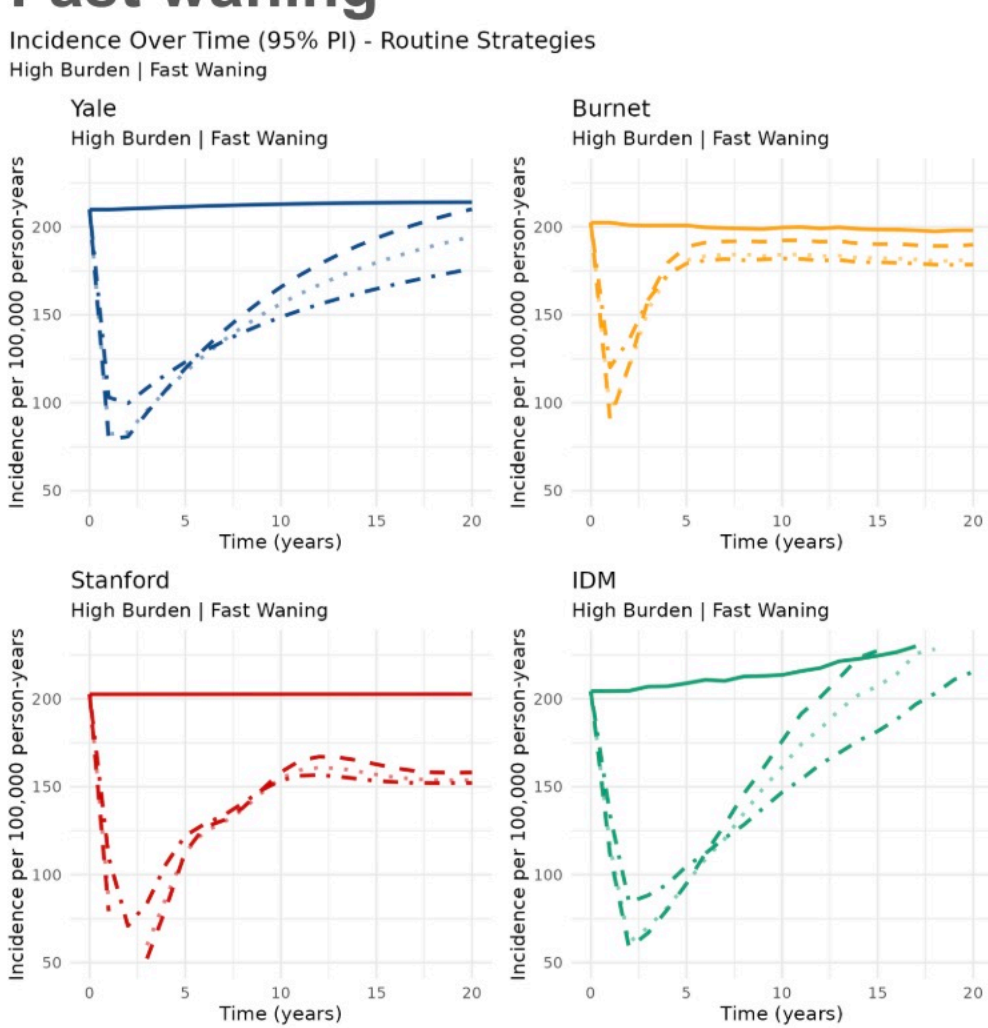


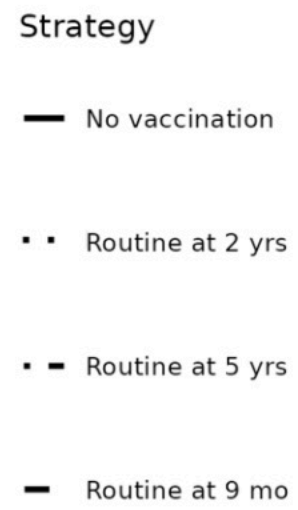
Routine strategies - High burden

Slow waning



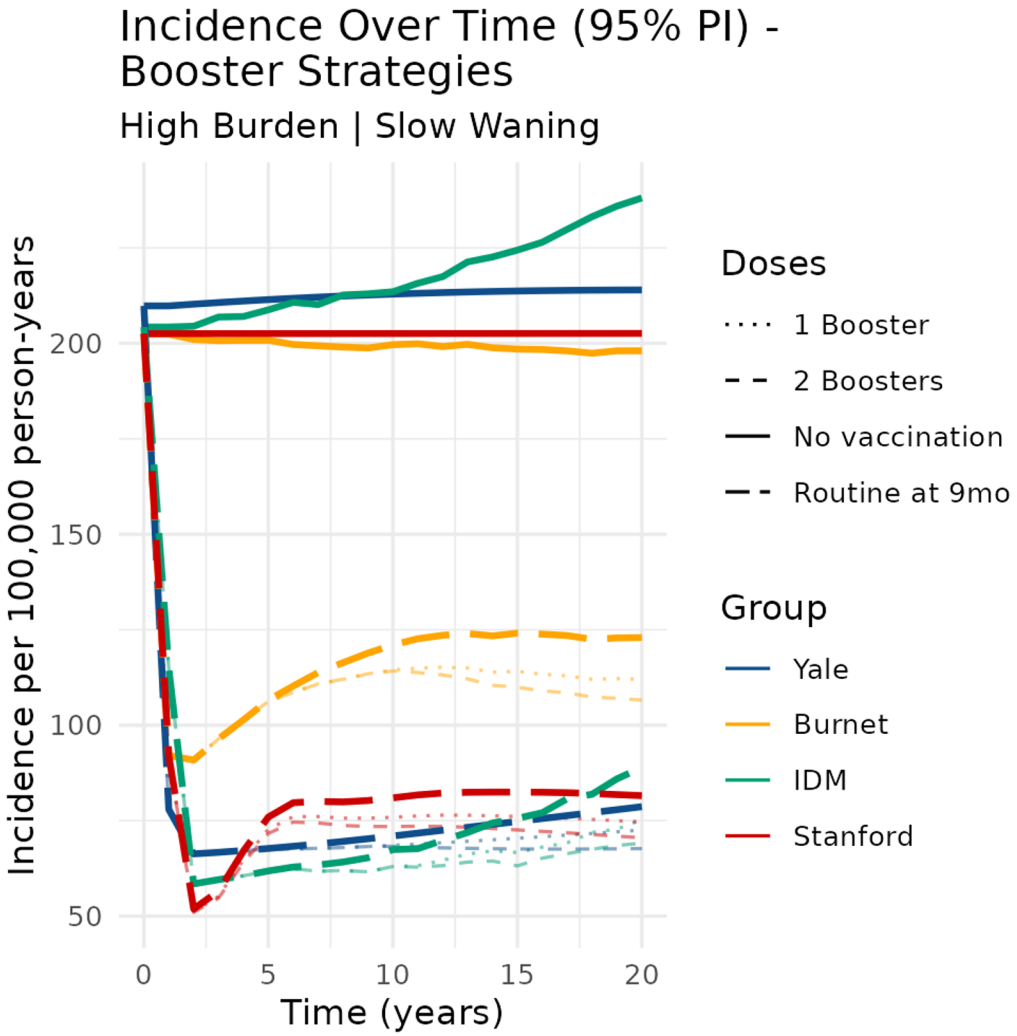
Fast waning



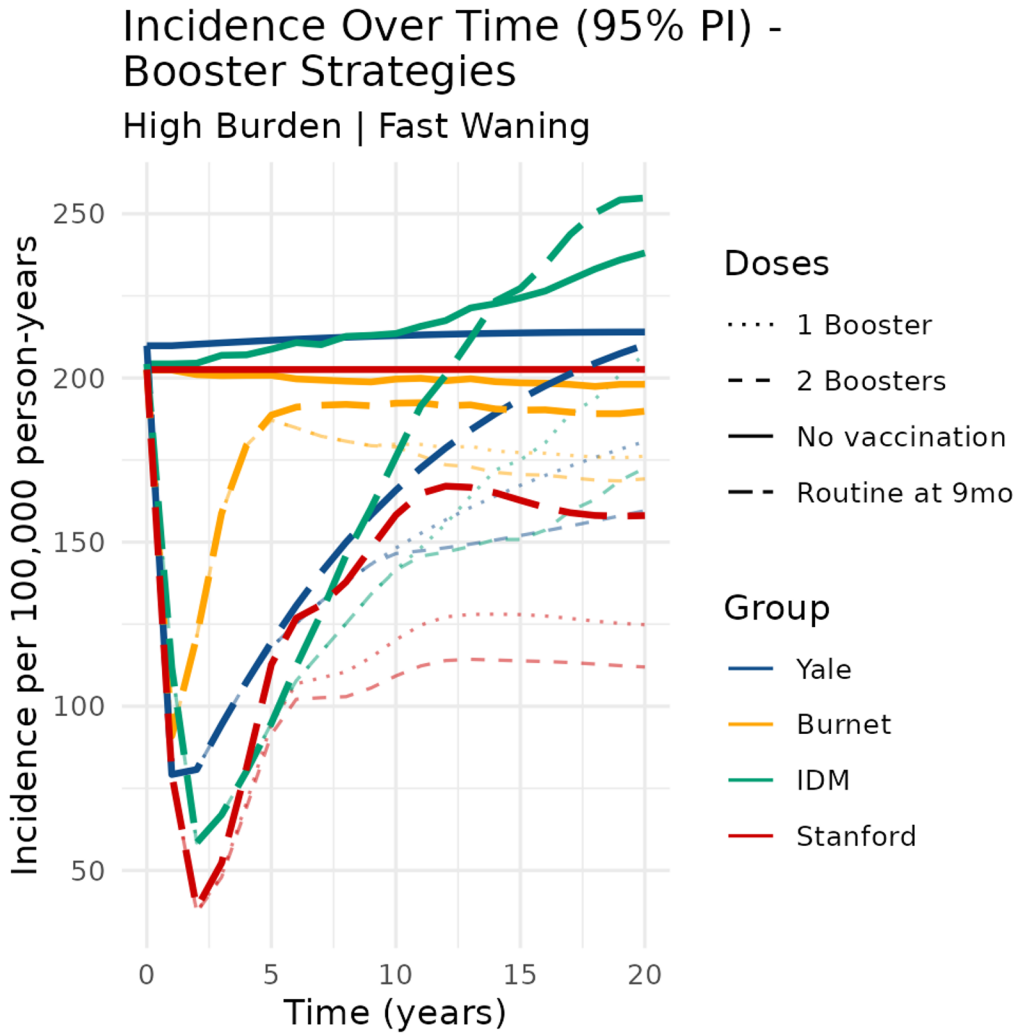


Booster strategies - High burden

Slow waning

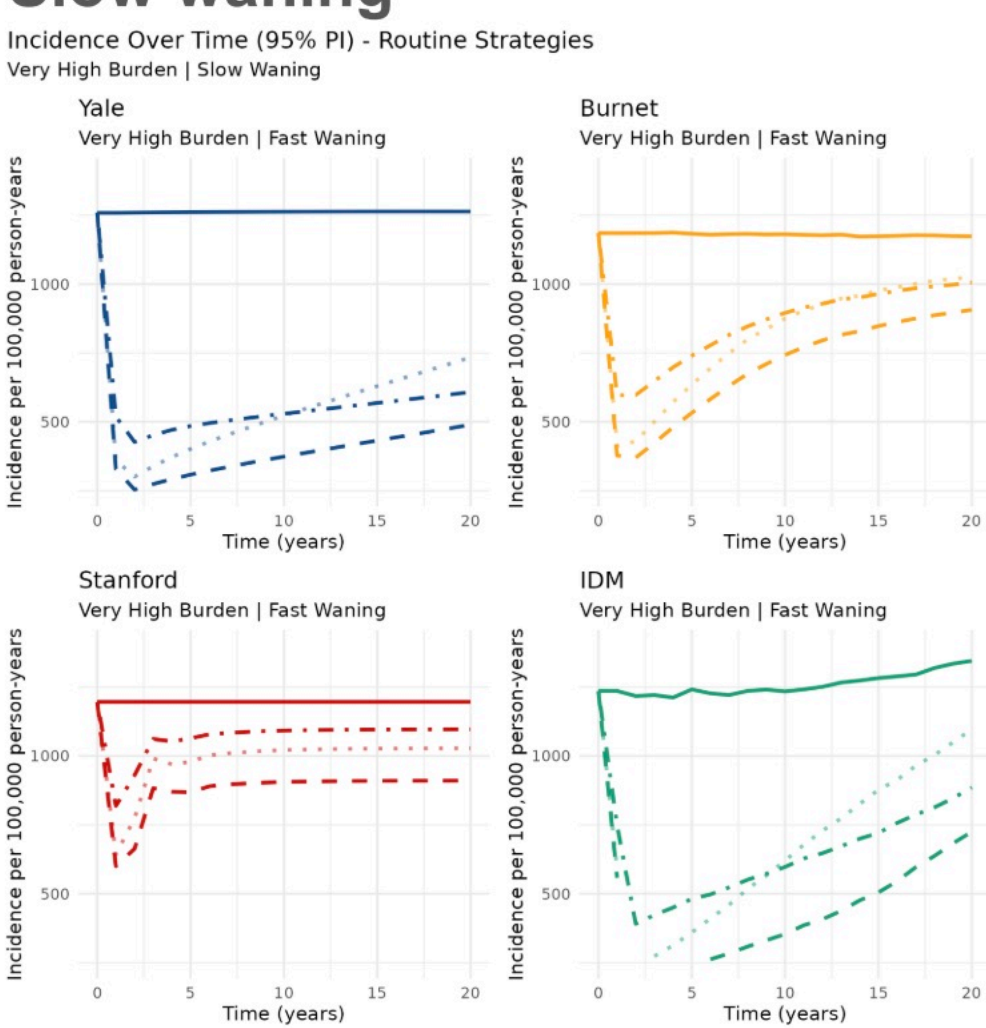


Fast waning

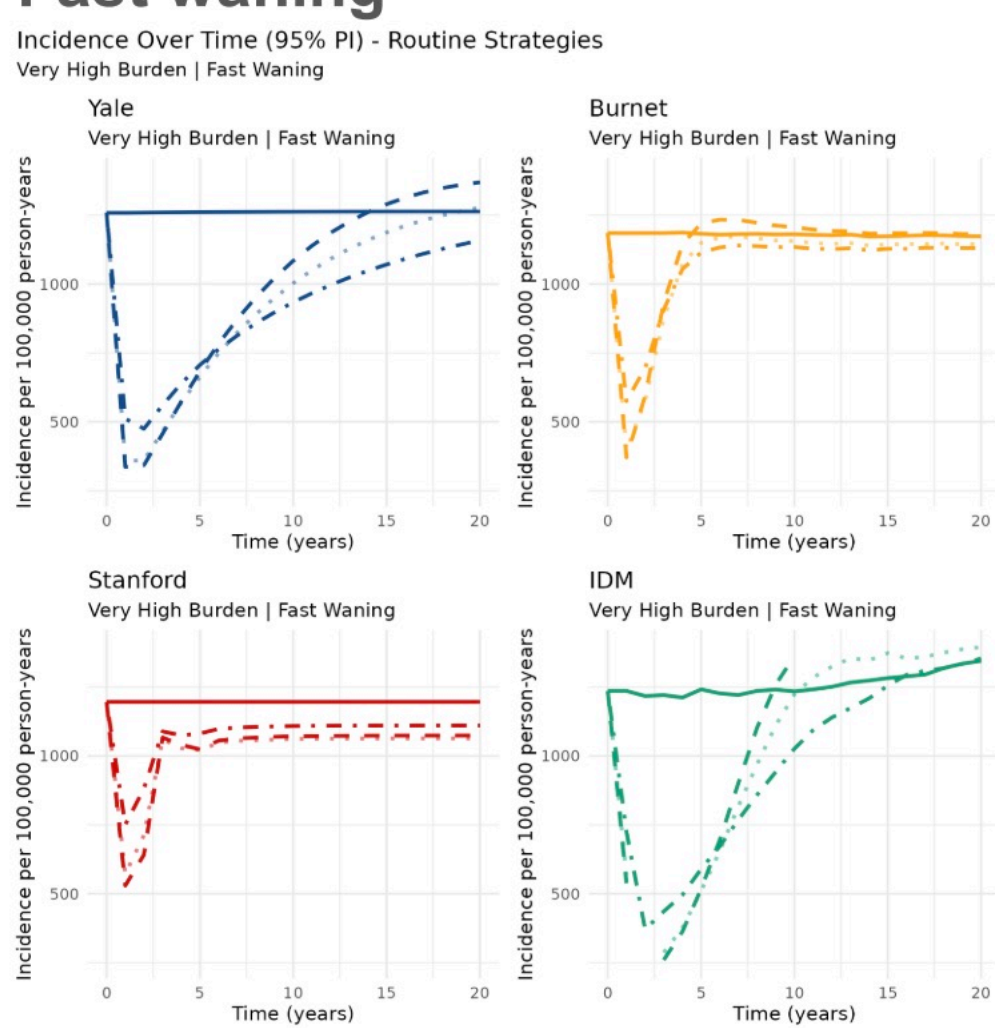


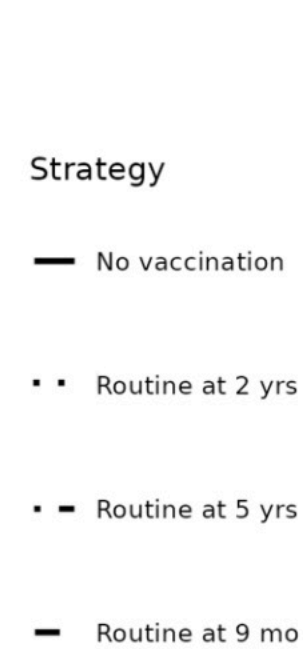
Routine strategies – Very high burden

Slow waning



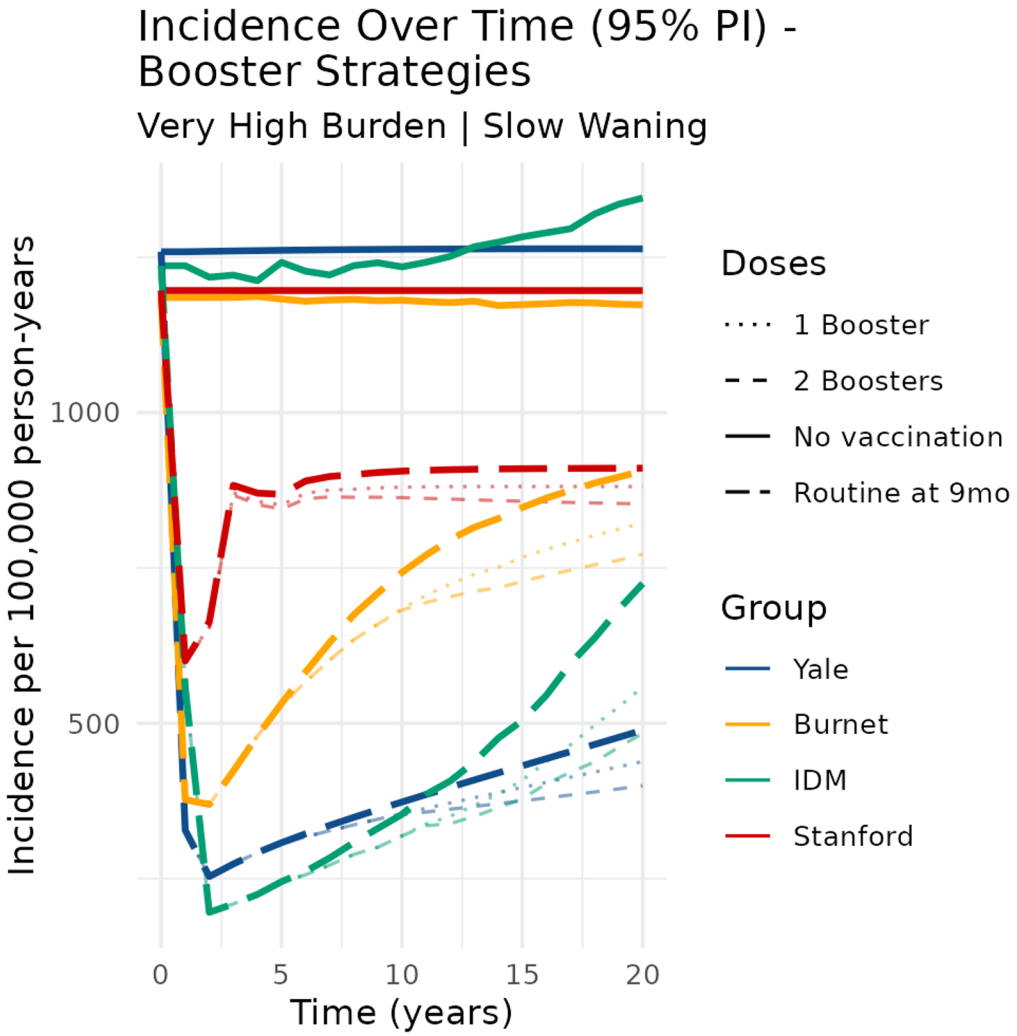
Fast waning



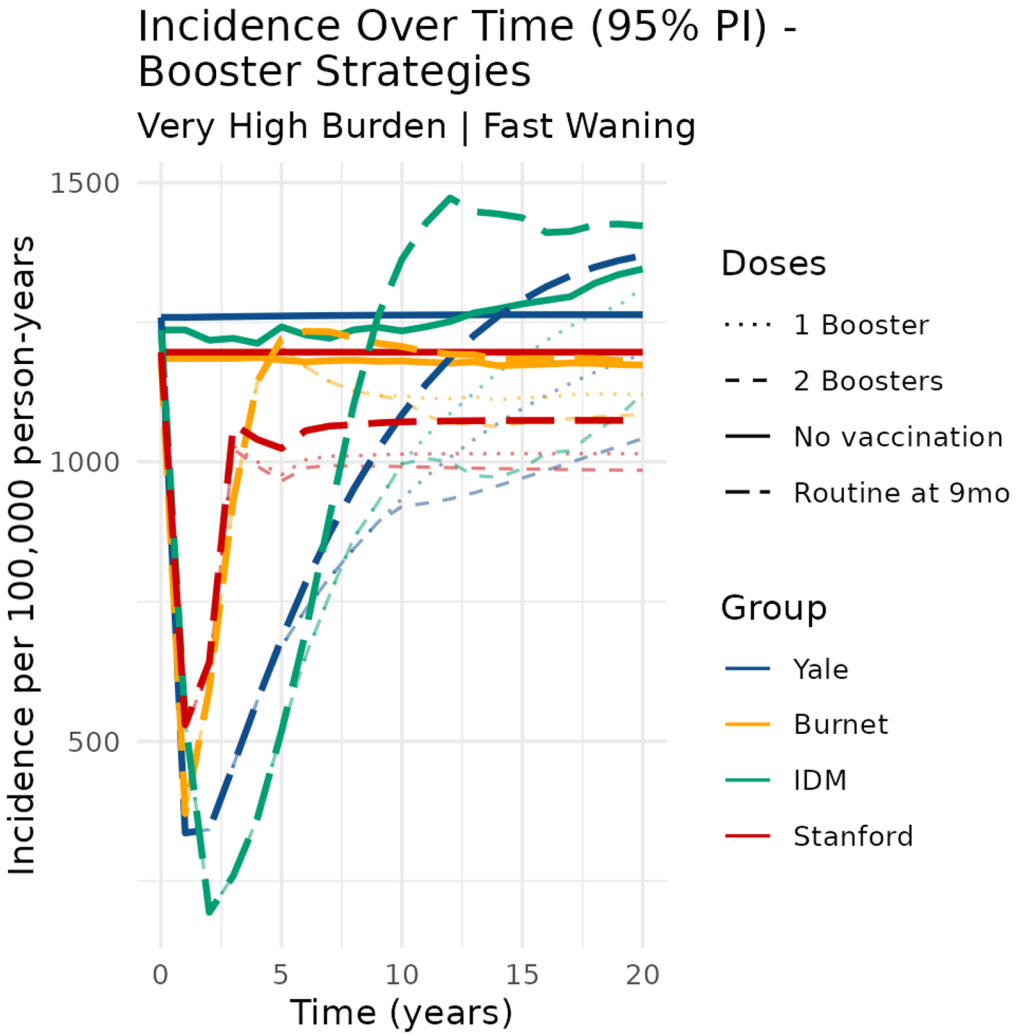


Booster strategies – Very high burden

Slow waning



Fast waning



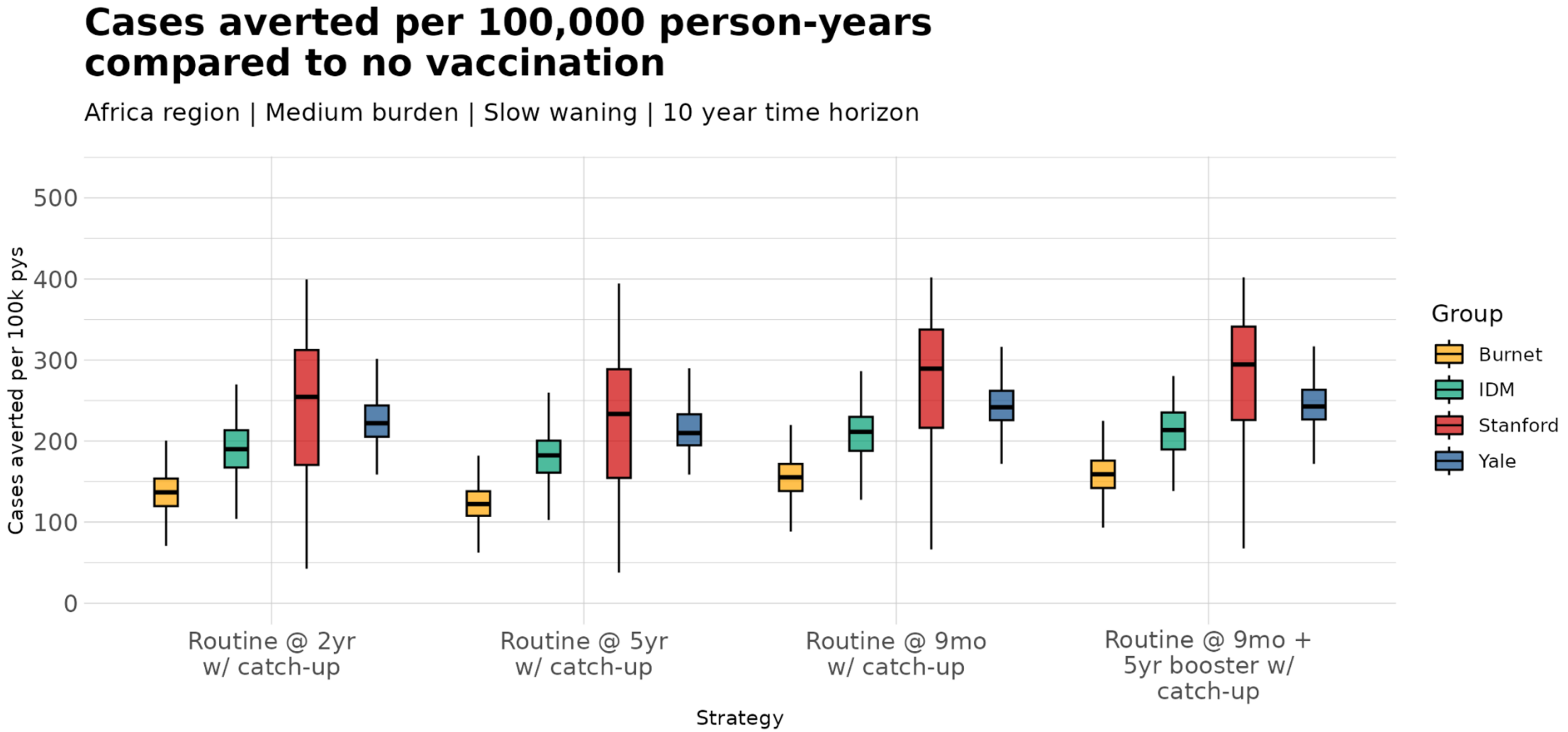
Vaccine Impact Results

Cases*

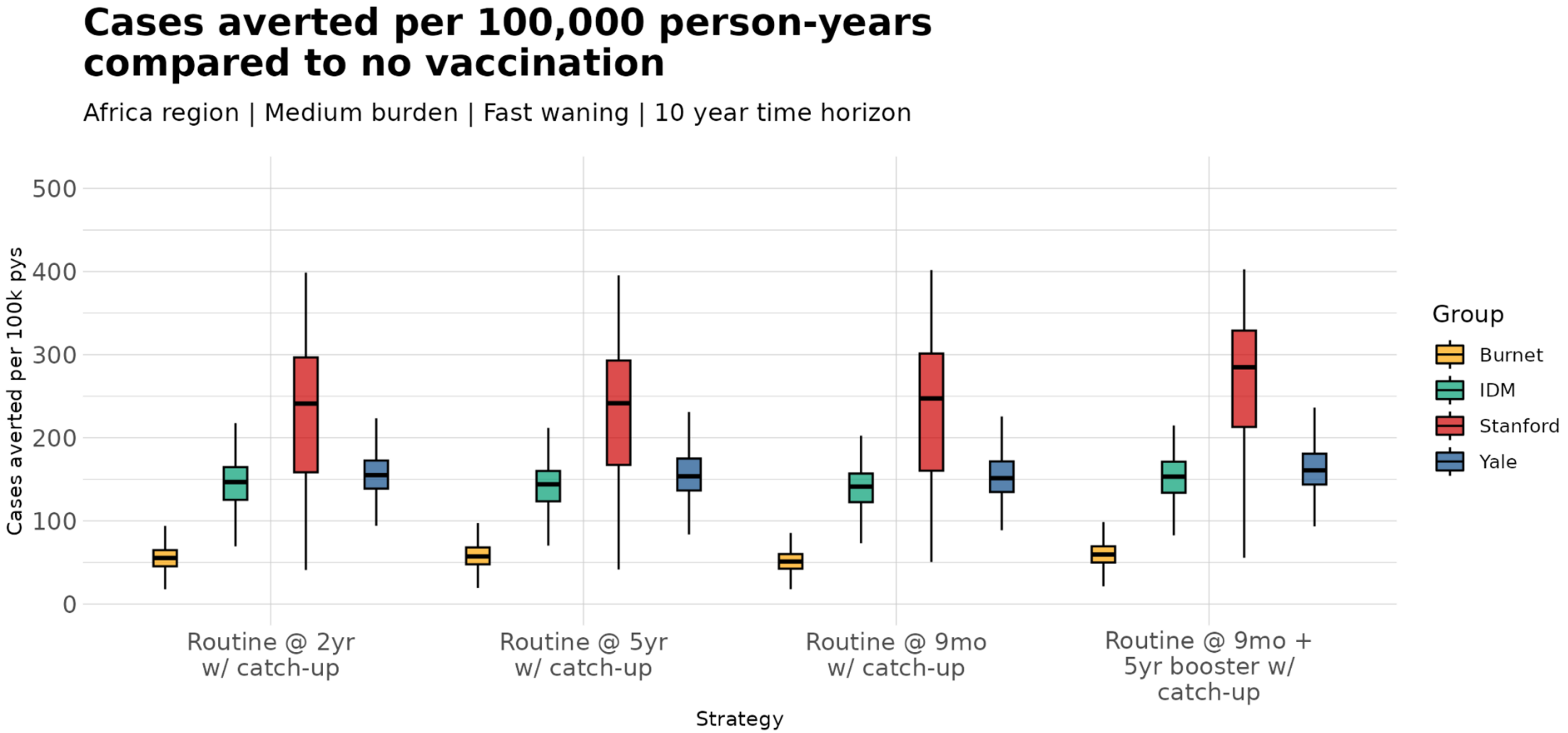
10 year time horizon

*Results do not differ by geographical region

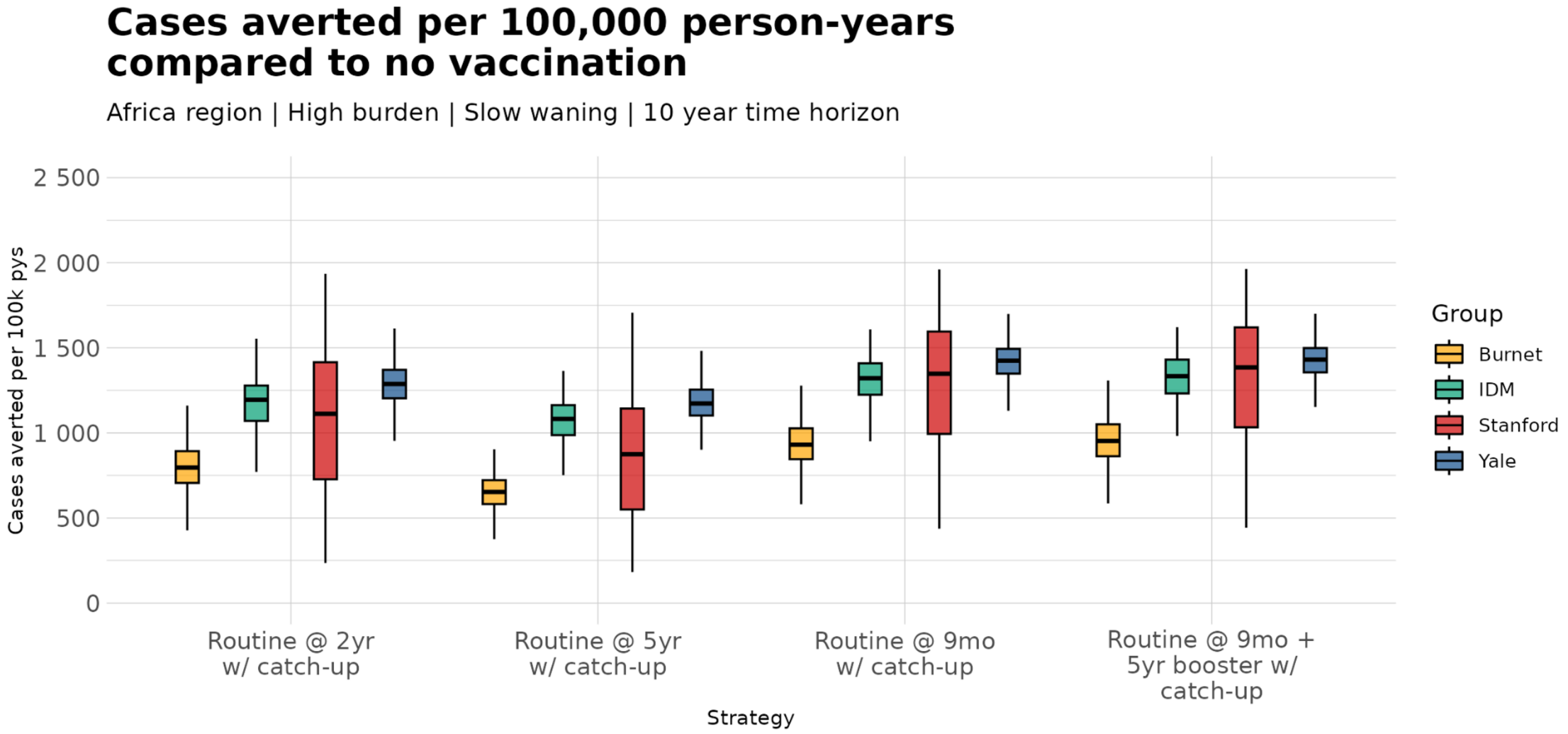
Cases averted - Slow waning, medium burden



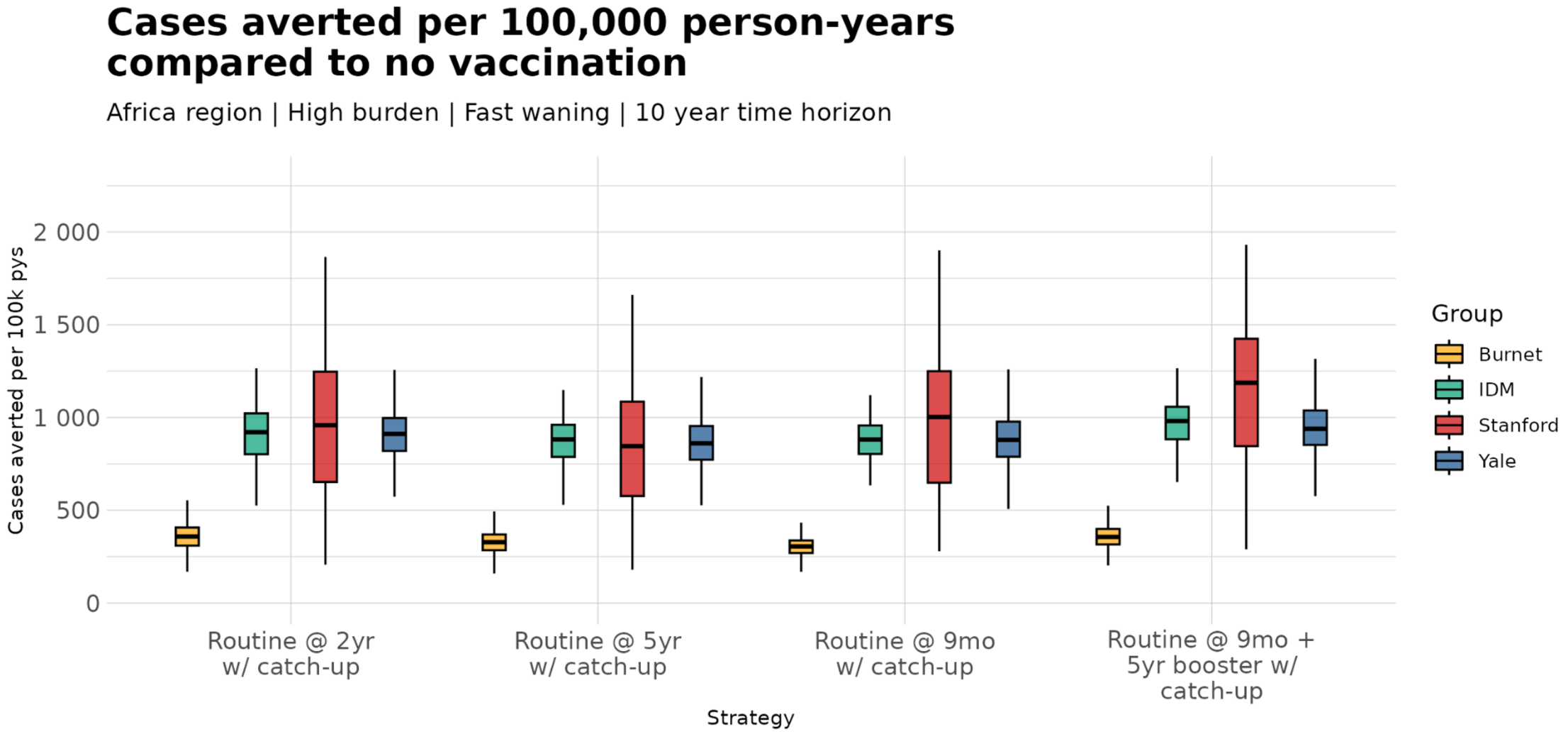
Cases averted - Fast waning, medium burden



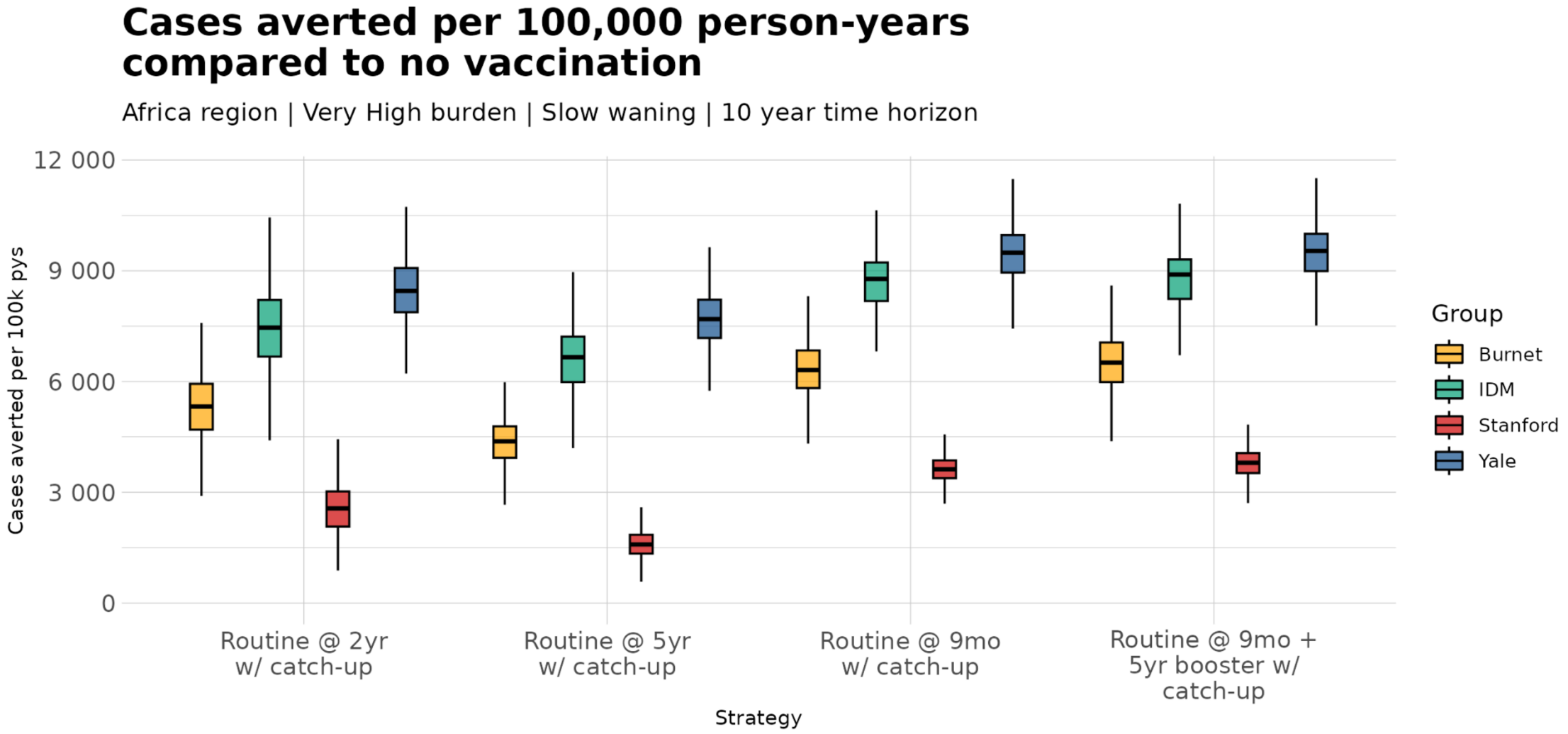
Cases averted - Slow waning, high burden



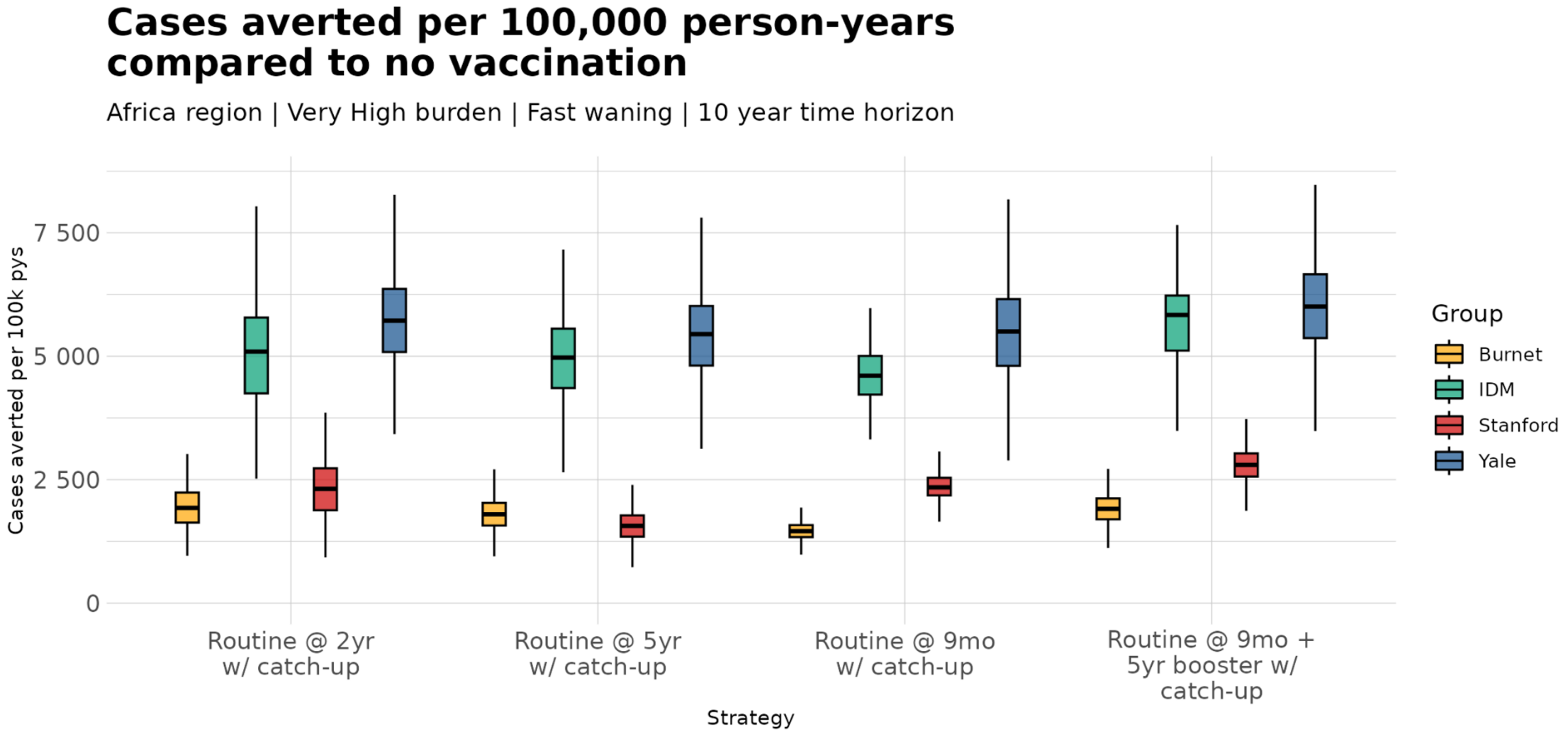
Cases averted - Fast waning, high burden



Cases averted - Slow waning, very high burden



Cases averted - Fast waning, very high burden



Vaccine Impact Results

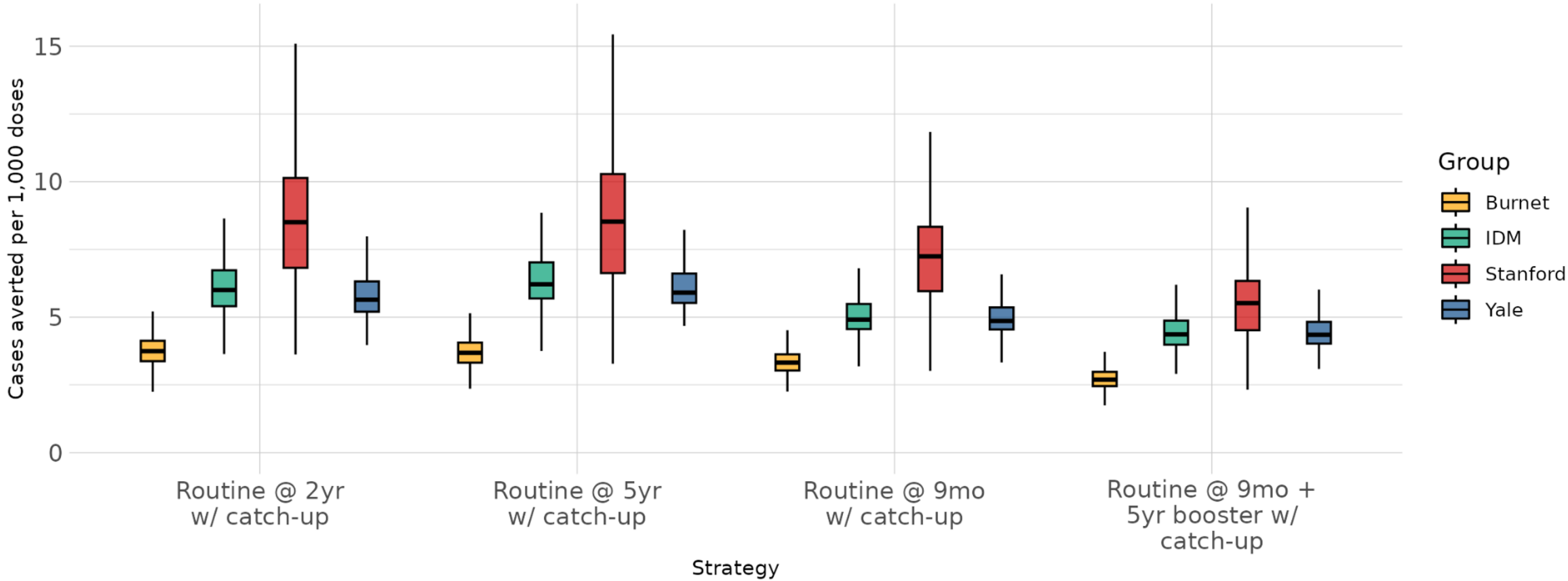
Cases averted per 1,000 doses*

10 year time horizon

*Results do not differ by geographical region

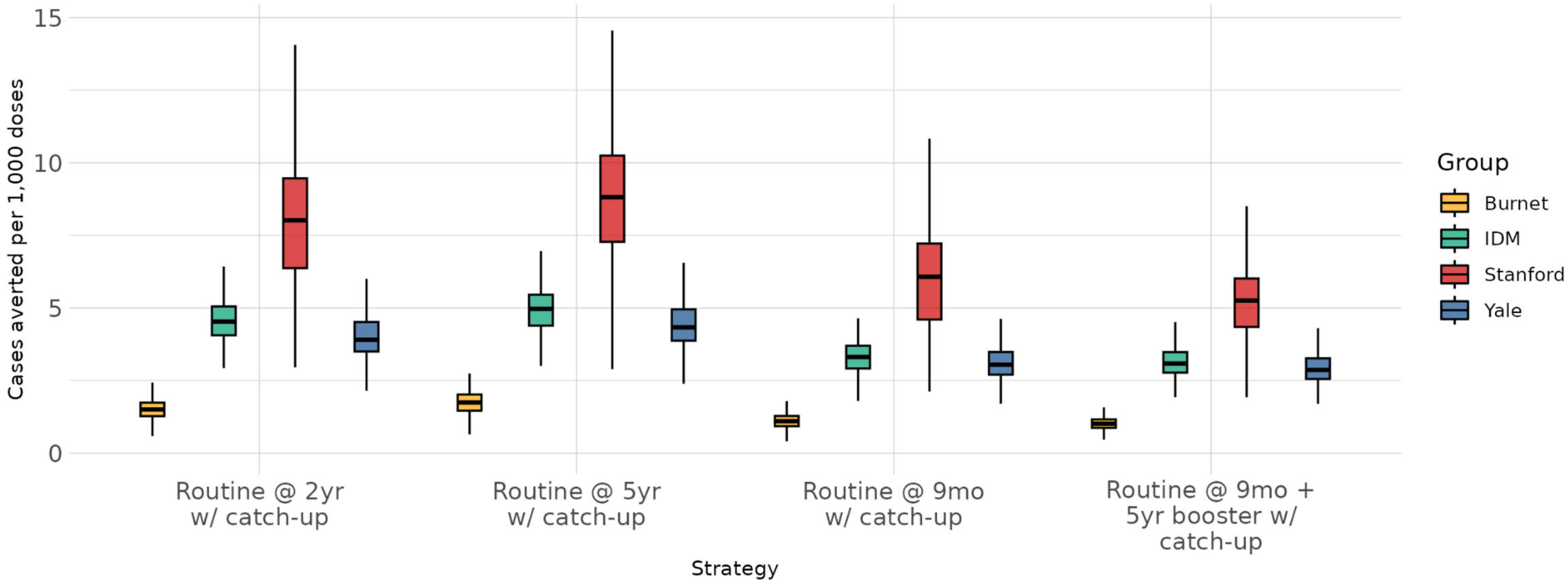
Cases averted per 1,000 doses compared to no vaccination

Africa region | Medium burden | Slow waning | 10 year time horizon



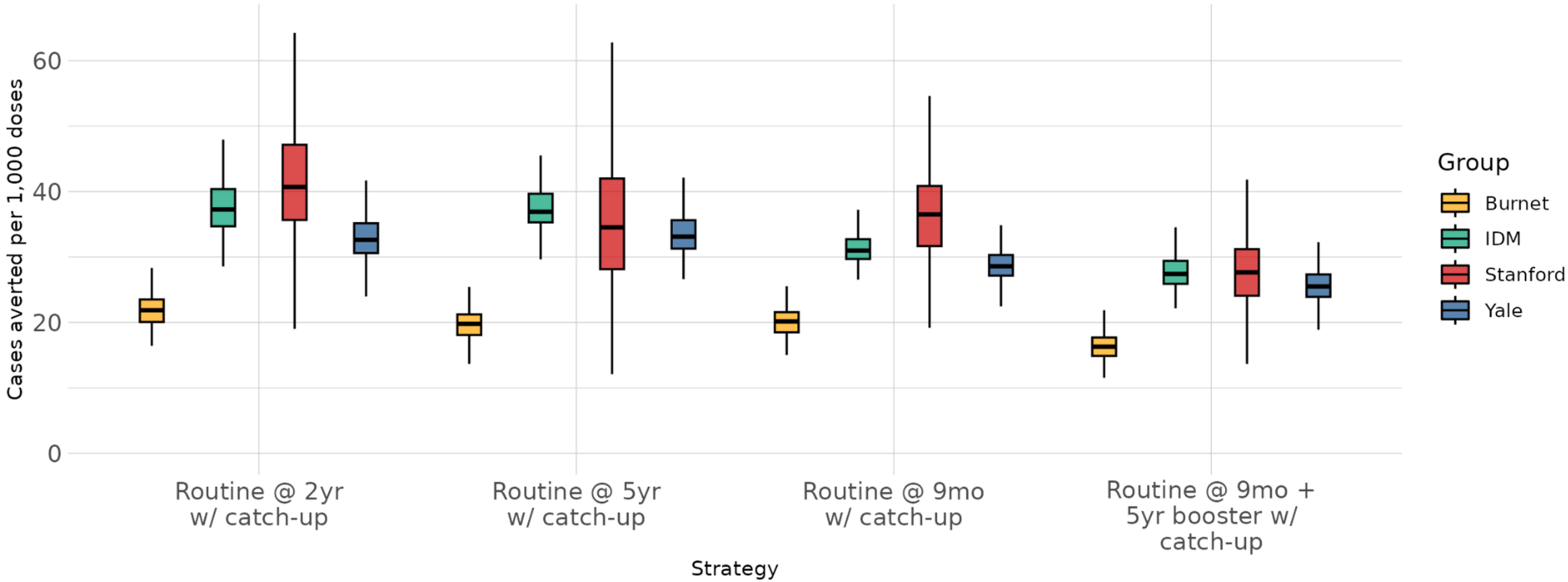
Cases averted per 1,000 doses compared to no vaccination

Africa region | Medium burden | Fast waning | 10 year time horizon



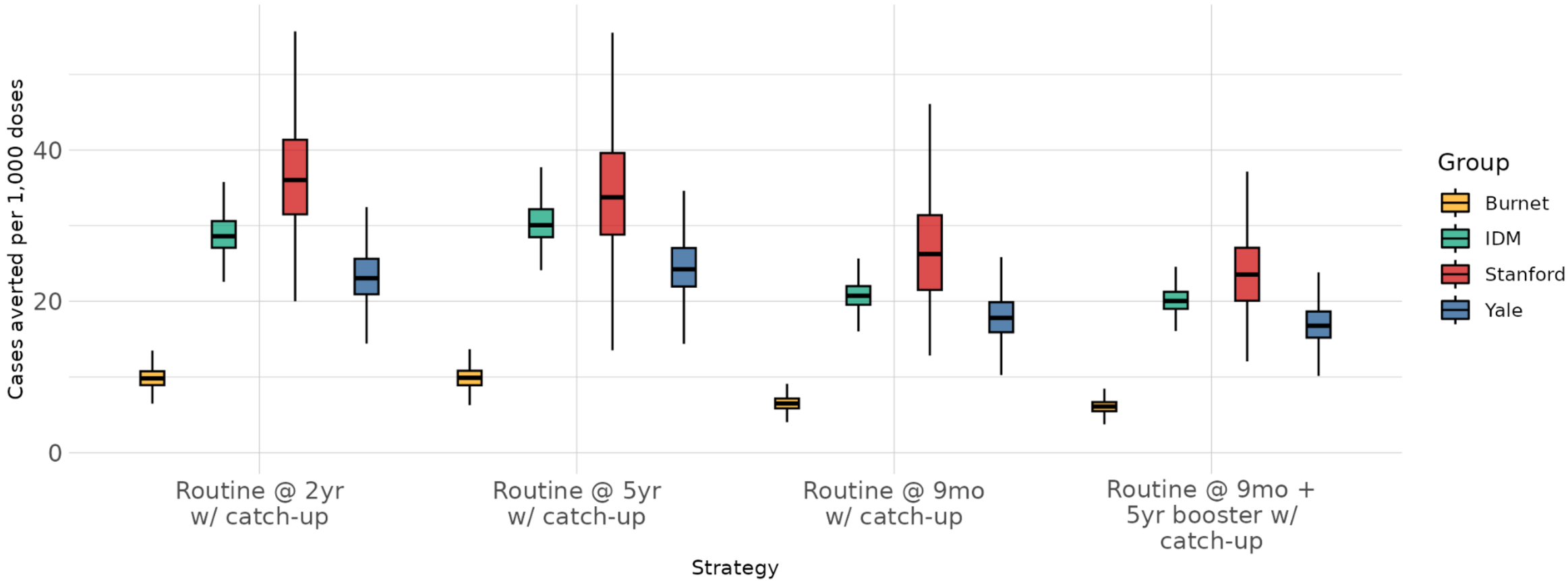
Cases averted per 1,000 doses compared to no vaccination

Africa region | High burden | Slow waning | 10 year time horizon



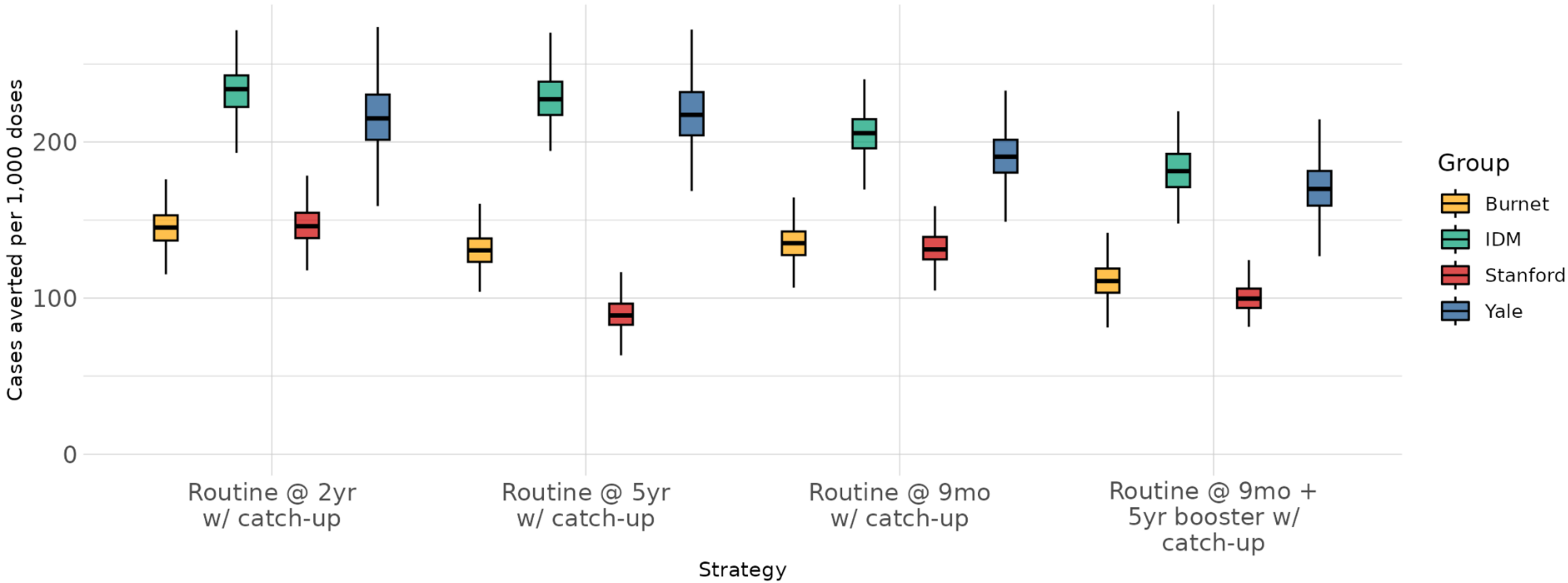
Cases averted per 1,000 doses compared to no vaccination

Africa region | High burden | Fast waning | 10 year time horizon



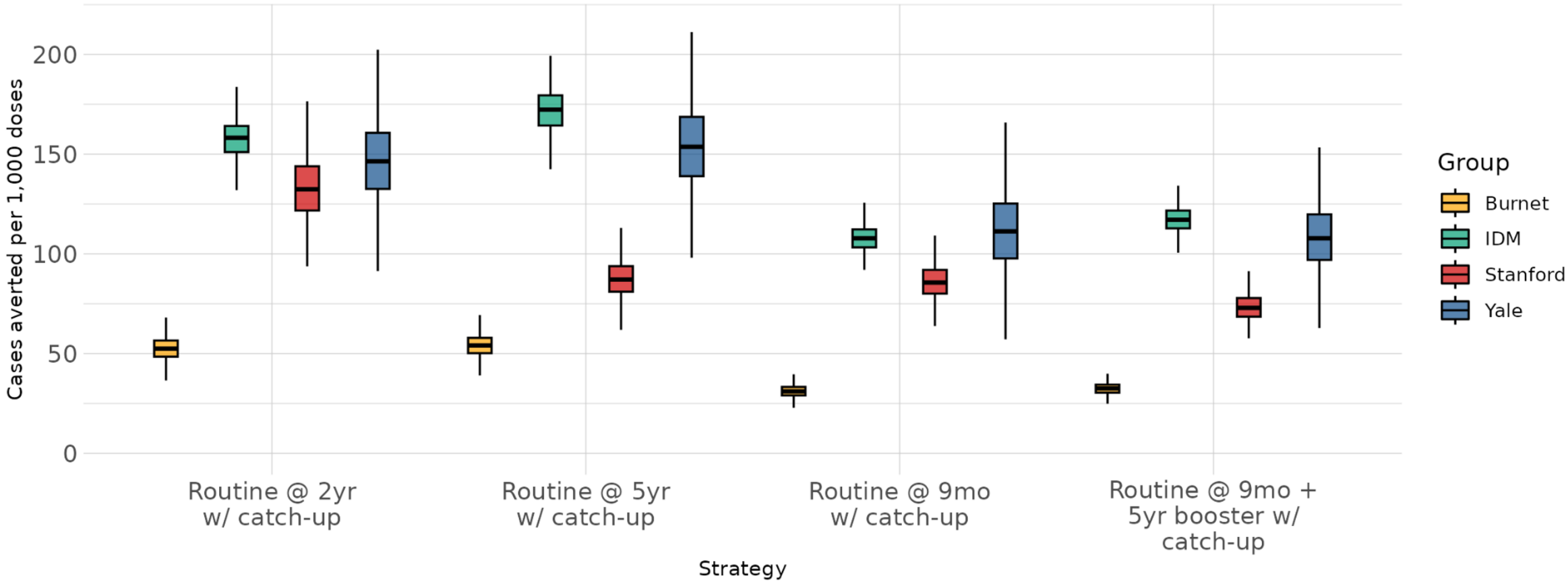
Cases averted per 1,000 doses compared to no vaccination

Africa region | Very High burden | Slow waning | 10 year time horizon



Cases averted per 1,000 doses compared to no vaccination

Africa region | Very High burden | Fast waning | 10 year time horizon



Vaccine Impact Results

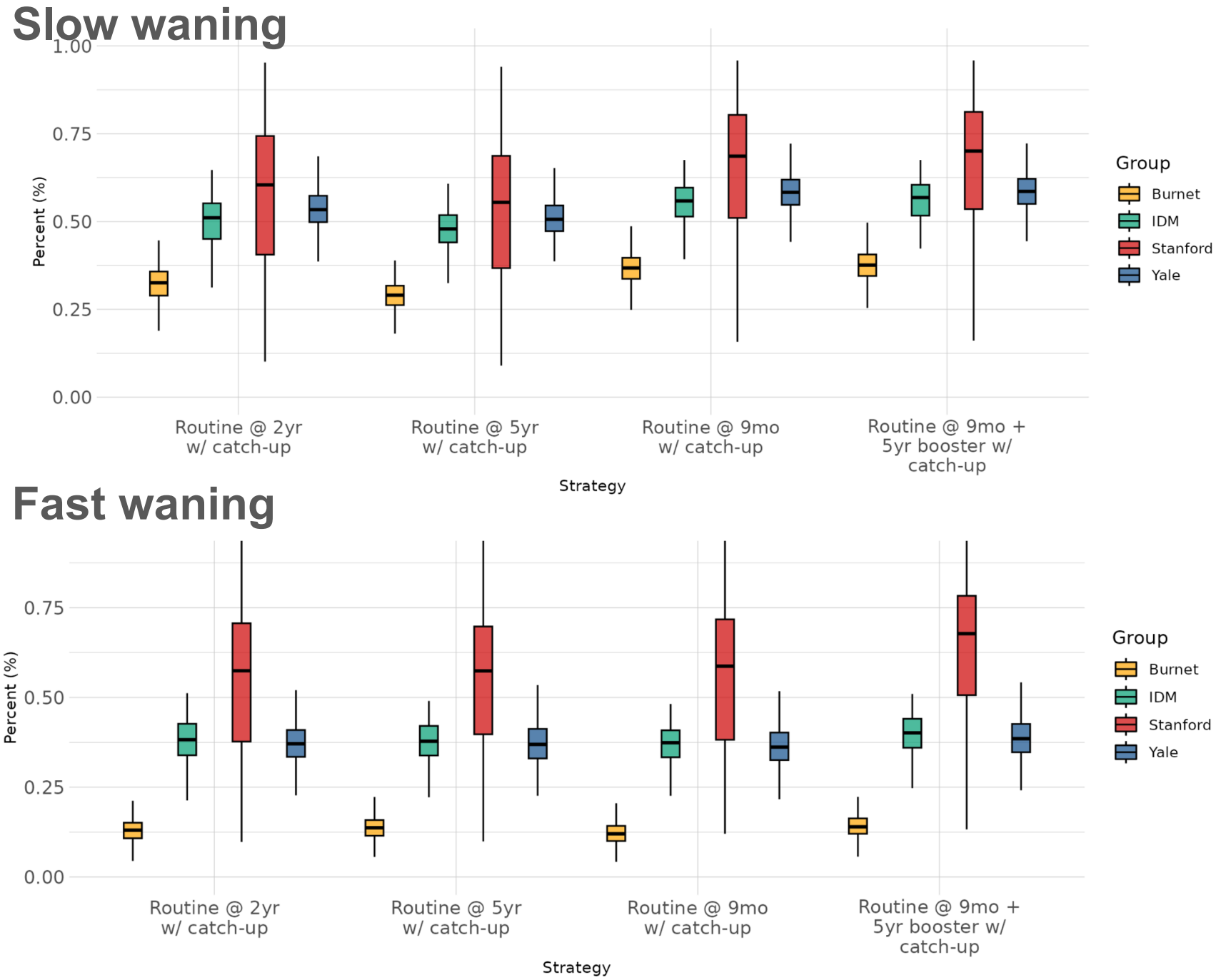
Percent of cases averted*

10 year time horizon

*Results do not differ by geographical region

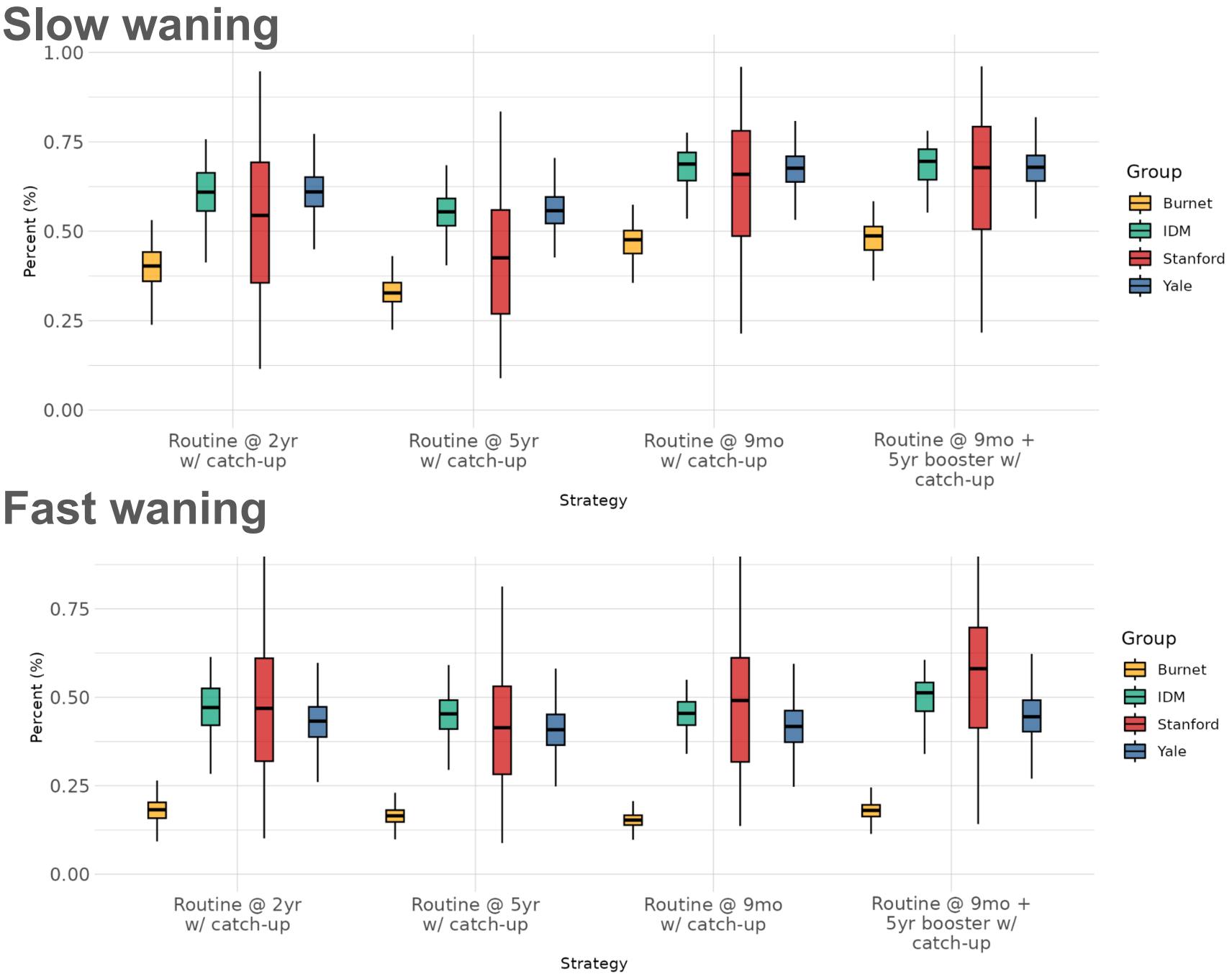
Percent of cases averted:

Medium burden



Percent of cases averted:

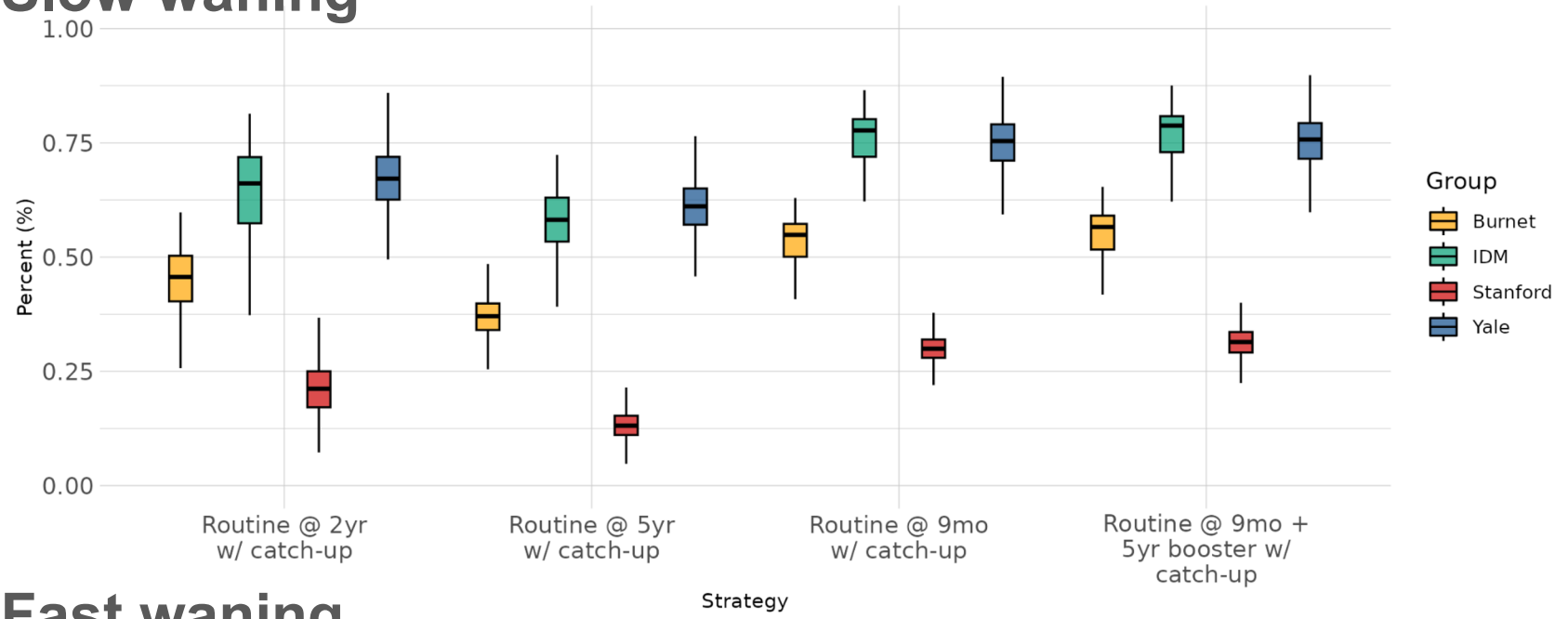
High burden



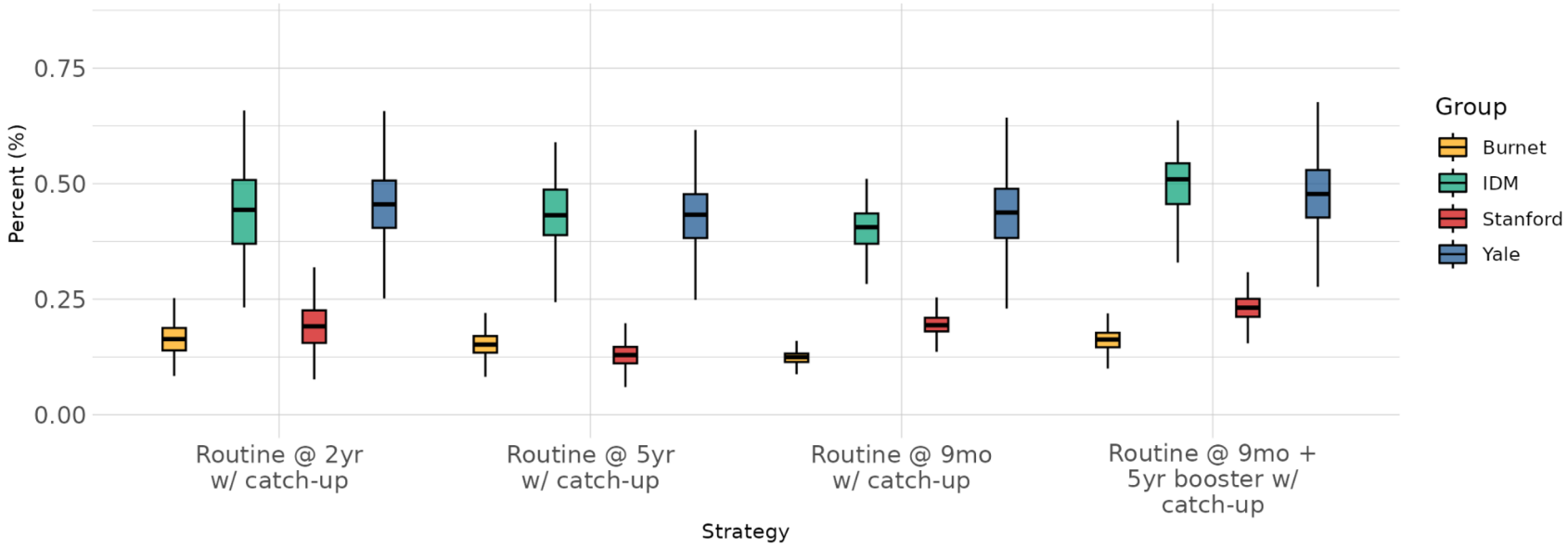
Percent of cases averted:

Very high burden

Slow waning



Fast waning



CEA parameters: Healthcare seeking & severity

Parameters	Africa	Asia	source
Healthcare seeking parameters			
Probability of seeking care	0.58 (0.42, 0.77)		Bilcke et al (2019)
Probability of inpatient treatment	0.24 (0.08, 0.53)	0.10 (0.03, 0.28)	Marks et al (2024), Longley et al (2020)
Probability of outpatient treatment	Complement of the above		Marks et al (2024), Longley et al (2020)
Probability of complications	0.32 (0.20, 0.47)	0.02 (0.001, 0.36)	Marks et al (2024), Longley et al (2020)
Severity parameters			
Duration of severe illness	20.0 days (IQR: 14.0 - 44.0 days)		Mejia et al (2020)
Duration of moderate illness	14.0 days (IQR: 7.0 - 25.0 days)		Mejia et al (2020)
Duration of untreated illness	14.0 days (IQR: 8.0 - 25.0 days)		Mejia et al (2020)
CFR	0.81% (0.10%-6.22%)	0.16% (0.07%-0.40%)	Murthy et al (unpublished) – based on meta-analysis of studies since 2010
Life expectancy	64.0 years	74.8 years	UN data portal

CEA parameters: Vaccination & treatment costs

Treatment costs	**Africa**	**Asia**	**source**
Inpatient pediatric costs	$285.01 ($199.29, $370.74)	$214.45 ($153.75, $326.76)	Limani et al (2020), Mejia et al (2010)
Outpatient pediatric costs	$50.41 ($41.16, $59.68)	$42.62 ($26.34, $72.01)	Limani et al (2020), Mejia et al (2020)
Inpatient adult costs	$445.65 ($295.27, $596.02)	$214.45 ($153.75, $326.76)	Limani et al (2020), Mejia et al (2010)
Outpatient adult costs	$46.77 ($35.18, $58.36)	$42.62 ($26.34, $72.01)	Limani et al (2020), Mejia et al (2020)
Vaccination costs			
Vaccine procurement costs (i.e. vaccine price)	$1.50		UNICEF, 2024
Syringes & safety equipment costs (unit price)	$0.29 ($0.28, $0.31)		Portnoy et al., Vaccine 2015
Delivery costs, routine	$2.34 ($1.96, $2.70)	$1.54 ($0.94, $2.14)	Bilcke et al., Lancet Infect Dis, 2019
Delivery costs, school-based	$1.42 ($0.71, $2.14)		Weyant et al., Vaccine, 2024
Delivery costs, catch-up campaign	$0.50 ($0.44, $0.56)	$0.54 ($0.46, $0.61)	Bilcke et al., Lancet Infect Dis, 2019

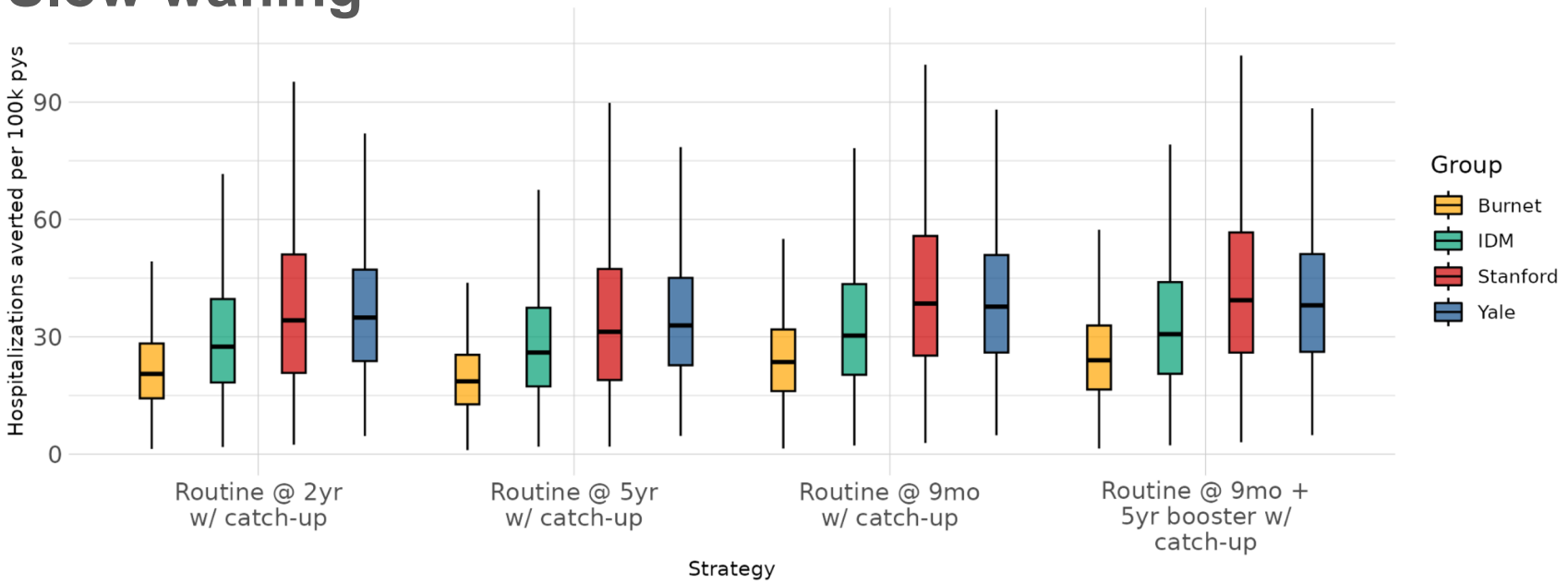
Vaccine Impact Results

Hospitalizations
10 year time horizon

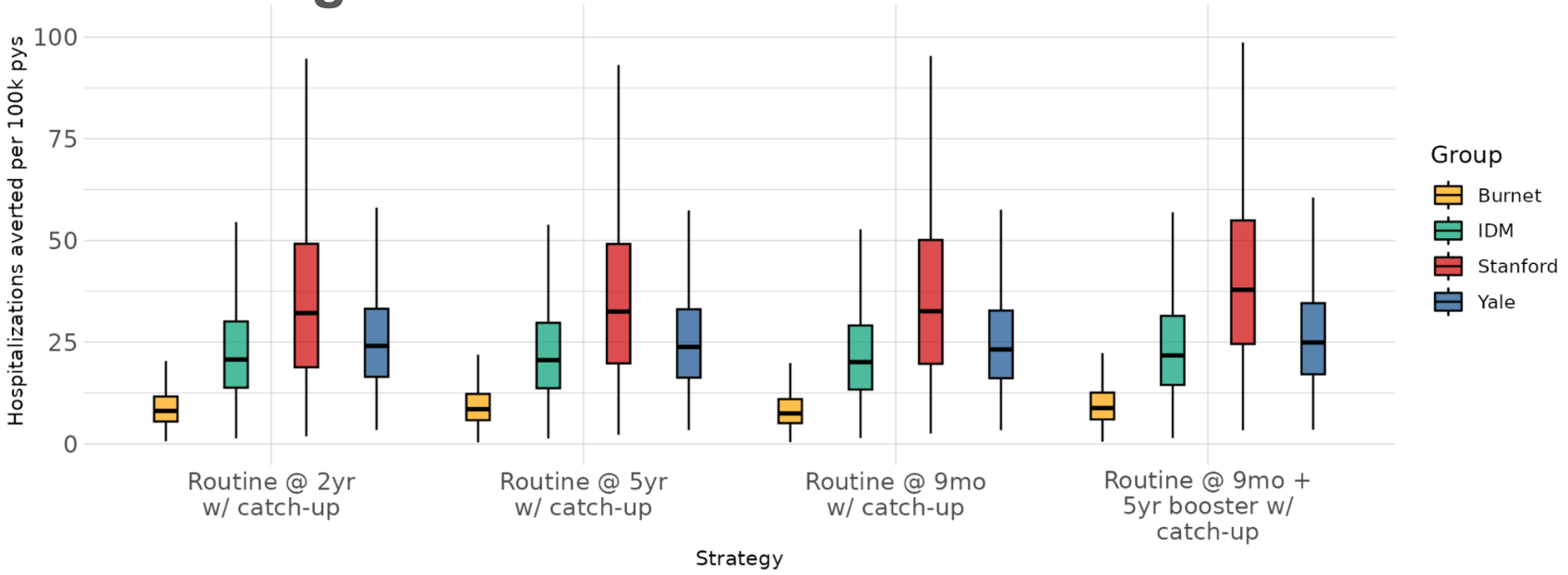
Hospitalizations averted per 100k person-years:

Medium burden, Africa region

Slow waning

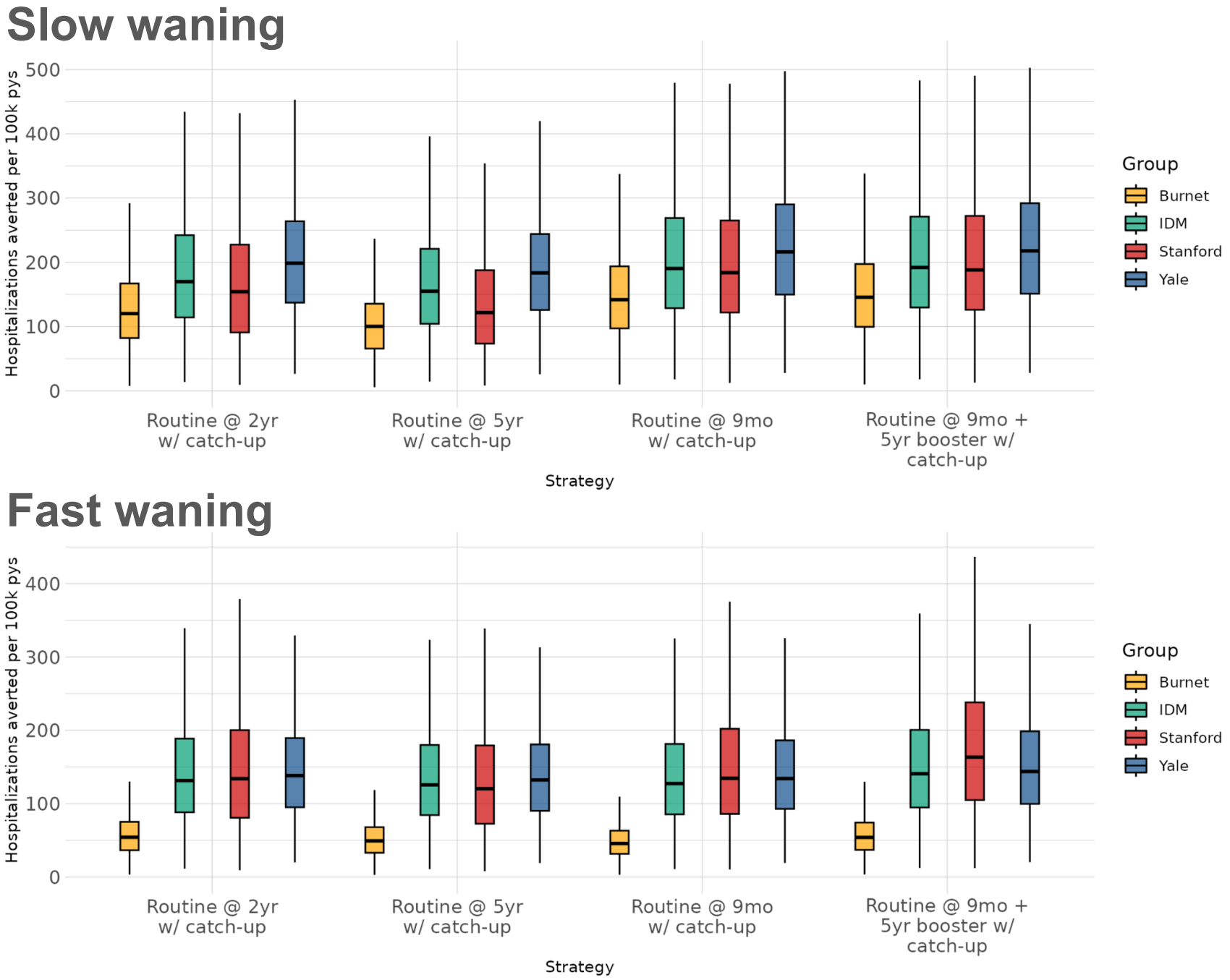


Fast waning



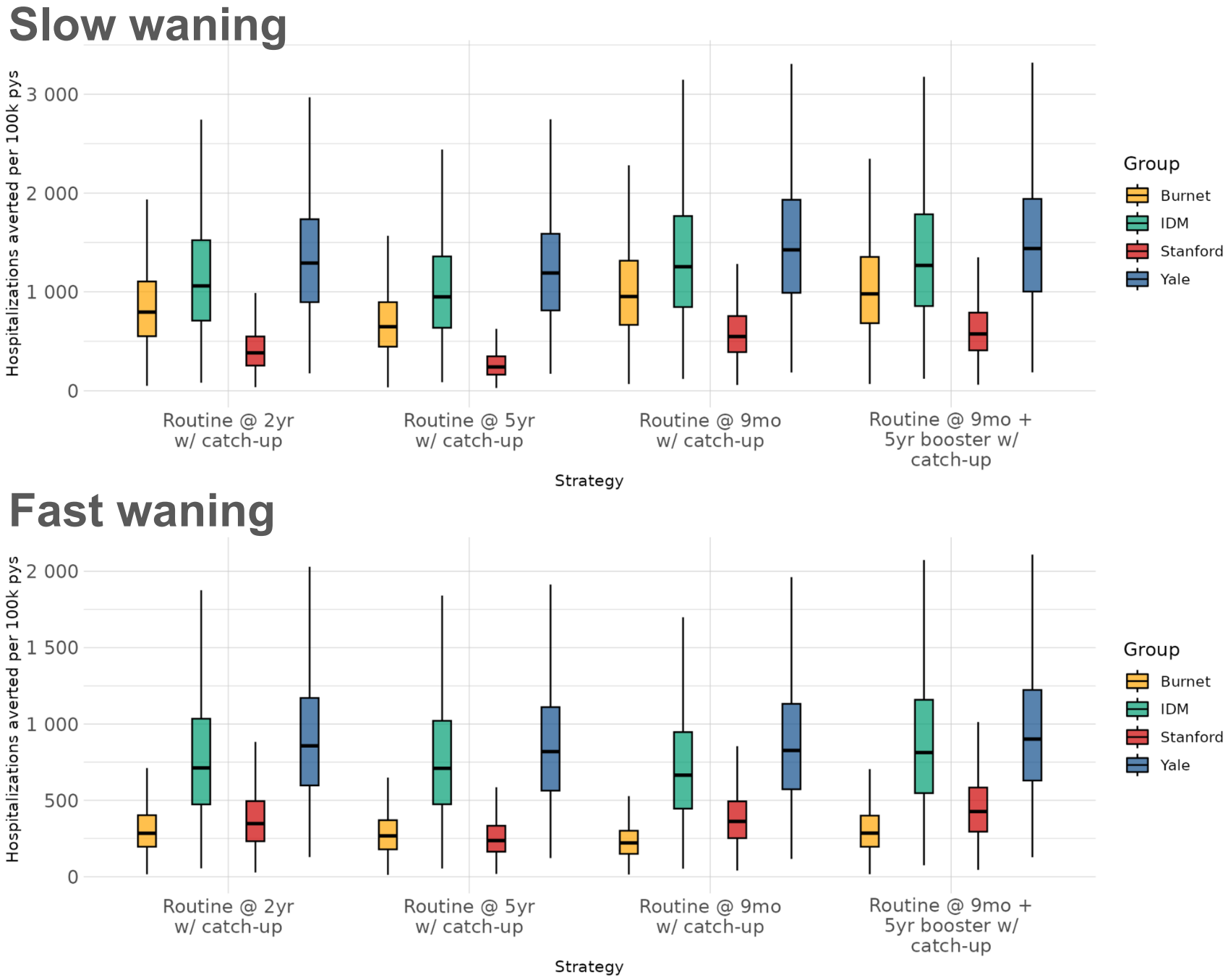
Hospitalizations averted per 100k person-years:

High burden, Africa region



Hospitalizations averted per 100k person-years:

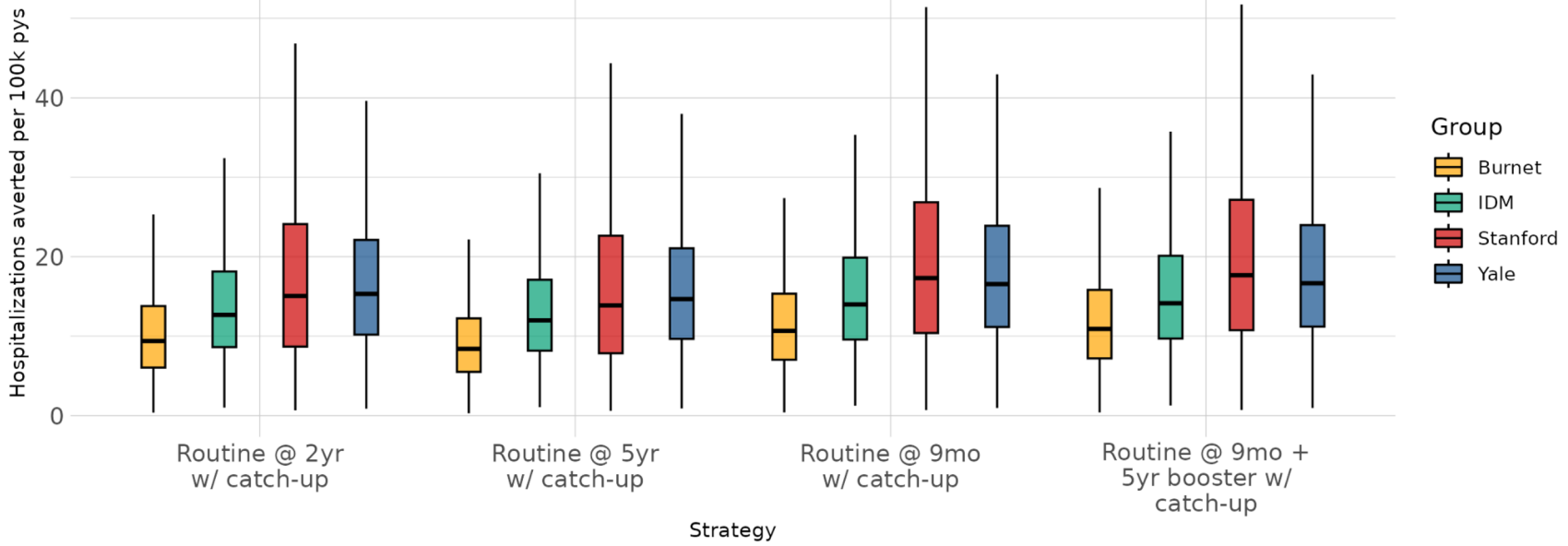
Very high burden, Africa region



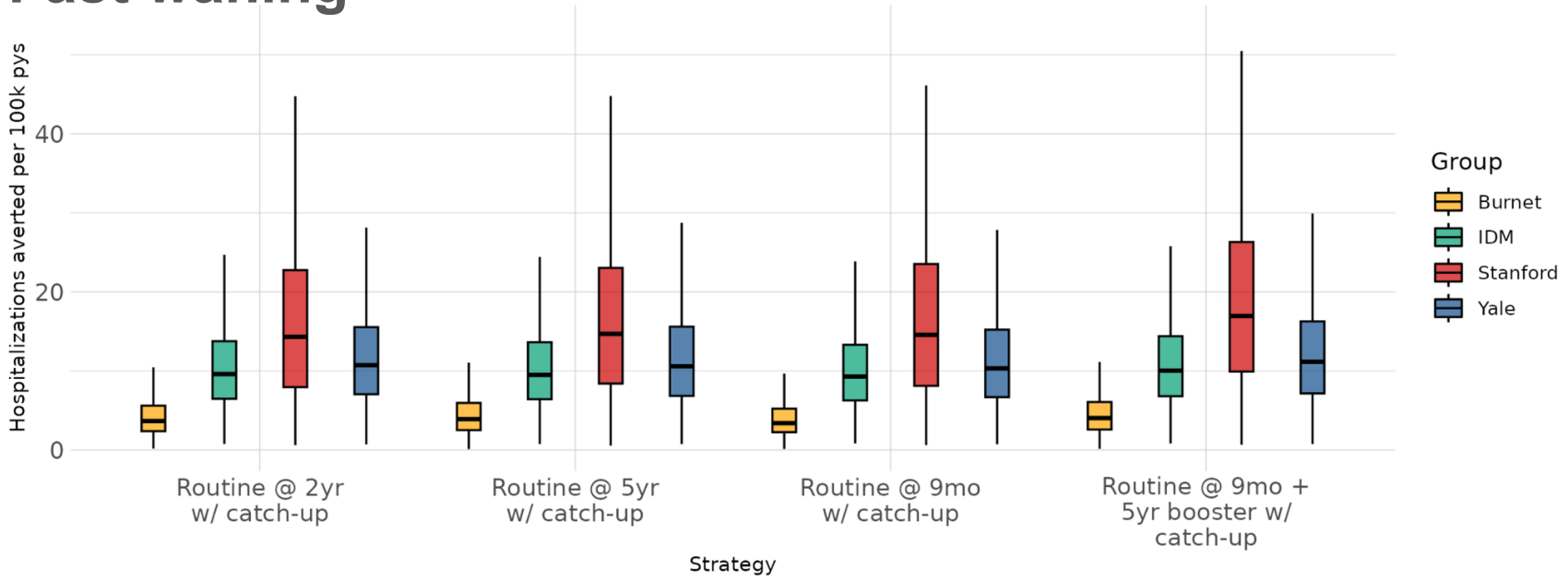
Hospitalizations averted per 100k person-years:

Medium burden, Asia region

Slow waning

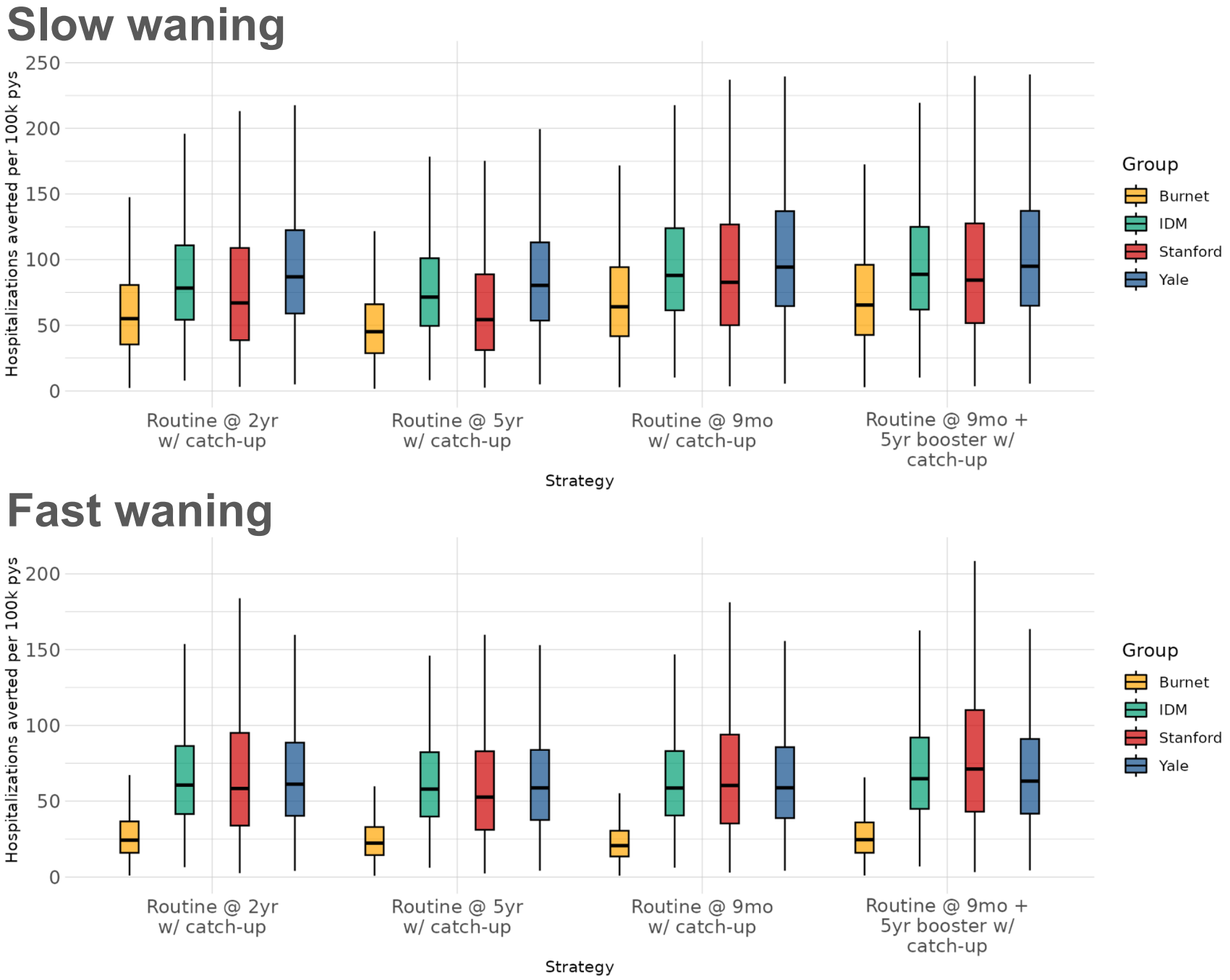


Fast waning



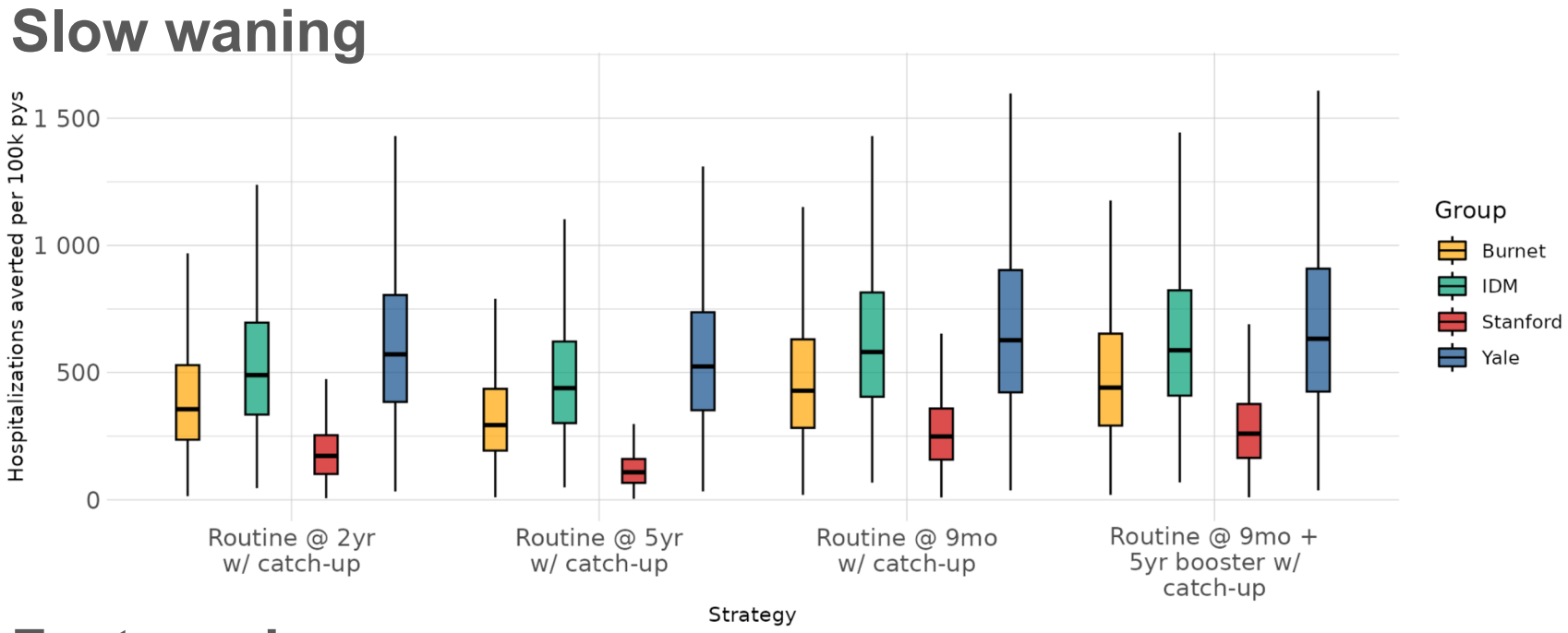
Hospitalizations averted per 100k person-years:

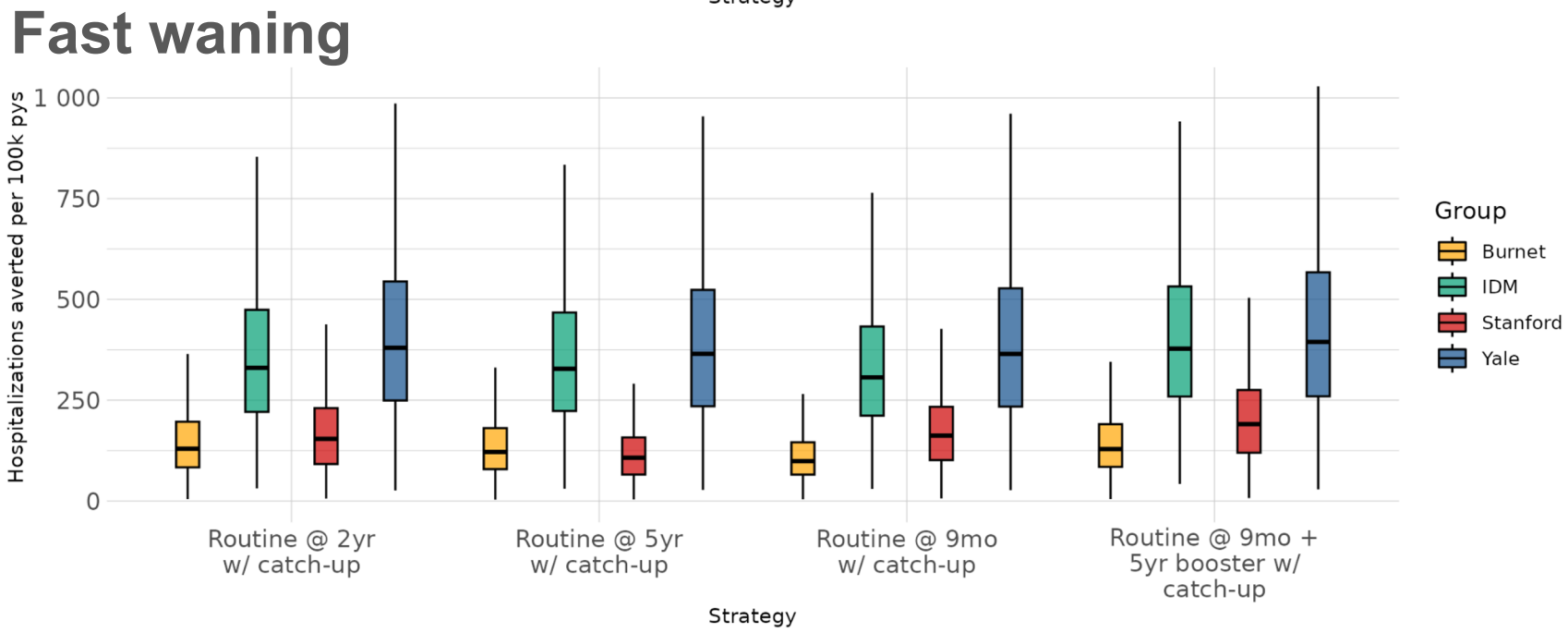
High burden, Asia region



Hospitalizations averted per 100k person-years:

Very high burden, Asia region





Vaccine Impact Results

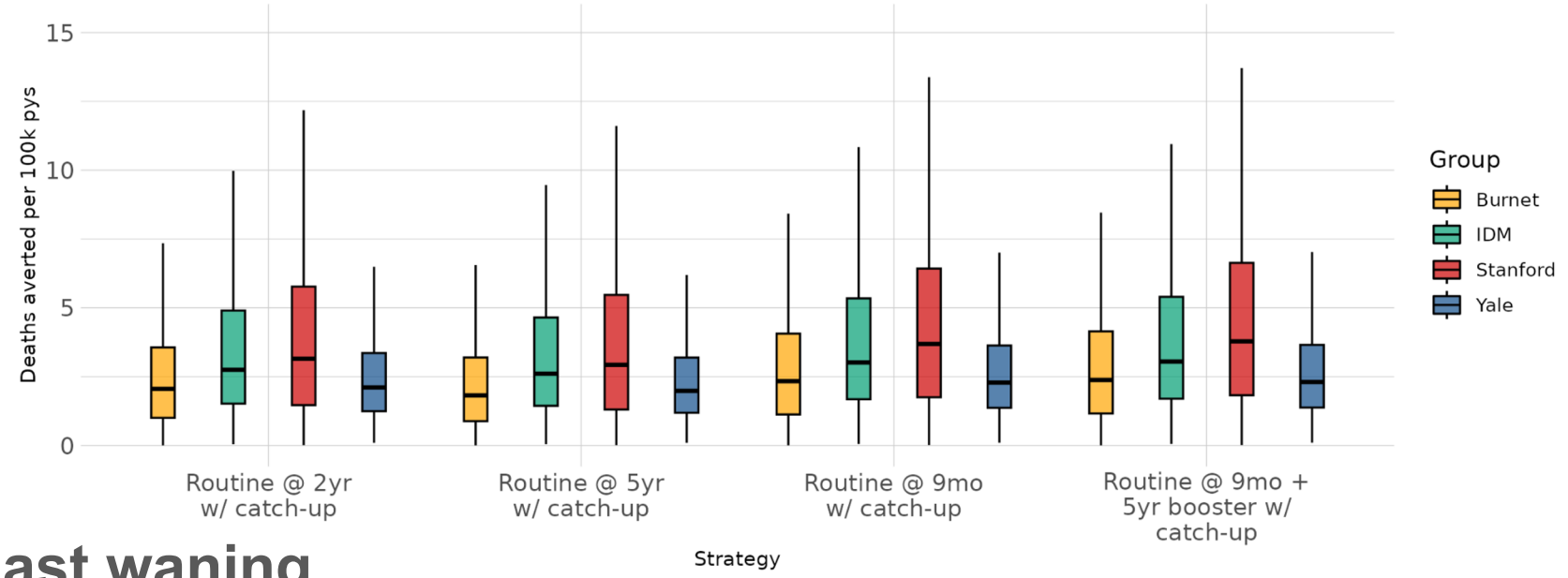
Deaths

10 year time horizon

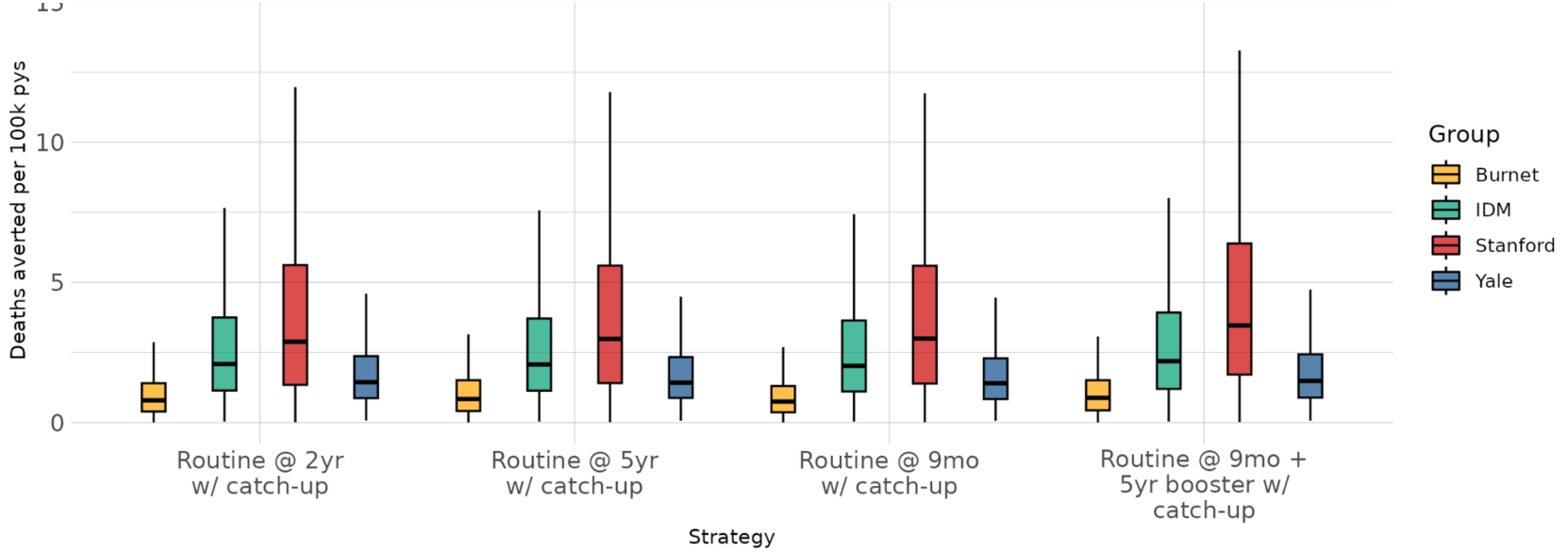
Deaths averted per 100k person-years:

Medium burden, Africa region

Slow waning



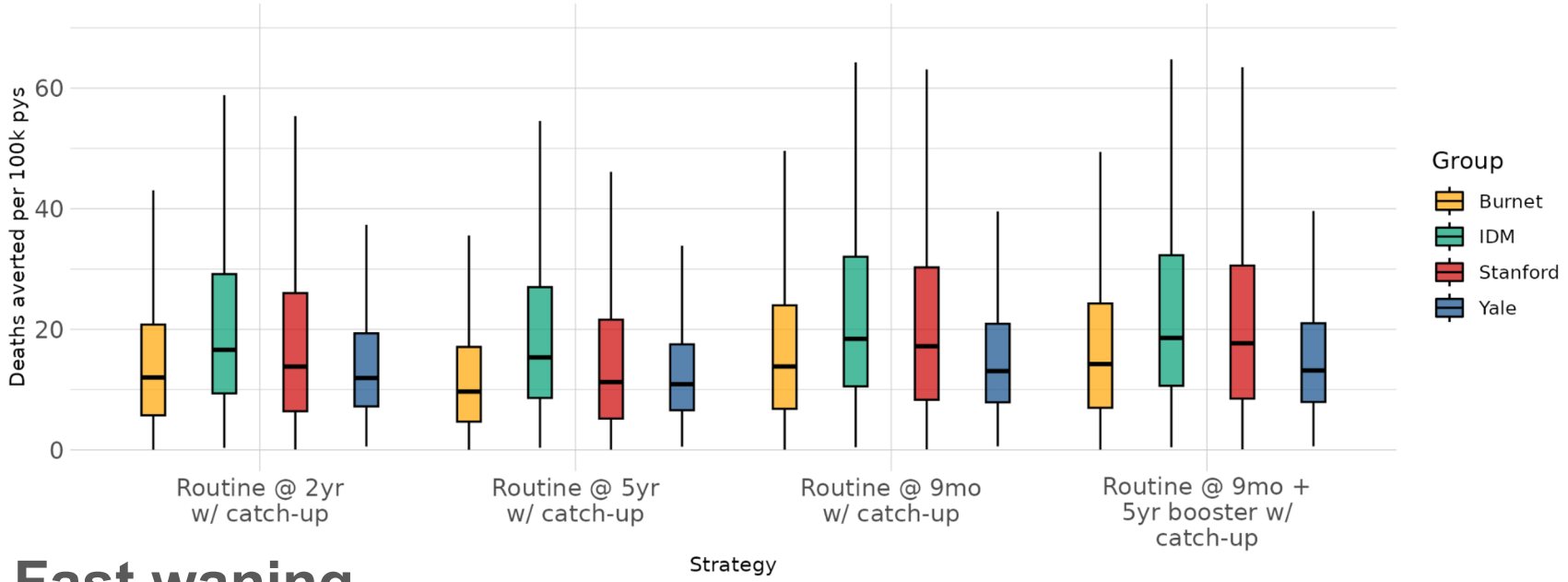
Fast waning



Deaths averted per 100k person-years:

High burden, Africa region

Slow waning



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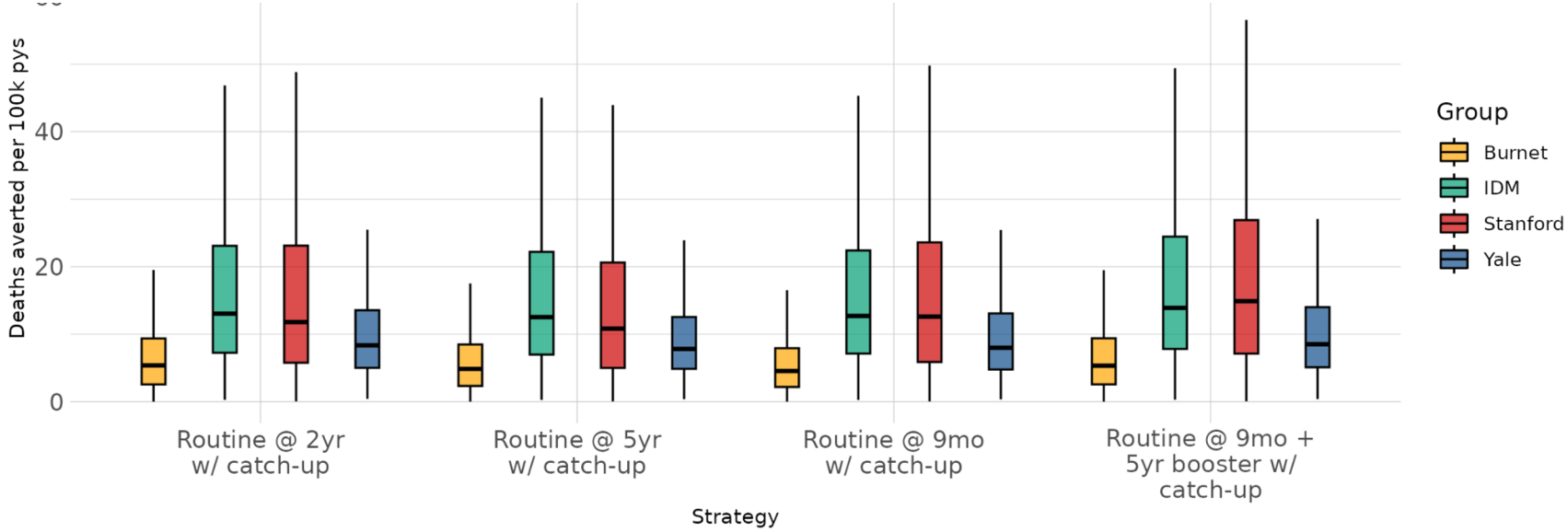
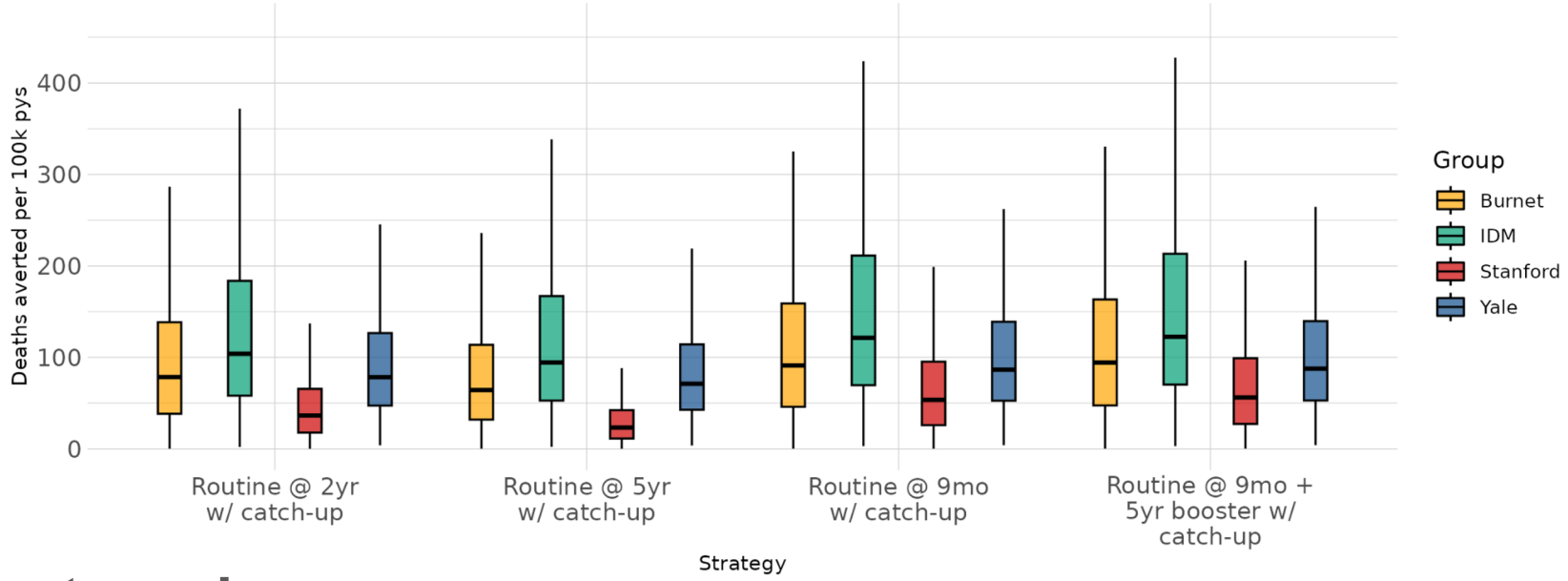


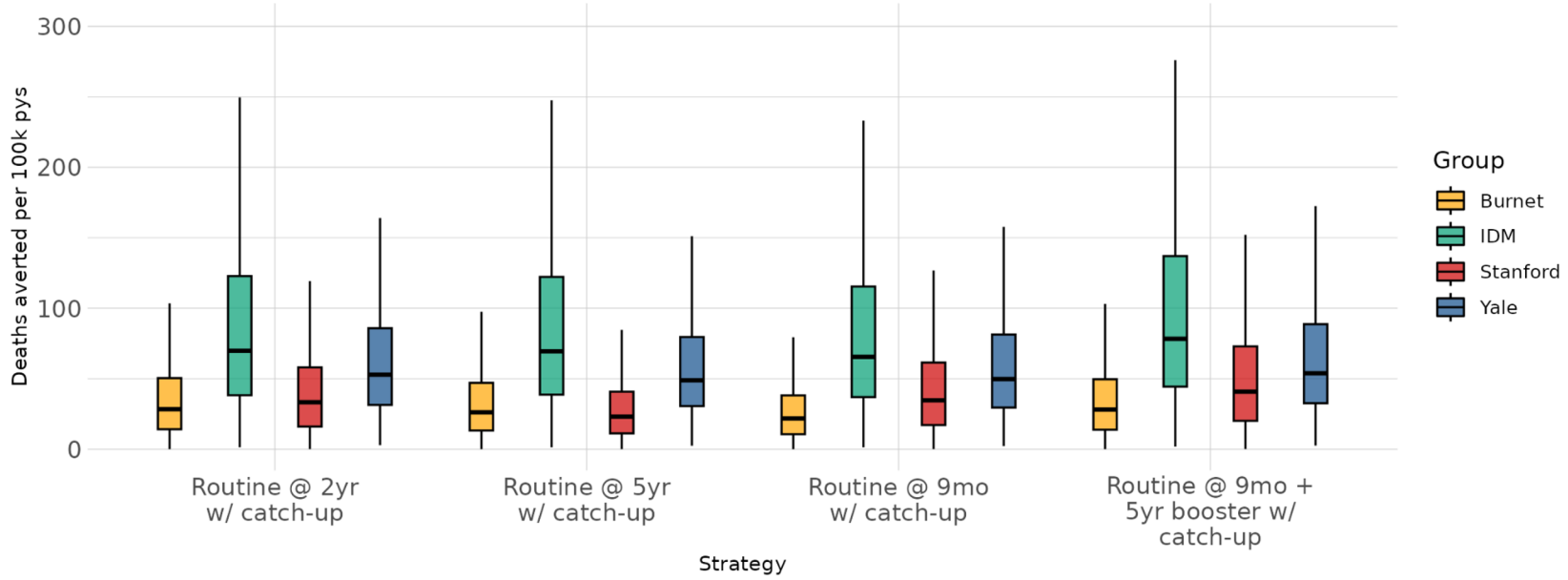
Deaths averted per 100k person-years:

Very high burden, Africa region

Slow waning



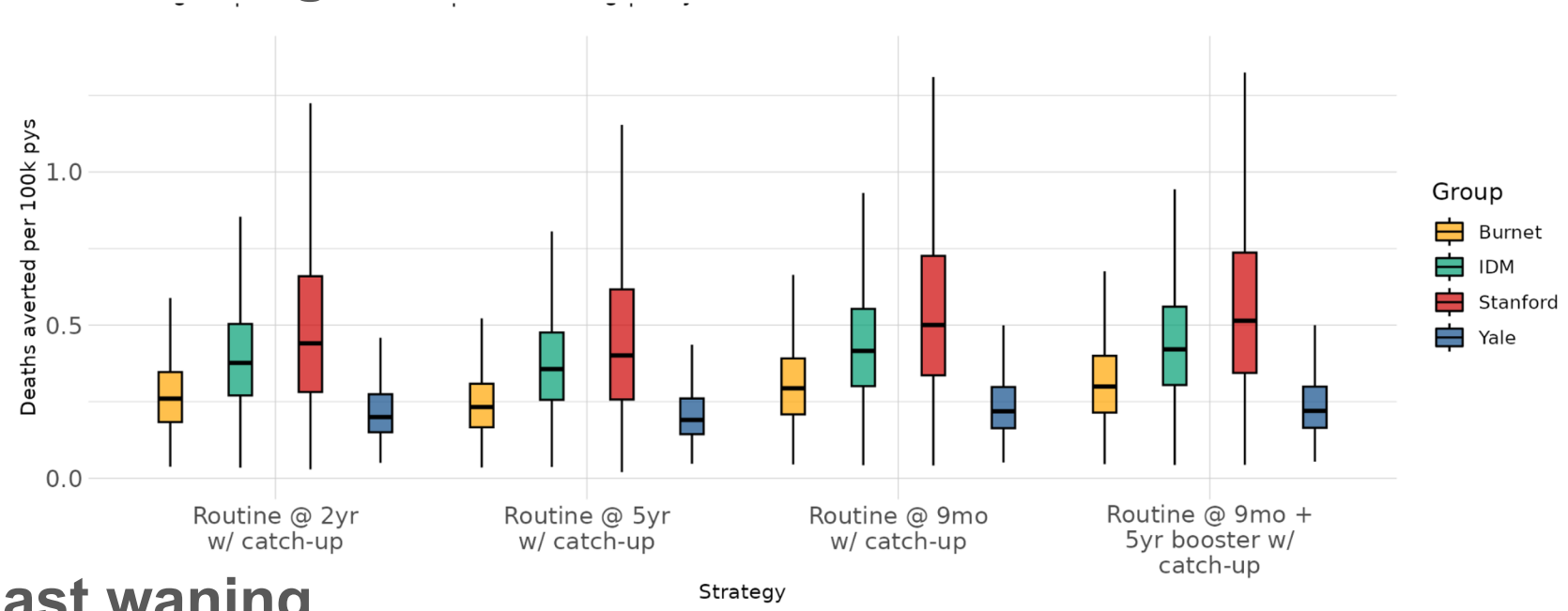
Fast waning



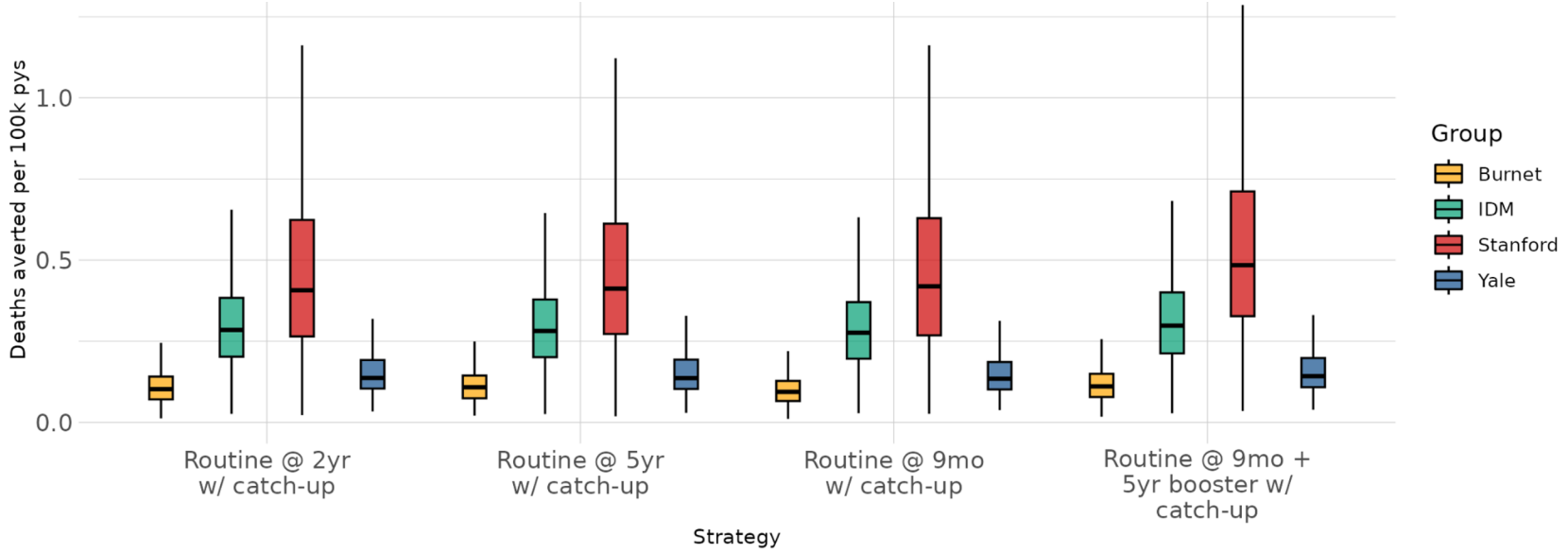
Deaths averted per 100k person-years:

Medium burden, Asia region

Slow waning



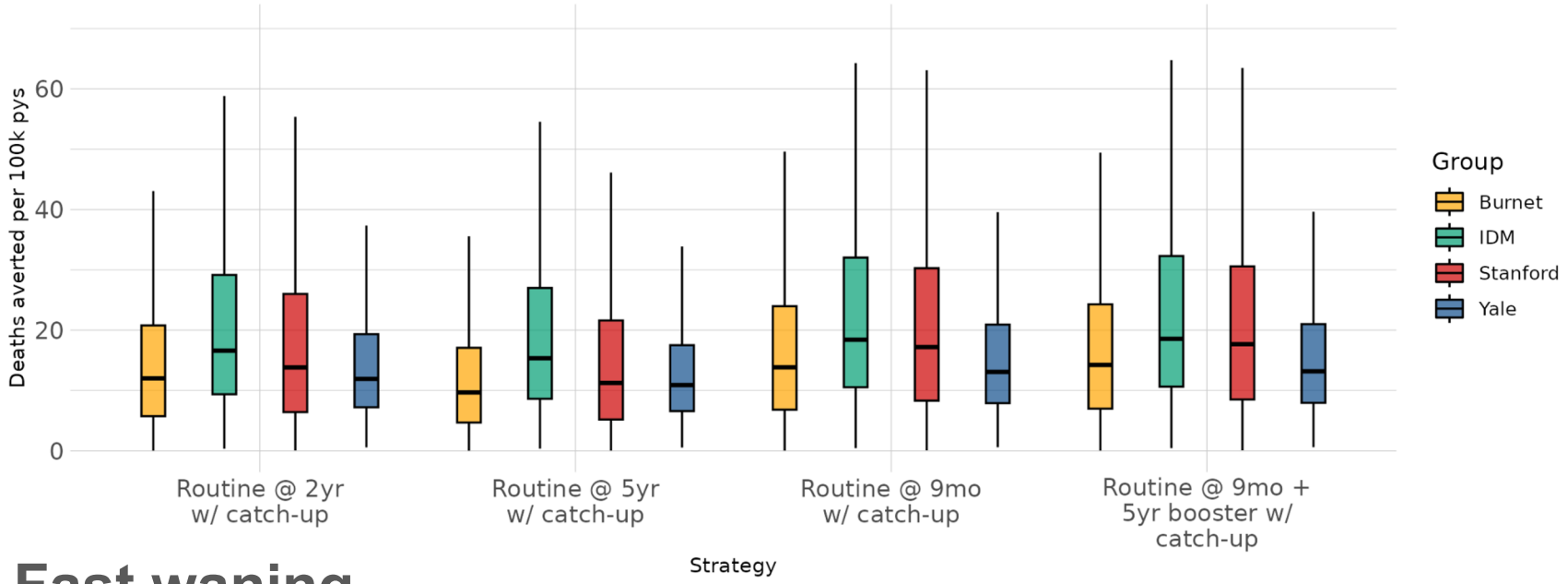
Fast waning



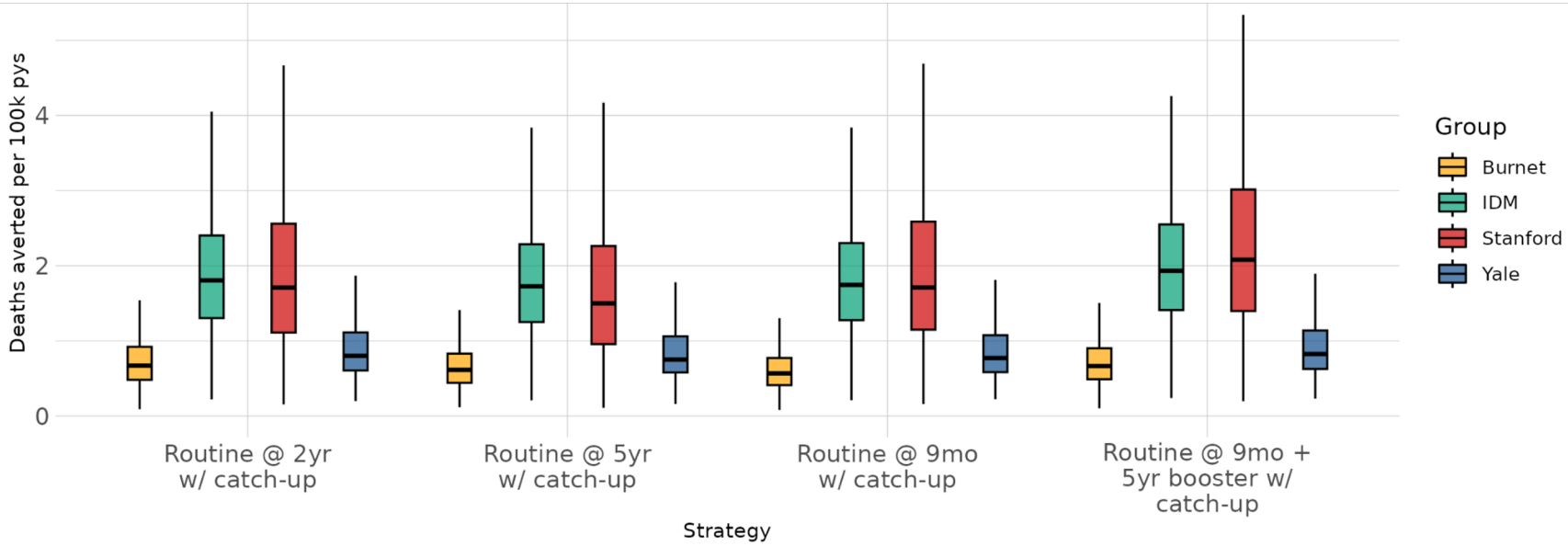
Deaths averted per 100k person-years:

High burden, Asia region

Slow waning



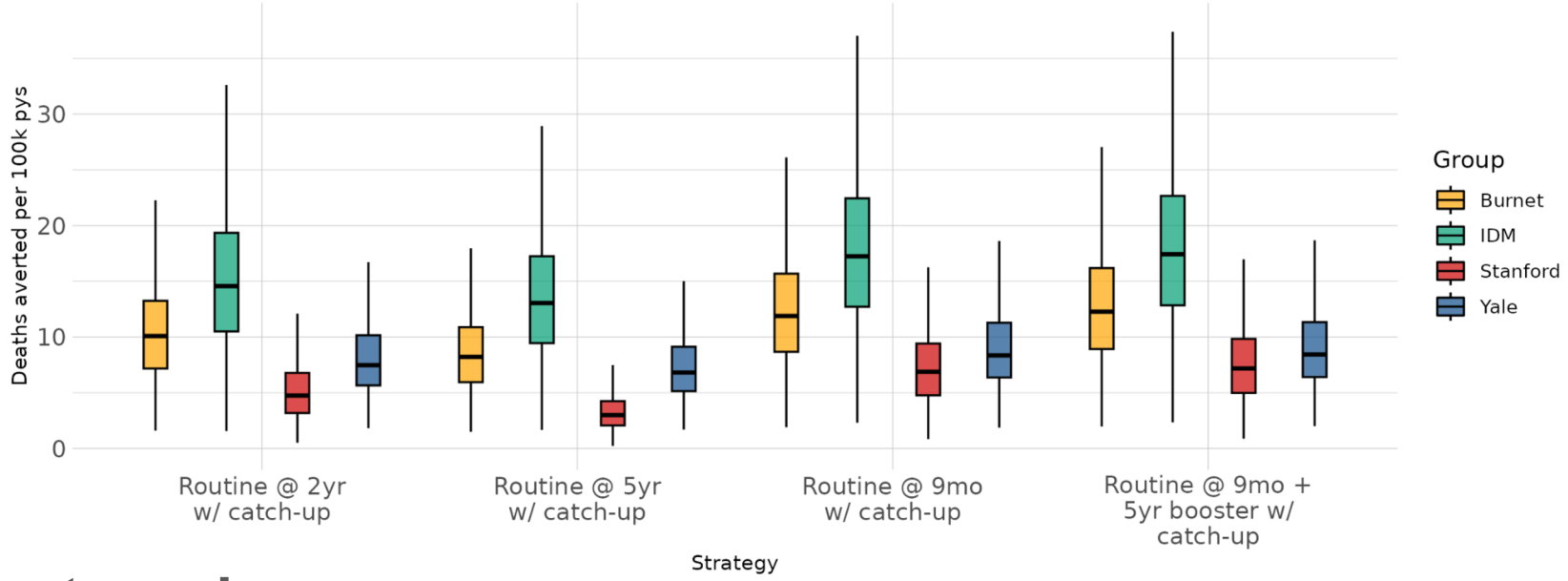
Fast waning



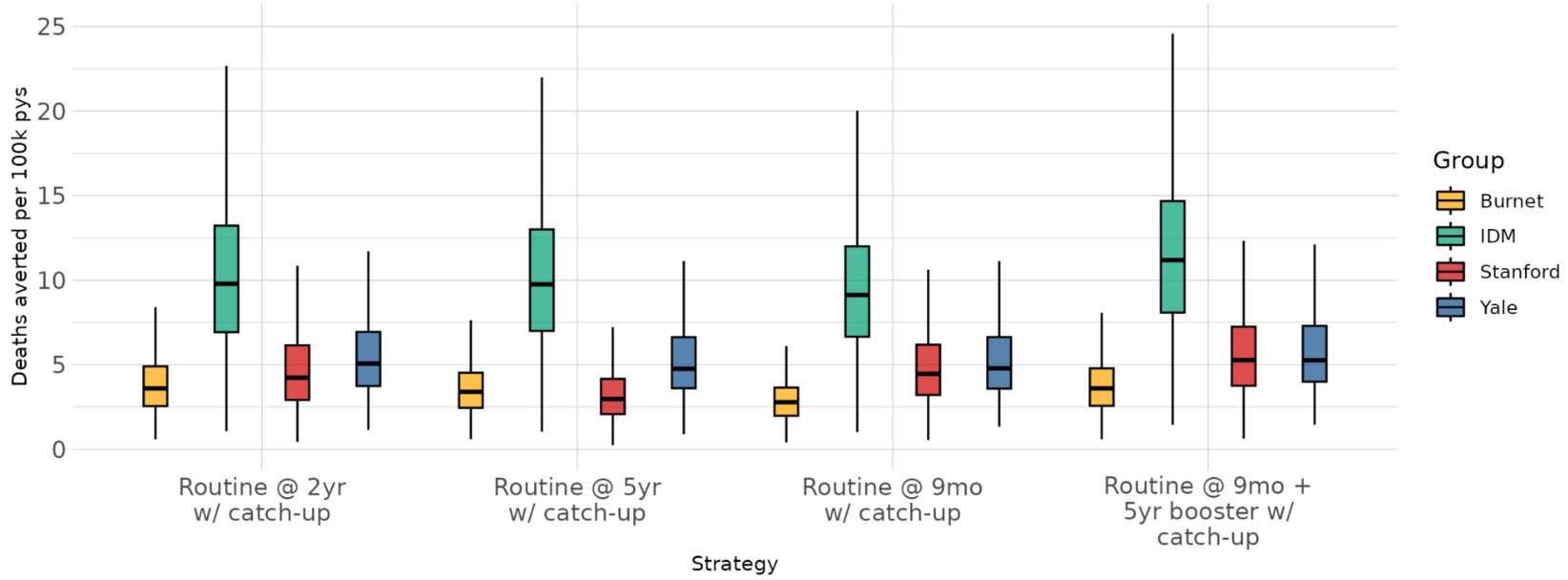
Deaths averted per 100k person-years:

Very high burden, Asia region

Slow waning



Fast waning



Vaccine Impact Results

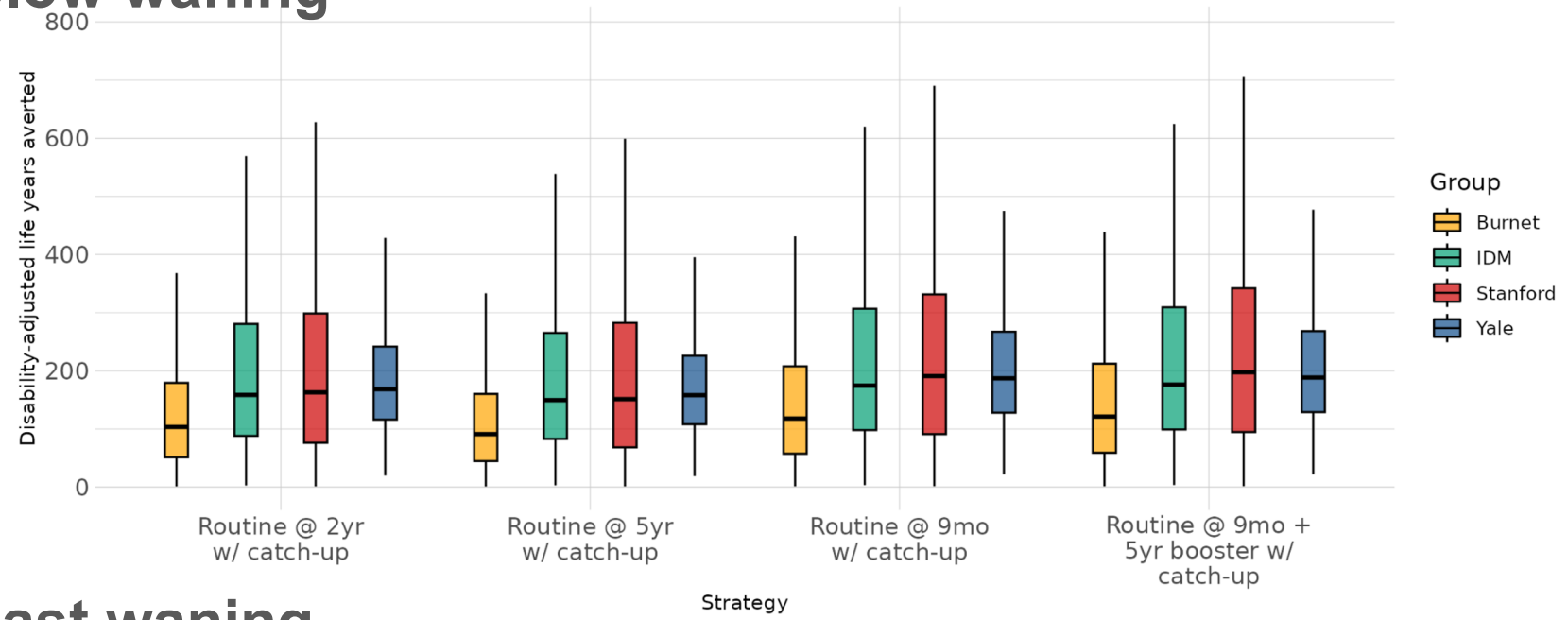
DALYs

10 year time horizon

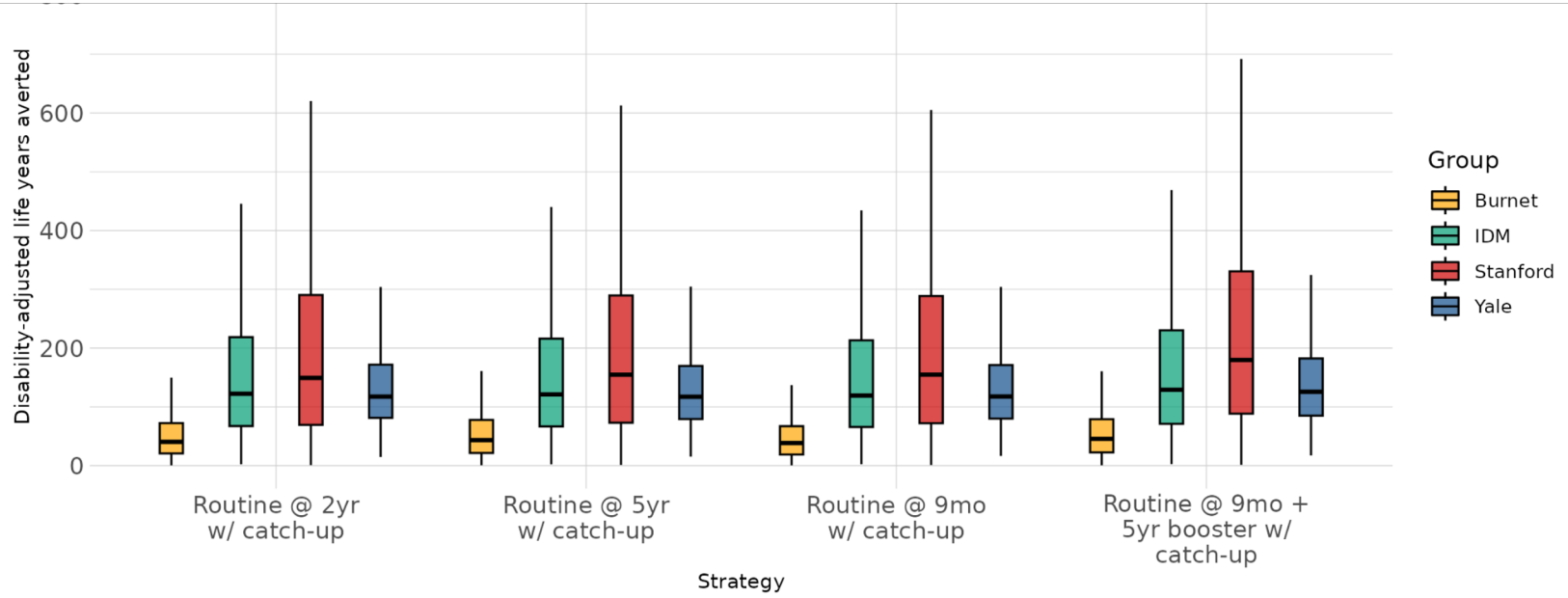
DALYs averted per 100k person-years:

Medium burden, Africa region

Slow waning

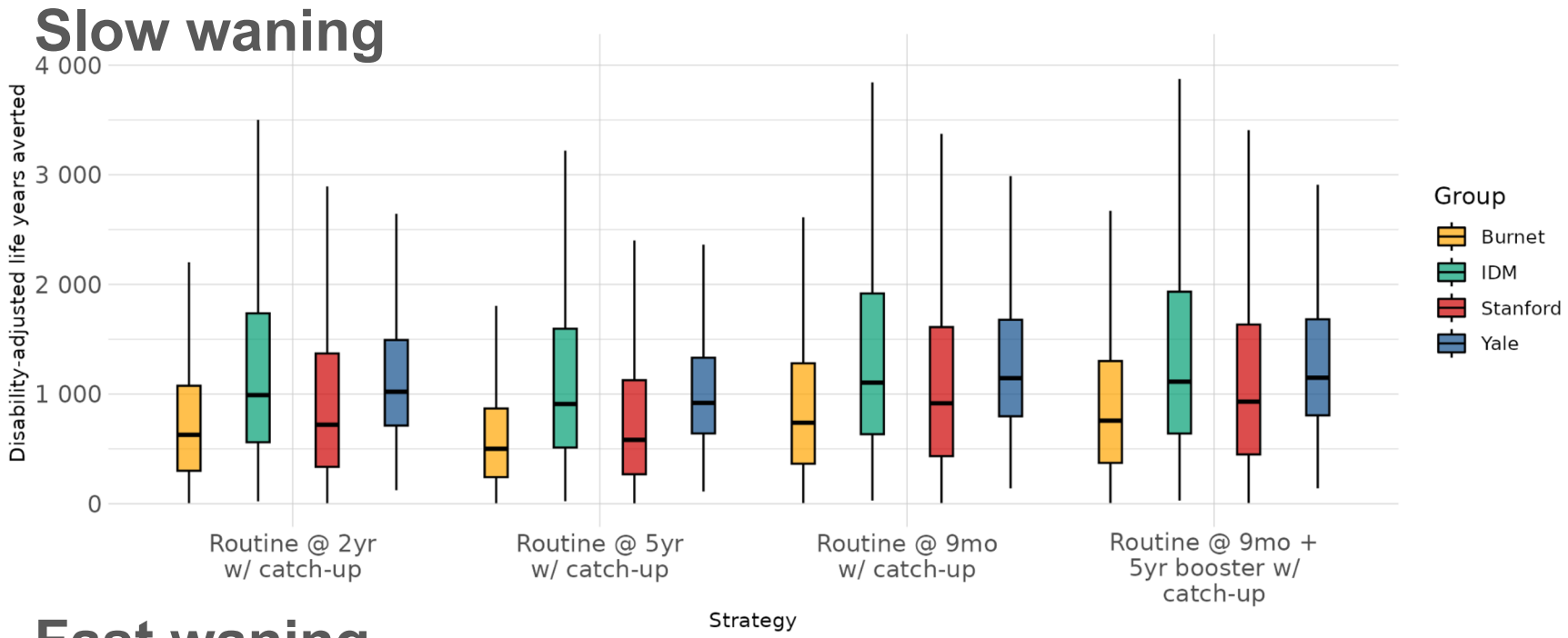


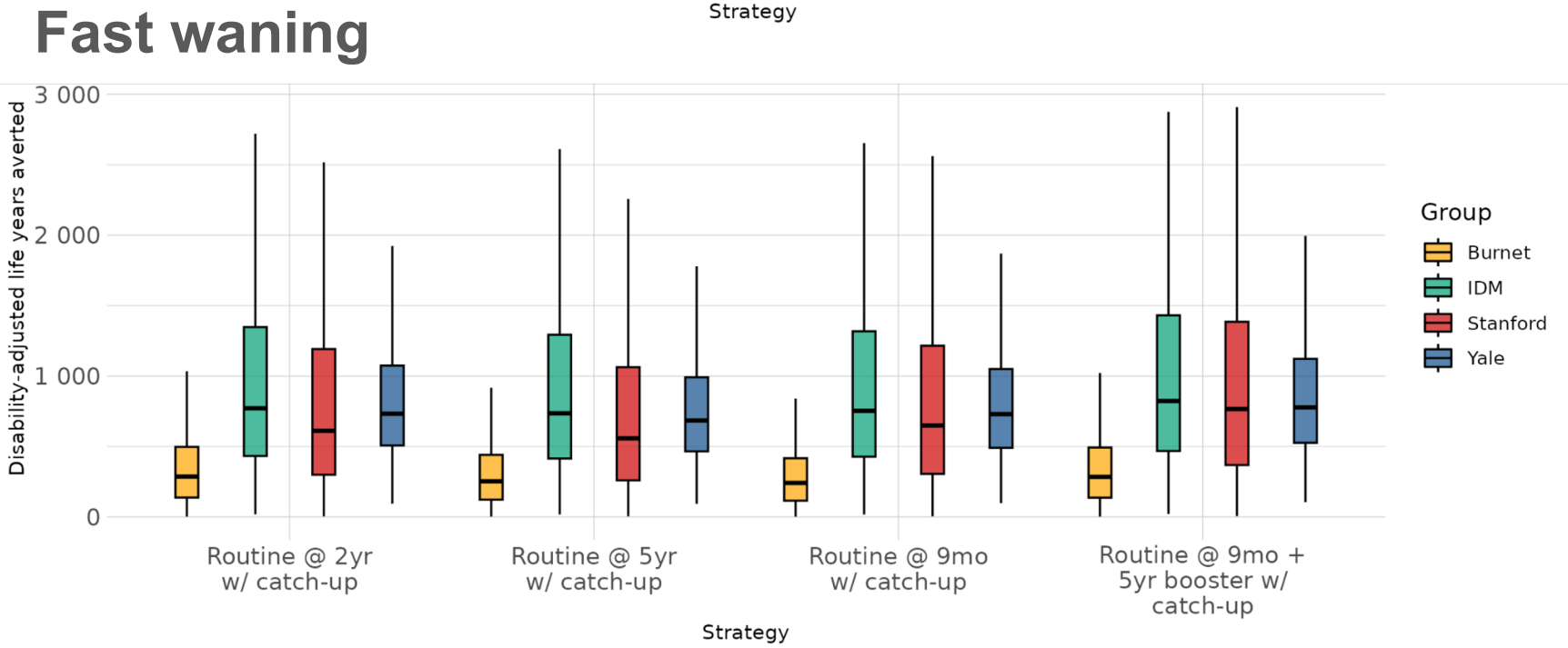
Fast waning



DALYs averted per 100k person-years:

High burden, Africa region





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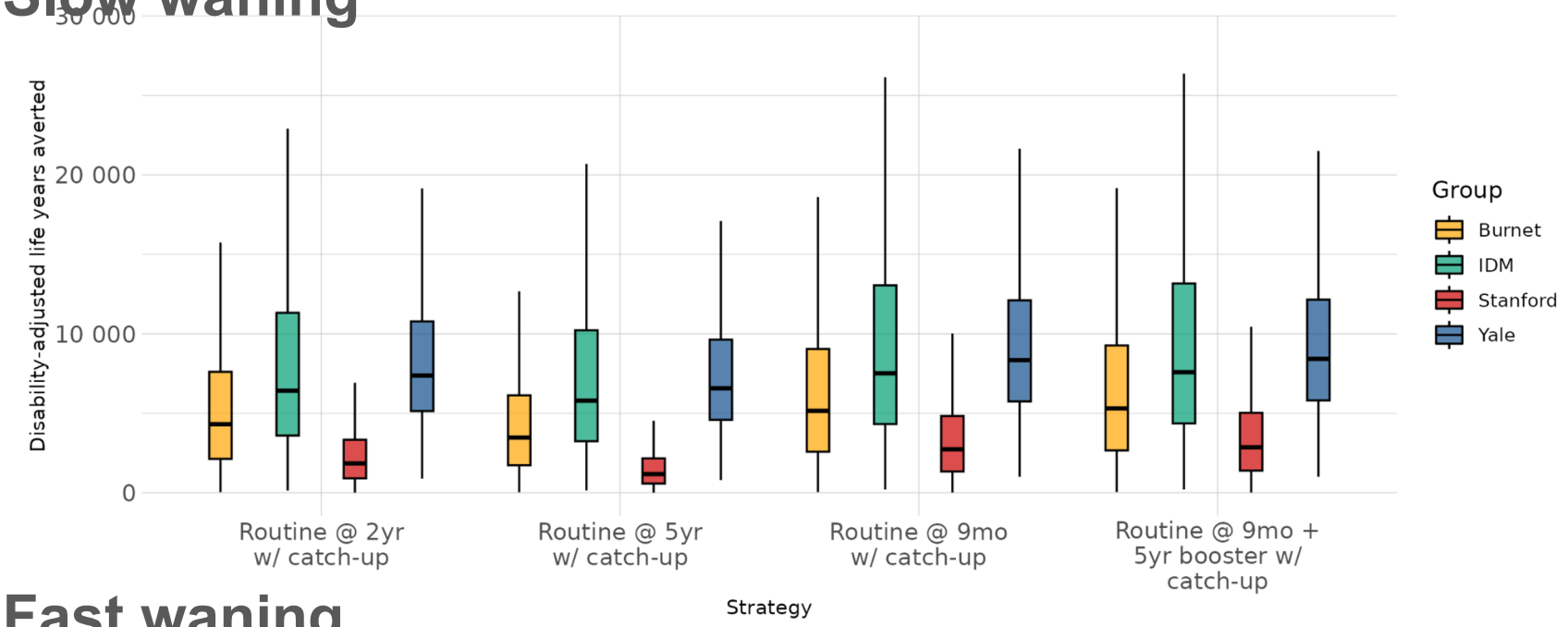
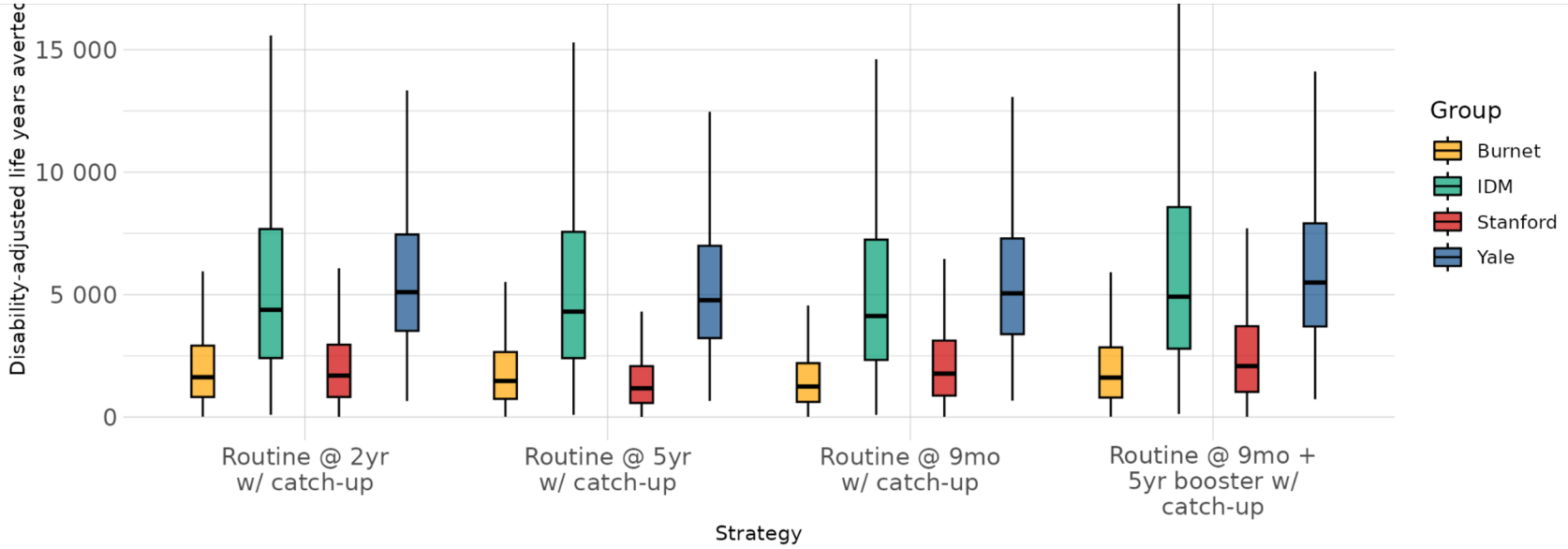


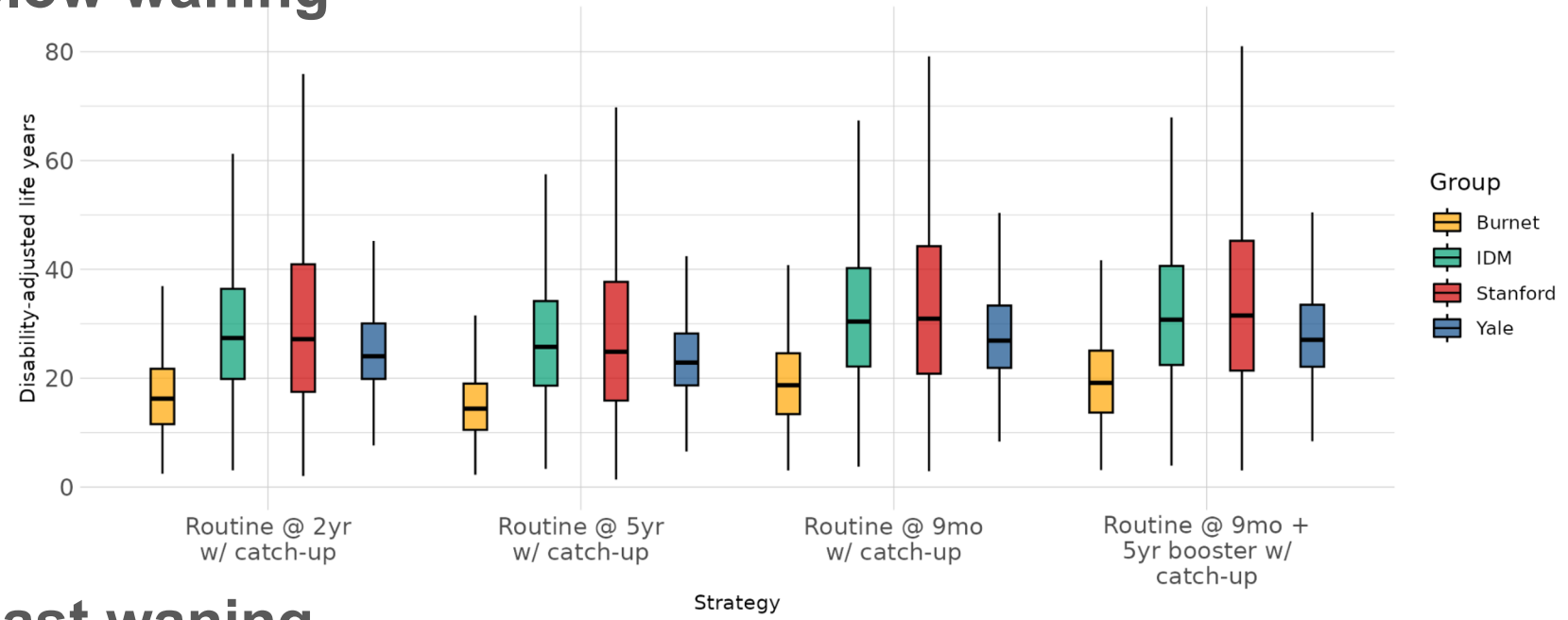
Fast waning



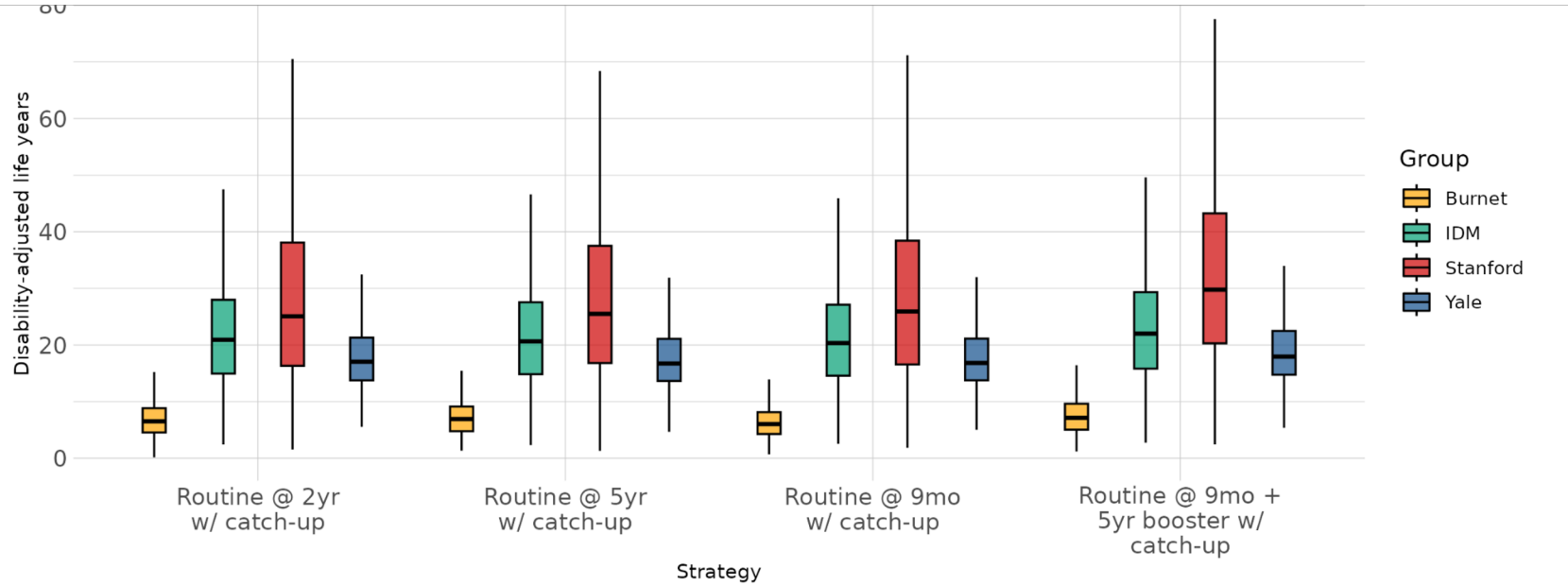
DALYs averted per 100k person-years:

Medium burden, Asia region

Slow waning

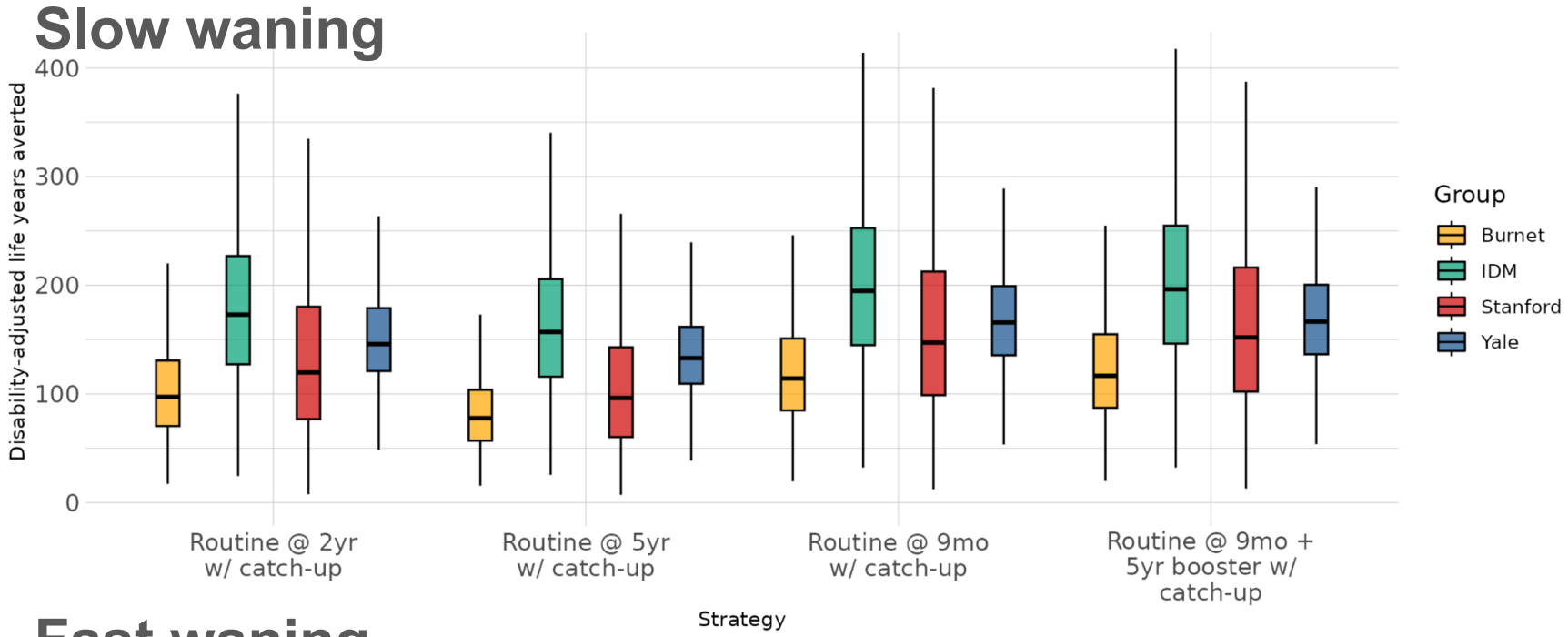


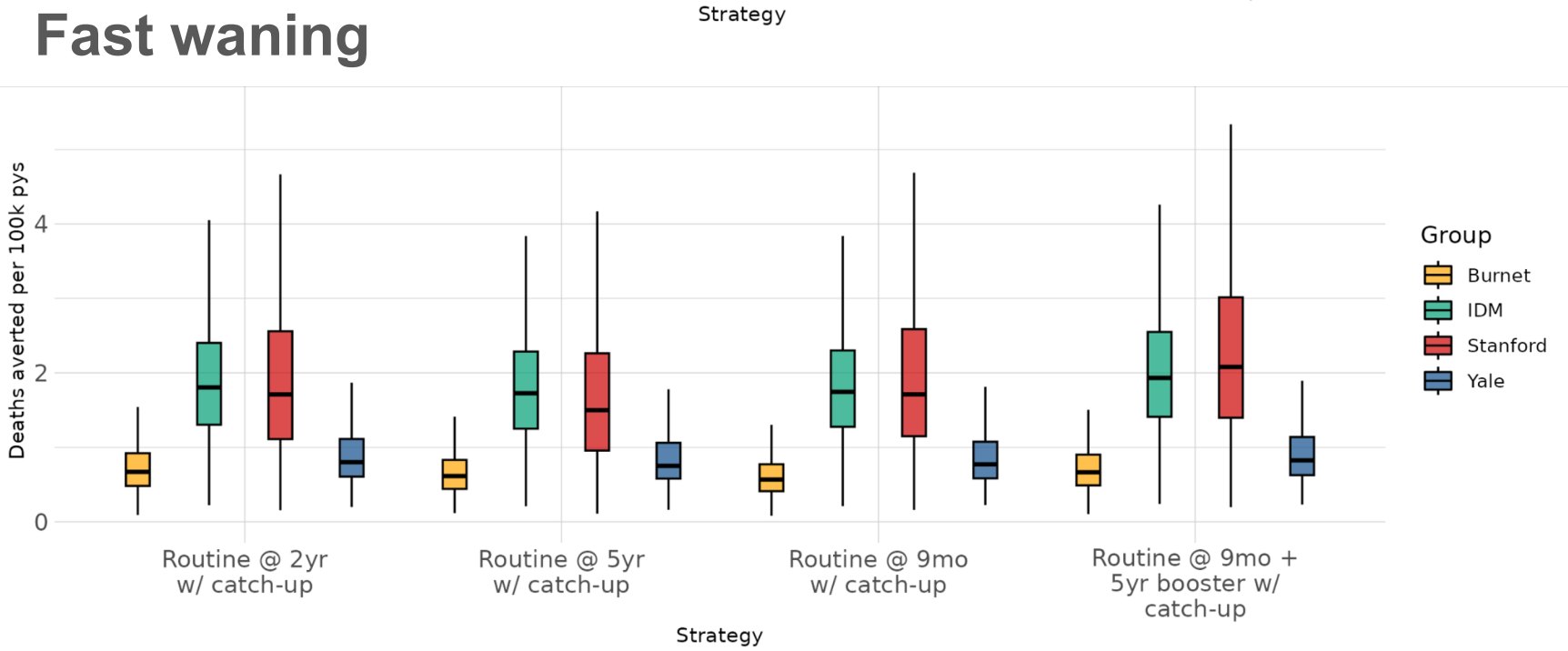
Fast waning



DALYs averted per 100k person-years:

High burden, Asia region

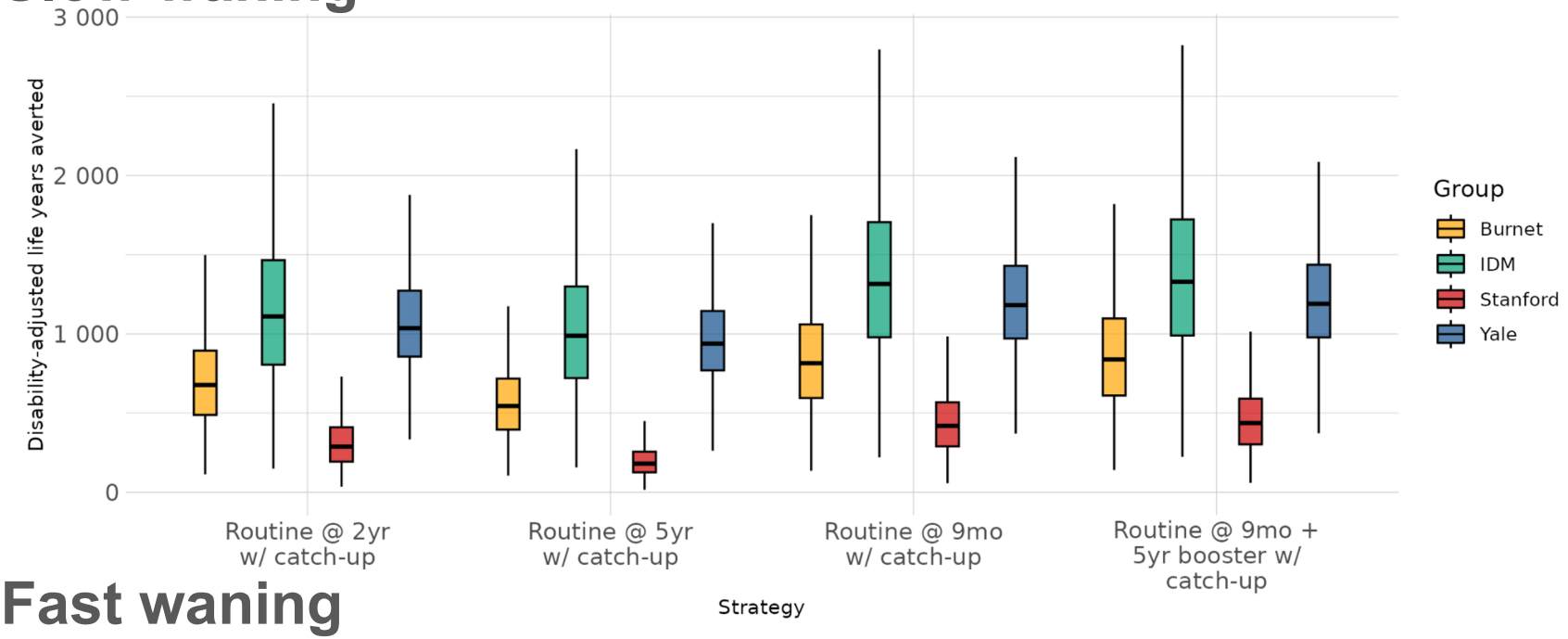




DALYs averted per 100k person-years:

Very high burden, Asia region

Slow waning



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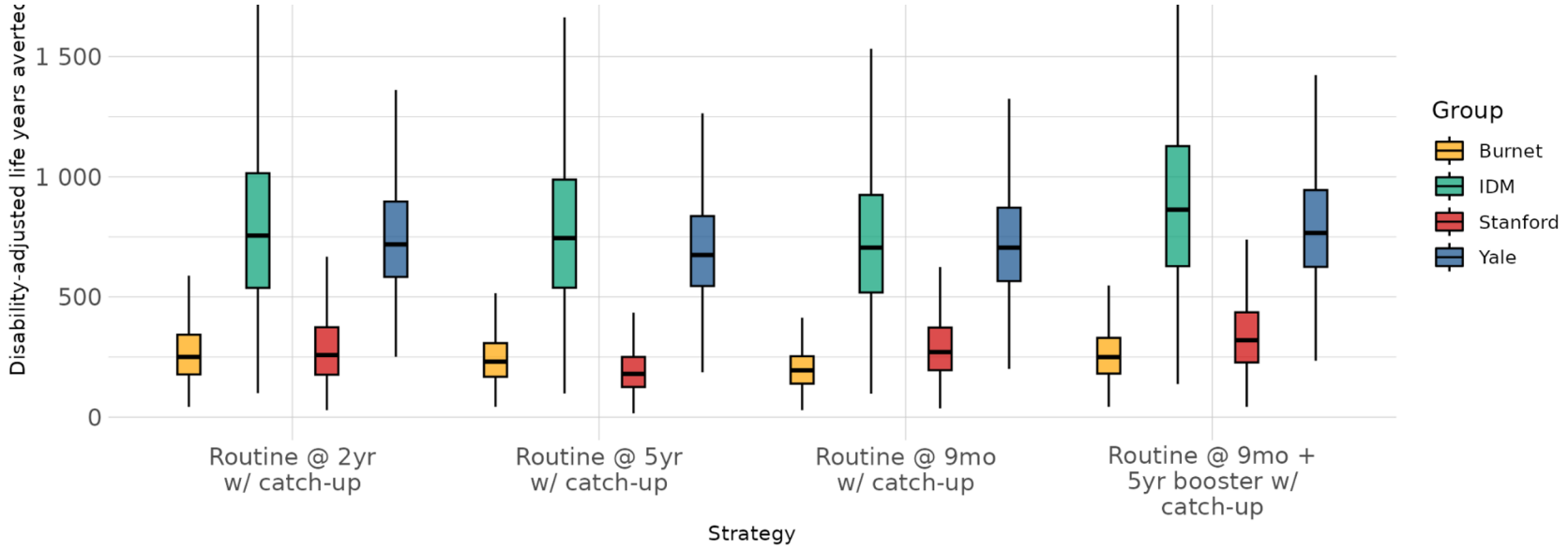


Vaccine Impact Results

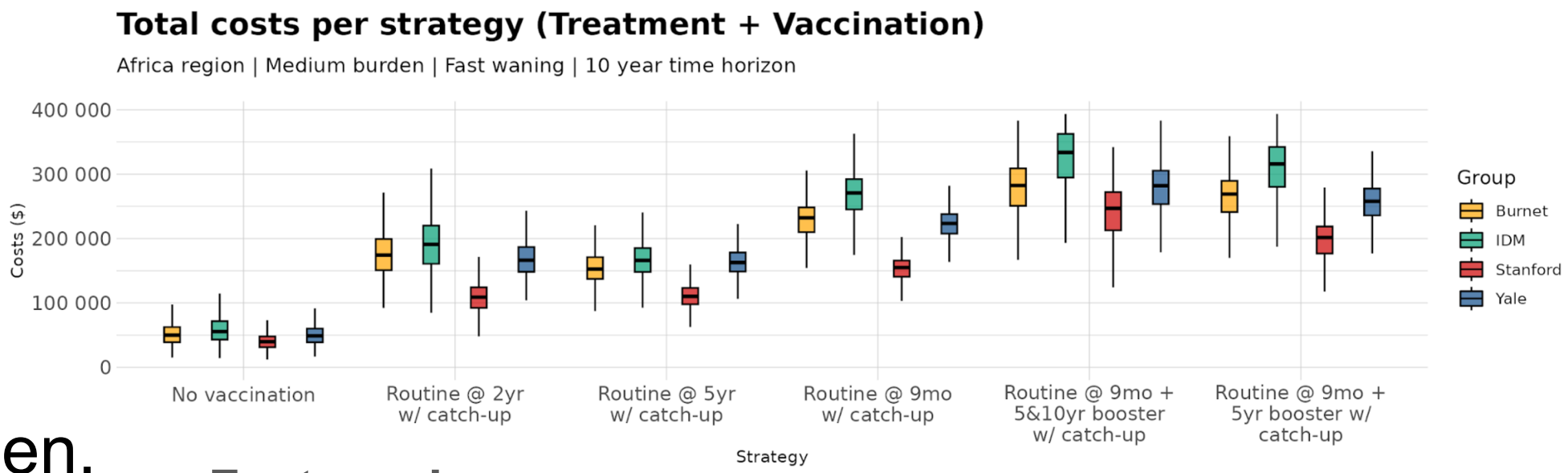
Costs

10 year time horizon

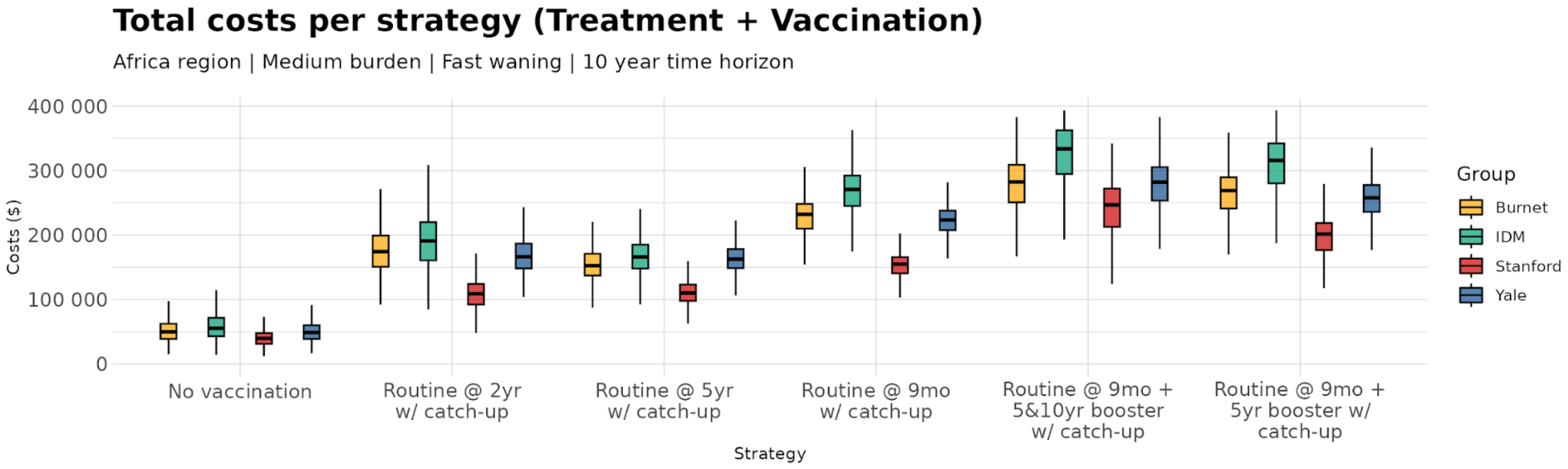
Total costs (discounted):

Medium burden, Africa region

Slow waning



Fast waning

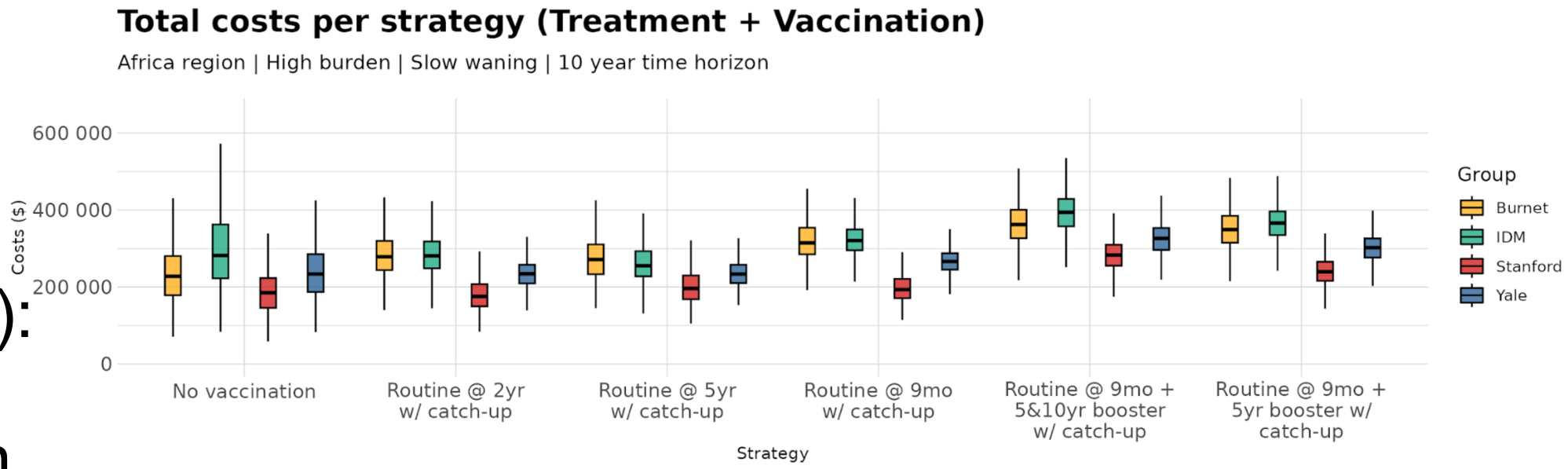


Note: Costs can differ between models due to differences in the assumed population size

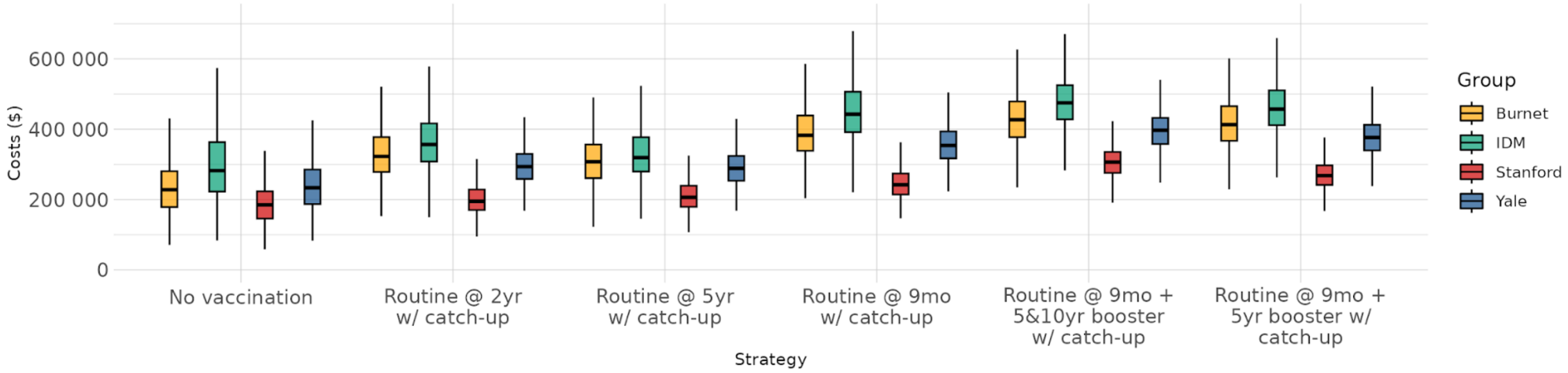
Total costs (discounted):

High burden, Africa region

Slow waning



Fast waning



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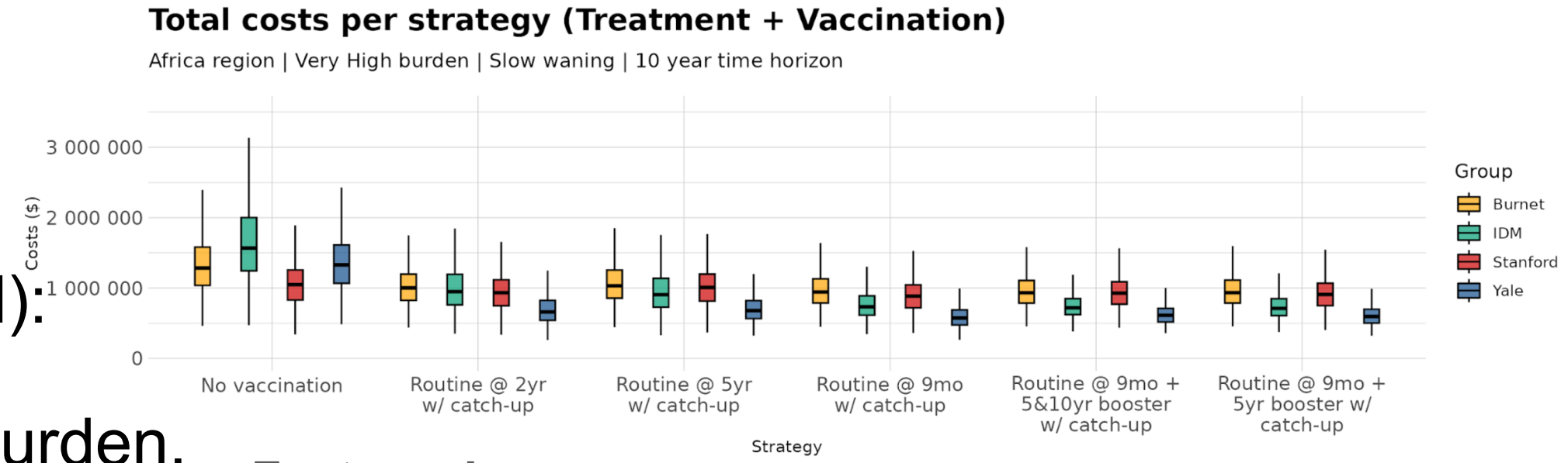
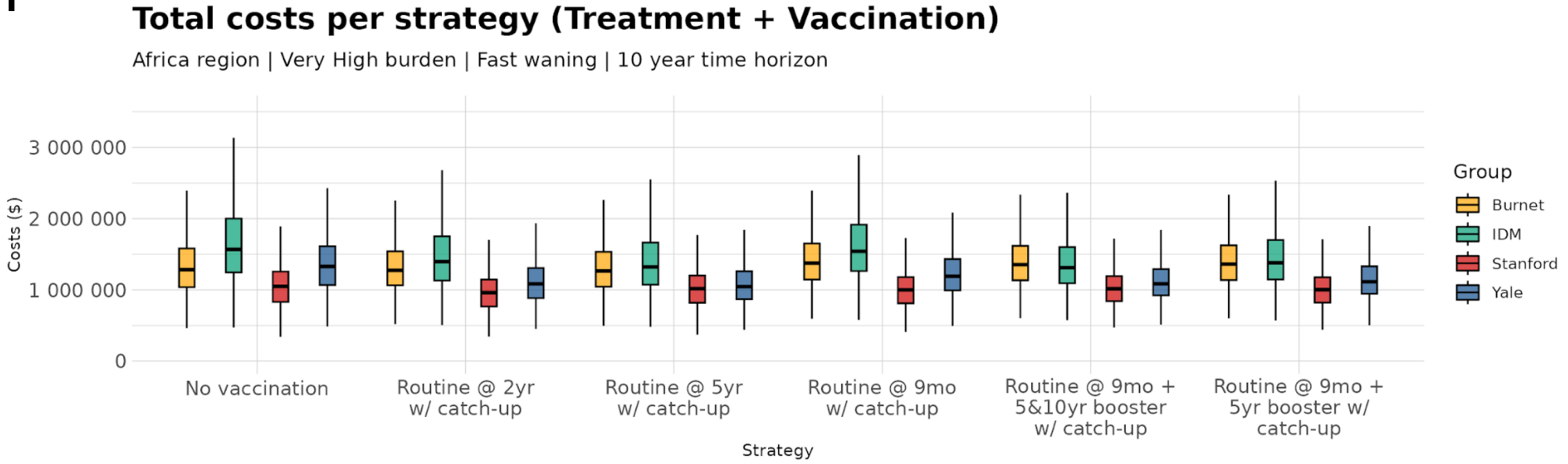


Fast waning



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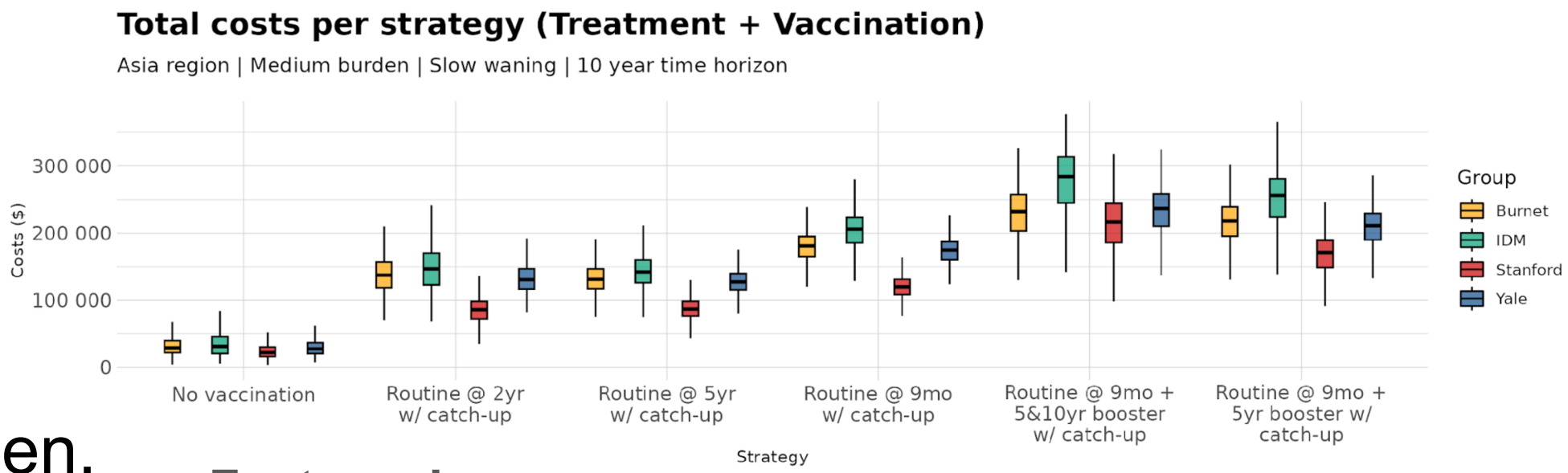
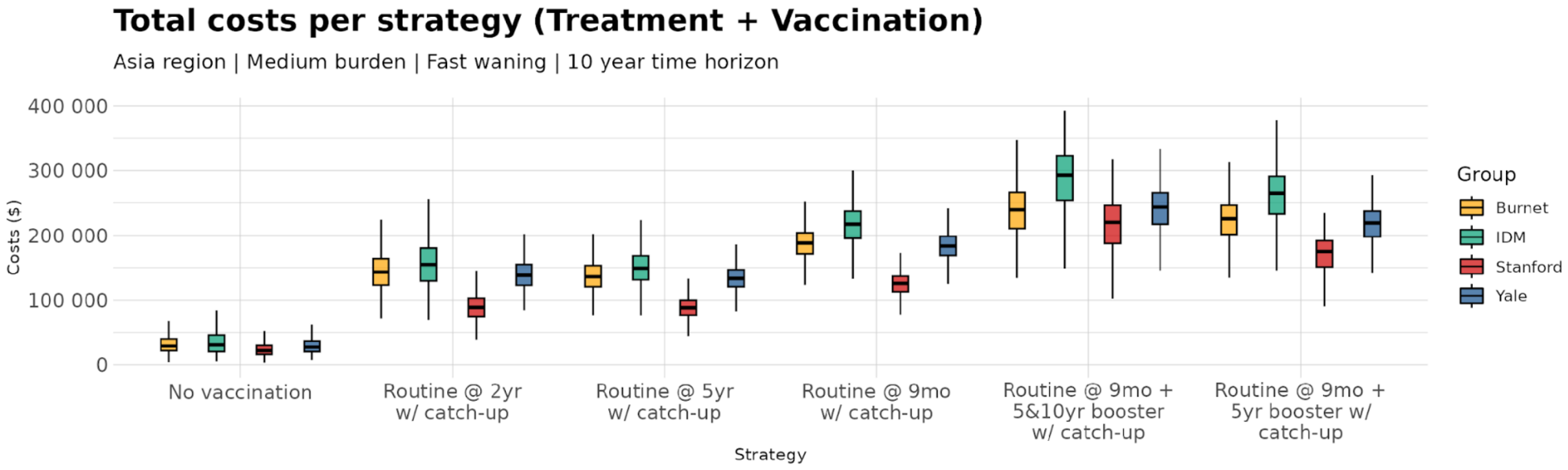
Slow waning

Total costs (discounted):

Medium burden, Asia region



Fast waning



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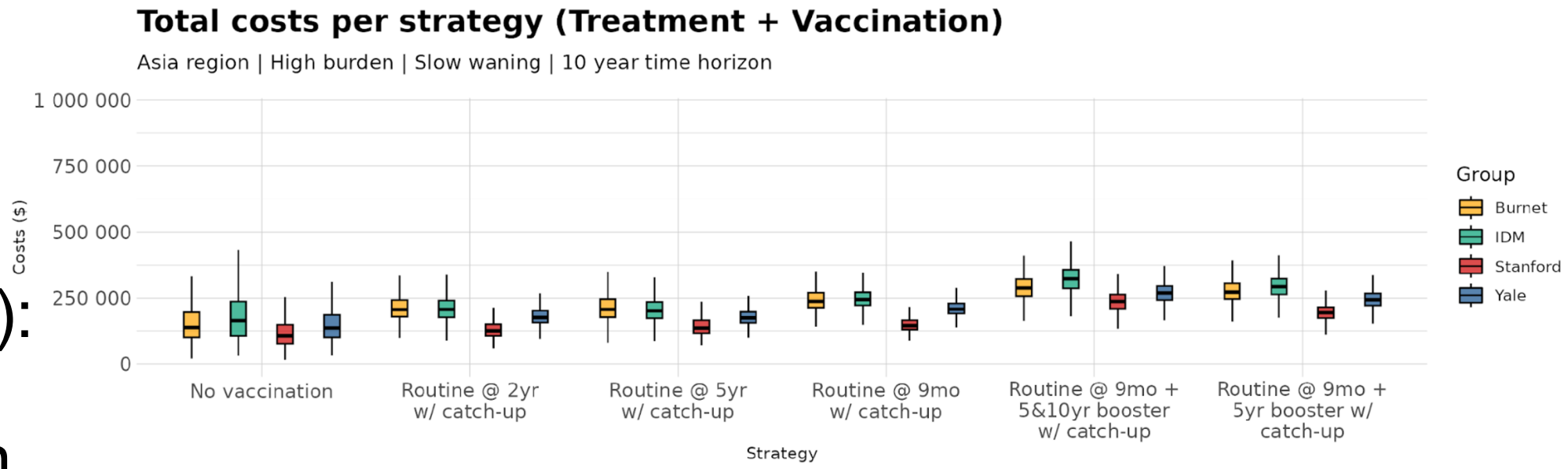
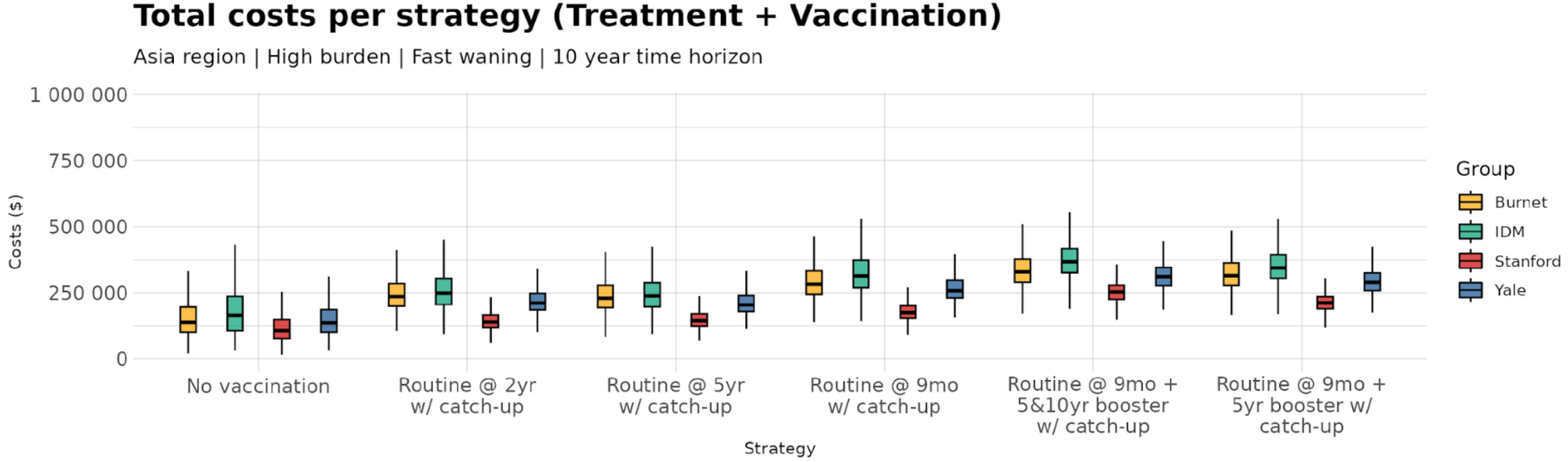
Total costs (discounted):

High burden, Asia region

Slow waning



Fast waning



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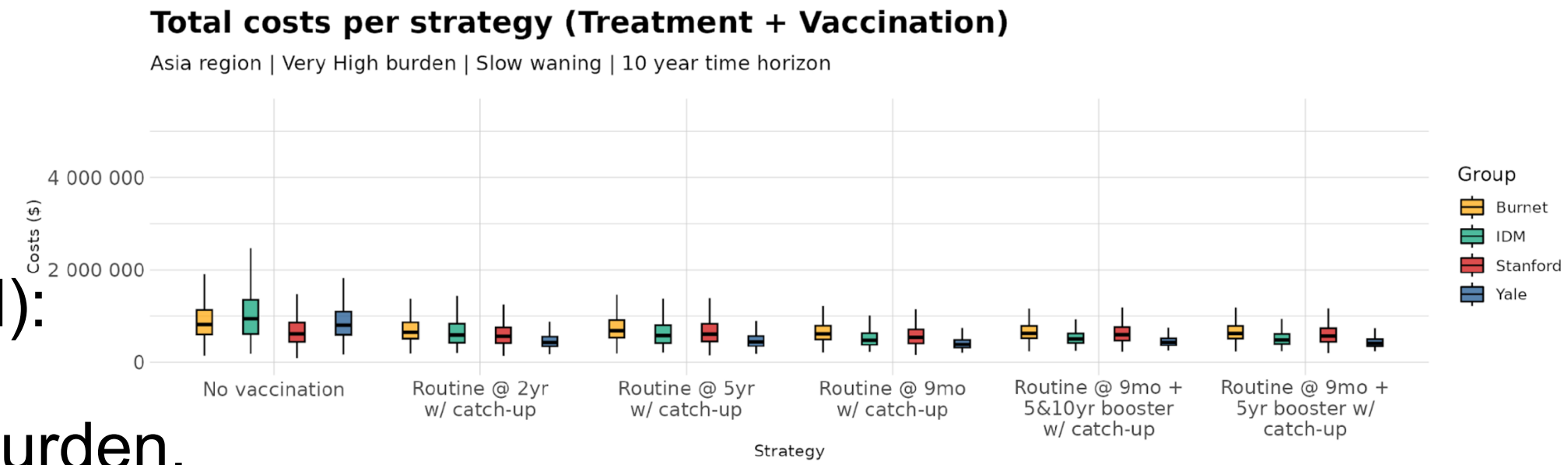
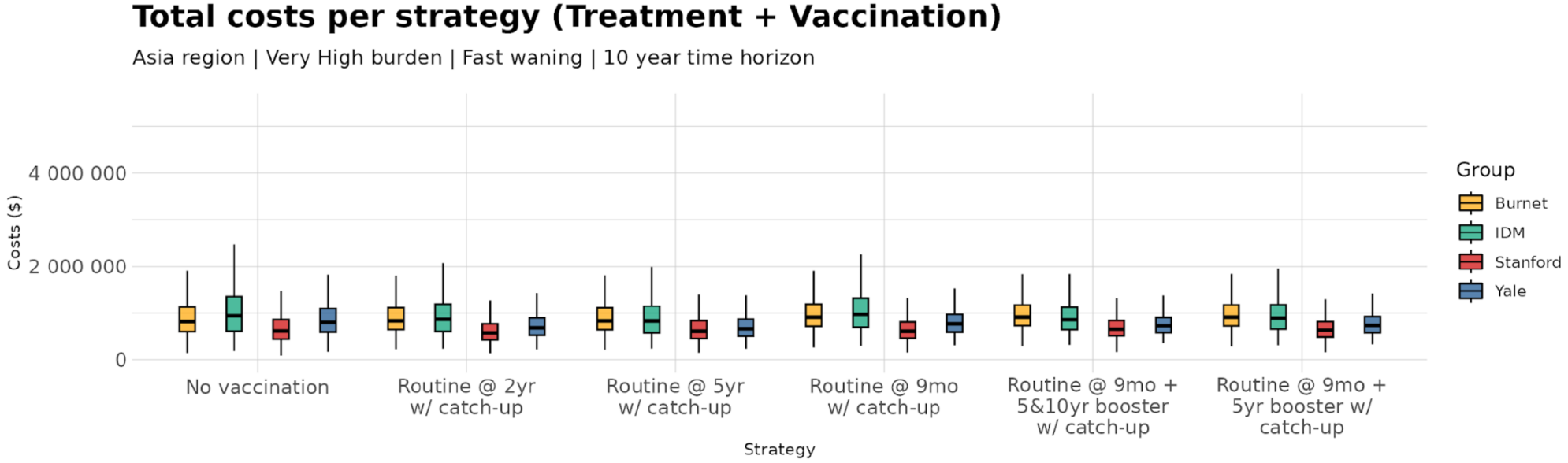


Fast waning



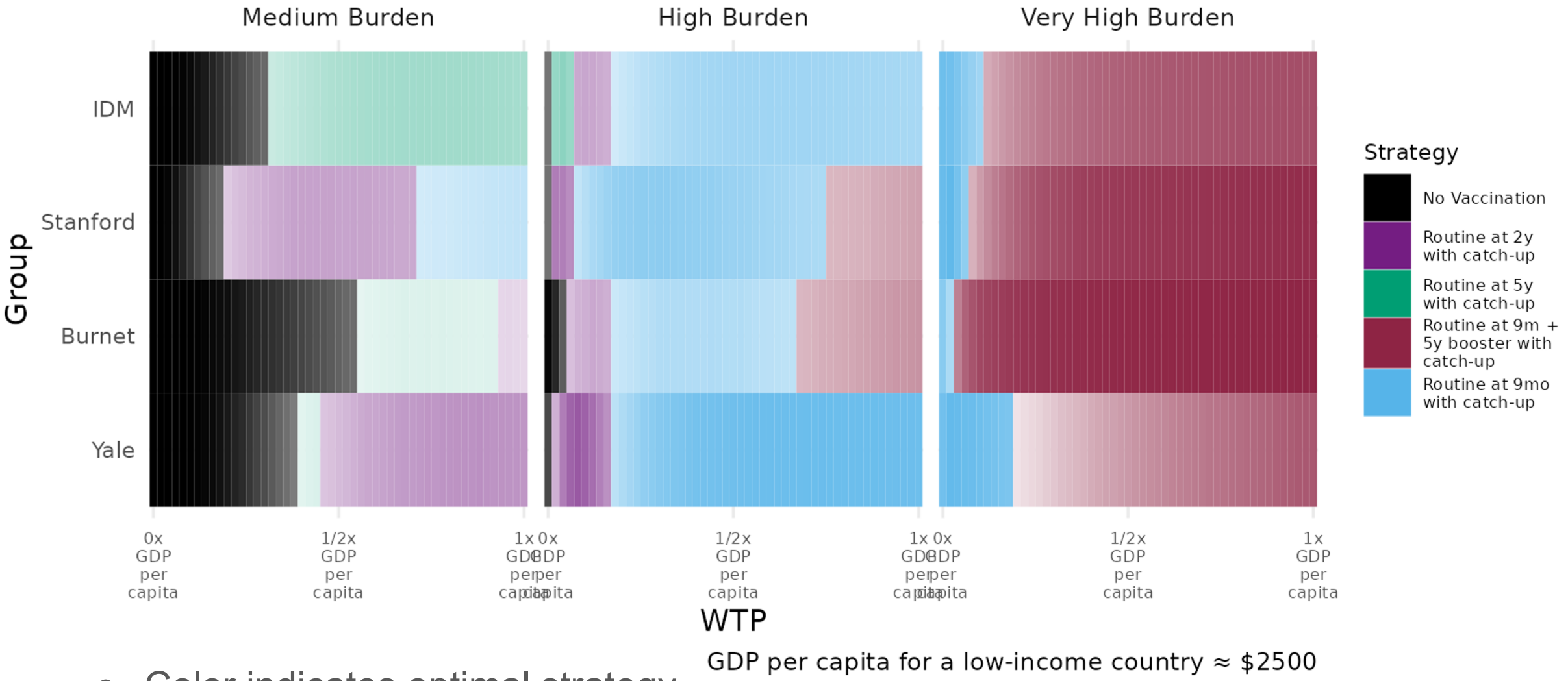
Note: Costs can differ between models due to differences in the assumed population size

Cost-Effectiveness Results

Cost-Effectiveness Acceptability Frontiers

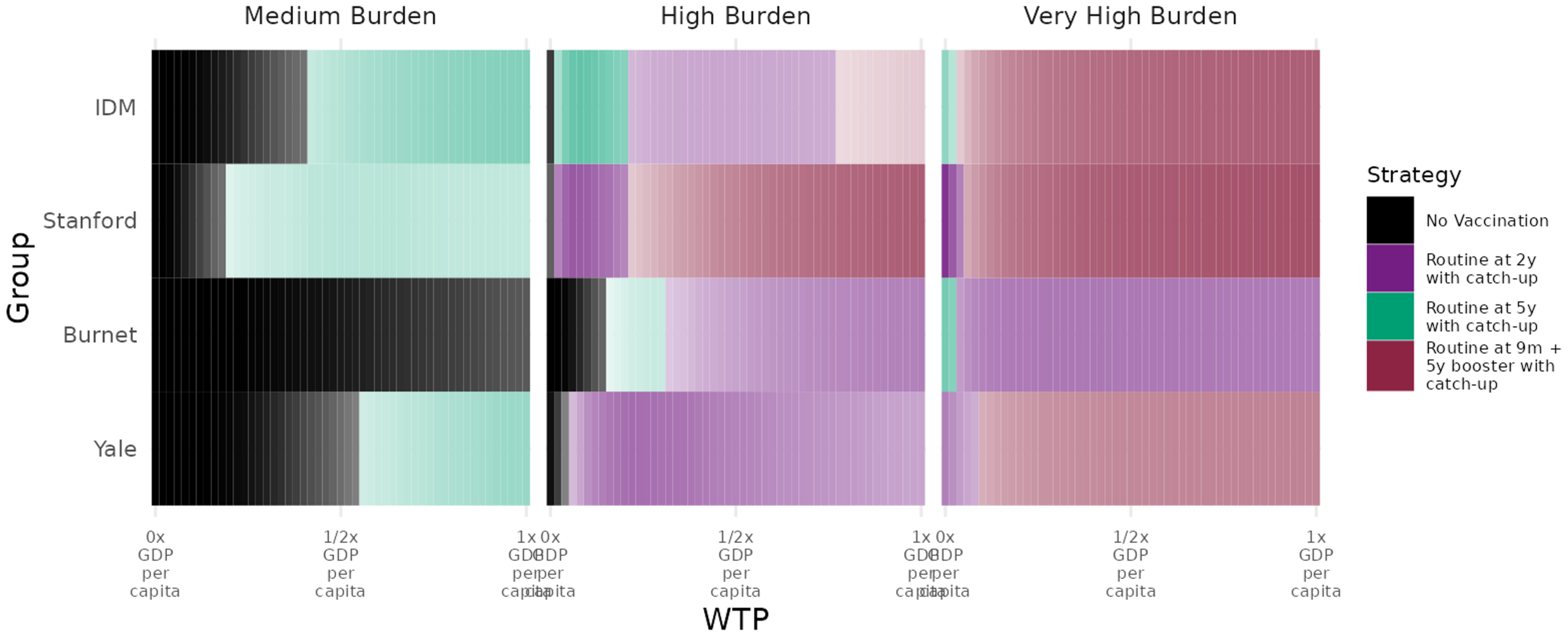
10 year time horizon

Cost-effectiveness Frontier
Africa | Slow waning



- Color indicates optimal strategy
- Shading represents probability it yields the highest net benefit (darker=higher probability)

Cost-effectiveness Frontier
Africa | Fast waning



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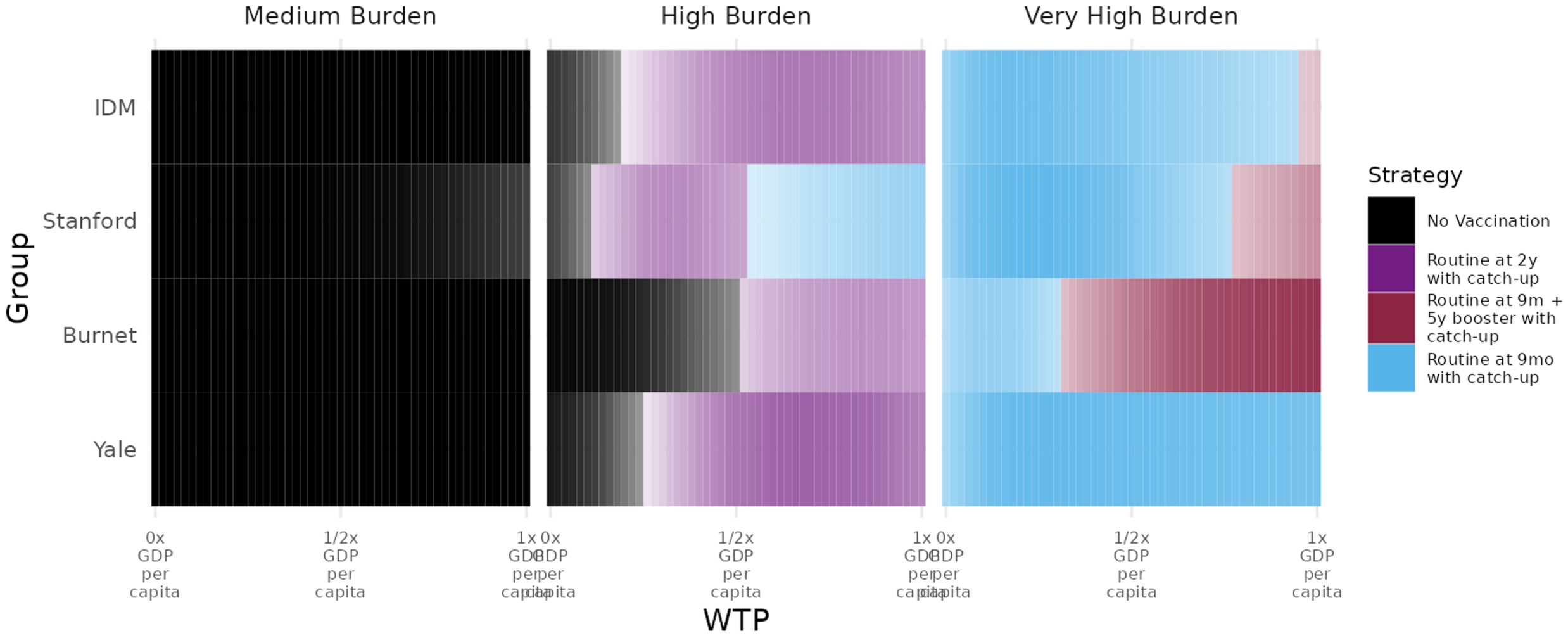
GDP per capita for a low-income country ≈ $2500

Cost-effectiveness Frontier
Asia | Slow waning



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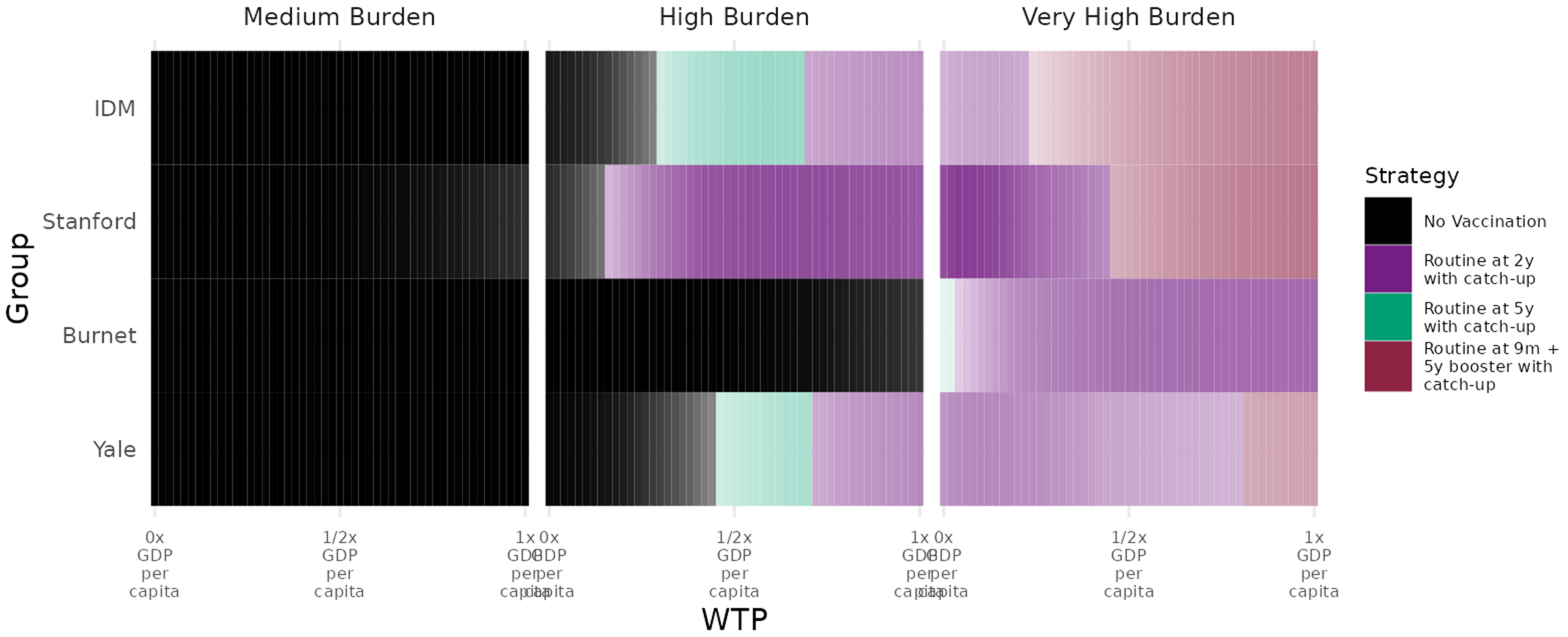
Cost-effectiveness Frontier
Asia | Fast waning



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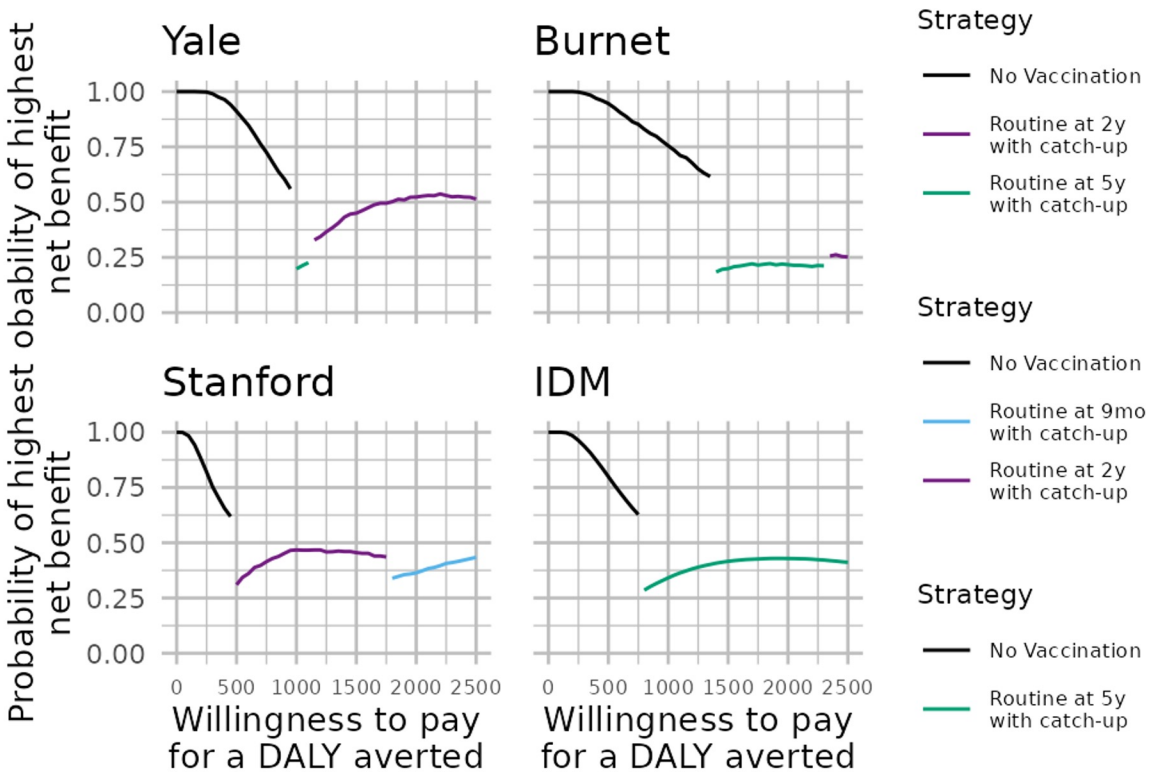
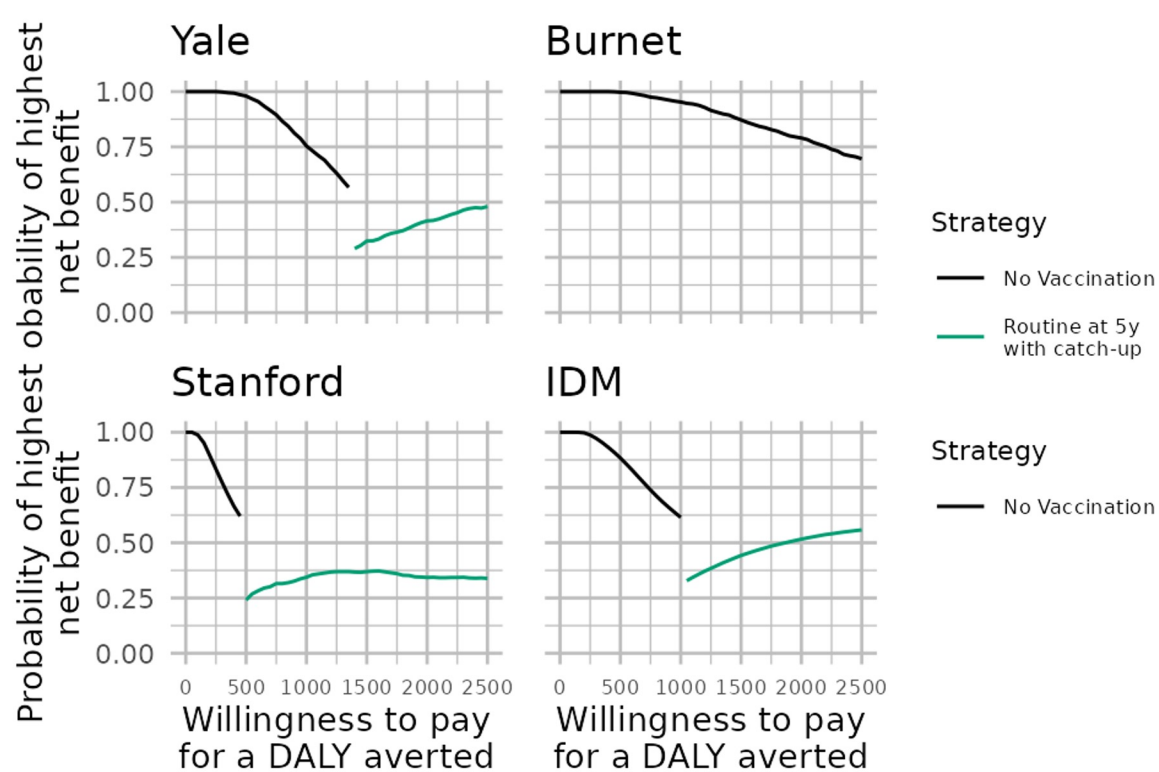
Cost-effectiveness Acceptability Frontiers 10yr time horizon

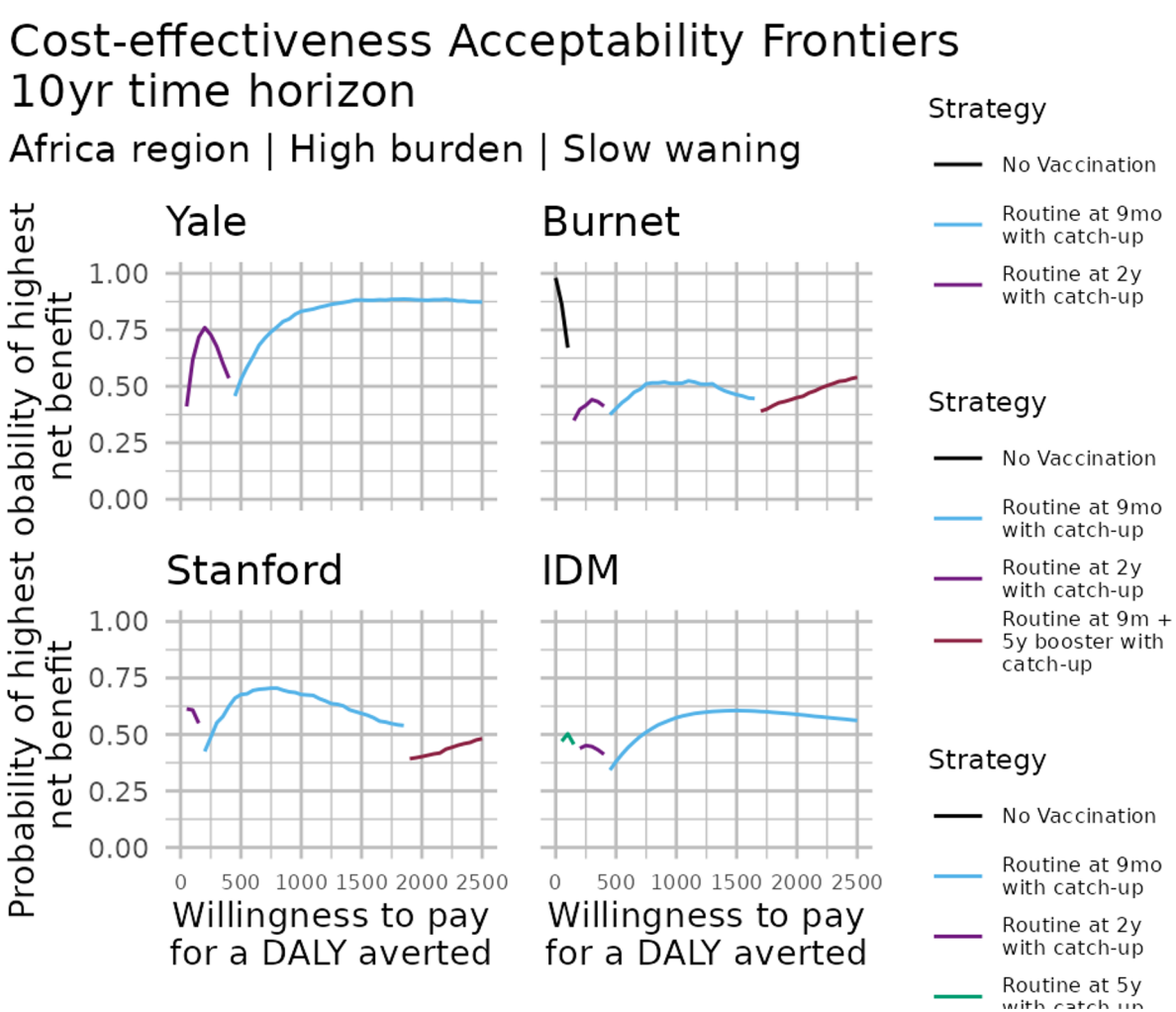
Africa region | Medium burden | Slow waning



Cost-effectiveness Acceptability Frontiers 10yr time horizon

Africa region | Medium burden | Fast waning




Cost-effectiveness Acceptability Frontiers
10yr time horizon
Africa region | High burden | Slow waning
Yale
Burnet
Stanford
IDM
Probability of highest obability of highest net benefit
1.00
0.75
0.50
0.25
0.00
0
500
1000
1500
2000
2500
Willingness to pay for a DALY averted
Strategy
No Vaccination
Routine at 9mo with catch-up
Routine at 2y with catch-up
Routine at 9m + 5y booster with catch-up
Routine at 5y with catch-up

Cost-effectiveness Acceptability Frontiers
10yr time horizon
Africa region | High burden | Fast waning
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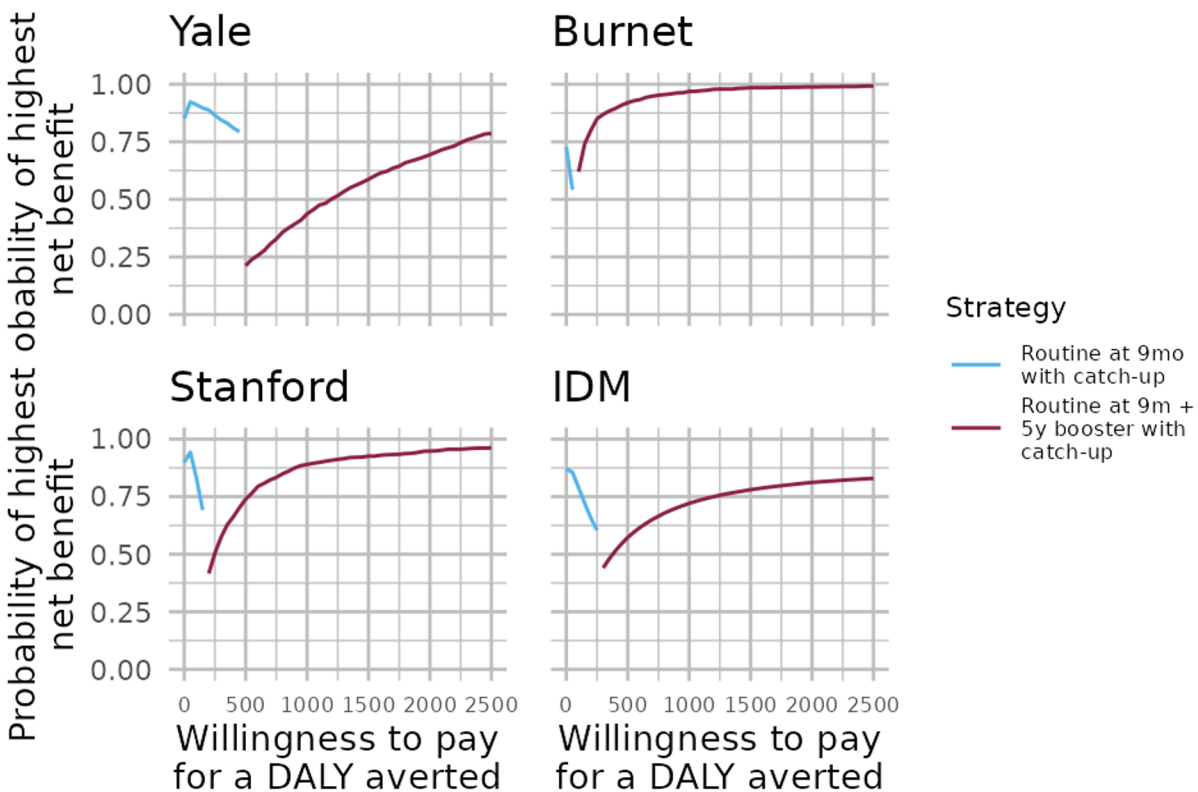
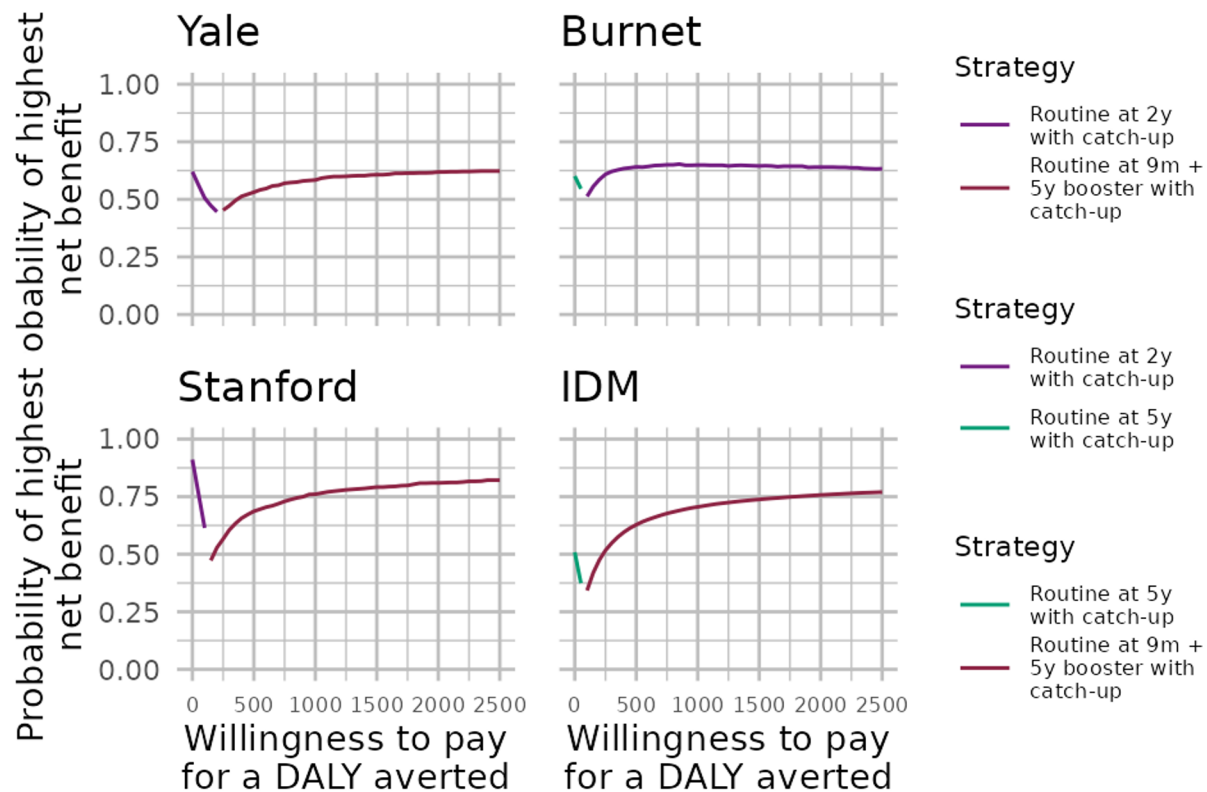
Cost-effectiveness Acceptability Frontiers 10yr time horizon

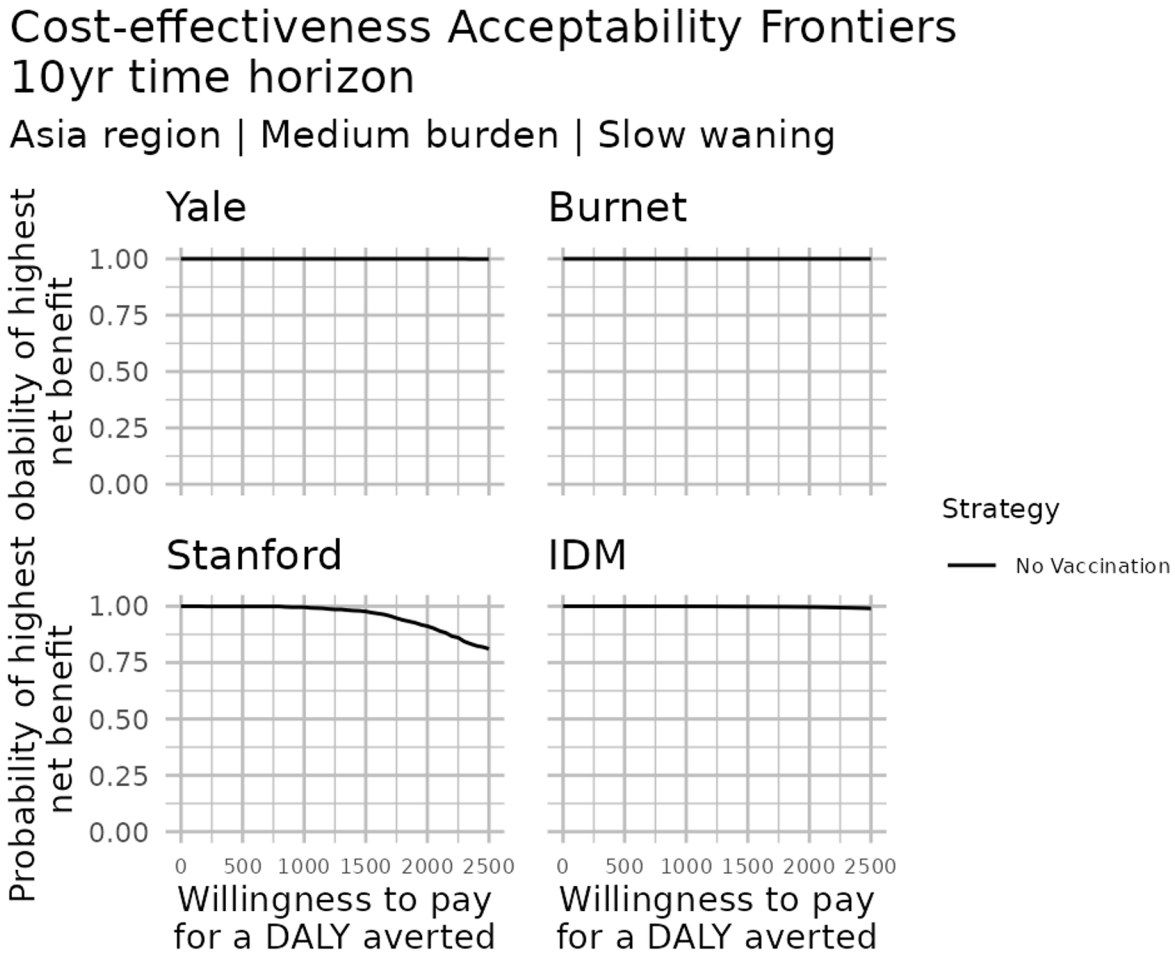
Africa region | Very High burden | Slow waning

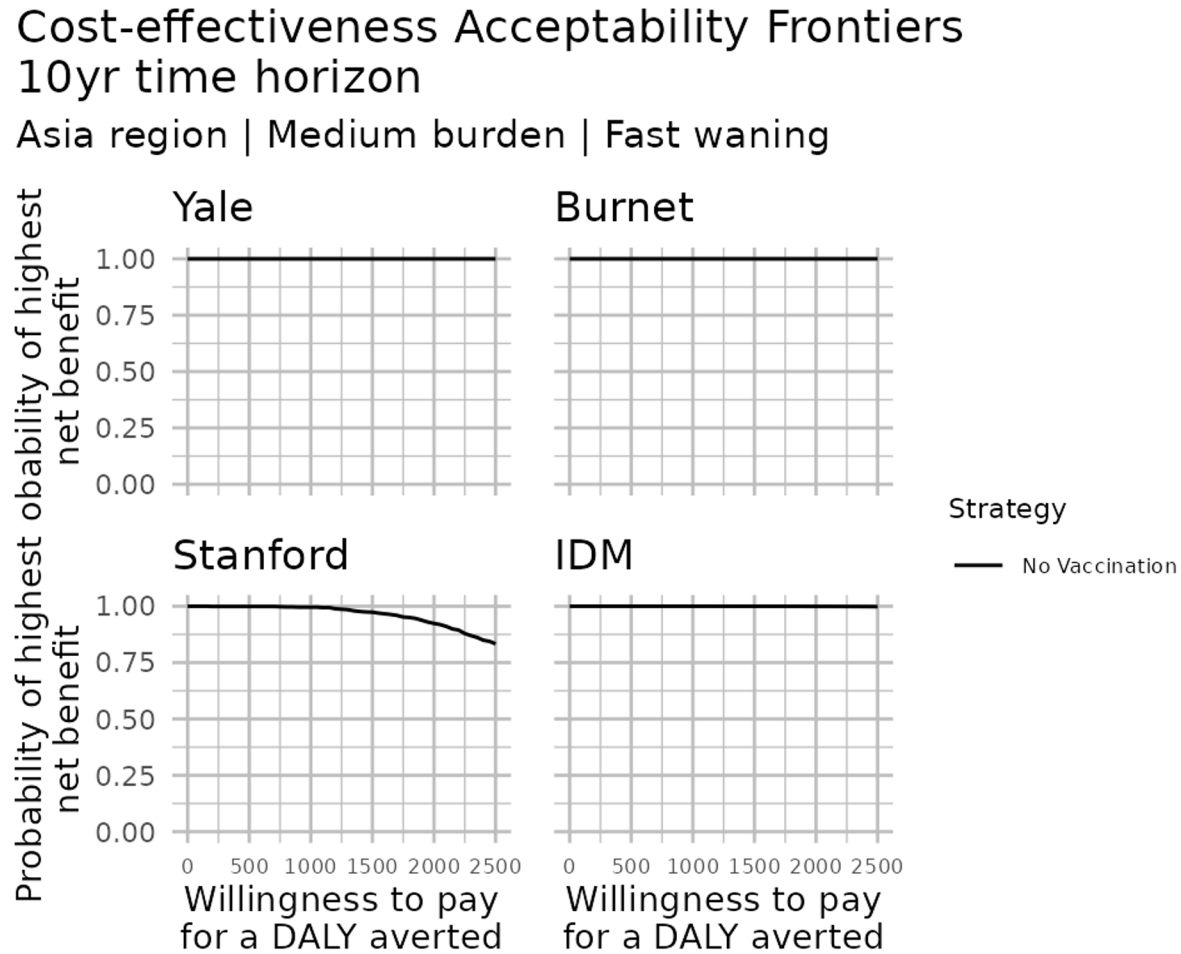


Cost-effectiveness Acceptability Frontiers 10yr time horizon

Africa region | Very High burden | Fast waning




Cost-effectiveness Acceptability Frontiers
10yr time horizon
Asia region | Medium burden | Slow waning
Yale
Burnet
Stanford
IDM
Probability of highest obability of highest net benefit
net benefit
1.00
0.75
0.50
0.25
0.00
0
500
1000
1500
2000
2500
Willingness to pay for a DALY averted
Strategy
No Vaccination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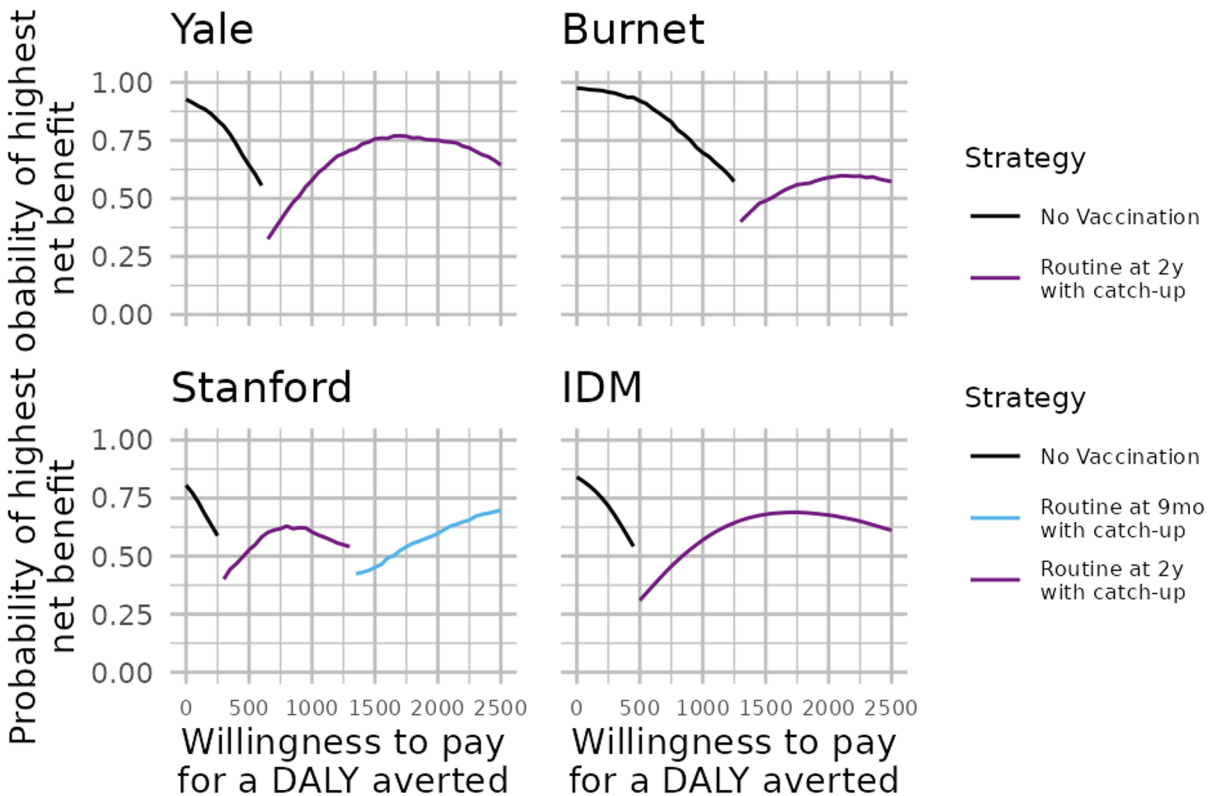
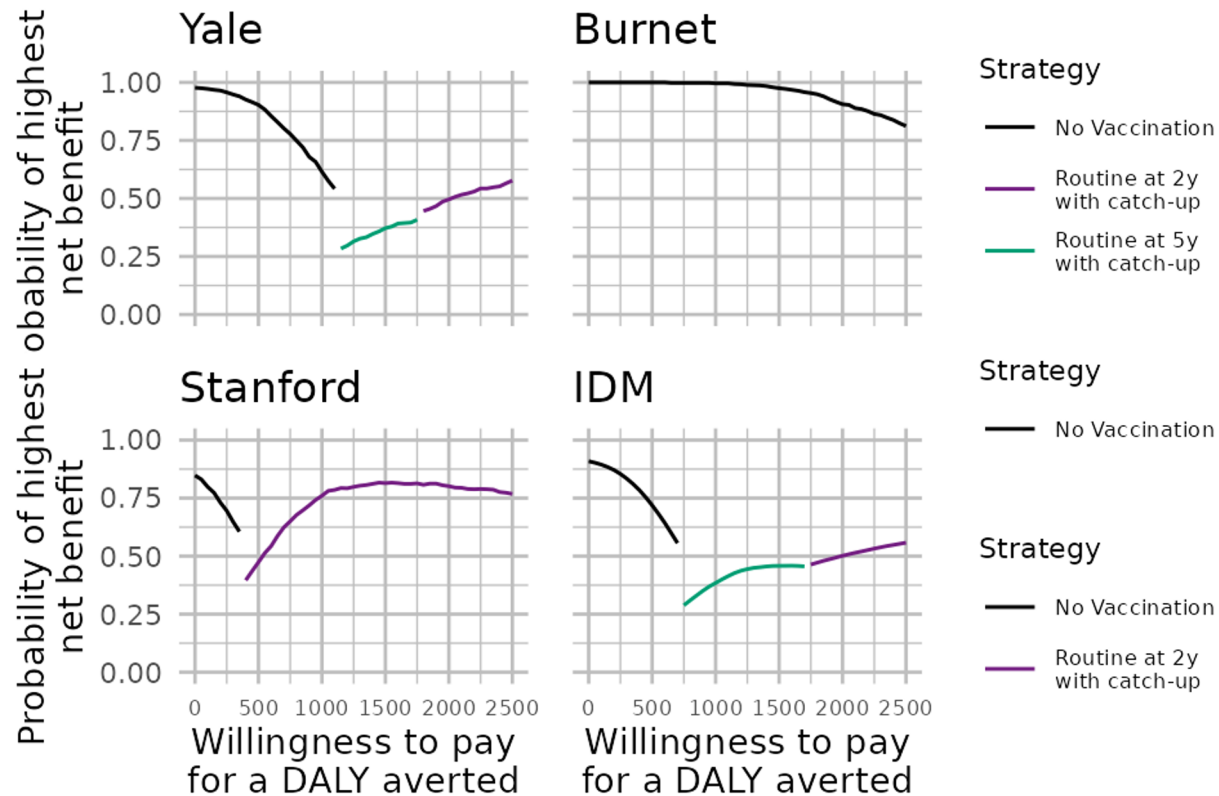
Cost-effectiveness Acceptability Frontiers 10yr time horizon

Asia region | High burden | Slow waning



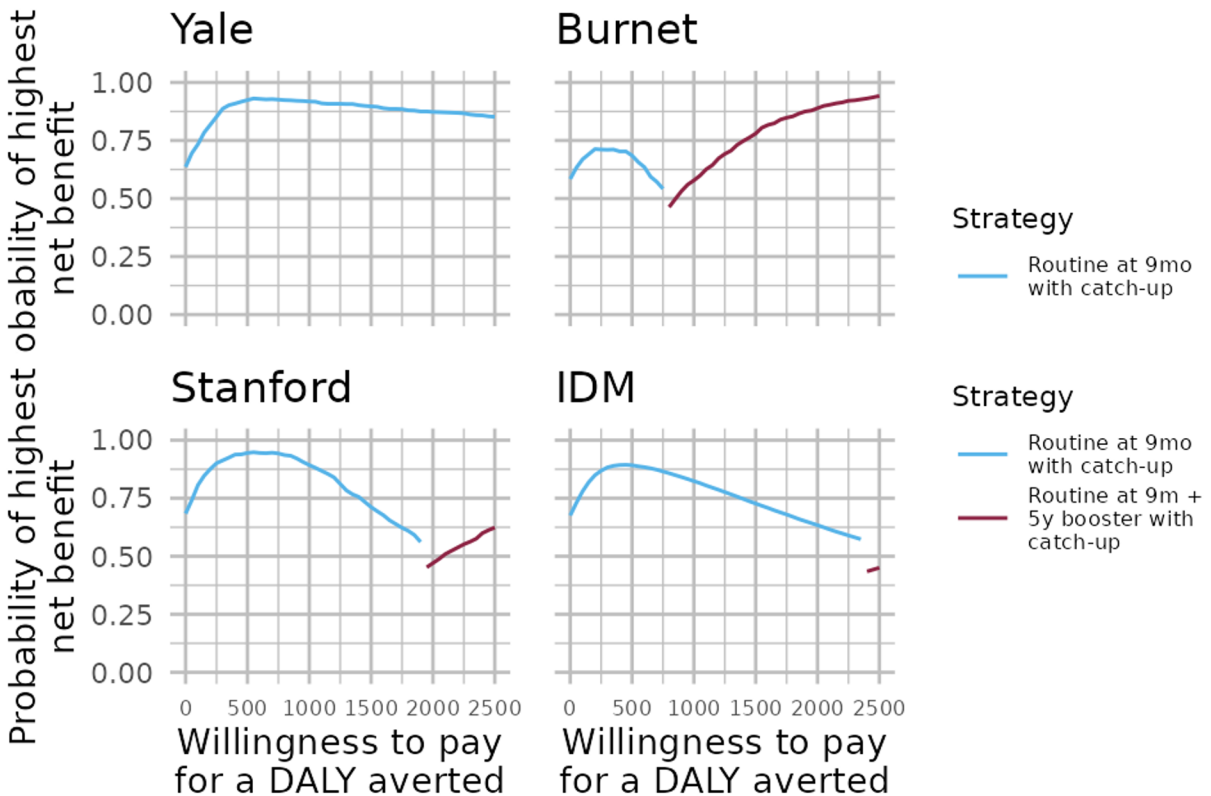
Cost-effectiveness Acceptability Frontiers 10yr time horizon

Asia region | High burden | Fast waning



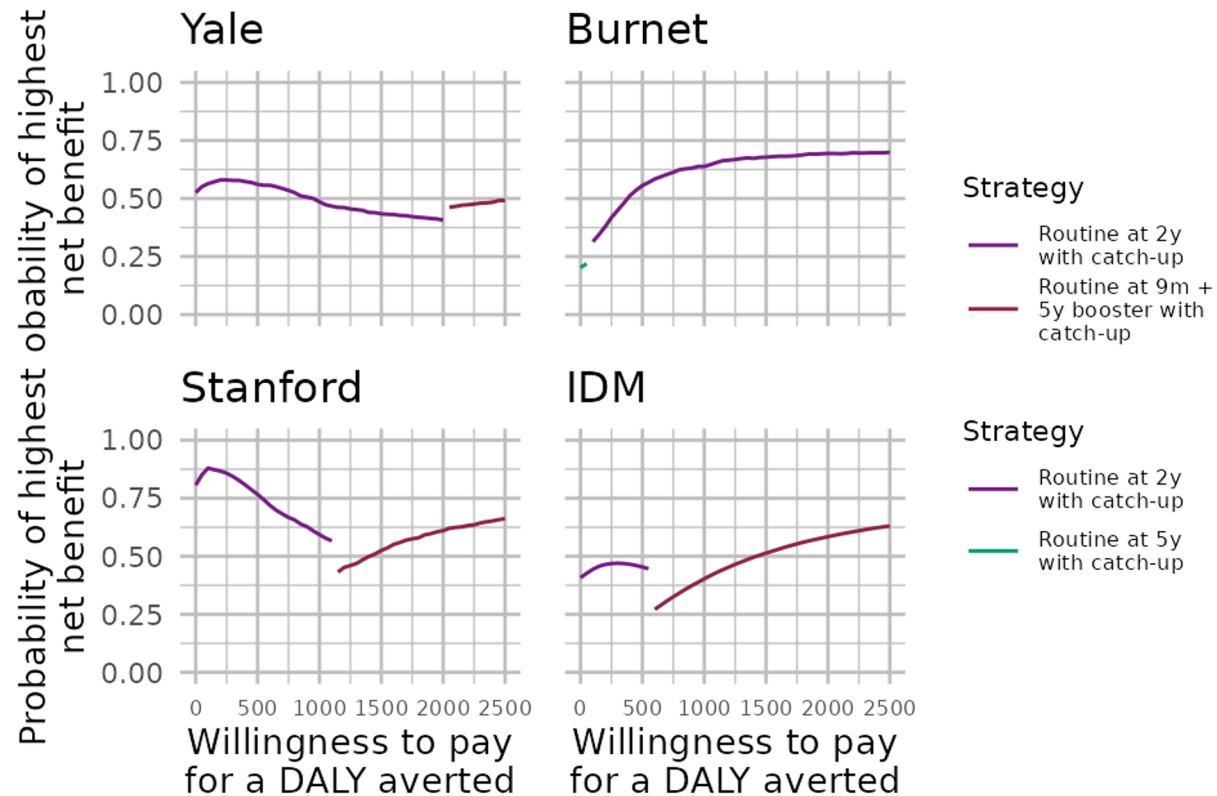
Cost-effectiveness Acceptability Frontiers 10yr time horizon

Asia region | Very High burden | Slow waning



Cost-effectiveness Acceptability Frontiers 10yr time horizon

Asia region | Very High burden | Fast waning



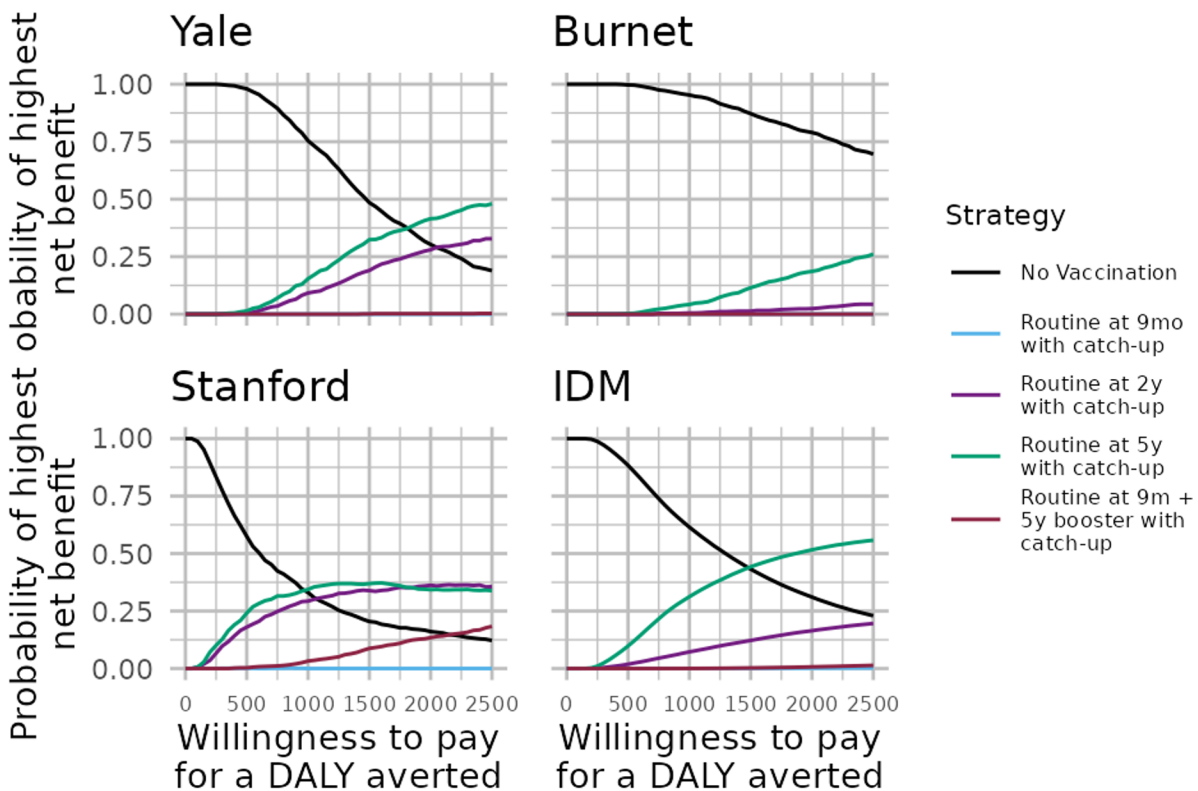
Cost-Effectiveness Results

Cost-Effectiveness Acceptability Curves

10 year time horizon

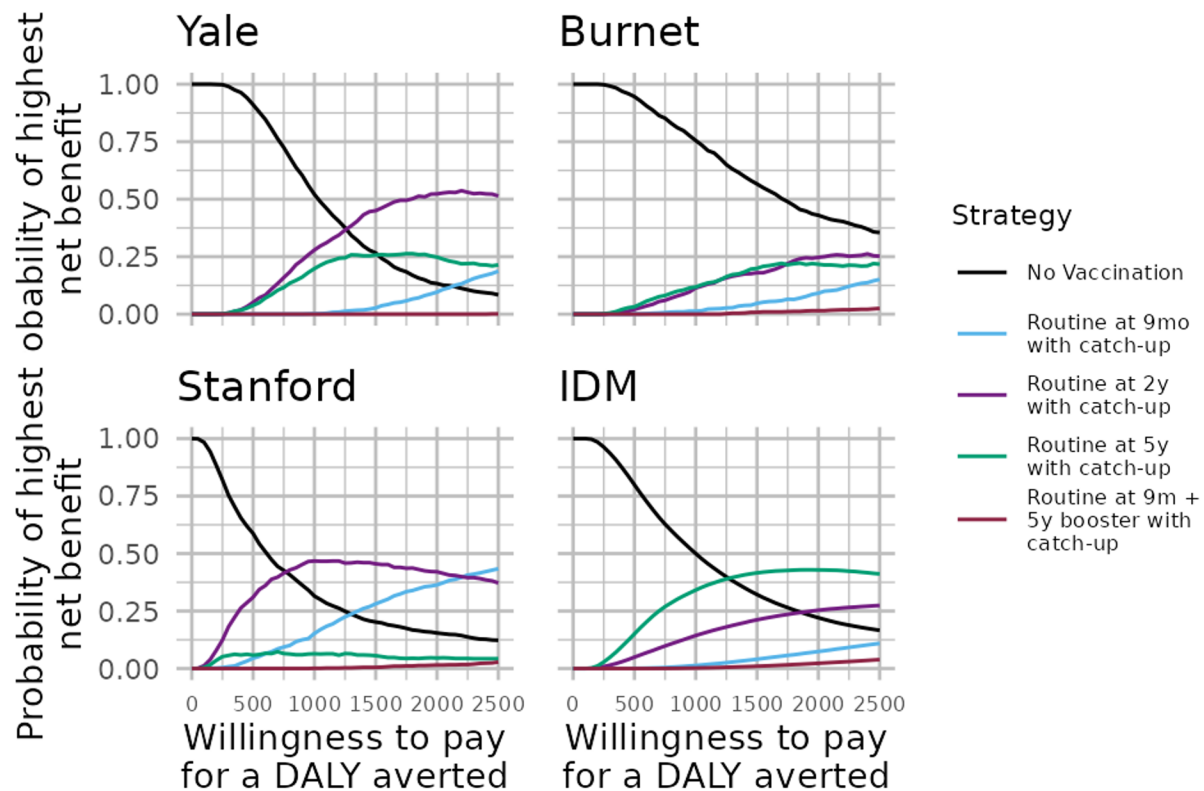
Cost-effectiveness Acceptability Curves
10yr time horizon

Africa region | Medium burden | Fast waning



Cost-effectiveness Acceptability Curves
10yr time horizon

Africa region | Medium burden | Slow waning



Cost-effectiveness Acceptability Curves
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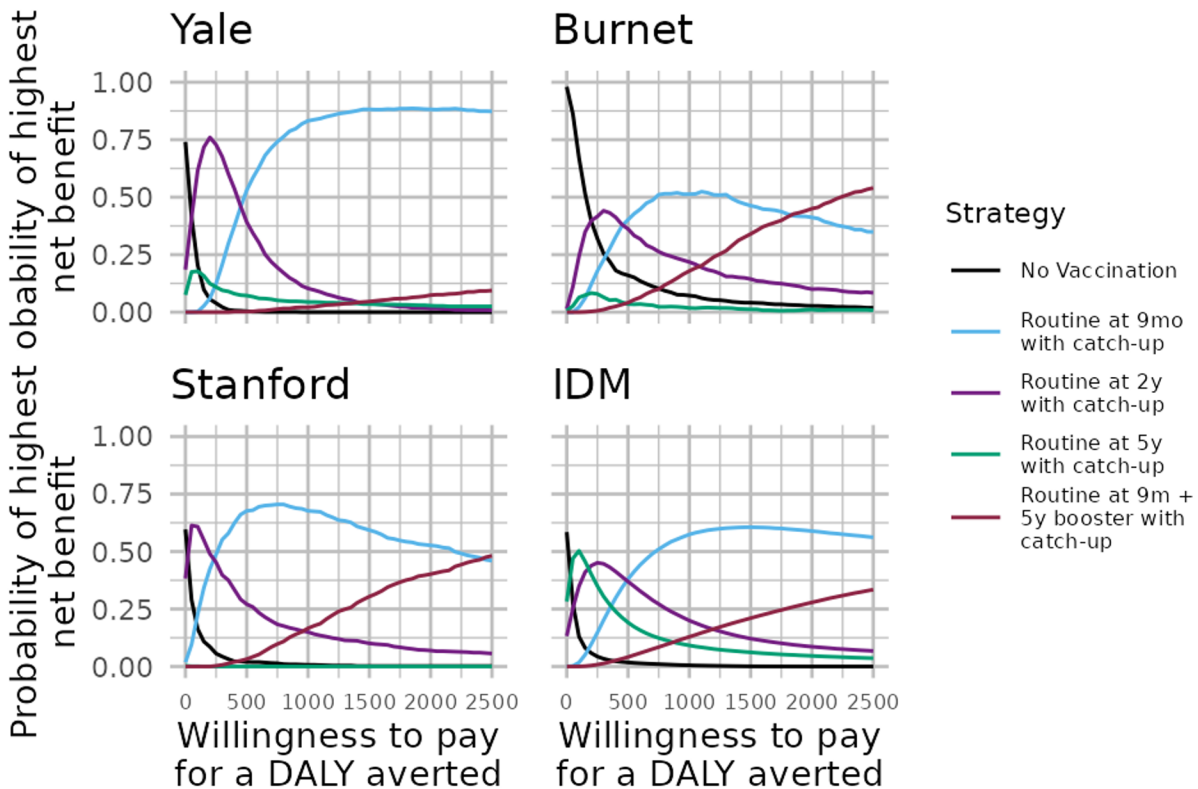
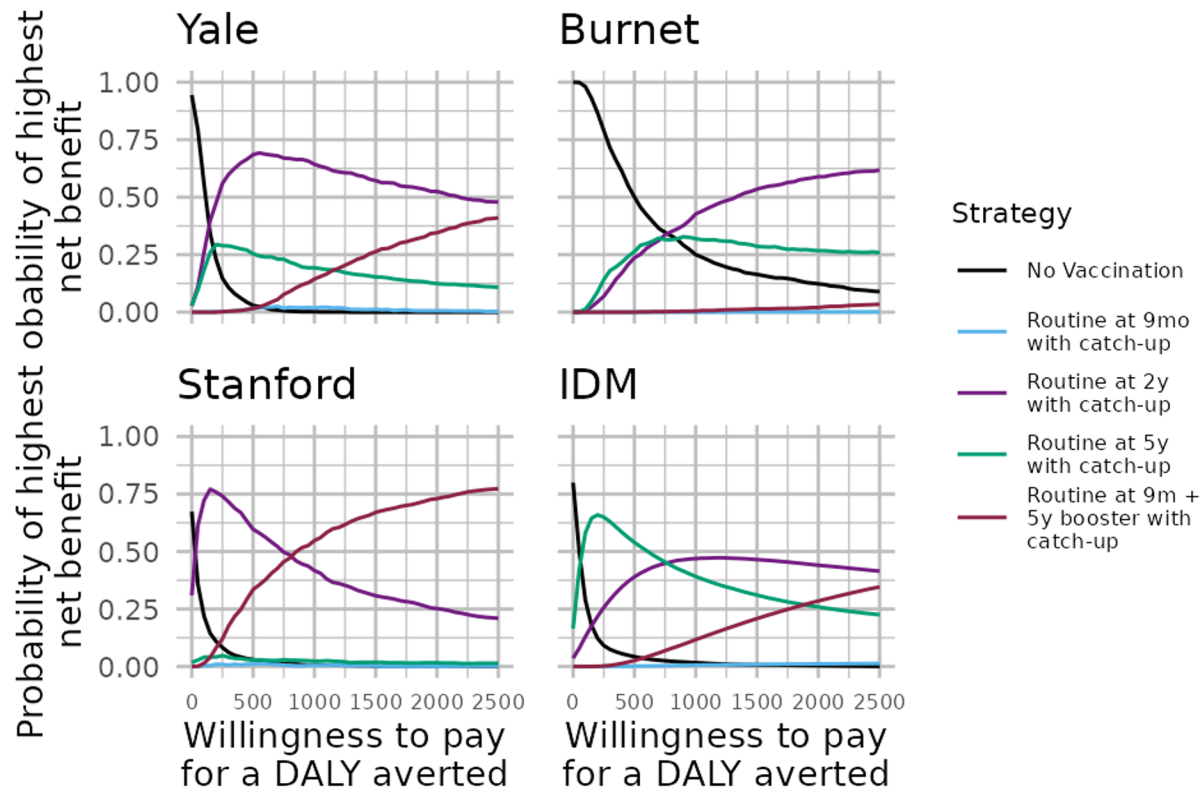
Africa region | High burden | Slow waning



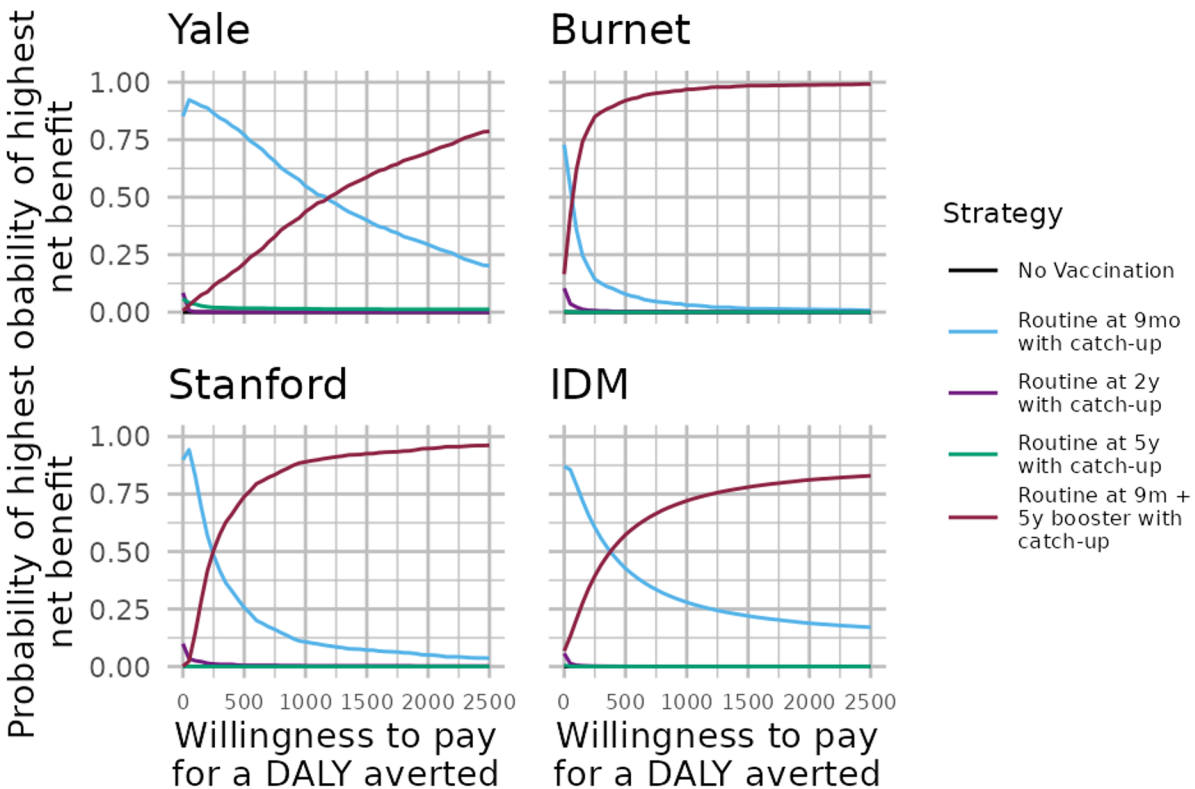
Cost-effectiveness Acceptability Curves
10yr time horizon

Africa region | High burden | Fast waning



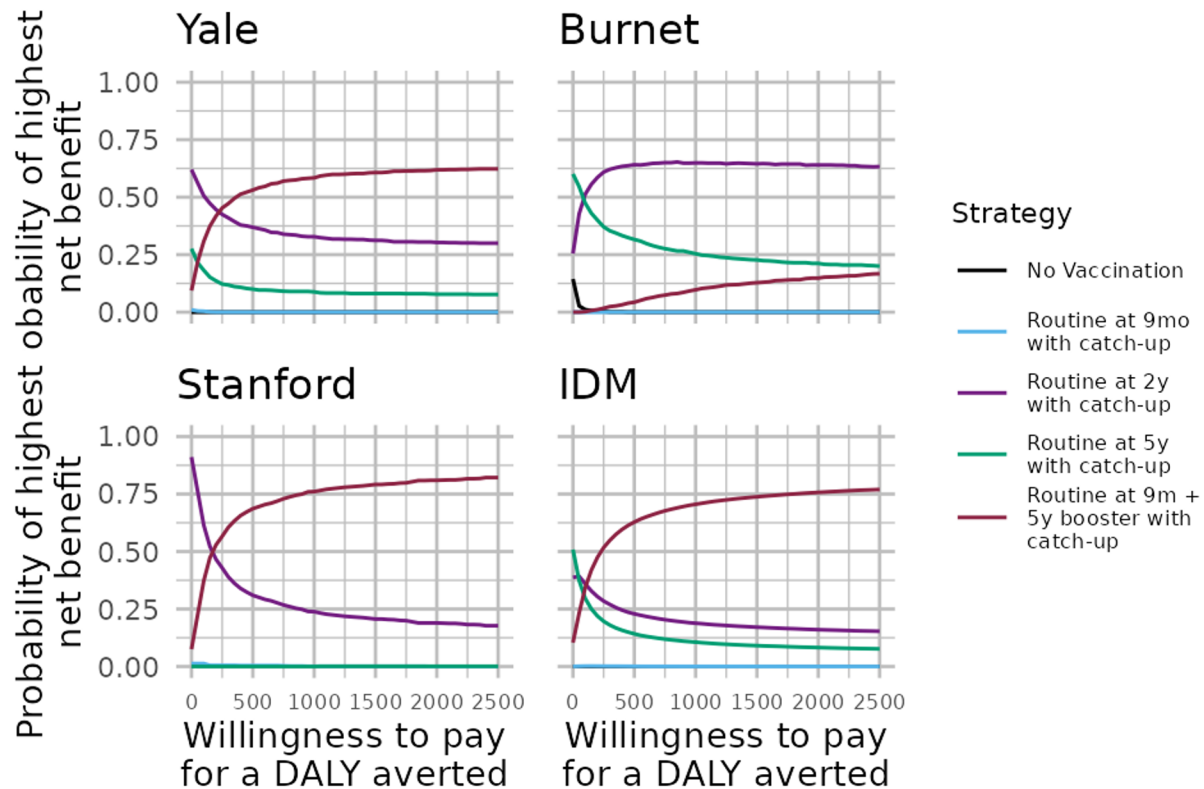
Cost-effectiveness Acceptability Curves 10yr time horizon

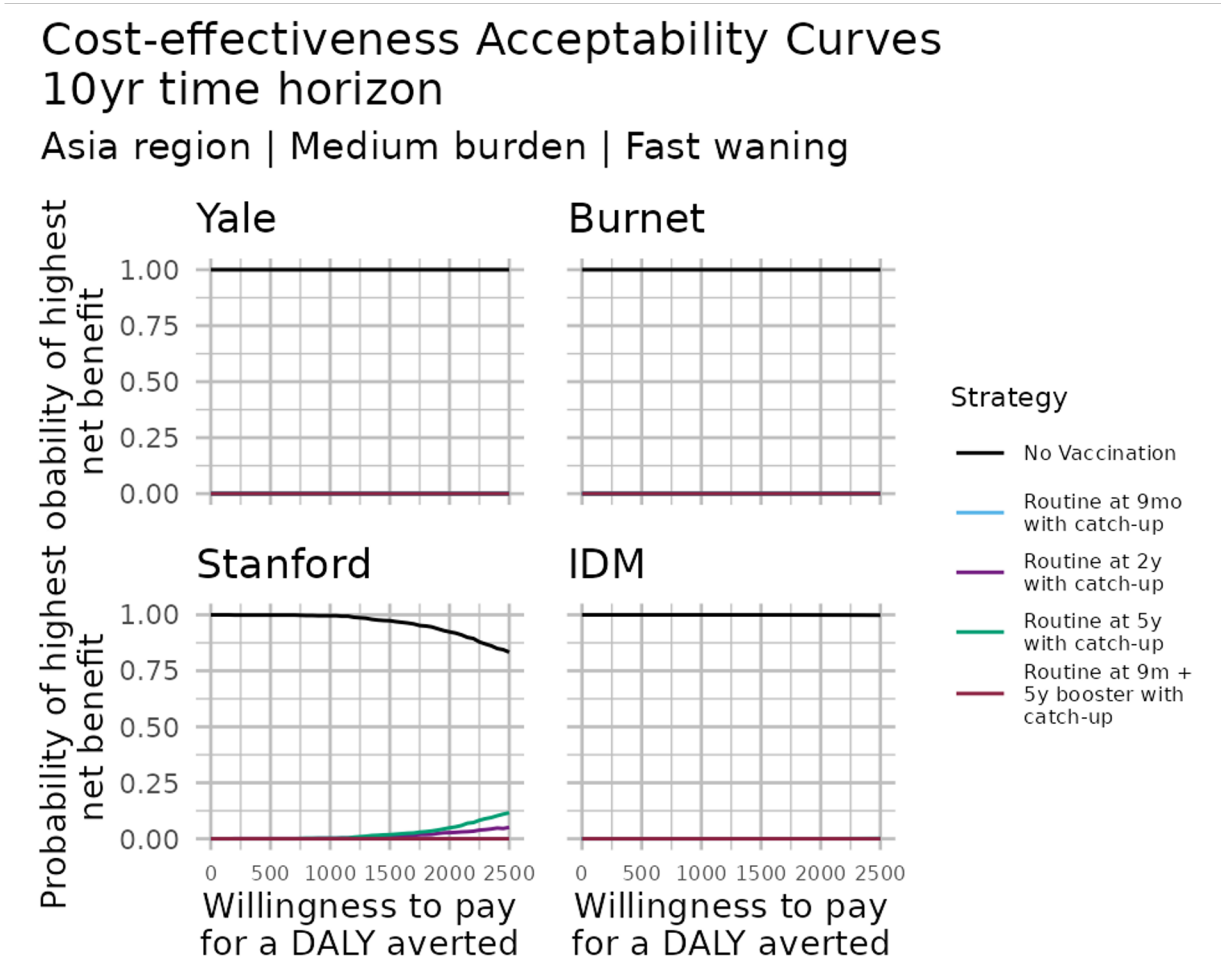
Africa region | Very High burden | Slow waning



Cost-effectiveness Acceptability Curves 10yr time horizon

Africa region | Very High burden | Fast waning




Cost-effectiveness Acceptability Curves
10yr time horizon
Asia region | Medium burden | Fast waning
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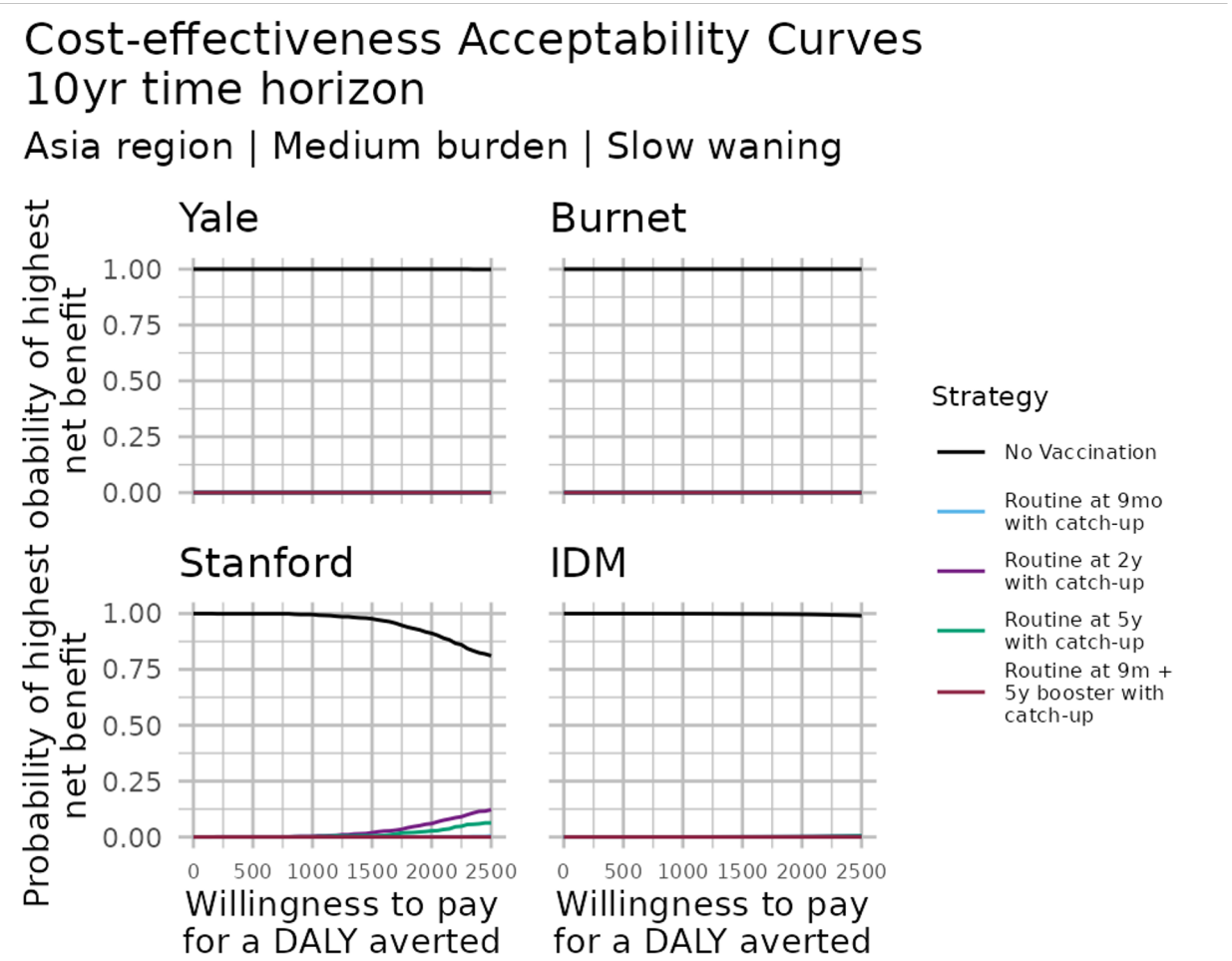
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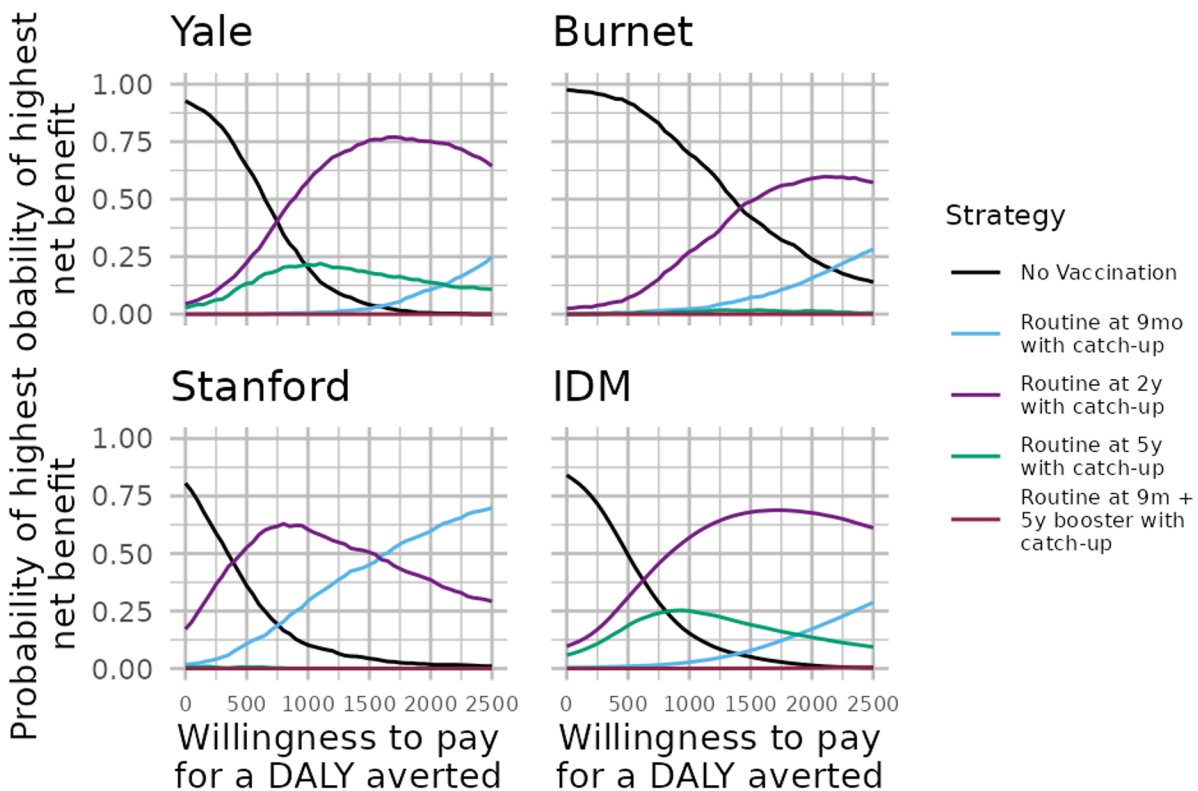
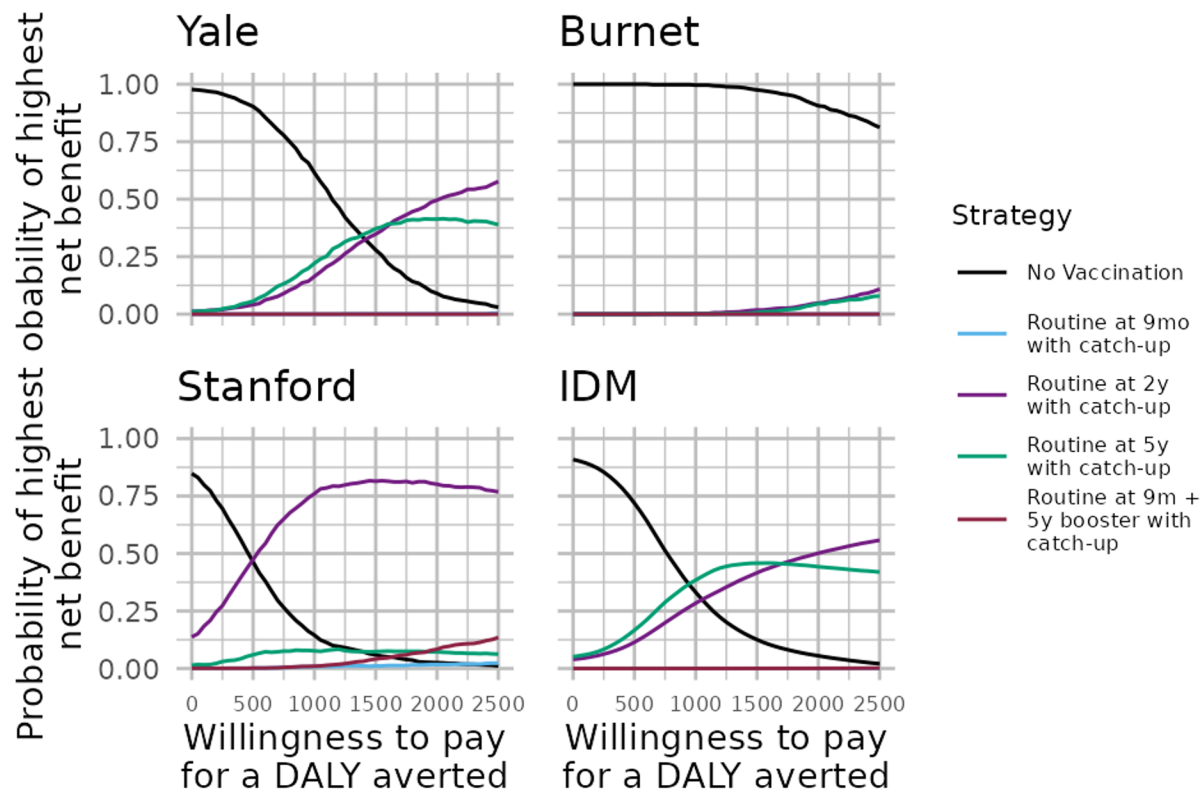
Cost-effectiveness Acceptability Curves
10yr time horizon

Asia region | High burden | Slow waning



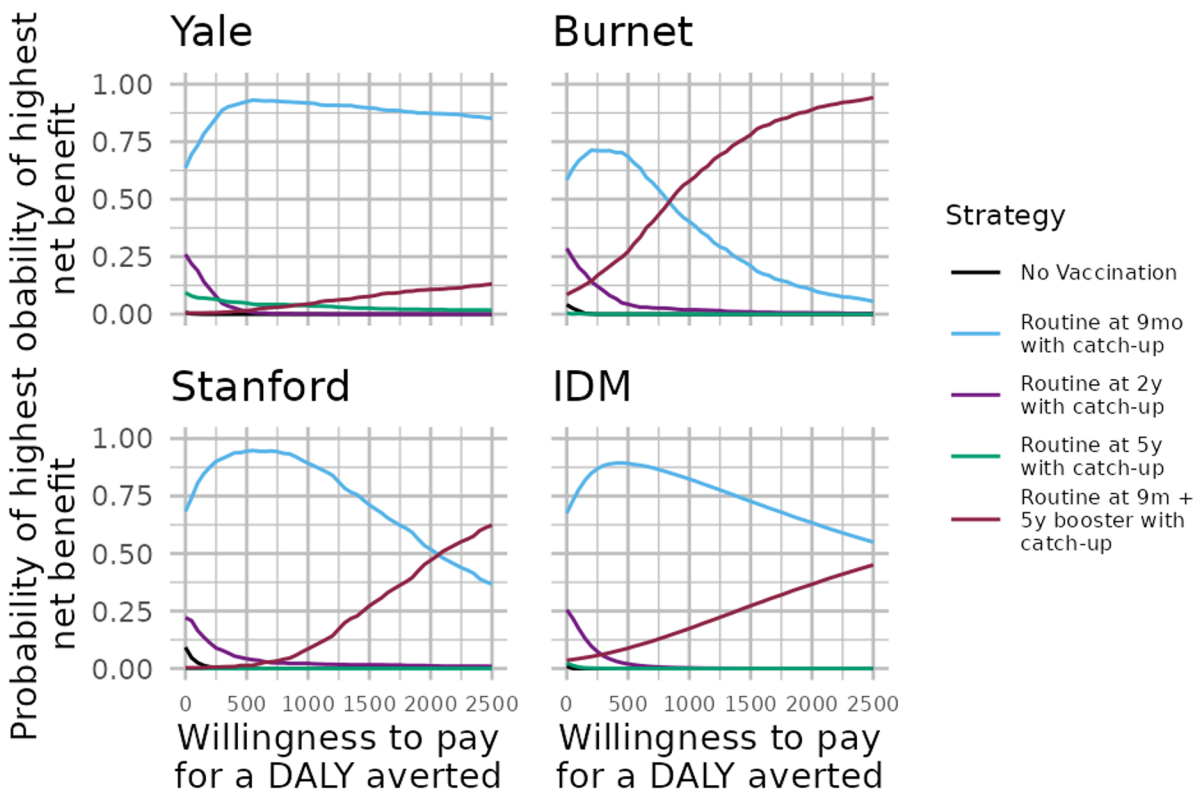
Cost-effectiveness Acceptability Curves
10yr time horizon

Asia region | High burden | Fast waning



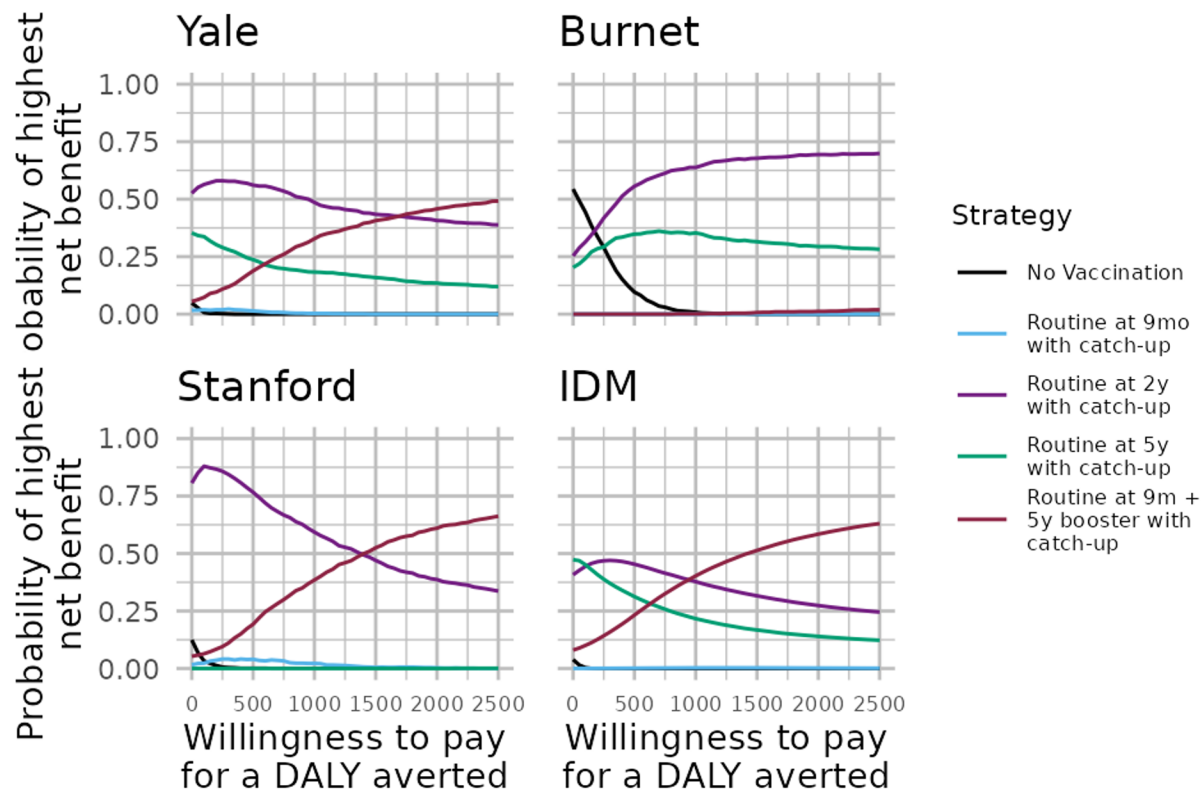
Cost-effectiveness Acceptability Curves 10yr time horizon

Asia region | Very High burden | Slow waning



Cost-effectiveness Acceptability Curves 10yr time horizon

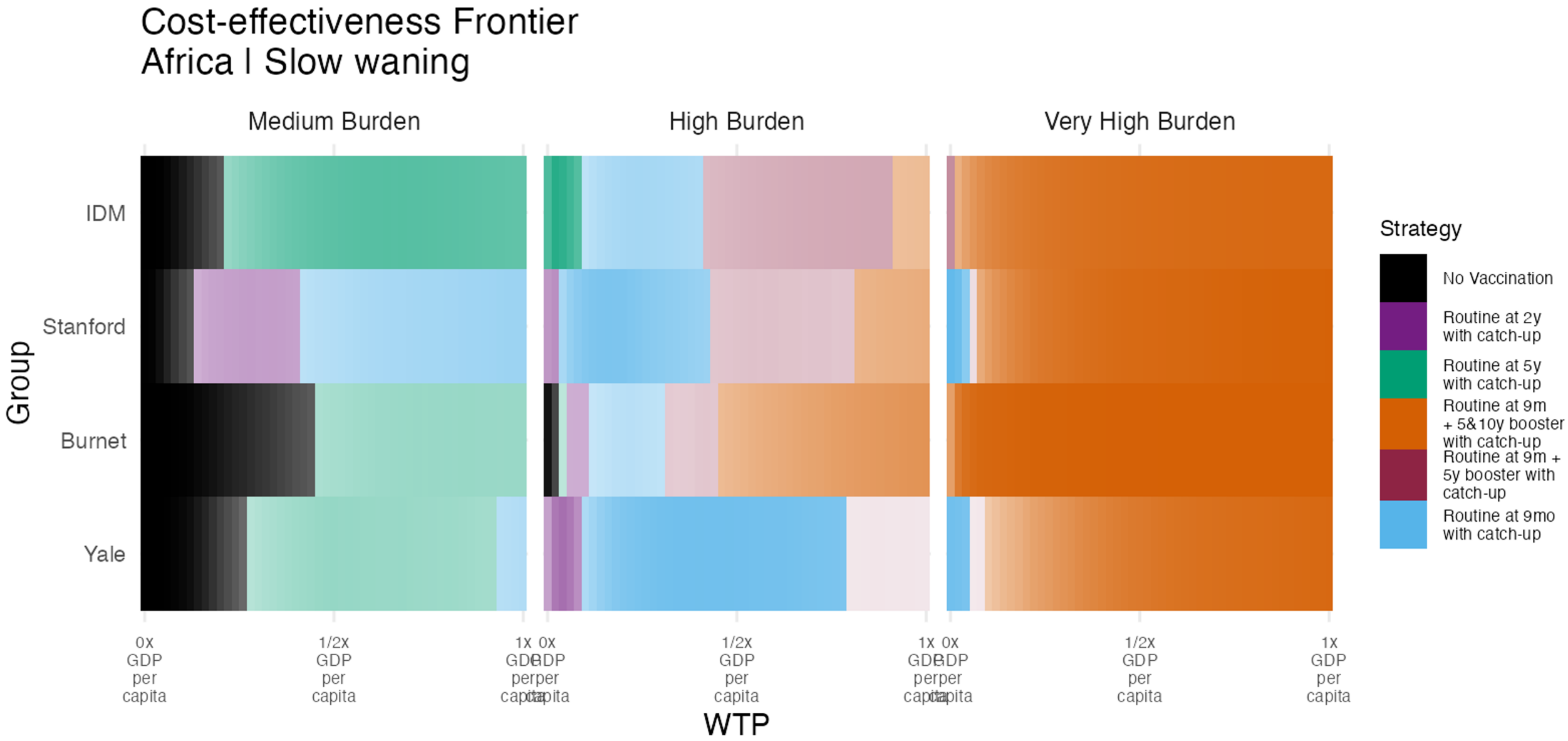
Asia region | Very High burden | Fast waning



Cost-Effectiveness Results

Cost-effectiveness Acceptability Frontiers

20 year time horizon



- Color indicates optimal strategy
- Shading represents probability it yields the highest net benefit (darker=higher probability)

GDP per capita for a low-income country ≈ $2500

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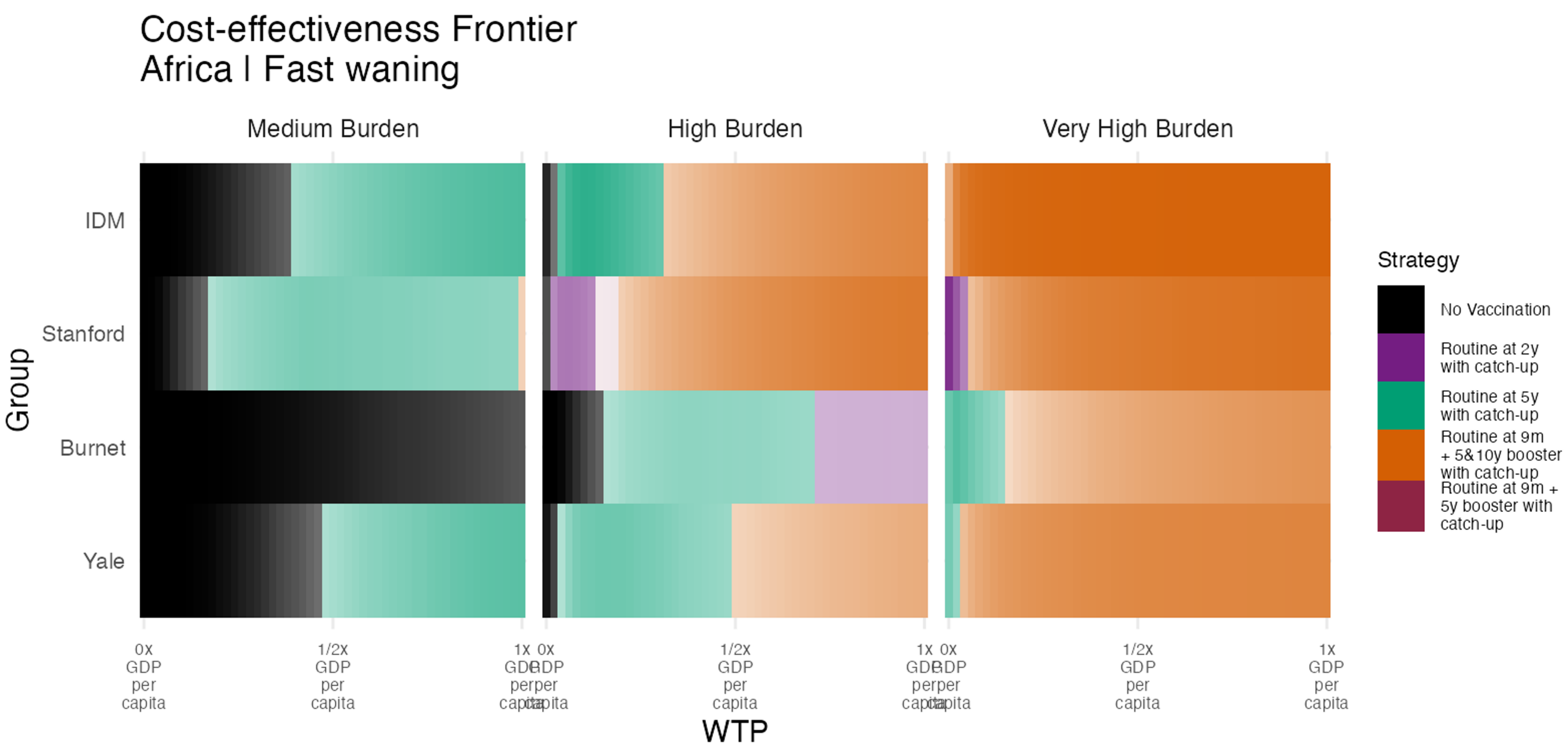

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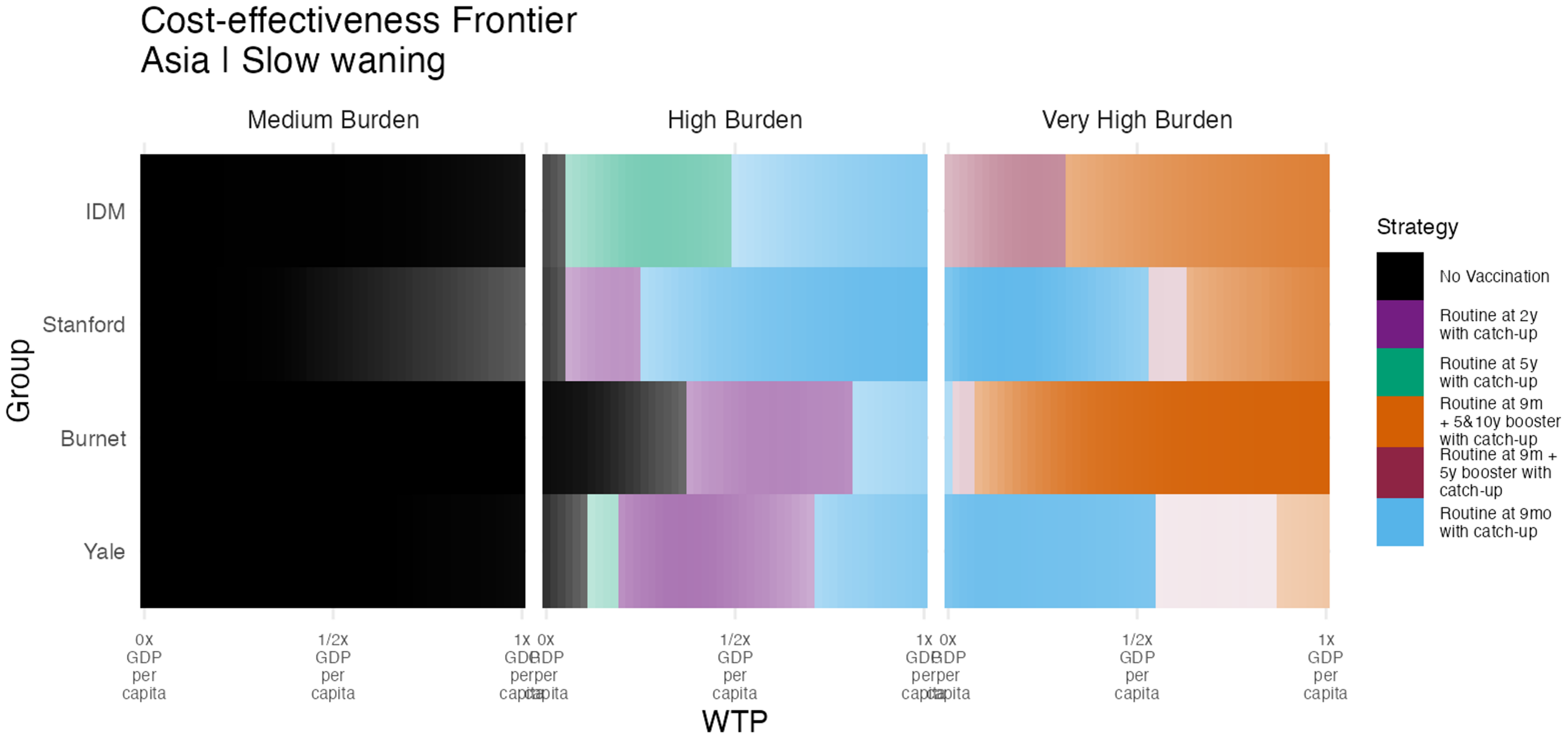

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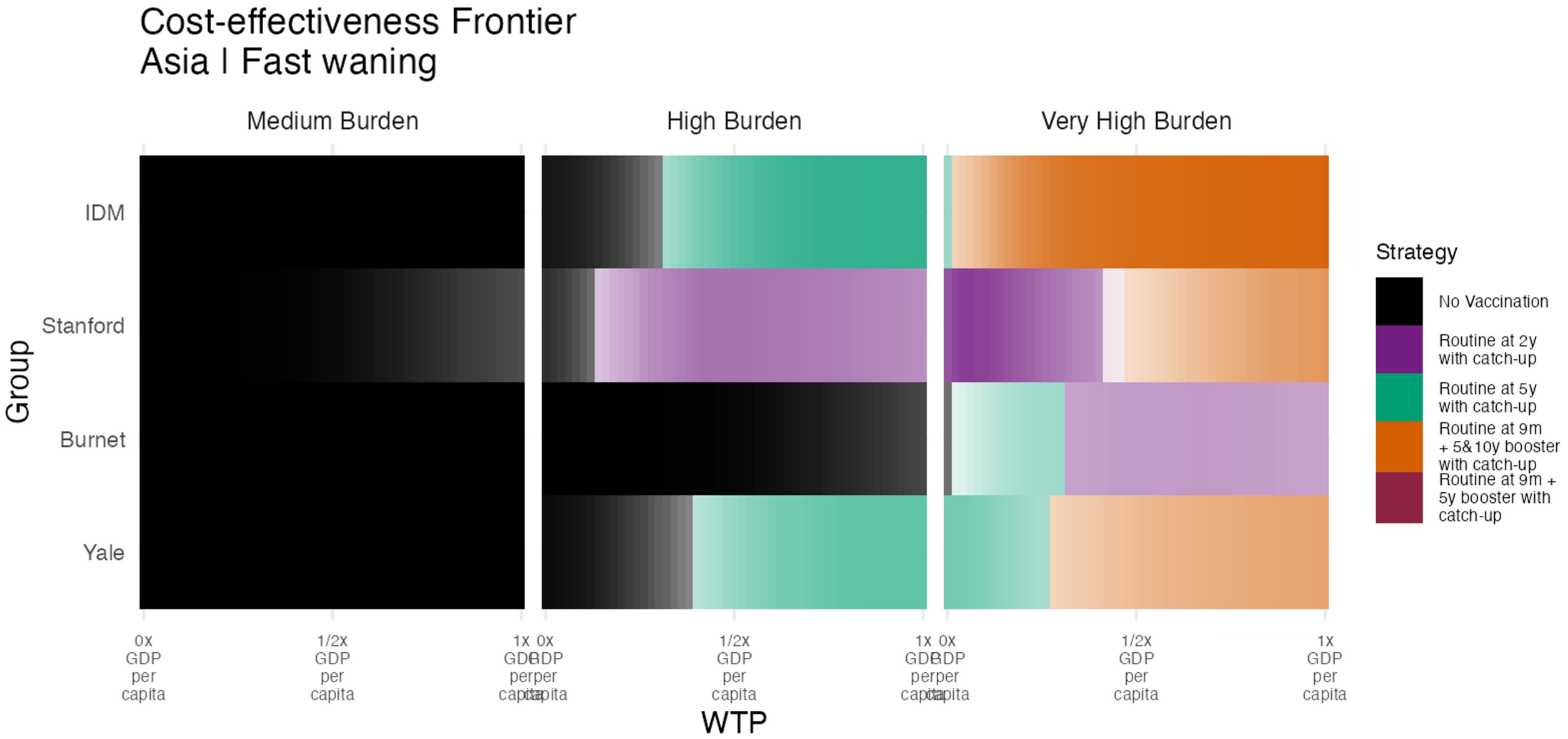

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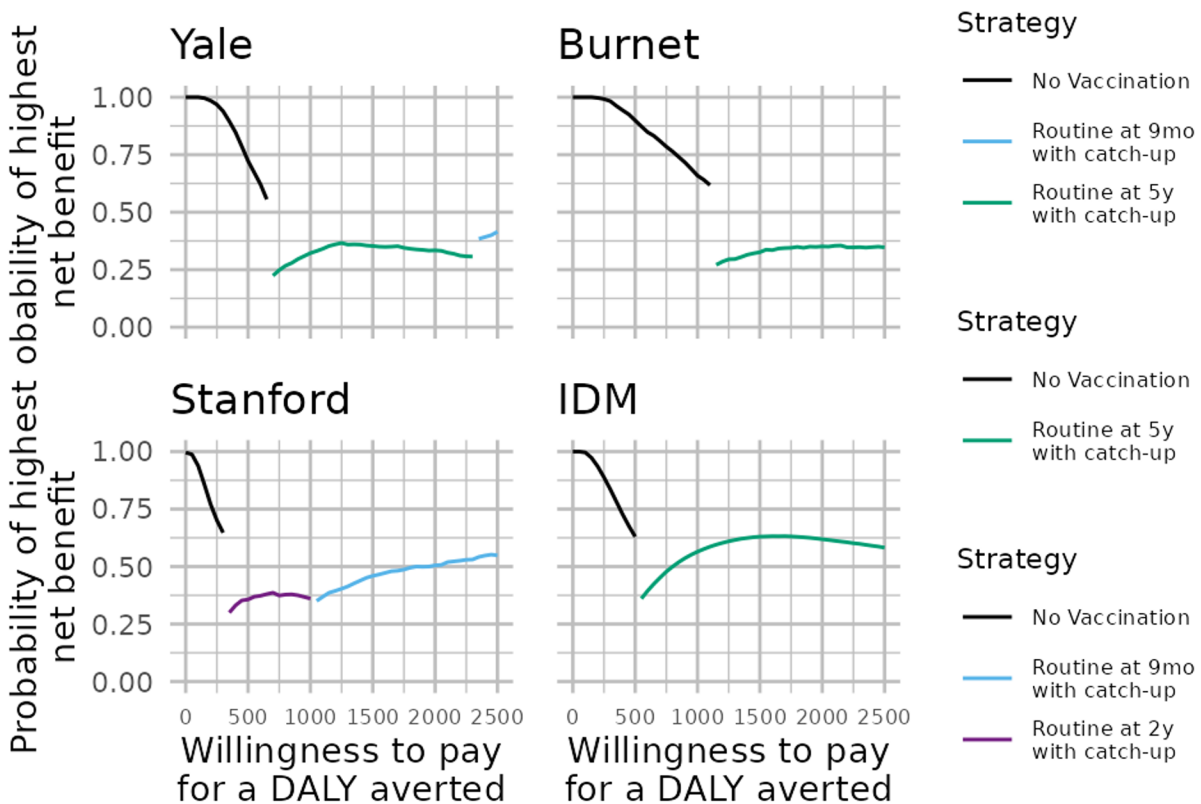
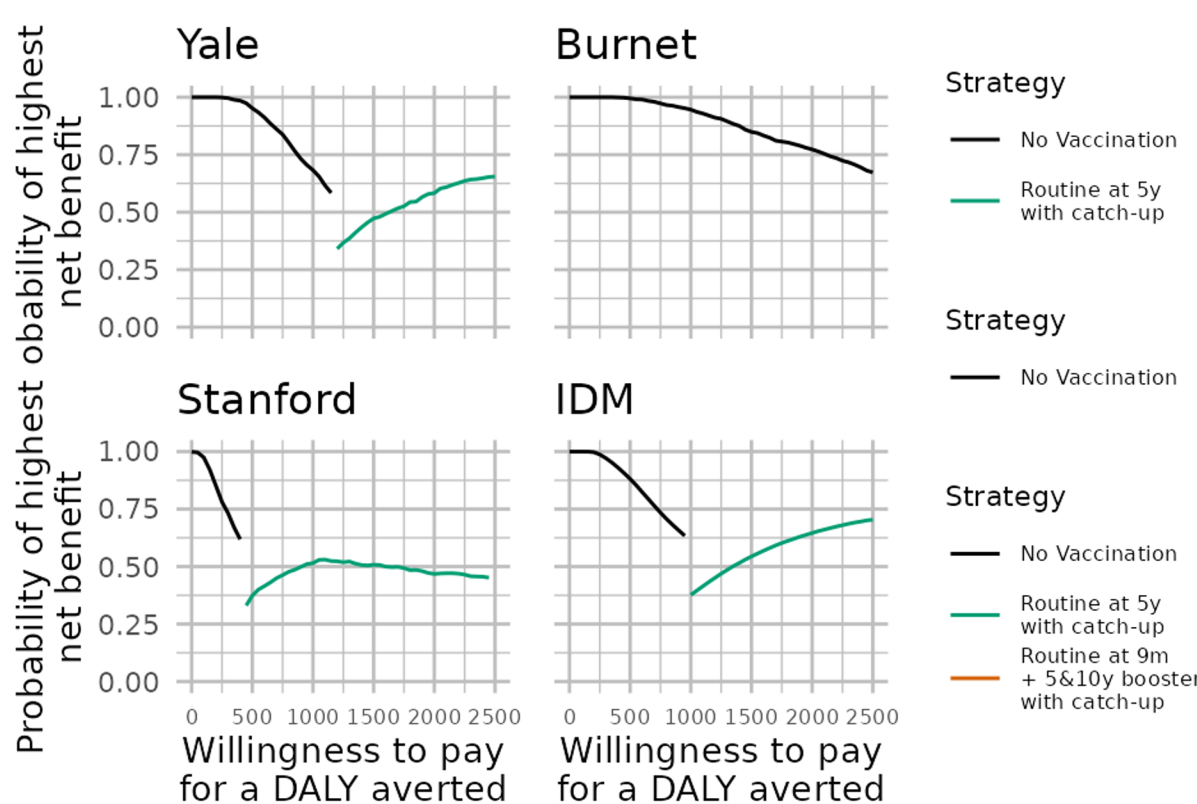
Cost-effectiveness Acceptability Frontiers 20yr time horizon

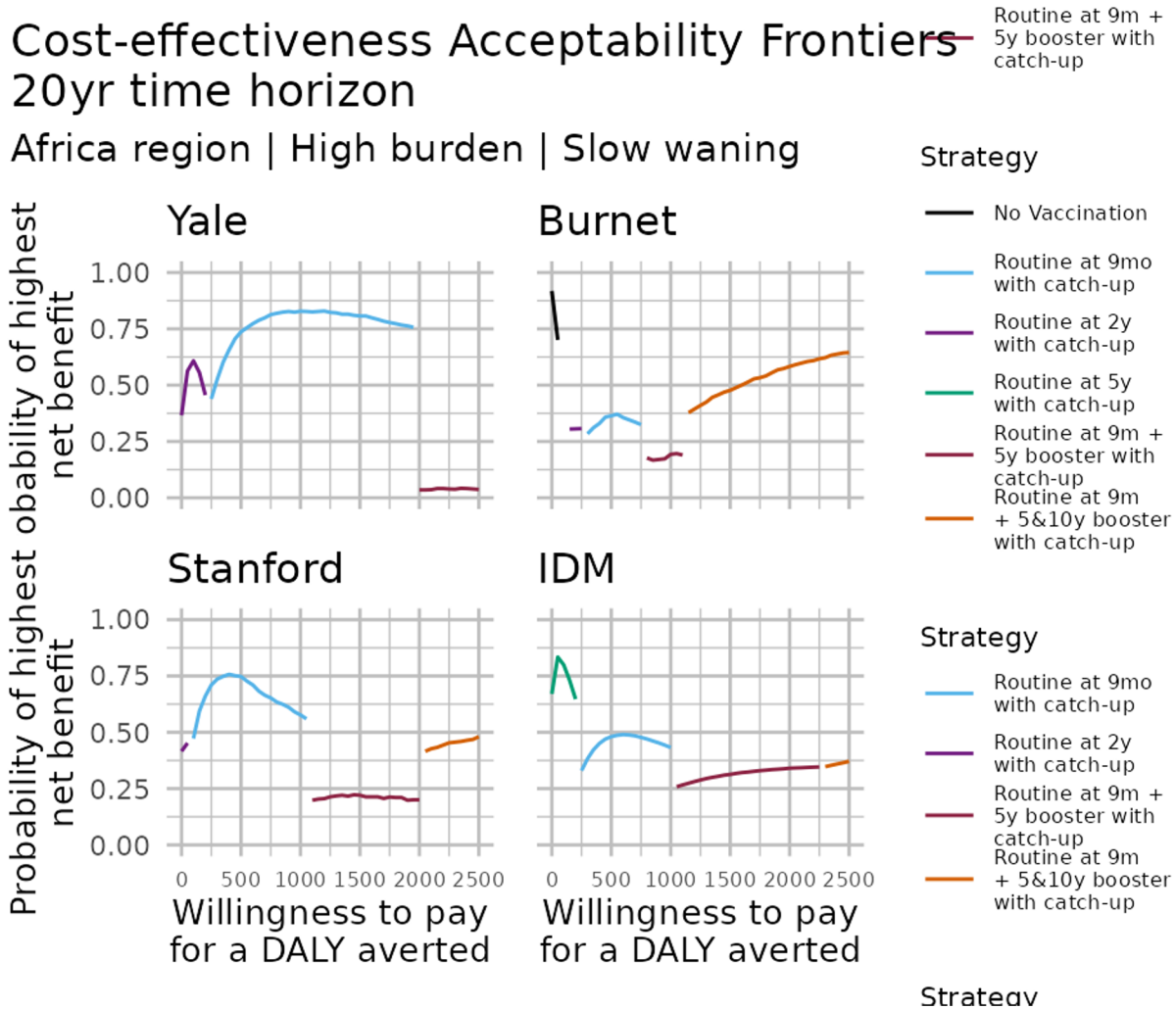
Africa region | Medium burden | Slow waning



Cost-effectiveness Acceptability Frontiers 20yr time horizon

Africa region | Medium burden | Fast waning




Cost-effectiveness Acceptability Frontiers
20yr time horizon
Africa region | High burden | Slow waning
Yale
Burnet
Stanford
IDM
Probability of highest obability of highest net benefit
1.00
0.75
0.50
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0 500 1000 1500 2000 2500
Willingness to pay for a DALY averted
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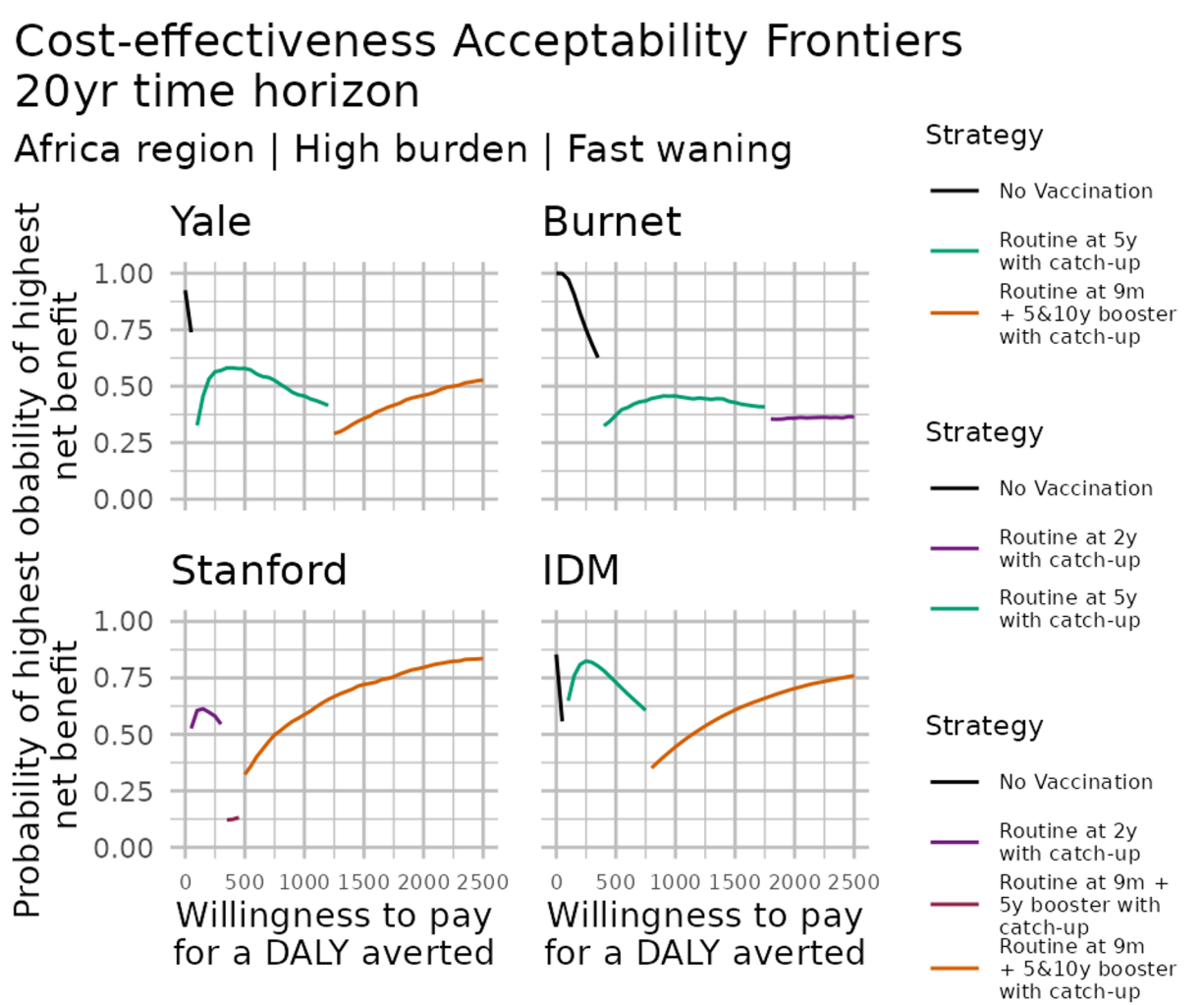
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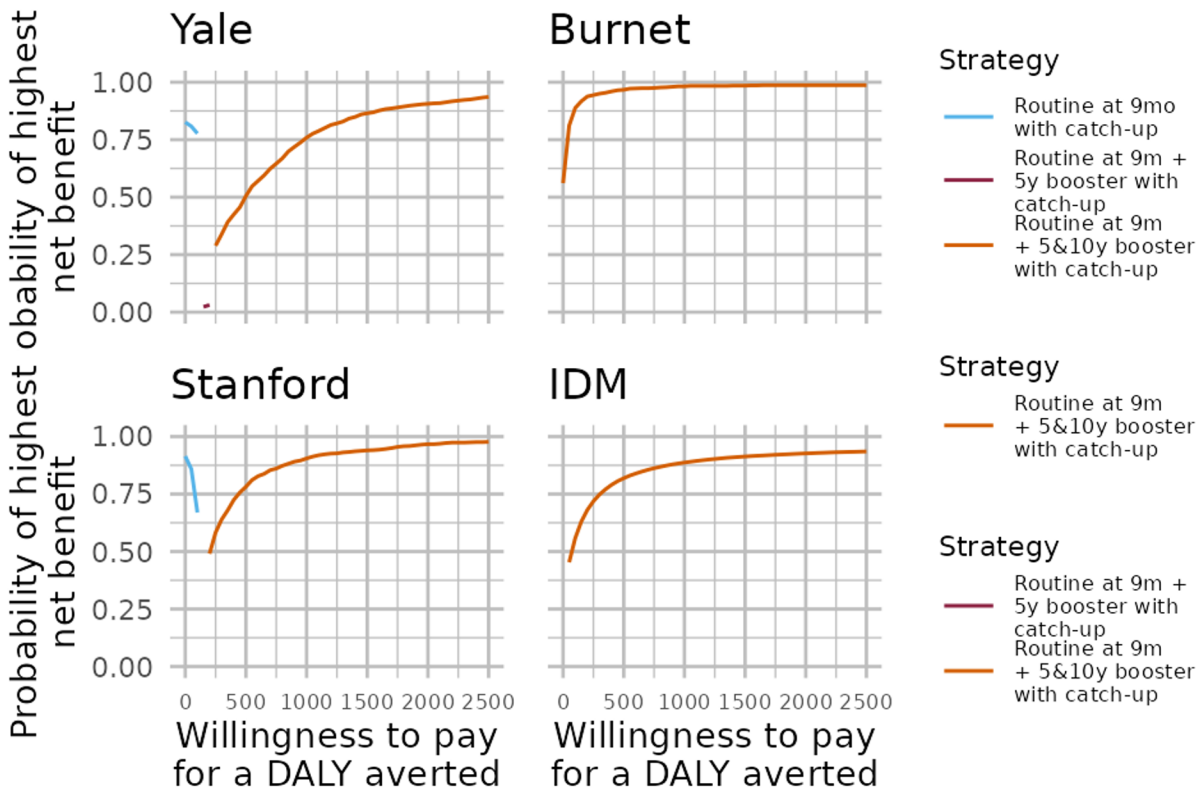
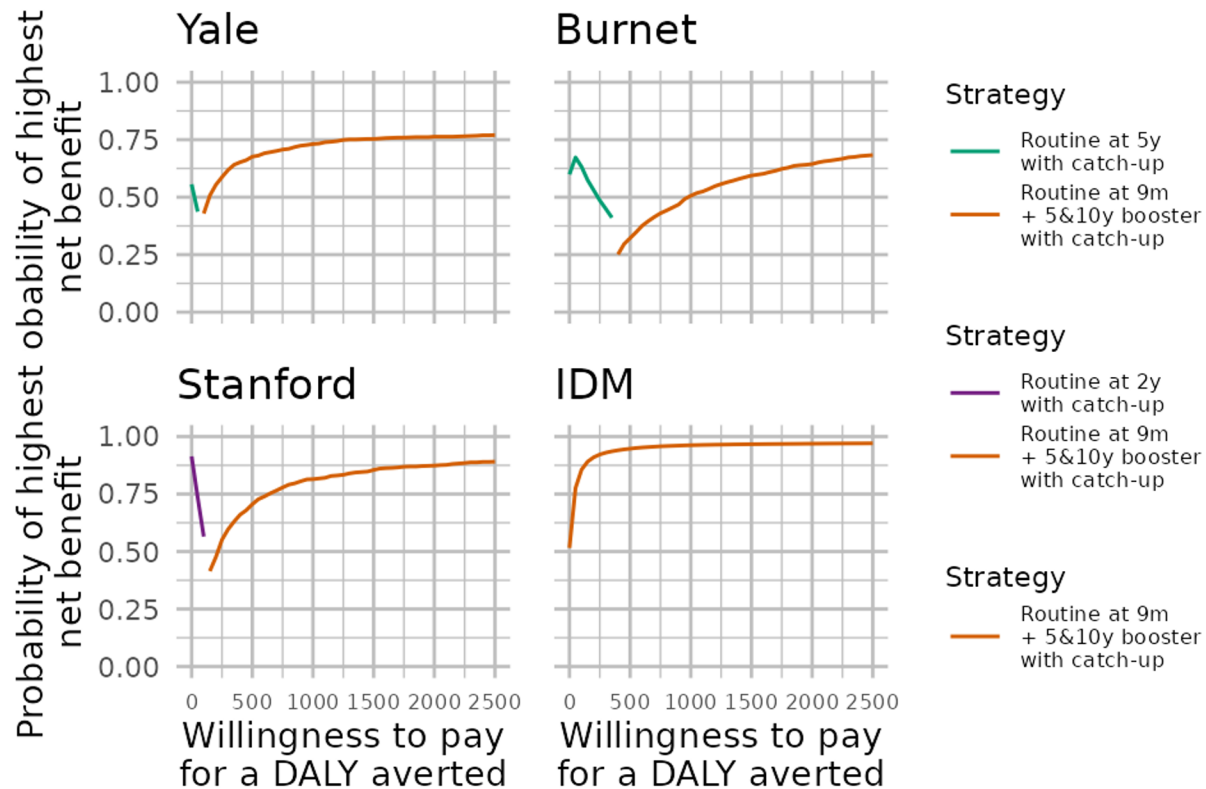
Cost-effectiveness Acceptability Frontiers 20yr time horizon

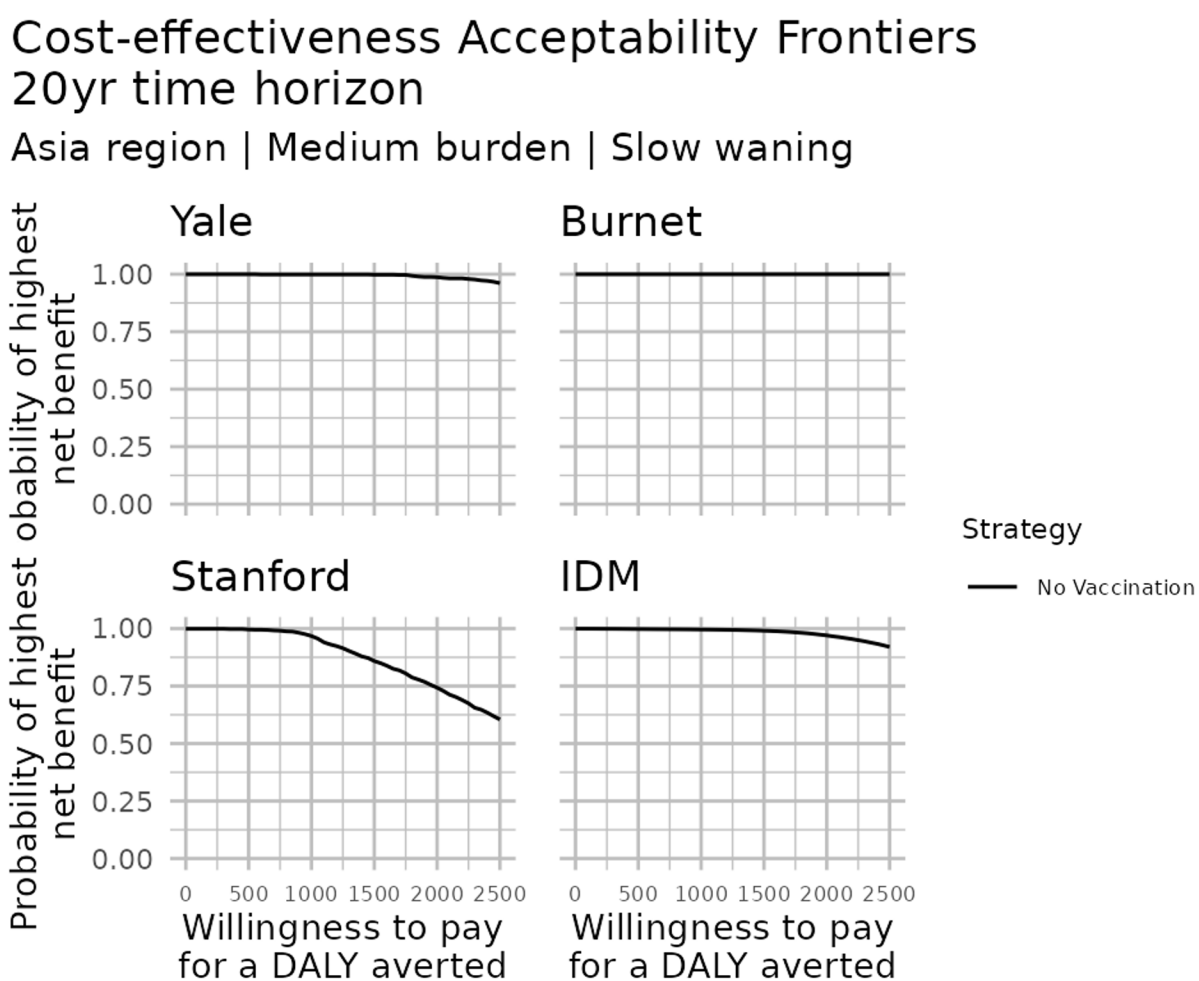
Africa region | Very High burden | Slow waning



Cost-effectiveness Acceptability Frontiers 20yr time horizon

Africa region | Very High burden | Fast waning

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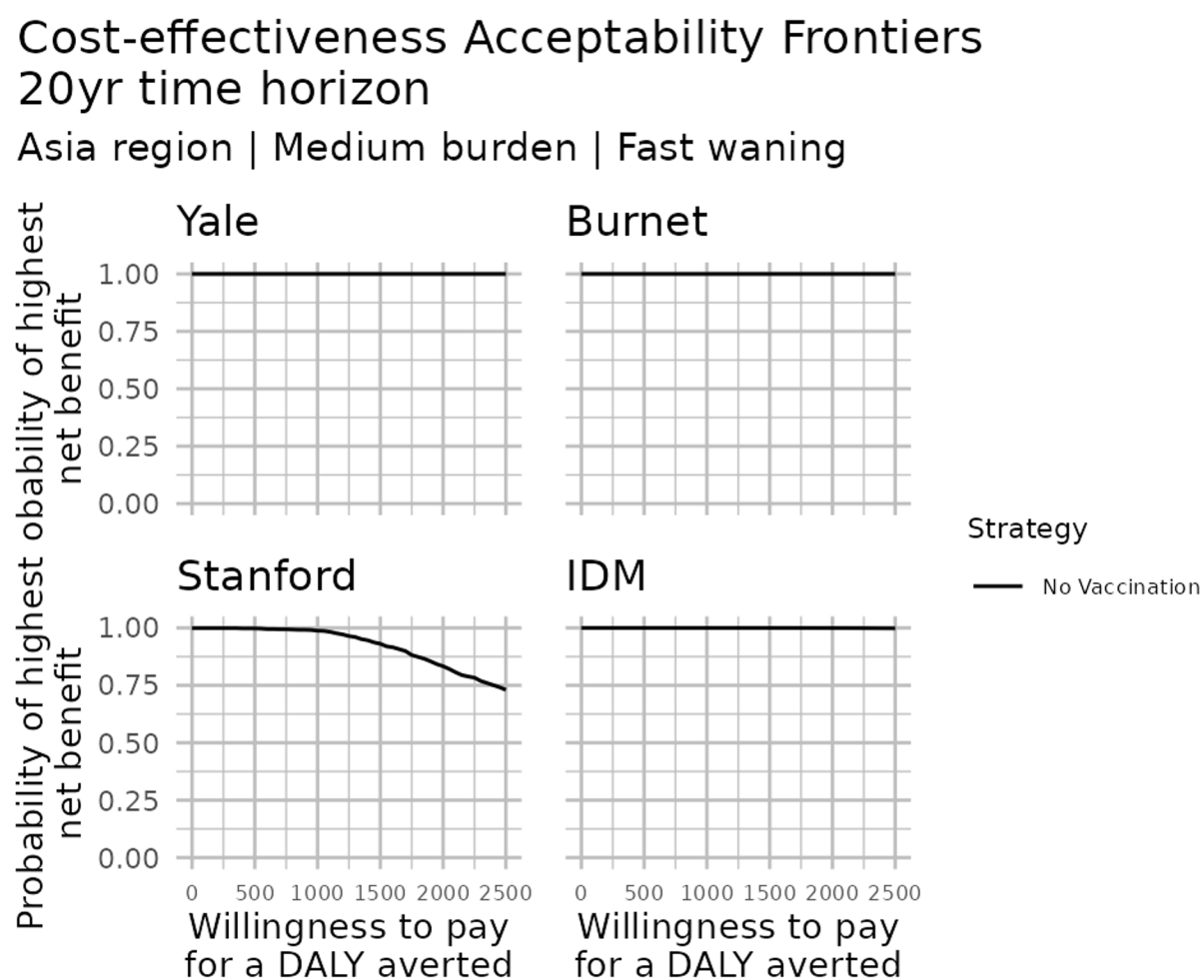
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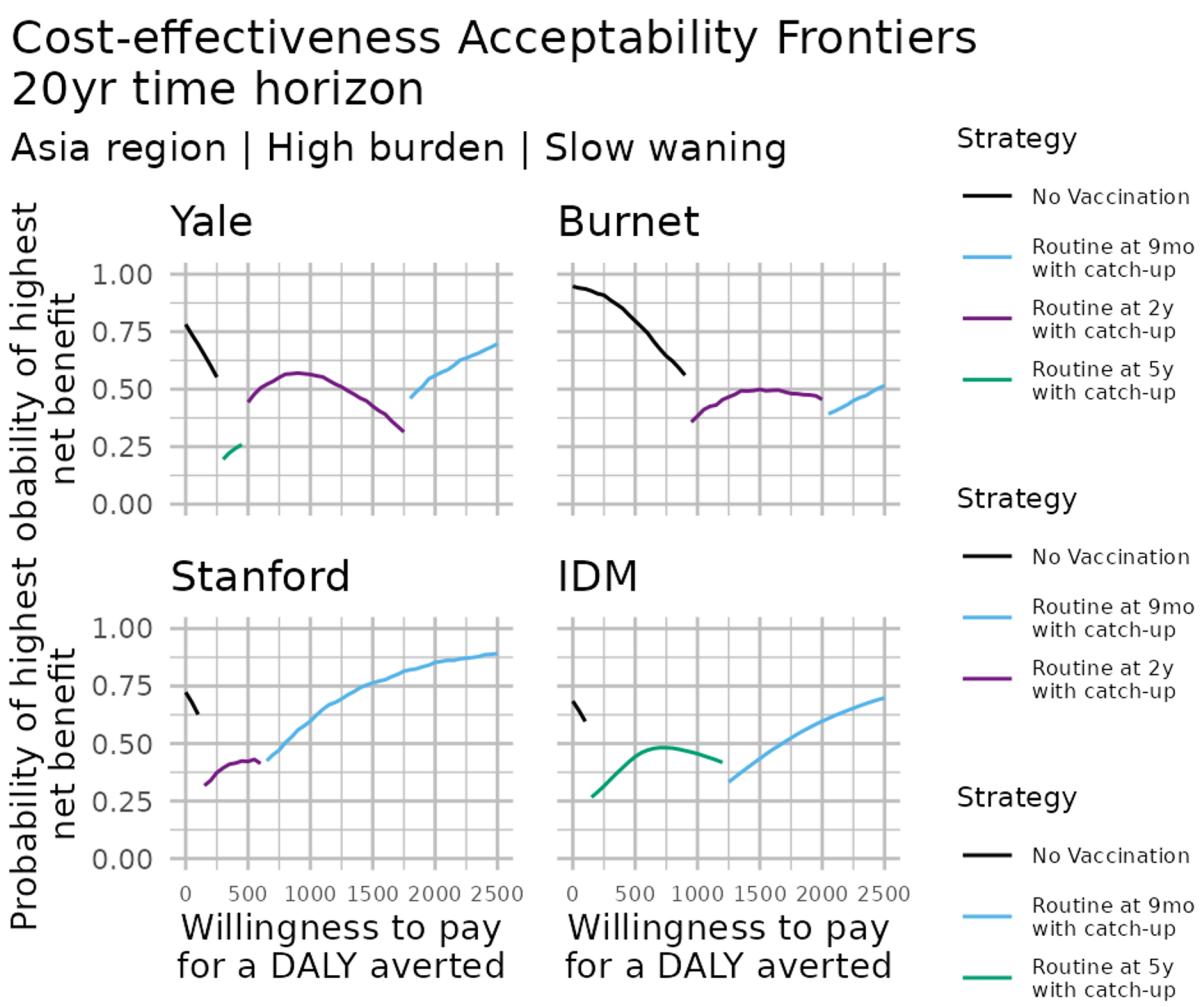
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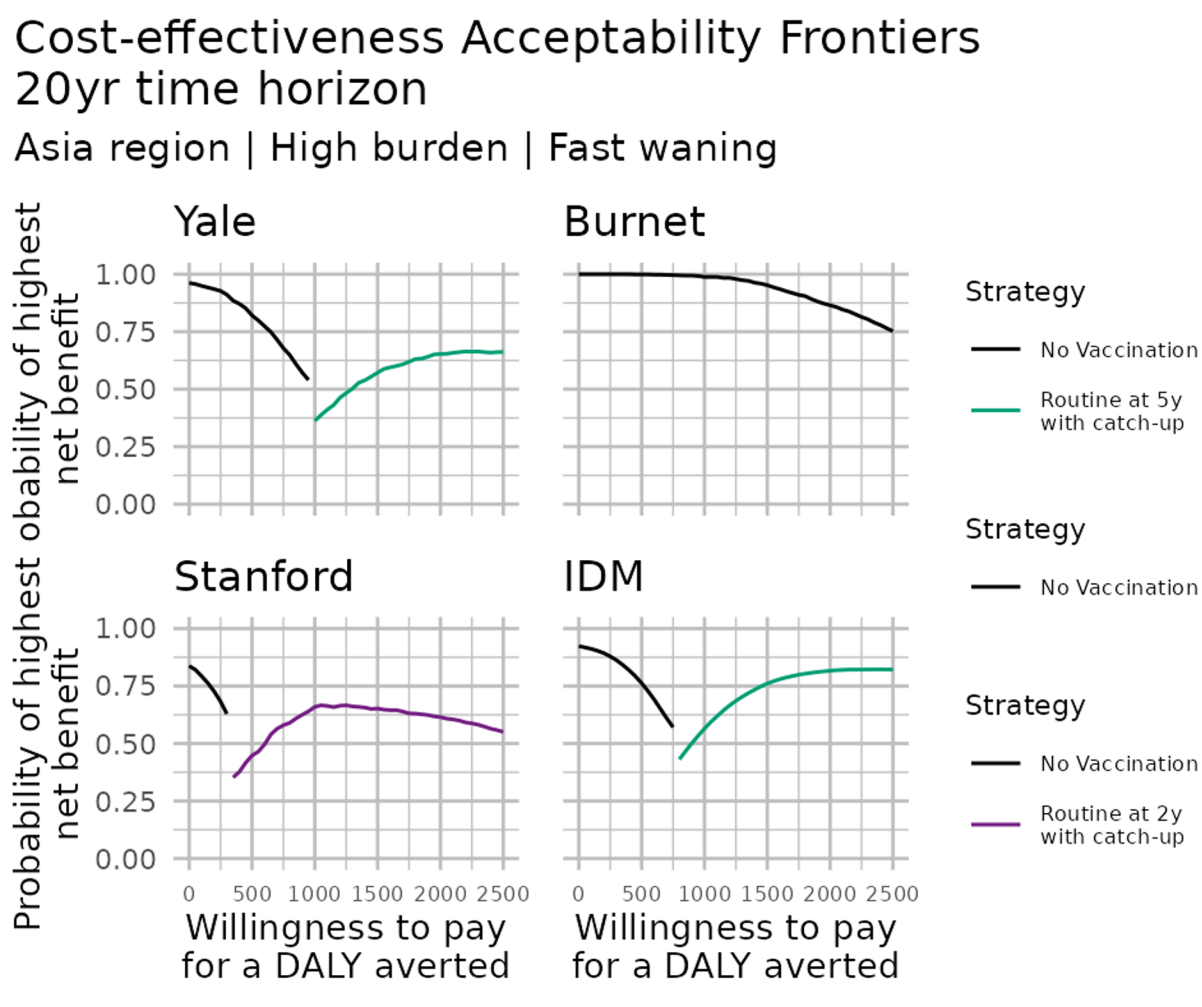
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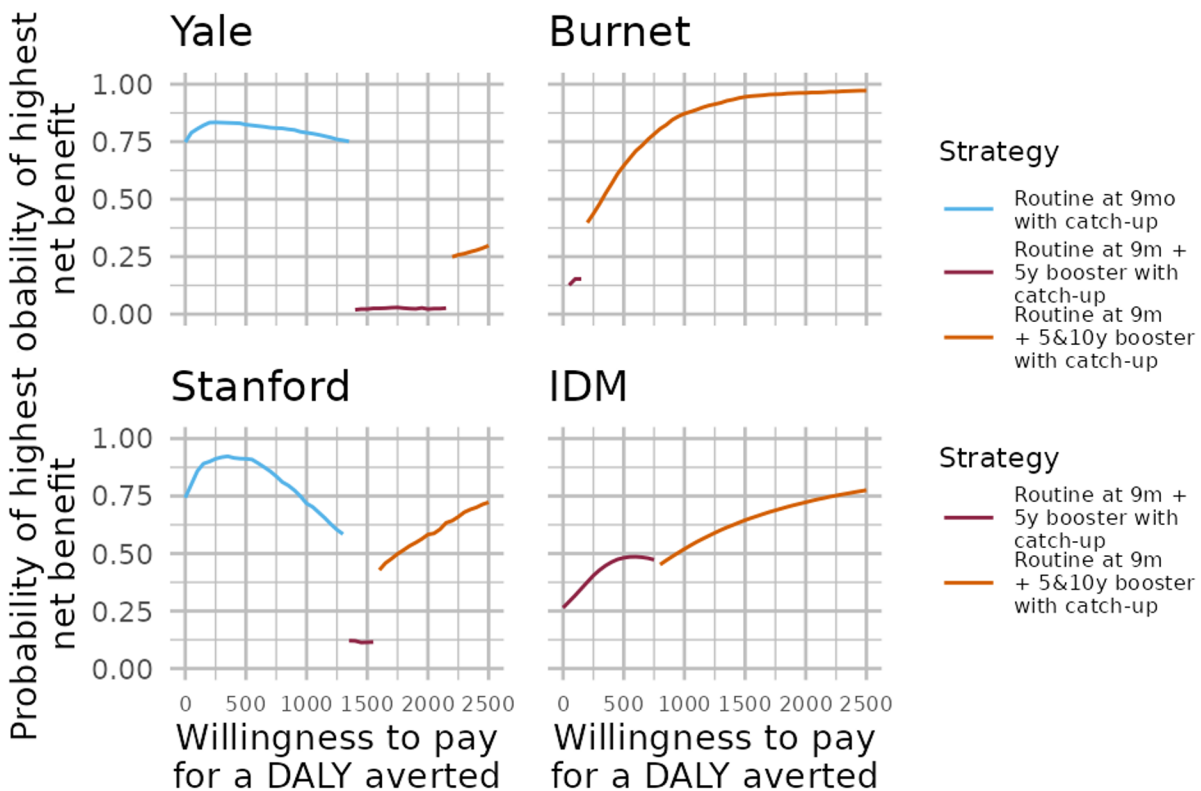
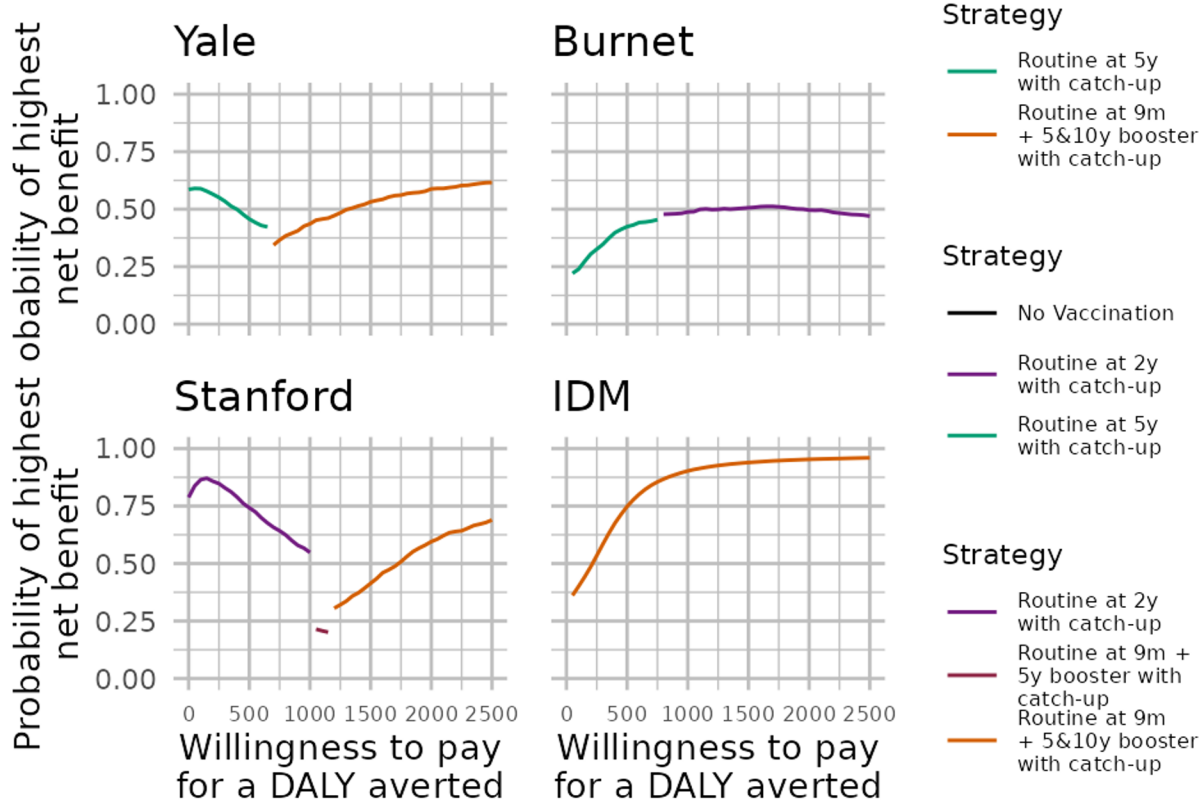
Cost-effectiveness Acceptability Frontiers 20yr time horizon

Asia region | Very High burden | Slow waning



Cost-effectiveness Acceptability Frontiers 20yr time horizon

Asia region | Very High burden | Fast waning



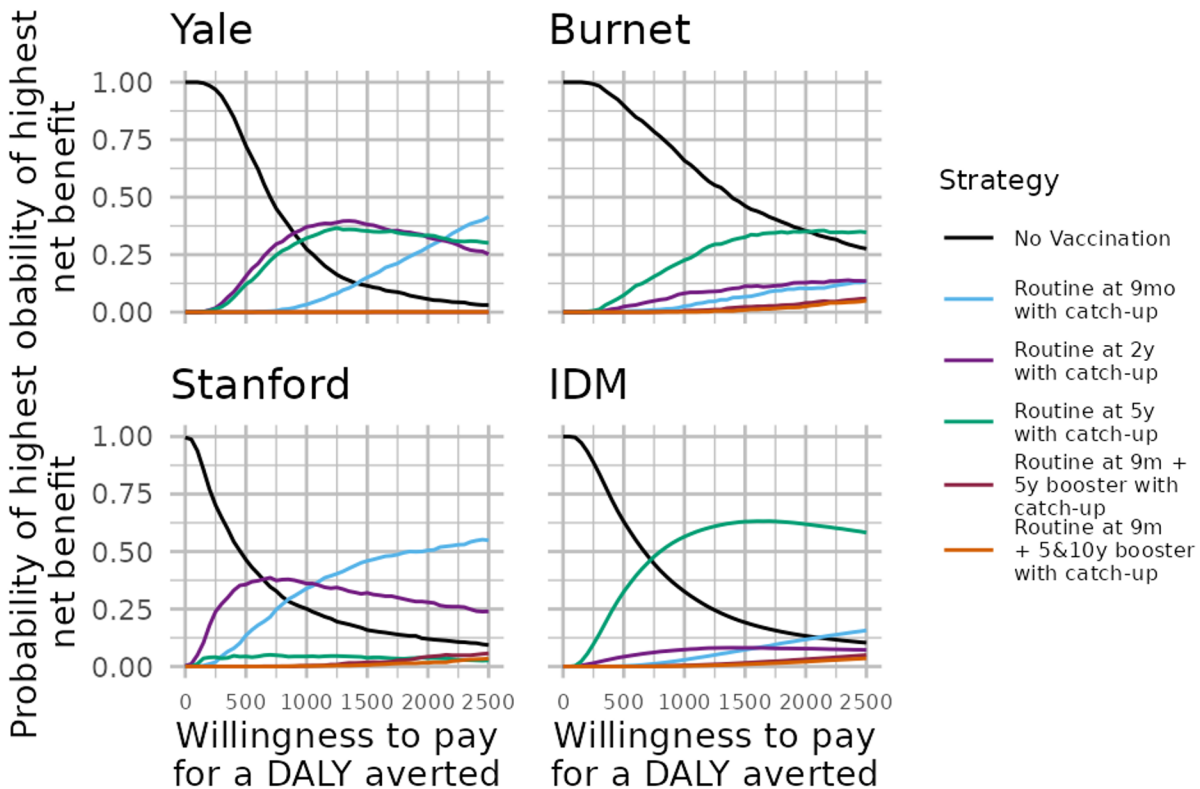
Cost-Effectiveness Results

Cost-effectiveness Acceptability Curves

20 year time horizon

Cost-effectiveness Acceptability Curves 20yr time horizon

Africa region | Medium burden | Slow waning



Cost-effectiveness Acceptability Curves 20yr time horizon

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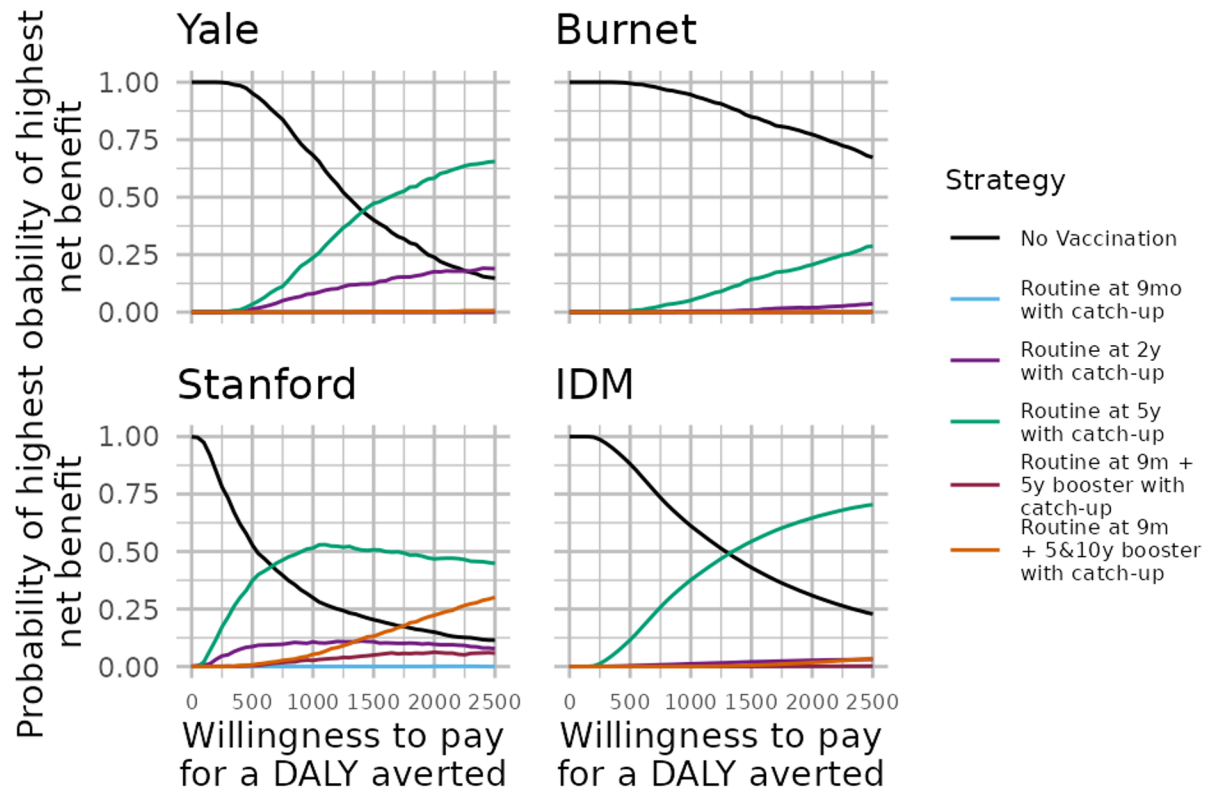
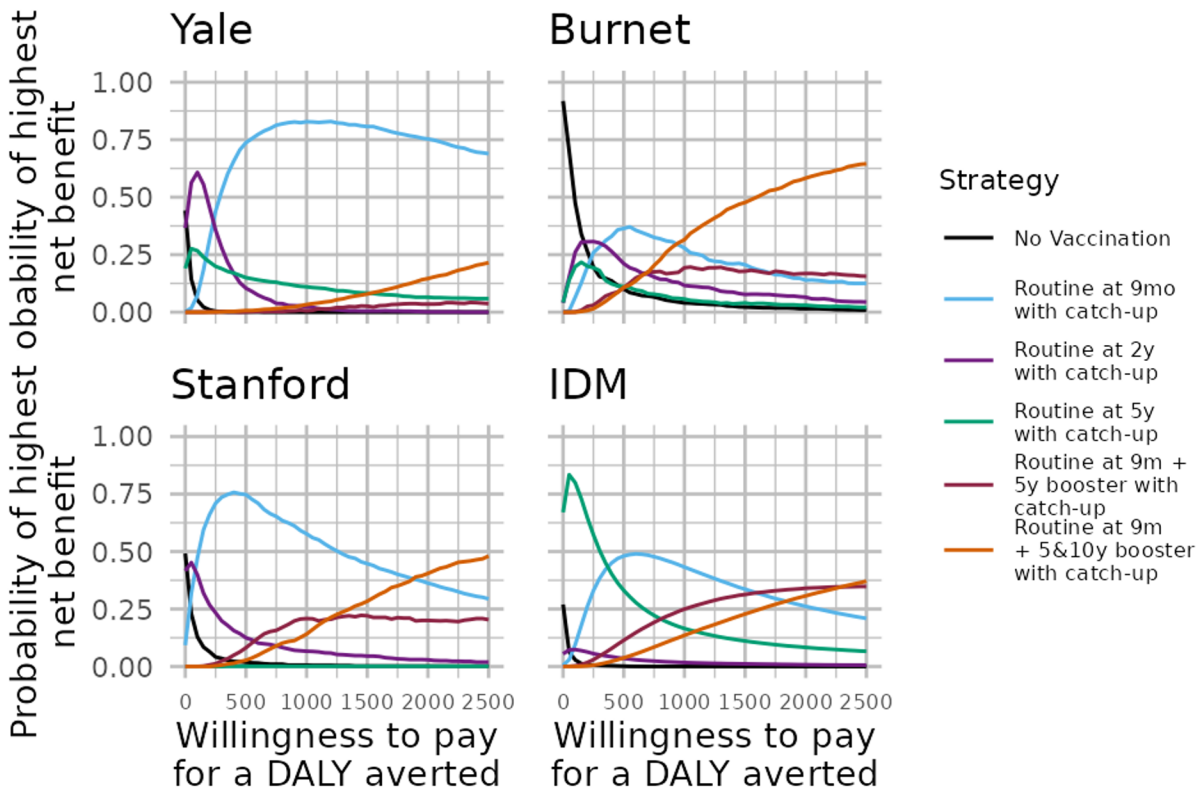


Cost-effectiveness Acceptability Curves
20yr time horizon

Africa region | High burden | Slow waning



Cost-effectiveness Acceptability Curves
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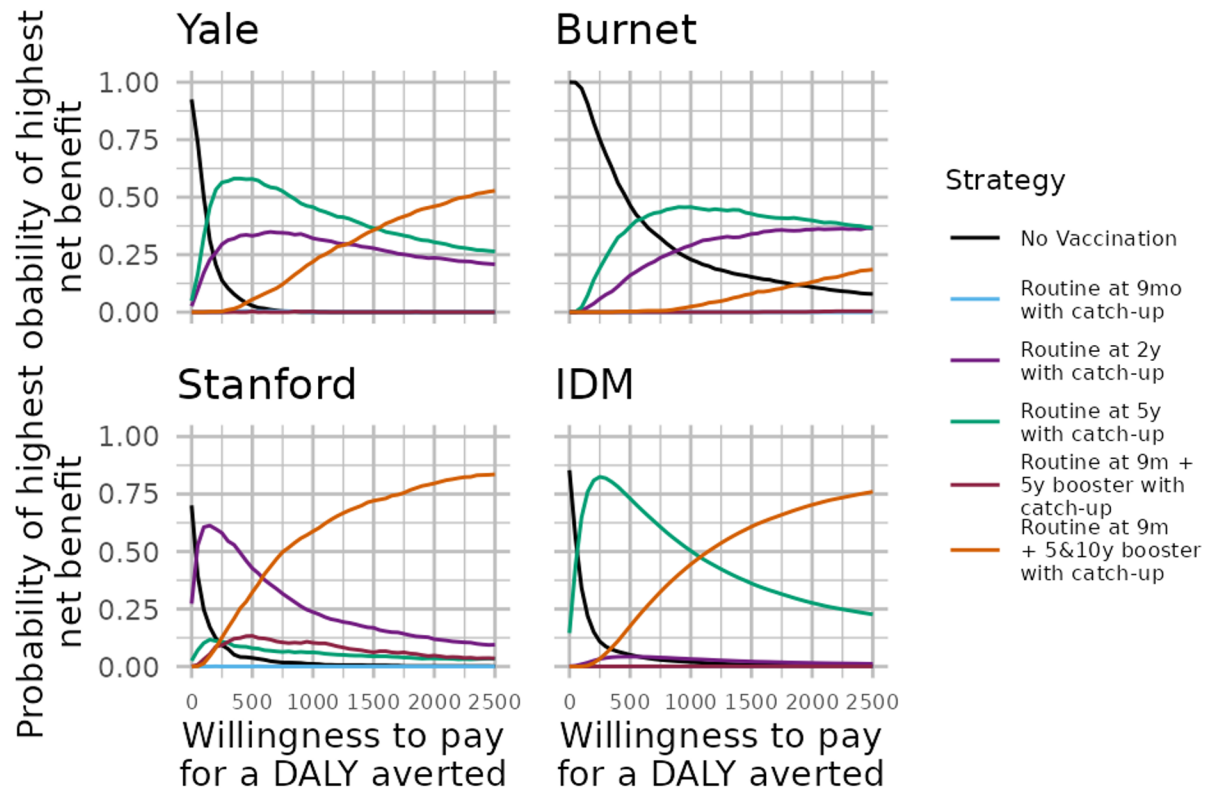
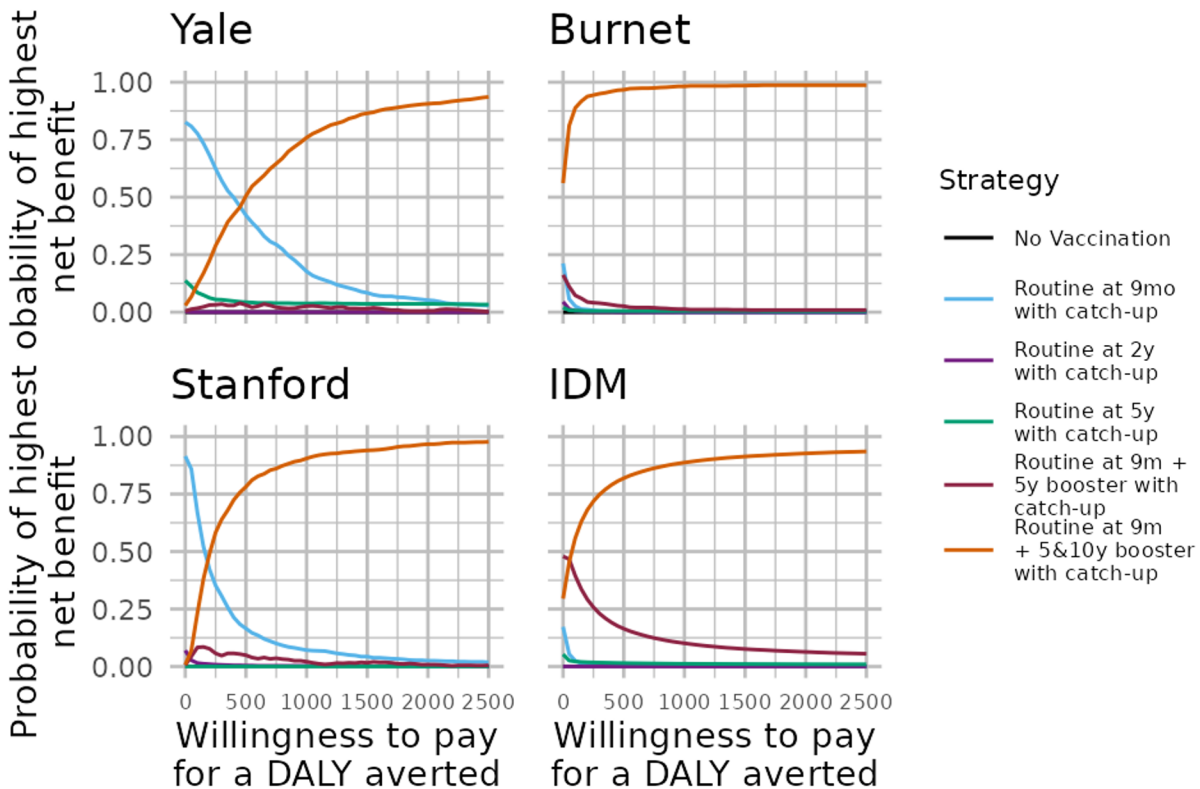
Africa region | High burden | Fast waning



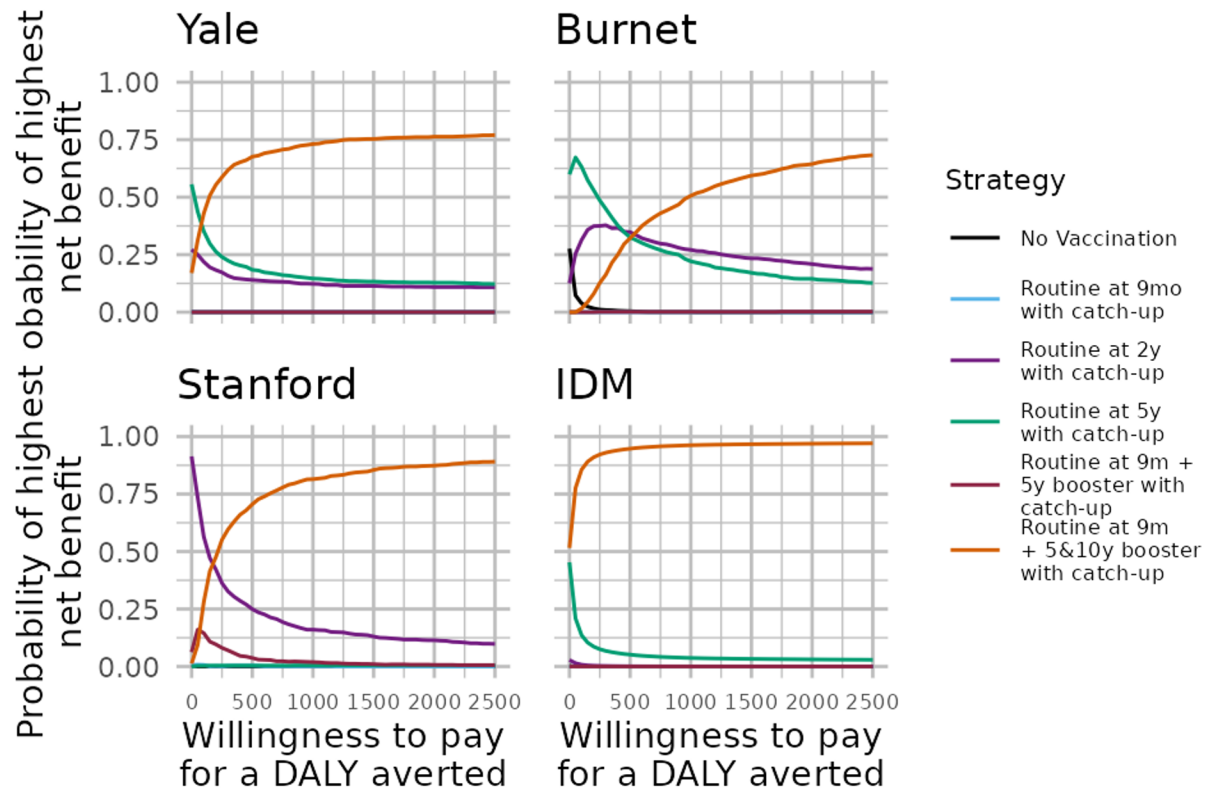
Cost-effectiveness Acceptability Curves
20yr time horizon

Africa region | Very High burden | Slow waning



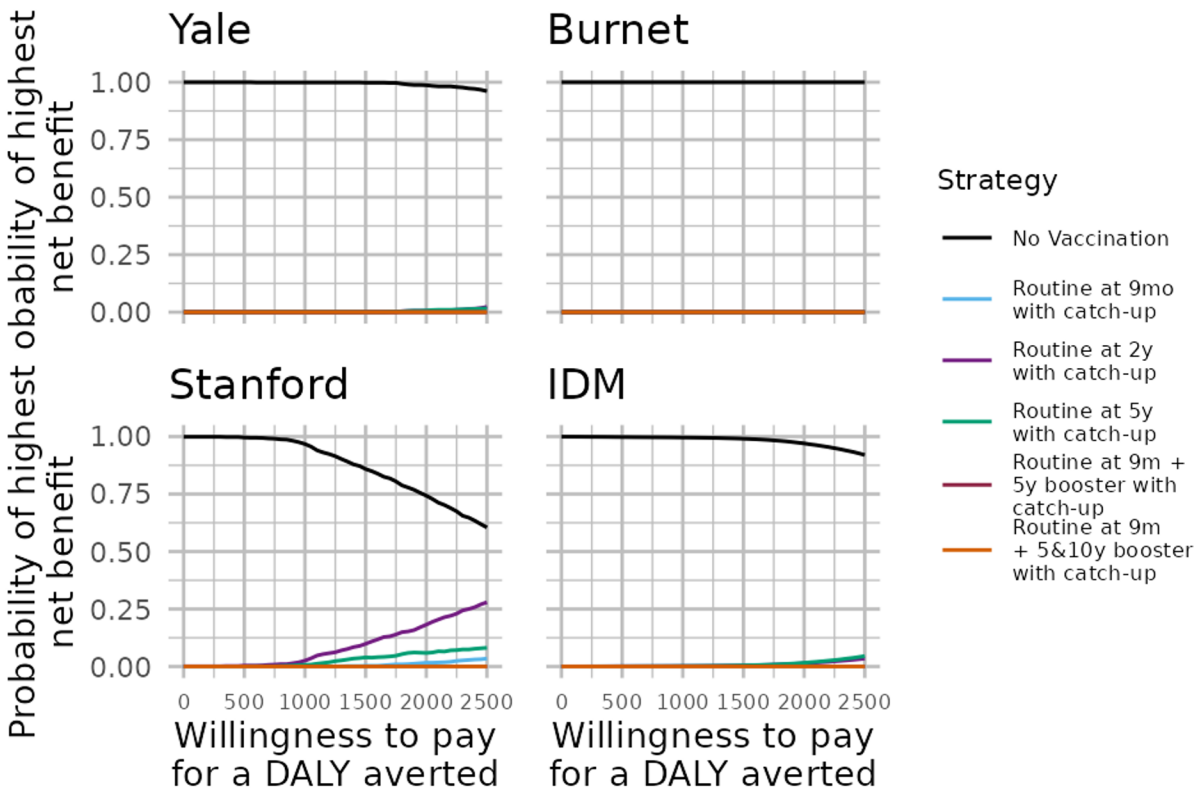
Cost-effectiveness Acceptability Curves
20yr time horizon

Africa region | Very High burden | Fast waning



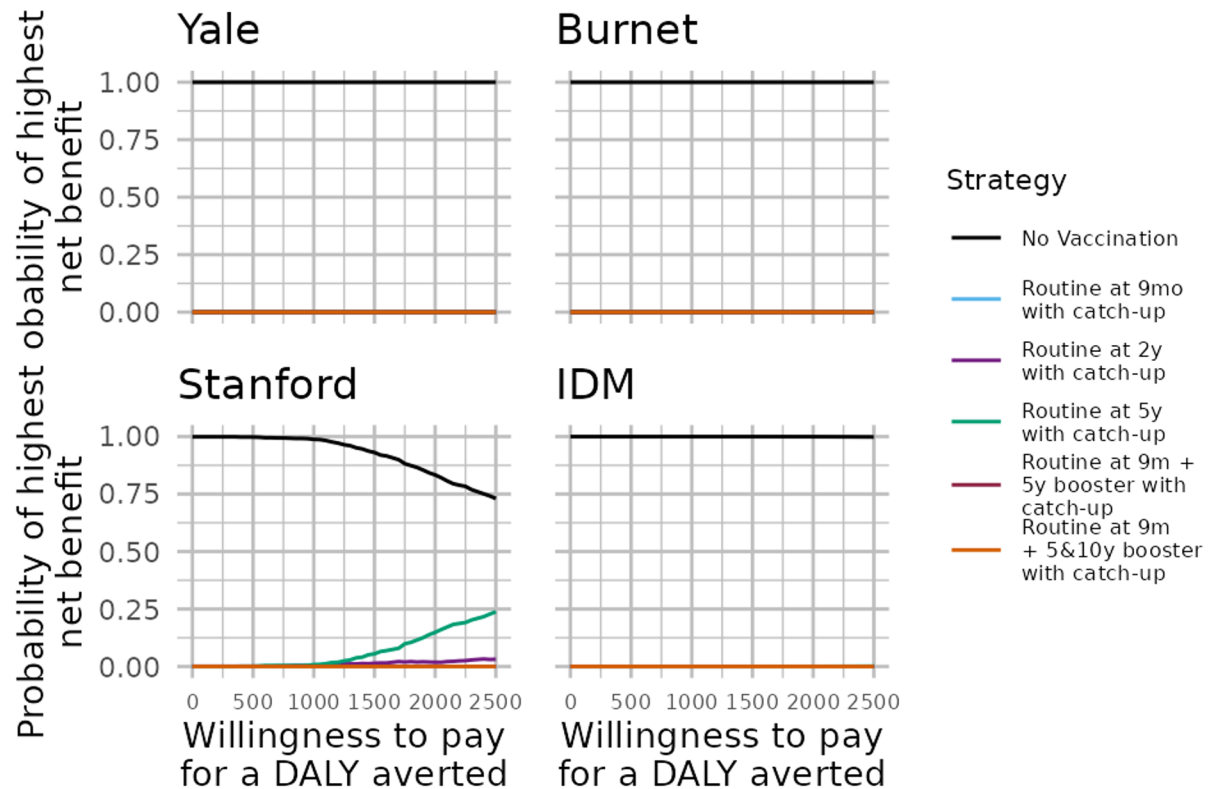
Cost-effectiveness Acceptability Curves 20yr time horizon

Asia region | Medium burden | Slow waning



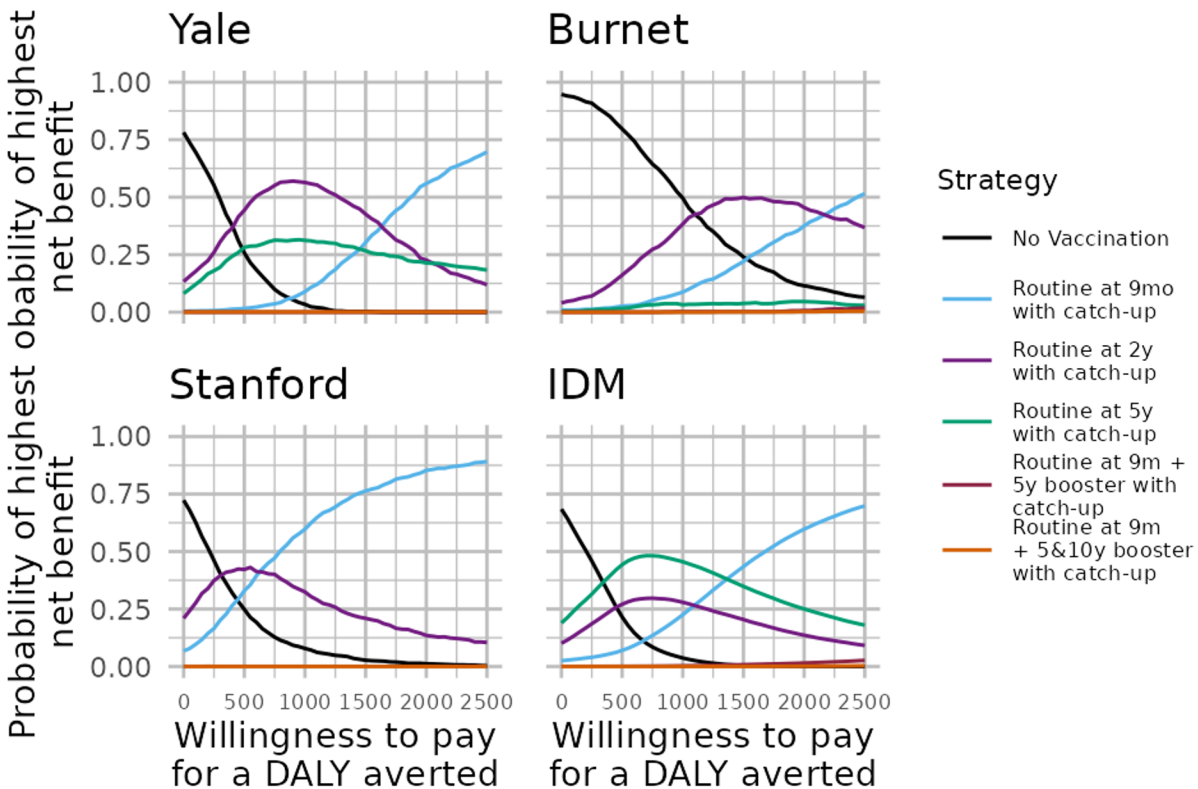
Cost-effectiveness Acceptability Curves 20yr time horizon

Asia region | Medium burden | Fast waning



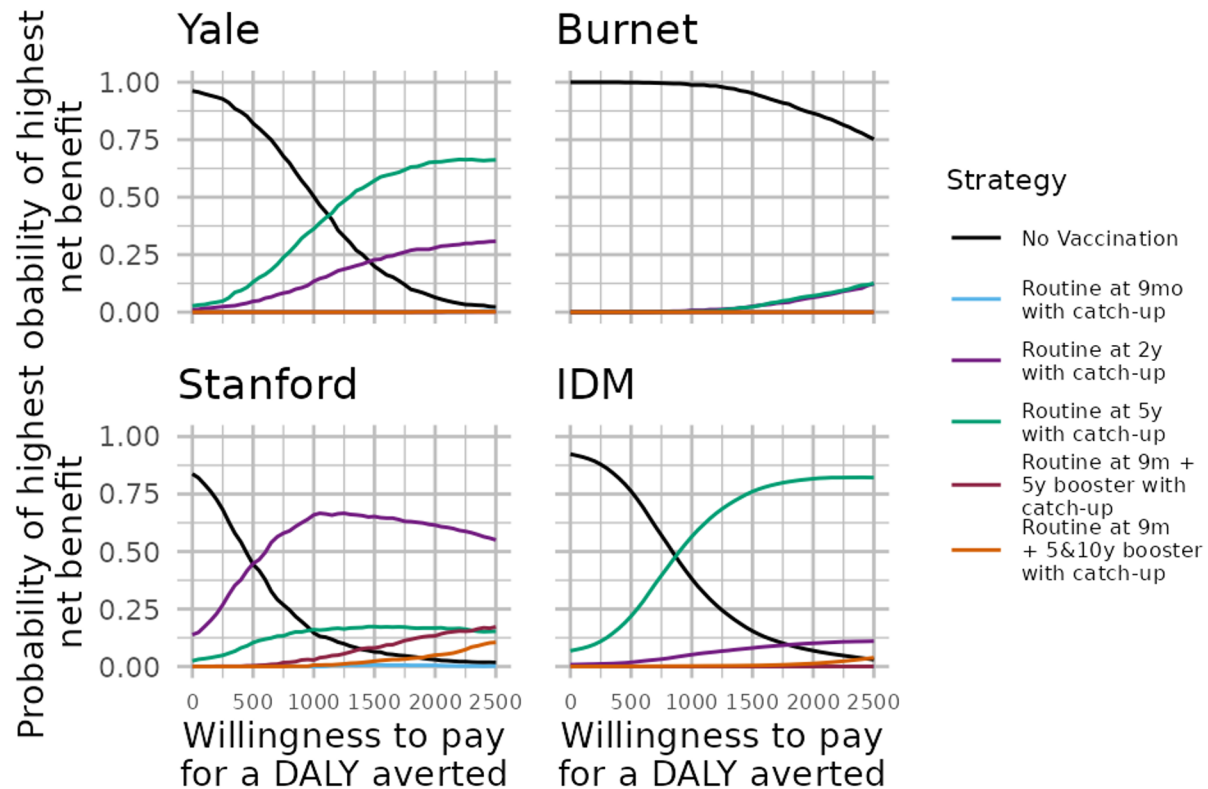
Cost-effectiveness Acceptability Curves 20yr time horizon

Asia region | High burden | Slow waning



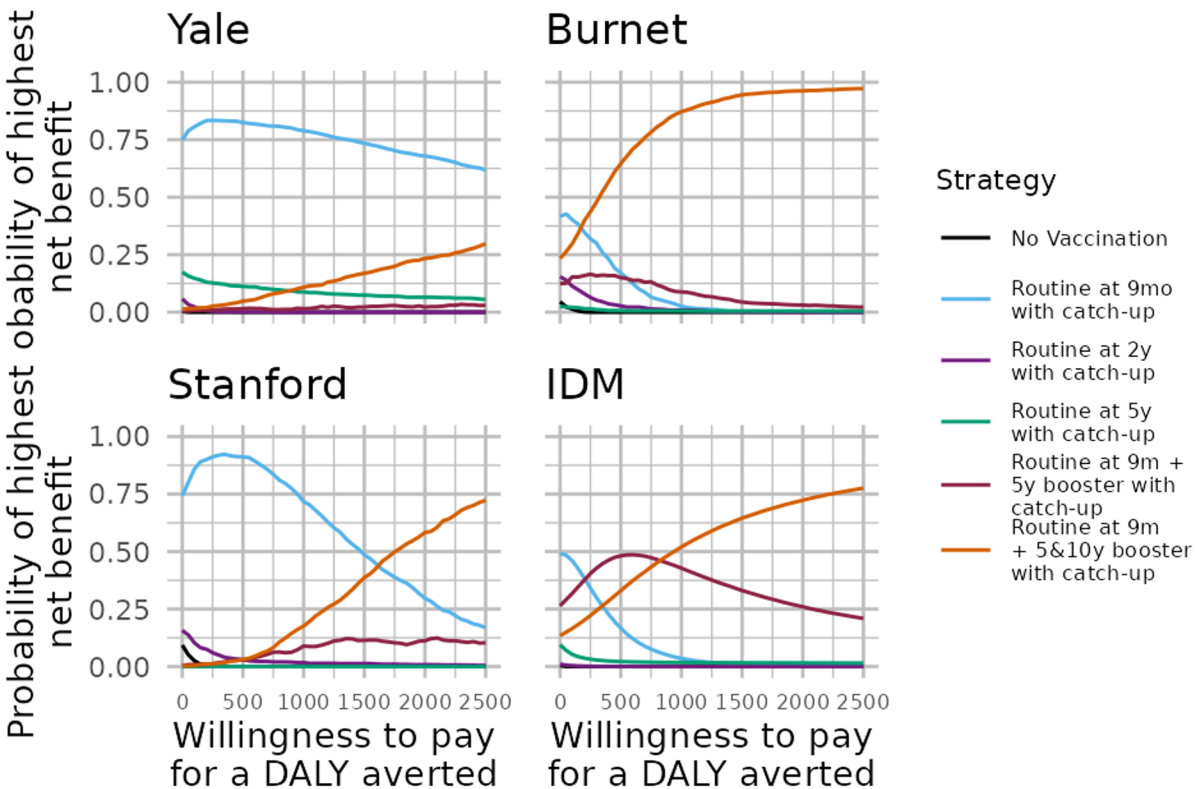
Cost-effectiveness Acceptability Curves 20yr time horizon

Asia region | High burden | Fast waning



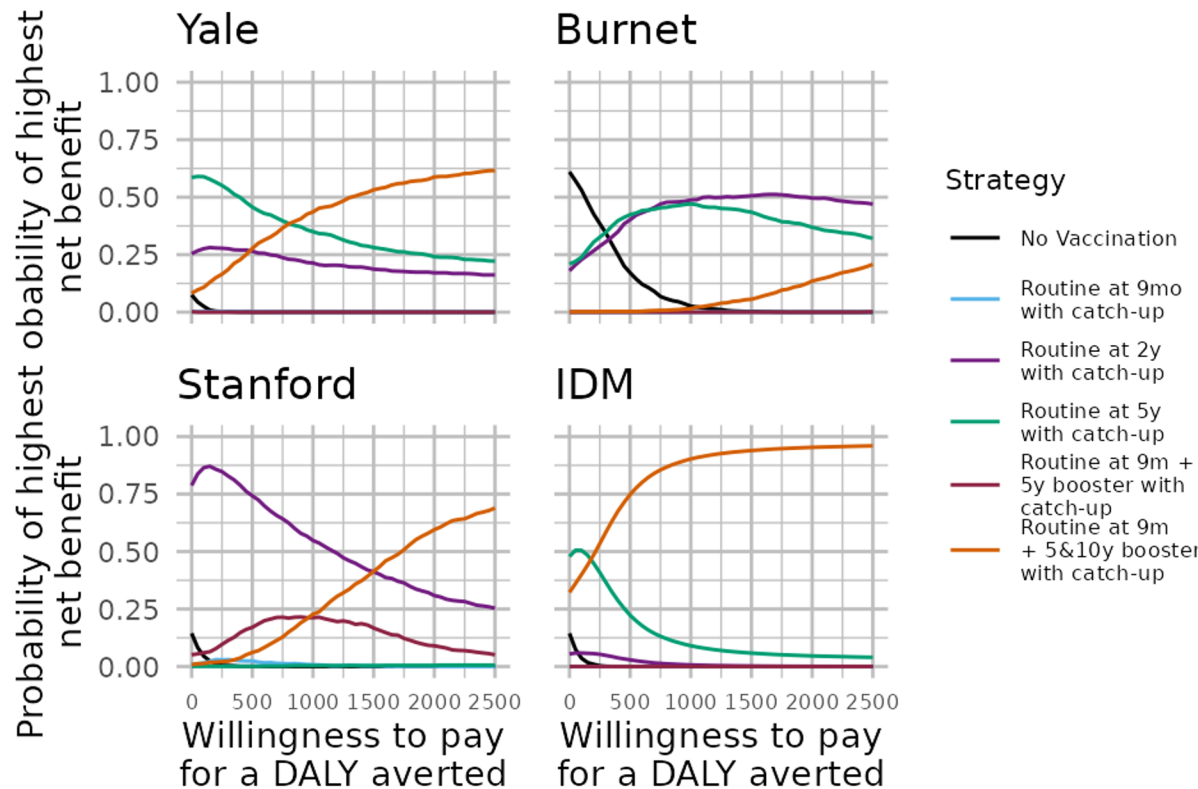
Cost-effectiveness Acceptability Curves
20yr time horizon

Asia region | Very High burden | Slow waning



Cost-effectiveness Acceptability Curves
20yr time horizon

Asia region | Very High burden | Fast waning



Threshold Analysis

For this analysis, we varied the symptomatic fraction (i.e. proportion of all typhoid infections that are symptomatic) to obtain different baseline incidence levels for a given age distribution of cases (depending on the incidence setting), then re-ran the cost-effectiveness analysis on the model output to examine how the optimal strategy varied depending on baseline incidence.

Cost-Effectiveness Acceptability Frontiers

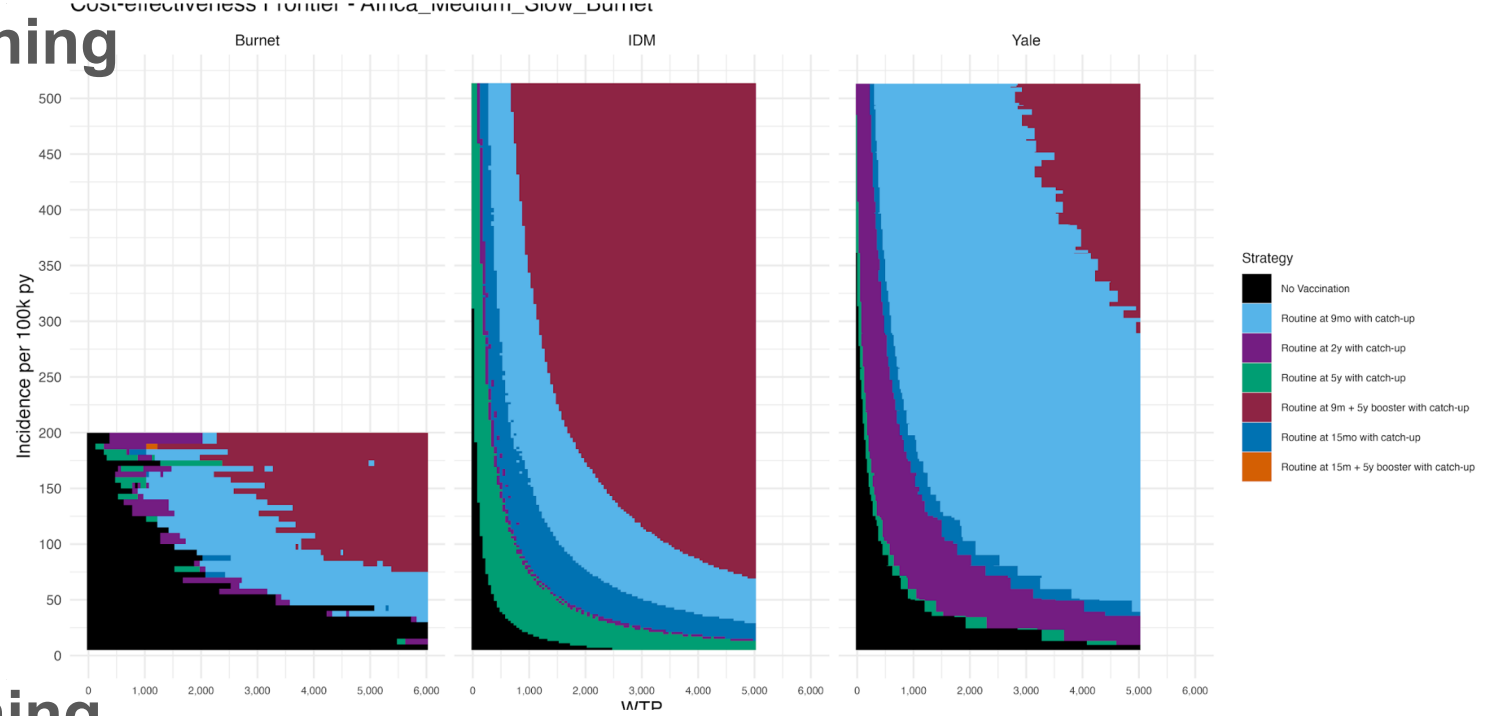
10 year time horizon

Cost-effectiveness frontier

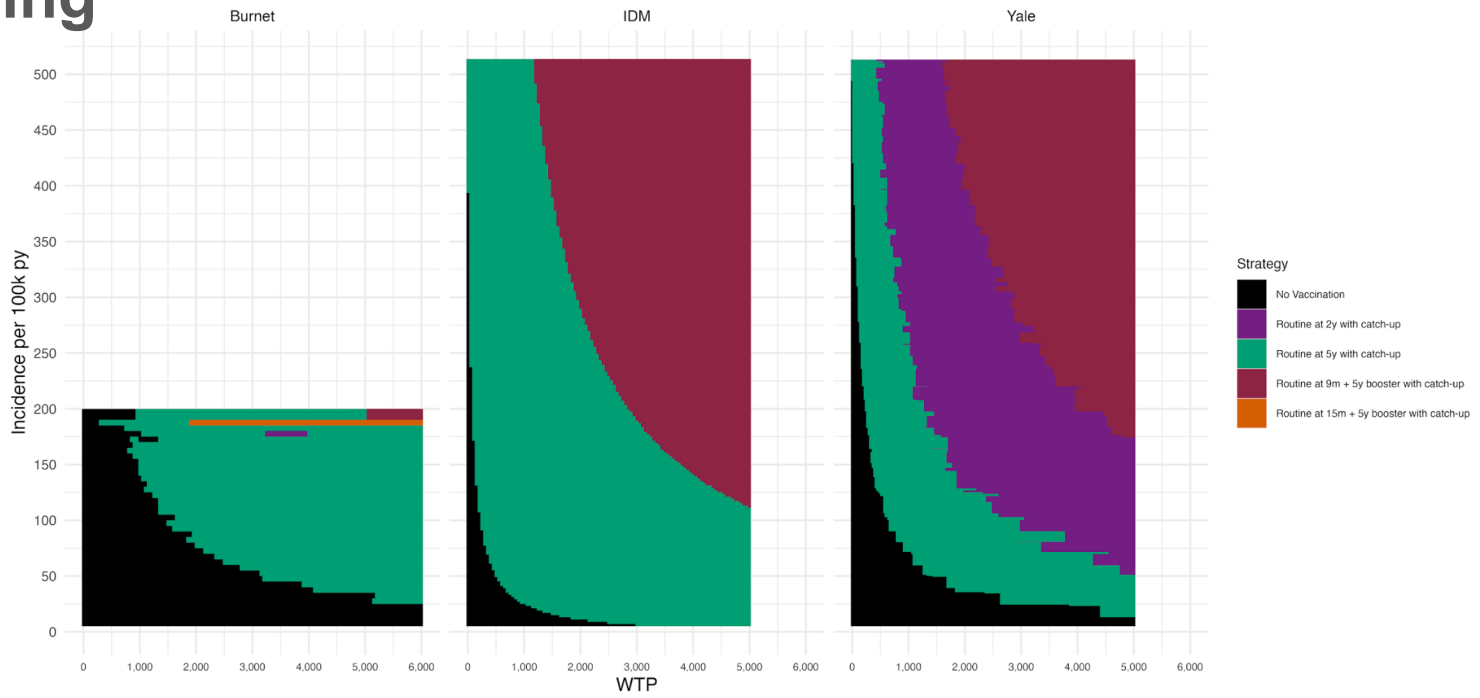
Medium burden*, Africa region

*Incidence is highest in the 5-15 yr age group

Slow waning



Fast waning

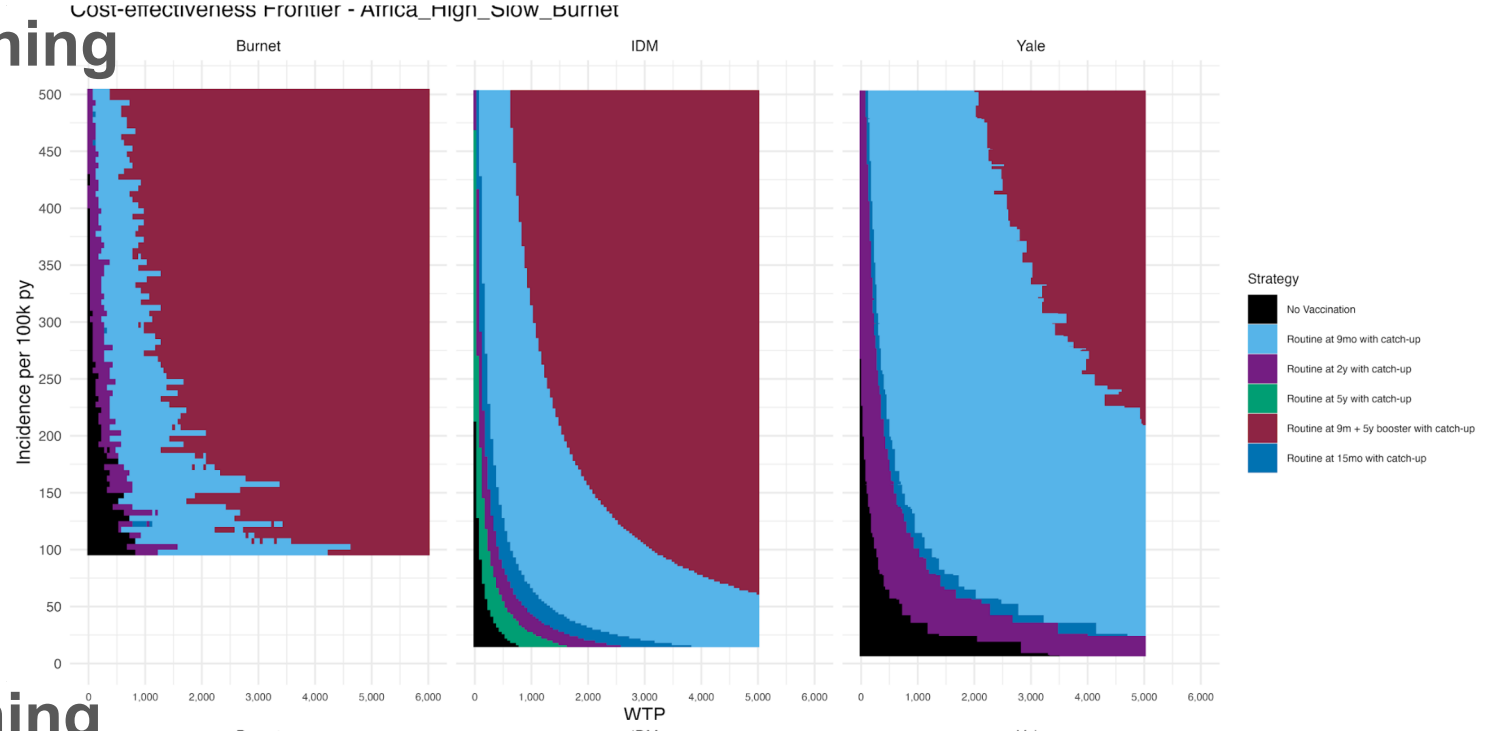


Cost-effectiveness frontier

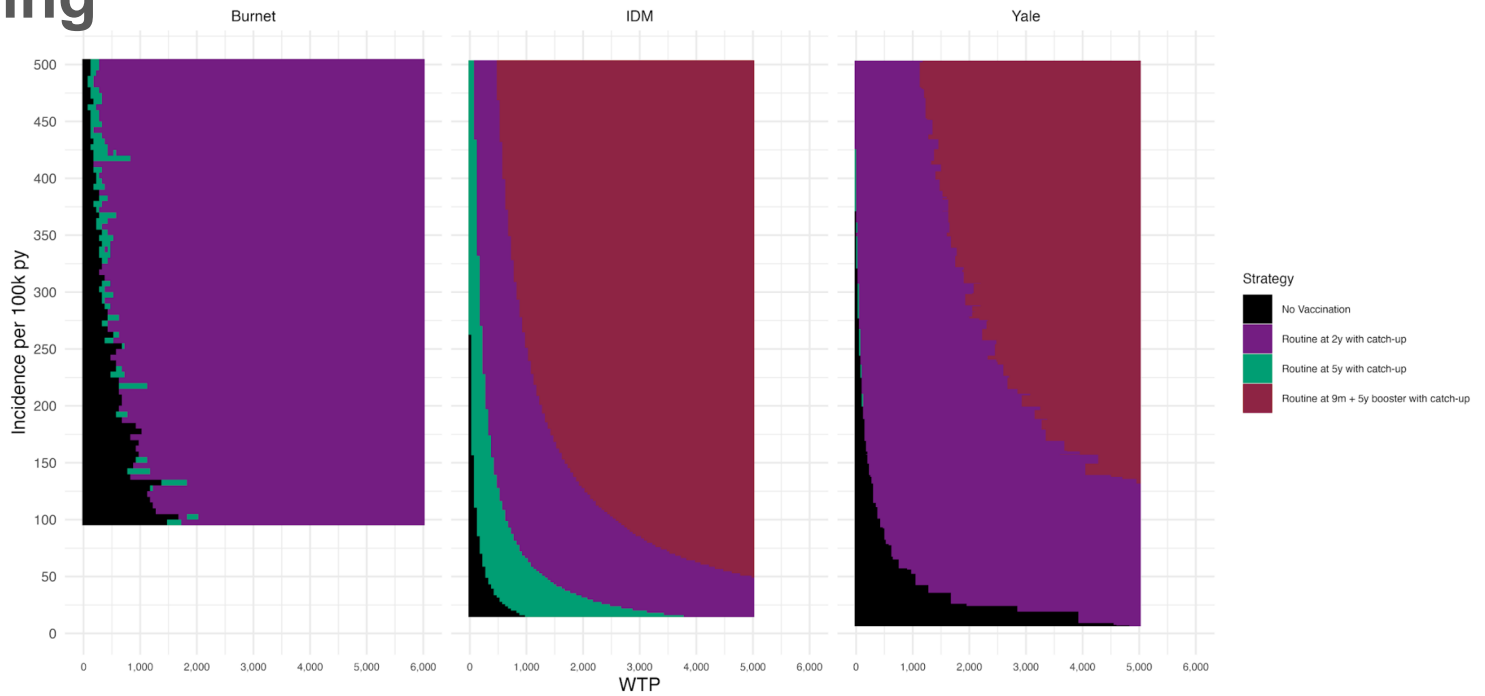
High burden*, Africa region

*Incidence is highest in the 2-5 yr age group

Slow waning



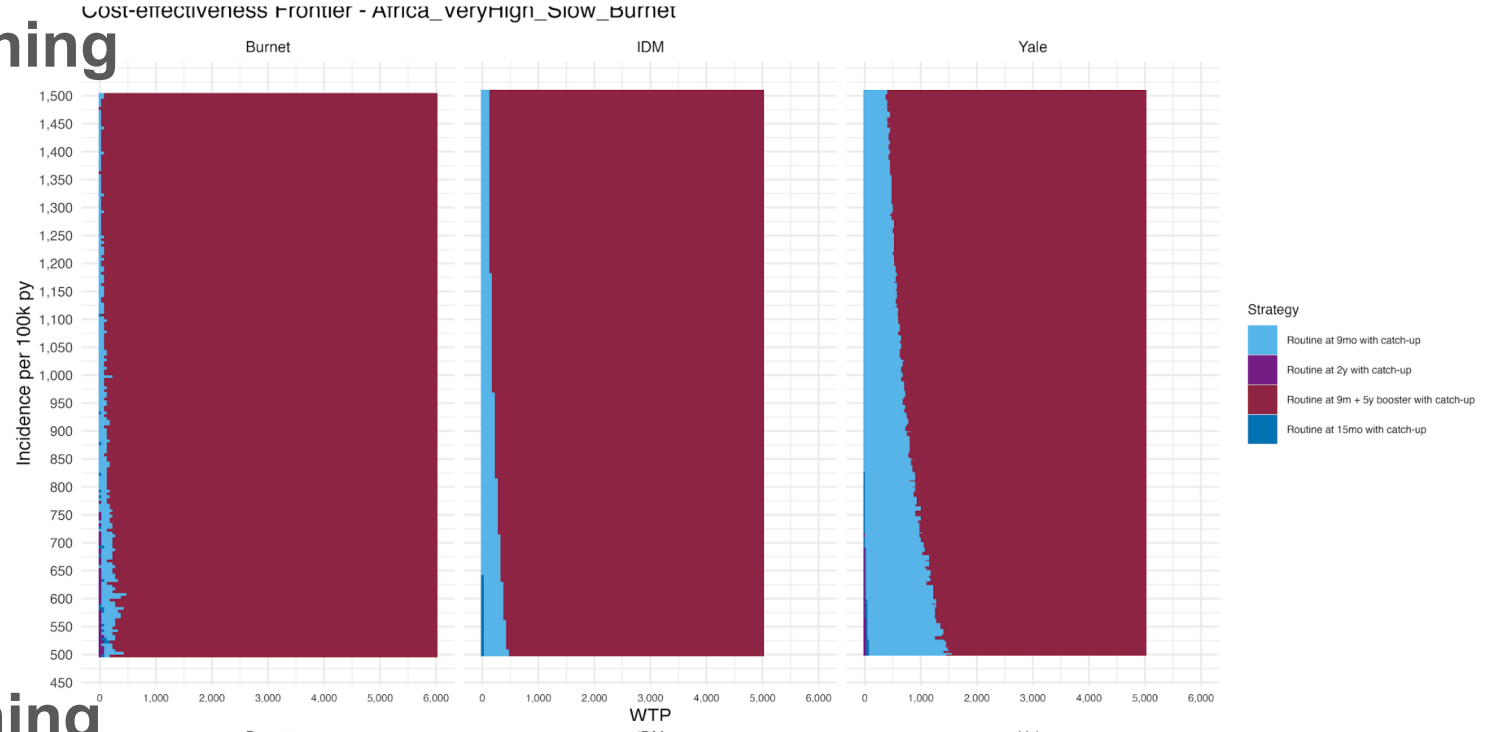
Fast waning



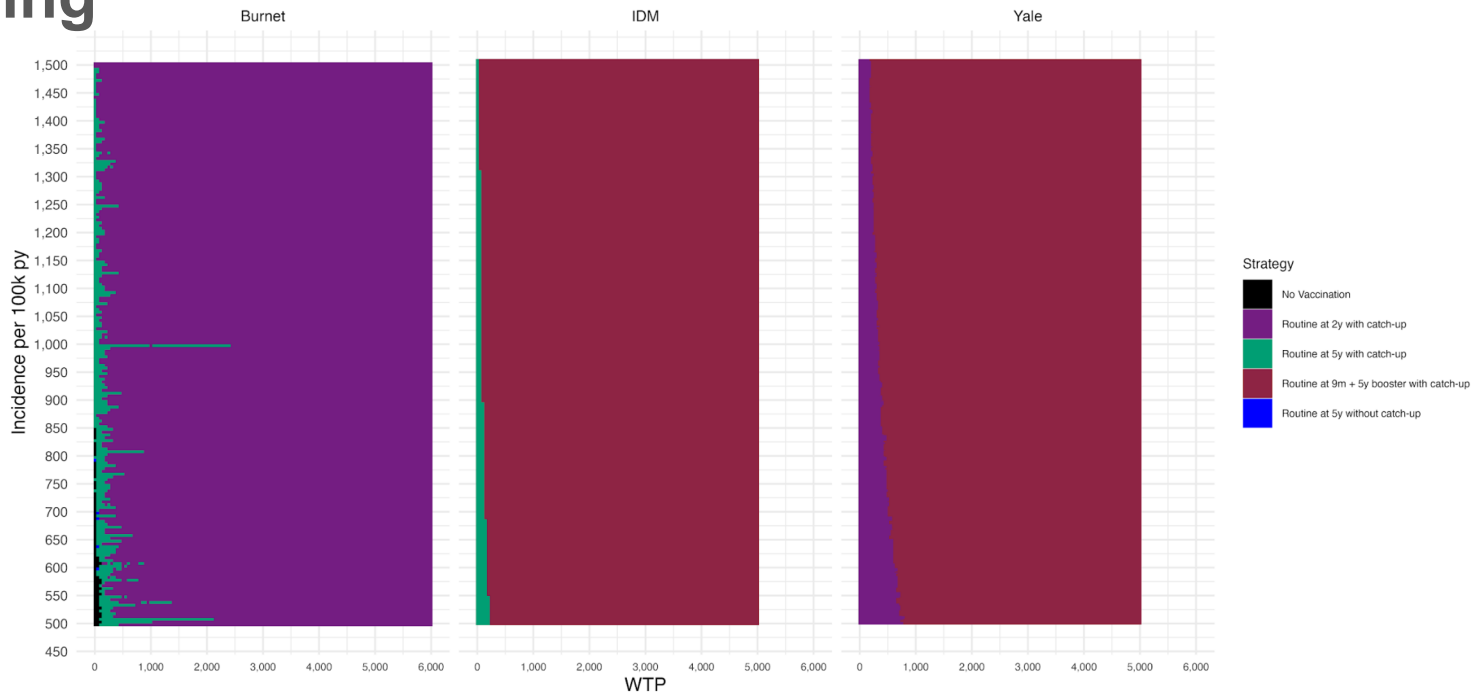
Cost-effectiveness frontier

Very high burden, Africa region

Slow waning



Fast waning

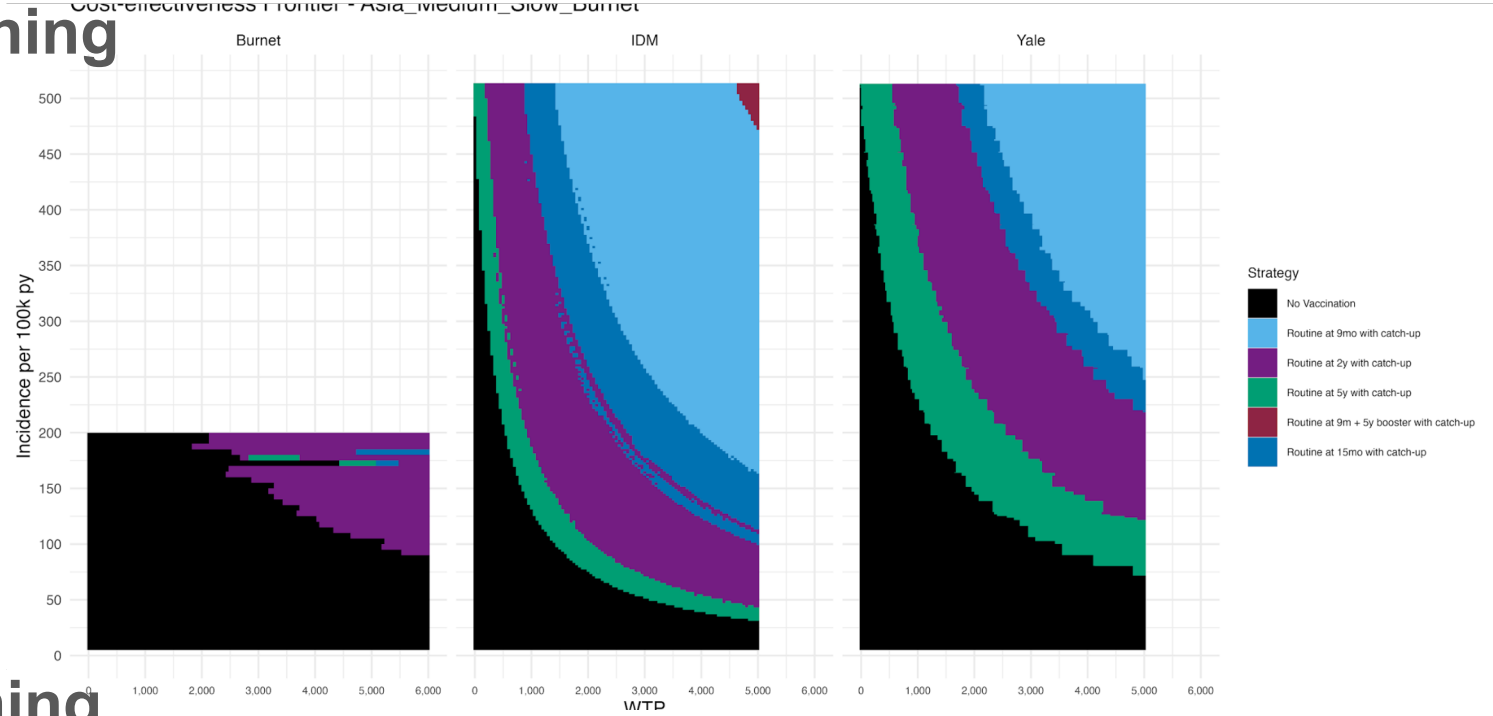


Cost-effectiveness frontier

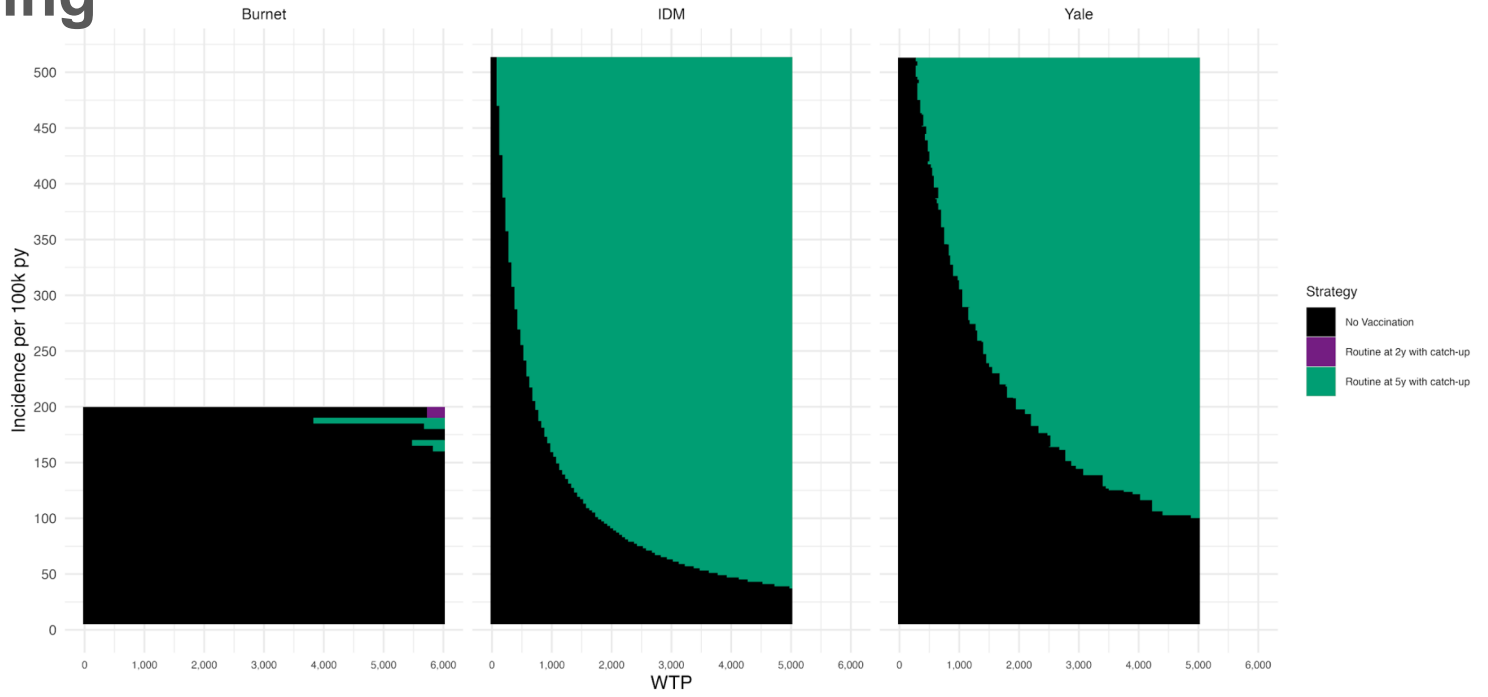
Medium burden*, Asia region

* Incidence is highest in the 5-15 yr age group

Slow waning



Fast waning

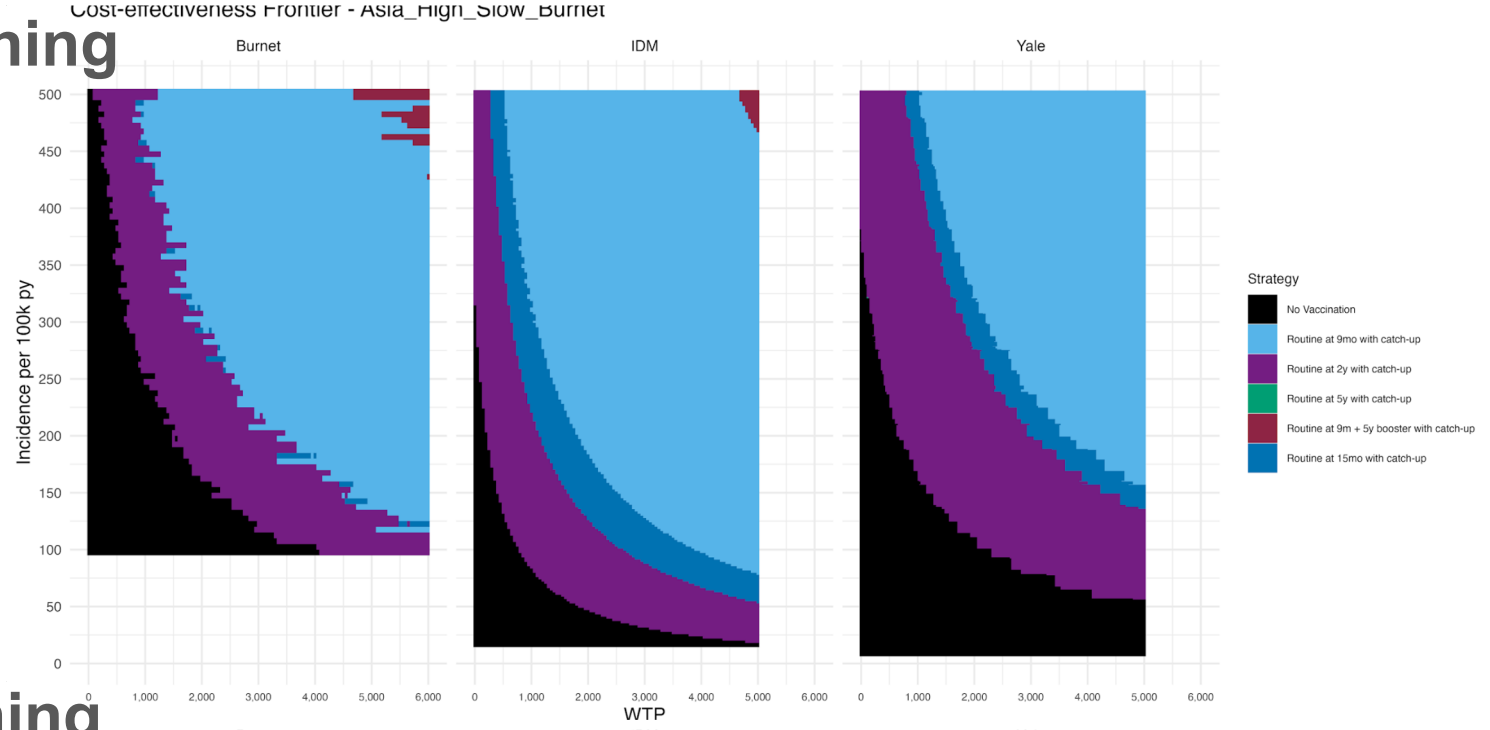


Cost-effectiveness frontier

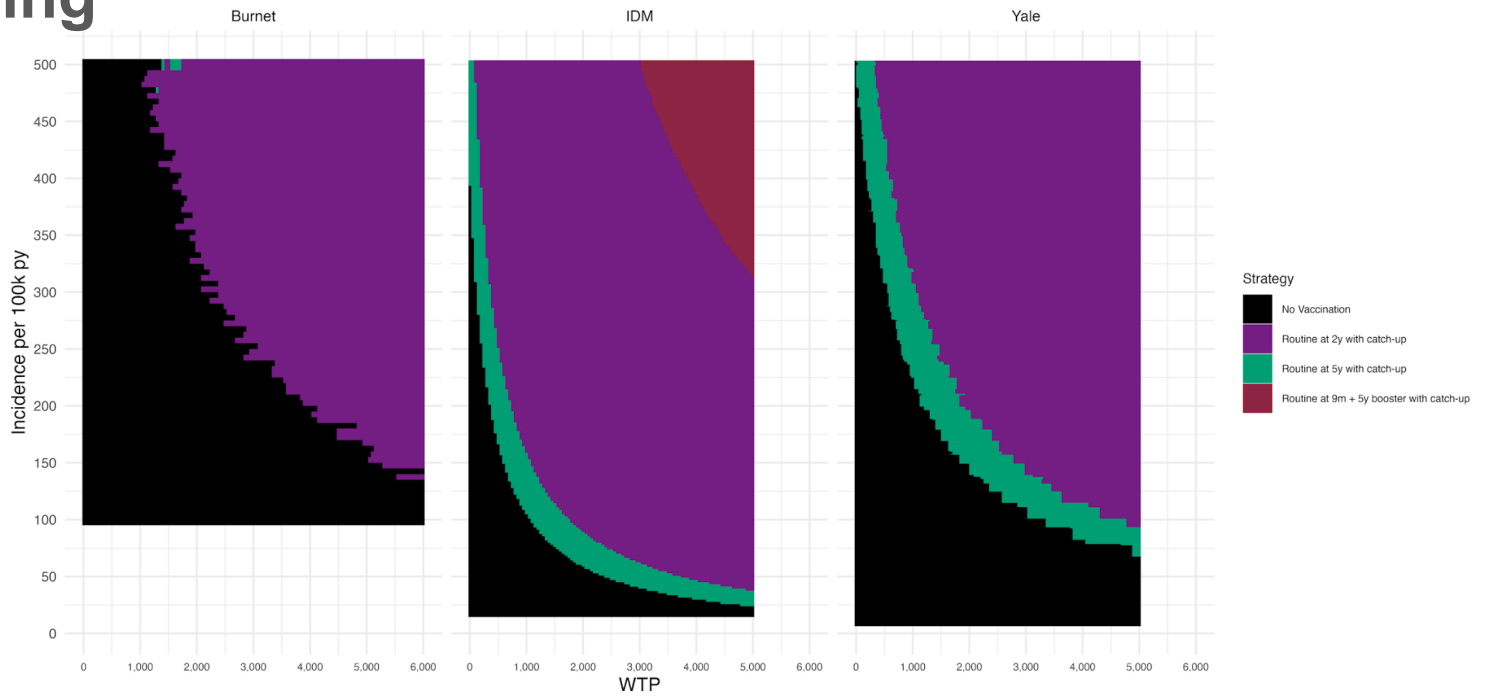
High burden*, Asia region

*Incidence is highest in the 2-5 yr age group

Slow waning



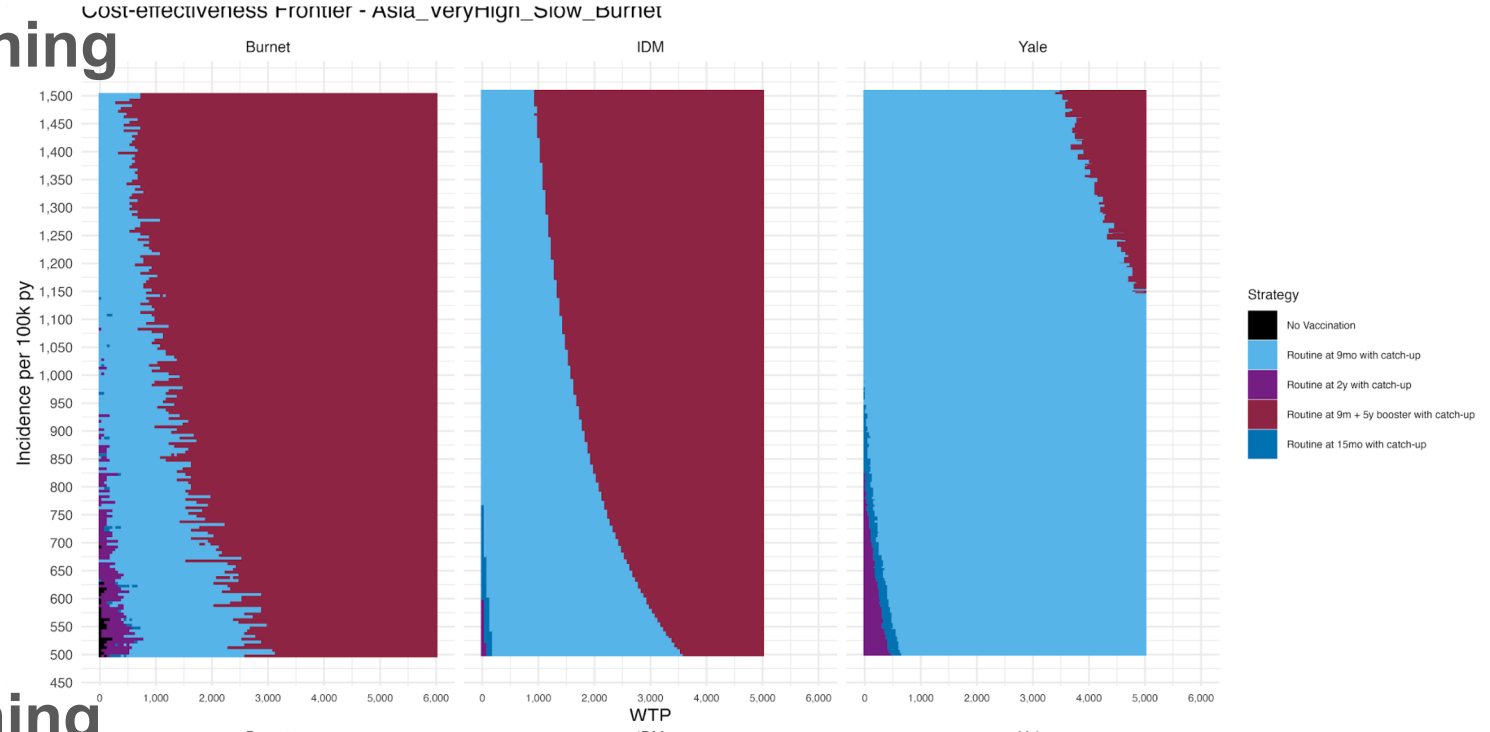
Fast waning



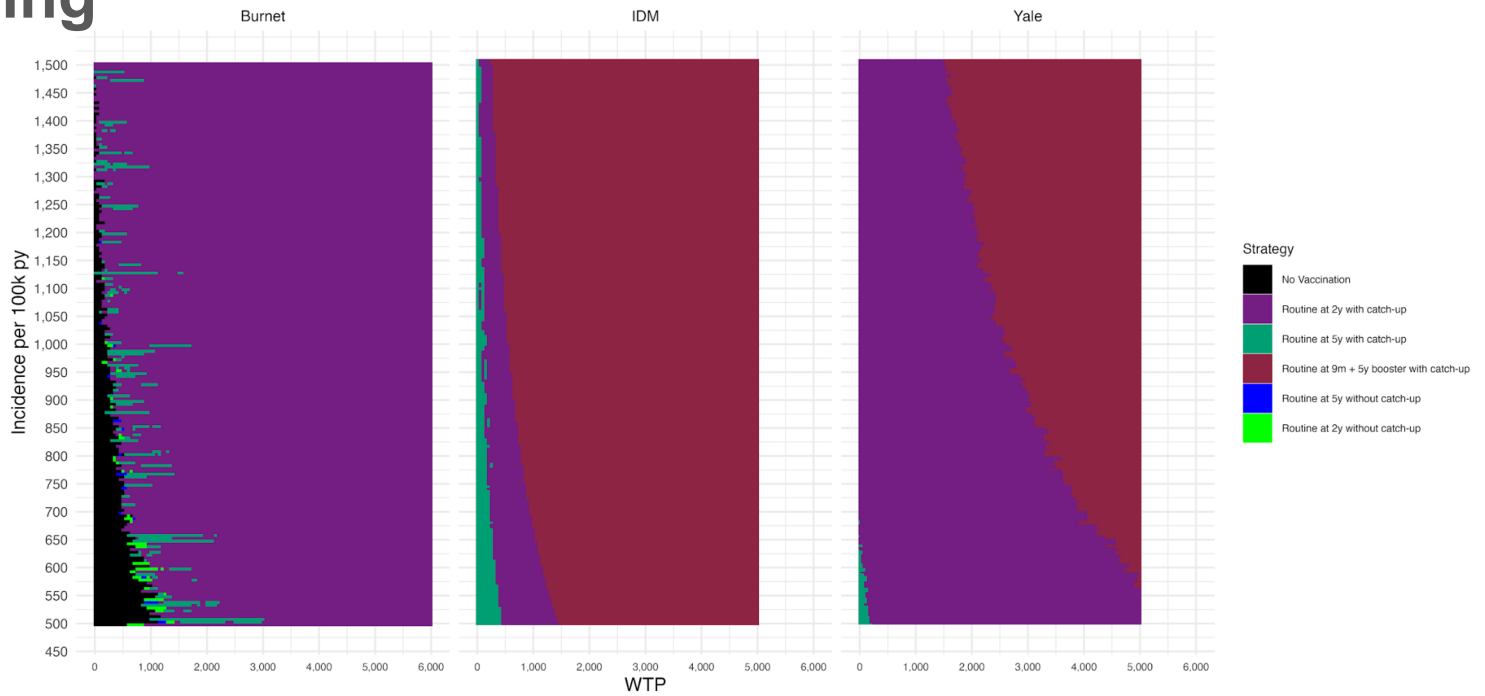
Cost-effectiveness frontier

Very high burden, Asia region

Slow waning



Fast waning



Link to Full Model Comparison Results

"Summary_stats_figures" folder includes vaccine impact results for:

- 20-year ("long") time horizon
- 2-year ("short") time horizon following addition of booster dose (compared to routine vaccination at 9m or 15m alone)

"CEA_Figures" folder includes corresponding CEAFs and CEACs

Response to IVIR-AC recommendations from April 2025 meeting

Recommendations:

- IVIR-AC commends the methodological and systematic approach to model comparisons, including model validation against trial findings and exploring scenarios that capture routine and booster vaccination at different coverage levels and assumptions about the durability of vaccine efficacy. To facilitate understanding of this comprehensive work, IVIR-AC recommends a summary to orientate stakeholders to the objectives and outcomes of each model in a digestible format.

In our presentation to the WHO SAGE typhoid working group, we provided a high-level summary of the differences between the models. All of the models have been validated against the observed indirect effectiveness from a cluster-randomized trial of TCV in Dhaka, Bangladesh. We have explored a comprehensive set of vaccination scenarios, coverage levels, and assumptions about duration of vaccine efficacy.

- IVIR-AC highlights the need for probabilistic sensitivity analyses (PSA) comparing slow versus fast waning of TCV effectiveness across very high-, high-, and medium-burden settings. IVIR-AC emphasizes the importance for the modelling groups to explain key differences in their outputs relative to other models in the multi-model comparison.

PSAs have been performed for both the vaccine impact and cost-effectiveness results. We sampled from uncertainty in transmission model parameters, vaccine efficacy and duration parameters from two different settings, vaccine coverage levels consistent with variability across LMICs, cost-effectiveness parameters, and different incidence settings. We also added a "threshold analysis" examining how the optimal strategy (from a cost-effectiveness standpoint) varies depending on incidence (and age distribution of cases) by varying the reporting rate parameter for the different age-specific incidence patterns. We are working to understand and explain the key differences between the conclusions of the four models.

- IVIR-AC recommends assessing the key drivers of difference between optimal routine vaccination schedules (e.g., 9 months vs. 5 years, with or without boosters) and evaluating their cost-effectiveness in a competing choice framework in relation to the force of infection in each setting. Additionally, systematic exploration of uncertainties—particularly around vaccination coverage differences between age-based strategies—should be prioritized.

We evaluated the cost-effectiveness of the different vaccine delivery strategies using the net benefits framework for each of the three incidence settings and two waning scenarios. For individual models, value of information analysis was used to identify key drivers of decision uncertainty.

- Given the substantial uncertainty in model outputs, IVIR-AC suggests strengthening the robustness assessment of vaccination strategies by quantifying how frequently simulations meet predefined effectiveness thresholds (e.g., percentage of simulations that achieve a specified reduction in incidence over time) and cost-effectiveness thresholds (e.g., cost-effectiveness acceptability curves).

Final results are based on cost-effectiveness acceptability curves for all groups. We have not (yet?) examined the percent of simulations that achieve a specified reduction in incidence because it is not clear what a meaningful threshold might be. Furthermore, rebounds in incidence following an initial catch-up campaign may mean that simulations that reach a pre-specified threshold over shorter time horizon may not achieve that threshold over longer time horizons.

- IVIR-AC recognizes that substantial uncertainty and wide prediction intervals in the presented PSA results preclude definitive conclusions about optimal vaccination strategies. The analysis should focus on identifying key uncertainty drivers, including vaccine waning rates, durability, force of infection, and cost variations, and use frontier curves and tornado diagrams for comparisons. Targeted investigation of these factors can help narrow prediction intervals, reduce ambiguity, and facilitate clearer comparisons between schedule options.

Our primary results are based on cost-effectiveness acceptability frontiers for all groups. The impact of parameter uncertainty is being explored by the individual modeling groups.

- Given substantial uncertainty surrounding vaccine durability and booster dose effectiveness, IVIR-AC advises careful consideration in communicating these model results for policy decisions until further evidence is available. IVIR-AC notes that re-evaluation of model scenarios may be necessary as new data emerge.

We have updated our analysis to incorporate the most recently available estimates of vaccine efficacy over time and re-estimated parameters for the initial VE and duration of vaccine-induced immunity based for the fast-waning scenario. While there is no data available yet on the clinical efficacy of booster doses, immunogenicity data suggests that booster doses (when given at least 2 years from the initial dose) generate an immune response that is somewhat more robust (slightly higher initial antibody and slower waning) than the first dose. Thus, our analysis of the potential impact and cost-effectiveness of booster doses may be conservative.

- IVIR-AC suggests that future modeling work may explore surveillance strategies to allow reactive booster dose implementation based on emerging evidence on durability of protection in the early years of life.

This is a valuable suggestion for future work, but beyond the scope of the current analysis.

Additional recommendations

- IVIR-AC recommends that modelling groups using individual-based models conduct additional analyses to evaluate how individual variability in vaccine efficacy contributes to overall uncertainty in their estimates and predictions.

The IDM group explored the relative impacts of individual variance in vaccine response and decay and in simulation-level variance in vaccine coverage on overall model uncertainty. They found that sampling vaccine coverage contributes substantially more uncertainty in model results than individual variance in VE0/decay. Much of the variance from VE0/decay is averaged out (within each model iteration) when calculating population-level metrics like incidence or total DALYs.

WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS)

Ginny Pitzer (on behalf of the modeling teams)

WHO SAGE typhoid working group meeting

7th May 2025

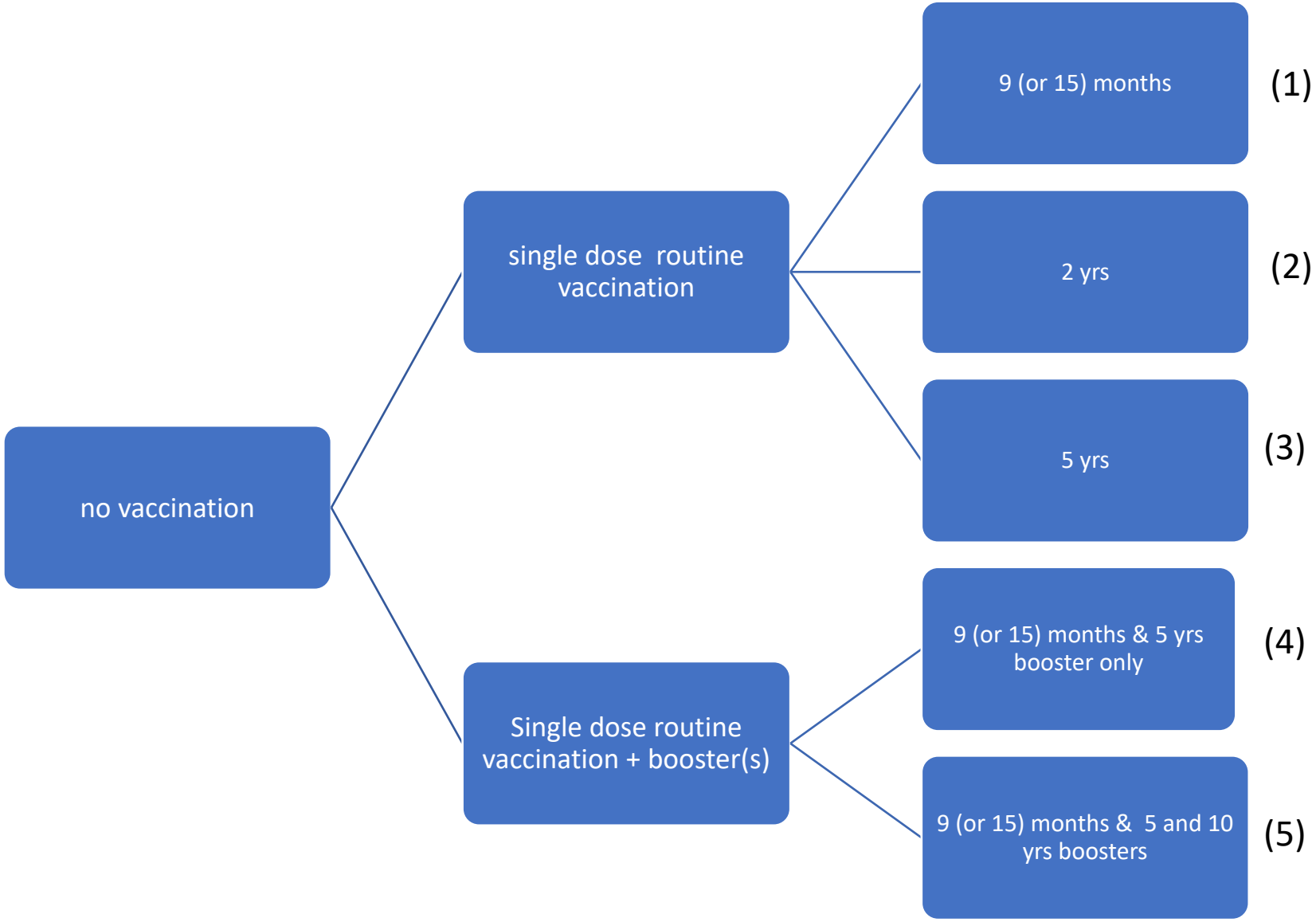
Yale SCHOOL OF PUBLIC HEALTH

Purpose of the models

- To determine the optimal schedule of Typhoid Conjugate Vaccine (TCV) through different schedule scenarios from the **public health impact** and **cost-effectiveness** perspective.

- Four modeling groups selected to conduct a multi-model comparison:
  - Yale School of Public Health
  - Stanford University
  - Gates Foundation Institute for Disease Modeling (IDM)
  - Burnet Intitute

Overview of modeling strategies and assumptions



Assumptions for all five strategies:

A. With and without **catch-up campaigns** to 15 yrs

B. Coverage

- **9 (or 15) months** based on first- (or second-) dose measles-containing vaccination (MCV1 or MCV2) coverage;
- **2 yrs** to be lower and uncertain (e.g., 50-90% of MCV2)
- **5 yrs** to be uncertain and based on school attendance

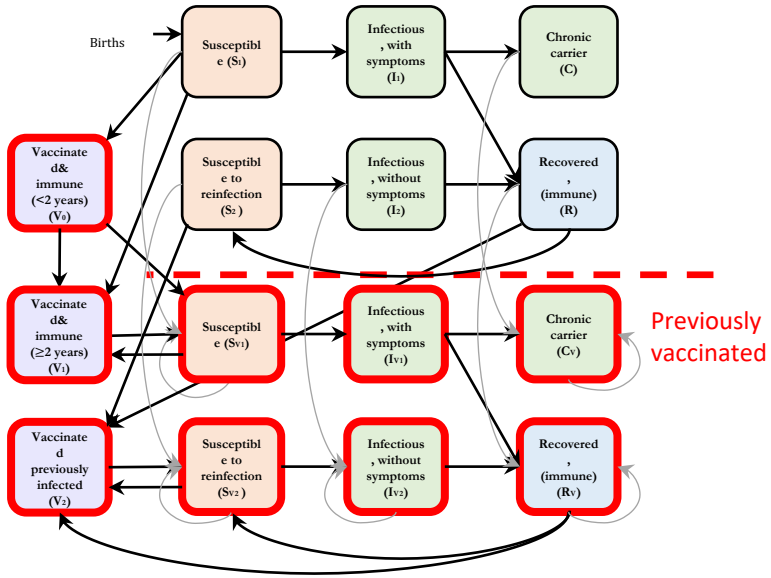
C. Waning efficacy scenarios

- Bangladesh-like (i.e., **faster**)
- Malawi-like (i.e., **slower**)

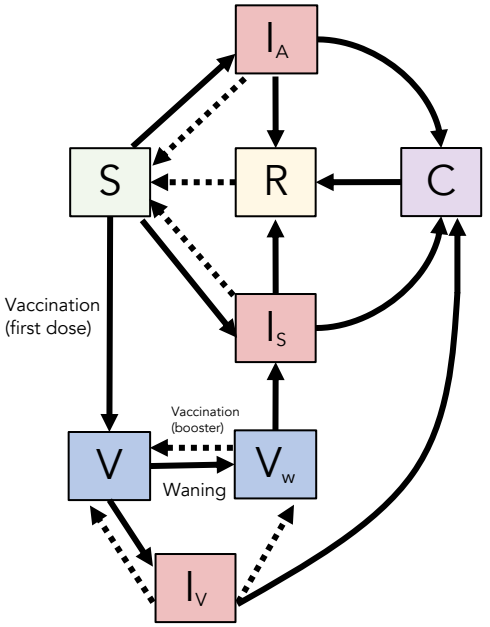
Overview of the transmission models

- Two compartmental, two agent-based models
- All models include the following states:
  - Susceptible, Infectious, Recovered
  - Acute vs subclinical infection
  - Chronic carriers
    - Age- (and sex-) specific probability following infection
    - Duration: 10 years to life-long
  - Vaccinated
    - Waning immunity (depending on age at vaccination)

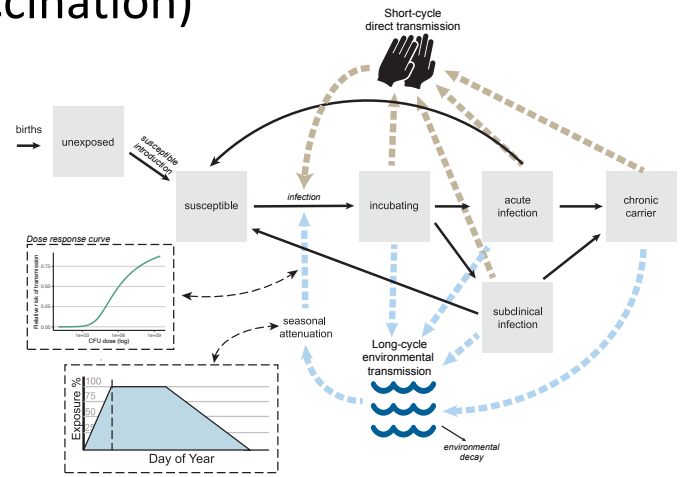
Yale model



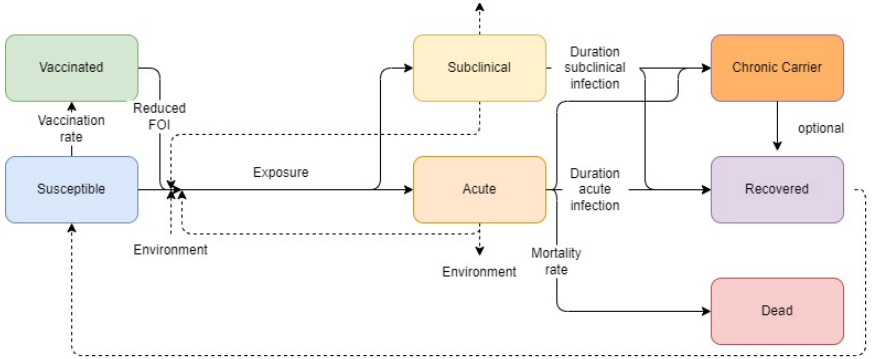
Stanford model



IDM model

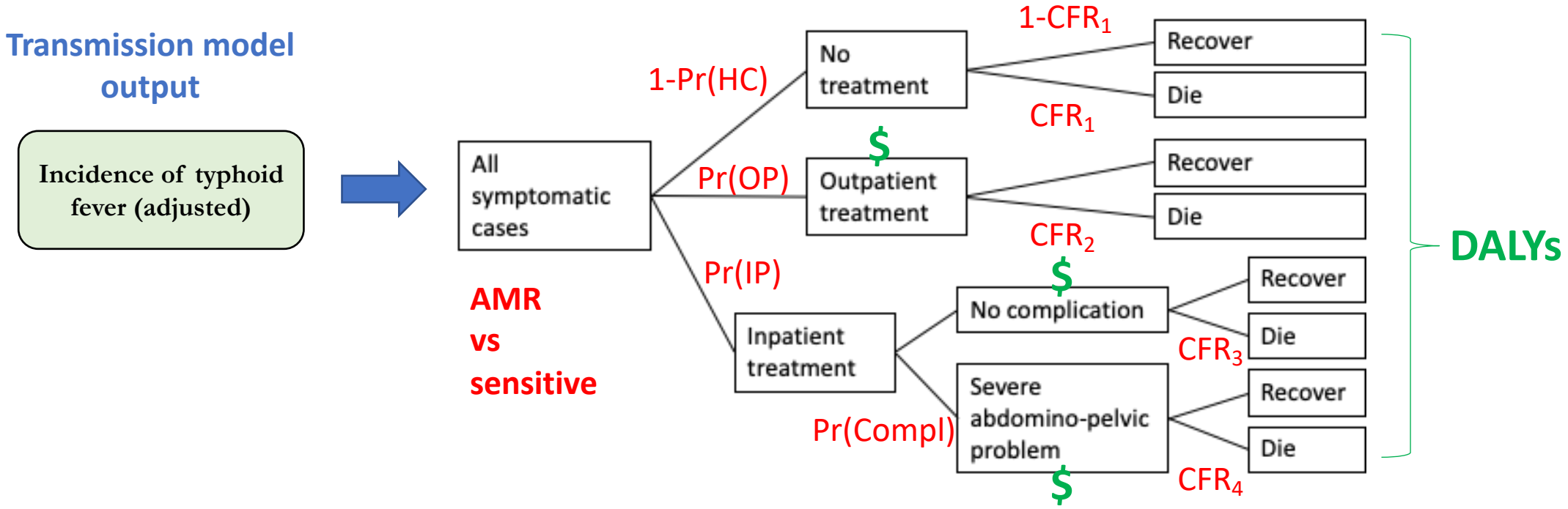


Burnet model



Health economic models

- Link to decision tree model for health economic analysis
  - Sample from uncertainty in **treatment probabilities**, **case fatality risks**, **treatment costs**, **DALY weights**, etc.



Model calibration:

Burden archetypes and incidence age distributions

Transmission model
R0, age-related risk or reporting, prob. of symptoms, etc.

Health economic model
Healthcare seeking, Probability of hospitalization, Risk of complications, CFR, costs of illness, cost of delivery

Medium incidence	High incidence	Very High incidence
Africa	**Africa**	**Africa**
Higher CFR, prob of hospitalization, risk of complications		
Higher treatment costs (especially adult inpatient)		
Asia/WPR	**Asia/WPR**	**Asia/WPR**
Lower CFR, prob of hospitalization, risk of complications		
Lower treatment costs (especially adult inpatient)		

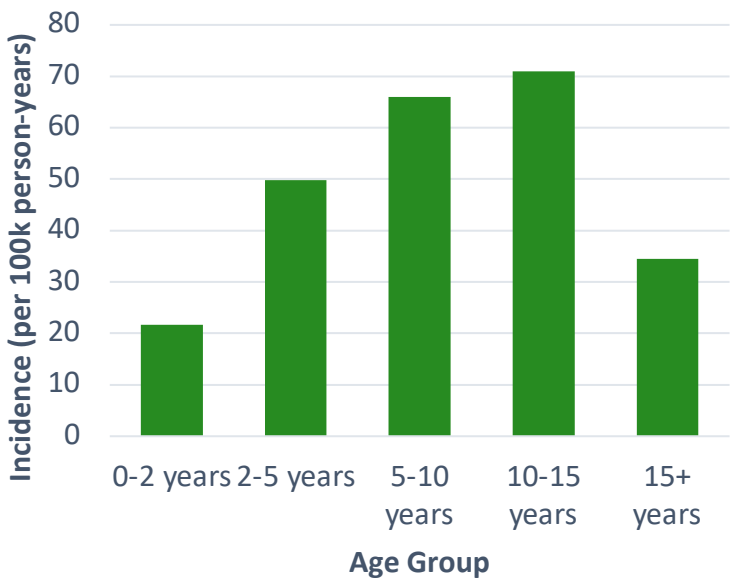
Evaluate **fast-waning** and **slow-waning** scenarios for vaccine protection across each incidence rate archetype

12 scenarios

Incidence Data by Burden Setting

Medium Burden

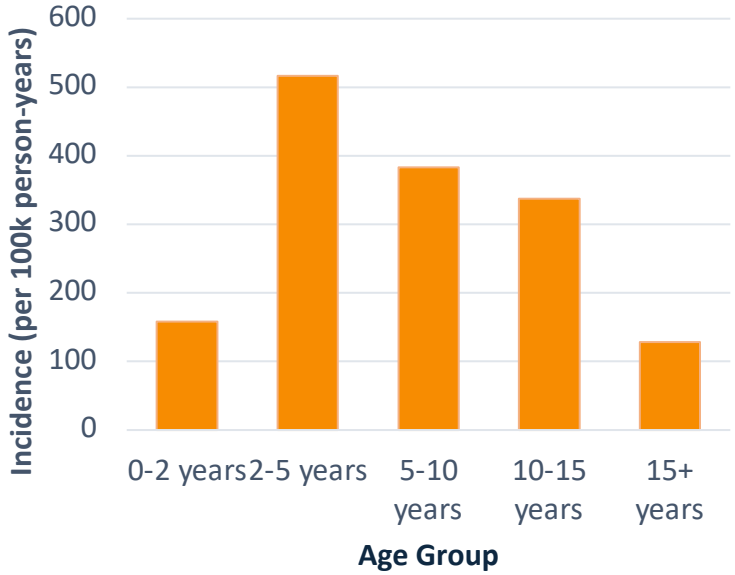
10 to <100 cases per 100k person-years



	Cases	Person-years	Incidence (per 100k pys)
0-<2y	3	13801	21.7
2-<5y	10	20074	49.8
5-<10y	30	45891	66
10-<15y	32	44580	71
15+y	18	52249	34.5
Overall	**93**	**176595**	**52.7**

High Burden

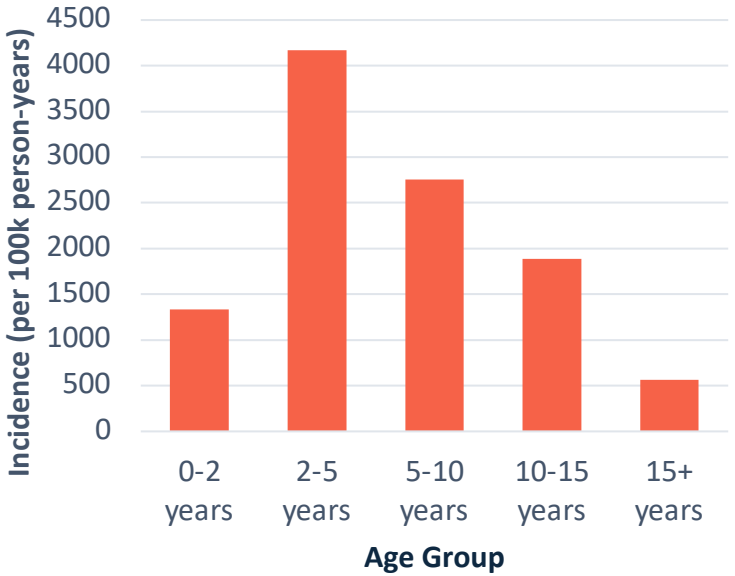
100 to <500 cases per 100k person-years



	Cases	Person-years	Incidence (per 100k pys)
0-<2y	39	24601	158.5
2-<5y	185	35784	517.0
5-<10y	275	71742	383
10-<15y	235	69692	337
15+y	450	350883	128.2
Overall	**1184**	**552702**	**214.2**

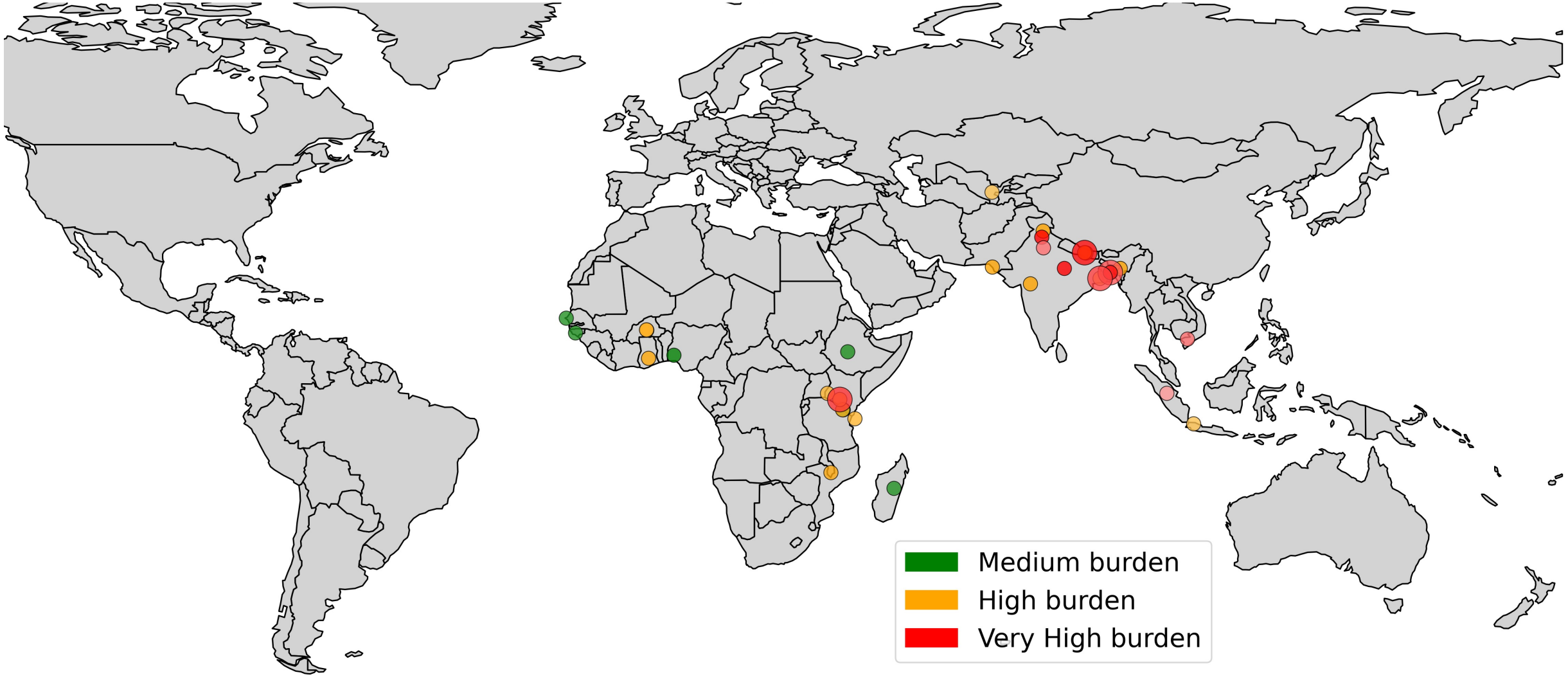
Very High Burden

≥ 500 cases per 100k person-years



	Cases	Person-years	Incidence (per 100k pys)
0-<2y	53	3976	1333.0
2-<5y	241	5784	4166.7
5-<10y	359	13019	2757
10-<15y	239	12647	1890
15+y	367	64928	565.2
Overall	**1259**	**100355**	**1254.5**

Incidence data by burden setting

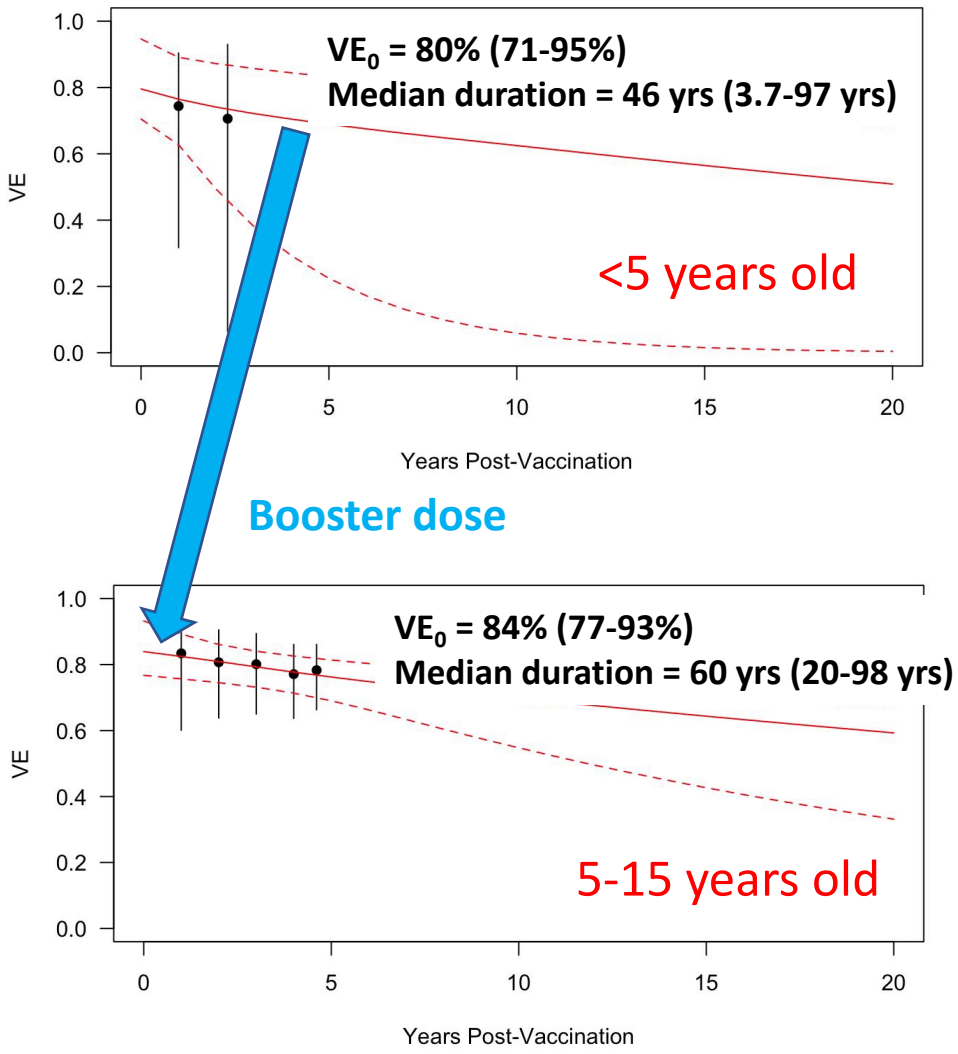


Waning of vaccine effectiveness

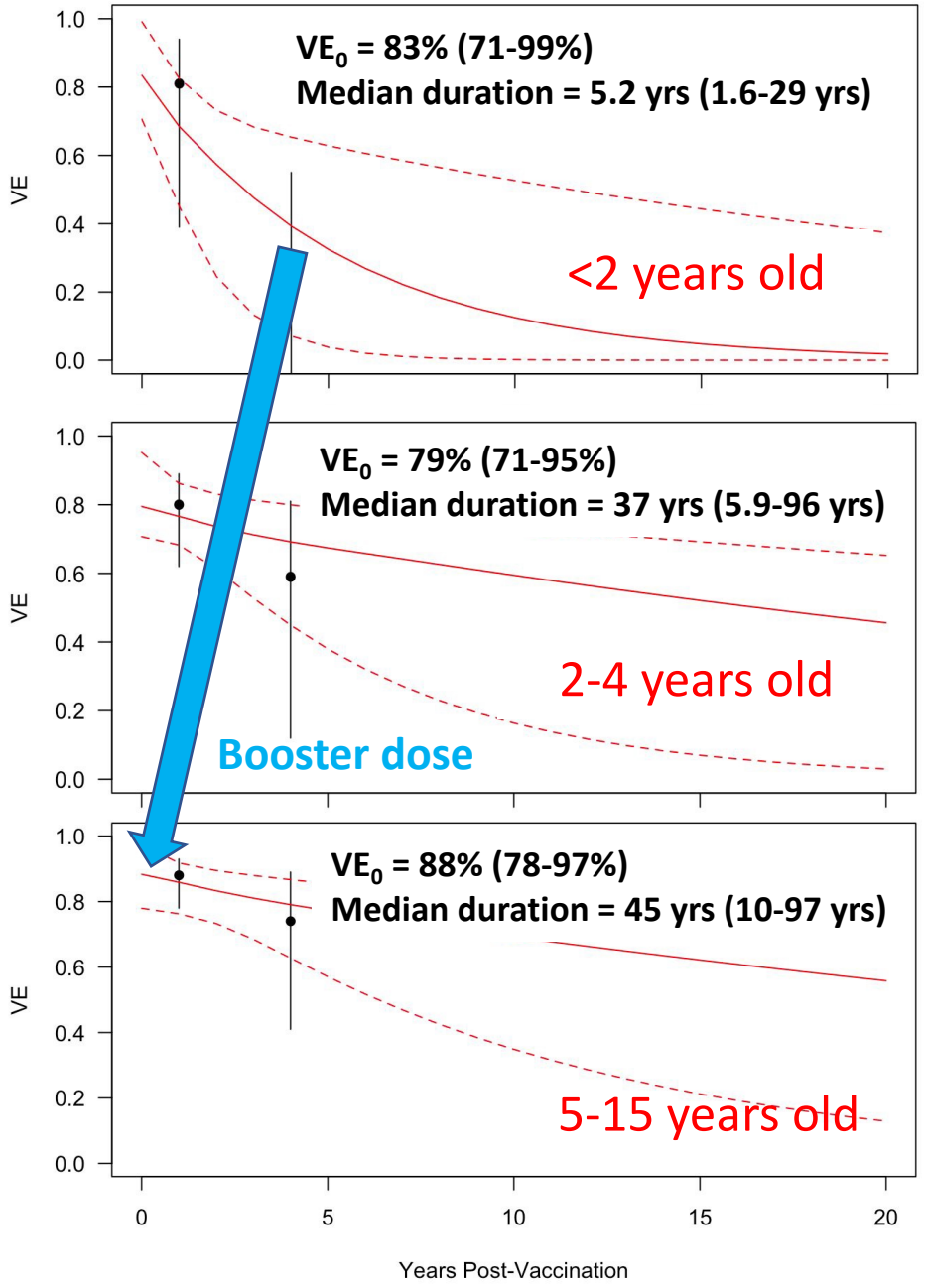
Routine vaccination doses (<5 yrs)

Campaign & booster doses (5-15 yrs)

Slow waning (Malawi)



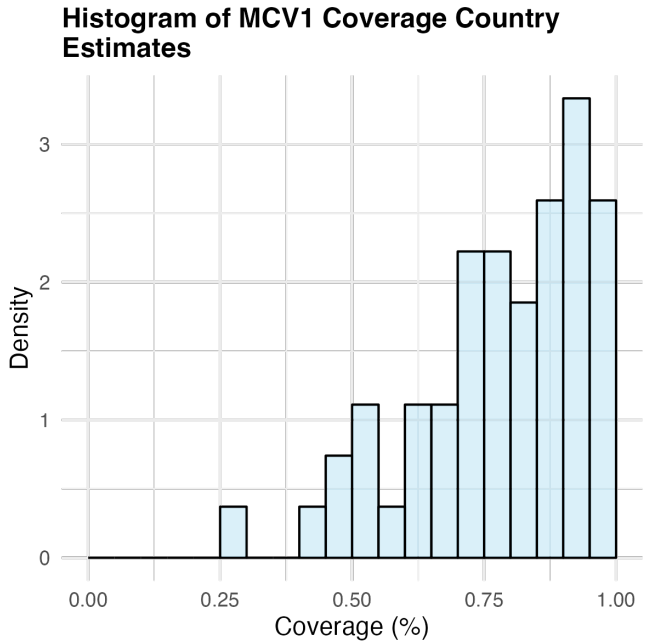
Fast waning (Bangladesh)

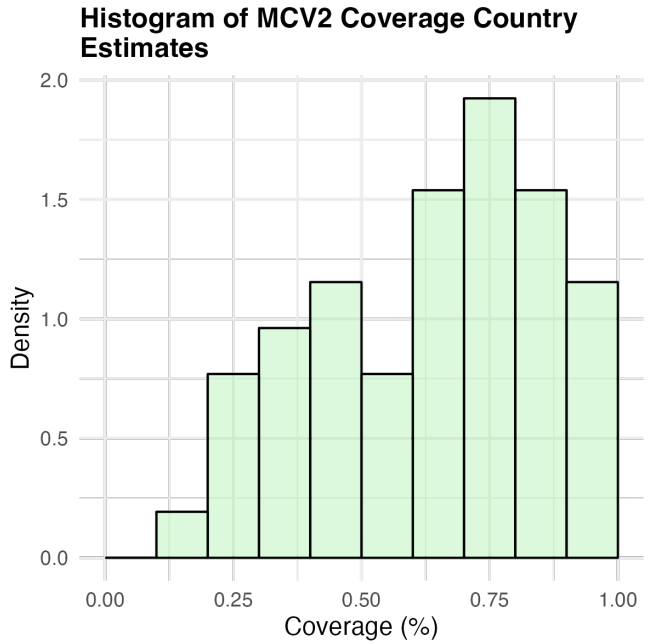


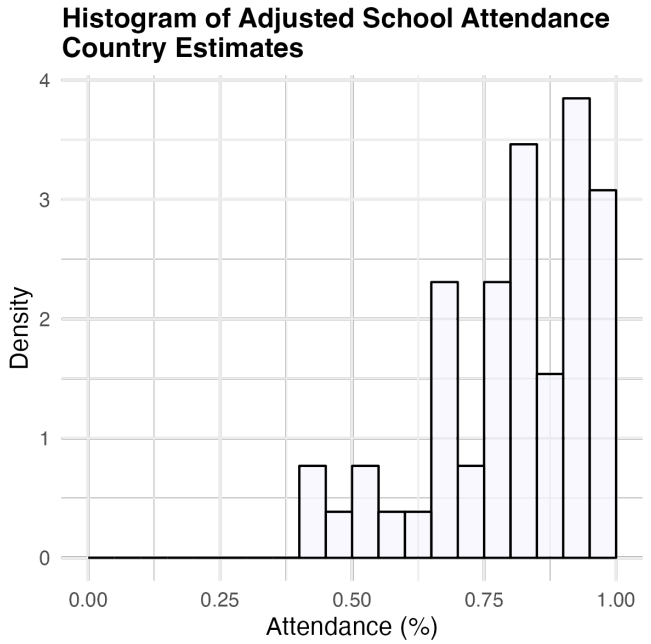
Vaccine Coverage

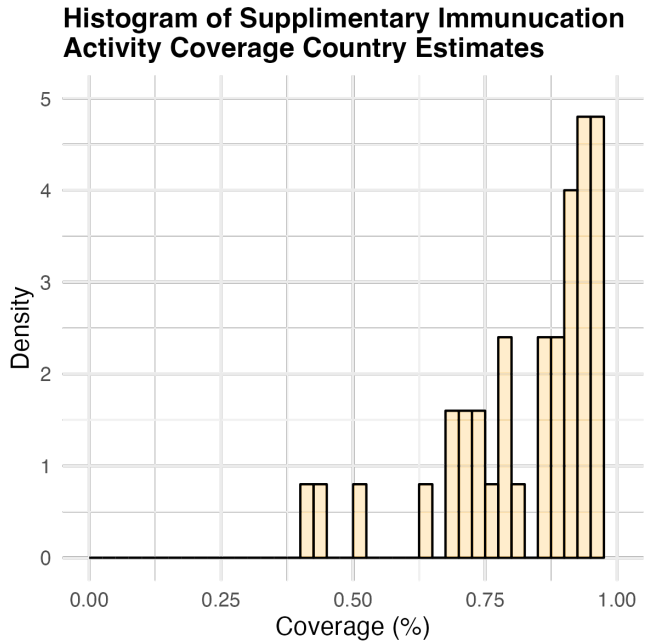
- **Routine coverage at 9 months:** MCV1 estimates for LMICs
- **Routine coverage at 15 months:** MCV2 estimates for LMICs
- **Routine coverage at 2 years:** 50-100% of MCV2 distribution
- **Routine/booster coverage at 5 years:** 50-100% of school attendance (UNICEF)
- **Catch-up campaign coverage**: based on TCV campaign coverage estimates

Coverage estimates were sampled to preserve correlation between coverage types while allowing for parameter uncertainty.









N=46

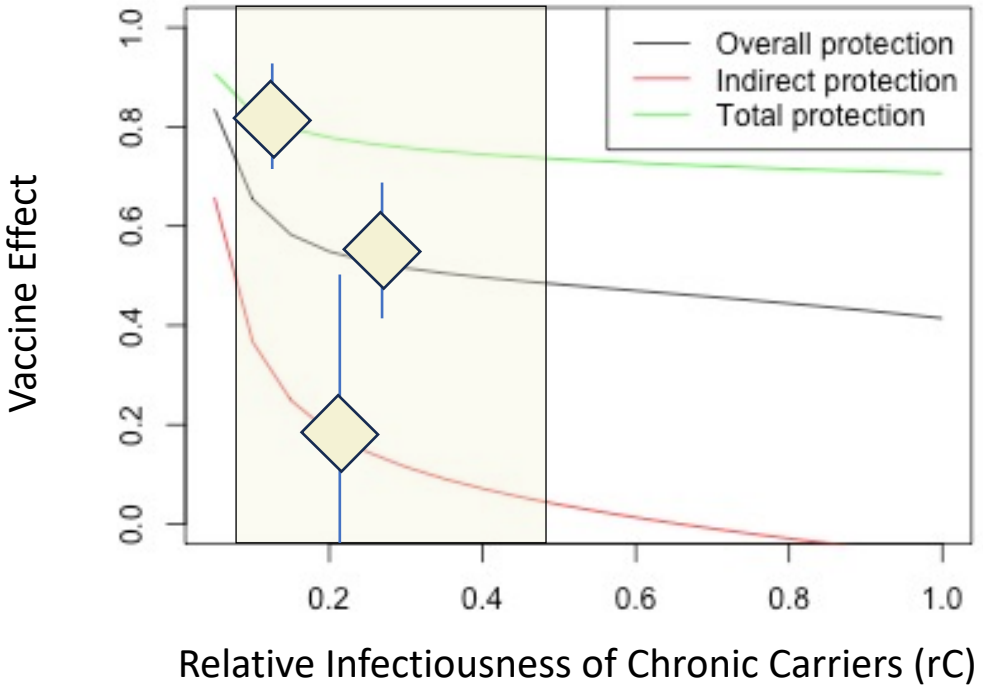
Model validation

- Demonstrate the models can reproduce observed indirect and overall effectiveness from Bangladesh cRCT

	SA 14-14-2 group	Vi-TT group	Protective effectiveness (%)
Total vaccine protection	n=30 685	n=30 882	..
Typhoid fever	192	29	..
Person-years of follow-up	30 253	30 349	..
Incidence rate, per 100 000 person-years	635 (548 to 731)	96 (64 to 137)	85% (97·5% CI 76 to 91)
Overall vaccine protection	n=155 448	n=155 841	..
Typhoid fever	331	144	..
Person-years of follow-up	155 458	154 449	..
Incidence rate, per 100 000 person-years	213 (191 to 237)	93 (79 to 110)	57% (97·5% CI 43 to 68)
Indirect vaccine protection	n=134 835	n=135 110	..
Typhoid fever	139	115	..
Person-years of follow up	125 205	124 100	..
Incidence rate, per 100 000 person-years	111 (93 to 131)	93 (77 to 111)	19% (95% CI −12 to 41)

Qadri et al (Lancet, 2021)

- Possible parameters to calibrate:
  - VE against infection (vs symptoms)
  - relative infectiousness of chronic carriers



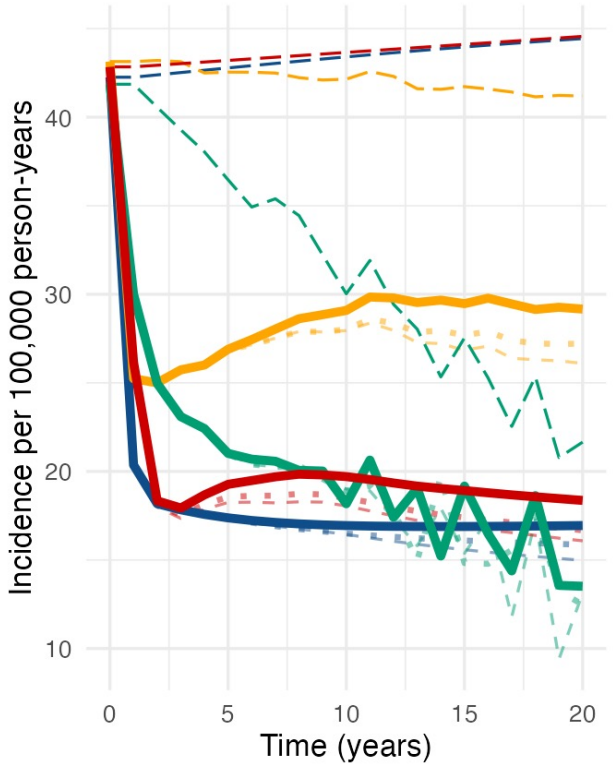
Preliminary results:

Vaccine Impact

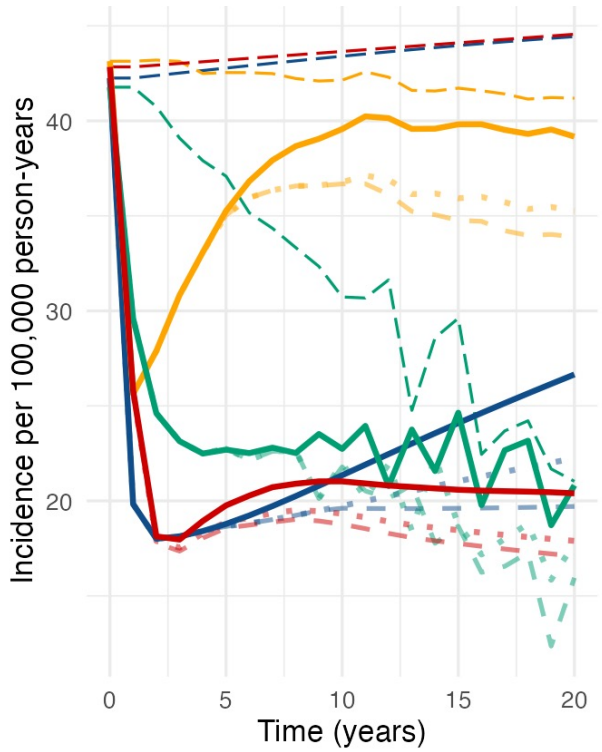
Medium incidence setting:

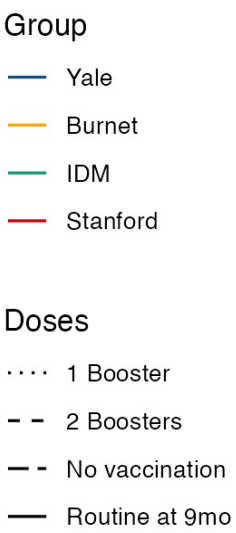
Routine vaccination at 9m with/without booster doses

Slow waning



Fast waning



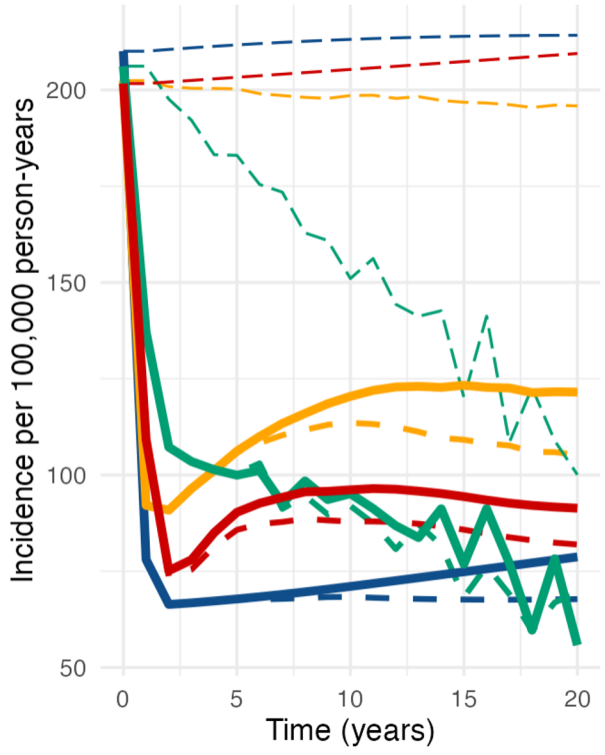


- Yale model predicts the largest initial decline in incidence, moderate rebound under ”fast waning” scenario
- Burnet model predicts moderate initial impact and large rebound in incidence under “fast waning” scenario
- IDM model predicts smallest initial impact, declining incidence even in the absence of vaccine
- Stanford model predicts similar initial decline in incidence, slight rebound under both waning scenarios

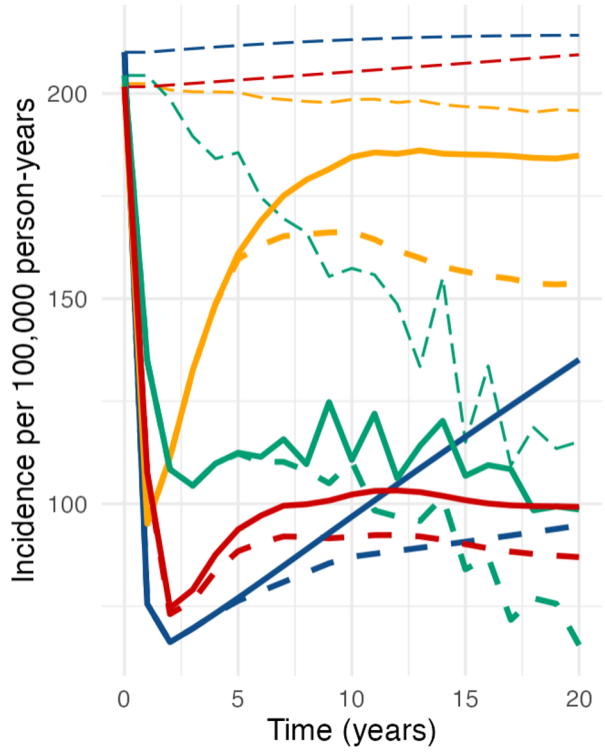
High incidence setting:

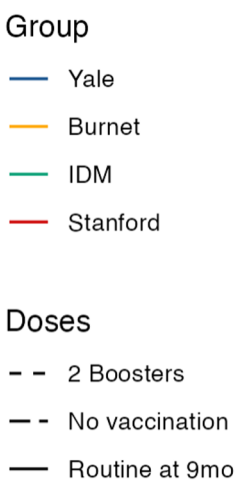
Routine vaccination at 9m with/without booster doses

Slow waning



Fast waning





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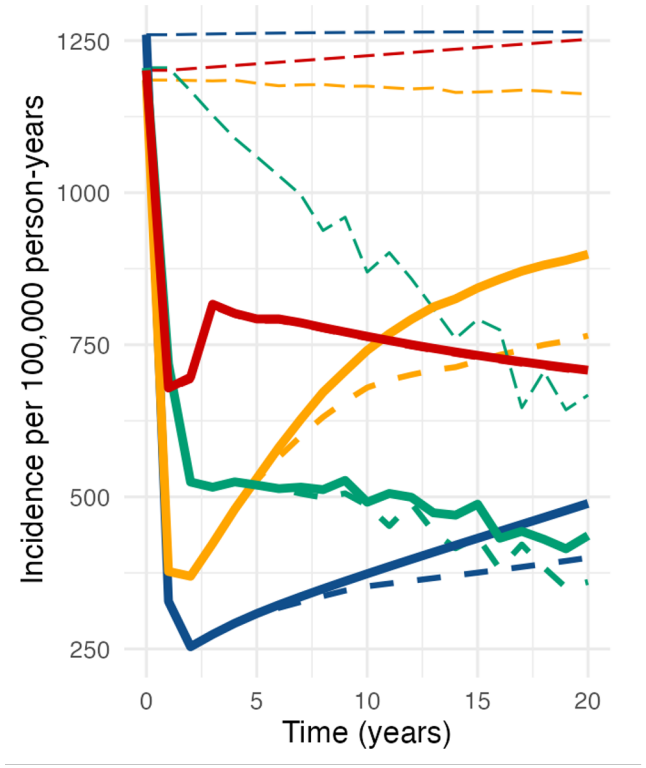
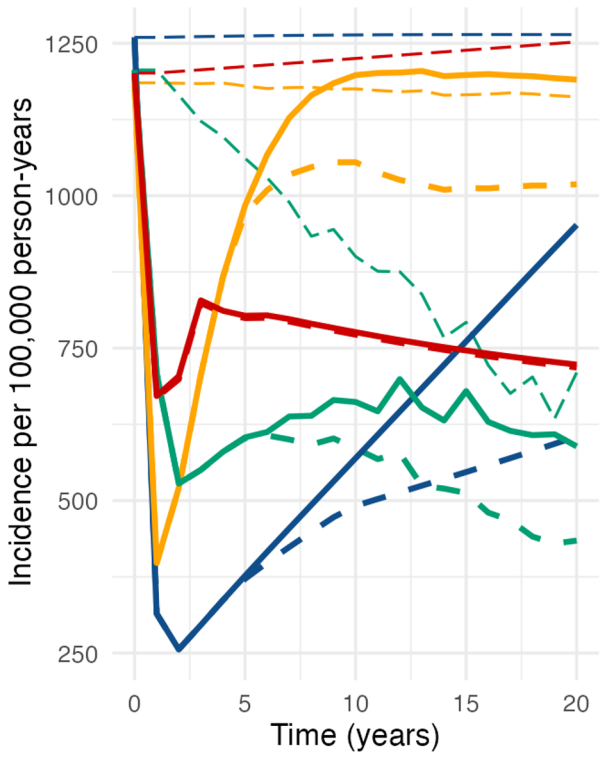
Very high incidence setting:

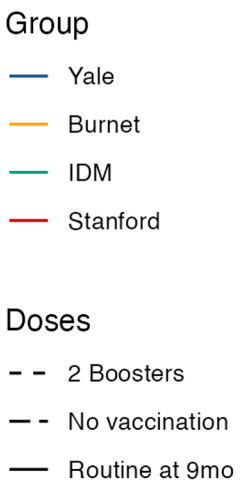
Routine vaccination at 9m with/without booster doses

Slow waning



Fast waning



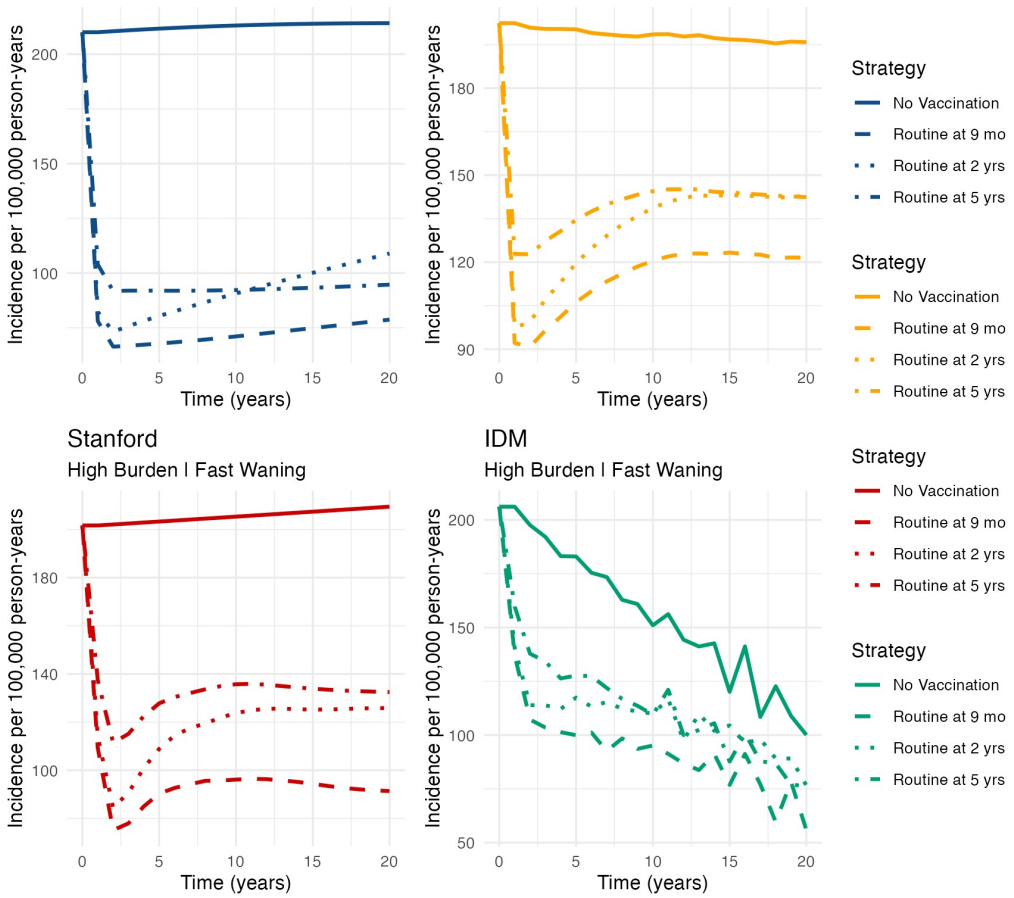


- Yale model again predicts the largest initial decline in incidence, moderate rebound under both waning scenarios
- Burnet model predicts larger initial impact and large rebound in incidence especially under “fast waning” scenario
- IDM model predicts moderate initial impact, slight rebound under ”fast waning” scenario
- Stanford model predicts lower initial decline in incidence, slight rebound followed by gradual decline under both waning scenarios

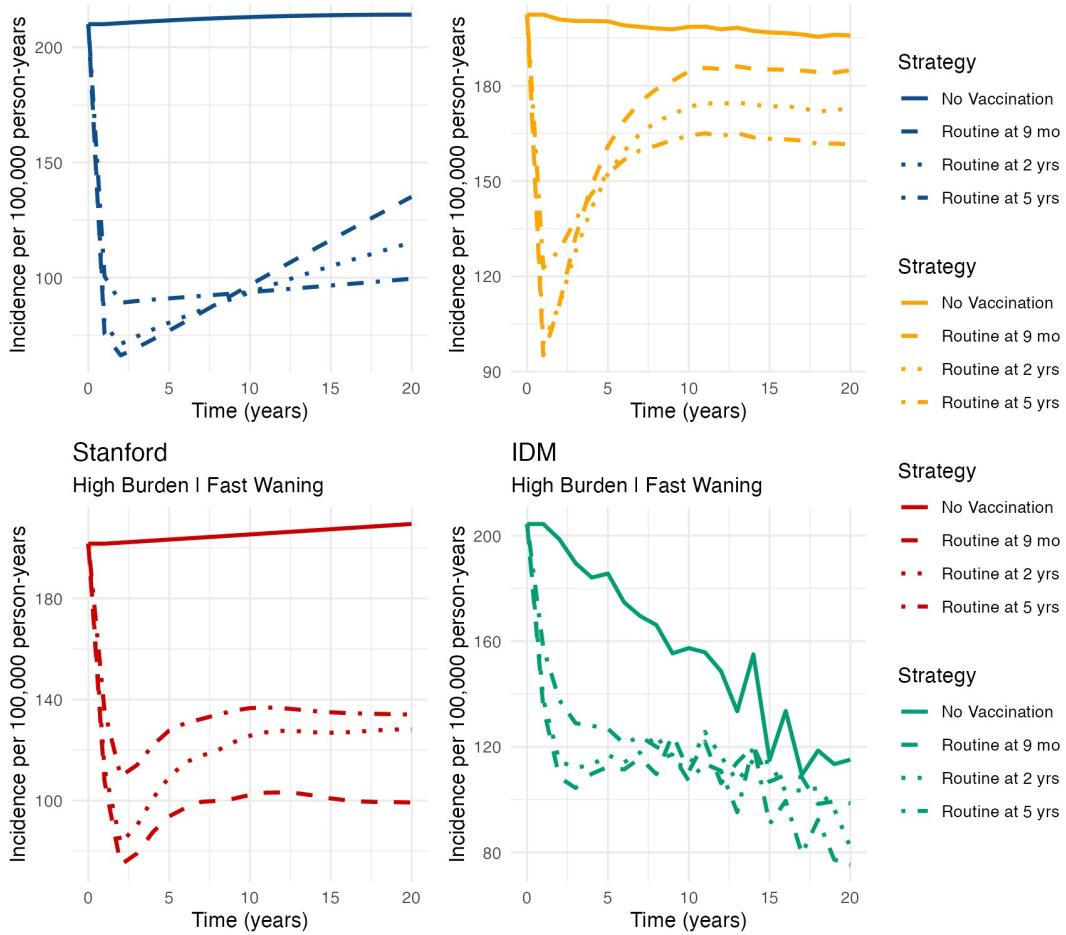
Age at routine vaccination (9m, 2y, or 5y)

High incidence setting

Slow waning



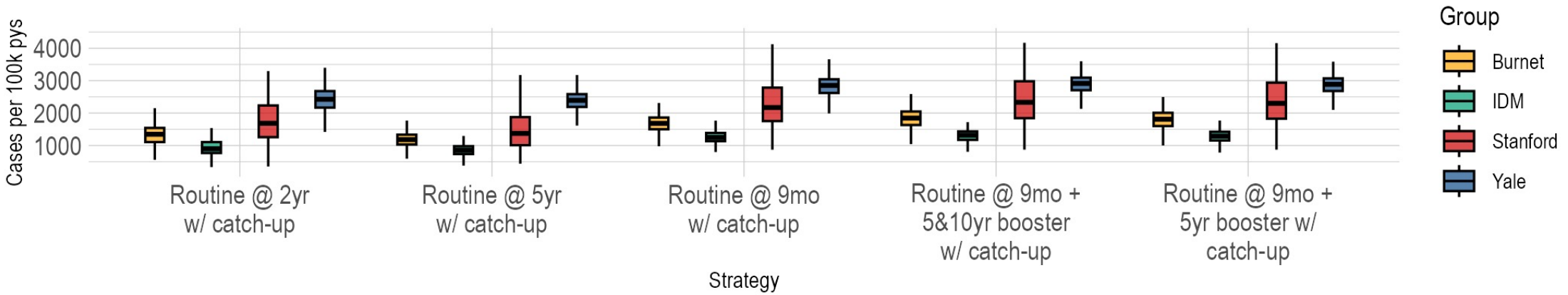
Fast waning



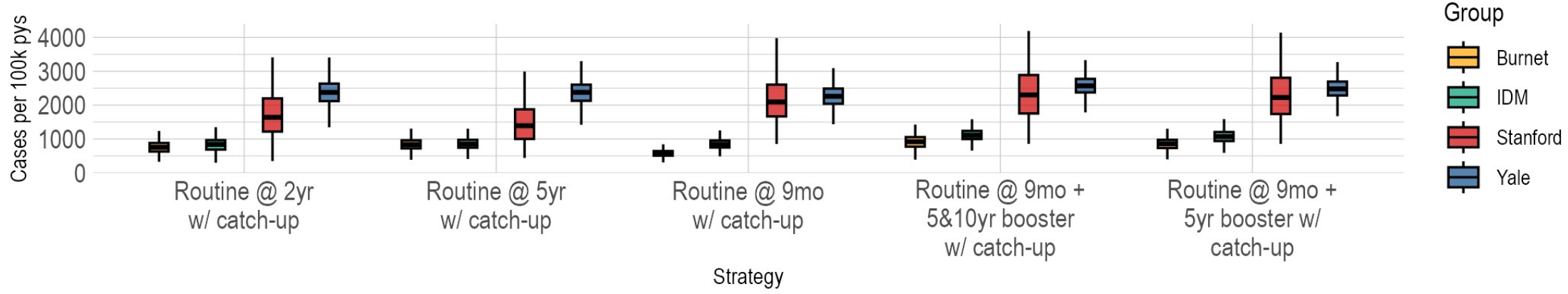
Cases averted

per 100K person-years: **High incidence, Africa**

Slow waning



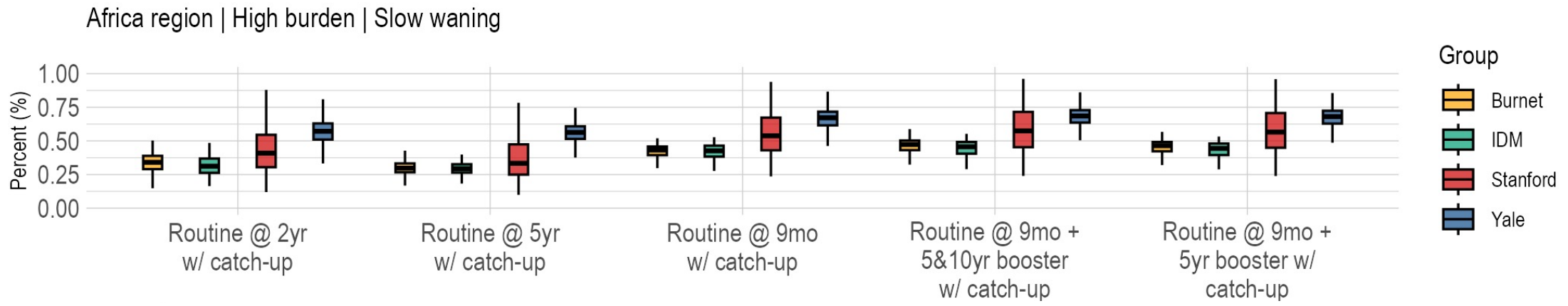
Fast waning



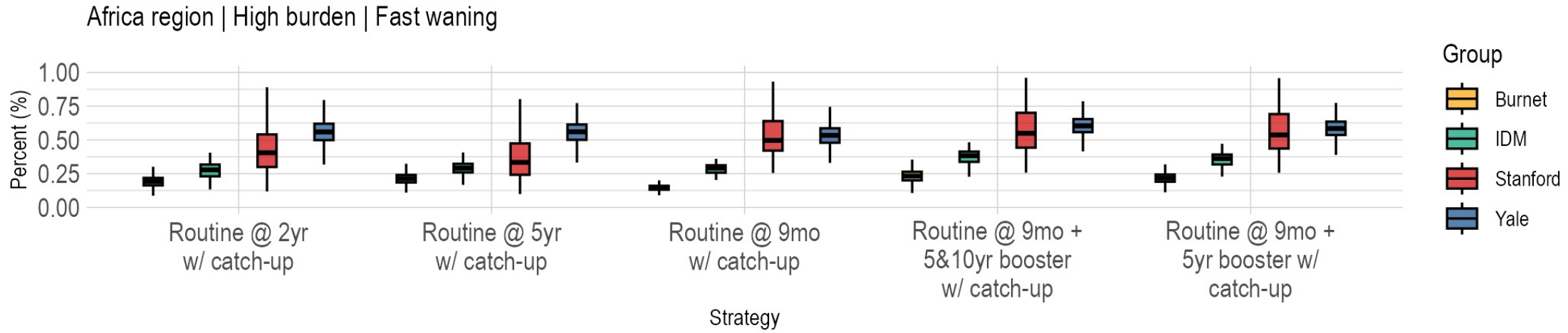
Percent of cases averted

High incidence, Africa

Slow waning



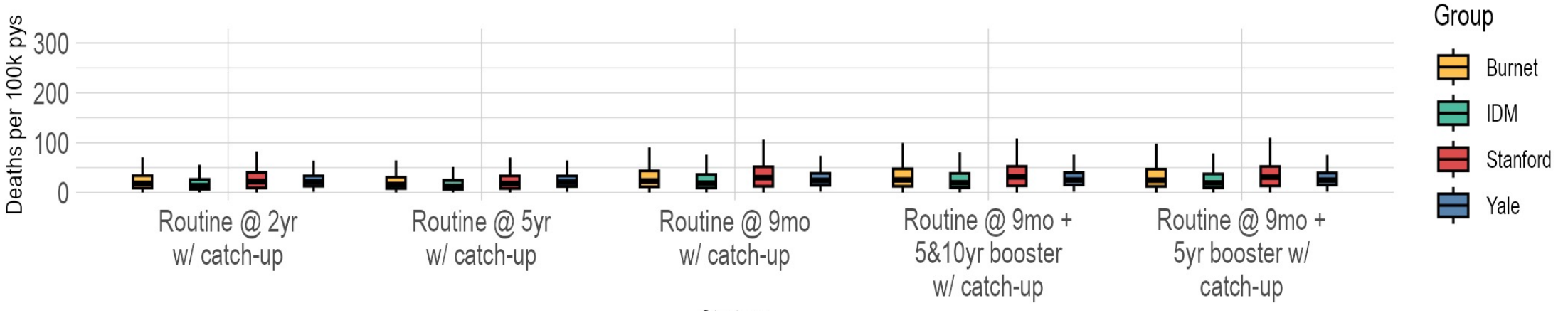
Fast waning



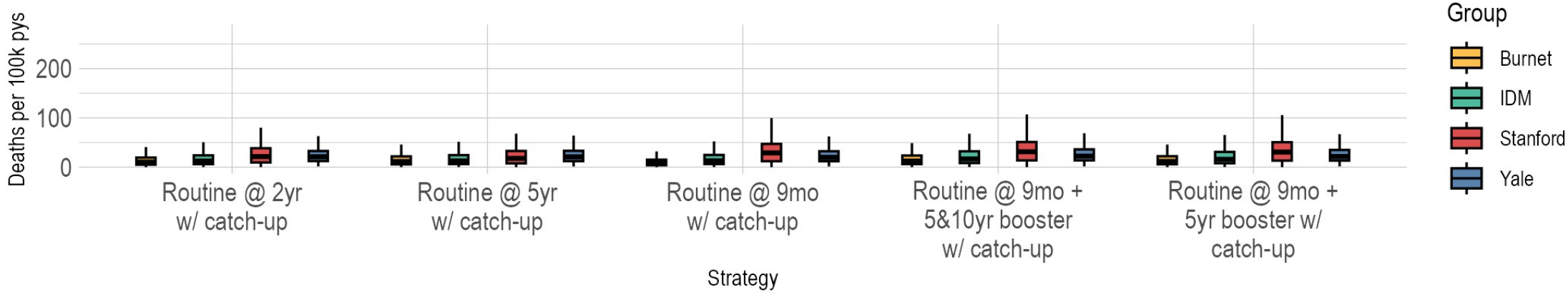
Deaths averted

per 100K person-years: **High incidence, Africa**

Slow waning



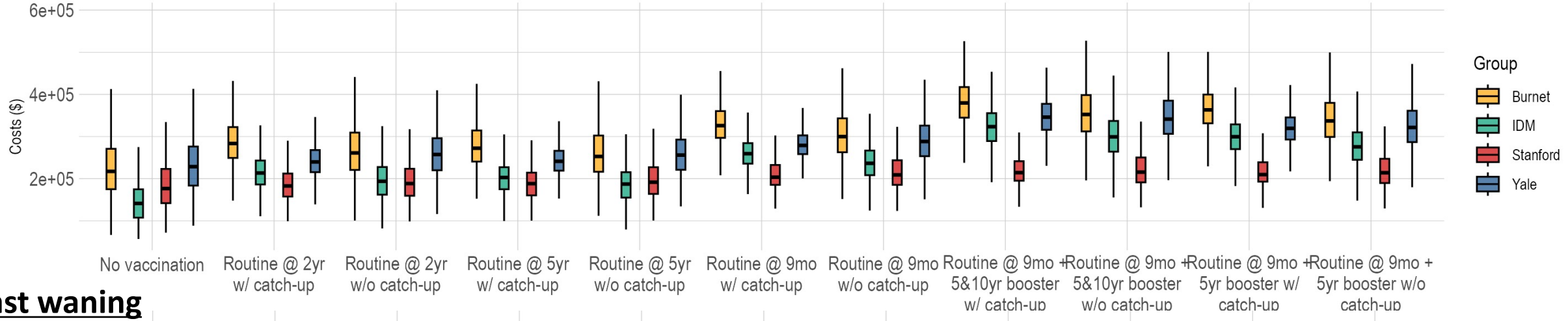
Fast waning



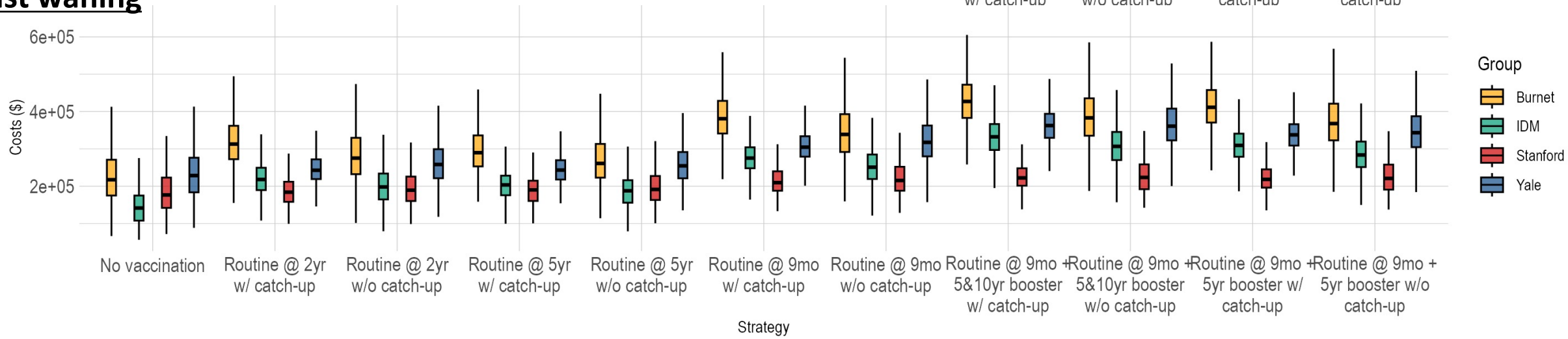
Total costs per strategy

Treatment + Vaccination costs: **High incidence, Africa**

Slow waning



Fast waning



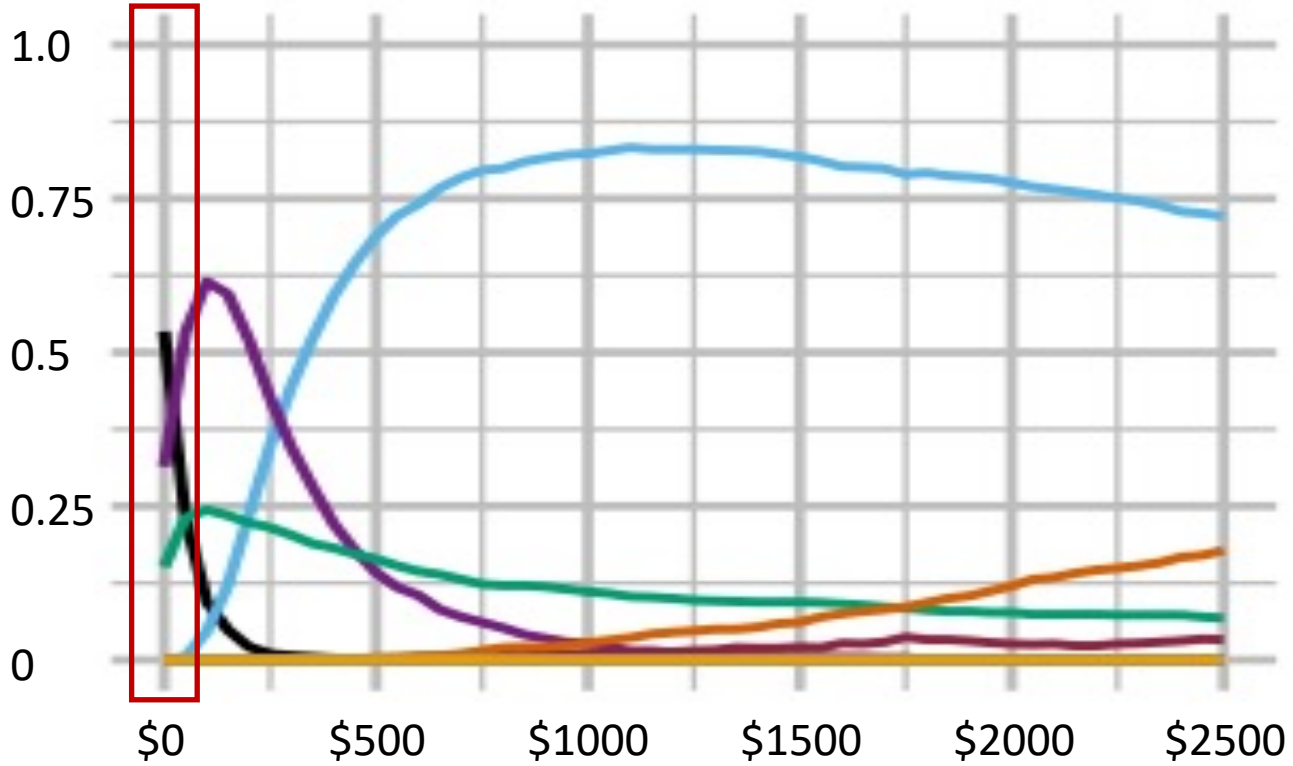
Preliminary results:

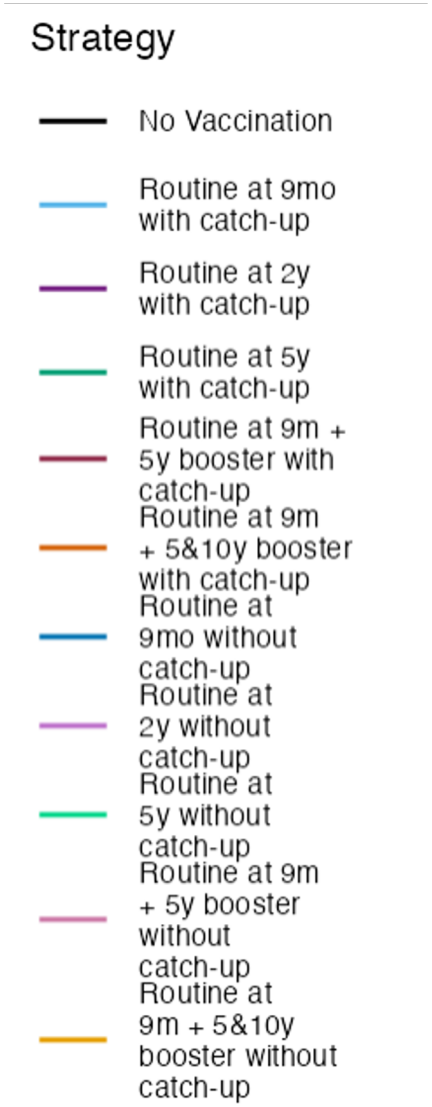
Cost-effectiveness

Cost-effectiveness acceptability curves:
Interpretation

If you are only willing to introduce TCV if it is **cost-saving**, then no vaccination is preferred. But there is a ~50% chance some TCV strategy will be cost-saving (~30% for routine at 2y, ~20% for routine at 5y with catch-up campaign)

Probability that the strategy provides the highest net benefit

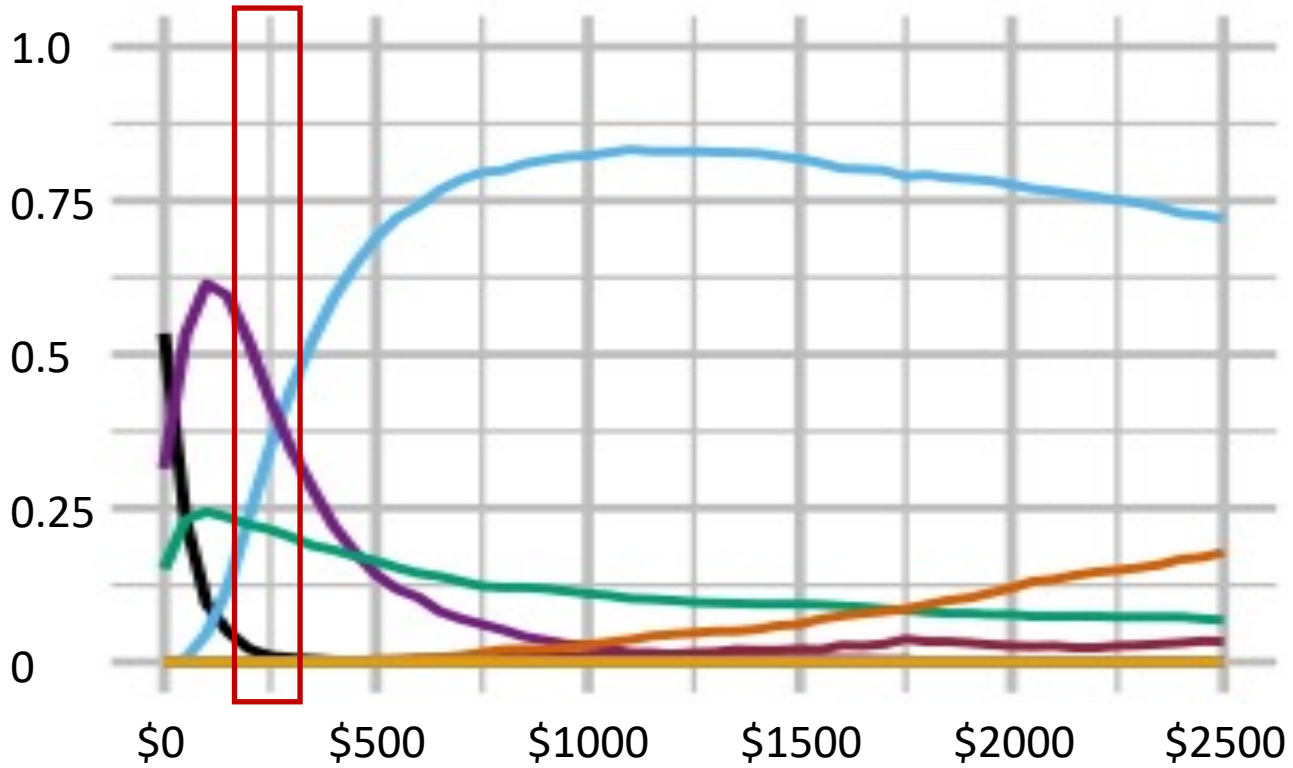


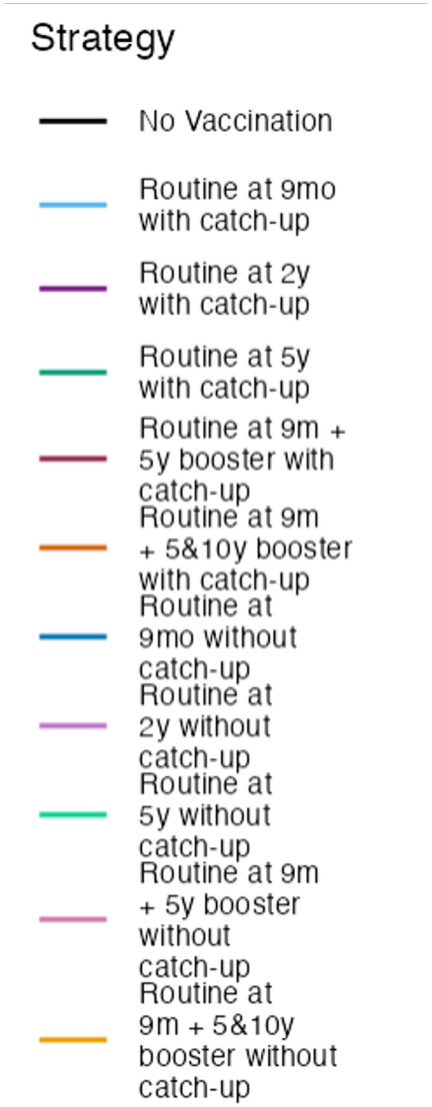


Cost-effectiveness acceptability curves:
Interpretation

For a willingness-to-pay threshold of <$300 per DALY averted (e.g. 0.5x GDP per capita for Malawi), introducing routine vaccination with TCV at 2y with a catch-up campaign is the preferred strategy (i.e. is **cost-effective**).

Probability that the strategy provides the highest net benefit

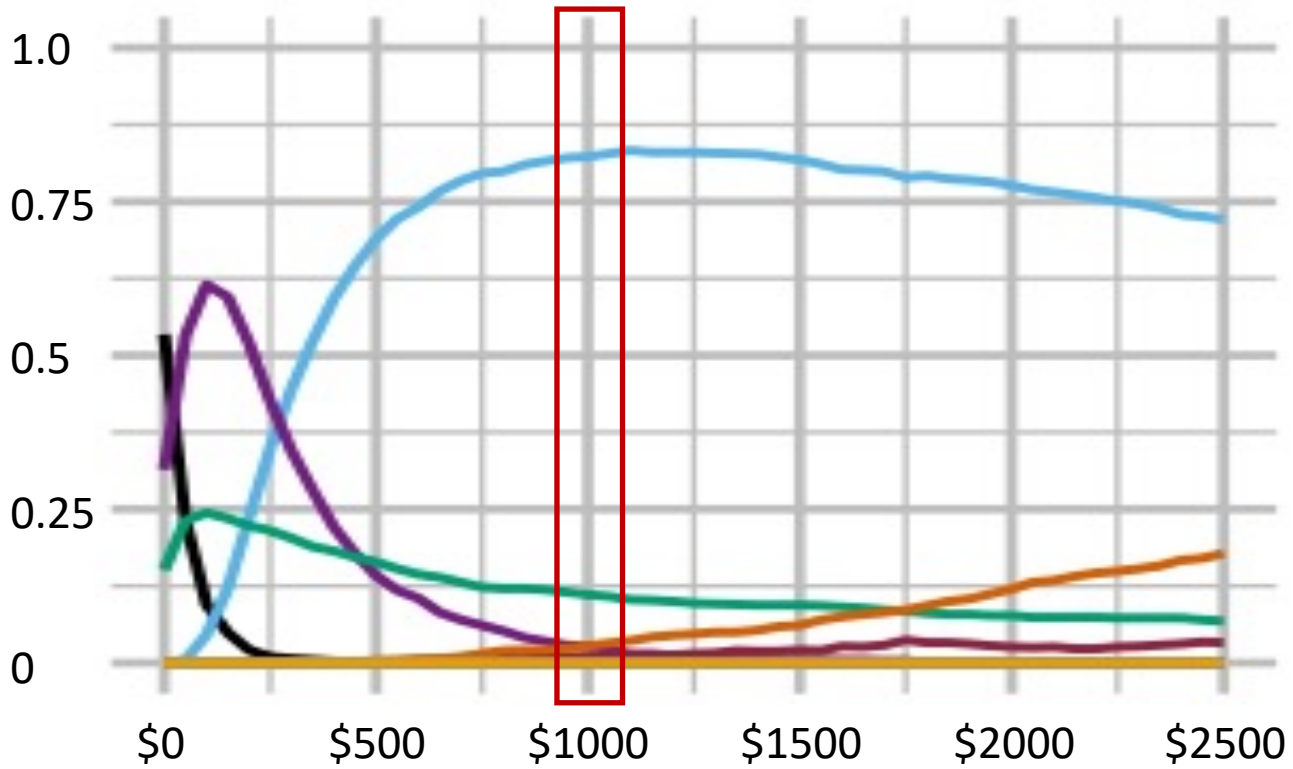


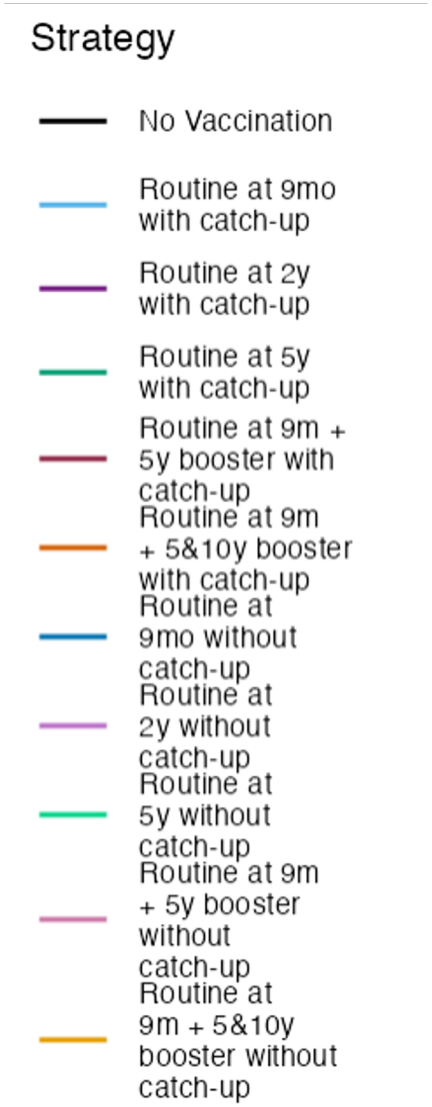


Cost-effectiveness acceptability curves:
Interpretation

For a willingness-to-pay threshold of $1000 per DALY averted (e.g. 0.5x GDP per capita for Kenya), introducing routine vaccination with TCV at 9m with a catch-up campaign is the preferred strategy (with high probability).

Probability that the strategy provides the highest net benefit

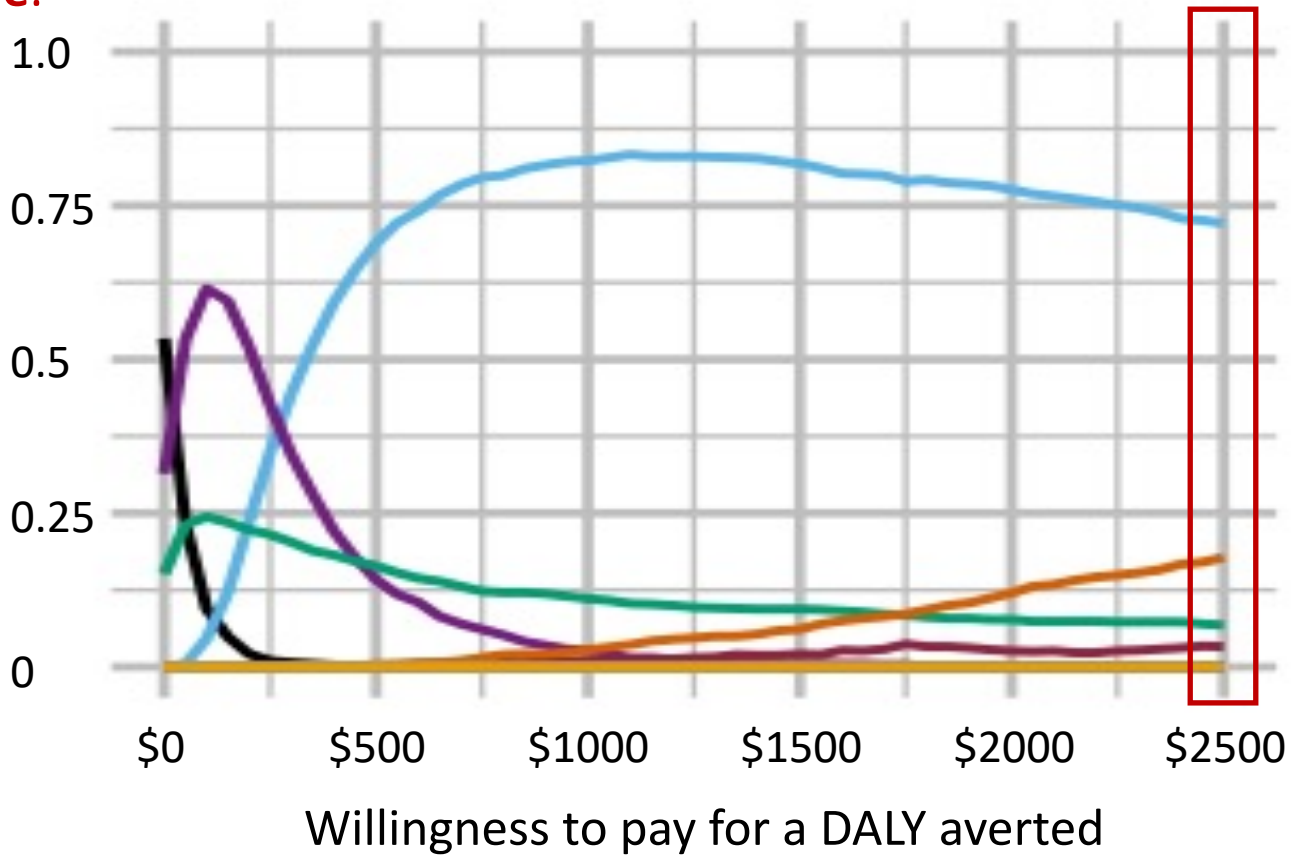


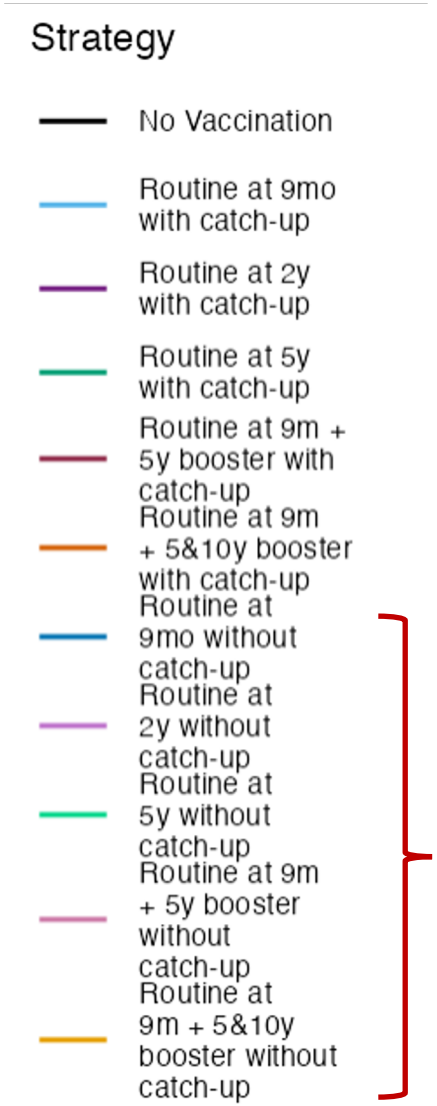


Cost-effectiveness acceptability curves:
Interpretation

For a willingness-to-pay threshold of $2500 per DALY averted (e.g. 1x GDP per capita for Côte d'Ivoire), vaccination at 9m is still preferred, but there is a ~20% probability that introducing booster doses at 5y and 10y of age would be **cost-effective**.

Probability that the strategy provides the highest net benefit



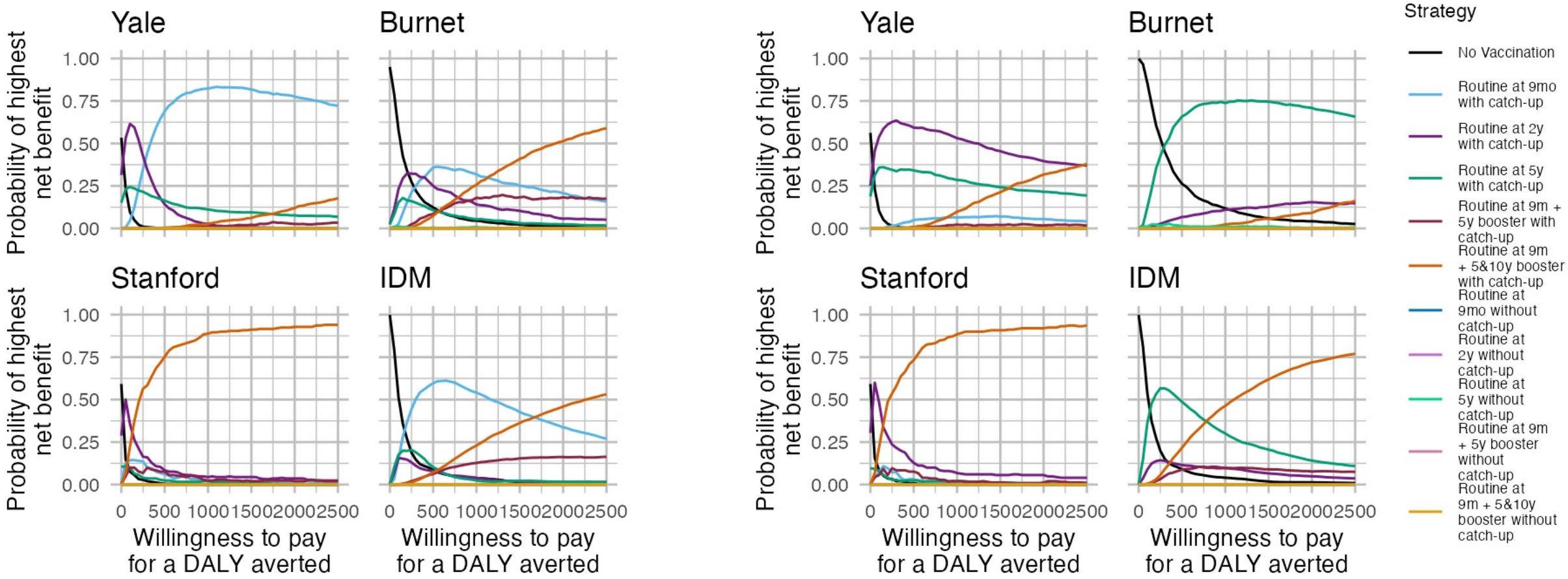


Strategies without a catch-up campaign are never preferred

High incidence | Africa region

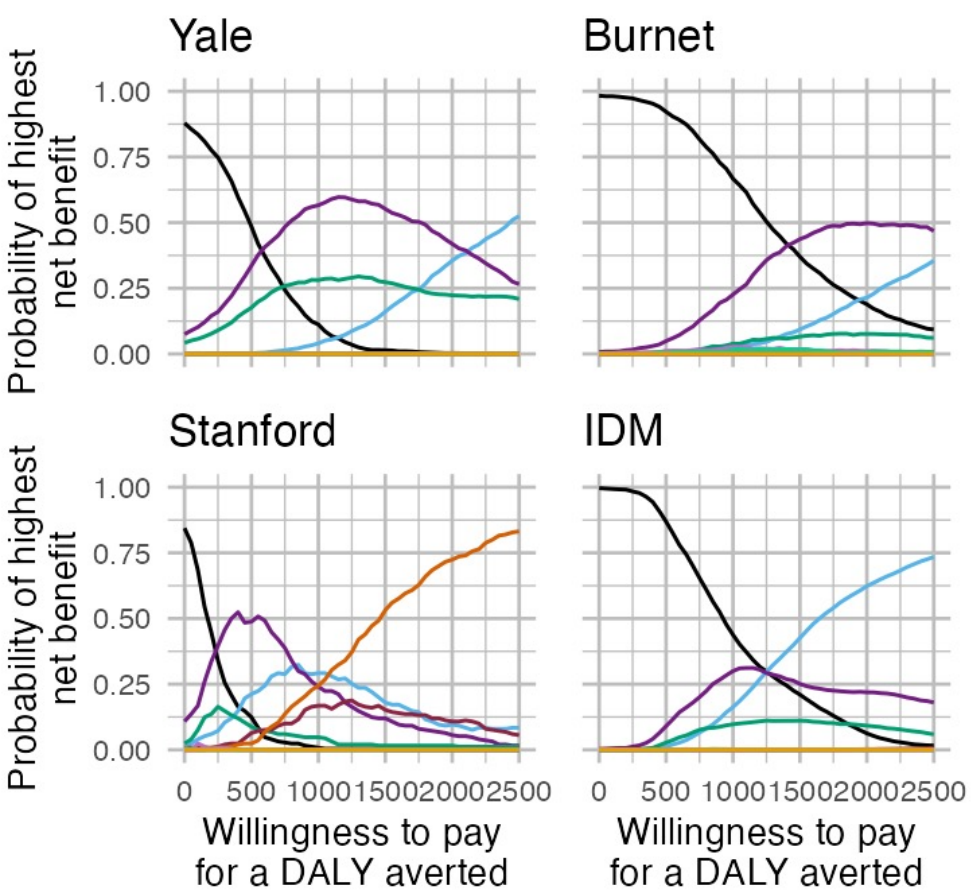
Slow waning

Fast waning

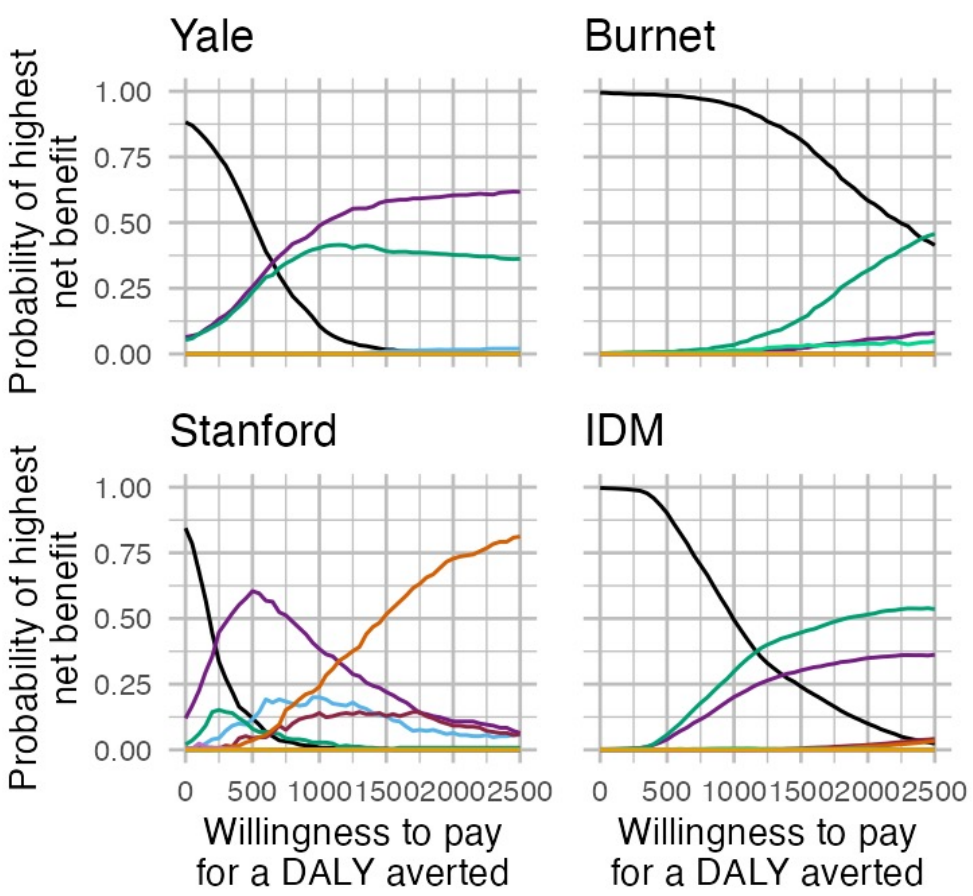


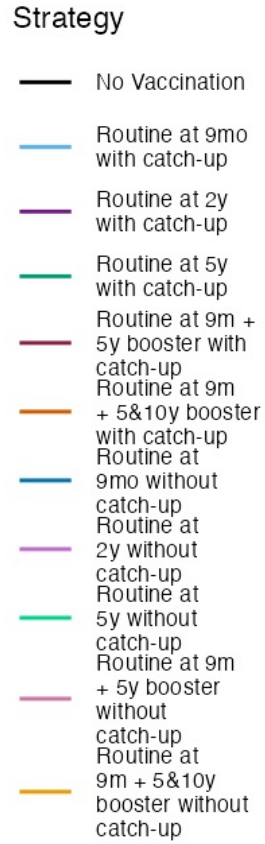
High incidence | Asia region

Slow waning

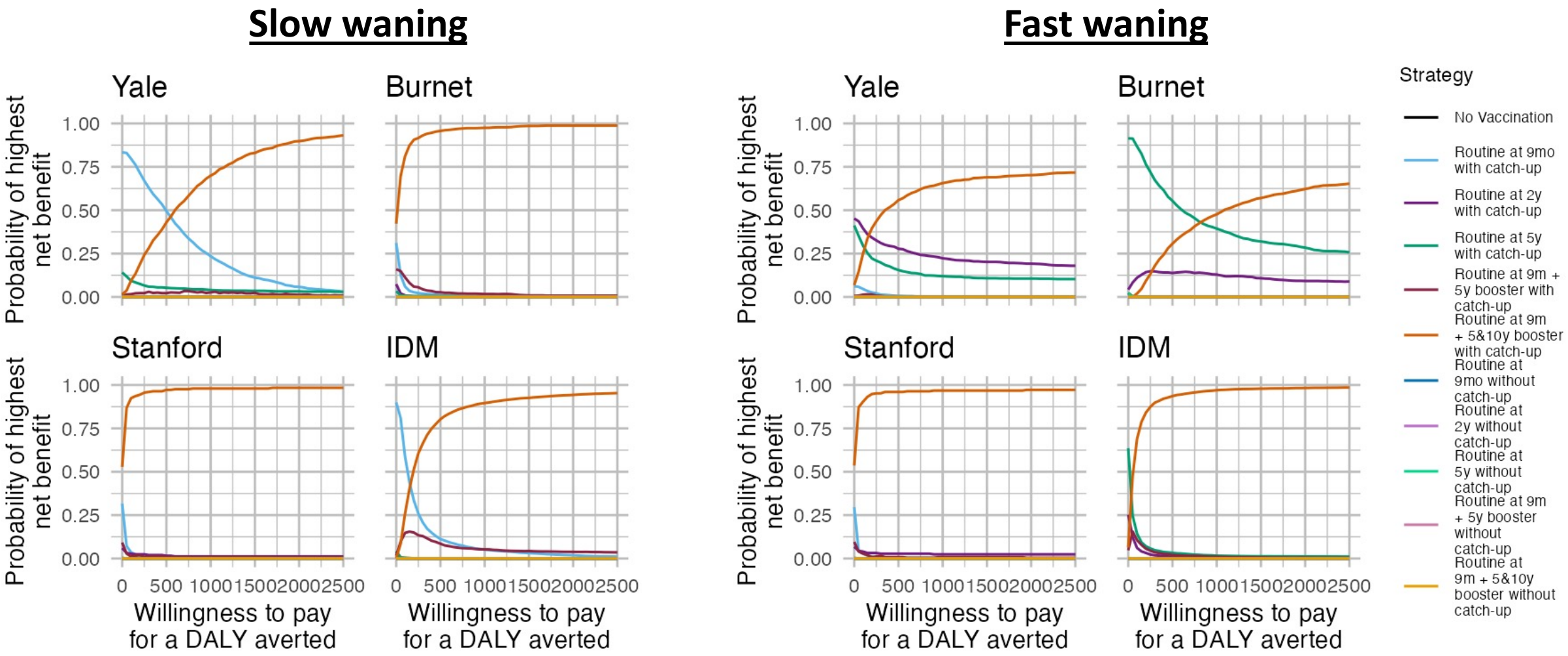


Fast waning

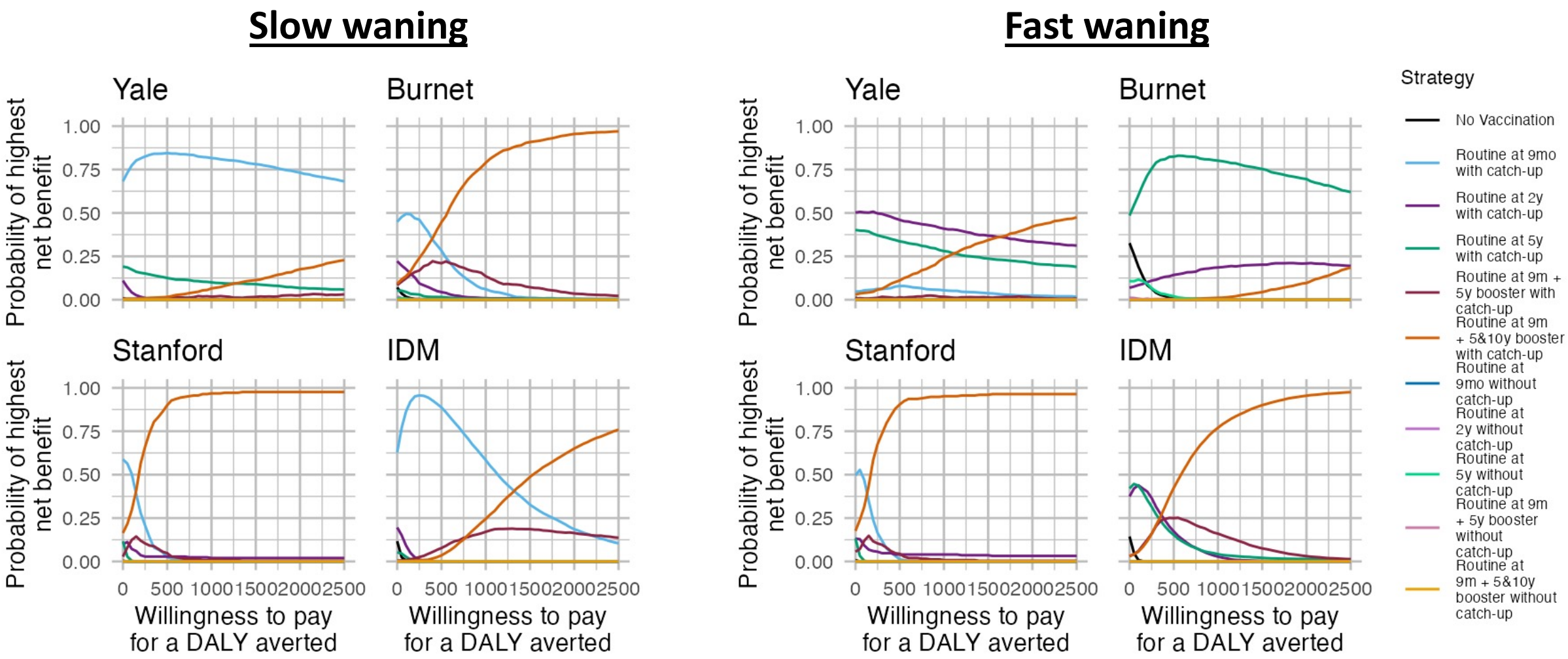




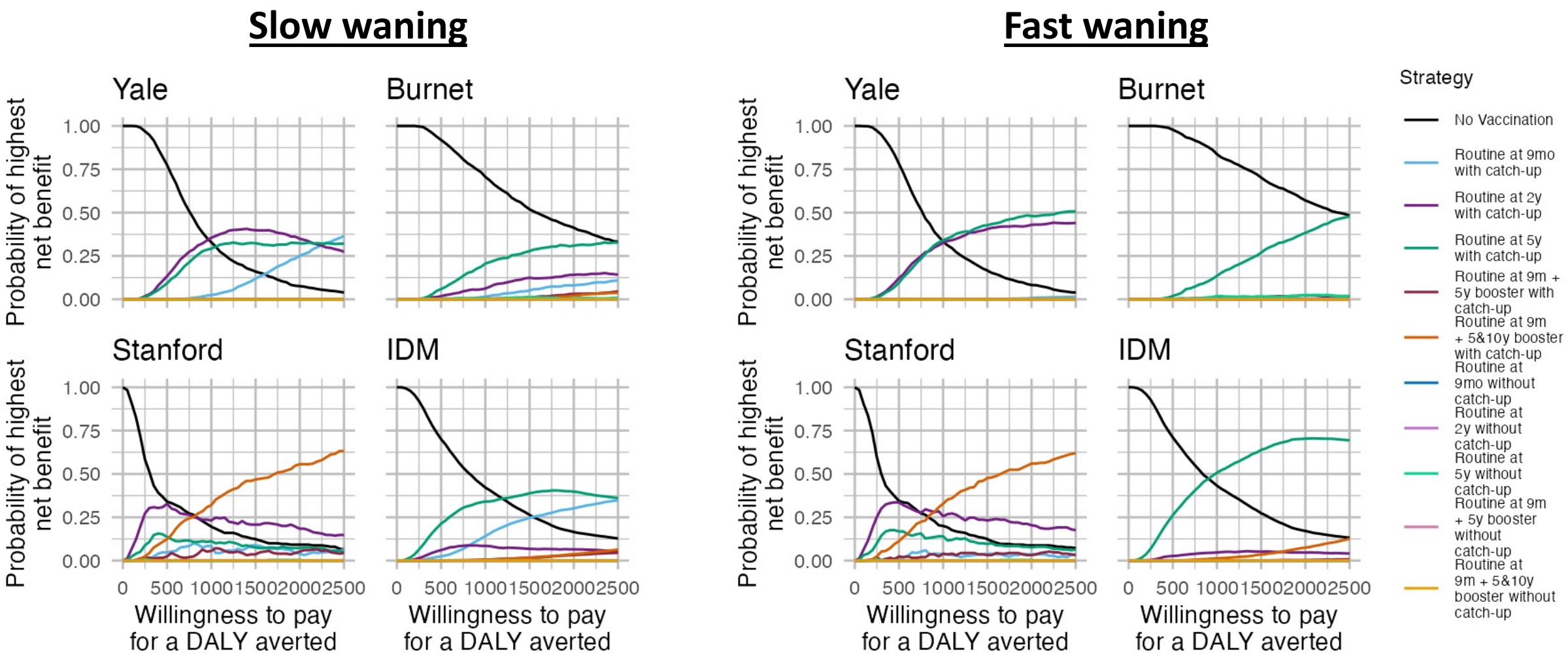
Very high incidence | Africa region



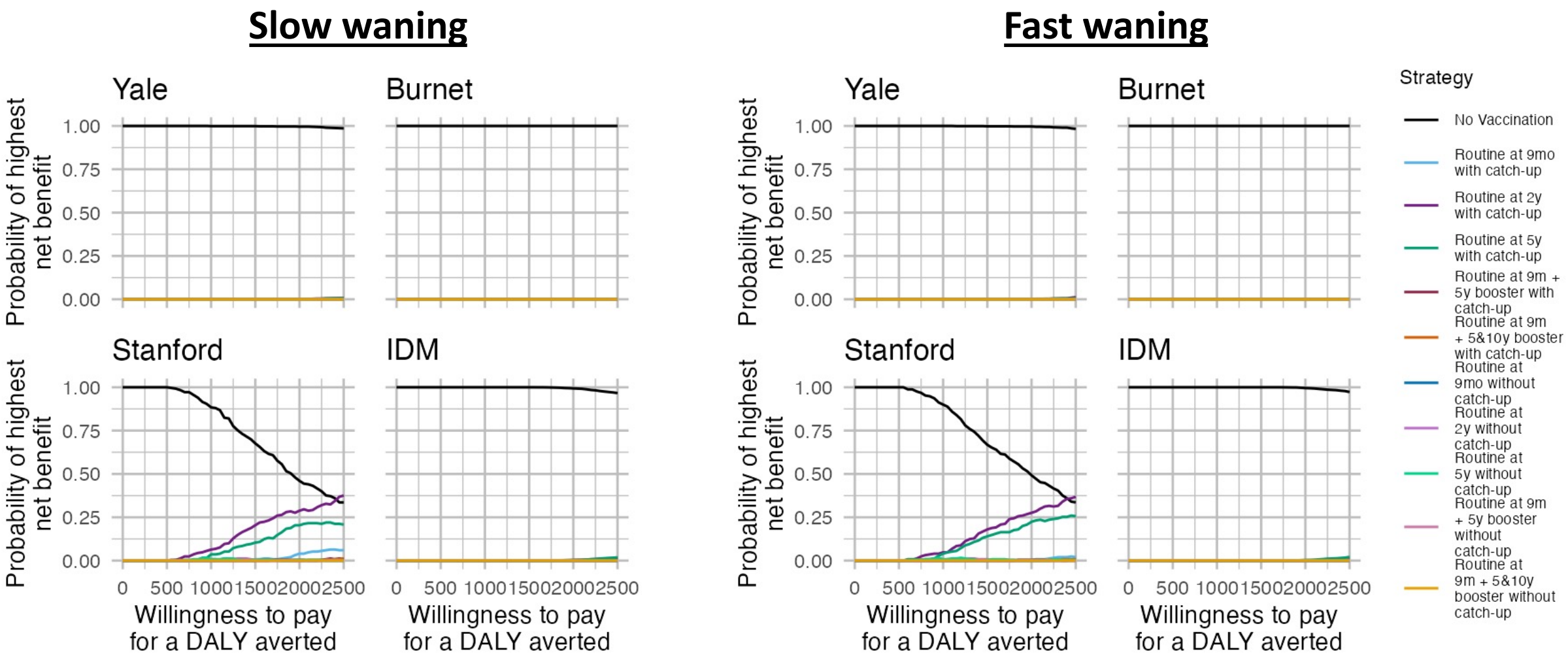
Very high incidence | Asia region



Medium incidence | Africa region



Medium incidence | Asia region



Medium incidence:
Summary results

GDP per capita for a low-income country ≈ $2500

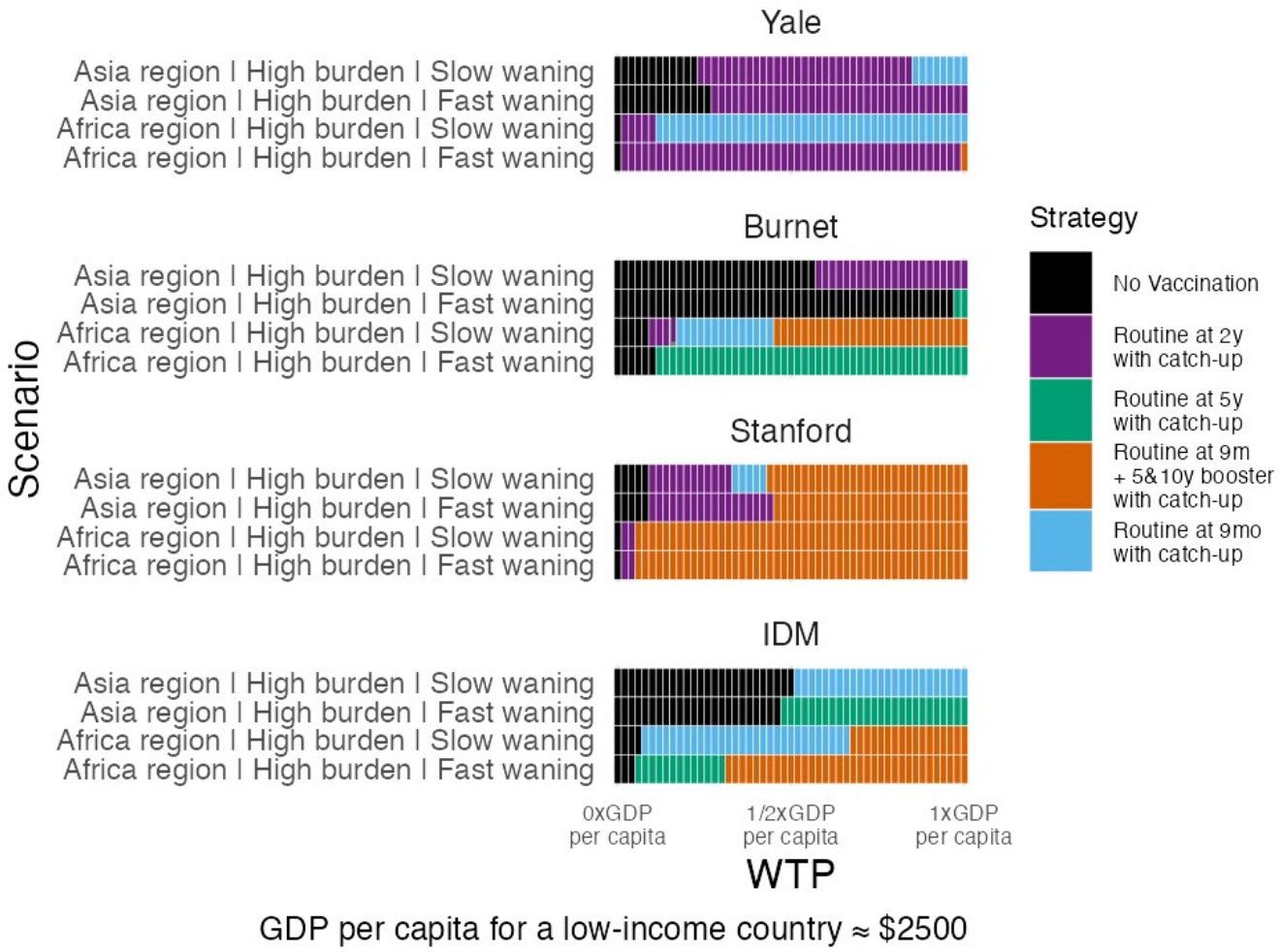
Africa:

- Routine vaccination at **2y or 5y of age with a catch-up campaign** might be cost-effective (for higher WTP thresholds)

Asia:

- Vaccination is **unlikely to be cost-effective**

High incidence:
Summary results



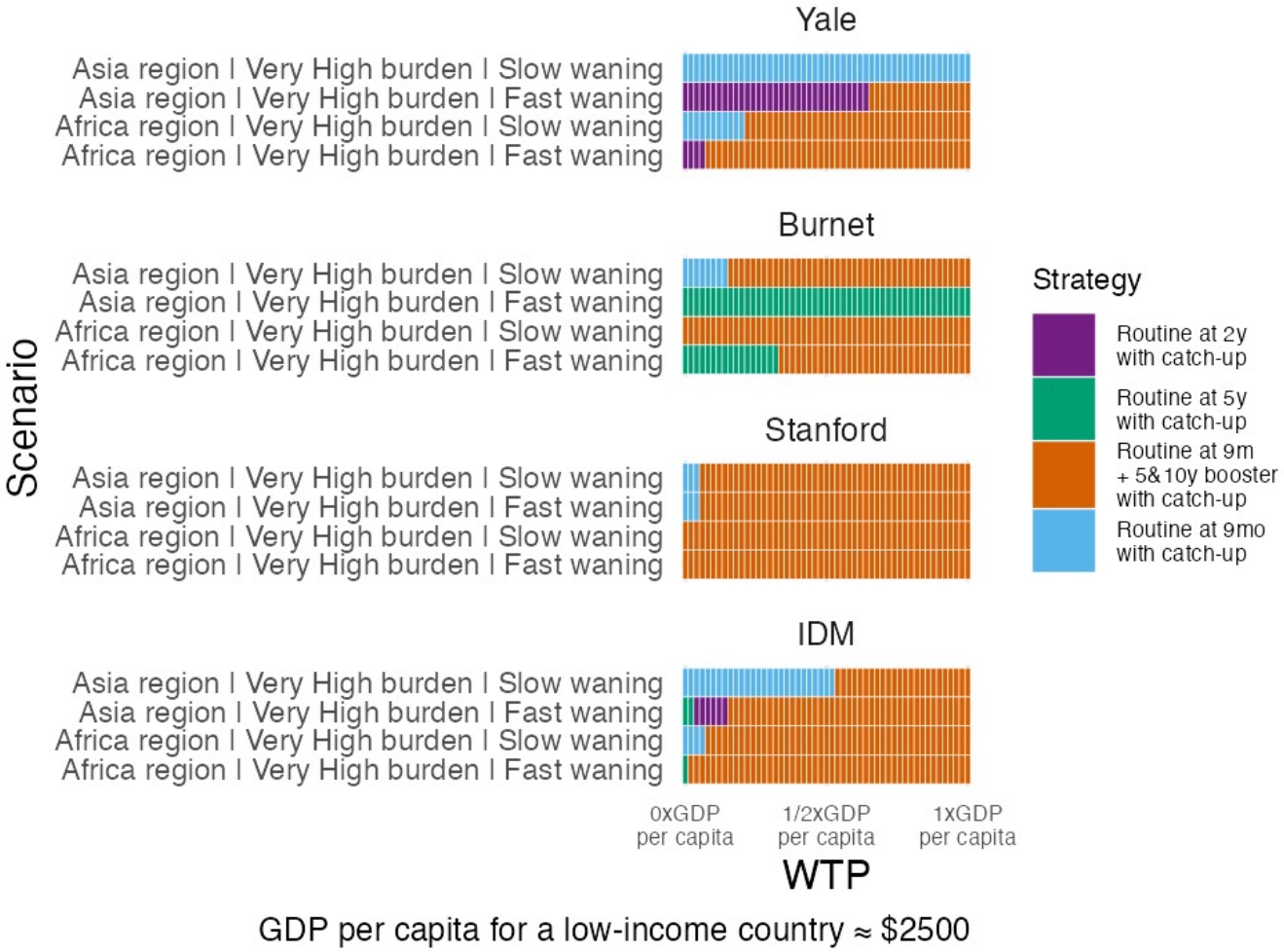
Africa:

- Routine vaccination at **9m with a catch-up campaign** is very likely to be cost-effective **if waning is slow**
- Consider delaying the first dose to 2y or 5y of age **if waning is fast**

Asia:

- Routine vaccination at **2y with a catch-up campaign** is might be cost-effective depending on the WTP threshold

Very high incidence:
Summary results



Africa:

- Routine vaccination at **9m with a catch-up campaign** is very likely to be cost-effective (and is potentially cost-saving)
- **Booster doses at 5y and 10y** are also likely to be cost-effective

Asia:

- Routine vaccination at **9m with a catch-up campaign** is very likely to be cost-effective (and is potentially cost-saving) **if waning is slow**
- Consider **delaying routine vaccination to 2y or 5y** of age **if waning is fast** and willingness to pay (for booster doses) is low

Key drivers of uncertainty

Yale model

- Waning rate in 0-2y and 2-5y age groups
- Vaccine coverage
  - Routine coverage at 2y
  - Booster dose coverage
- CFR
  - particularly for medium incidence setting in Africa

Identified issues and next steps

- Potential issues with each of the models
  - Incidence is declining in the absence of vaccination in IDM model
  - Incidence rebounds quickly following vaccination in Burnet model
  - Very few booster doses administered in Stanford model
  - Yale model predicts more cases averted, but similar deaths/DALYs averted, compared to other models
- Groups might be using different approaches for discounting DALYs
- Explore shorter time horizons
  - 10 years, 2 years following booster introduction
- **Further explore key drivers of uncertainty with and between models**

Next steps following SAGE presentation

- Refit VE waning parameters for the fast waning scenario to the latest data from Bangladesh
- Consider incorporating uncertainty in the incidence rate within (and between) medium, high, and very high settings, e.g. by sampling from a range of values for the symptomatic fraction
- Determine whether additional data is available to account for differences in risk of complications and CFR by age and AMR
- Update model structure/calibration as needed

Acknowledgements

Yale

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Tigist Menkir, , Nathan Lo, Jason Andrews

IDM

Kyra Grantz, Alicia Kraay, Jillian Gauld

Burnet Institute

Romesh Abeysuriya, Alina Muellenmeister, Nick Scott

Extra slides:
Cost-effectiveness parameters

CEA parameters – Healthcare seeking & severity

Parameters	Africa	Asia	source
Healthcare seeking parameters			
Probability of seeking care	0.58 (0.42, 0.77)		Bilcke et al (2019)
Probability of inpatient treatment	0.24 (0.08, 0.53)	0.10 (0.03, 0.28)	Marks et al (2024), Longley et al (2020)
Probability of outpatient treatment	Complement of the above		Marks et al (2024), Longley et al (2020)
Probability of complications	0.32 (0.20, 0.47)	0.02 (0.001, 0.36)	Marks et al (2024), Longley et al (2020)
Severity parameters			
Duration of severe illness	20.0 days (IQR: 14.0 - 44.0 days)		Mejia et al (2020)
Duration of moderate illness	14.0 days (IQR: 7.0 - 25.0 days)		Mejia et al (2020)
Duration of untreated illness	14.0 days (IQR: 8.0 - 25.0 days)		Mejia et al (2020)
CFR	0.81% (0.10%-6.22%)	0.16% (0.07%-0.40%)	Murthy et al (unpublished) – based on meta-analysis of studies since 2010

CEA parameters – Treatment & vaccine costs

Parameters	Africa	Asia	source
Treatment costs			
Inpatient pediatric costs	$265.87 ($194.99, $362.75)	$224.98 ($138.91, $364.36)	Limani et al (2020), Sur et al (2010)
Outpatient pediatric costs	$48.52 ($40.28, $58.39)	$39.02 ($8.73, $174.41)	Limani et al (2020), Mejia et al (2020)
Inpatient adult costs	$410.35 ($288.91, $583.17)	$118.51 ($33.41, $420.37)	Limani et al (2020), Sur et al (2010)
Outpatient adult costs	$44.35 ($34.42, $57.11)	$39 ($8.73, $174.41)	Limani et al (2020), Mejia et al (2020)
Vaccination costs			
Vaccine procurement costs (i.e. vaccine price)	$1.50		UNICEF, 2024
Syringes & safety equipment costs (unit price)	$0.37 ($0.35, $0.39)		Portnoy et al., Vaccine 2015
Delivery costs, routine	$2.66 ($2.15, $3.19)		Bilcke et al., Lancet Infect Dis, 2019
Delivery costs, school-based	$1.77 ($0.88, $2.66)		Weyant et al., Vaccine, 2024
Delivery costs, catch-up campaign	$0.54 ($0.49, $0.68)		Bilcke et al., Lancet Infect Dis, 2019

CEA parameters – DALYs (YLD & YLL)

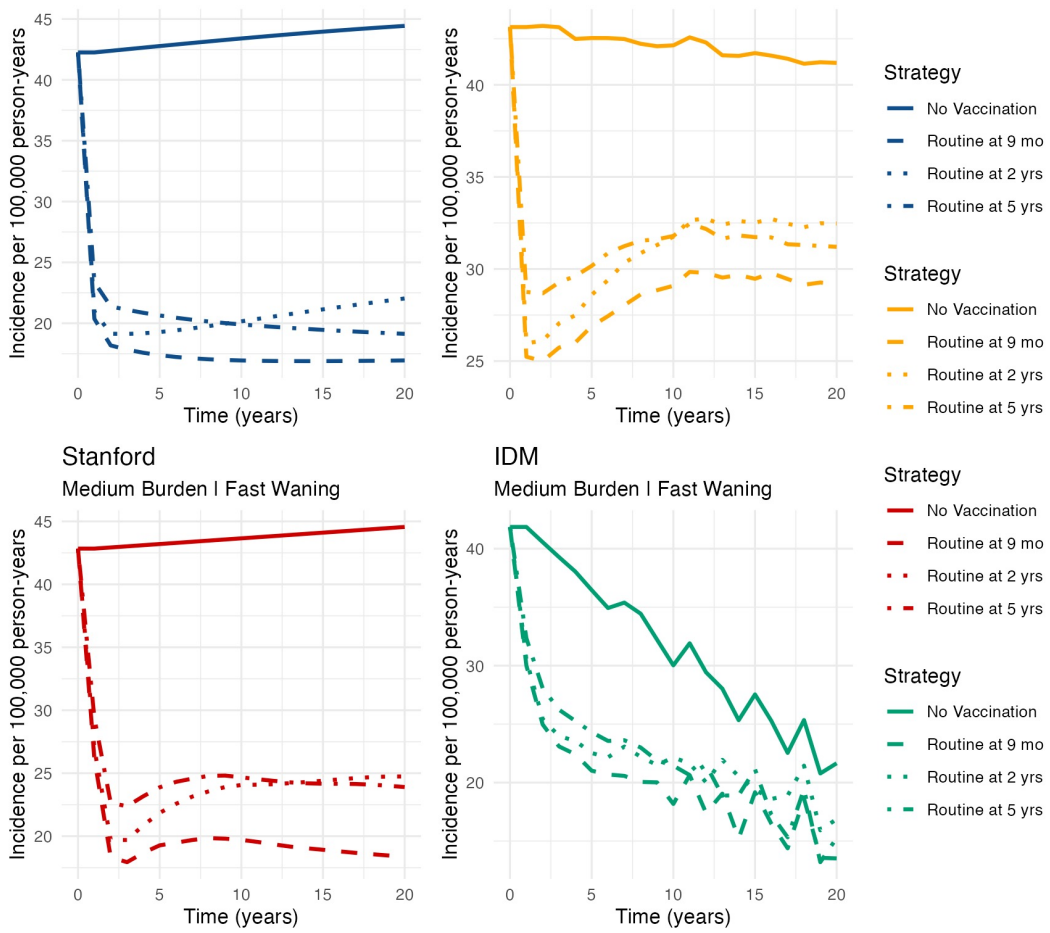
Parameters	Africa	Asia	source
Treatment costs			
Disability weight (moderate typhoid)	0.0506 (0.0324, 0.0741)		GBD 2021 Study: Disability Weights
Disability weight (severe typhoid)	0.133 (0.0885, 0.190)		GBD 2021 Study: Disability Weights
Disability weight (severe typhoid with ileal perforation)	0.324 (0.220, 0.442)		GBD 2021 Study: Disability Weights
Disability weight (untreated typhoid)	0.0506 (0.0324, 0.0741)		GBD 2021 Study: Disability Weights
Life expectancy			
Life expectancy at birth	64.02 years	74.76 years	UN data portal

Supplementary results

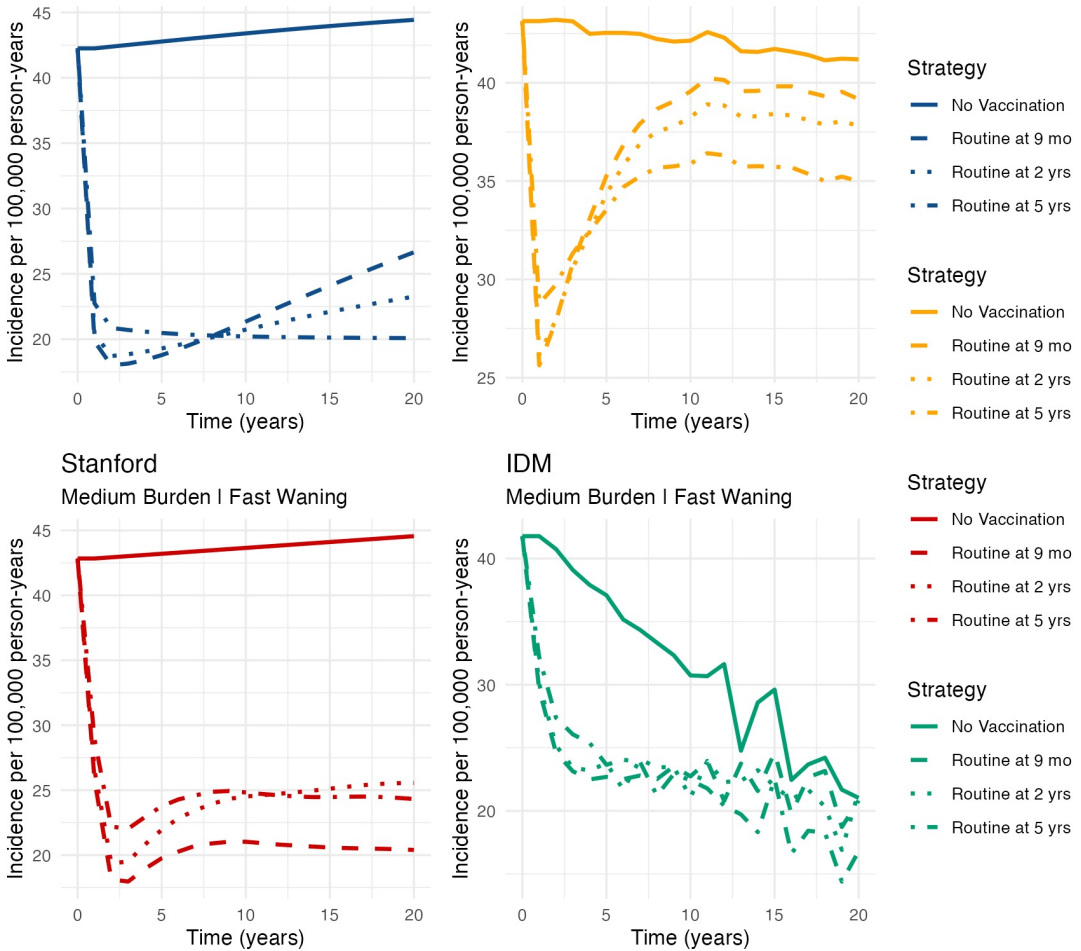
Medium incidence setting:

Routine vaccination at 9m, 2y, or 5y

Slow waning



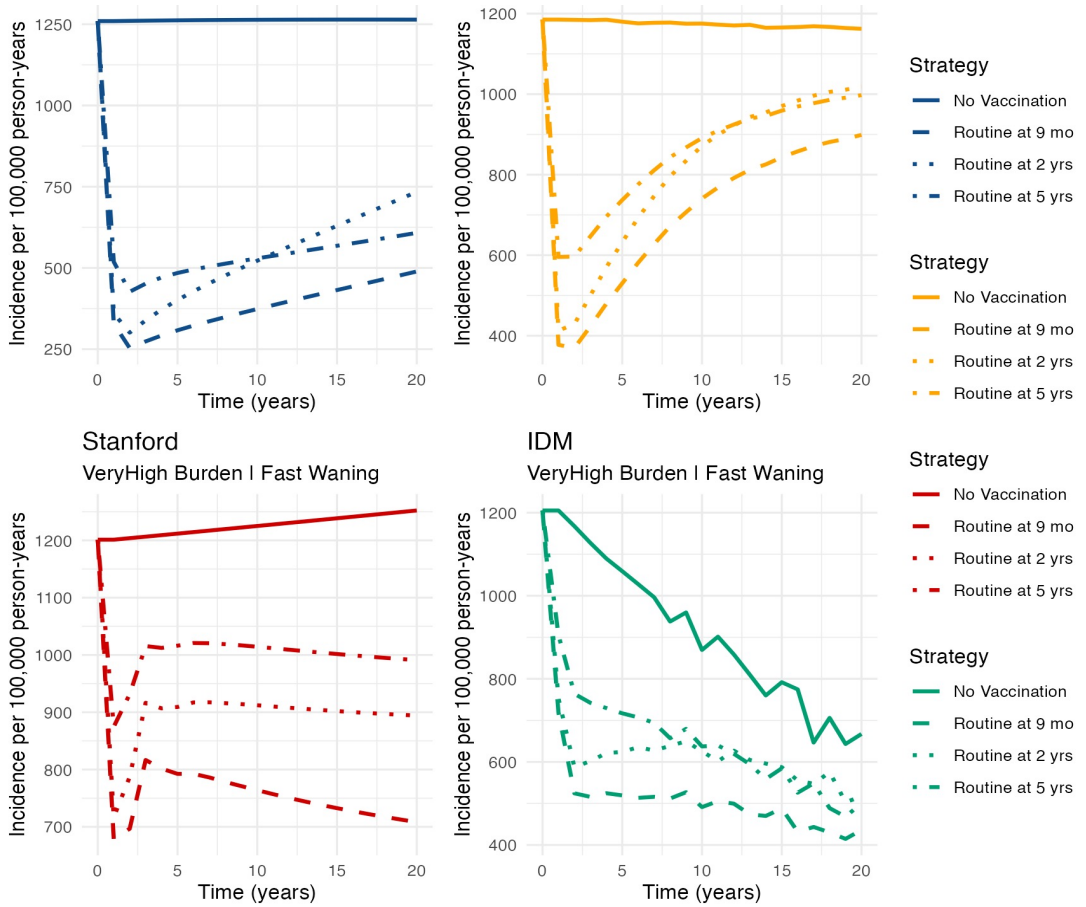
Fast waning



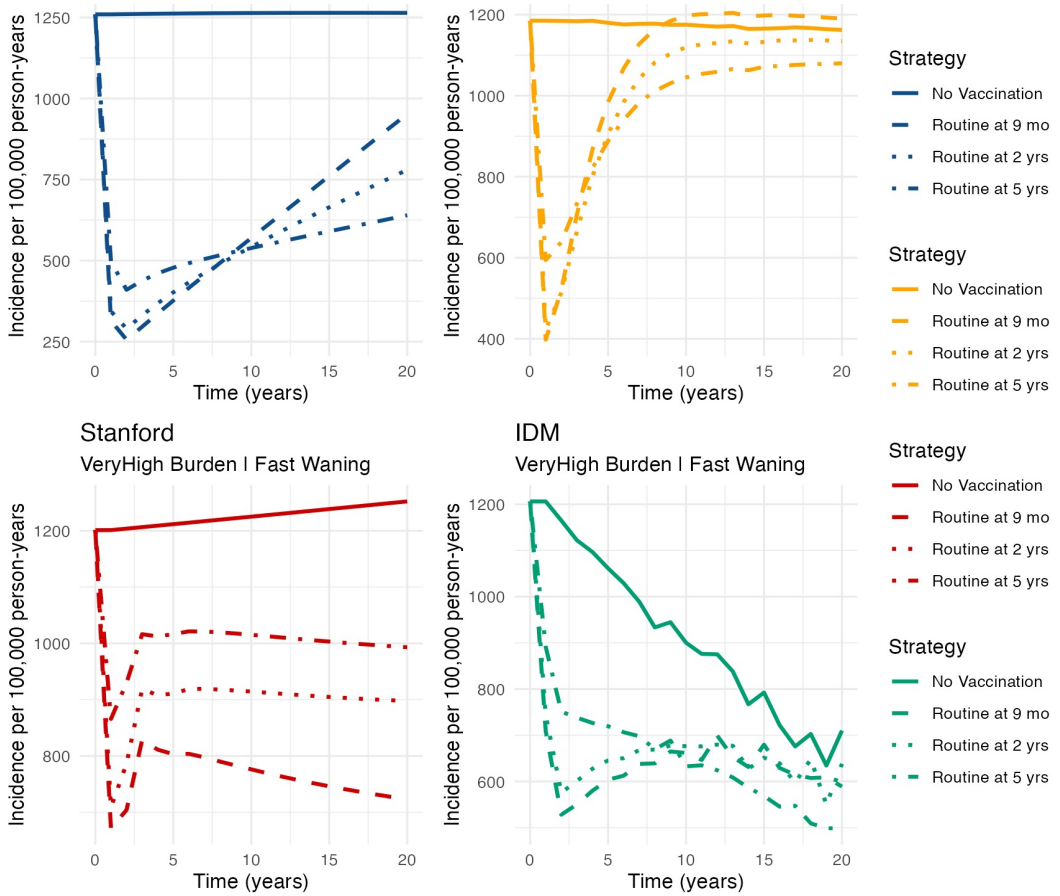
Very high incidence setting:

Routine vaccination at 9m, 2y, or 5y

Slow waning



Fast waning



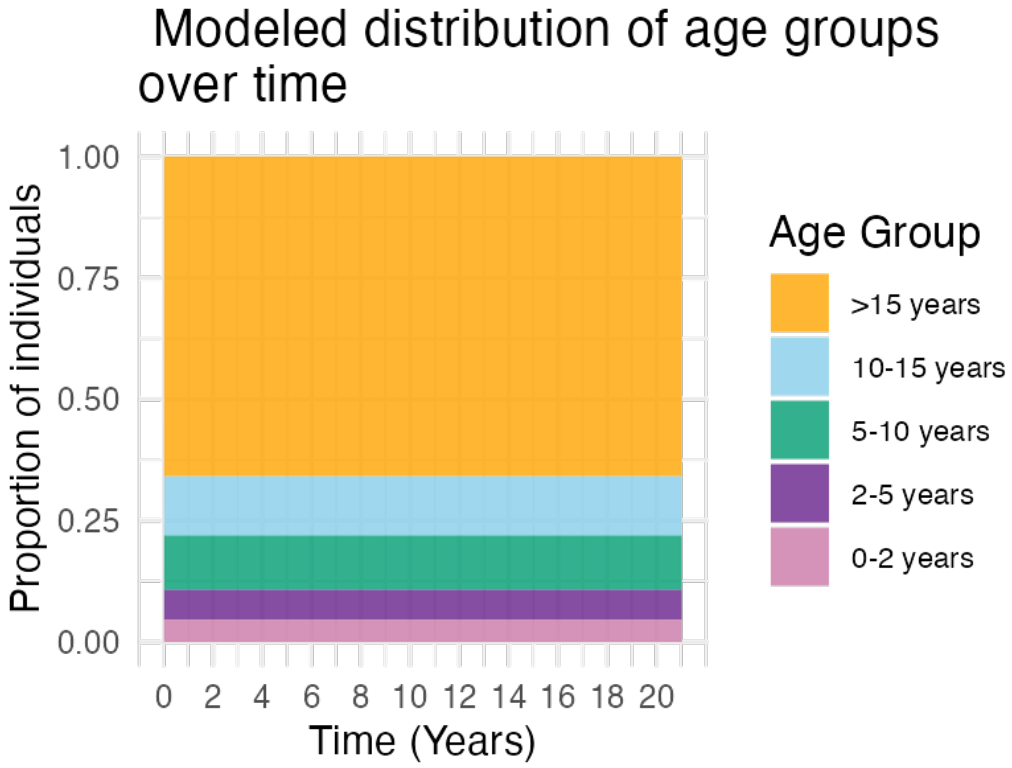
Extra slides:

Model calibration

Model parameters and demographic fit

- Used demographic parameters, birth rate and population age proportions, from the World Population Prospects to
- Fit death rates to maintain a stable population over time in the model

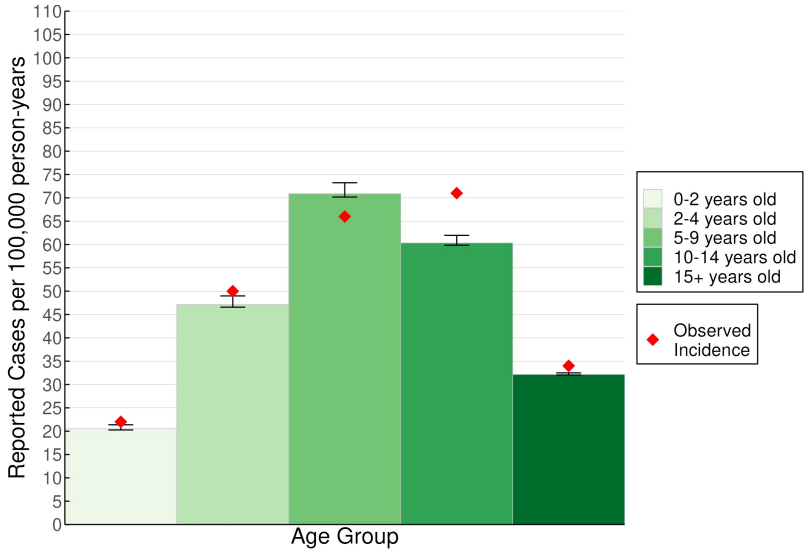
Fixed Parameters	Symbol	Value	source
Rate of waning immunity from natural infection	$1/\omega$	104 weeks	Hornick et al (1970)
Duration of primary infection	$1/\delta$	4 weeks	Hornick et al (1970)
Probability of symptoms for subsequent infection	p_{symp2}	0	Assumption
Probability of dying from typhoid infection	α	0.001	Assumption (deaths are modeled in CEA)
Proportion of individuals who become chronic carriers (age-specific)	ϑ	0.003-0.09	Ames and Robins (1943)
Birthrate	b	0.000438	World population prospects



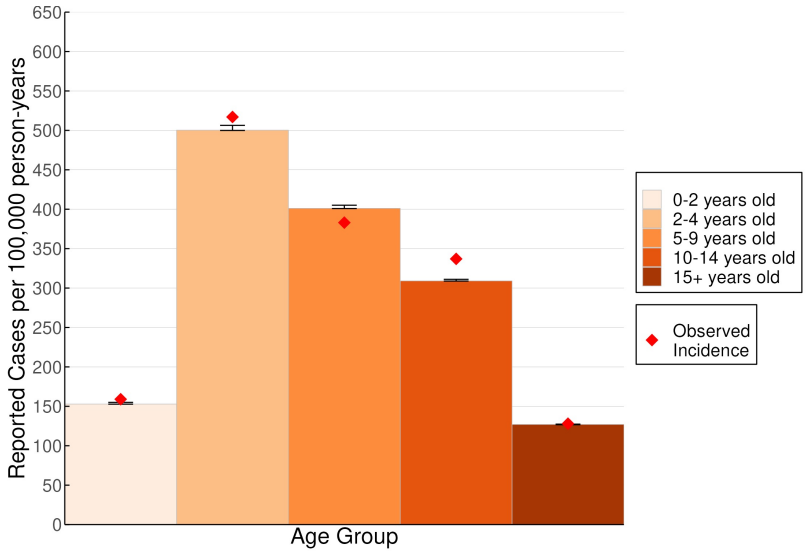
Model fit

Fitted parameters	Symbol	Values by Burden Setting		
		Medium	High	Very High
Basic reproductive number (*dependent on sampled rC value)*	R_0	3 - 11	3 - 22	5 - 30
Relative risk of infection for <2 years	b_1	0.23	0.25	0.25
Relative risk of infection for 2-5 years	b_2	0.57	0.97	1.00
Probability of symptoms for primary infections	p_{symp1}	0.03	0.11	0.61

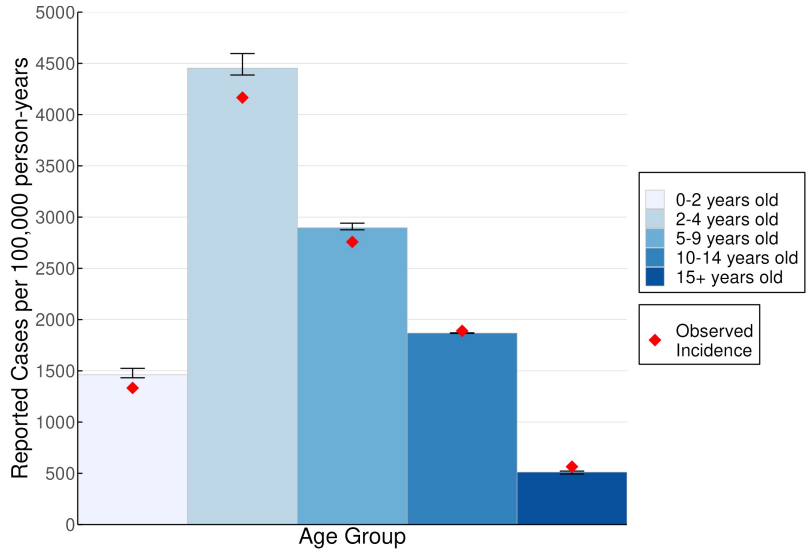
Medium Incidence



High Incidence



Very High Incidence



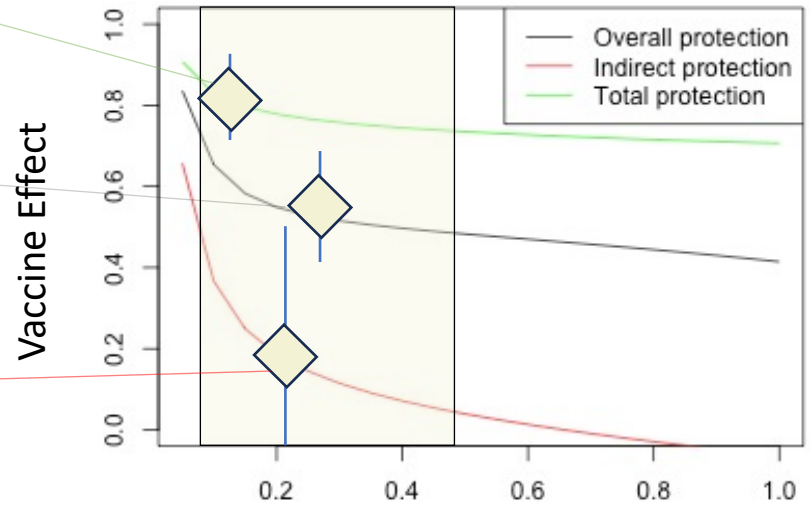
Yale model calibration to observed indirect and overall effectiveness

- Simulate data from cluster RCT
- Calculate the **total**, **overall**, and **indirect effect** of vaccine
- Sample relative infection of chronic carriers (rC) values consistent with observed vaccine effects

	SA 14-14-2 group	Vi-TT group	Protective effectiveness (%)
Total vaccine protection	n=30 685	n=30 882	..
Typhoid fever	192	29	..
Person-years of follow-up	30 253	30 349	..
Incidence rate, per 100 000 person-years	635 (548 to 731)	96 (64 to 137)	85% (97·5% CI 76 to 91)
Overall vaccine protection	n=155 448	n=155 841	..
Typhoid fever	331	144	..
Person-years of follow-up	155 458	154 449	..
Incidence rate, per 100 000 person-years	213 (191 to 237)	93 (79 to 110)	57% (97·5% CI 43 to 68)
Indirect vaccine protection	n=134 835	n=135 110	..
Typhoid fever	139	115	..
Person-years of follow up	125 205	124 100	..
Incidence rate, per 100 000 person-years	111 (93 to 131)	93 (77 to 111)	19% (95% CI −12 to 41)

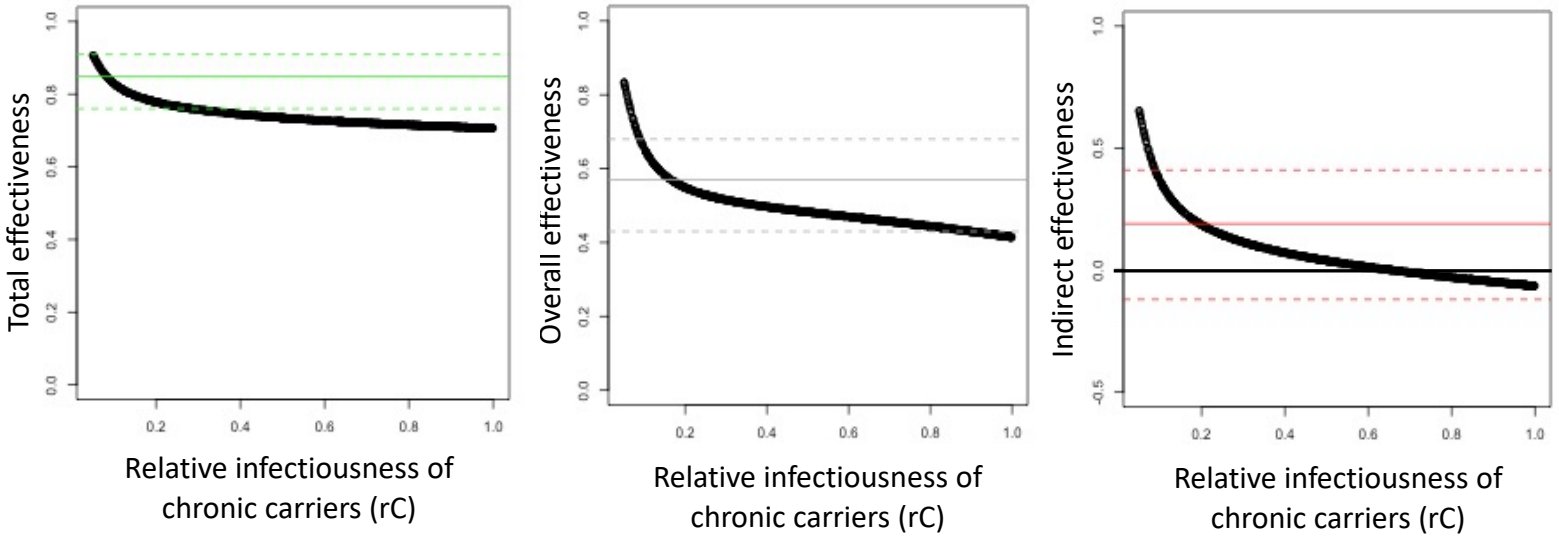
Qadri et al (Lancet, 2021)

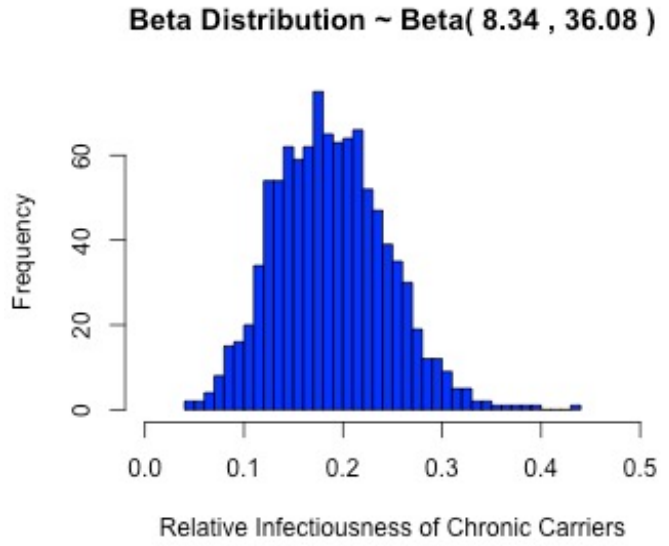
Simulated Vaccination
(Dhaka RCT)



Yale model validation: Chronic carrier parameterization using modeled vaccine effect

Sampled rC values consistent with Dhaka trial estimates



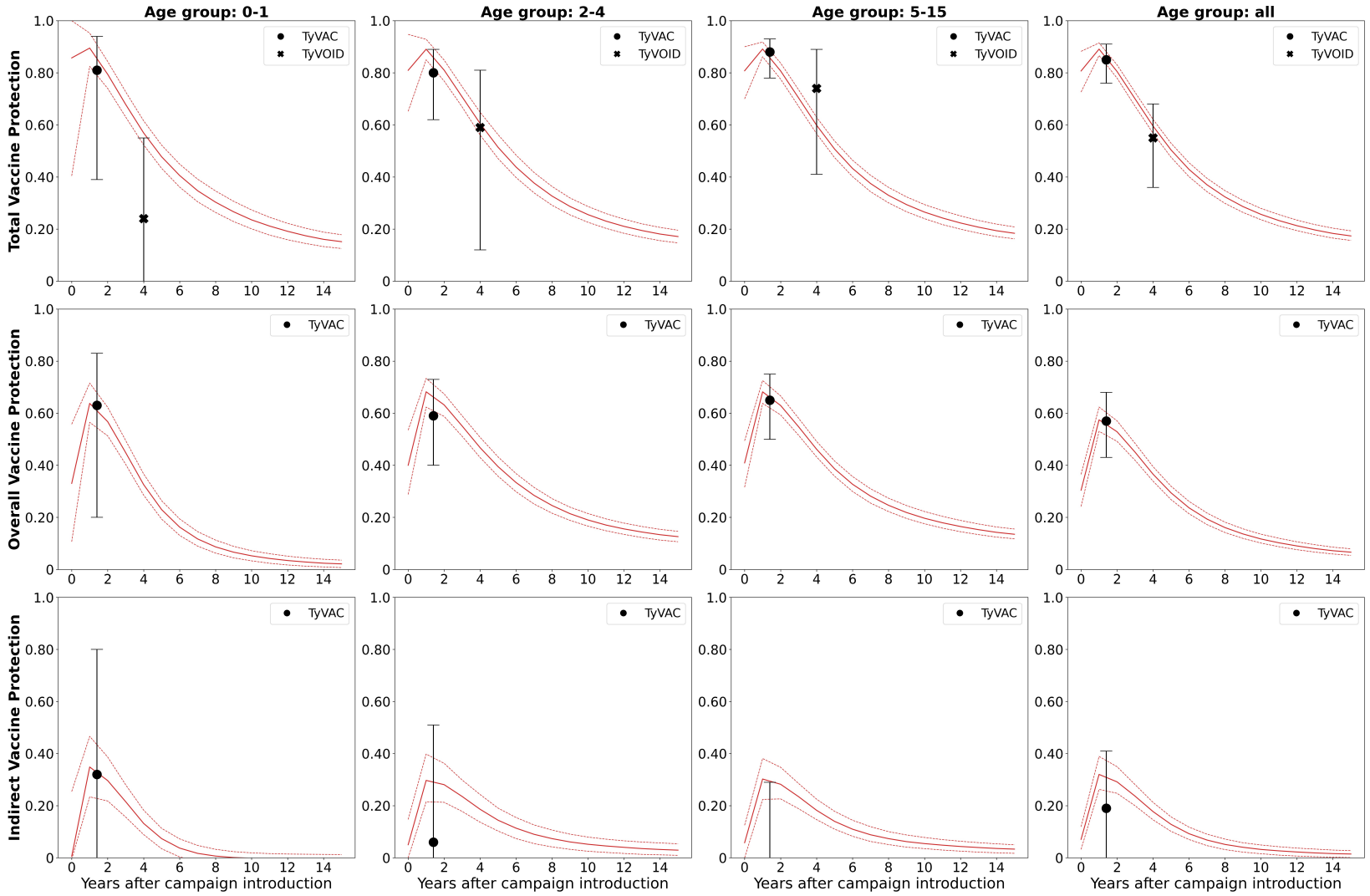


Mean(rC) = 0.18

Burnet Institute: Fast waning validation: Bangladesh

Very High Burden

- Assuming a fixed waning rate and vaccine efficacy across all age groups
- Model aligns with observed data for total and overall protection
- Model currently overestimates indirect protection in most age groups – however, data for indirect protection shows no significant effects
- **Consider revising calibration to reduce indirect protection?**

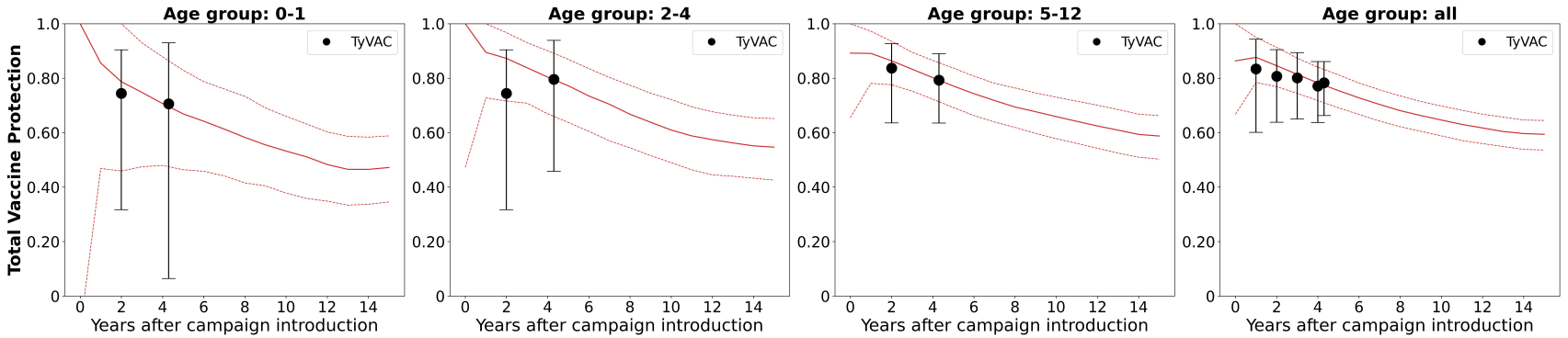


PRELIMINARY RESULTS

Burnet Institute: Slow waning validation: Malawi

High Burden

- Assuming a fixed waning rate and vaccine efficacy across all age groups
- Model aligns with observed data for total protection
- No data on overall or indirect protection



PRELIMINARY RESULTS

Bangladesh

Age groups considered:

- < 2 years old
- 2 - 4 years old
- ⩾ 5 years old
- All ages

Study midpoints for

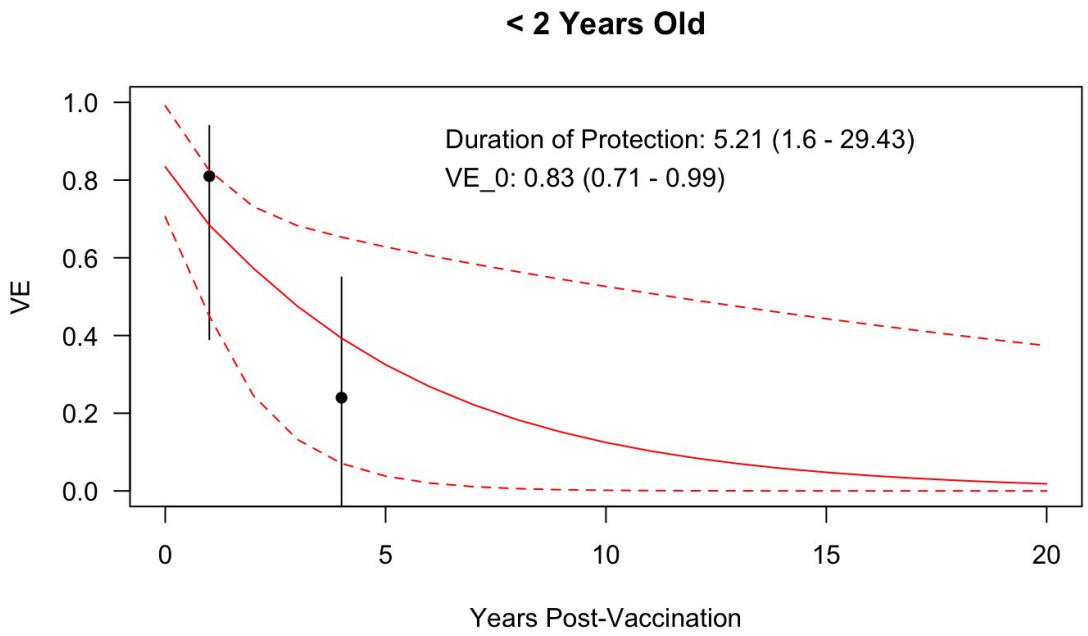
- TyVac: 1 year
- TyVoid: 4 years

Possible assumptions for waning:

- Exponential
- Gamma

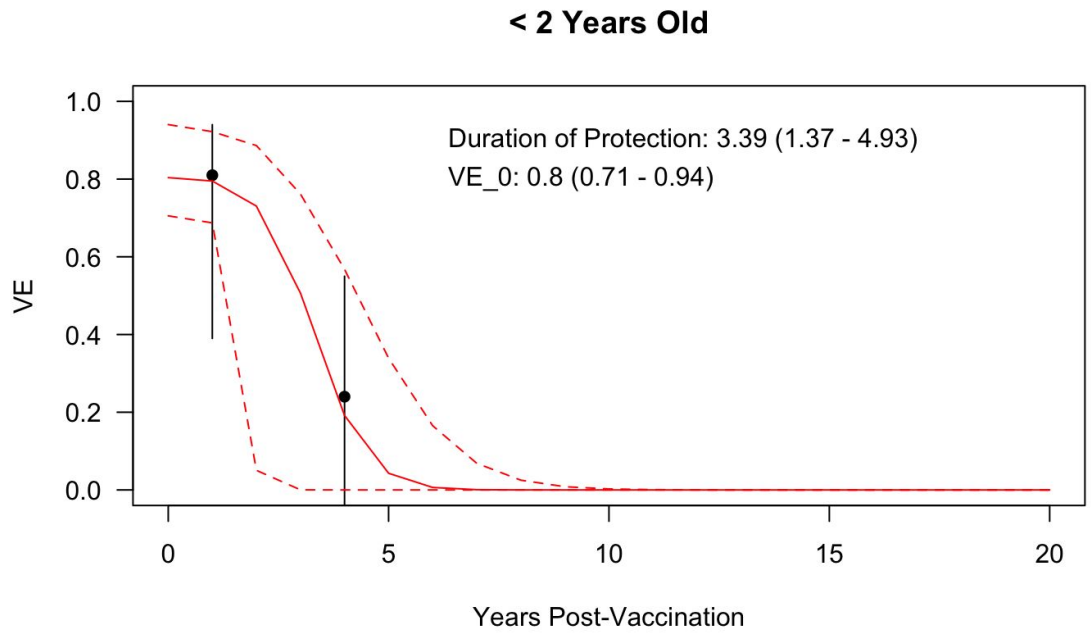
For age group: < 2 years old

Exponential Waning



Median AIC: 5.941
Median BIC: 3.327

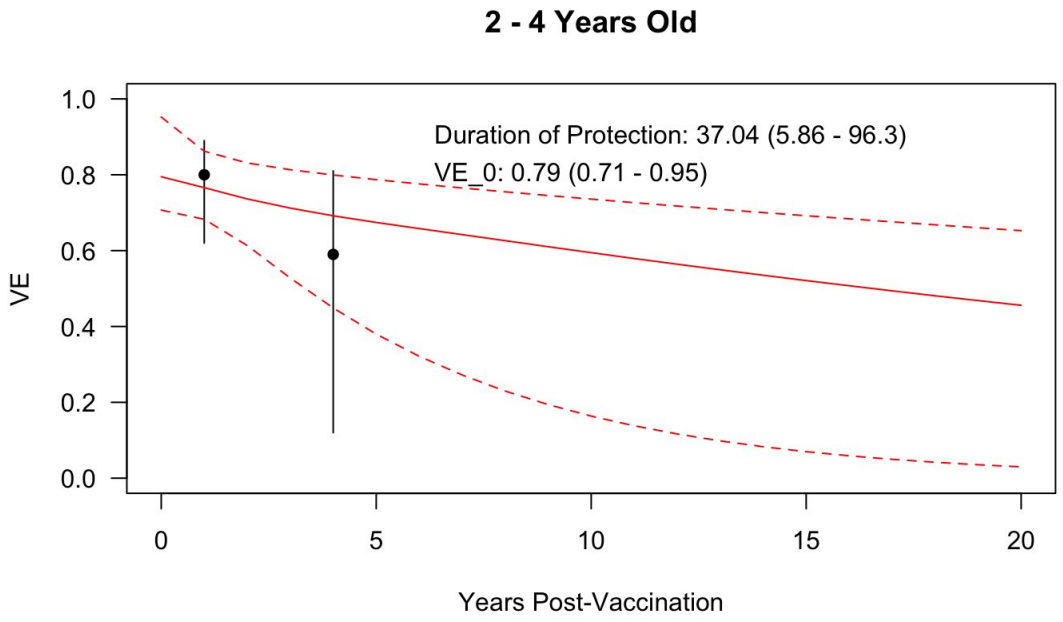
Gamma Waning



Median AIC: 6.924
Median BIC: 3.003

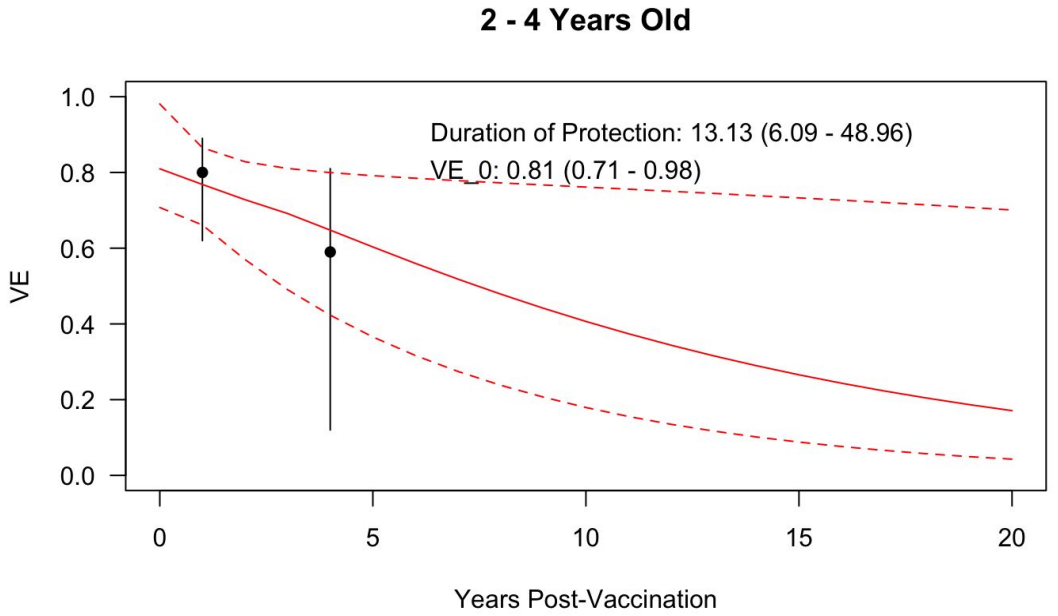
For age group: 2 - 4 years old

Exponential Waning



Median AIC: 4.953
Median BIC: 2.340

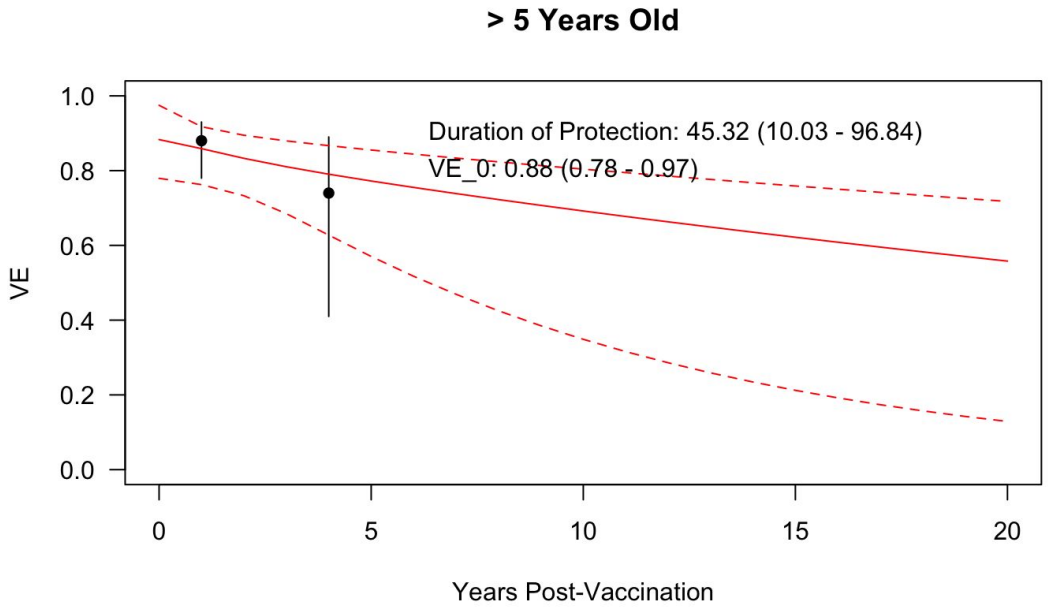
Gamma Waning



Median AIC: 6.665
Median BIC: 2.744

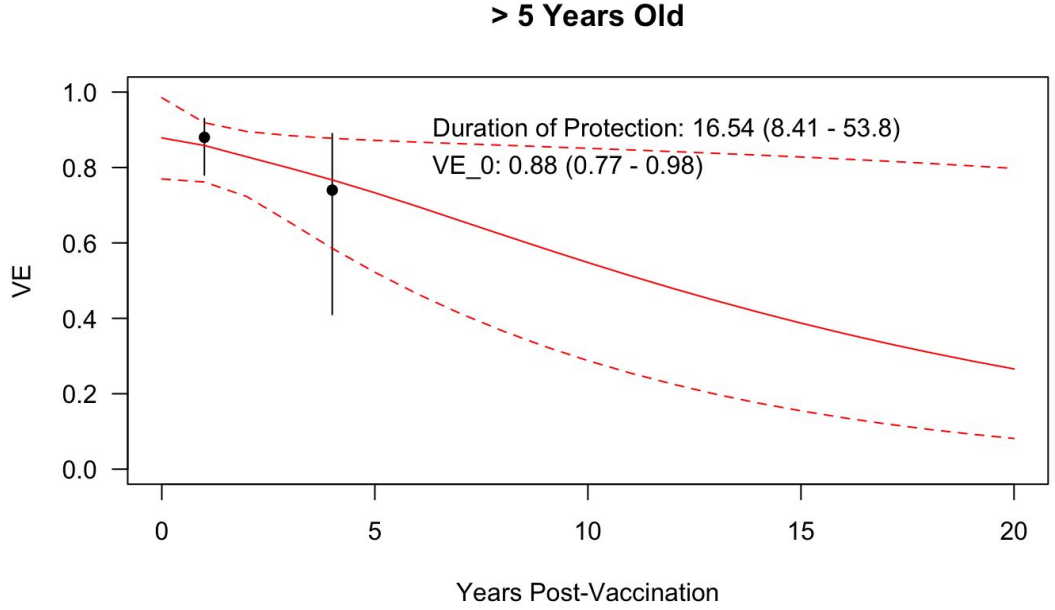
For age group: ⩾ 5 years old

Exponential Waning



Median AIC: 4.855
Median BIC: 2.416

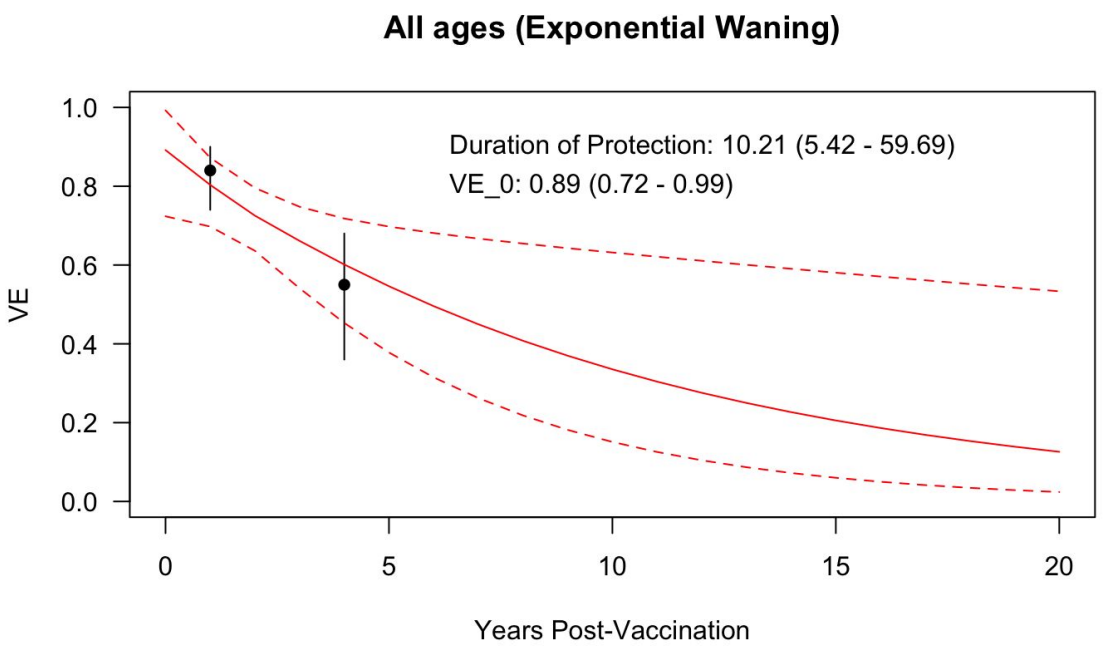
Gamma Waning



Median AIC: 6.984
Median BIC: 3.063

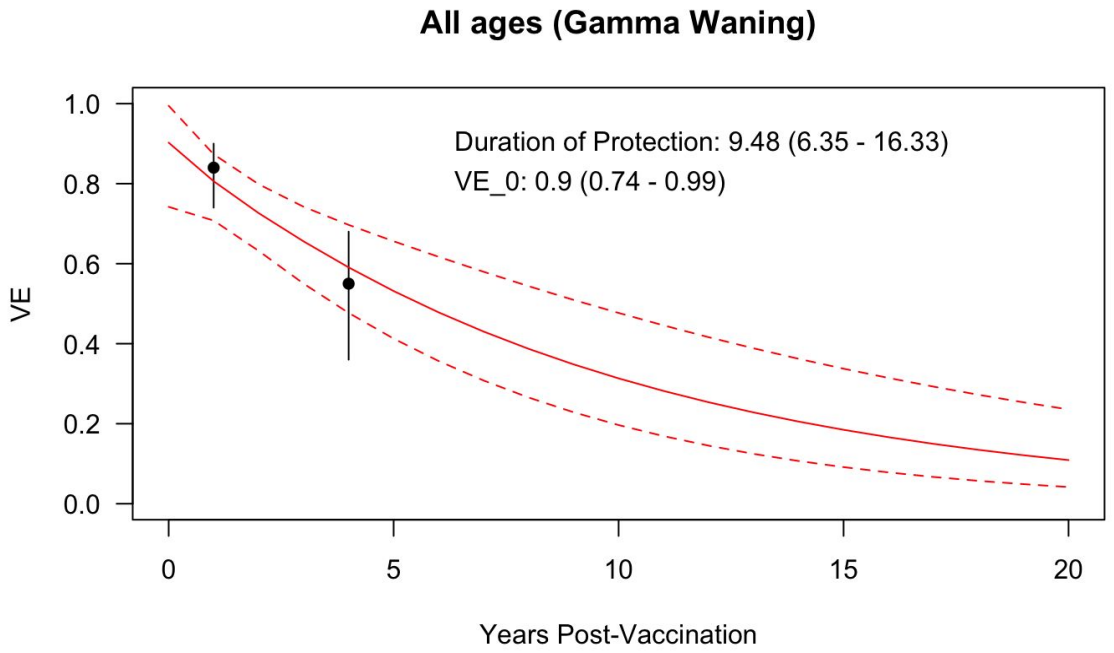
For age group: All ages

Exponential Waning



Median AIC: 3.552
Median BIC: 0.938

Gamma Waning

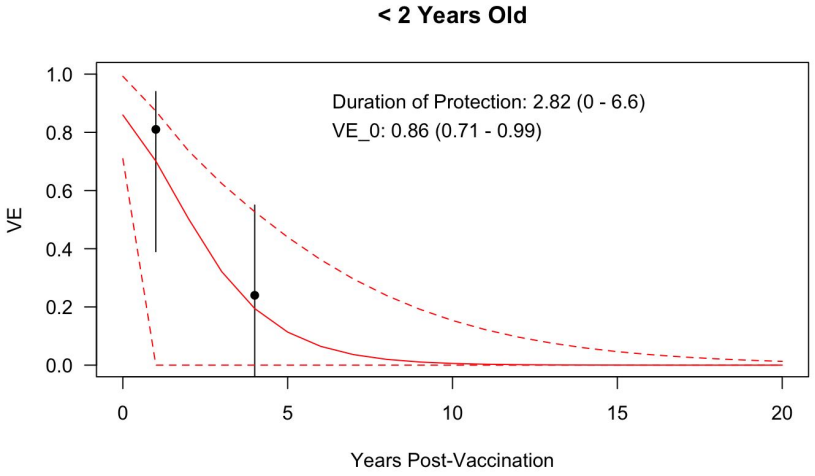


Median AIC: 5.097
Median BIC: 1.177

Setting a fixed Shape parameter, and estimating Scale parameter.

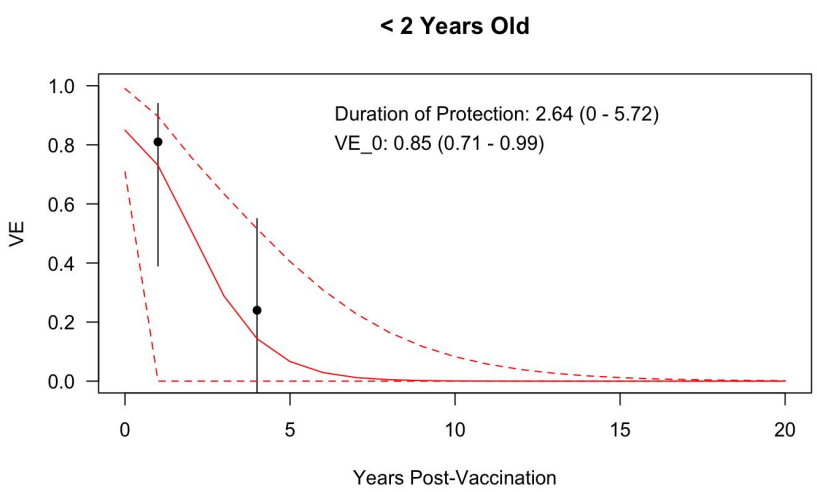
For age group: < 2 Years Old. For Exponential waning, AIC = 5.941 and BIC = 3.327

Shape = 2



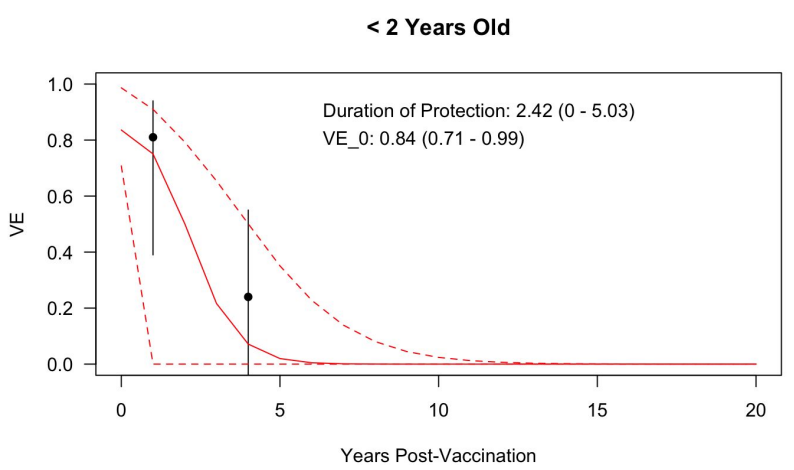
Median AIC: 7.185
Median BIC: 3.264

Shape = 3



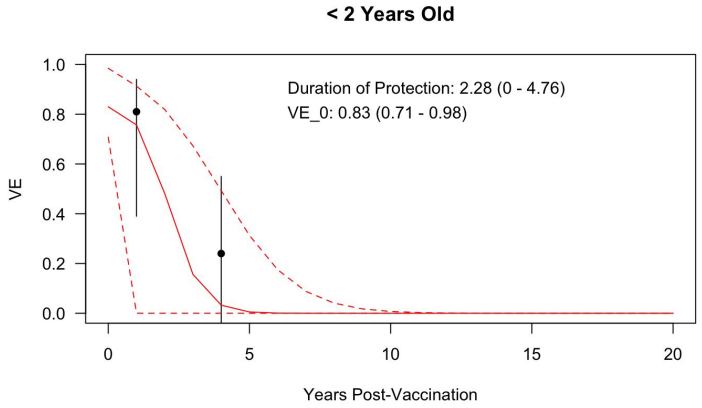
Median AIC: 7.007
Median BIC: 3.086

Shape = 5



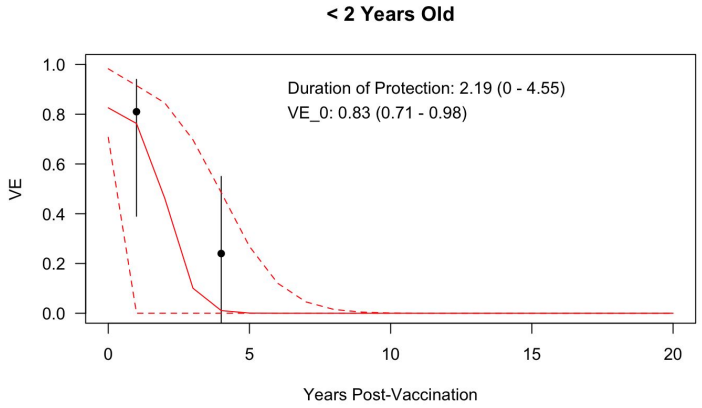
Median AIC: 7.101
Median BIC: 3.180

Shape = 7



Median AIC: 7.187
Median BIC: 3.266

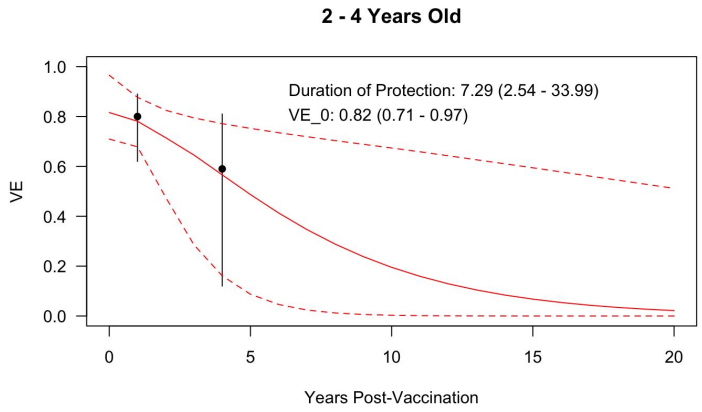
Shape = 10



Median AIC: 7.221
Median BIC: 3.301

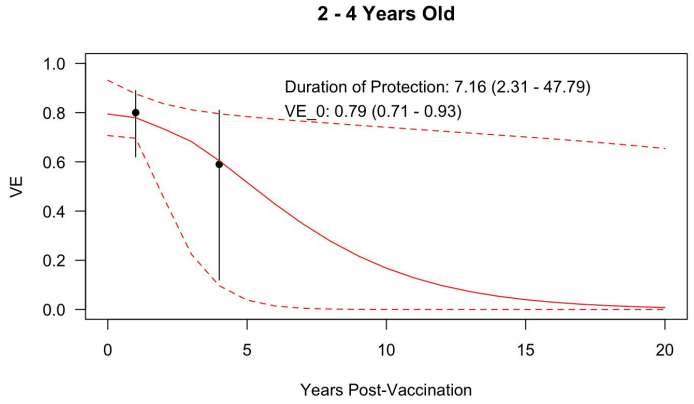
For age group: 2 - 4 Years Old. For Exponential waning, AIC = 4.953 and BIC = 2.340

Shape = 2



Median AIC: 6.686
Median BIC: 2.765

Shape = 3



Median AIC: 6.898
Median BIC: 2.977

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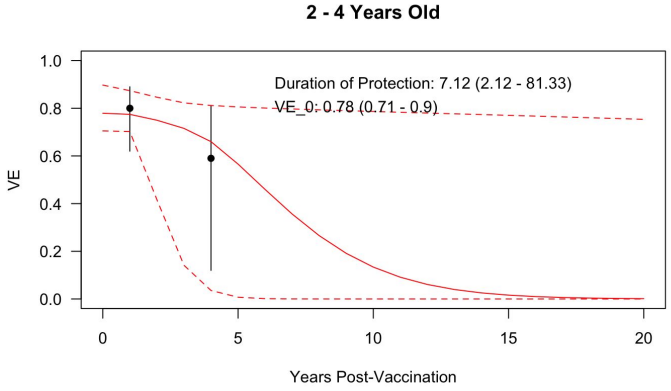
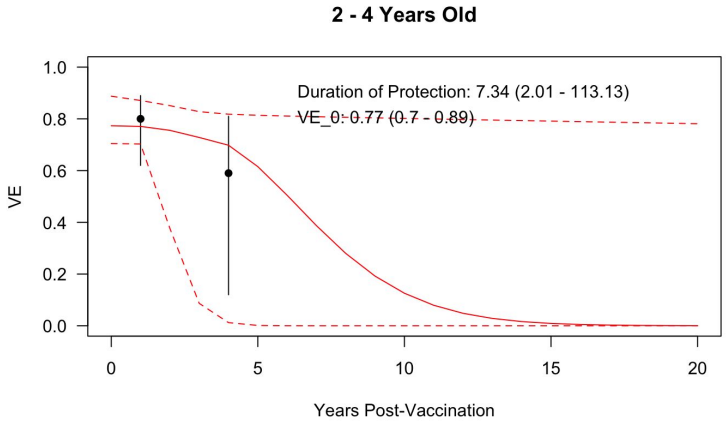


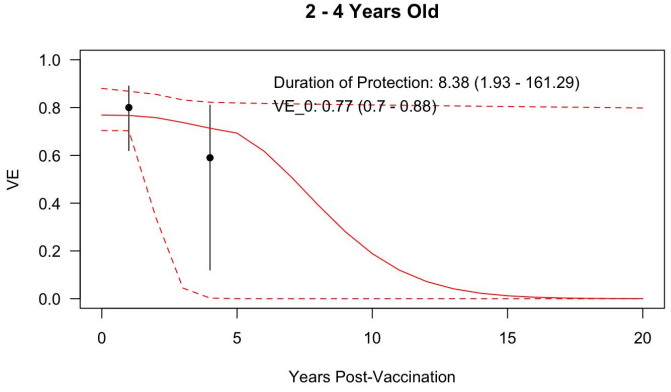
Median AIC: 7.282
Median BIC: 3.361

Shape = 7



Median AIC: 7.533
Median BIC: 3.612

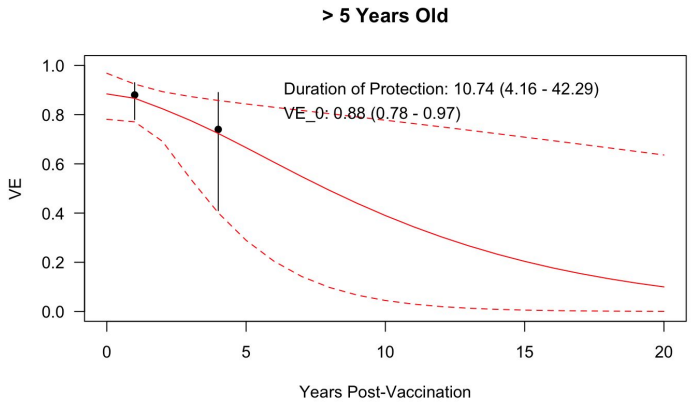
Shape = 10



Median AIC: 7.566
Median BIC: 3.646

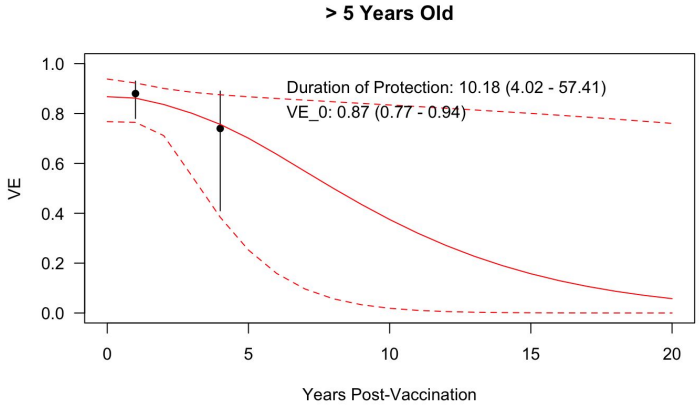
For age group: ⩾ 5 Years Old. For Exponential waning, AIC = 4.855 and BIC = 2.416

Shape = 2



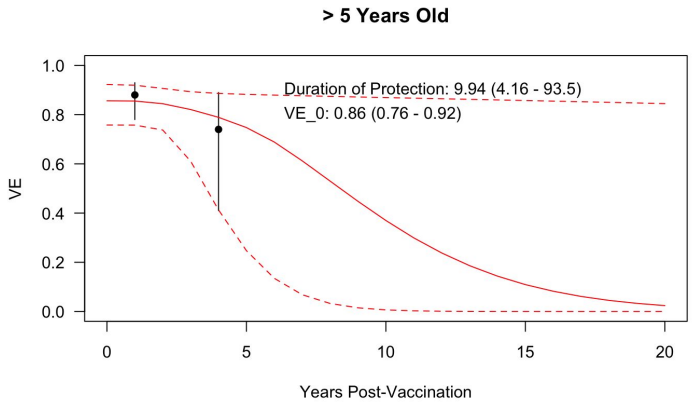
Median AIC: 6.879
Median BIC: 2.959

Shape = 3



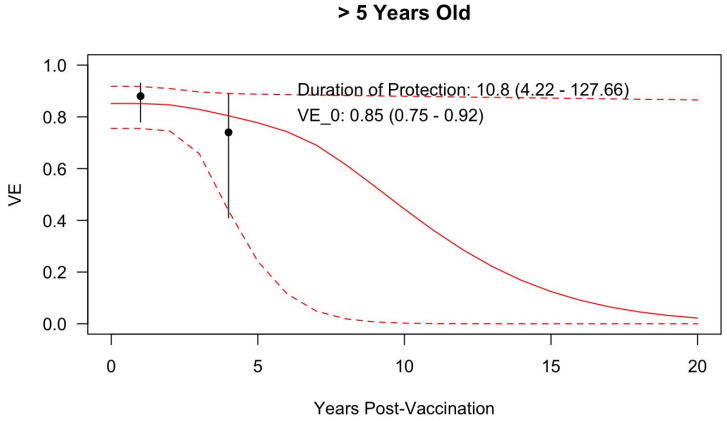
Median AIC: 7.222
Median BIC: 3.301

Shape = 5



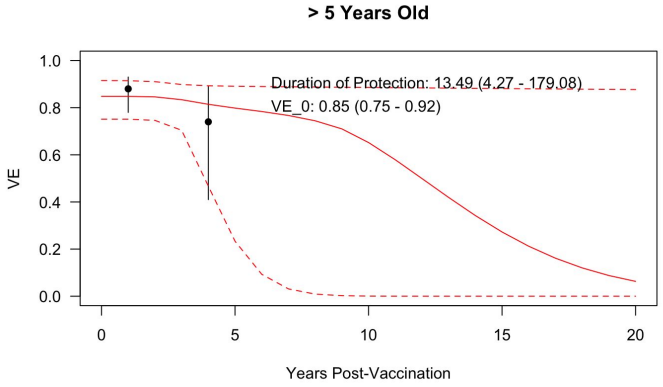
Median AIC: 7.740
Median BIC: 3.820

Shape = 7



Median AIC: 7.840
Median BIC: 3.920

Shape = 10



Median AIC: 7.942
Median BIC: 4.021

Malawi

Age groups considered:

- < 5 years old
- ≥ 5 years old
- All ages

Study midpoints for

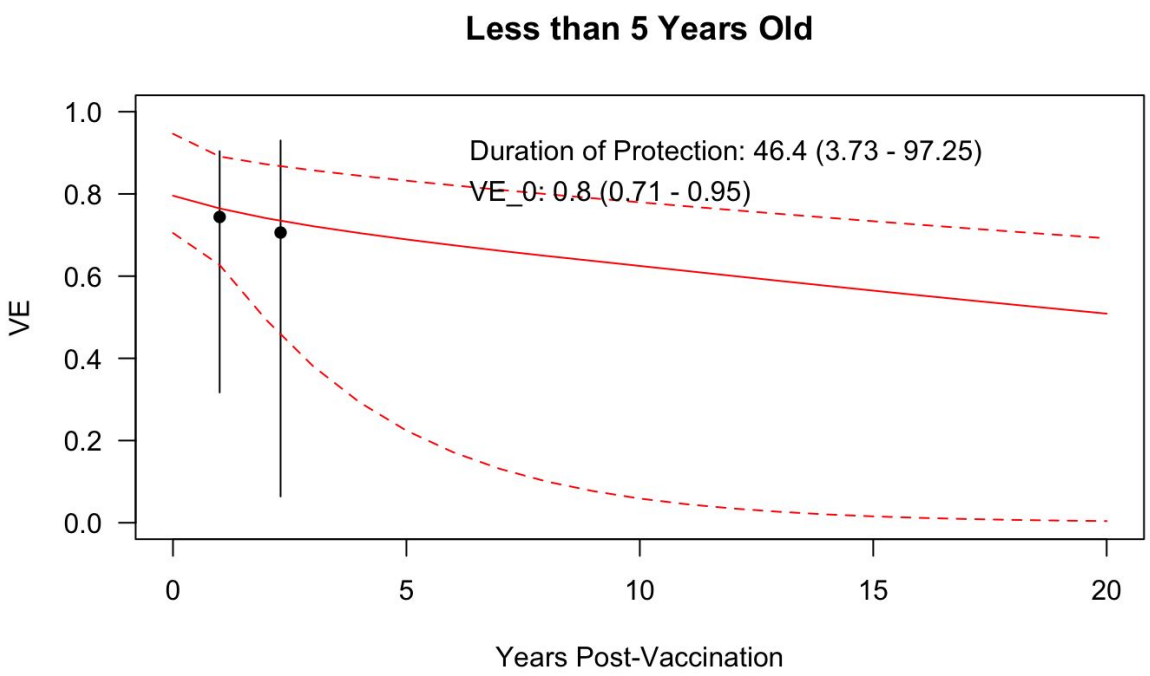
- 2021 NEJM Paper : 1.75 years
- 2024 Lancet Paper : 2.305 years

Possible assumptions for waning:

- Exponential
- Gamma

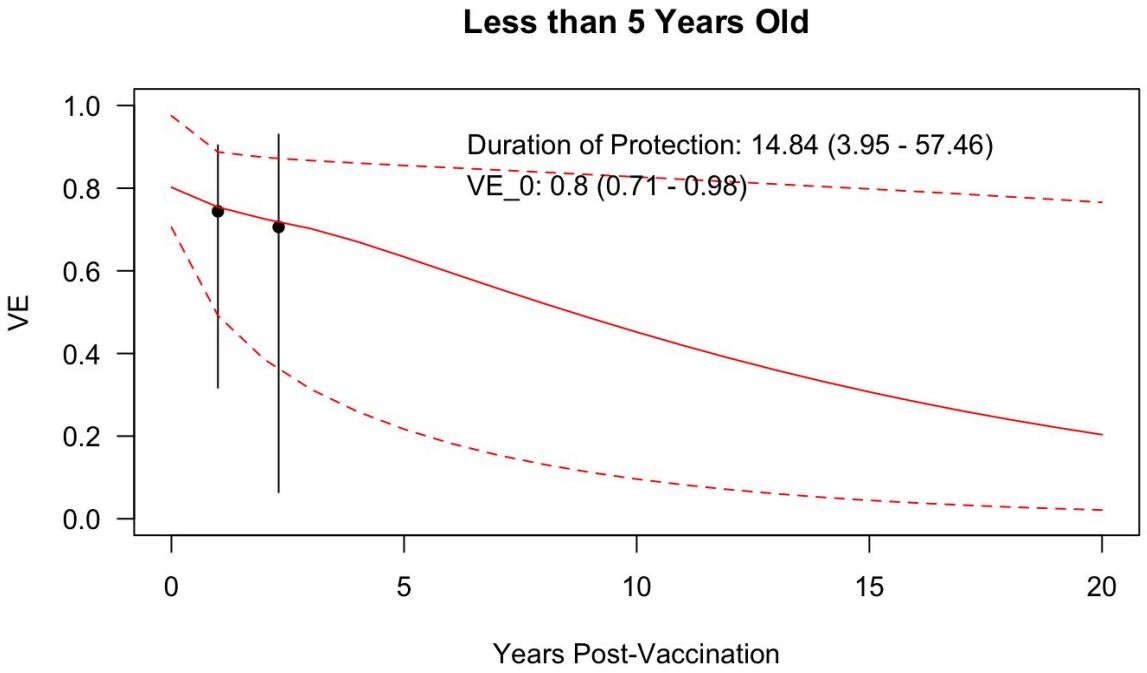
For age group: < 5 years old

Exponential Waning



Median AIC: 5.704
Median BIC: 3.090

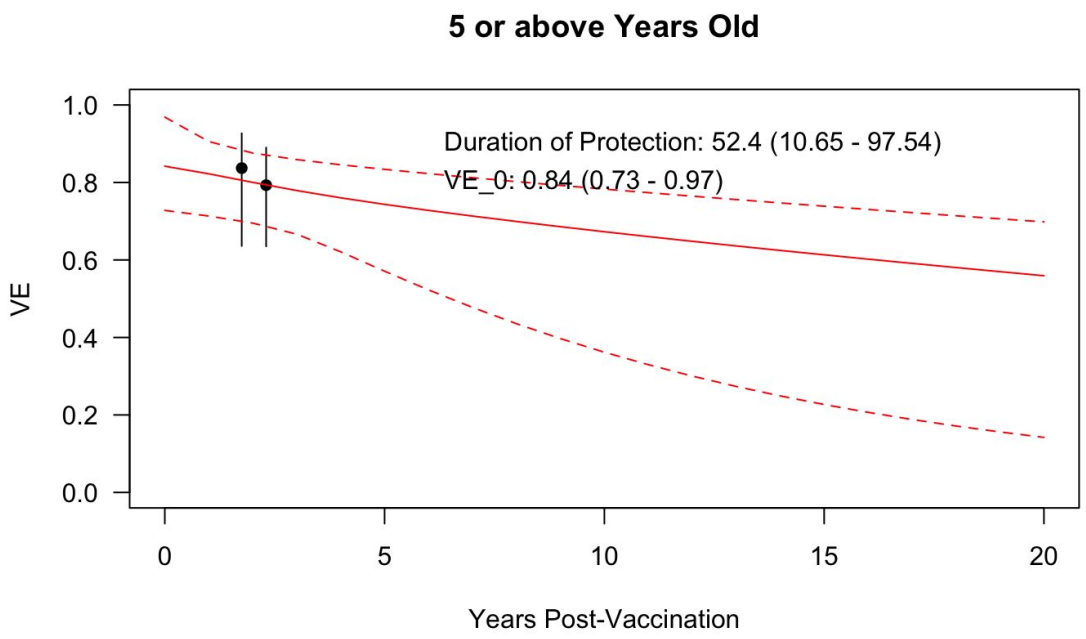
Gamma Waning



Median AIC: 7.782
Median BIC: 3.861

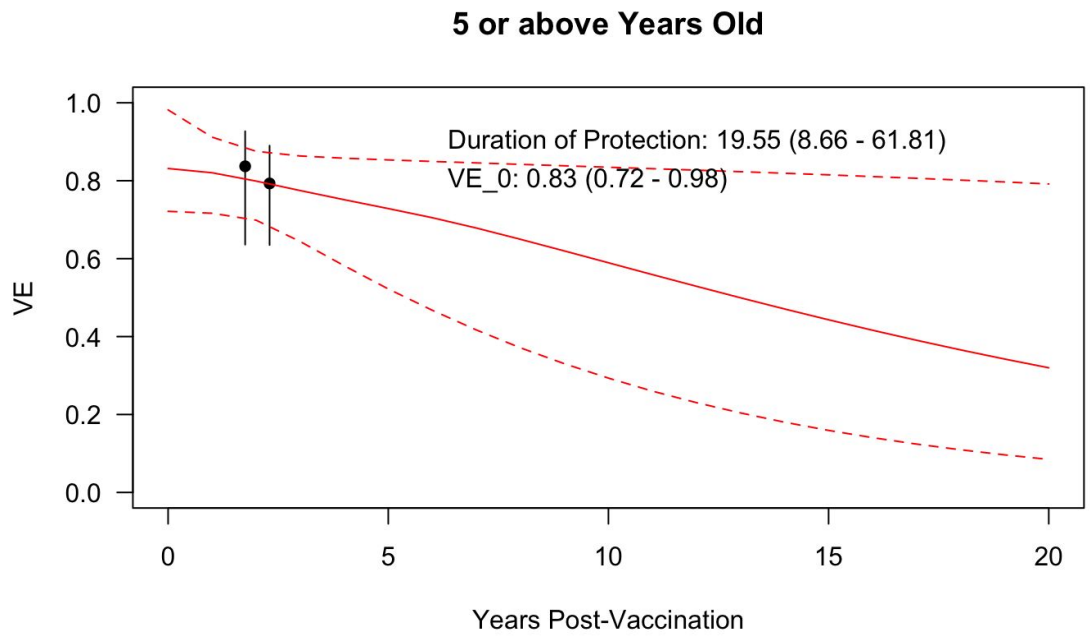
For age group: ≥ 5 years old

Exponential Waning



Median AIC: 4.116
Median BIC: 1.502

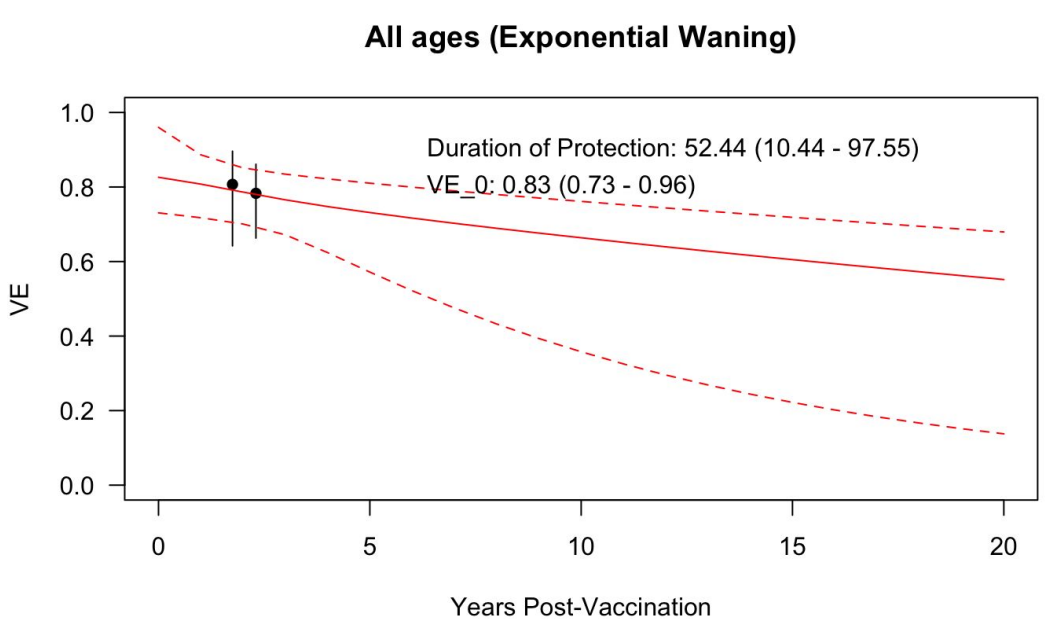
Gamma Waning



Median AIC: 6.124
Median BIC: 2.203

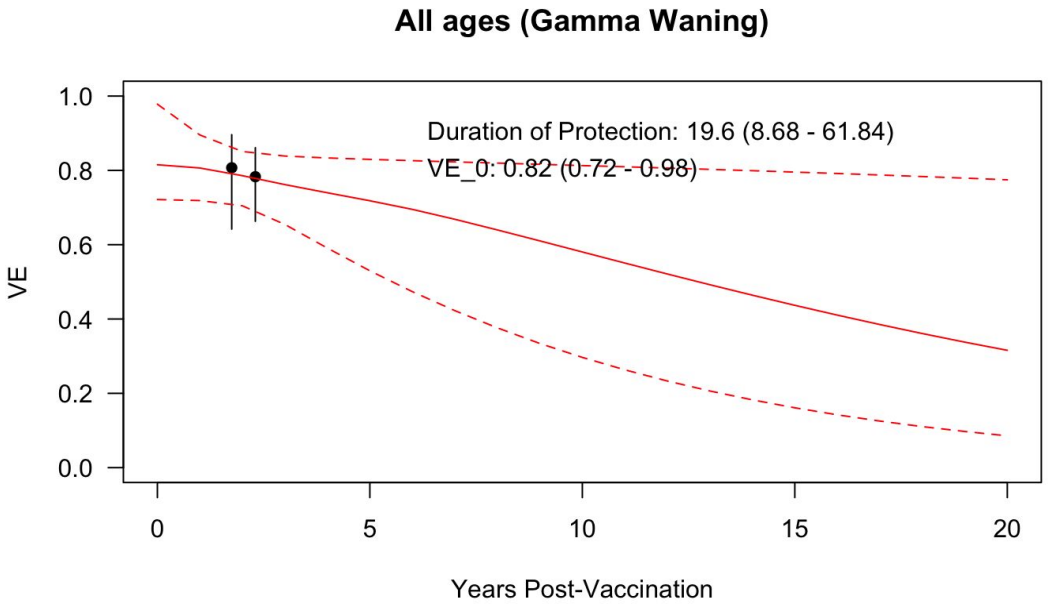
For age group: All ages

Exponential Waning



Median AIC: 2.892
Median BIC: 0.278

Gamma Waning



Median AIC: 4.910
Median BIC: 0.989

Time points considered for vaccine efficacy over time in intention-to-treat population of malawi
(Table 3 in 2024 Lancet Paper)

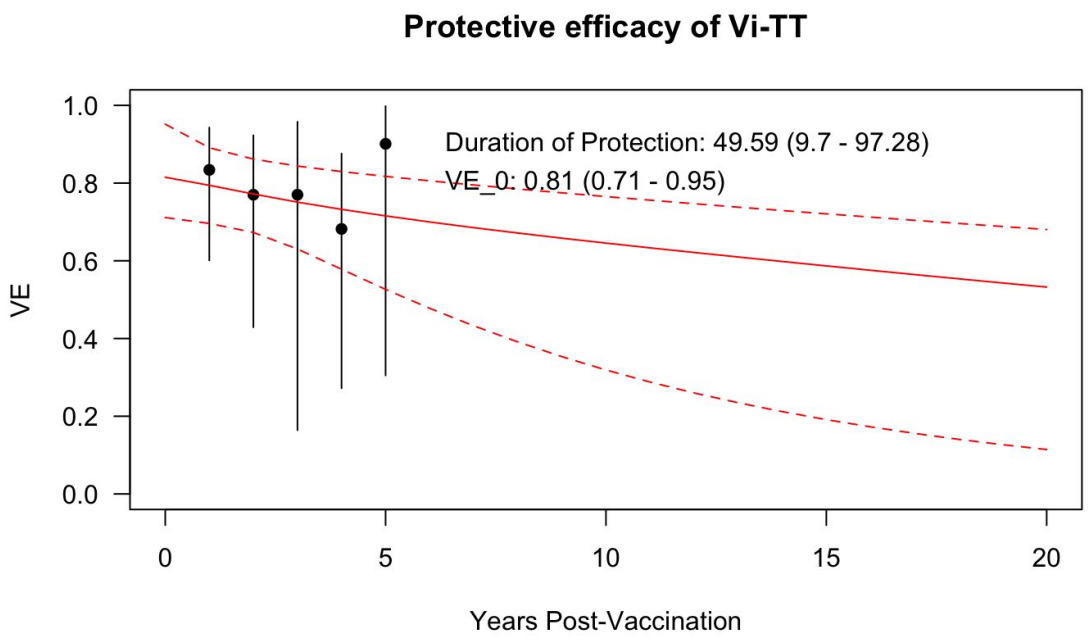
- Discrete time since vaccination. (time = 1, 2, 3, 4, 5)
- Cumulative time since vaccination. Assuming time points to be the mid points of the cumulative range. Therefore, time = (1-0)/2, (2-0)/2, (3-0)/2, (4-0)/2, (4.61-0)/2). (time = 0.5, 1, 1.5, 2, 2.305)
- Cumulative time since vaccination. Assuming time points to be the end point of the cumulative range. (time = 1, 2, 3, 4, 4.61)

Possible assumptions for waning:

- Exponential
- Gamma

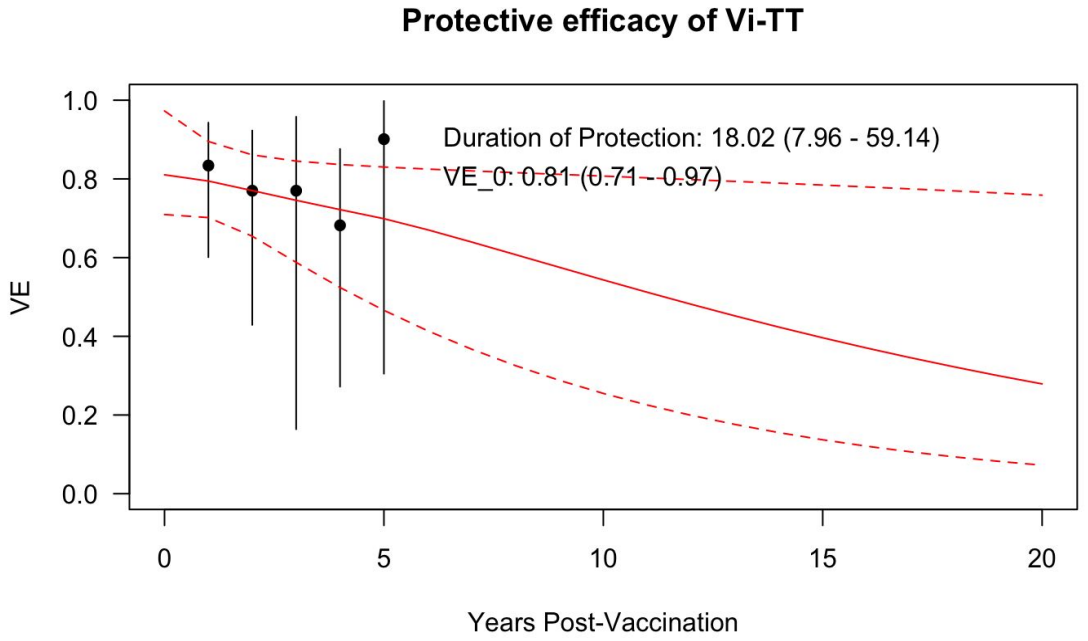
VE for all age groups by discrete time since vaccination

Exponential Waning



Median AIC: 10.440
Median BIC: 9.659

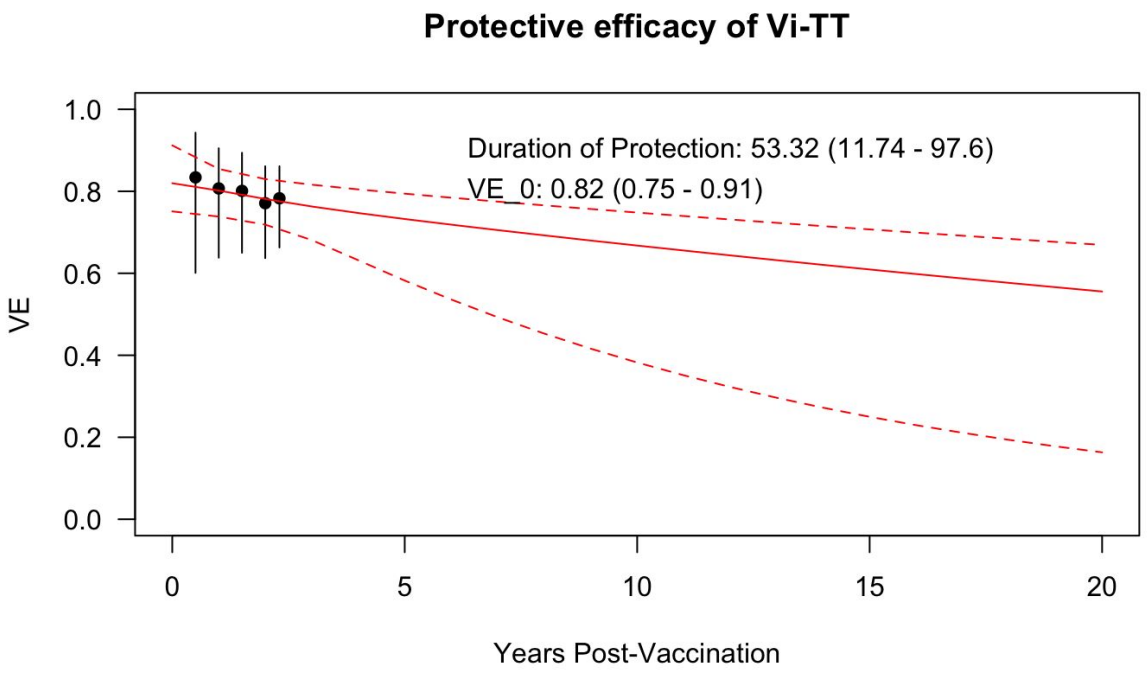
Gamma Waning



Median AIC: 12.582
Median BIC: 11.410

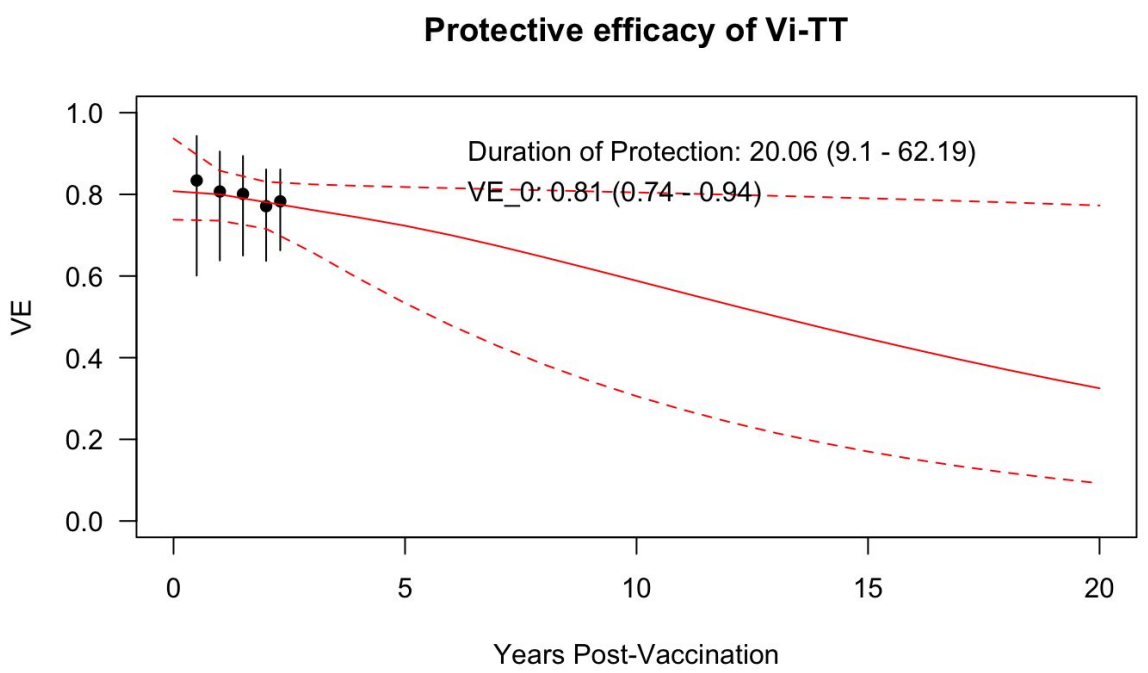
VE for all age groups by cumulative time since vaccination (time = 0.5, 1, 1.5, 2, 2.305)

Exponential Waning



Median AIC: 2.186
Median BIC: 1.405

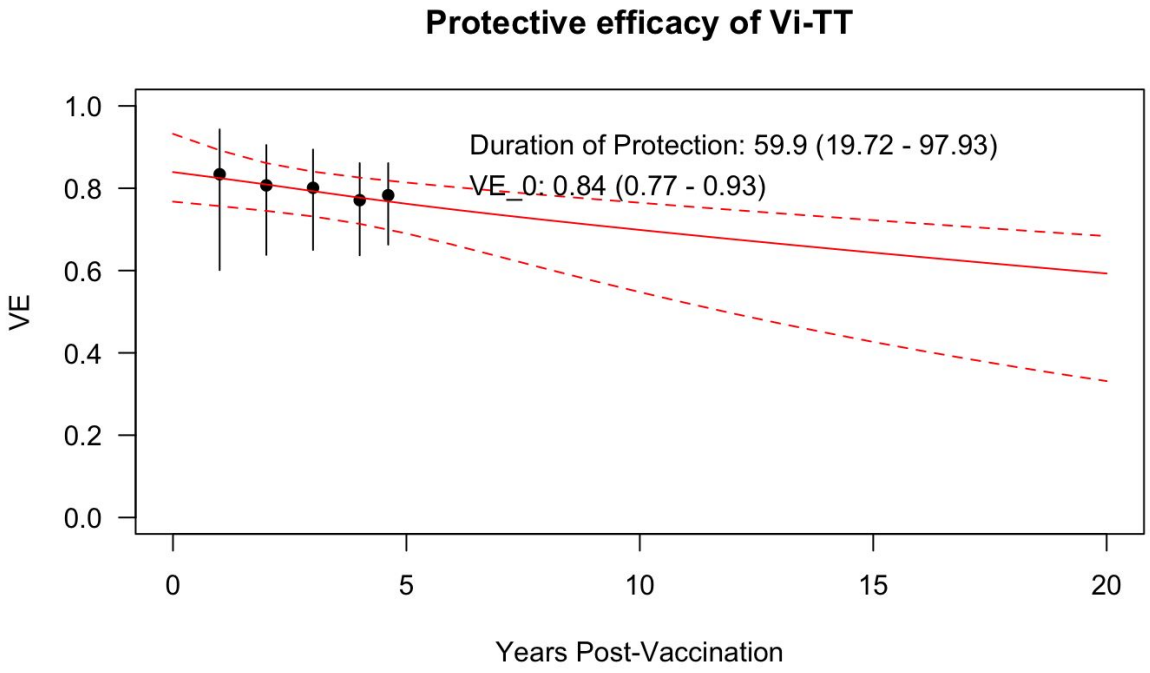
Gamma Waning



Median AIC: 4.370
Median BIC: 3.198

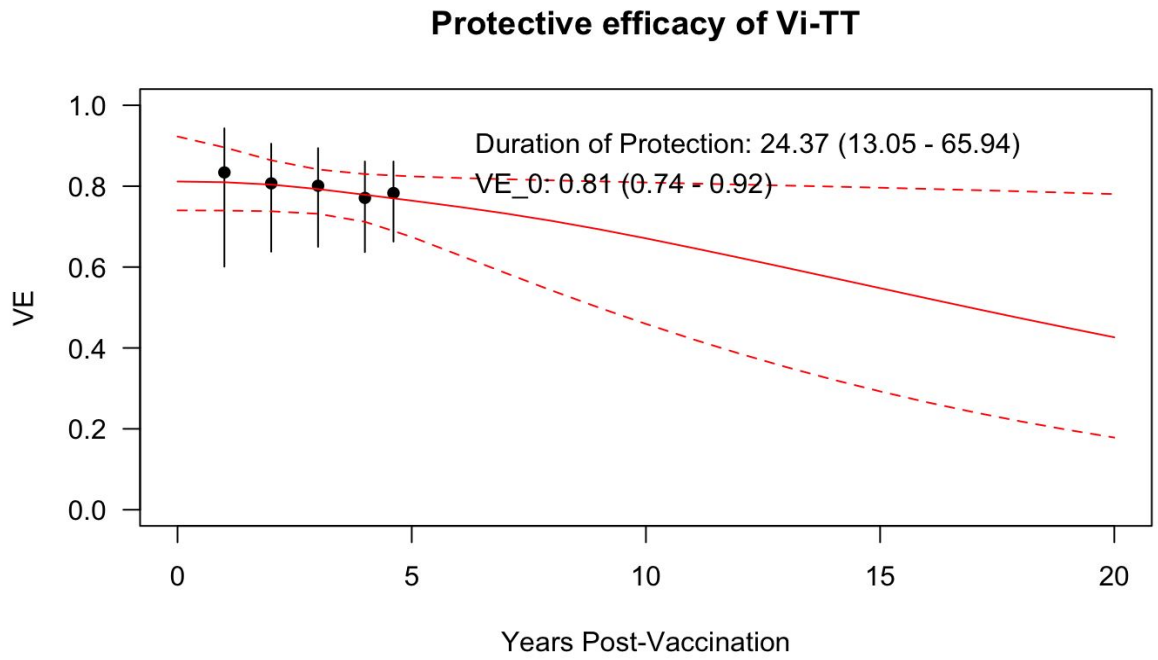
VE for all age groups by cumulative time since vaccination (time = 1, 2, 3, 4, 4.61)

Exponential Waning



Median AIC: 2.199
Median BIC: 1.417

Gamma Waning

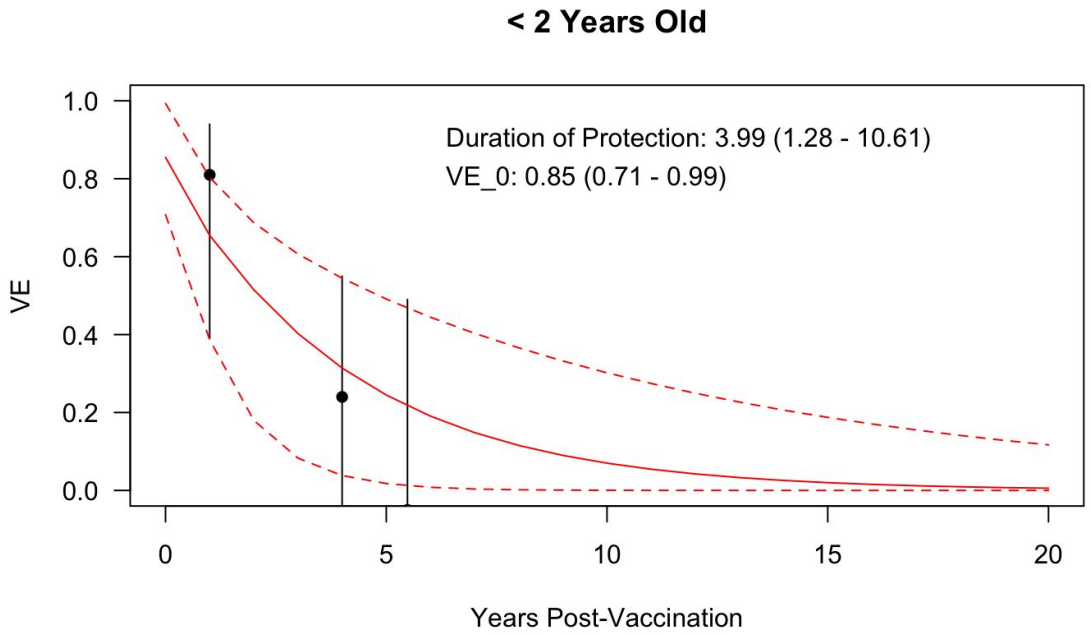


Median AIC: 4.419
Median BIC: 3.247

New VE estimates for Bangladesh (provided by Xinxue)

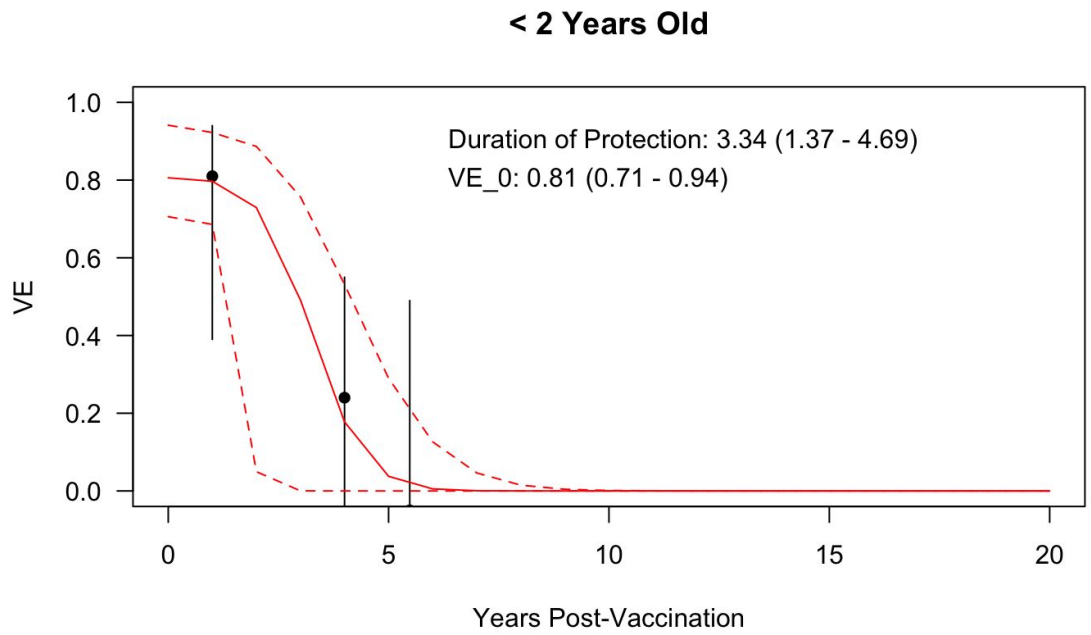
For age group: < 2 years old

Exponential Waning



DIC: 2.67
Median AIC: 6.21
Median BIC: 4.41

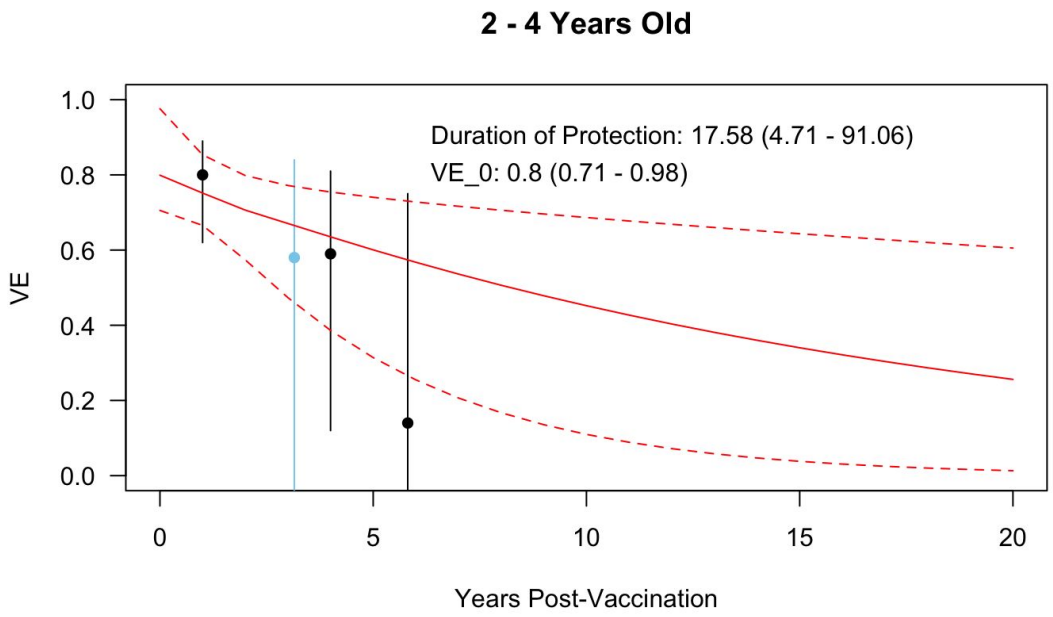
Gamma Waning



DIC: 1.09
Median AIC: 6.80
Median BIC: 4.10

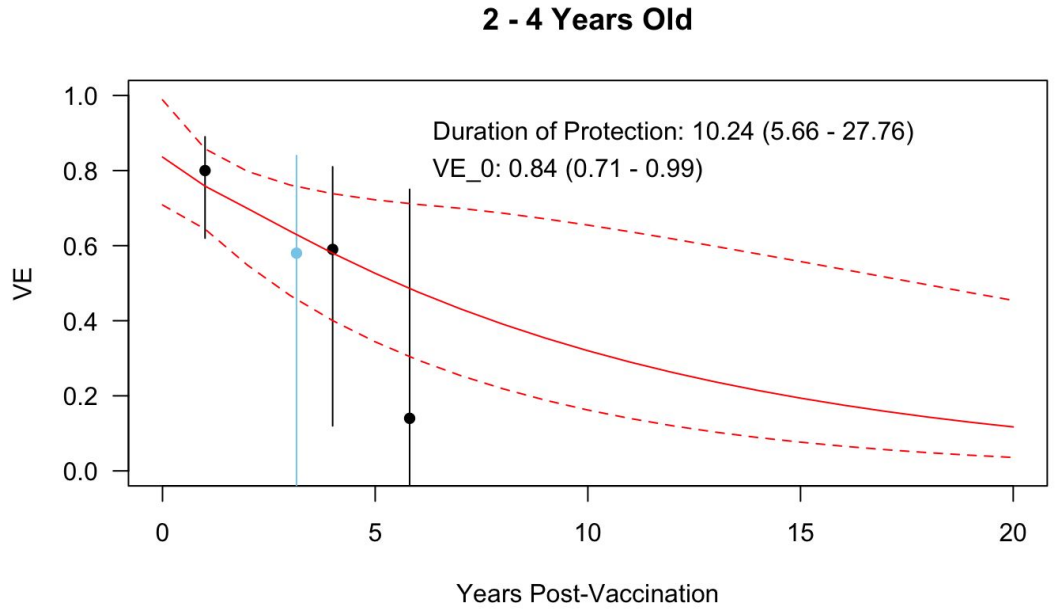
For age group: 2 - 4 years old

Exponential Waning



DIC: 3.83
Median AIC: 7.68
Median BIC: 6.46

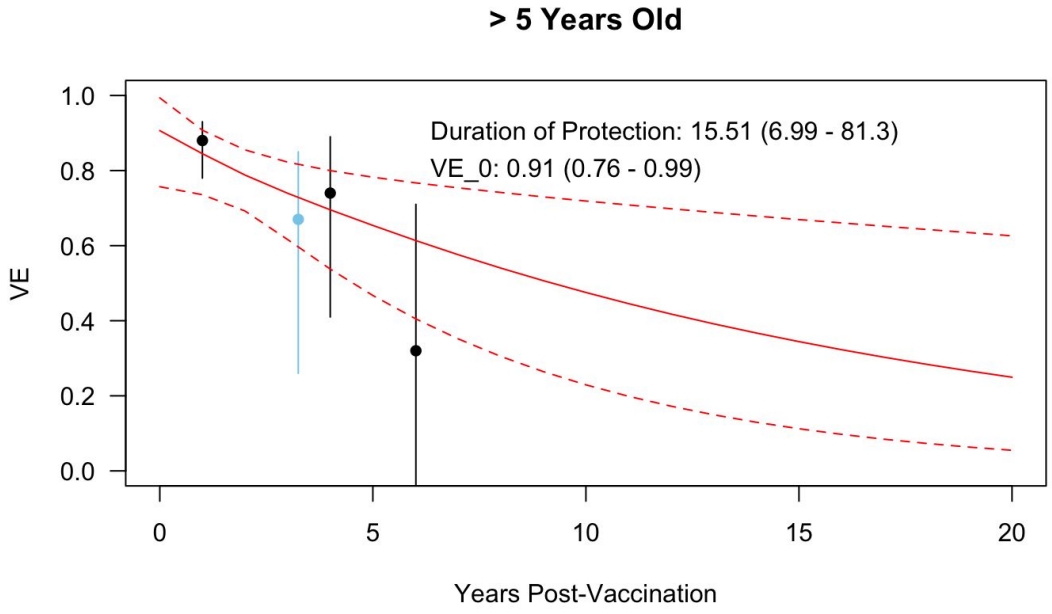
Gamma Waning



DIC: 3.12
Median AIC: 8.67
Median BIC: 6.83

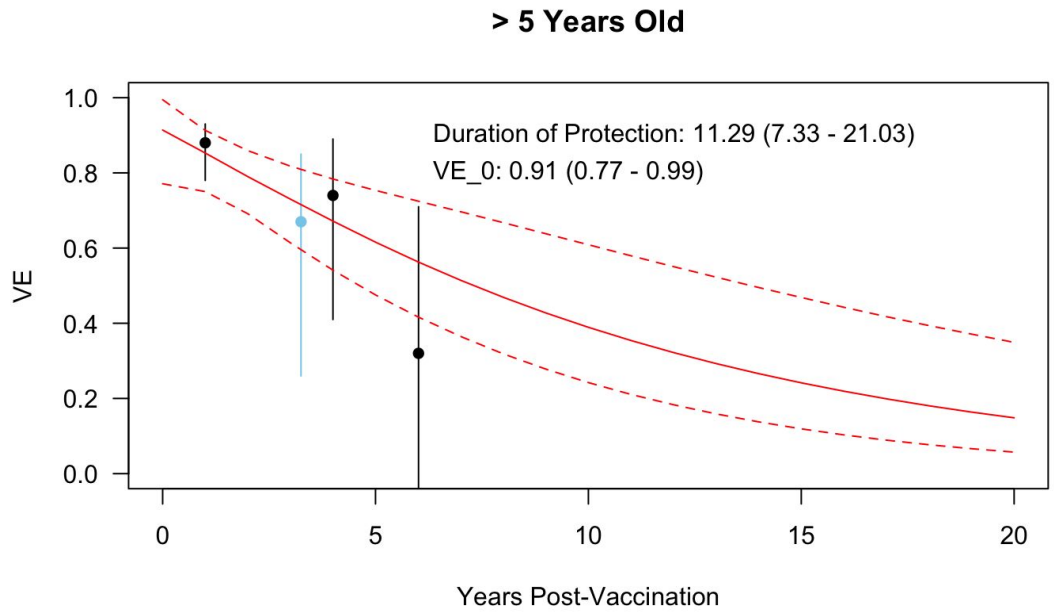
For age group: ⩾ 5 years old

Exponential Waning



DIC: 4.35
Median AIC: 7.53
Median BIC: 6.31

Gamma Waning

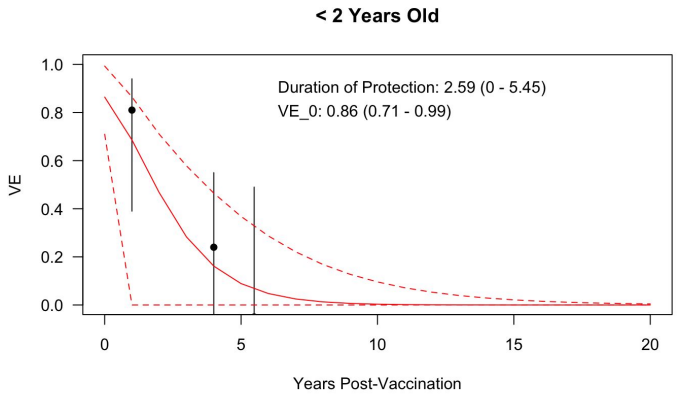


DIC: 3.21
Median AIC: 8.51
Median BIC: 6.67

Setting a fixed Shape parameter, and estimating Scale parameter.

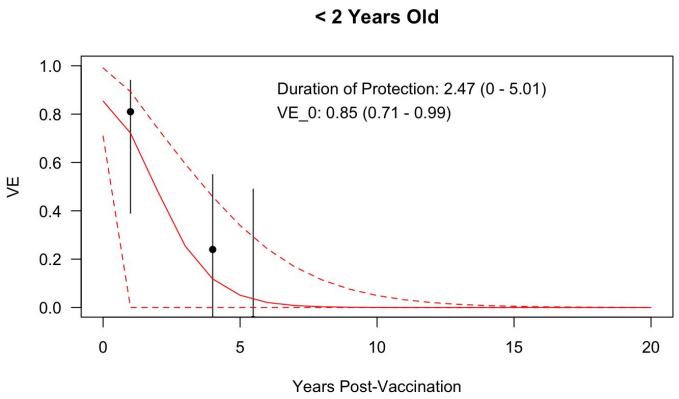
For age group: < 2 Years Old. For Exponential waning, DIC = 2.67, AIC = 6.21 and BIC = 4.41

Shape = 2



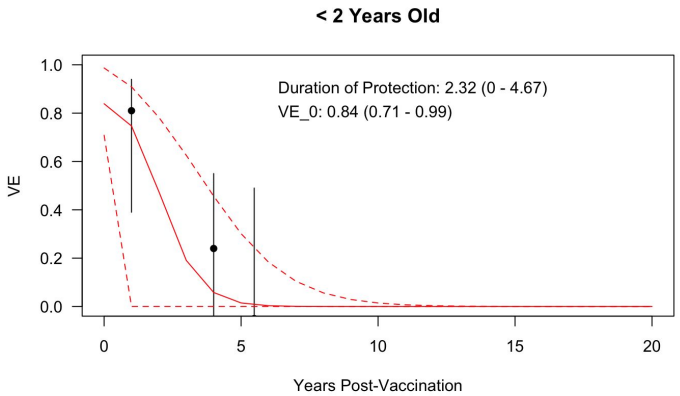
DIC: 2.47
Median AIC: 5.34
Median BIC: 3.53

Shape = 3



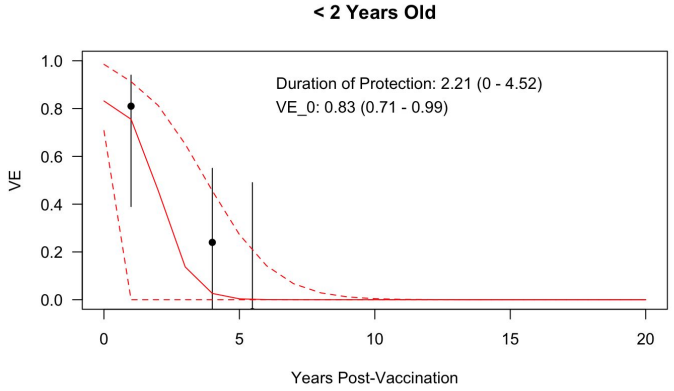
DIC: 2.58
Median AIC: 5.04
Median BIC: 3.24

Shape = 5



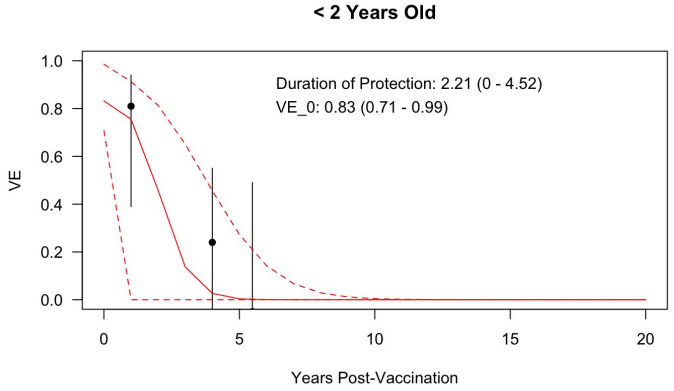
DIC: 2.31
Median AIC: 5.03
Median BIC: 3.23

Shape = 7



DIC: 2.27
Median AIC: 5.08
Median BIC: 3.28

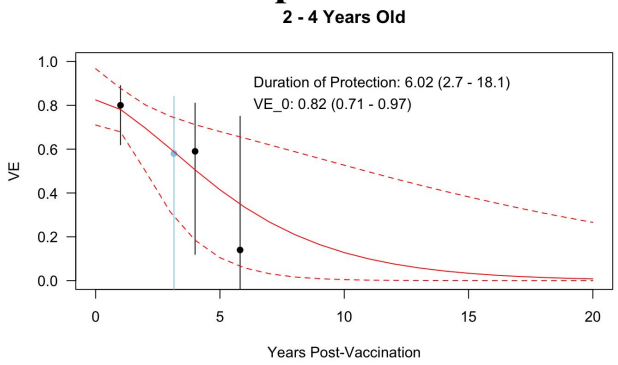
Shape = 10



DIC: 2.26
Median AIC: 5.10
Median BIC: 3.29

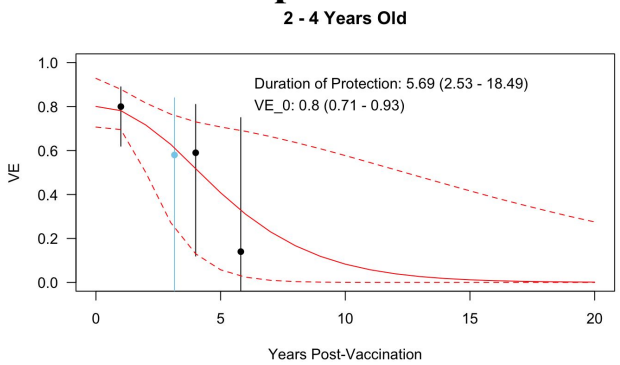
For age group: 2 - 4 Years Old. For Exponential waning, DIC = 3.83, AIC = 7.68 and BIC = 6.46

Shape = 2



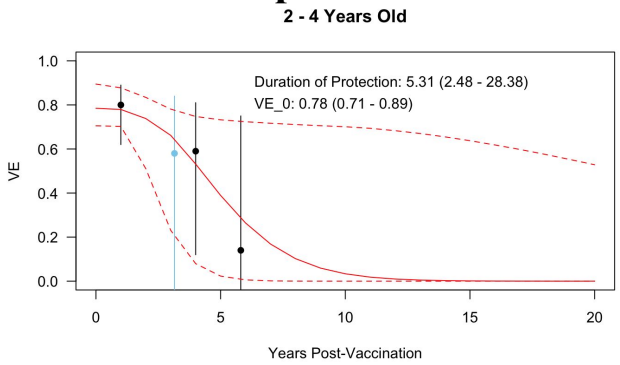
DIC: 2.96
Median AIC: 6.55
Median BIC: 5.32

Shape = 3



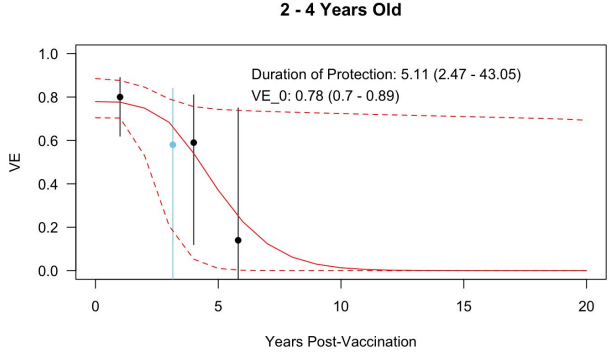
DIC: 3.11
Median AIC: 6.55
Median BIC: 5.32

Shape = 5



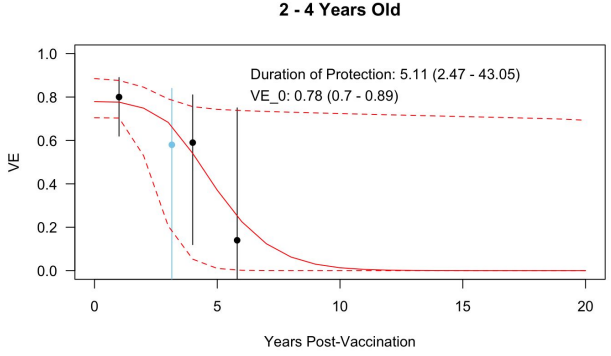
DIC: 3.28
Median AIC: 6.56
Median BIC: 5.33

Shape = 7



DIC: 3.40
Median AIC: 6.64
Median BIC: 5.41

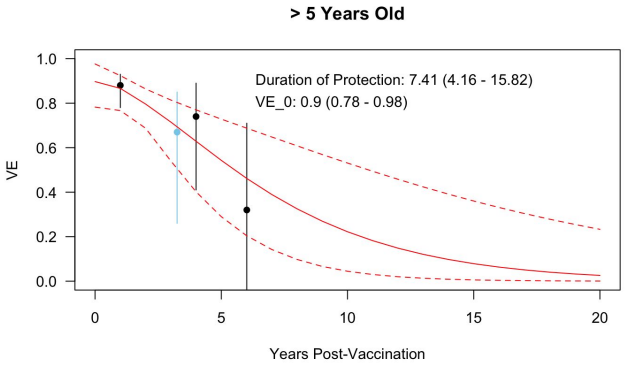
Shape = 10



DIC: 3.69
Median AIC: 6.80
Median BIC: 5.57

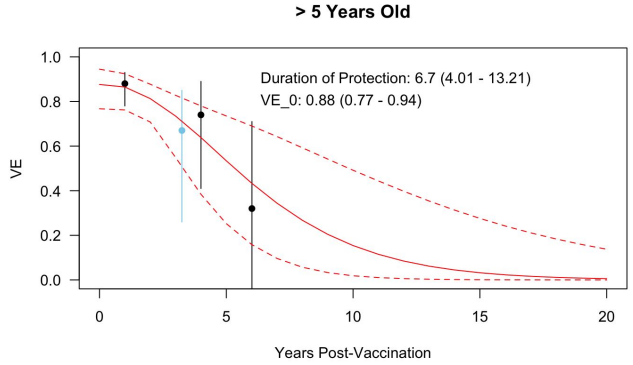
For age group: ⩾ 5 Years Old. For Exponential waning, DIC = 4.35, AIC = 7.53 and BIC = 6.31

Shape = 2



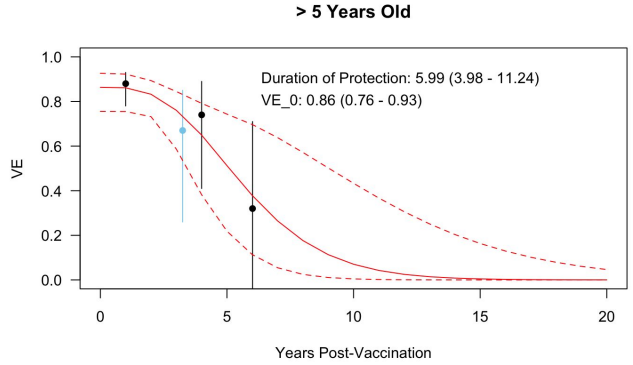
DIC: 2.83
Median AIC: 6.25
Median BIC: 5.02

Shape = 3



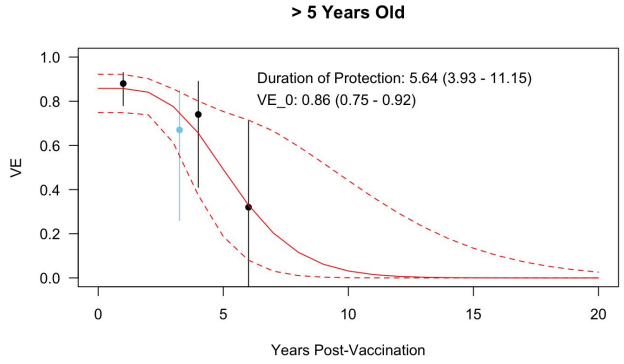
DIC: 2.95
Median AIC: 6.23
Median BIC: 5.00

Shape = 5



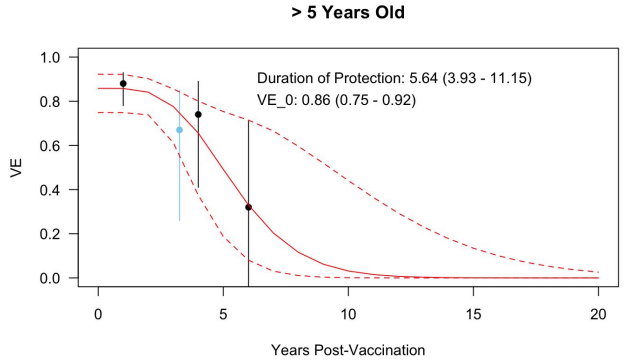
DIC: 3.33
Median AIC: 6.32
Median BIC: 5.09

Shape = 7



DIC: 3.28
Median AIC: 6.55
Median BIC: 5.32

Shape = 10



DIC: 3.71
Median AIC: 6.98
Median BIC: 5.75

Burnet typhoid model description

Model architecture: We have implemented an agent-based model, with optional environmental transmission, natural and vaccine-acquired immunity, and no antimicrobial resistance. The model uses the *Starsim* framework, an open-source agent-based framework developed by the Institute for Disease Modeling in collaboration with the Burnet Institute and other partners.

Disease dynamics: Agents in the model represent individuals. Each time step they have a probability of becoming infected that depends on the prevalence of infection among the population and their immunity status (vaccinated and/or previously infected). Following infection, they enter an infectious state that is either acute or subclinical. People in either state can recover and develop immunity to further infection or can become chronic carriers based on an age- and sex-specific probability. Those with an acute infection can also die based on a typhoid-specific mortality rate. The duration of chronic carriage can be varied but is currently assumed to be lifelong.

Transmission: Transmission in the model occurs through two dynamic mechanisms. First, direct person-to-person transmission occurs between infected and susceptible contacts, reflecting the infectiousness of freshly shed bacteria and the contact rate between individuals. Second, active typhoid infection prevalence (including chronic carriers) drives the prevalence of typhoid bacteria in the environment, increasing the risk of diffuse environmental transmission to all susceptible people in the model.

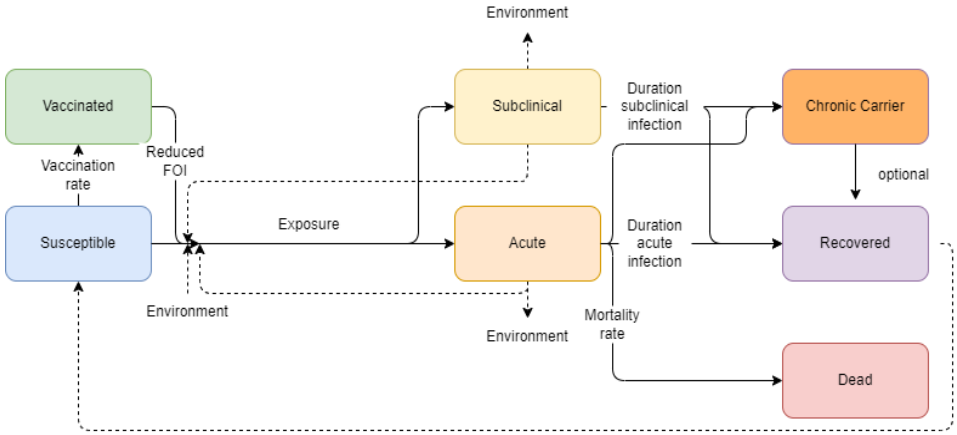


Figure 1: Model schematic showing disease and vaccination-related states and possible transitions between them.

Immunity: Agents in the model can acquire immunity through infection or vaccination. Both forms of immunity are leaky, wane over time, and can act on both susceptibility to any infection and on the probability that an infection causes acute disease.

Calibration: Age-specific background mortality is calculated to balance the birth rate in order to achieve a constant population size and stable age distribution over time. Calibration involves estimating the transmission coefficient, the initial conditions such as the initial acute, subclinical and chronic prevalences, the probability of an infection leading to acute disease, and the age-specific relative risks of infection, to achieve age-specific target incidence rates.

Health economics: Health economic outcomes associated with scenarios are calculated as a post-processing step using a decision tree, based on epidemiological outcomes from the model.

typhoidsim: an agent-based model of typhoid transmission and control
Institute for Disease Modeling, Gates Foundation

We have developed an individual-based model, typhoidsim, using the starsim platform to model the transmission and control of typhoid (Figure 1), as an update to the previously developed EMOD typhoid model (1–3). In this model, agents are born with maternal immunity to typhoid and enter the unexposed class. Children gradually become susceptible to infection, with an age-specific probability of entering the susceptible class that follows an exponential curve whose concavity is a fitted model parameter. Susceptible individuals can become infected through direct contact with an infectious person (short cycle transmission) or by being exposed to environmental reservoirs (long-cycle transmission). The rates of each transmission route are fitted parameters. We account for age-specific differences in relative rates of direct contacts using data from the expanded POLYMOD mixing data (4). The environmental reservoir is subject to seasonal attenuation, as previously fitted in a model of typhoid transmission in Chile (3). Exposure to the environmental reservoir is mediated by a dose response curve, to reflect the fact that multiple small exposures may have different risk of infection than a single, large-dose exposure.

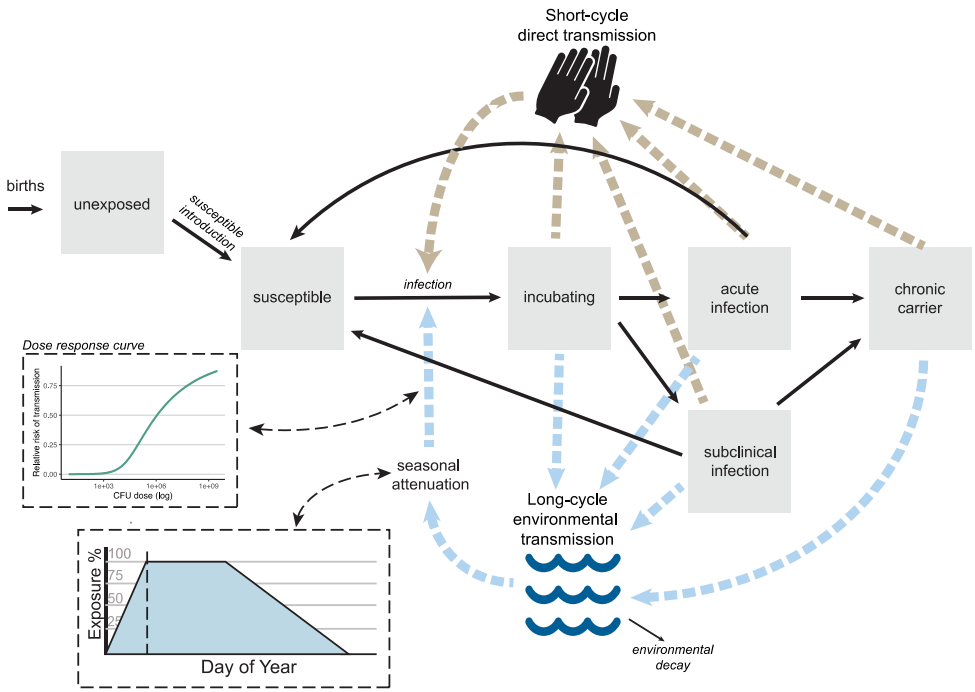


Figure 1. Schematic representation of the typhoidsim individual-based model of typhoid transmission and control.

After infection, individuals enter a latent infection stage (average duration, 2 days) before progressing to either subclinical or acute infection (symptomatic fraction, 16%; can be fitted). A small fraction of both acute and subclinical infections can become chronic carriers and continue to transmit the infection, albeit at a lower rate relative to acutely infected individuals (relative

infectiousness of chronic carriers, 24%; can be fitted). Risk of chronic carriage is age- and sex-specific, derived from risk of gallstone disease. In the absence of treatment interventions, chronic carriers are assumed to be infected for life. Individuals who do not become chronic carriers return to being susceptible to infection (average duration of non-chronic infection, X weeks), but get infected at a reduced rate depending on their number of prior exposures resulting in natural immunity from infection.

Vaccination is modeled as reducing susceptibility to infection by an amount proportional to age-specific vaccine efficacy. Age-specific waning of vaccine-derived protection is assumed to follow a box-exponential decay, which can reduce to exponential decay if the initial delay period is set equal to 0. Vaccines can be targeted to specific time periods and/or specific age cohorts. Booster vaccine doses can be delivered conditionally (i.e., only to those who received an initial dose) or unconditionally (i.e., to anyone in the eligible age cohort).

This model can be calibrated to disease incidence and prevalence targets using a tree-structured Parzen estimator algorithm in the optuna Python package. Age-specific contact rates can trade-off with susceptibility to fit the age-specific incidence between locations. We are testing whether differences in age-specific contact rates between locations can account for varying age-specific incidence, while fixing the age-specific susceptibility curve.

We will estimate total healthcare system costs associated with vaccination campaigns and typhoid-associated care and DALYs attributable to typhoid fever from a decision tree model based on typhoidsim output. Cost effectiveness for each potential vaccine strategy can then be summarized as the cost to avert 1 DALY and the incremental cost-effectiveness ratio (ICER).

References

1. starsimhub/starsim [Internet]. StarsimHub; 2025 [cited 2025 Jan 29]. Available from: https://github.com/starsimhub/starsim

2. Alicia N. M. Kraay, Yousafzai MT, Qureshi S, Gauld J, Qamar FN. Modeling the drivers of differential Typhoid Conjugate Vaccine (TCV) impact in Pakistan: force of infection and age-specific duration of protection [Internet]. medRxiv; 2024. Available from: https://www.medrxiv.org/content/10.1101/2024.08.30.24312839v1

3. Gauld JS, Hu H, Klein DJ, Levine MM. Typhoid fever in Santiago, Chile: Insights from a mathematical model utilizing venerable archived data from a successful disease control program. PLoS Negl Trop Dis. 2018 Sep 6;12(9):e0006759.

4. Prem K, Cook AR, Jit M. Projecting social contact matrices in 152 countries using contact surveys and demographic data. PLOS Comput Biol. 2017 Sep 12;13(9):e1005697.

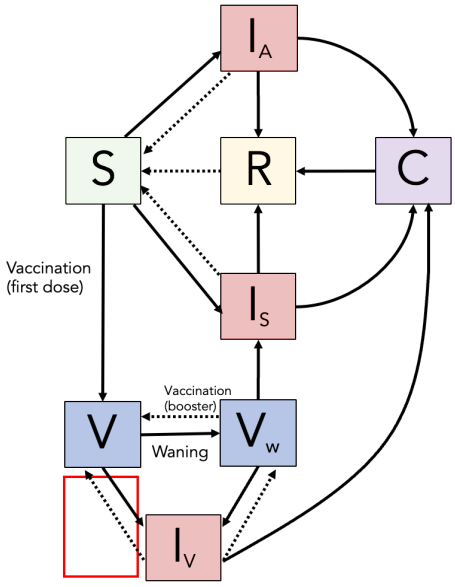
Stanford Model - Typhoid Model and TCVs

Team: Tigist Menkir, Nathan Lo, and Jason Andrews

Model structure

We use a Susceptible-Infected-Recovered-Carrier age-stratified compartmental model structure with inclusion of single- and multi-dose vaccination with the typhoid conjugate vaccine. The model schematic is shown in Figure 1. In brief, a susceptible (S) person can become infected at a transmission rate related to the number of infected persons, and can either become asymptomatically (I_a) or symptomatically infected (I_s), depending on the symptomatic fraction. Once their infectious period has elapsed, if their immune response is robust enough, they can recover to a fully immune state (R); if this is not the case, they become re-susceptible to infection (S). A subset of them can also enter a state of long-term carriage (C), where they continue to infect others at a lower level. Recovered individuals also become re-susceptible after their natural immunity wanes.

Our model will consider different vaccine-derived modes of protection consistent with the trial data. In the primary model, vaccine-directed protection will be all-or-nothing against symptomatic infection, although vaccinated people with protection (V) can still be asymptomatically infected (I_V). We will evaluate different formulations of the risk of asymptomatic infection and relative transmission rates among the previously vaccinated and will evaluate a leaky protection model. In all cases, we will target 20% or less indirect effects due to vaccination (Qadri et al., *The Lancet* 2021).



Initial vaccination will be applied to those in the susceptible state (S), moving a fraction of them to the vaccinated and protected (V) compartment based on vaccine coverage and the vaccine effectiveness (VE). Waning can occur from V to V_w where people are fully susceptible again. Multi-dose vaccination strategies will be administered to all those who received a first dose of the vaccine, but they will only meaningfully impact (benefit) those in the waned compartment (V_w). Finally, we assume that, upon being administered the booster, a fraction of individuals equal to VE return to the full vaccine-protected state (V) and the remaining stay in the no protection, waned state (V_w).

Model parameters and calibration

The model will use literature based estimates for natural history, epidemiologic, and health economic measures related to the model structure and study. The model will calibrate, using Nelder Mead optimization, parameters to both demographic and typhoid age-stratified incidence case data.

Model outcomes and cost-effectiveness analysis

Our primary outcomes are typhoid age-specific incidence, deaths, costs associated with vaccination, medical treatment, and other healthcare expenditures, and disability-adjusted life years, for which we account for different disability weights depending on the severity category of symptomatic cases (i.e. moderate, severe, and severe with intestinal perforation). From this, we estimate cost-effectiveness by comparing the differences in costs per reductions in incidence associated with each vaccination strategy.

Yale typhoid model description

Our model is an age-structured, deterministic compartmental model that follows an SIRS-like framework (Figure 1). The model includes six infection states: S_1, fully susceptible to typhoid infection; I_1, infected with the potential for symptomatic illness and diagnosis with clinical disease; R, recovered from infection and temporarily immune to reinfection; S_2, susceptible to subclinical infection; I_2, subclinically infected with *Salmonella* Typhi; and C, chronically infected with *S.* Typhi. We assume individuals are born into the S compartment of the lowest age-stratum. In the absence of immunizations, the susceptible population is infected and enters the I_1 compartment at a rate λ, i.e. the force of infection. Following primary infection, an age-specific fraction of infectious individuals become life-long chronic carriers (C), and the remaining (majority) fraction recover and gain temporary immunity to reinfection (R). Individuals lose immunity and enter compartment S_2, where they are susceptible to subclinical reinfection (I_2). Individuals who experience re-infection are all assumed to recover and again enter the R compartment, where they are temporarily immune to reinfection. We assume no waning of partial immunity to symptomatic reinfection (i.e. from S_2 to S_1), since previous estimates of this rate were not significantly different from zero. The force of infection is proportional to the infectious states (I_1, I_2, and C), with the relative infectiousness of chronic carriers calibrated to reproduce the level of indirect and overall protection observed in cluster-randomized trials of Vi-polysaccharide and conjugate vaccines.

The model also includes compartments for vaccinated and protected individuals; we differentiate between fully susceptible individuals who were vaccinated when they were infants (<2 years old) (V_0) versus those who were vaccinated as children ($\geq$2 years old) (V_1) to account for different rates of waning immunity, and those who were vaccinated after a previous infection (V_2). Individuals return to the respective previously vaccinated susceptible state (S_{V1} or S_{V2}) following the waning of vaccine-induced immunity. The model is set up to assume either "all-or-nothing" or "leaky" protection from vaccination. Under the "all-or-nothing" assumption, we assume those who "respond" to vaccine doses (=VE_0) transfer to the V_n compartments and are completely protected from infection until vaccine-induced immunity wanes, while those who fail to respond to vaccine doses (=1-VE_0) also transfer to the corresponding previously vaccinated state so that we can keep track of prior vaccination status when modeling booster doses. Under the "leaky" assumption, all vaccinated individuals move to the corresponding V_n compartment, and the rate of infection for individuals in these compartments is equal to (1-VE_0) λ. For our primary analysis, we plan to assume leaky protection.

For both mechanisms of vaccine protection, we assume that those who are currently infected with typhoid (I_1, I_2, and C) do not respond to vaccination, but rather move to the corresponding vaccinated compartment. Furthermore, we assume that vaccine protection is against infection, rather than modeling separate protection against infection versus disease given infection, since ongoing work in our group shows that it is possible to reproduce the observed level of indirect and overall protection observed in the cluster-randomized trial of TCVs conducted in Bangladesh either by assuming lower vaccine protection against infection or by calibrating the relative infectiousness of chronic carriers (see "Model Validation" below).

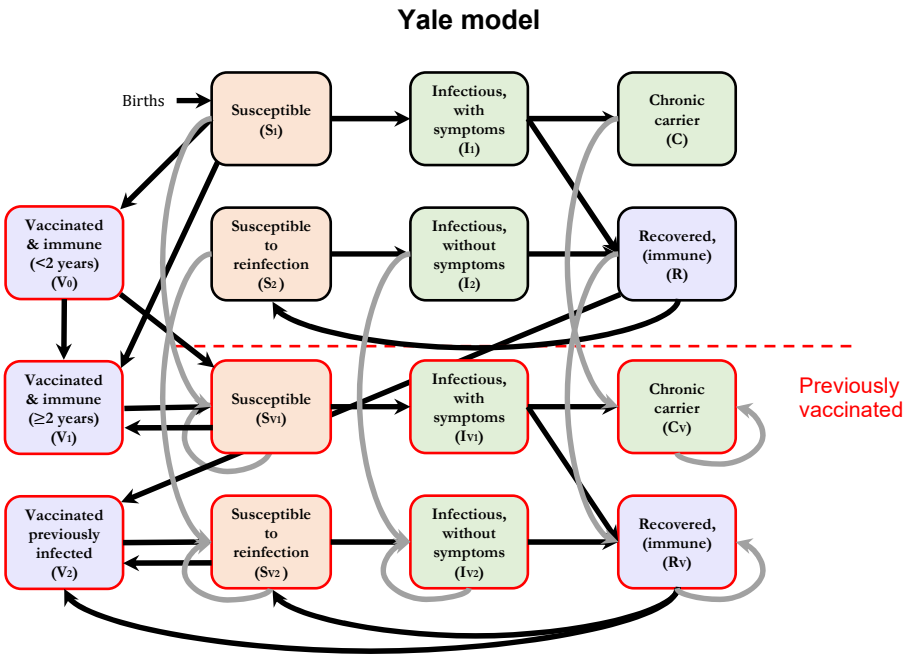


Figure 1. Compartmental model diagrams. The updated compartmental model diagram for the Yale model is presented. The model differentiates between previously unvaccinated compartments (outlined in black) and previously vaccinated compartments (outlined in red) to account for potential targeting of booster doses to previously vaccinated individuals; the grey arrows represent individuals who fail to respond to vaccination.

Model calibration and validation

For model calibration, we will fit our model to the age distribution of typhoid fever cases in country archetypes representing settings with medium (10-100 cases per 100K person-years), high (100-500 cases per 100K person-years), and very high (>500 cases per 100K person-years) typhoid fever incidence[1]. For each setting, we will model a hypothetical population of 100,000 people. Demographic parameters, including crude birth rates and population age structures, will be based on average values for countries falling within each of the three country archetypes based on data from the United Nations World Populations Prospects database. We will assume a steady-state population with the following age groups: 0-9m, 9m-2y, 2y-4y, 5y-9y, 10-14y, 15y-24y, 25y+. Estimated parameters include the basic reproductive number (R_0), factors for the relative risk of infection for children under age 2 (m_1) and children ages 2 to 5 (m_2), and a symptomatic fraction.

For model validation, we will simulate the TyVAC Bangladesh cluster-randomized clinical trial and compare the model-predicted vaccine effects to the observed estimates of overall and indirect protection. As previously shown for our typhoid transmission model (Pitzer et al, *PLOS Negl Trop Dis*, 2014), the indirect protection from vaccination is a function of the contribution of chronic carriers to the overall force of infection. The contribution of the chronic carriers is

[1] Incidence adjusted for underreporting of blood-culture-confirmed cases. We will not model the impact and cost-effectiveness of TCV strategies in low-incidence settings (<10 cases per 100K person-years) based on previous analyses concluding single-dose TCV strategies are unlikely to be cost-effective in such settings.

the product of two components: 1) the prevalence of chronic carriers in the population and 2) the relative infectiousness of chronic carriers (r_C) as compared to acute typhoid infections. The prevalence of chronic carriers (the first component) is based on the model output, while the trial data allows us to estimate the relative infectiousness of chronic carriers (the second component).

Previously, we fit the transmission model to incidence data from Kolkata, India while fixing r_C at values from 0.01 to 1 in increments of 0.01 (Antillón et al, *Vaccine*, 2017). We estimated the transmission rate parameter conditional on each value of r_C, and then simulated the overall and indirect effects of a mass vaccination campaign using the Vi-polysaccharide vaccine, assuming 60% coverage of individuals 2 years of age and older, as described in Sur et al (*NEJM*, 2009). The indirect effect of vaccination is the percent decrease in incidence among unvaccinated individuals in a partially vaccinated population compared to the incidence in a completely unvaccinated population. The overall effect is defined as the incidence among both vaccinated and unvaccinated individuals in the population with vaccination compared to the incidence in the unvaccinated population. We then evaluated the likelihood of each parameter set (including r_C) by comparing the value of the simulated indirect effect against the observed indirect effect in the trial, which we parameterized using a beta distribution. We sampled from the 100 values of r_C weighted by the likelihood of the predicted indirect protection. We recovered a comparable sample of parameter sets if we evaluated the likelihood against the observed overall effect. Finally, we fit a beta distribution to the sampled values of r_C, resulting in Beta(3.69, 6.79), which we will use as the prior distribution for r_C when fitting to the cluster-randomized controlled trial data for TCV in Dhaka, Bangladesh using the same approach.

Estimating vaccine protection

In TyVAC Malawi, VE declined from 83.4% in the first year after vaccination to 68.2% in the fourth year (Patel et al, *NEJM*, 2024). In the TyVAC Bangladesh cluster-randomized trial, total VE was 85% (97.5% CI: 76%, 91%) over an average of 17 months of follow-up (Qadri et al, *Lancet*, 2021). In the subsequent TyVOID Bangladesh study, conducted in the 2.5 years following the last trial visit, VE was estimated to be 84% (95% CI: 74%, 90%) in the first 2.5 years post-vaccination (among trial participants in the control arm who received TCV at the end of the trial), but only 57% (95% CI: 39%, 70%) between 2 and 5.5 years post-vaccination (among trial participants in the treatment arm, who received TCV at the initial time of enrollment) (Qadri et al, *Lancet*, 2024). This suggests that TCV protection may be waning more quickly at the Bangladesh study site than in Malawi, possibly due to the higher intensity of transmission in Bangladesh.

Based on this data, we will use Markov chain Monte Carlo (MCMC) inference, implemented with the JAGS software, to jointly estimate the initial level ($VE_{0,a}$) and rate of waning ($\omega_{v,a}$) of TCV protection by age group. This model will link our known data (VE estimates for different time periods) to our unknown parameters of interest (initial VE and the mean duration of protection) using two components: a time-varying protection model and an observation model.

In the protection model, the expected VE in those vaccinated in age group *a* at time *t* post-vaccination is described by the function $VE_a(t) = VE_{0,a}\, exp(-\omega_{v,a}t)$, where $VE_{0,a}$ is the probability that a TCV recipient is protected against typhoid fever shortly after vaccination (before any waning has occurred), and the duration of TCV protection is exponentially distributed with mean $1/\omega_{v,a}$, where $\omega_{v,a}$ is the rate of waning of TCV-induced immunity in age group *a*.

Since vaccine trials are conducted in a limited sample of the full population, VE measurements are subject to intrinsic uncertainty. To ensure that our estimates of $VE_{0,a}$ and $\omega_{v,a}$ account for this uncertainty, we will use an observation model to define the likelihood of the measured values of $VE_a\,(t)$ from the TyVAC Malawi and TyVOID Bangladesh studies, given the "true" level of protection and the precision of the trial measurements. Since relative risk (=1-VE) follows an approximately normal distribution once it is log-transformed, we will $log(1 - \widehat{VE}(t)) \sim Normal(log(1 - VE(t), \sigma^2)$model, where the variance, σ^2, can be approximated from the confidence interval of the observed VE, $\widehat{VE}(t)$.

By applying this approach to the available VE data from the trials, we will estimate the duration of TCV protection at each study site among young children (those vaccinated in the first 2 years of life), and older vaccinees (2-15 years of age). The age-specific VE estimates and waning rates from the TyVAC Malawi and TyVOID Bangladesh studies will be used to parameterize the "slow" and "fast" vaccine waning scenarios, respectively. We will also explore whether serological data could be used to bridge between these two scenarios by comparing serological data from children vaccinated at different ages in Malawi and Bangladesh to the clinical vaccine effectiveness estimates over time.

Public health impact

The output of the mathematical models is the number of symptomatic typhoid fever by age group and year, as well as the number of vaccine doses (routine, catch-up, and booster) administered under each strategy. To estimate the public health impact of each strategy, including the number of cases, hospitalizations, death, and disability-adjusted life-years (DALYs) averted by each strategy compared to the status quo, we will sample from region-specific estimates for the probability of seeking care and being treated as an inpatient or outpatient, the probability of complications, and the probability of death within each level of care (Figure 2). Probability distributions will be based on summary measures from our previous analyses and recent systematic reviews of the case fatality risk for typhoid fever for Africa, Asia, Oceania, and the Americas. Treatment probabilities and CFRs will be parameterized using beta distributions; shape parameters for each probability and utility (i.e. disability weights for the corresponding health states) in the decision tree will be calculated from sample means and standard errors (derived from 95% confidence intervals). Years of life lost (YLLs) will be calculated based on the average life expectancy within each region minus the model-predicted age distribution of deaths. We can also stratify the treatment probabilities and outcomes by antimicrobial resistance status (AMR vs sensitive), and multiply the number of symptomatic typhoid fever cases from the mathematical model by estimates of AMR prevalence in each region. Our previous analysis suggest that TCV use may lead to a small decrease in the prevalence of AMR,

depending on the role of chronic carriers in transmission and how recently AMR has emerged (Birger et al, *Lancet Infect Dis*, 202, but in the absence of information to validate our previous model predictions, this approach is likely to be conservative.

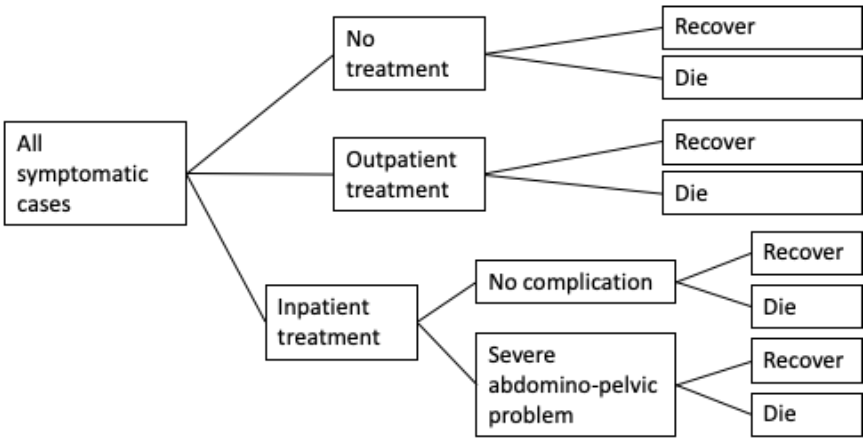


Figure 2. Decision-tree model for health outcomes of symptomatic typhoid fever cases from the transmission model. The probability of each branch of the decision tree will vary by region according to data from our prior analyses and recent systematic reviews.

Cost-effectiveness analysis

We will then conduct a cost-effectiveness analysis comparing the different TCV dosing strategies across the three incidence categories using a net benefits framework in which we will evaluate the optimal strategy across a range of willingness-to-pay thresholds. Using the net benefit framework, the optimal strategy is defined as the one that results in the highest *average* incremental net monetary benefit (NB) for a given willingness-to-pay (WTP) value. The incremental net benefit (ΔNB) of each alternative vaccination strategy compared to the status quo will be calculated as: $\Delta NB = \Delta E * WTP - \Delta C$, where ΔE is the DALYs averted through a vaccination strategy compared to the status quo (no vaccination), and ΔC is the incremental costs of a vaccination strategy (in 2024 US$) compared to the status quo, and WTP is the willingness-to-pay threshold.

Treatment costs and vaccination costs will be estimated separately for each region based on our prior analyses and recent systematic reviews. The cost per episode will be multiplied by the number of outpatients and inpatients (with and without severe complications) in each region and incidence level. The number of vaccine doses administered under each strategy will be multiplied by the vaccine price (US$1.50) and estimated delivery costs, which will vary by region and for routine, campaign, and booster doses. We will conduct the analysis from both the healthcare payer perspective (accounting only for direct medical costs) and the societal perspective (additionally accounting for direct non-medical costs and indirect costs). Following WHO guidance, 3% annual discounting will be applied to costs but not health outcomes.

We will conduct a probabilistic sensitivity analysis by combining the 1,000 model predictions of vaccine impact from the transmission models with 1,000 samples from each of the probability distributions describing the potential health outcomes (e.g. outpatient versus inpatient

treatment), treatment and vaccination costs, case fatality rate, and disability weights. This will generate 1,000 output values for the corresponding total costs and DALYs associated with each strategy. The percentage of the 1,000 samples for which a given strategy has the highest incremental net benefit among all strategies reflects how certain we are that a strategy is cost-effective. Results will be plotted for a range of WTP thresholds to generate a cost-effectiveness acceptability curve (CEAC) and cost-effectiveness acceptability frontier (CEAF). The WTP value at which a strategy becomes optimal corresponds to the incremental cost-effectiveness ratio.

Model outcomes. The model outcomes will be total costs (US$), disease burden (measured in cases, deaths, and DALYs), and optimal strategy in terms of cost-effectiveness over a range of WTP thresholds and for various time horizons. We will characterize model uncertainty in costs and disease burden outcomes with 95% prediction intervals, accounting for both the transmission model parameters as well as the economic model parameters.

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Session 6: WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS) (for decision)

Background:

- SAGE is currently revising the policy guidance of TCV use, based on emerging evidence of waning effectiveness of the vaccine 4-5 years after primary dose.
- Policy guidance from SAGE is expected by countries that have recently introduced TCV in their routine program and countries planning to introduce.
- To assess the epidemiological, economic and equity impact of different TCV schedules in different country settings a multi-model comparison analyses has been undertaken to develop robust modeled-based evidence on the optimal TCV schedule as an input to SAGE deliberations March 2026.

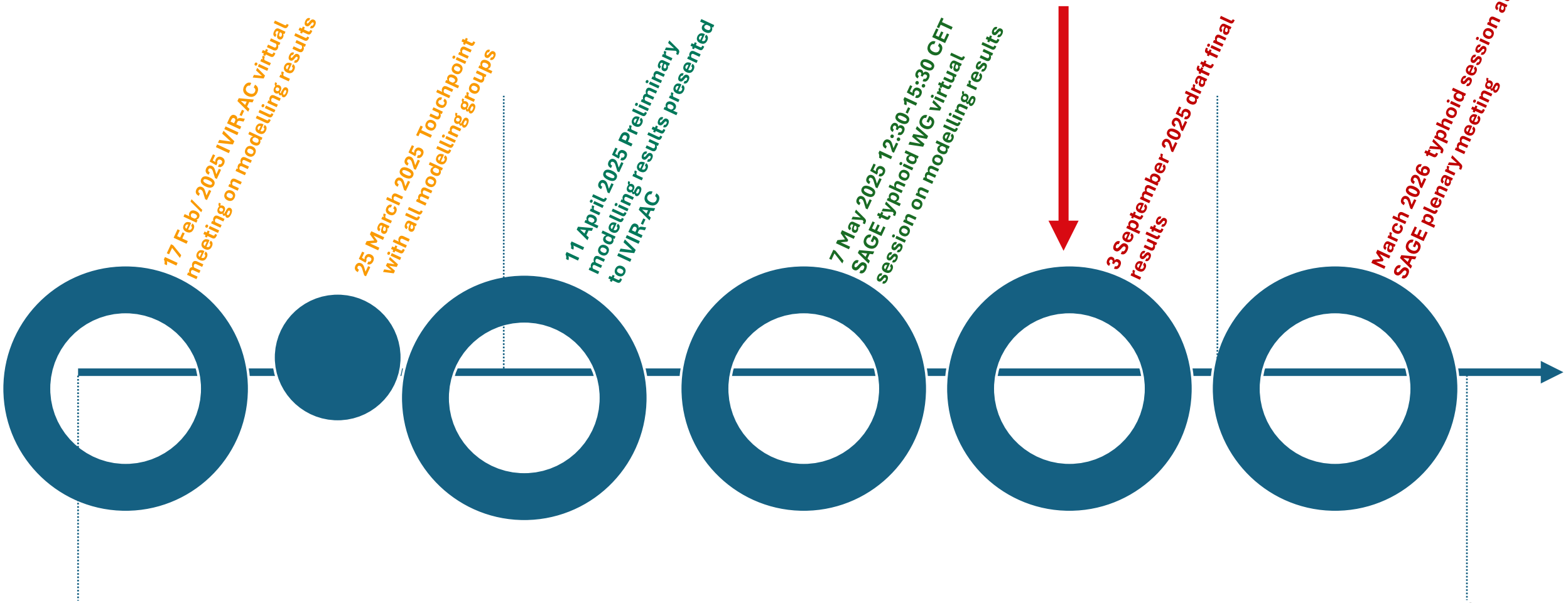
Objectives:

- Summary from SAGE-WG modeling discussions in May 2025
- Synthesis multi-model comparison results from four modeling groups on optimal TCV schedules

Feedback from IVIR-AC on draft final results:

1. Implementation of the IVIR-AC February 2025 recommendations
2. Harmonization of the data including the interpretation of the potential outliers from the different models
3. How to interpret and translate the multi-model results including uncertainty for deliberations of the SAGE WG to support their policy recommendations

Timeline SAGE typhoid WG and modelling up to March 2026



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WHO Multi-Model Comparisons for Typhoid Conjugate Vaccine Adequate Schedules (MMC-TAS)

Catherine Wenger *(on behalf of the modeling teams)*

WHO IVIR-AC meeting

3 September 2025

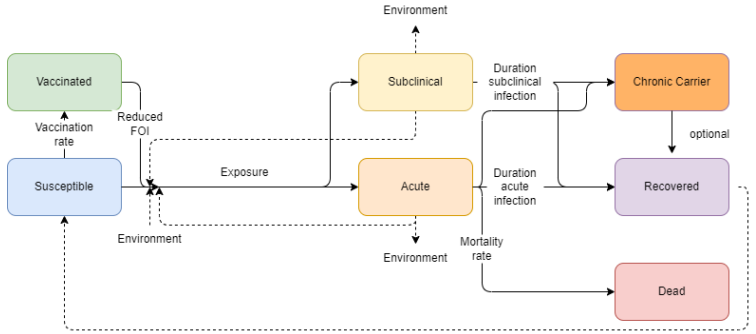
Feedback and next steps following SAGE typhoid working group meeting in May

- Recent data from Bangladesh suggests lower VE after 4-6 years than previously modeled
  - **ACTION:** Refit VE waning parameters for the fast-waning scenario to the latest data
- Consider incorporating uncertainty in the incidence rate within (and between) medium, high, and very high settings
  - **ACTION:** Conducted a "threshold analysis" sampling from a range of values for the symptomatic fraction to examine how cost-effectiveness varies with incidence for a given age distribution
- Determine whether additional data is available to account for differences in risk of complications and CFR by age and AMR
  - **ACTION:** Discussed with John Crump, but could not identify additional data needed for stratification
- Update model structure/calibration as needed
  - **ACTION:** IDM increased burn-in period and recalibrated model; Stanford changed how booster doses were modeled

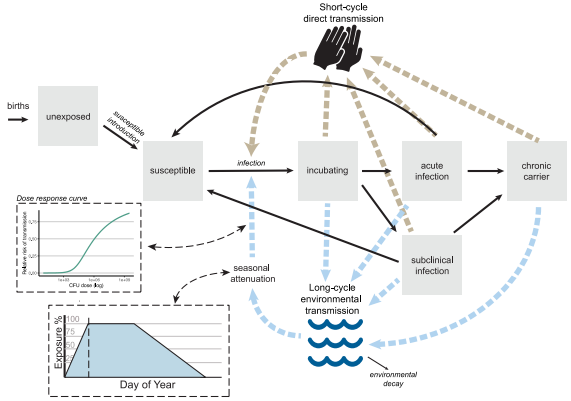
Overview of the transmission models

- Two agent-based models (Burnet, IDM), two compartmental (Stanford, Yale)
- All models include the following states:
  - Susceptible, Infectious, Recovered
  - Acute vs subclinical infection
  - Chronic carriers
  - Vaccinated

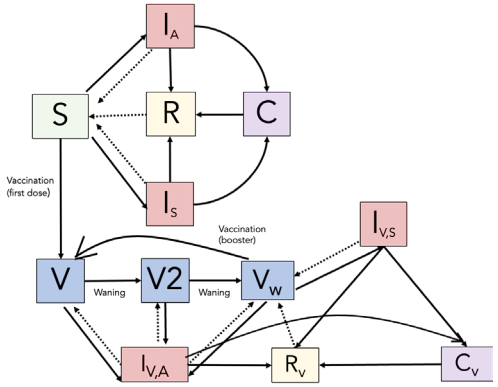
Burnet model



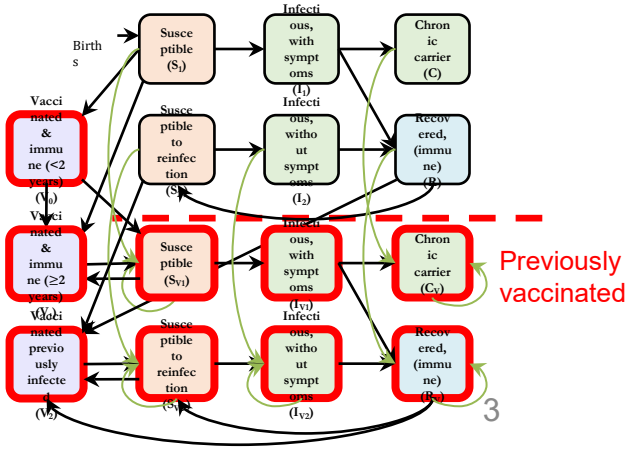
IDM model



Stanford model



Yale model



Overview of modeling strategies and assumptions

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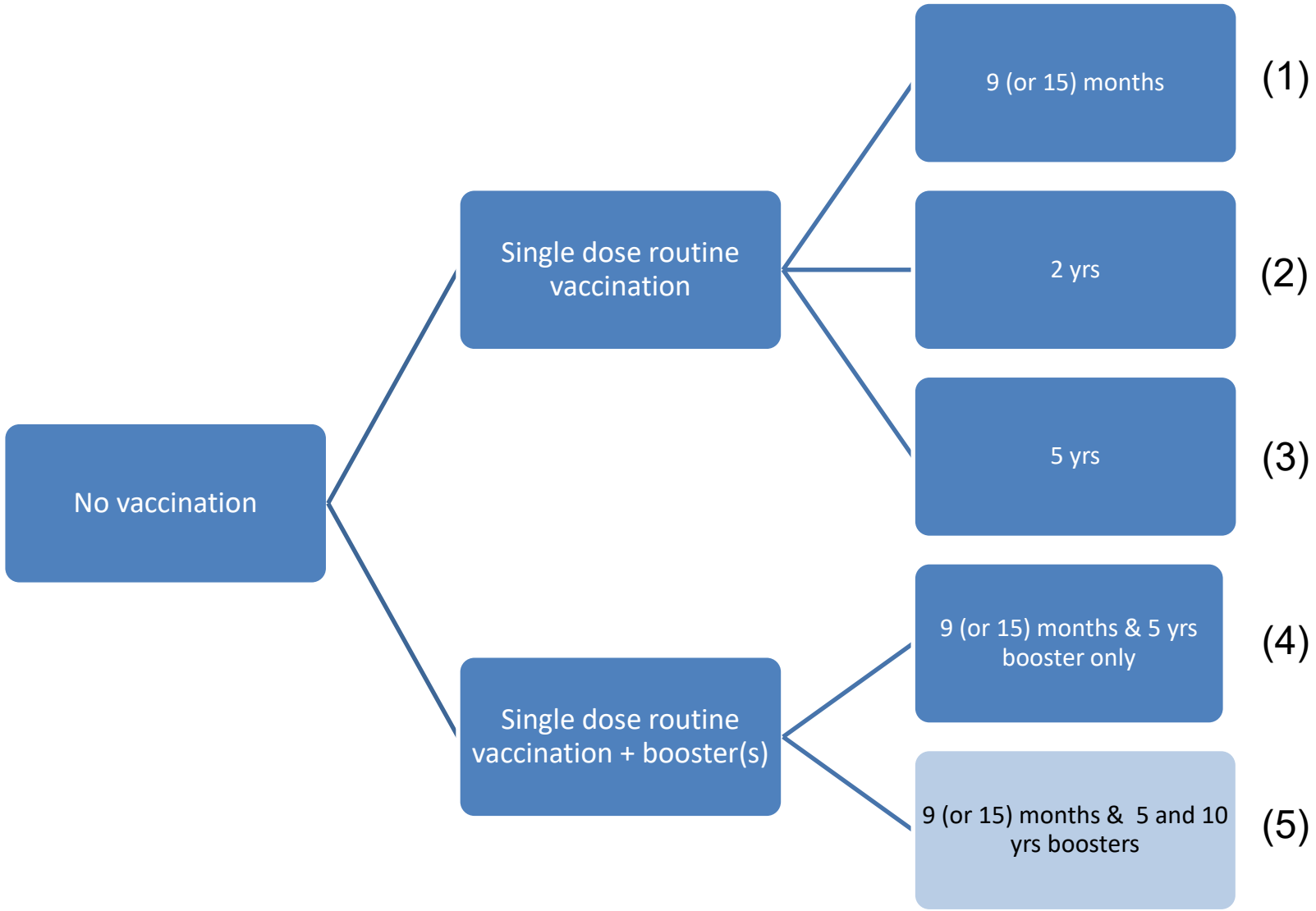

Assumptions for all five strategies:

A. With **catch-up campaigns** to 15 yrs

B. Coverage

- **9 (or 15) months** based on first- (or second-) dose measles-containing vaccination (MCV1 or MCV2) coverage;
- **2 yrs** to be lower and uncertain (e.g., 50-90% of MCV2)
- **5 yrs** to be uncertain and based on school attendance

C. Waning efficacy scenarios

- Bangladesh-like (i.e., **faster**)
- Malawi-like (i.e., **slower**)

Model calibration

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Burden archetypes and incidence age distributions

Transmission model
R0, age-related risk or reporting, prob. of symptoms, etc.

Health economic model
Healthcare seeking, Probability of hospitalization, Risk of complications, CFR, costs of illness, cost of delivery

Medium incidence	High incidence	Very High incidence
Africa		
Higher CFR, prob of hospitalization, risk of complications		
Higher treatment costs (especially adult inpatient)		
Asia/WPR		
Lower CFR, prob of hospitalization, risk of complications		
Lower treatment costs (especially adult inpatient)		

Evaluate **fast-waning** and **slow-waning** scenarios for vaccine protection across each incidence rate archetype

12 scenarios

Routine strategies - High burden

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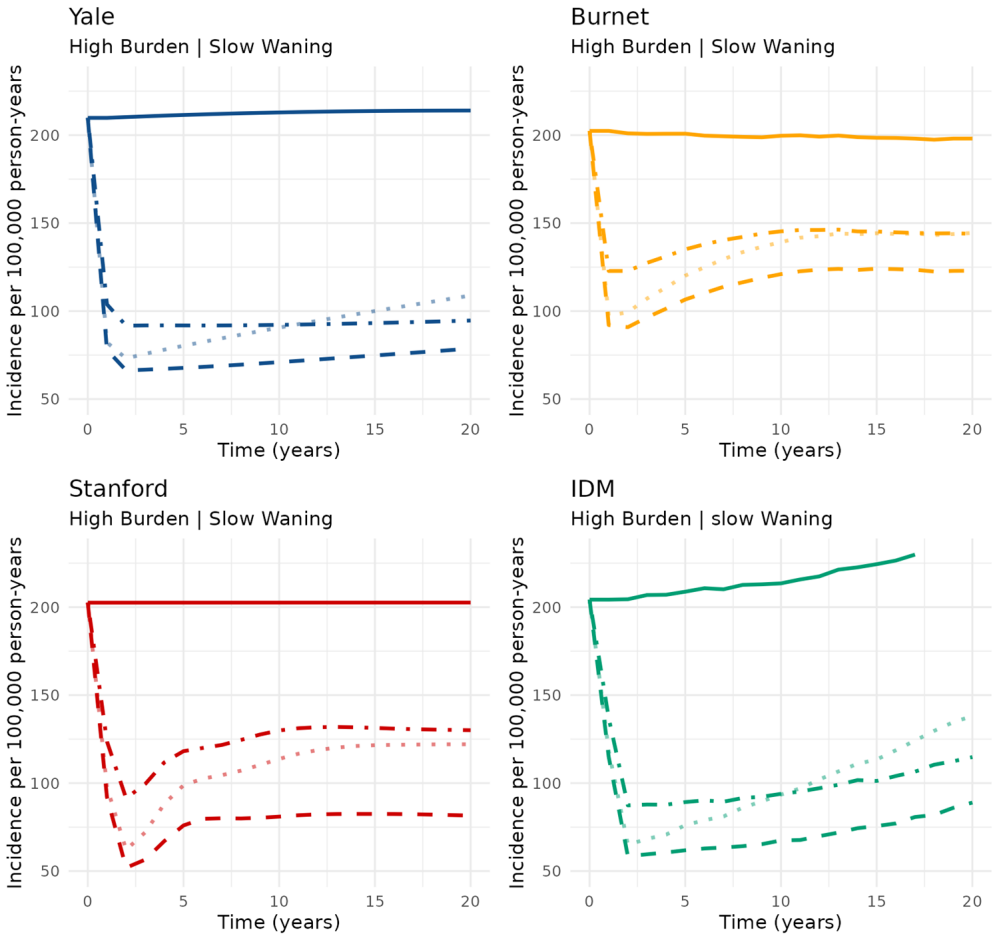
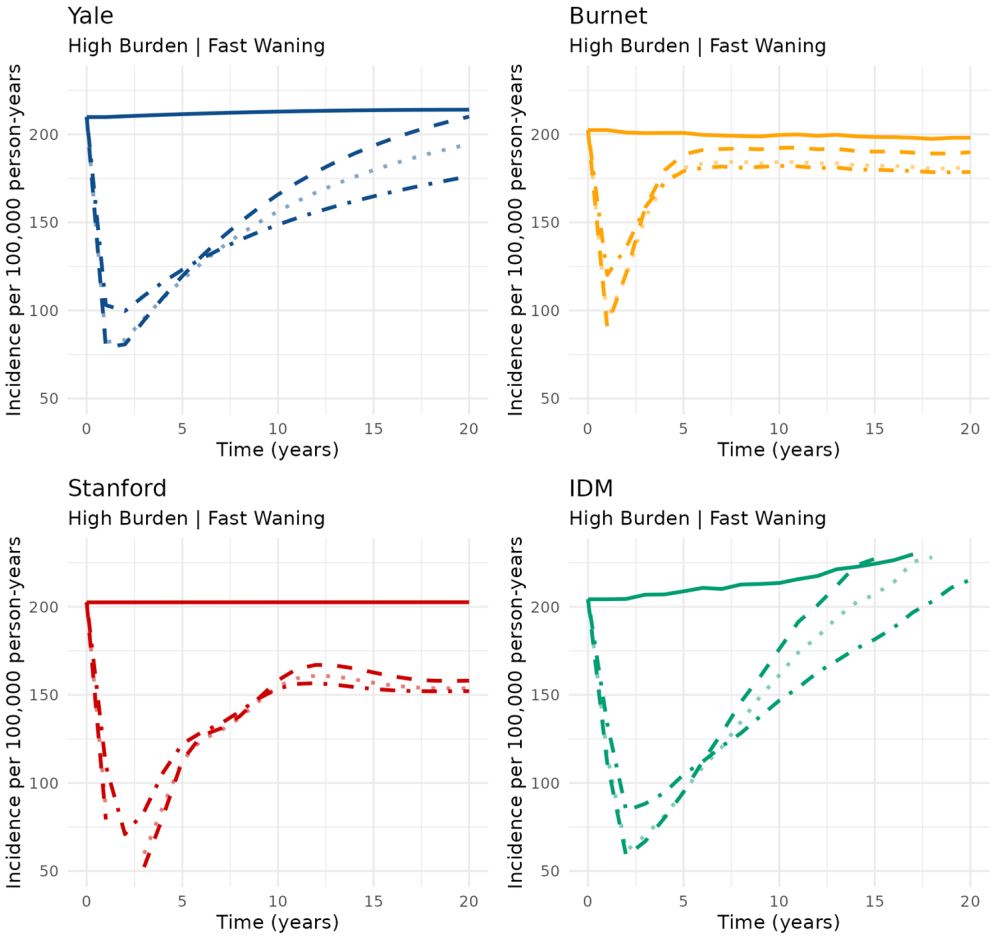
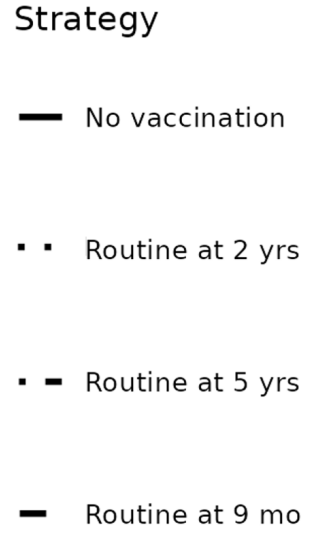
Slow waning



Fast waning





Booster strategies - High burden

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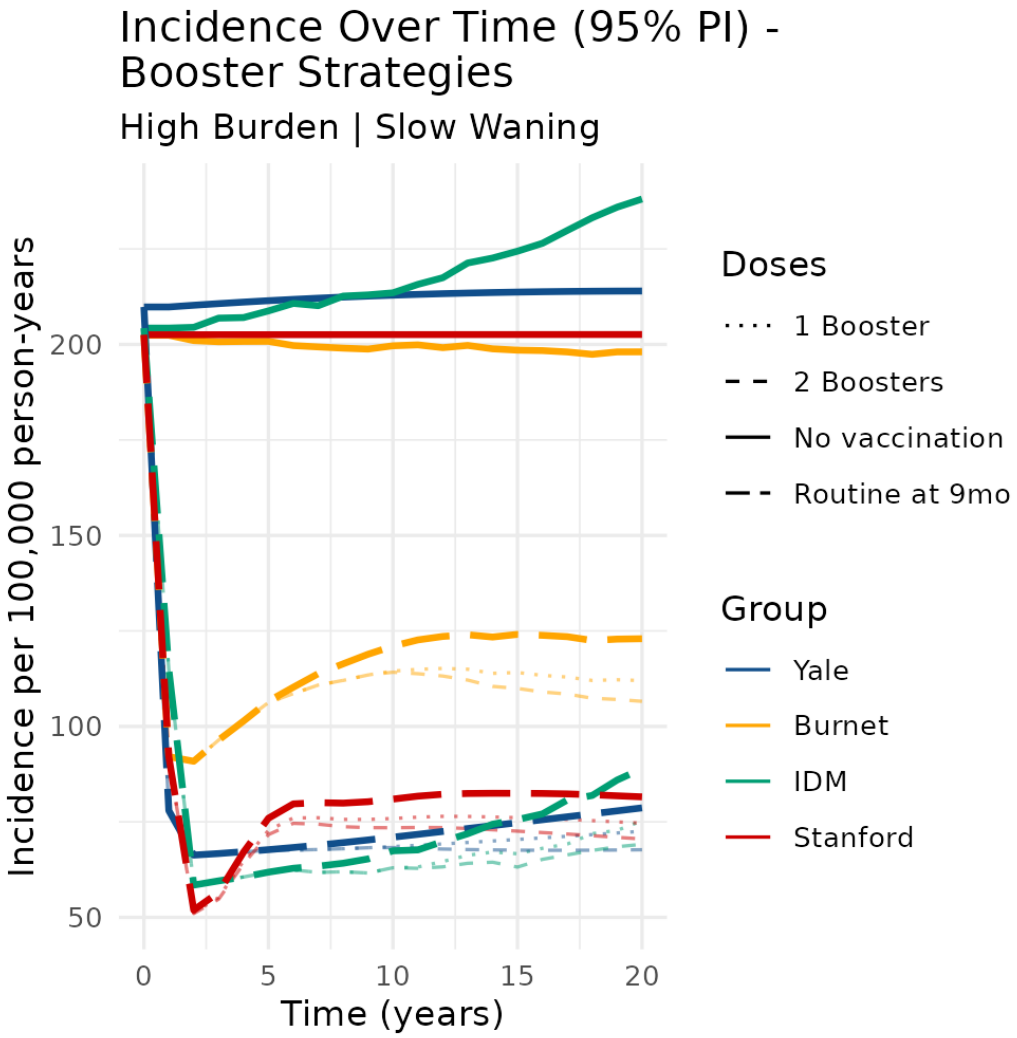
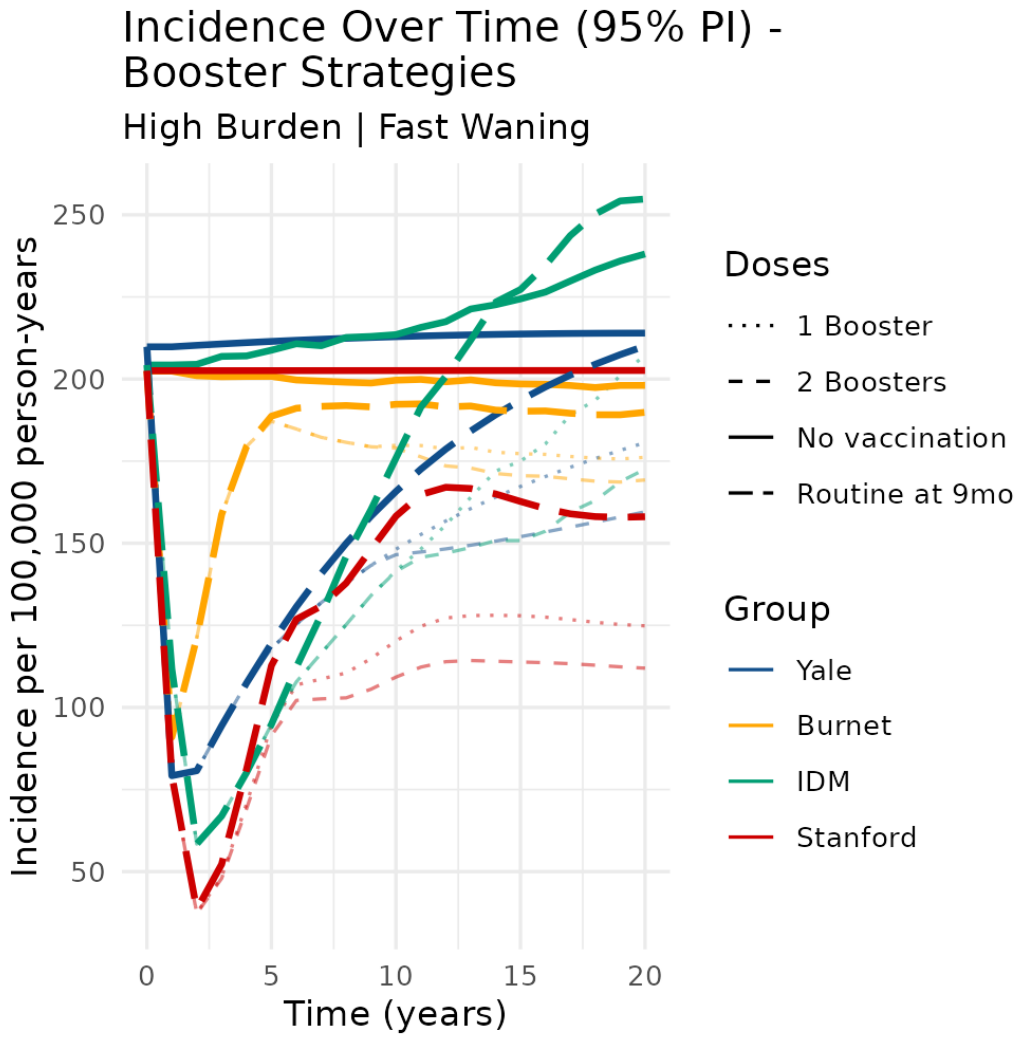
Slow waning



Fast waning



Percent of cases averted: High burden

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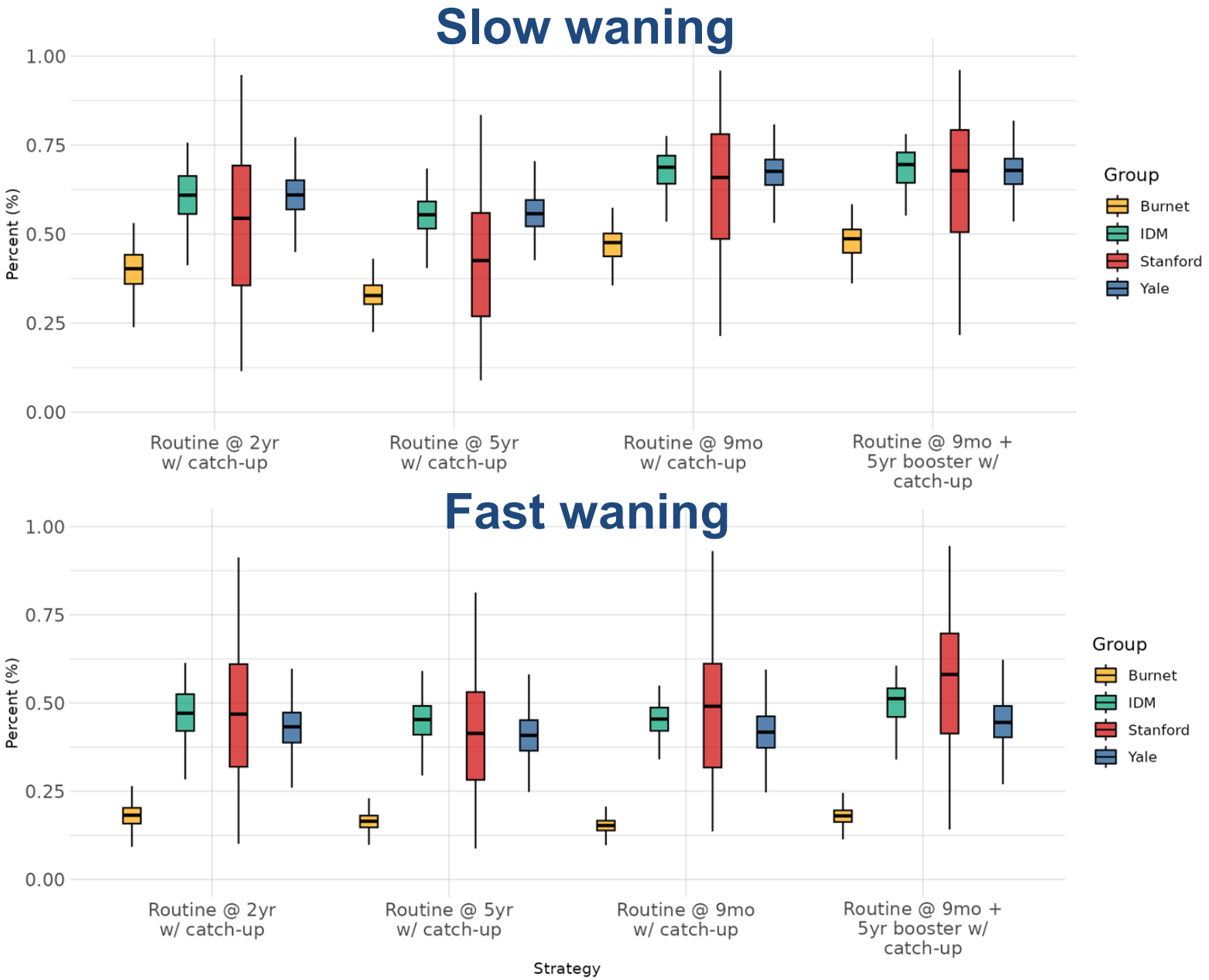


<u>Over a 10-year time horizon, TCV introduction can avert</u>:

- 250-1,500 cases
- 5-45 cases per 1,000 doses
- 15-300 hospitalizations
- 0.5-32 deaths
- 25-2,000 DALYs

per 100,000 people in a high incidence setting (~200 cases per 100k py)

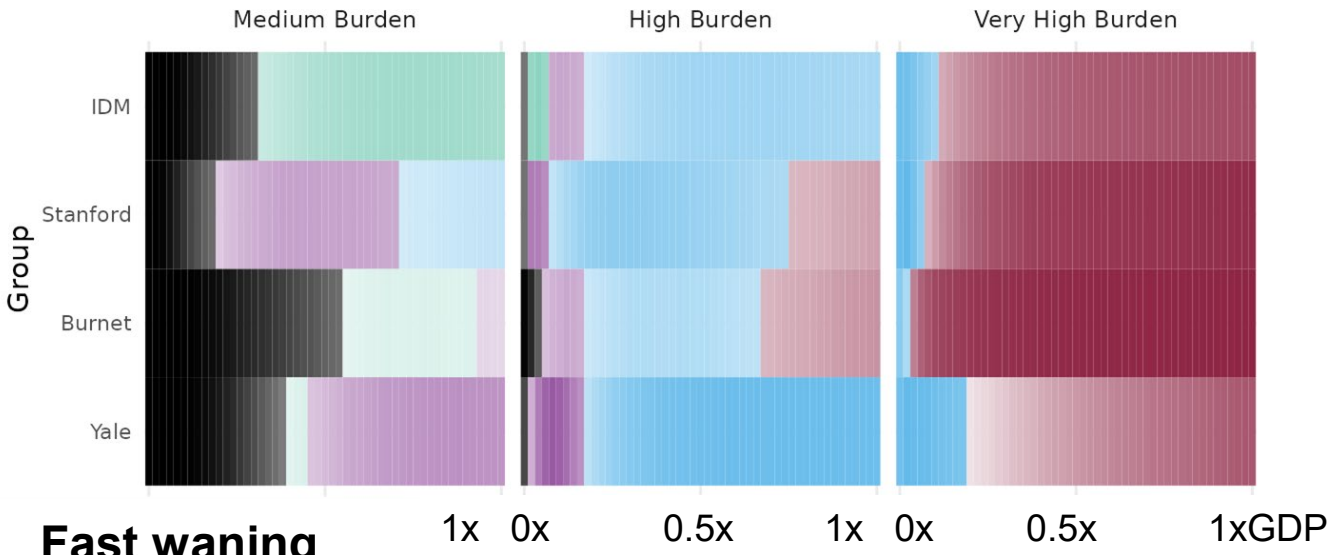
<u>Model comparison takeaways:</u>

- Burnet model predicted lowest burden averted
- IDM and Yale models predicted (similar) higher burden averted
- Stanford model varied by setting

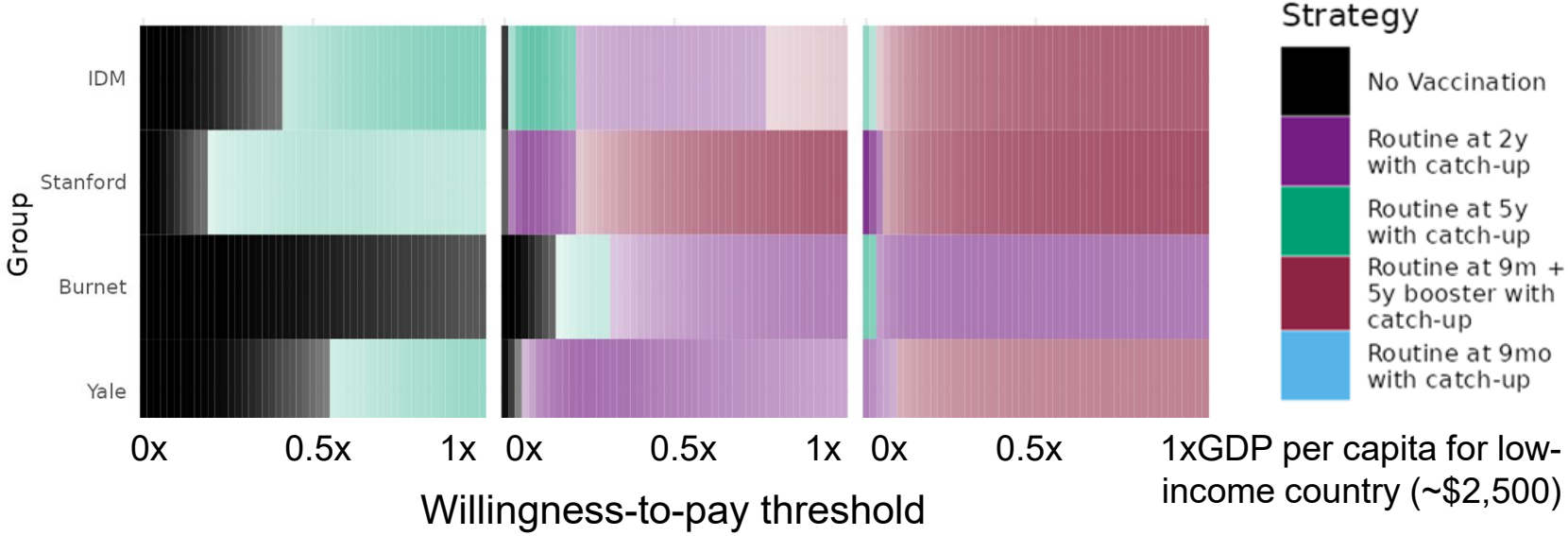
Cost-effectiveness results: Africa

Yale

Slow waning



Fast waning



1xGDP per capita for low-income country (~$2,500)

Medium incidence (~50 cases per 100k py):

- Routine vaccination at 2 or 5 years old (with a catch-up campaign) may be cost-effective

High incidence (~200 cases per 100k py):

- TCV introduction very likely to be cost-effective; consider delaying to 2 years of age or adding a booster dose if waning is fast

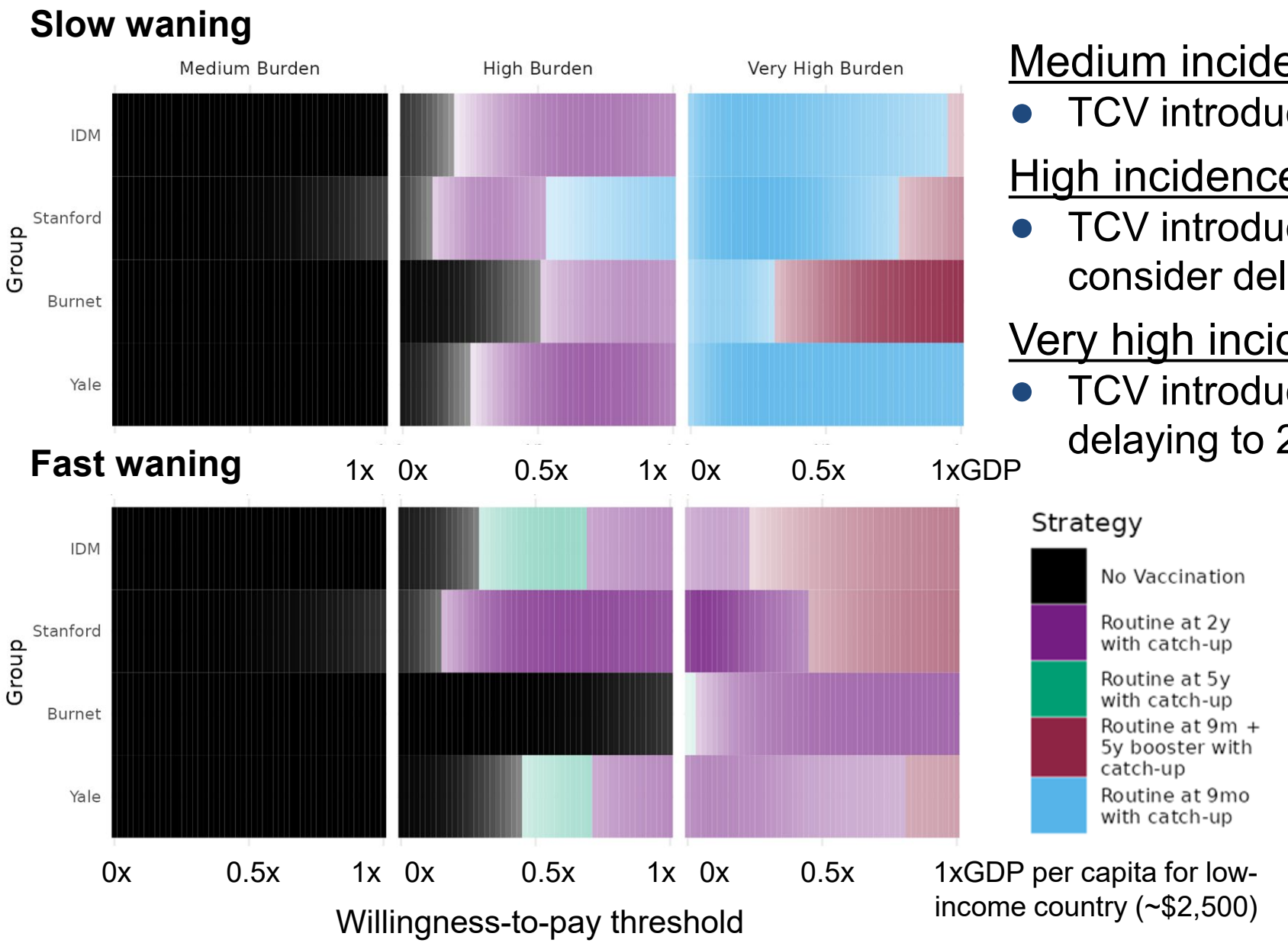
Very high incidence (~1500 cases per 100k py):

- TCV introduction is cost-saving, and adding booster dose is very likely to be cost-effective

- Color indicates optimal strategy
- Shading represents probability it yields the highest net benefit (darker=higher probability)

Cost-effectiveness results: Asia

Yale



Medium incidence (~50 cases per 100k py):

- TCV introduction is NOT cost-effective

High incidence (~200 cases per 100k py):

- TCV introduction may be cost-effective, but consider delaying to 2-5 years of age

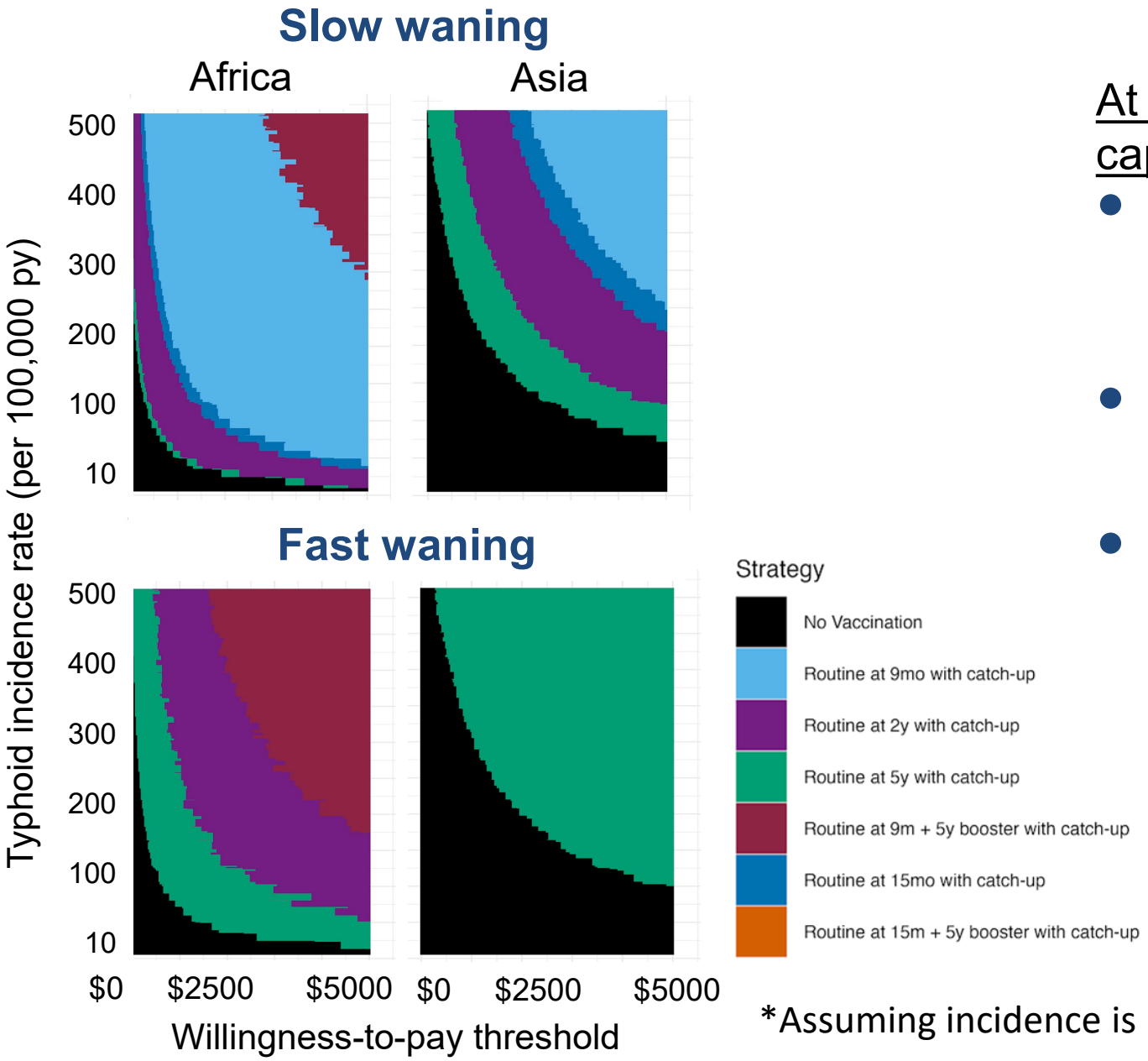
Very high incidence (~1500 cases per 100k py):

- TCV introduction is cost-saving, but consider delaying to 2y or adding booster dose

- Color indicates optimal strategy
- Shading represents probability it yields the highest net benefit (darker=higher probability)

Threshold analysis

Yale



At a WTP threshold of $2,500 (~1xGDP per capita for a low-income country):

- TCV introduction is cost-effective when typhoid incidence is:
  - **> 10-60 cases per 100k py in Africa**
  - **> 75-250 cases per 100k py in Asia**
- A delayed vaccination schedule (2y or 5y of age) is more cost-effective at lower incidence levels (and lower WTP thresholds)
- Routine vaccination at 9m + booster dose at 5y is cost-effective when typhoid incidence is:
  - **> 100-250 cases per 100k py in Africa**
  - **> 500-1000 cases per 100k py in Asia**

*Assuming incidence is highest in the 5-15 yr age groups

Key drivers of differences between models

Yale

- Main driver of differences between models was the average duration of vaccine-induced immunity
  - IDM and Yale used parameters estimated from a statistical model fitted directly to VE data
  - Burnet and Stanford group re-calibrated these parameters in their transmission models as part of the validation

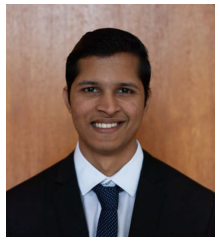
- Within models, the key sources of uncertainty were:
  - CFR
  - waning rate (Yale)
  - relative infectiousness of chronic carriers→indirect effect (Yale)

Fast waning	Burnet (fixed)	Stanford	Yale/IDM
0-1y	0.72 years	1.1 (1.07-1.17)	2.8 (0.01-6.6)
2-4y	1.5 years	7.0 (2.7-18.5)	7.3 (2.6-34.0)
5+y	1.9 years	7.1 (5.2-10.6)	10.7 (4.2-42.3)
Slow waning	**Burnet**	**Stanford**	**Yale/IDM**
0-4y	8.4 years	73.9 (41.2-83.3)	46.4 (3.7-97.3)
5+y	8.4 years	36.9 (21.8-81.4)	52.4 (10.4-97.6)

Acknowledgements

Yale

Catherine Wenger, Zeaan Pithawala, Jo Walker, Ginny Pitzer



IDM

Kyra Grantz, Alicia Kraay, Jillian Gauld

Stanford

Tigist Menkir, Nathan Lo, Jason Andrews

Burnet Institute

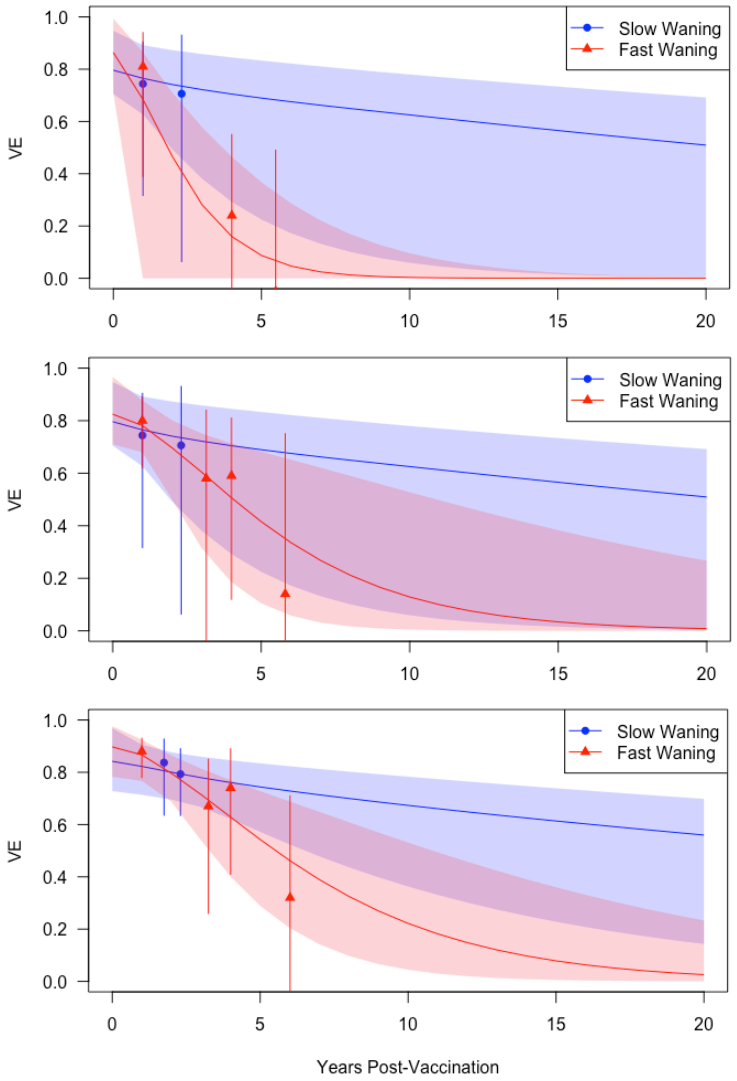
Romesh Abeysuriya, Alina Muellenmeister, Nick Scott

Supplemental Slides

Vaccine efficacy – Yale and IDM

Yale

Yale

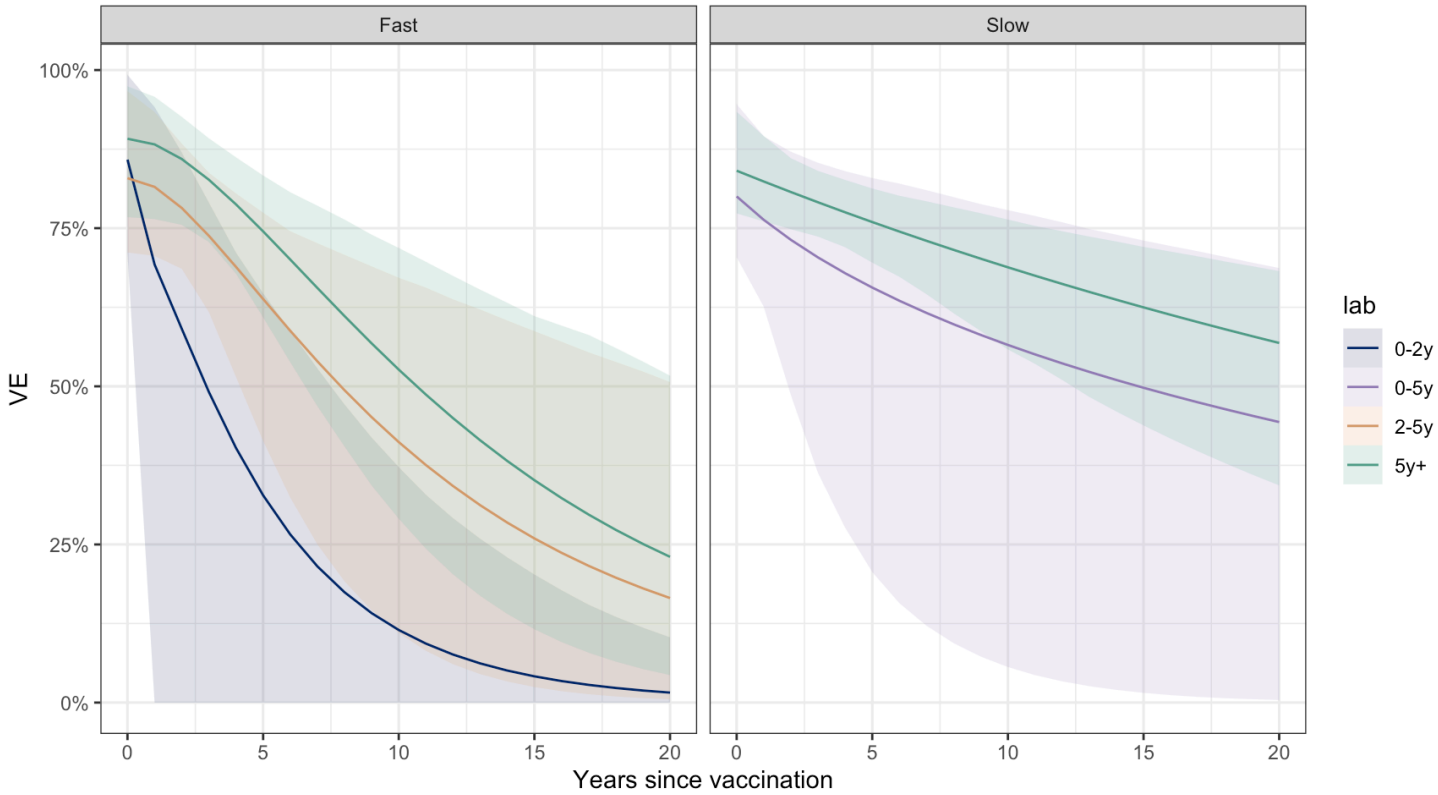


0-<2y

2-<5y

5+y

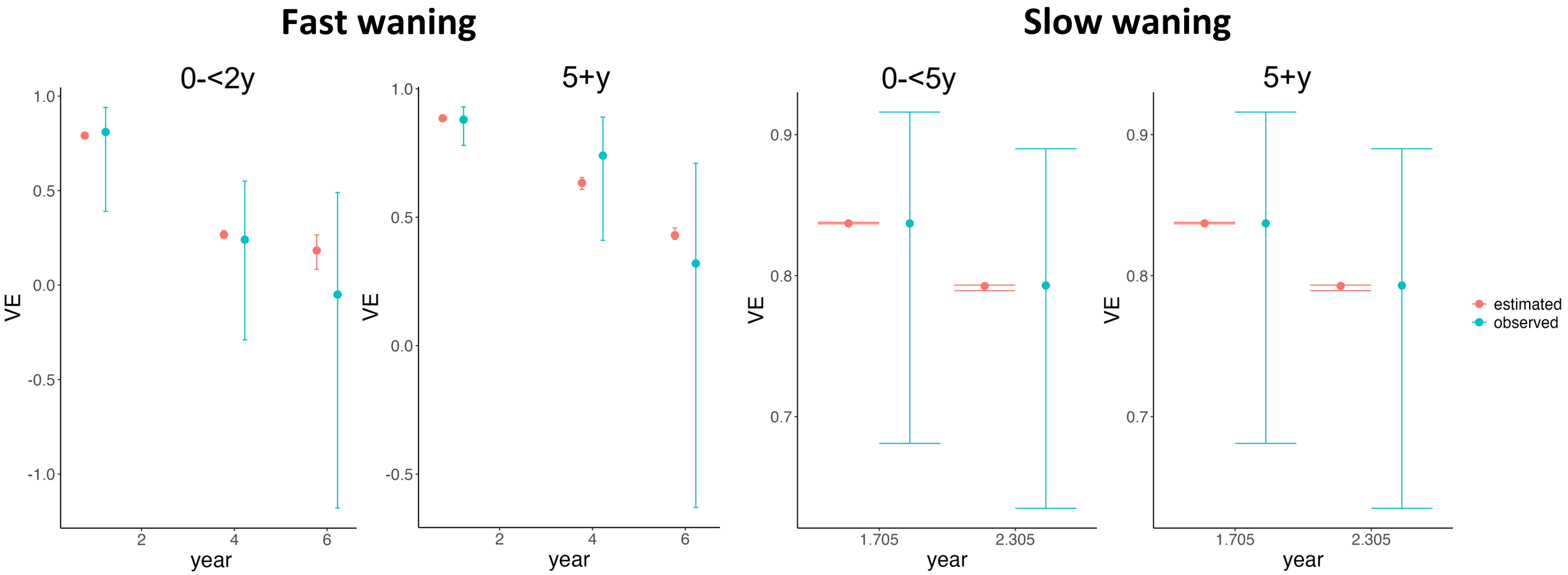
IDM



- IDM model assumes individual-level heterogeneity in vaccine response and duration, whereas other models assumes population-level heterogeneity
- IDM model assumes VE0 and waning rate are independent

Vaccine efficacy – Stanford

Yale

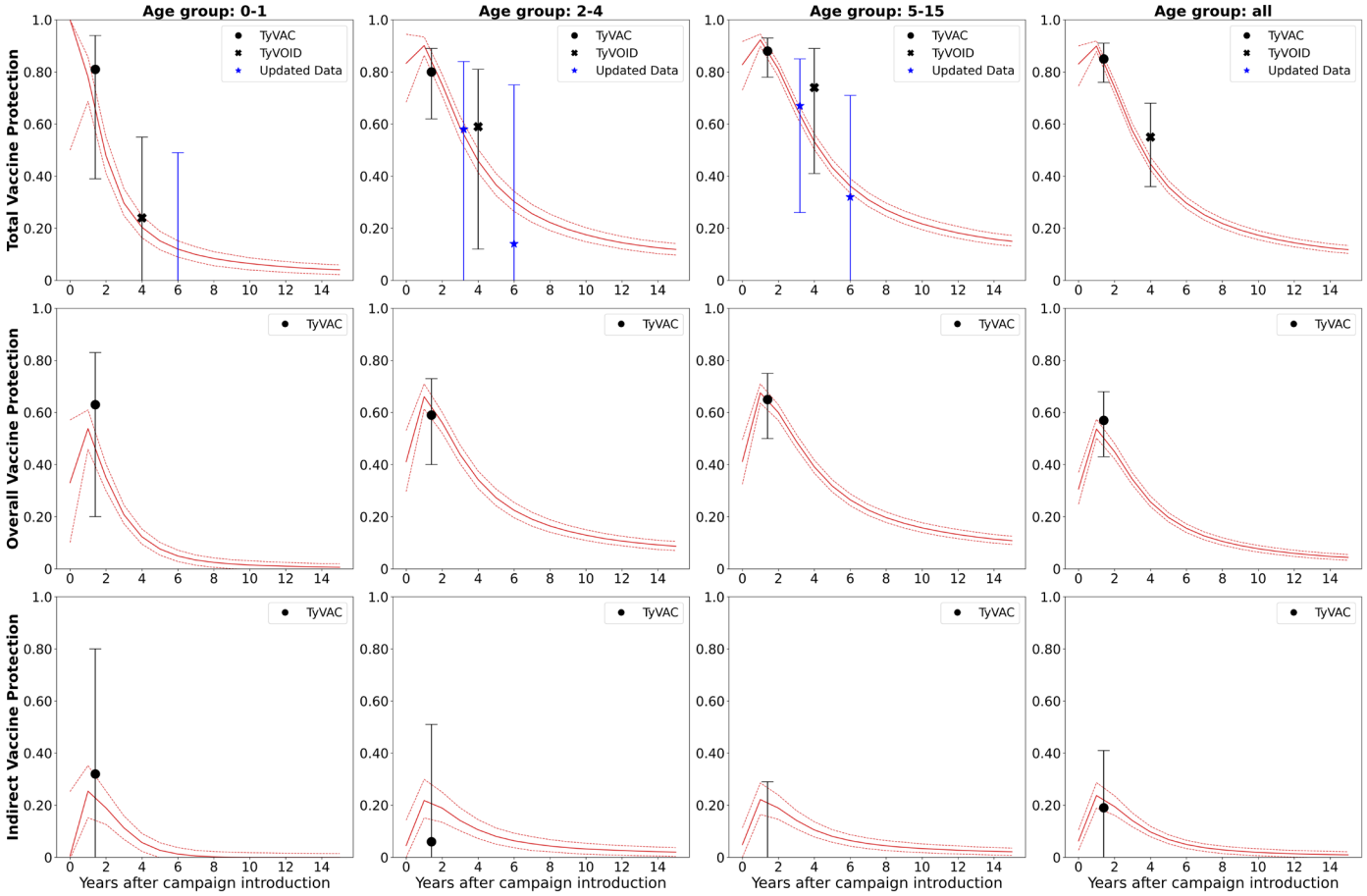


- Calibrated quantities: overall I (risk of asymptomatic infection among those in the partially protected V and V2 states*) & r_v (reduction in transmission risk among asymptomatically infected previously partially protected), alpha_v (rate of transition from V to V2 and V2 to Vw) & VE by age group

Burnet - Fast waning validation: Bangladesh

Yale

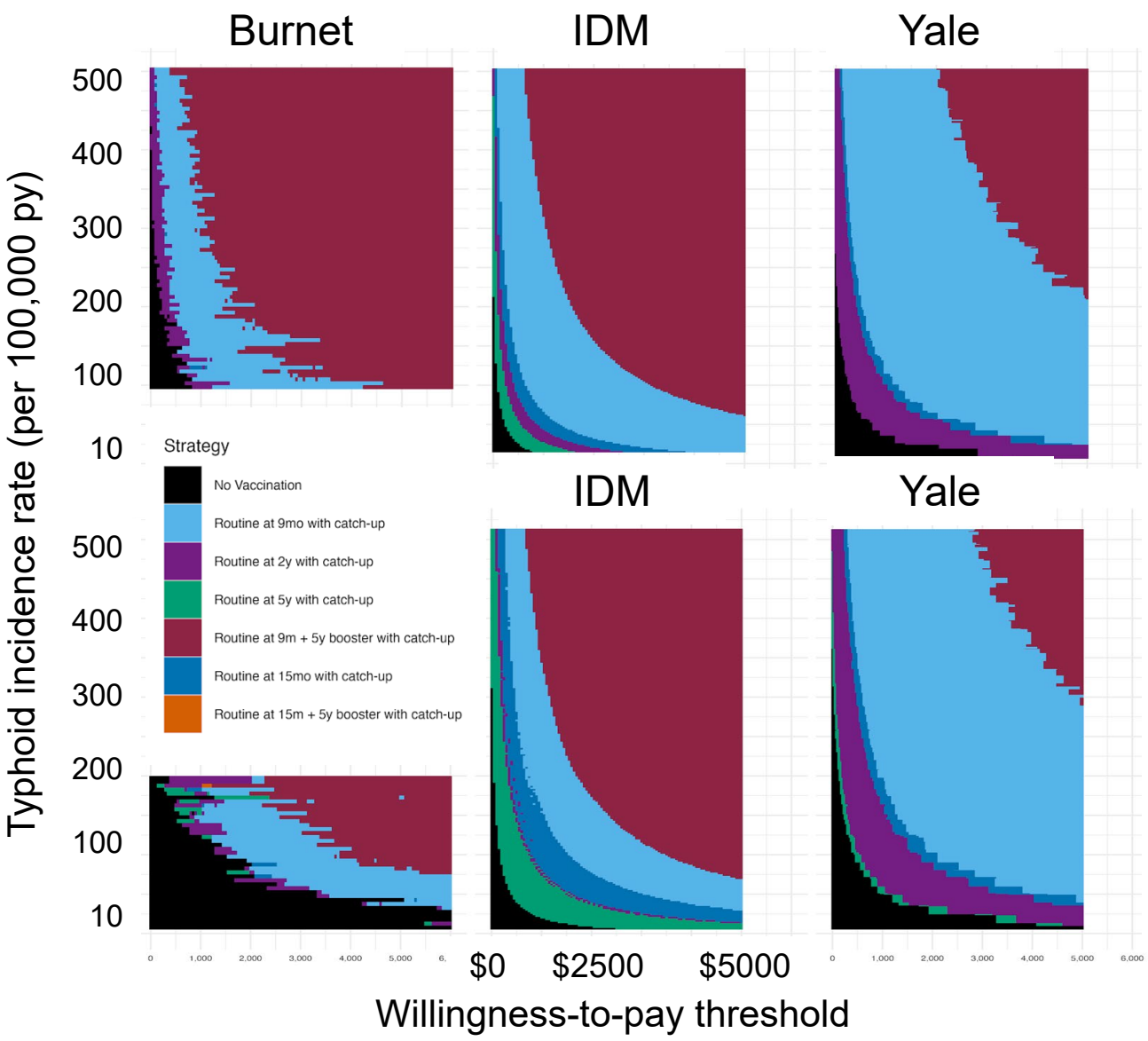
- We estimated waning rates by explicitly simulating the trial cohort structure and vaccine coverage, enabling direct comparison with trial data
- Efficacy parameters and waning rates were estimated and applied per age group (no individual variability)
- Infectiousness of chronic carriers was calibrated to align with observed indirect protection
- **Red curves represent model-calculated protection over time**
- The model aligns with observed data for total, overall and indirect protection, although the level of indirect protection in the data was not significant.



Threshold analysis: Africa (med-high burden)

Yale

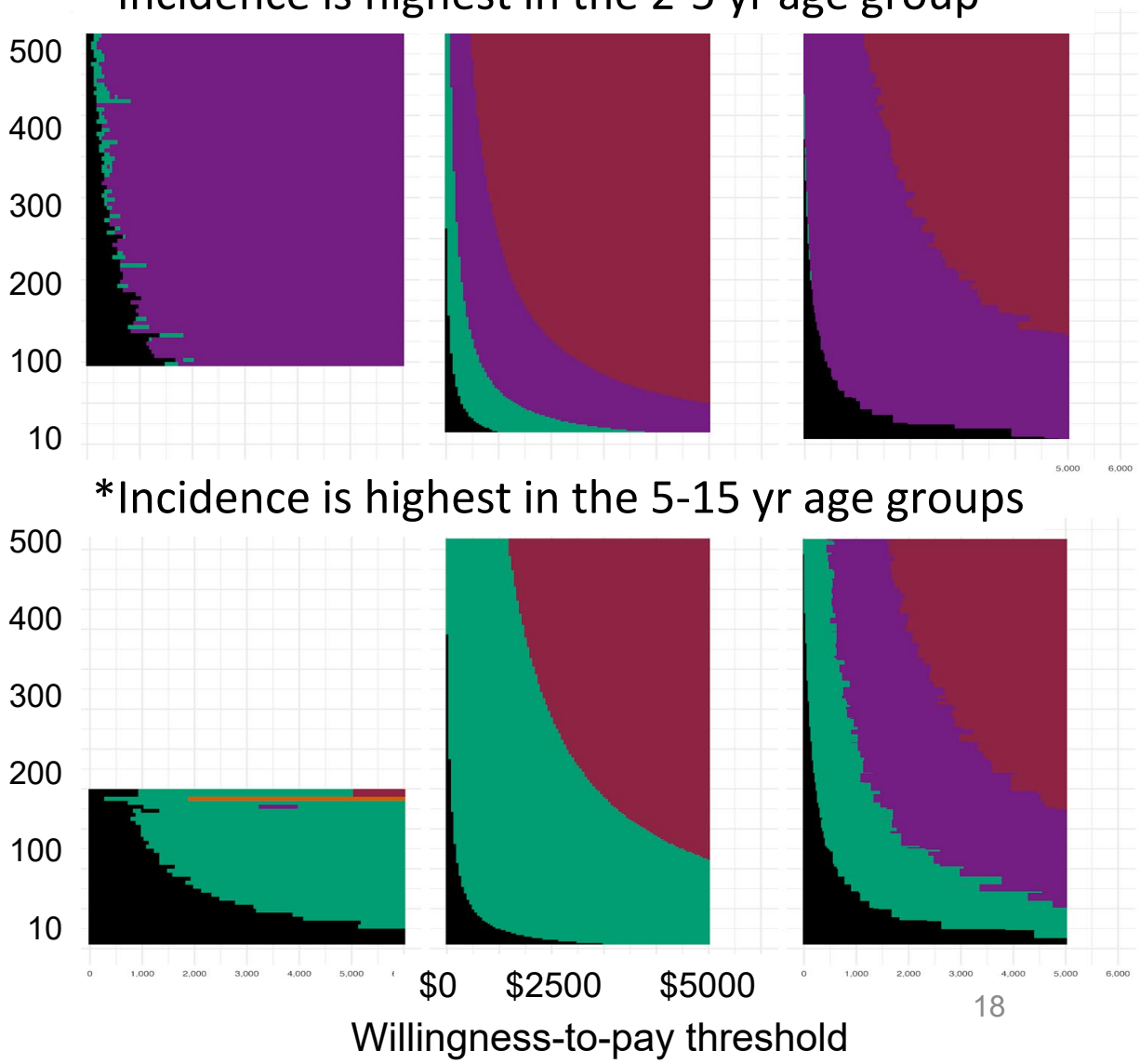
Slow waning



Fast waning

*Incidence is highest in the 2-5 yr age group

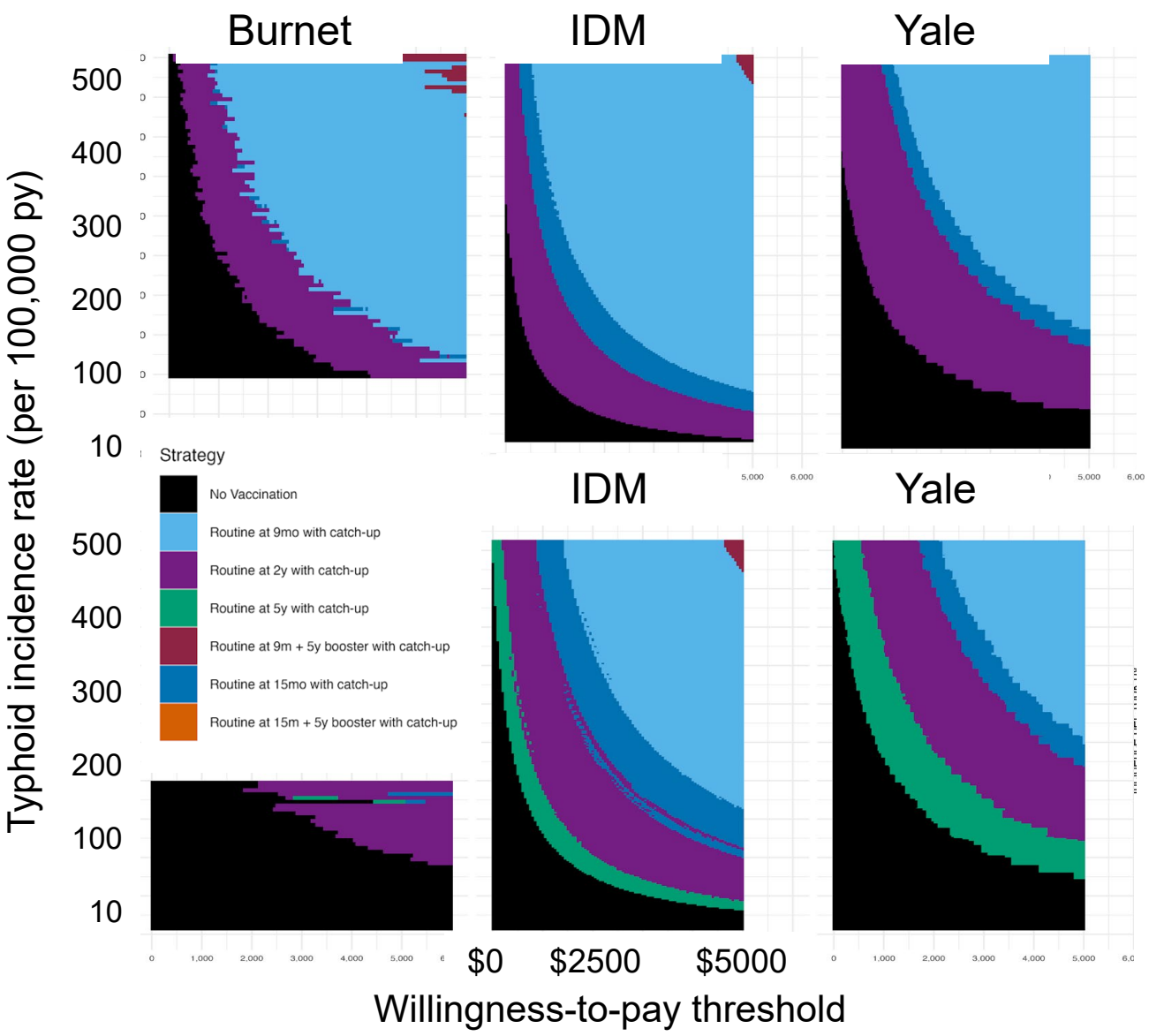
*Incidence is highest in the 5-15 yr age groups



Threshold analysis: Asia (med-high burden)

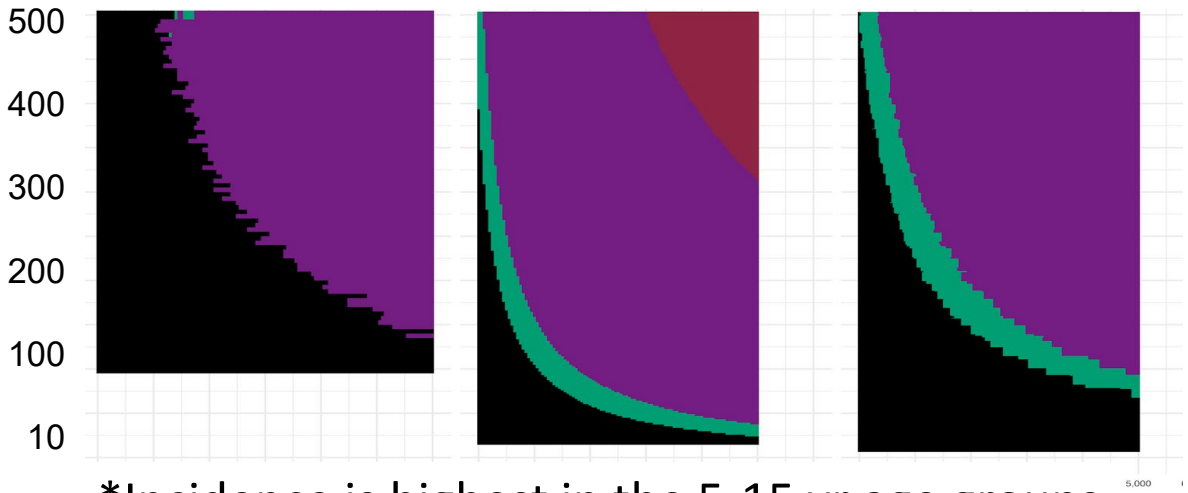
Yale

Slow waning

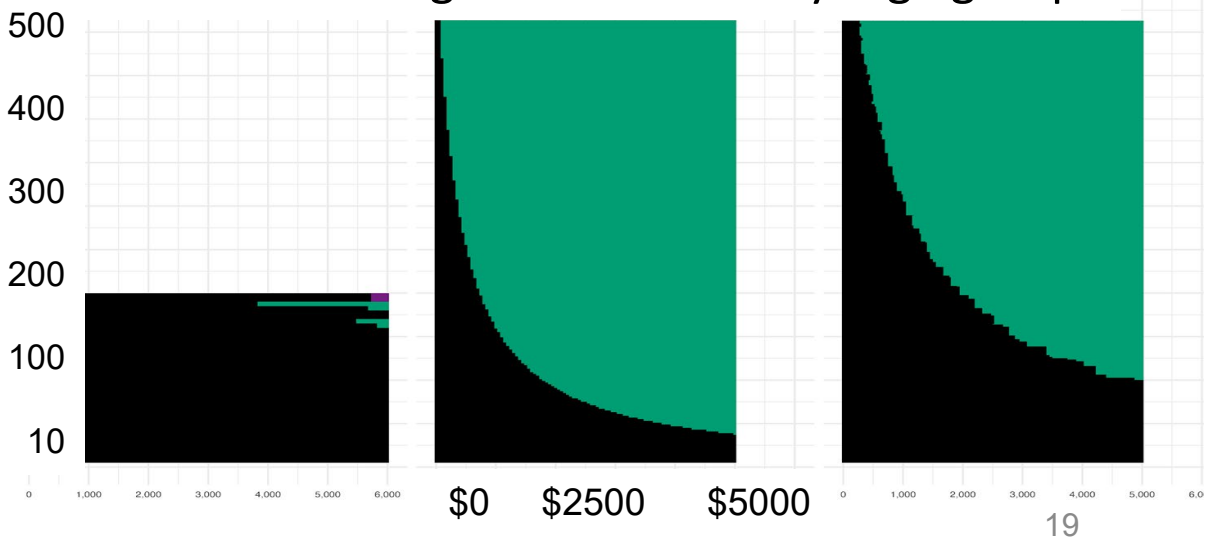


Fast waning

*Incidence is highest in the 2-5 yr age group



*Incidence is highest in the 5-15 yr age groups

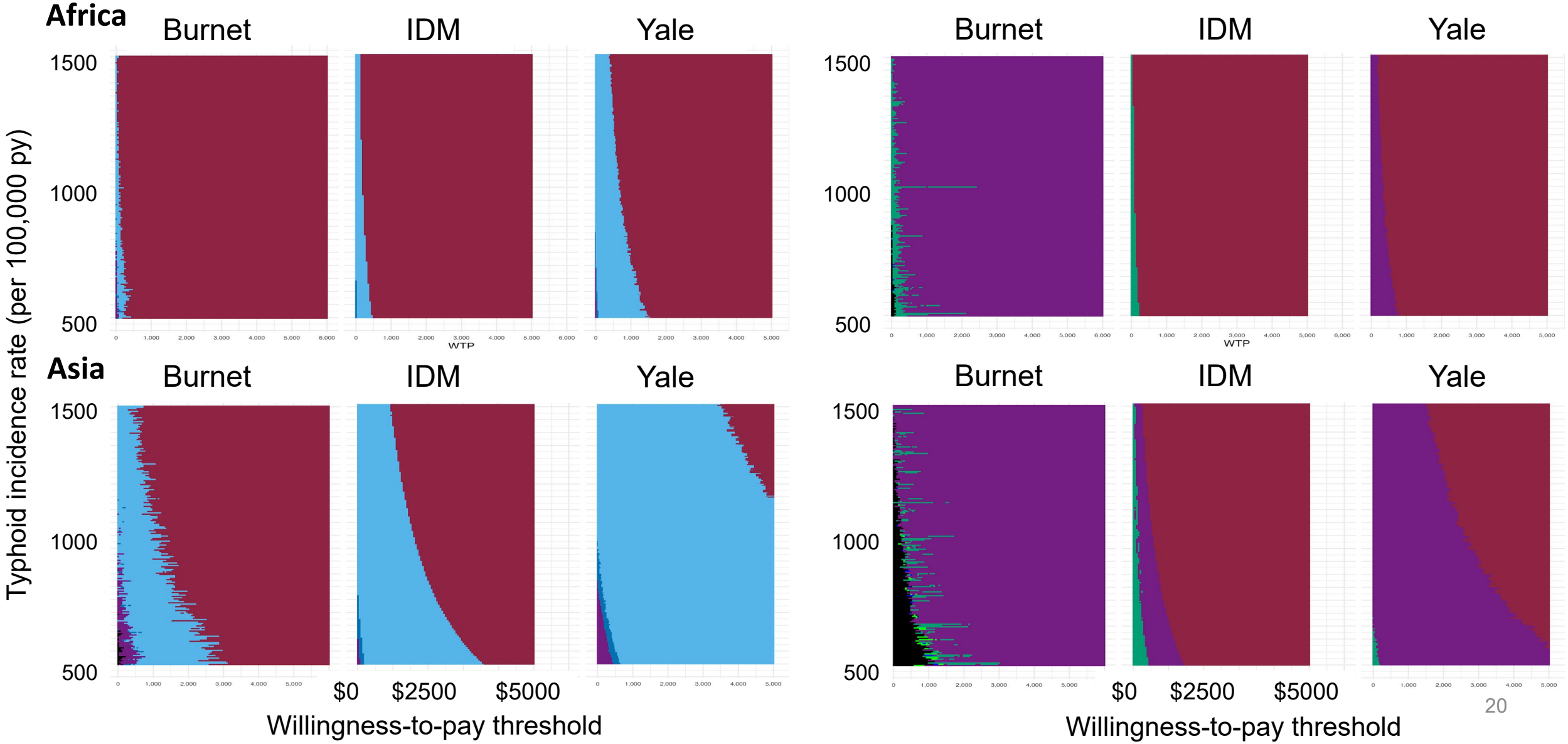


Threshold analysis: Very high burden

Yale

Slow waning

Fast waning



CEA parameters: Healthcare seeking & severity

Yale

Parameters	Africa	Asia	source
Healthcare seeking parameters			
Probability of seeking care	0.58 (0.42, 0.77)		Bilcke et al (2019)
Probability of inpatient treatment	0.24 (0.08, 0.53)	0.10 (0.03, 0.28)	Marks et al (2024), Longley et al (2020)
Probability of outpatient treatment	Complement of the above		Marks et al (2024), Longley et al (2020)
Probability of complications	0.32 (0.20, 0.47)	0.02 (0.001, 0.36)	Marks et al (2024), Longley et al (2020)
Severity parameters			
Duration of severe illness	20.0 days (IQR: 14.0 - 44.0 days)		Mejia et al (2020)
Duration of moderate illness	14.0 days (IQR: 7.0 - 25.0 days)		Mejia et al (2020)
Duration of untreated illness	14.0 days (IQR: 8.0 - 25.0 days)		Mejia et al (2020)
CFR	0.81% (0.10%-6.22%)	0.16% (0.07%-0.40%)	Murthy et al (unpublished) – based on meta-analysis of studies since 2010
Life expectancy	64.0 years	74.8 years	UN data portal

CEA parameters: Vaccination & treatment costs

Yale

Treatment costs	**Africa**	**Asia**	**source**
Inpatient pediatric costs	$285.01 ($199.29, $370.74)	$214.45 ($153.75, $326.76)	Limani et al (2020), Mejia et al (2010)
Outpatient pediatric costs	$50.41 ($41.16, $59.68)	$42.62 ($26.34, $72.01)	Limani et al (2020), Mejia et al (2020)
Inpatient adult costs	$445.65 ($295.27, $596.02)	$214.45 ($153.75, $326.76)	Limani et al (2020), Mejia et al (2010)
Outpatient adult costs	$46.77 ($35.18, $58.36)	$42.62 ($26.34, $72.01)	Limani et al (2020), Mejia et al (2020)
Vaccination costs			
Vaccine procurement costs (i.e. vaccine price)	$1.50		UNICEF, 2024
Syringes & safety equipment costs (unit price)	$0.29 ($0.28, $0.31)		Portnoy et al., Vaccine 2015
Delivery costs, routine	$2.34 ($1.96, $2.70)	$1.54 ($0.94, $2.14)	Bilcke et al., Lancet Infect Dis, 2019
Delivery costs, school-based	$1.42 ($0.71, $2.14)		Weyant et al., Vaccine, 2024
Delivery costs, catch-up campaign	$0.50 ($0.44, $0.56)	$0.54 ($0.46, $0.61)	Bilcke et al., Lancet Infect Dis, 2019

World Health Organization

Session 7: Novel matrix for valuing combination vaccines.

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Some of the documents related to this session are currently confidential and not available for public access.

World Health Organization

Session 8: Stockpiling and vaccination strategies for Ebola response: insights from Integrated epidemiological and epidemic modelling

Cost effectiveness of vaccination against Ebola Virus Disease

IVIR-AC meeting , 4th September 2025

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Aims

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- What is the most beneficial vaccination strategy against Ebola virus disease?
  - preventative vs. reactive
  - geographical targeting vs ring vaccination (less targeted vs more targeted)
  - priority groups e.g. HCWs
- What is the most cost-effective vaccination strategy?
- How many doses should be maintained in the stockpile?
- Is the current price of an Ervebo dose justified?

Method overview

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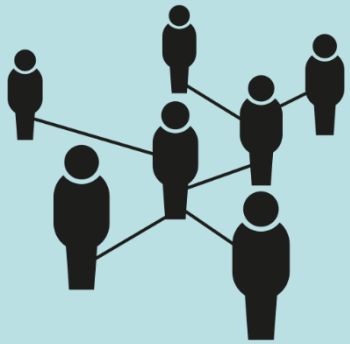
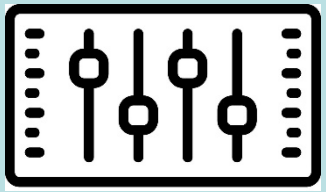
Individual-based transmission model

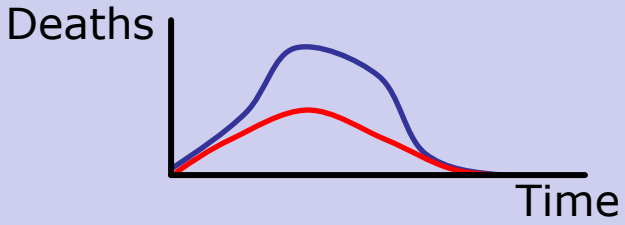


- Varied parameters



Simulated health outcomes

Under counterfactual scenarios

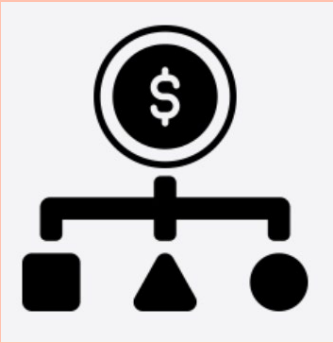


For:
- single epidemics
- five-year horizons

Multiple repetitions

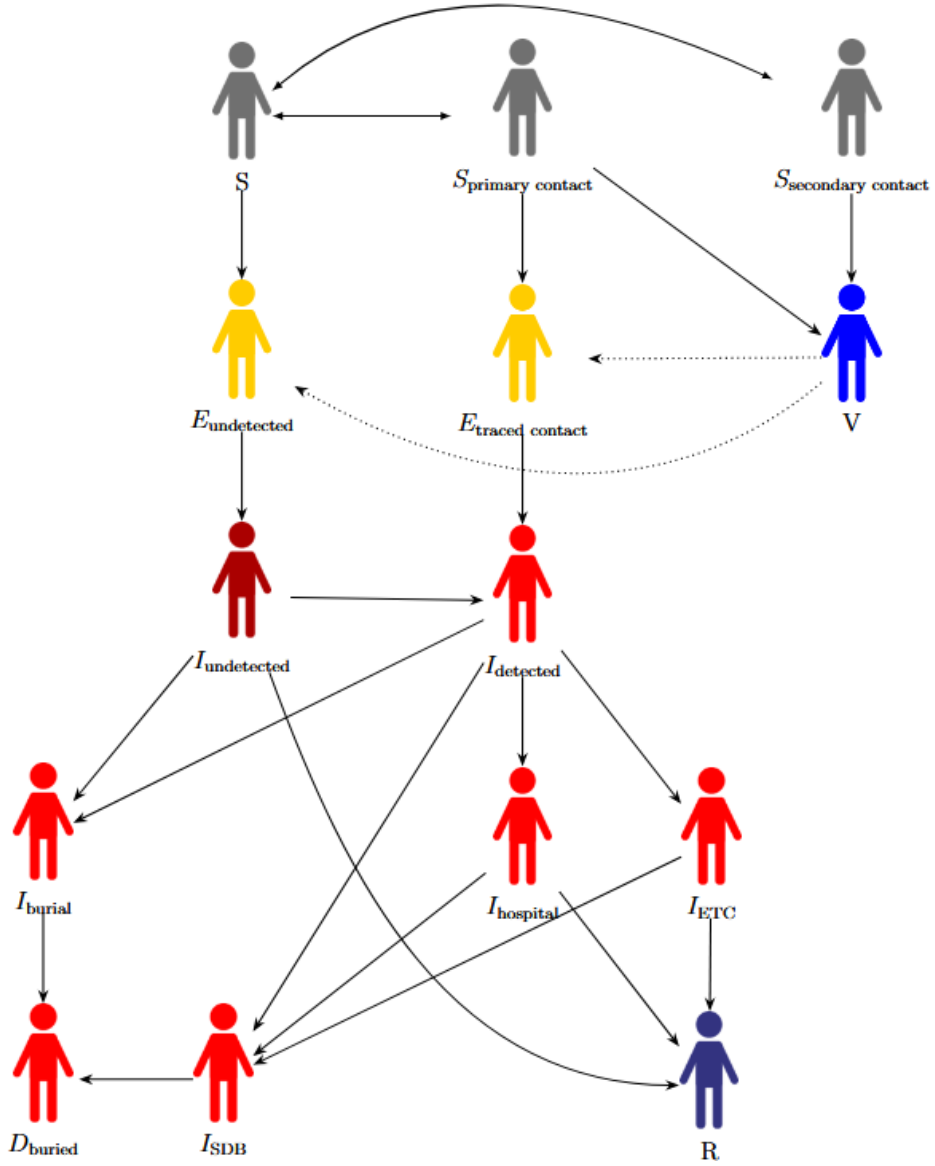
+

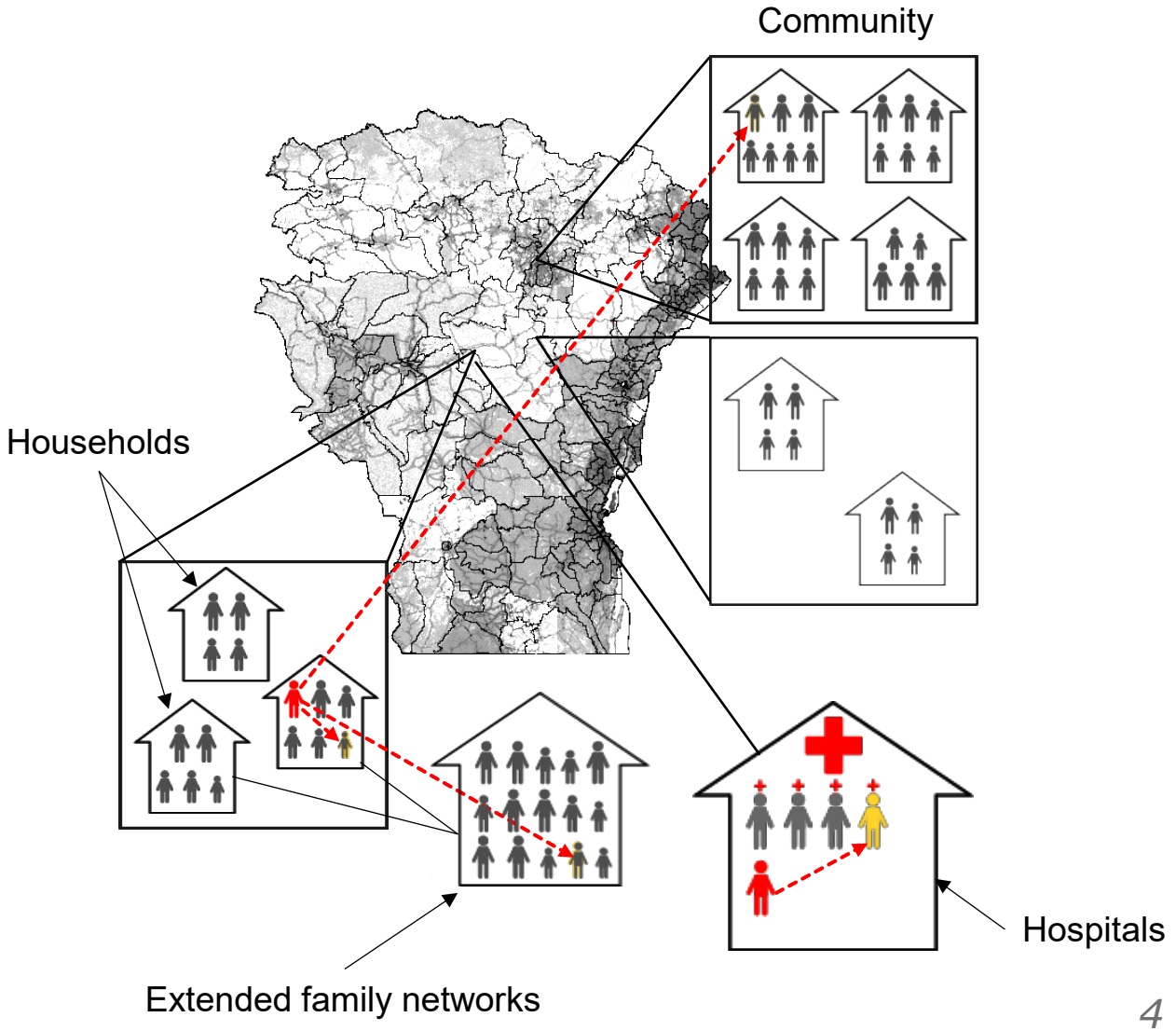
Costing model



→ Benefits, costs & cost effectiveness of different interventions
→ Simulated across multiple scenarios

Modelling EVD outbreak response
Disease transmission





Modelling EVD outbreak response
Interventions

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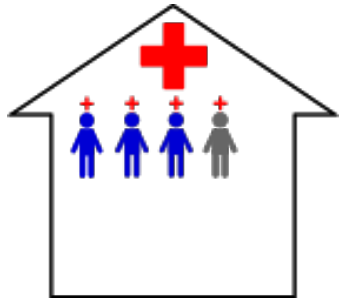
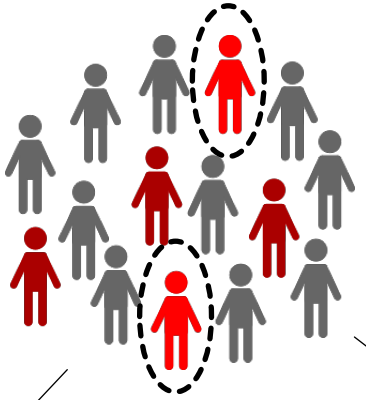
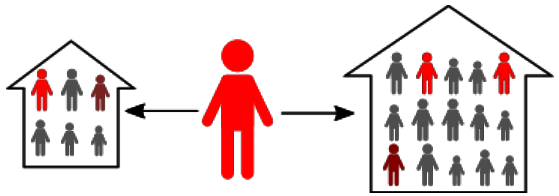
HCW vaccination
(preventative or reactive)



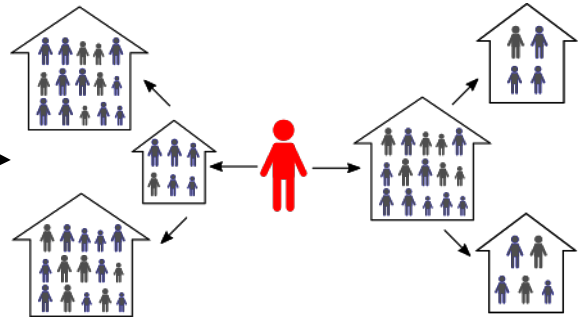
Case finding



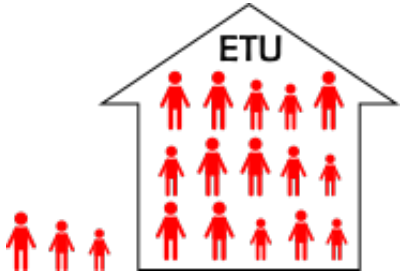
Contact tracing



Vaccination
(ring or geographical)



ETU admissions



Safe and dignified
burials

Model parameterisation

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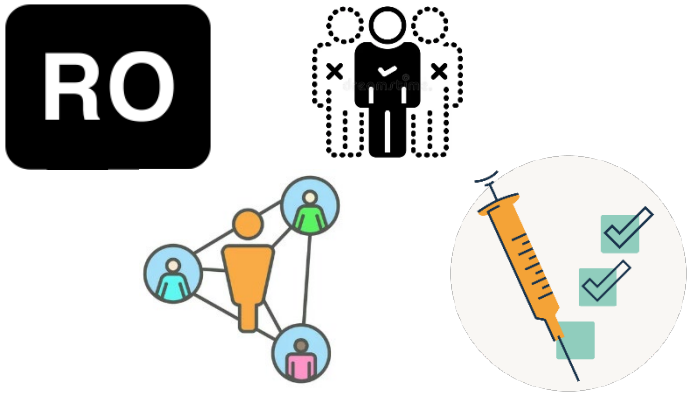
- **Model NOT calibrated**
  - Some parameters fixed
  - Some varied
  - + stochasticity across many simulations

- **Demography** & **geography** of DRC

- **Ebola natural history** from literature [Nash et al. Lancet ID 2024]

- Varied parameters relate to:
  - **Transmission** (Basic reproduction number)
  - **Case ascertainment** timeliness and coverage
  - **Contact tracing** performance
  - **Vaccination** coverage

→ Worst-case, realistic and best-case scenarios considered



- **Costs** from literature

Is the Ervebo vaccine cost-effective against Ebola virus disease?

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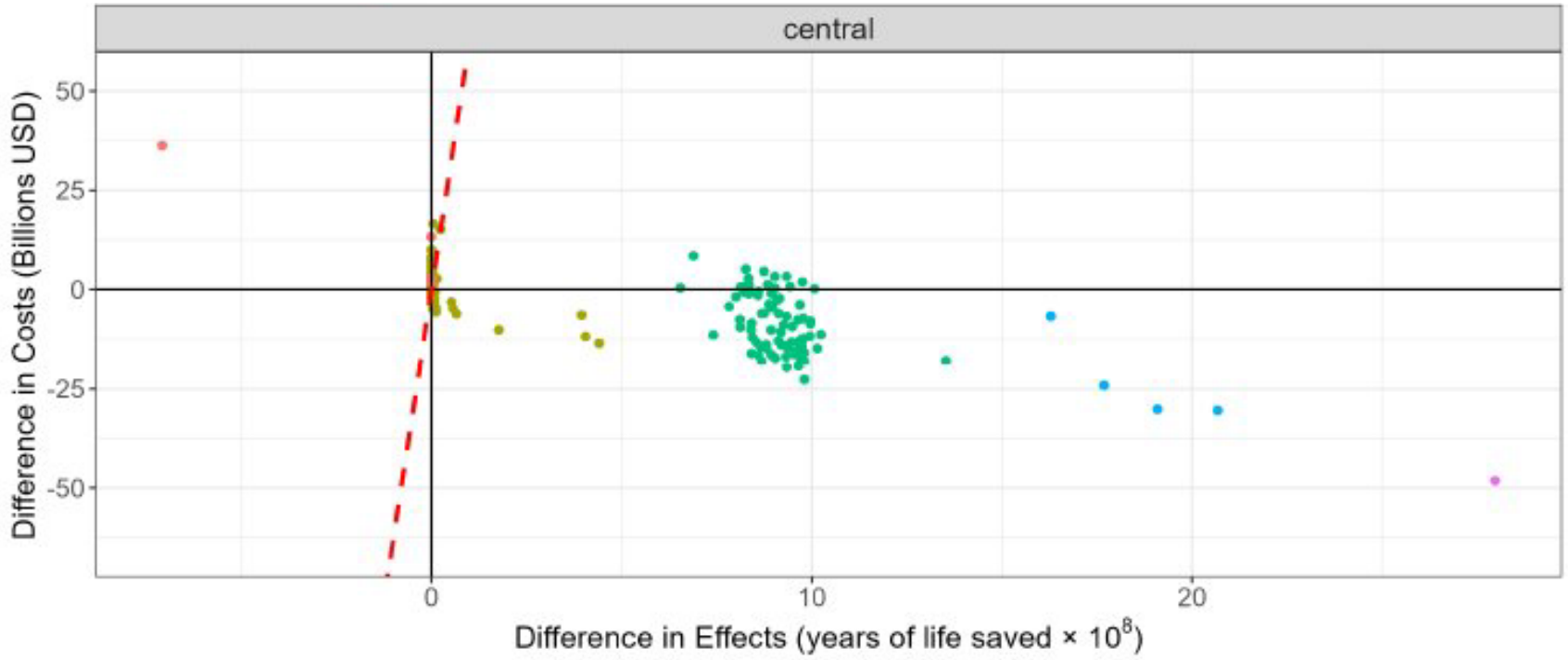
PRELIMINARY RESULTS

- Reactive ring vaccination with Ervebo tends to be cost-saving if at least one large EVD outbreak occurs during a 5-year projection horizon



What is the most beneficial vaccination strategy – ring or geographic?

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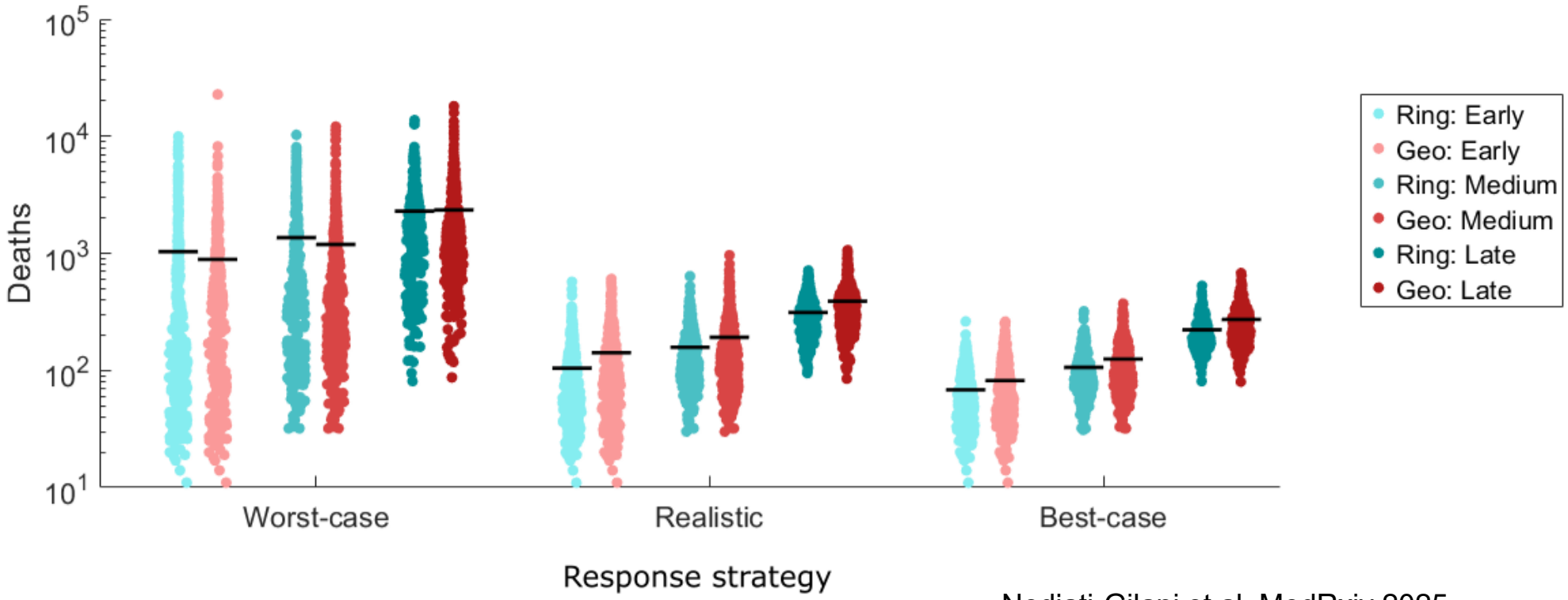
- The performance of both strategies is similar, but on average:
  - For worst-case responses: geographic preferred, uses fewer doses
  - For realistic/best-case responses: ring preferred, uses fewer doses
- Improving standard response activities is more critical than vaccination strategy



Nedjati-Gilani et al, MedRxiv 2025

Should we preventively vaccinate healthcare workers?

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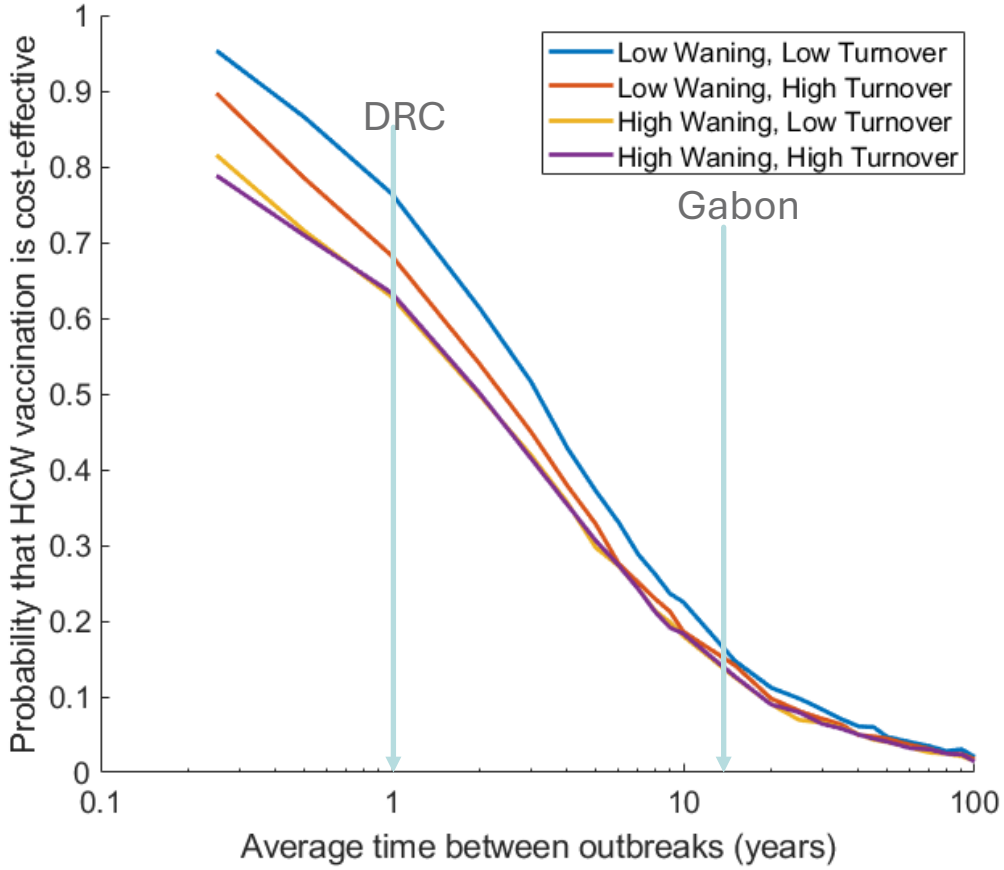
- Cost-effectiveness depends on:
  - Outbreak emergence frequency – main driver
  - Immunity waning & HCW turnover – to some extent



Nedjati-Gilani et al, IDM 2024

How many doses should be maintained in the stockpile?

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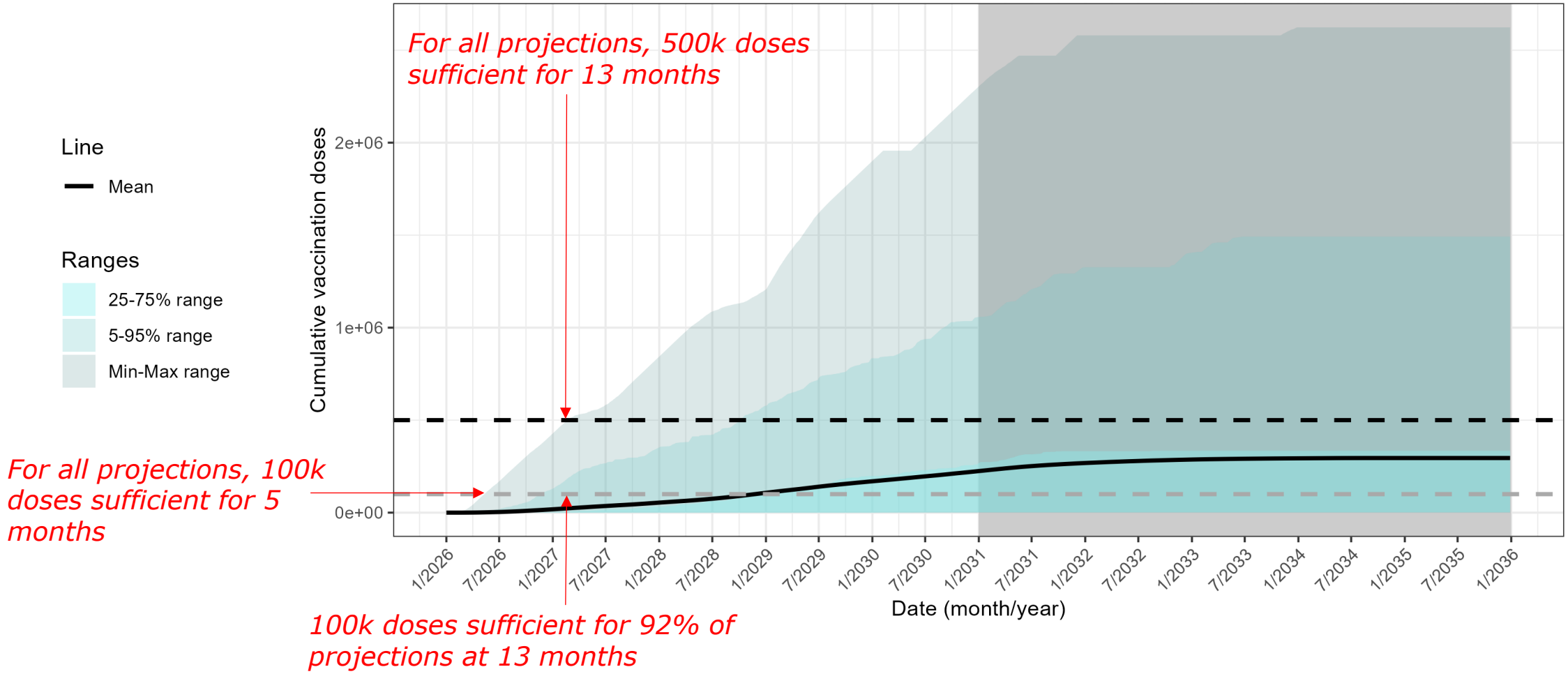
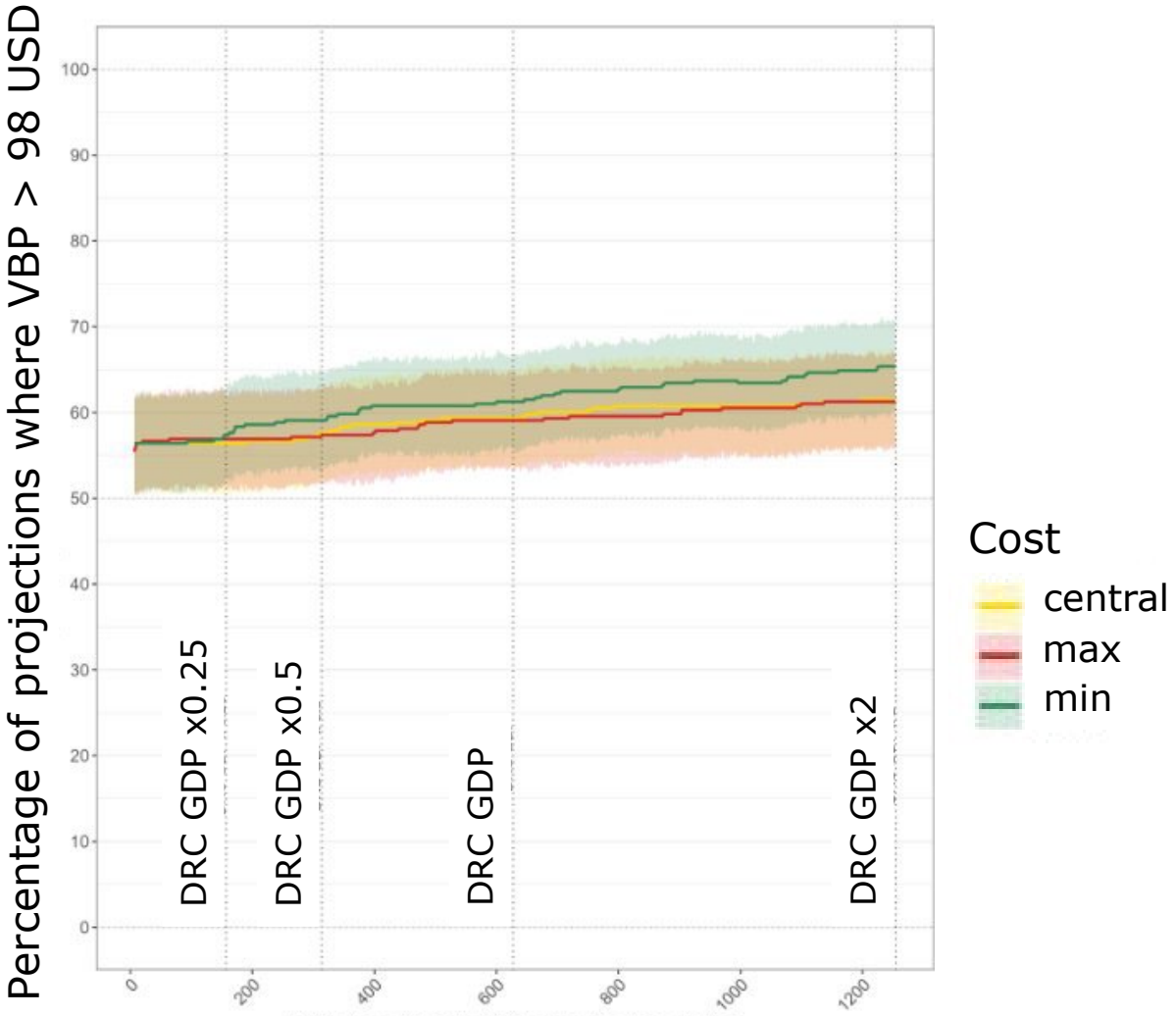
PRELIMINARY RESULTS

- Optimal stockpile size depends on the risk we are willing to take and dose replenishment speed



Is the current price of an Ervebo dose justified?

PRELIMINARY RESULTS



- Percentage of five-year projection horizons for which the value-based price per Ervebo dose is > 98 USD
- There is a bimodality in the VBP
  - either it is a very valuable component of the outbreak response, or not a very useful addition to existing measures
- If the aim is to be prepared for a large EVD outbreak occurring within the next 5 years, the current price of an Ervebo dose is justified

Limitations

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- Model simplifies reality
- Model not calibrated to outbreak data
- DRC only
- Limited cost data
- Results sensitive to parameter choices
- No correlation between parameters (work in progress)
- Imperfect counterfactual matching

Questions

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- Is this transmission model suitable given the aims of our work?
- Are there any other factors that we should be considering (e.g. in terms of disease natural history or interventions)?
- Are the parameter ranges we are using appropriate?
- Are the key output metrics we use suitable?
- Are the outcomes presented clearly?
- How is it best to represent and show value-based price?

Acknowledgements

Imperial College London:

Anne Cori

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Sarah Pallas

Ruth Kallay

Pierre Muhoza

Emma Aberle Grasse

UKRI
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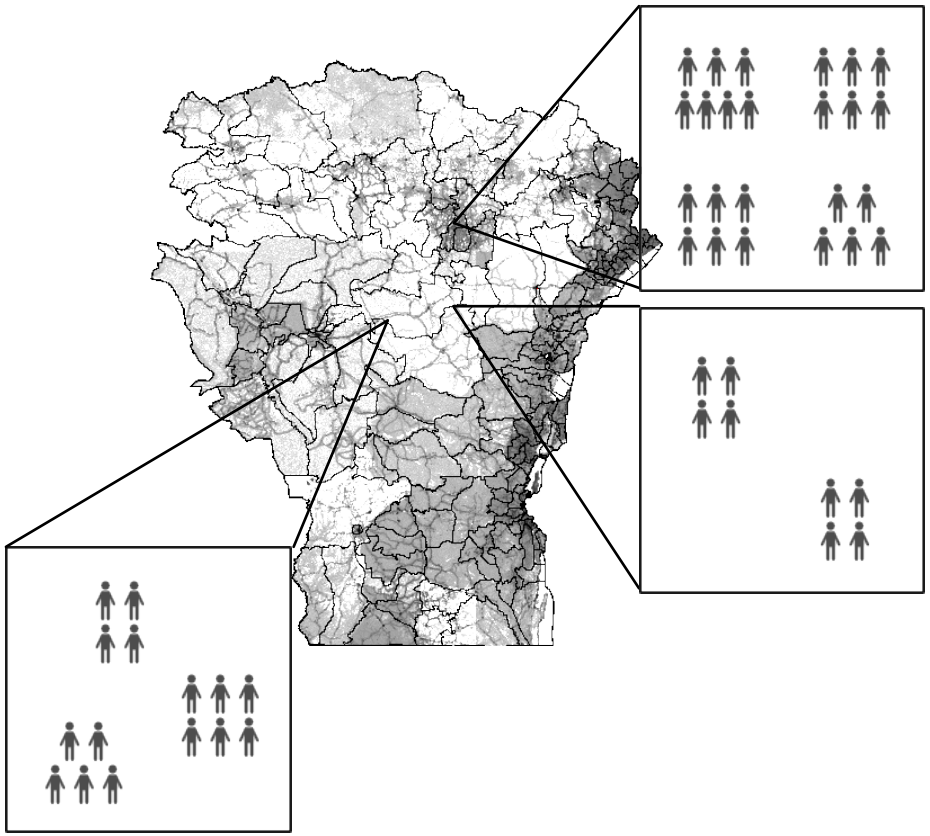
Additional slides

Transmission model

Modelling EVD outbreak response
Population demographics



- Locate individuals in our simulated population according to population density information[6]

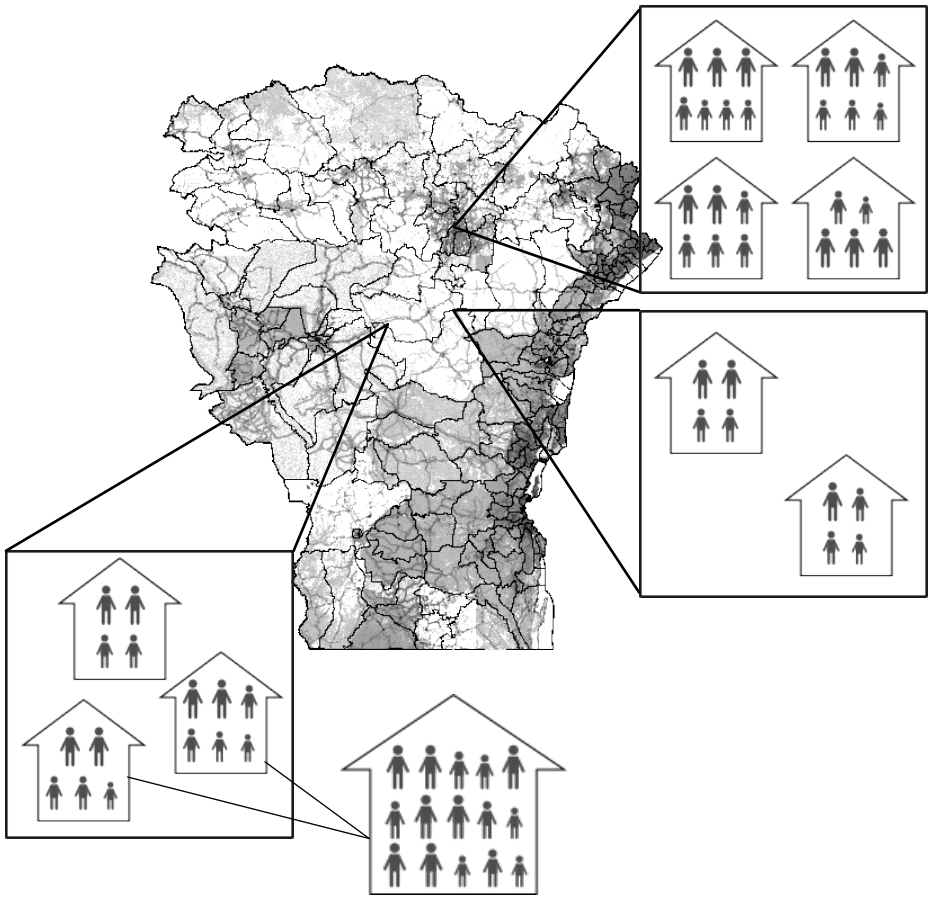
[6]Landscan Global 2018

Modelling EVD outbreak response
Population demographics

- Locate individuals in our simulated population according to population density information
- We assign ages to individuals and group them into households according to available demographic data[7]

[7]DHS Survey for DRC, 2013-2014

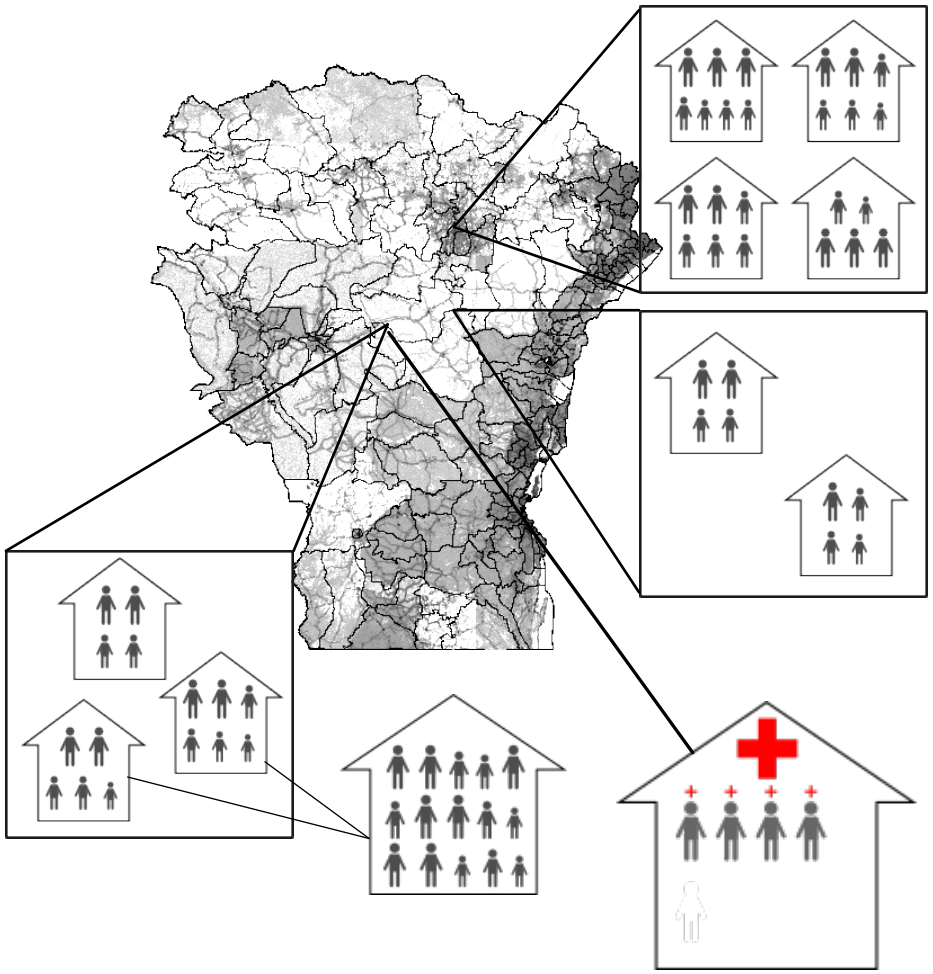
Modelling EVD outbreak response
Population demographics



- Locate individuals in our simulated population according to population density information
- We assign ages to individuals and group them into households according to available demographic data
- Link households together to form extended family groups that match vaccination ring data[8]

[8]WHO Situation Reports, DRC 2018-2020

Modelling EVD outbreak response
Population demographics



- Locate individuals in our simulated population according to population density information
- We assign ages to individuals and group them into households according to available demographic data
- Link households together to form extended family groups that match vaccination ring data
- Situate hospitals near high density areas: every individual is assigned a local hospital. Catchment areas of hospitals and number of HCWs match available data[9,10]

[9]Medical Country of Origin Information Report for DRC 2021
[10]World Bank

Key intervention parameters

- We vary the parameters that have a direct impact on vaccination strategy:
  - Basic reproduction number
  - Contact tracing
  - Case ascertainment
  - Vaccination
- These parameters are often unobserved (i.e. proportion of (non-contact traced cases that is ascertained) or not reported (i.e. proportion of contacts traced, proportion of contacts lost to follow-up)
- Intervention parameters which do not have a direct impact on vaccination and are better characterised are not varied

		Scenario		
Parameter type	Parameter	Worst-case	Realistic	Best-case
Basic reproduction number	Basic reproduction number (Nash et al 2024)	2.1	1.8	1.5
Contact tracing	Proportion of contacts traced	0.74	0.85	0.96
	Proportion of contacts lost to follow-up. (Senga, Koi et al 2017, Ilunga Kalenga, Moeti et al 2019)	0.20	0.10	0.05
Case ascertainment	Proportion of cases who are not traced contacts who are ascertained (Unwin, Cori et al 2022)	0.33	0.61	0.83
	Mean case ascertainment delay (days) (World Health Organization. Ebola Virus Response 2019)	8	6	3
Vaccination	Delay from cases ascertainment to vaccination triggered (days) (Henao-Restrepo, Camacho et al 2017)	10	7	3.5
	Probability of establishing a ring for ring vaccination (World Health Organization. Ebola Virus Response 2019)	0.66	0.83	1
	Probability of accepting vaccination, for geographic vaccination	0.63	0.78	0.95

Cost effectiveness
Costs and benefits

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- **Costs include**:
  - Initial HCW vaccination, outbreak response vaccination, safe burials, rapid response teams, laboratory testing, safe burials, case ascertainment, case management (ETUs)

- We represent **benefits** as years of life lost (YLL) averted

- **Incremental Net Monetary Benefit** for *i*th pair of simulations is

$$INMB_i = \left(YLL_{NoVacc,i} - YLL_{HCWVacc,i}\right) \times VSLY - \left(Cost_{HCWVacc,i} - Cost_{NoVacc,i}\right)$$

- VSLY is a multiple of gross national income (GNI) where we consider a range from 0.5xGNI to 4.5xGNI

Cost effectiveness
Cost data

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- We use unit cost data from the 2018-2020 North Kivu outbreak (Zeng et al, BMJ 2023)

Table 3 Share of funding by public health response (pillar 1) activities

Interventions	Amount (US$ in million)	Percentage (%)
Coordination	143.89	18.8
Risk communication and community engagement	105.21	13.7
Surveillance, contract tracing, POE/C and vaccination	122.24	15.9
Laboratories	14.97	2.0
Clinical management of Ebola cases	141.13	18.4
IPC/WASH	105.81	13.8
Safe and dignified burials	40.33	5.3
Psychosocial support	33.88	4.4
Operational support (including incentive payment)	59.07	7.7
Total	766.53	100

IPC, infection prevention and control; POE/C, point of entry/control; WASH, water, sanitation and hygiene.

Note: some response activities (IPC/WASH, safe burials) only have a budget, not a unit cost

Table 4 The unit costs of key interventions for the Ebola control

Services/ interventions	Total spending (US$ million)	Quantity	Unit cost
Rapid response team (per team per month)	–	–	US$66 182
Contact tracing and surveillance (per identified case)	11.92	2687	US$4435
POE/C (per POE/C per month)	11.34	76	US$18 293
Laboratory test (per lab test)	14.97	244 193	US$59.40
Laboratory test (per identified Ebola case)	14.97	3481	US$4166
Confirmed cases in treatment centre (per case)	1.85	1264	US$1464
Suspected cases in treatment centre (per case)	–	–	US$358.38
Confirmed cases in transit centre (per case)	0.32	1476	US$219.28
Suspected cases in transit centre (per case)	–	–	US$220.01
Vaccination (per vaccinated individual)	18.95	157 067	US$120.70
Psychosocial support (per beneficiary)	30.00	171 423	US$175.00
Prevention, coordination, community engagement, operation and monitoring and evaluation (per capita per month)	427.1	6 300 365	US$2.71

POE/C, point of entry/control.

Questions

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- Is this use of INMB to characterise cost-effectiveness appropriate?
- Should we consider a wider range for VSLY, or characterise it in a different way completely?
- Is the cost data we are using appropriate?
- Should we represent cost-effectiveness in a different way?
  - ICER clouds

Planned updates for scenario modelling

Questions to be answered with this work

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1. What is the effect of stockpile size on the costs and benefits of comprehensive outbreak response?
2. What are the optimal (cost minimising) mitigation and stockpiling strategies for the DRC?
3. What is the maximum acceptable price per Ervebo vaccine dose that achieves a satisfactory return on investment to the international community?

Scenarios considered

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Stockpile assumptions: 10K (baseline), 50K, 100K, 200K, 300K, 400K, 500K

We will also run simulations with no stockpile (to assess the benefit of any stockpile) and infinite stockpile (to calculate the shortfall in doses in the event the stockpile runs out before replenishment)

Parameter(s)	Worst-case	Realistic	Best-case
Transmissibility (R_0)	2.1	1.8	1.5
Vaccine replenishment time	18 months	15 months	12 months
Outbreak detection	20 hospitalised cases	10 hospitalised cases	5 hospitalised cases
Response capacity	Low	Realistic	High
Community acceptance	Low	Realistic	High

Ring vaccination around a case is preferred; if the ring cannot be established, geographically targeted vaccination takes place.

We run the analysis both with and without prior preventative HCW vaccination campaigns

Assumptions: Response capacity

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Response capacity comprises multiple parameters, which we assume are correlated, i.e. if the response has high capacity for contact tracing, we assume that it also has high capacity for vaccination.

Response capacity	Worst-case	Realistic	Best-case
Time from symptom onset to case ascertainment (days)	8	6	3
Contact tracing capacity (per admin unit per day)	1000	2500	5000
Ring vaccination capacity (per team per day)	50	100	150
Geographic vaccination capacity (per team per day)	200	250	300
ETU capacity (beds)	12	24	36
Safe burials (per team per day)	4	6	8

Assumptions: Capacity constraints

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Team	Initial	Increased 1	Increased 2	Maximum (100%)
Safe and dignified burials	40%	60%	80%	22 (min-max: 11-33) teams
Contact tracing	40%	60%	80%	150 (min-max: 50-250) contact tracers
Geographic vaccination	40%	60%	80%	35 (min-max: 20-50) teams
Ring vaccination	40%	60%	80%	35 (min-max: 20-50) teams

- Proposed capacity constraints are presented **per territory** (2nd level administration division in DRC).
  - We are making the same assumptions for worst-case, realistic, and best-case scenarios
  - Within each step, the capacity is therefore not directly tied to the number of events that are occurring (i.e. acceptance)
  - The increase from initial response capacity to the following capacity level is triggered once capacity is 80% filled

Assumptions: Community acceptance

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Similarly for **community acceptance**, we assume that if the community is receptive to contact tracing, we assume they will also be receptive to vaccination.

Community acceptance	Worst-case	Realistic	Best-case
Proportion of cases ascertained who are not traced contacts	33%	61%	83%
Proportion of ascertained cases who seek healthcare	50%	70%	90%
Proportion of contacts found	74%	86%	95%
Proportion of contacts lost to follow up	50%	25%	5%
Proportion of cases around whom a vaccination ring is established	66%	83%	100%
Probability that a ring member accepts vaccination	95%	95%	95%
Probability that a community member accepts vaccination	63%	81%	95%

Discontinuous costing of outbreaks

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- This approach takes into account set-up costs and scale-up costs

- Outbreak response activities split across **six main components**:
  - Ebola Treatment Centre
  - Intensified surveillance and community sensitisation
  - Case detection and laboratories
  - Contact tracing
  - Vaccination
  - Safe and dignified burials

Component of outbreak response	**Example**
Occurs for every outbreak	Lead epidemiologist salary
Scales with number of geographical regions affected	ETC building
Scales with individuals affected	Vaccine doses used

Categorising costs

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Component	Fixed outbreak	Fixed territory	Variable unit
ETC/hospitalisation	International response team	ETC building (contains transit centre) ETC extension Salary (nurse, doctor, cleaning, admin) Medical and other equipment Running costs (electricity, maintenance etc.)	Medications Perishables PPE Cleaning equipment
Case detection /laboratories	International response team	Mobile laboratory + relocating it to desired area Running costs Salary (lab technician, lab scientist, admin) Vehicles	PCR test Rapid test PPE Sample transport Test transport Transporting nurses to take tests IT + stationery
Contact tracing	International response team Salary (lead epidemiologist, national data manager)	Vehicles Office space Salary (CT team supervisor)	Petrol IT + stationery Salary (contact tracing team) CT team kit PPE
Safe and dignified burials	International response team	Vehicles Office space Salary (SDB team supervisor)	SDB team kit Petrol IT + stationery Salary (SDB team)
Vaccination	International response team Central vaccine storage	Vehicles Local vaccine storage Office space Local training	Petrol Salary (vaccination team) PPE Vaccine doses Vaccinating equipment IT + stationery
Surveillance and community sensitisation	International response team Central surveillance activities	Office space Vehicles Salary (PoE teams, community health worker supervisors, community engagement unit) PoE station	IT + stationery Petrol Salary (community health worker)

Outcomes

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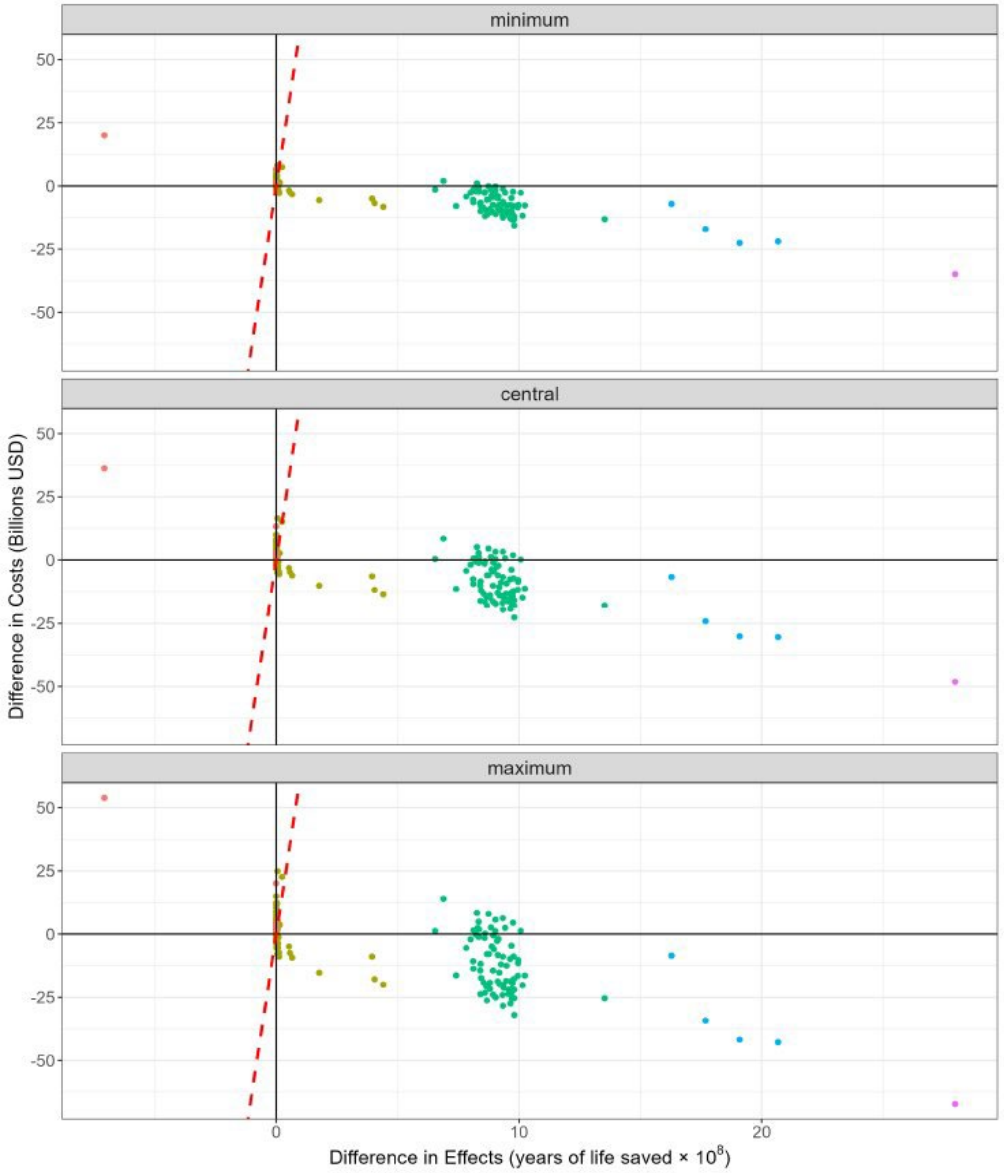
Type of outcome	Description
Epidemiological	• Key simulation outcome metrics • deaths, infections, epidemic length, shortfall in vaccine doses • Number of vaccine doses needed for outbreak response • Number of vaccines to administer to save one life • Proportion of outbreaks controlled with each stockpile level scenario • Proportion of scenarios for which the chosen stockpile scenario is not sufficient for the first 12/15/18 months of the epidemic • An analysis of the features (e.g. transmissibility) that result in the stockpile not being sufficient
Outbreak response cost	• Cost per death averted • Cost per DALY averted • Cost per YLL averted • Incremental cost-effectiveness ratios with incremental DALYs • Baseline: 10k doses • Total cost over 5 years for each stockpile size
Vaccine cost	• Price of a vaccine dose that makes the stockpile scenario cost-effective • The marginal costs of the increasing the stockpile so that instead of being sufficient for 90% of outbreaks, it is sufficient for 95% and 99% of outbreaks.

How many doses should be maintained in the stockpile?

PRELIMINARY RESULTS



- ICER plot with points coloured by how many large EVD outbreaks during five-year projection horizon were successfully mitigated with reactive ring vaccination with Ervebo
  - Baseline: no vaccination
  - Counterfactual: vaccination
  - Red line: per capita GDP of DRC (627.50 USD 2024)
- Reactive ring vaccination with Ervebo tends to be cost-saving if at least one large EVD outbreak occurs during a projection horizon

What is the most beneficial vaccination strategy?

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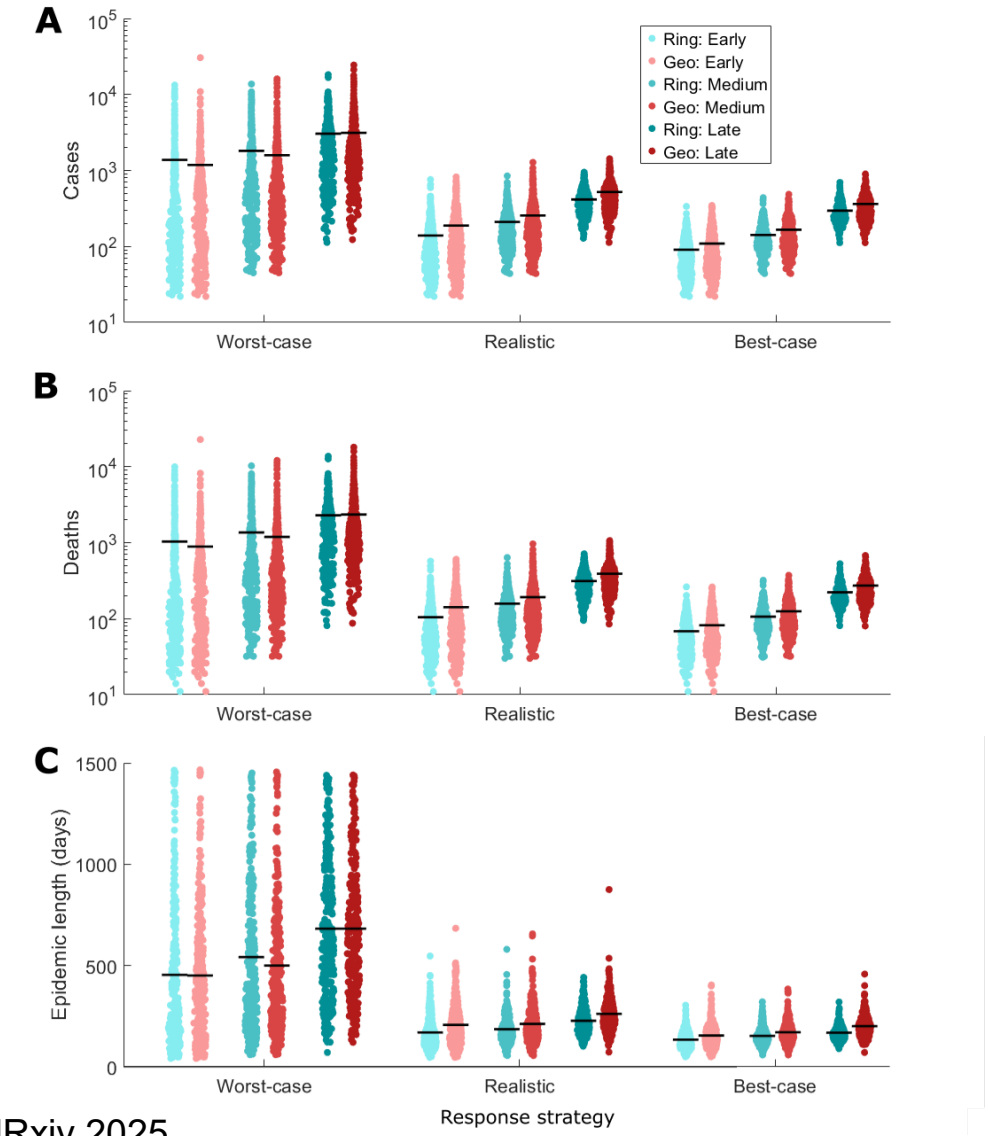
- Compare ring and geographic vaccination for a wide range of scenarios, varying transmissibility, outbreak detection time and response level.
- The performance of both strategies is similar, but on average:
  - Geographically-targeted vaccination preferred for worst-case responses, uses fewer doses
  - Ring vaccination preferred for realistic and best-case responses, uses fewer doses.

		Worst-case		Realistic		Best-case	
Detection time	Summary statistic	Ring	Geo	Ring	Geo	Ring	Geo
Early	Mean	109,500	87,700	15,100	23,600	11,200	15,700
	50th	30,400	43,200	10,100	16,600	8,200	12,200
	95th	523,800	298,300	47,300	72,600	29,000	42,000
Medium	Mean	143,600	113,100	22,400	30,200	17,000	22,300
	50th	66,700	63,300	17,800	23,600	14,000	19,000
	95th	579,900	378,800	57,400	91,400	39,500	52,500
Late	Mean	235,400	196,800	42,500	53,400	32,600	39,500
	50th	175,400	165,600	38,500	51,000	28,900	38,800
	95th	676,200	477,300	87,400	109,500	60,900	70,700

Summary statistics of the number of vaccine doses used in different scenarios and for different vaccination strategies



Nedjati-Gilani et al, MedRxiv 2025

Should we preventively vaccinate healthcare workers?

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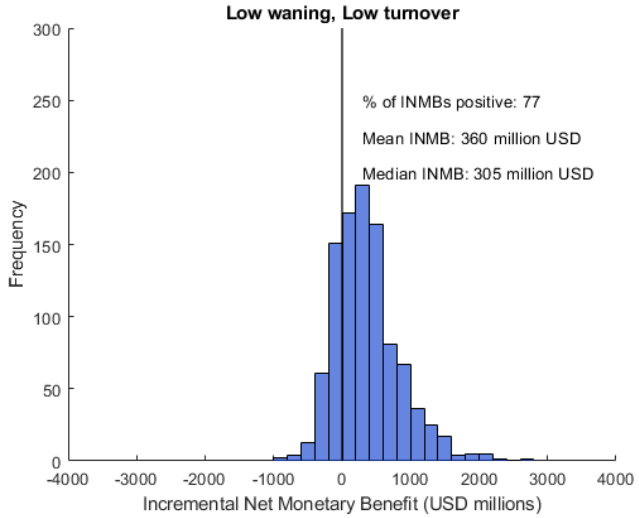
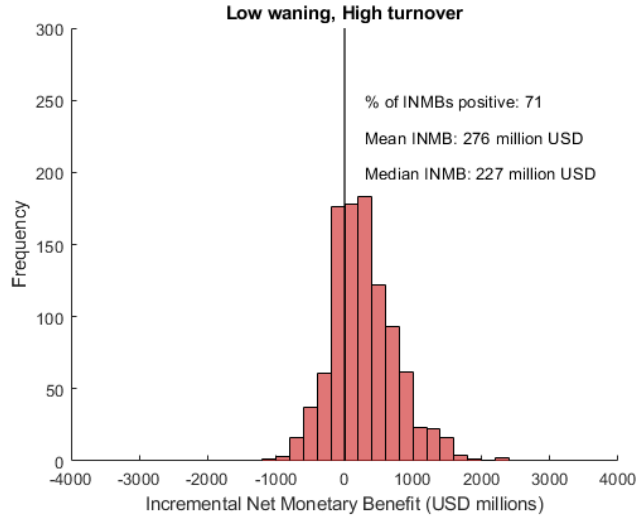
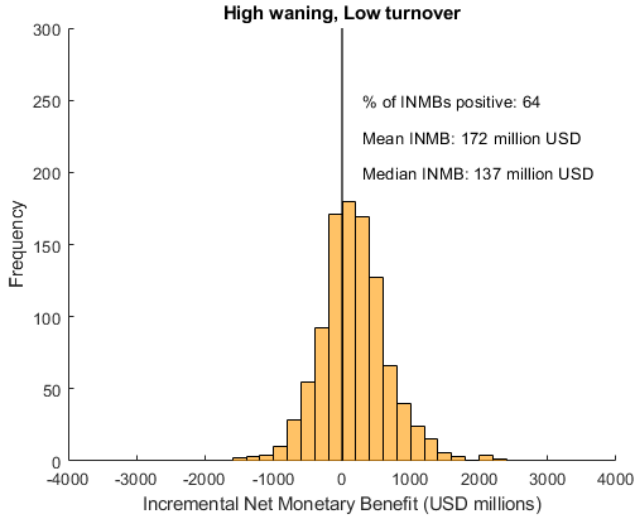
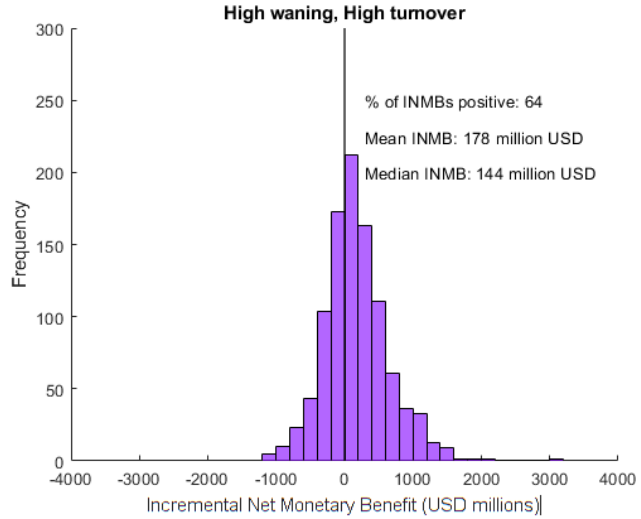
- Assume 95% of healthcare workers vaccinated preventatively,
- Assume outbreak risk like Democratic Republic of Congo and simulate outbreaks over 5 years,
- Consider different immunity waning and healthcare worker turnover rates,
- INMB histograms mostly positive -> preventative vaccination likely to be cost-effective:
  - As outbreaks occur less frequently, it is less cost effective
  - For frequent outbreaks, low waning and staff turnover result in higher cost-effectiveness









Nedjati-Gilani et al, IDM 2024

Infection state colours

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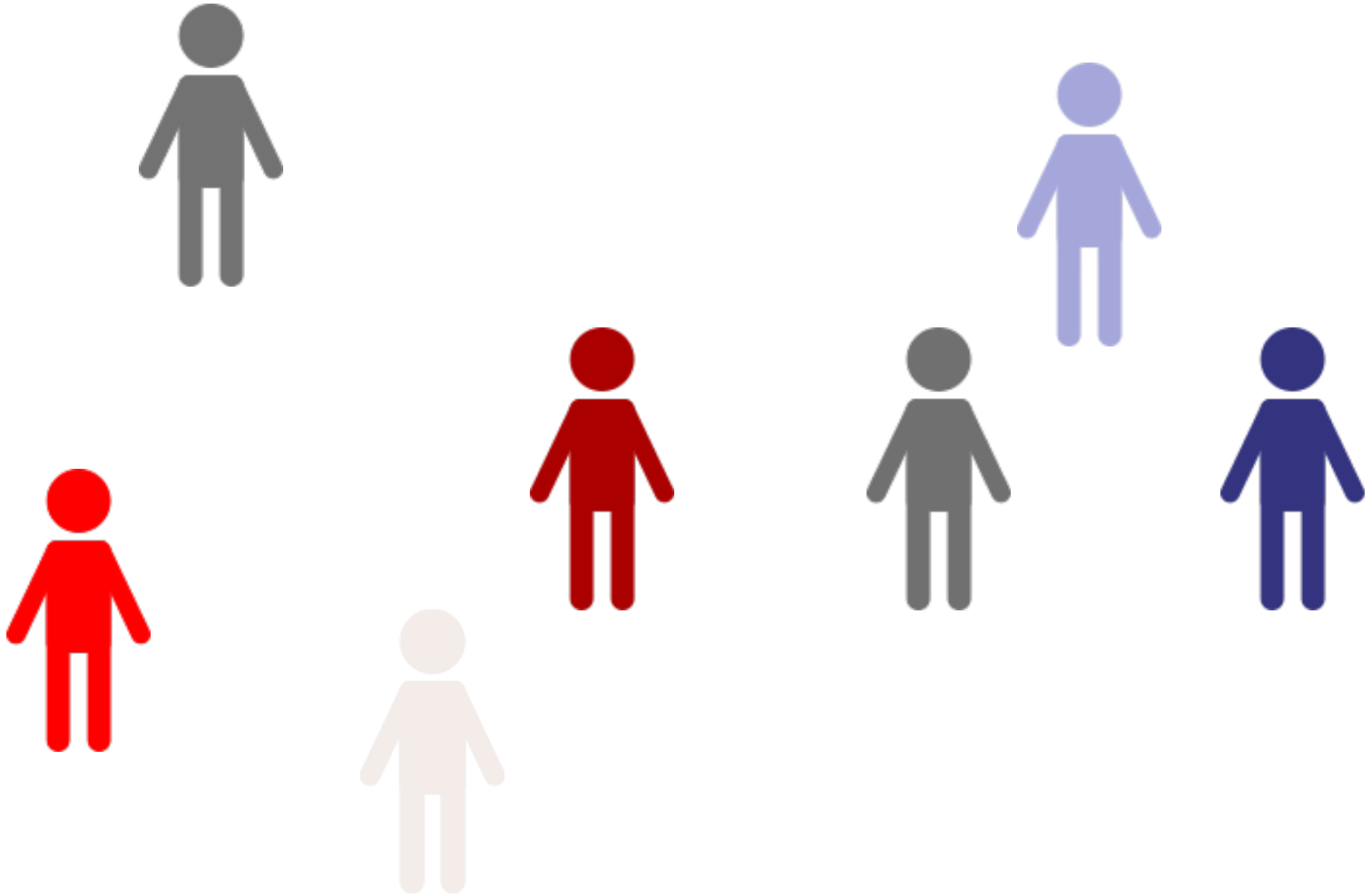

Published background documents for this session

Nedjati-Gilani, G., Pearson, C. A. B., Skarp, J. E., Hinsley, W., Riley, S., Hunter, A., Ferguson, N. M., Hauck, K. D., & Cori, A. (2025). *Cost-effectiveness of geographically targeted versus ring vaccination campaigns in response to an outbreak of Ebola Virus Disease*. medRxiv. https://doi.org/10.1101/2025.05.22.25328133

World Health Organization

Session 9: Malaria multi-model comparison of prioritized interventions (M3CPI)

WHO Malaria multi-model comparison of prioritized interventions (M3CPI)

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Research for Health Department, Science Division

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Department of Immunization, Vaccines and Biologicals

WHO Secretariat

Science Division (SCI)

- Jeremy Farrar
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- Kate O'brien
- Raymond Hutubessy
- Philipp Lambach
- Mary Hamel
- Karene Yeung

Health Financing & Economics (HFE)

- Anna Vasssall
- Vittal Mogasale
- Filip Meheus

The M3CPI project is financially supported by the Gates Foundation

Overall aim and purpose M3CPI project

Aim

The WHO M3CPI project will contribute to

- malaria strategic goals to **drive down disease and economic burden** and get ahead of resistance

- enable the decision making needed to **optimize malaria programs' resource allocation and prioritization**, and complement existing investments in malaria modelling, capacity building and support for normative institutions

- Through a multi-model comparison exercise and under guidance of independent WHO technical and policy advisory groups in GPM and IVB, the M3CPI project aims to **generate modeled evidence to eventually inform global recommendations** on the **optimal mix of malaria interventions** in any endemic *P. falciparum* malaria setting

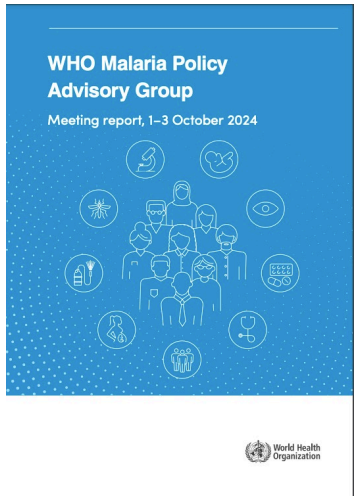
Purpose

To identify the most **resource-efficient intervention mix to reduce malaria burden** in different **archetypal settings** through a **multi-model comparison approach** based on WHO guidance, advice and technical support

Expected outcomes of M3CPI project

The expected outcome is that this analysis will contribute to further clarify the most **cost-effective mix of interventions** from the **country perspectives** to achieve maximal reduction of malaria burden in different settings (archetypes)

The results of this modeling work and its translation into **WHO global guidance** by mid 2026 will inform country-level prioritization decisions, relevant for the application for funding to GC8 of the Global Fund and to GAVI



IVIR-AC's recommendations in Feb 2025

- IVIR-AC recommends **capturing and communicating uncertainty** due to the lack of empirical data to fully explore the impact of various interventions and their combinations
- IVIR-AC recommends **prioritizing combinations of malaria interventions with the most programmatic relevance**, ensuring that modeling analyses align with programmatic needs
- IVIR-AC emphasizes the importance of **in-depth stakeholder engagement** to determine the appropriate prioritization of interventions for the modeling analyses

Timelines

December 2024:
1st Technical Consultation

- Project initiation

February 2025:
IVIR-AC meeting (virtual)

- Review methods

June 2025:
2nd Technical Consultation (virtual)

- Review and solve emerging issues
- Agree on main outputs

September 2025:
IVIR-AC meeting (virtual)

- Review methods and communication plan

November 2025:
3rd Technical Consultation

- Agree and finalize final results

December 2025:
Joint SAGE-MPAG

- **Feed results into updated prioritization guidance**

World Health Organization

Session 9: Malaria multi-model comparison of prioritized interventions (M3CPI) *(for information)*

Background:

- To inform WHO guidance on prioritization of malaria interventions under resource constraints, WHO is proposing a multi-model analyses to analyse impact and cost the mixes of malaria interventions, with assumptions about performance and coverage, in different scenarios in Sub-Saharan Africa
- The objective of the multi-model comparison approach is to inform global WHO guidance taking into consideration MPAG and SAGE advice on the conclusions from multiple mathematical models
- Since the February 2025 IVIR-AC meeting, a second M3CPI technical consultation with the modeling groups took place in June 2025. It is expected to present the final M3CPI project results to SAGE and MPAG in November 2025.

Objectives:

- To present the methods of the multi-model comparisons of mix of malaria interventions including communication plan of the results

Questions to IVIR-AC:

1. Provide feedback on the methodologies used for modeling malaria intervention prioritization, including the approach to model comparison
2. Provide strategic recommendations on how to effectively present and communicate results to support decision-making by SAGE and MPAG
3. Provide specific guidance of the translation of modeling results into WHO guidance on prioritization of malaria interventions document with explicit consideration of the target audience
4. Provide recommendations on priority areas for expansion in future phases of the project

Technical presentation

1. Present the methods of the multi-model comparisons of mix of malaria interventions including communication plan of the results (Monica Golumbeanu)

Meeting Report

WHO Technical Consultation to Review Progress on Malaria Multi-Model Comparison of Prioritized Interventions (M3CPI)

3-4 June 2025

Virtual meeting from WHO room D45043

Executive summary

The World Health Organization (WHO) convened the second technical consultation on the Malaria Multi-Model Comparison of Prioritized Interventions (M3CPI) on 3–4 June 2025. This initiative, led by WHO's Research for Health Department, Science Division (RFH), and involving Global Malaria Programme (GMP) and the Department of Immunization, Vaccines and Biologicals (IVB), aims to inform the revision of WHO's *Guiding principles for prioritizing malaria interventions in resource-constrained country contexts to achieve maximum impact (GPP)*. The updated GPP will incorporate cost-effectiveness of different mixes of interventions to better support strategic decision-making in resource-constrained settings.

The consultation brought together WHO secretariat, modeling teams, academic experts, and policy advisors to review progress and align on next steps. Two independent models (*malariasimulation* and *OpenMalaria*) are being used to simulate 24 intervention combinations across 600 diverse settings in sub-Saharan Africa. These simulations incorporate historical data, intervention coverage, and contextual characteristics to identify cost-effective strategies under varying budget thresholds.

Participants confirmed key methodological assumptions, including fixed case management coverage, context-specific intervention scaling-up and suspensions, and the exclusion of new tools under development. The costing methodology was reviewed and endorsed, with consensus on using both published and grey literature to build a comprehensive intervention cost database. While limitations such as the inability to model scale effects and/or country-specific costs were acknowledged, the approach was deemed appropriate for informing global guidance.

Preliminary results from pilot settings demonstrated the feasibility of modeling diverse intervention strategies and highlighted the influence of contextual factors such as vector species, rainfall seasonality, and demographic profiles. The models captured uncertainty through multiple iterations and produced comparative outputs for both scale-up and scale-down scenarios in the context of the current global financial situation for public health investments. These findings will inform the development of representative archetypes to guide global policy. The analysis plan will be updated based on the discussion during the meeting, including a section on model comparison to harmonize outputs and interpret differences across models.

The consultation also addressed several strategic and methodological issues, including alignment with WHO guidelines, and the timing of archetype definition. Participants endorsed a flexible, output-driven approach and emphasized the need for high-level

guidance that can adapt to future innovations. The group also emphasized that the intention of the M3CPI project is not to guide country-level decision making on the optimal mix of malaria interventions. For that, customized analyses would be required taking into consideration local data, evidence and involvement of local decision makers.

Looking ahead, participants identified several areas for potential expansion in a second phase of M3CPI, such as modeling also indirect malaria mortality, evaluating synergies between interventions and cost-effectiveness of multiple delivery strategies, exploring efficiency-equity trade-offs, and extending the time horizon to capture long-term effects. These additions would enhance the comprehensiveness and policy relevance of the modeling work.

The group proposed streamlining the process of systematic review on malaria intervention costs and increasing number of experts to complete the development of the cost database to facilitate the completion of M3CPI project towards the end of 2025. This will allow time for updating GPP to inform country applications to Global Fund's Eighth Replenishment (GC8) in March 2026. In the meantime, modeling teams will continue refining simulations using placeholder cost data.

Key future milestones include the presentation of revised methodological approach and communication plan to IVIR-AC in September 2025, a third technical consultation in October, submission of the final report to MPAG and SAGE in November, and publication of the updated GPP by February 2026, in alignment with the timelines of GC8, as country allocation letters will be sent early March 2026.

The meeting participants agreed on the value of the multi-model approach in generating robust, generalizable insights. While not intended for country-specific guidance, the findings will inform WHO's updated GPP, supporting policymakers in prioritizing interventions for maximum impact in resource-constrained environments.

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Background

The World Health Organization (WHO) launched the Multi-Model Comparison of Prioritized Interventions (M3CPI) to estimate the health impact and cost-effectiveness of various combinations of malaria control interventions across different settings. The results of this initiative will inform the revision of WHO's Guiding principles for prioritizing malaria interventions in resource constrained country contexts to achieve maximum impact (GPP). [1] The current GPP does not consider intervention combinations nor costs, and the updated version aims to better support policymakers in mobilizing resources and making strategic decisions on scaling interventions to optimize impact.

The M3CPI project is a collaborative effort led by the WHO's Research for Health Department, Science Division (RFH), involving Global Malaria Programme (GMP), and the Department of Immunization, Vaccines and Biologicals (IVB). It is guided by expert input from the Immunization and Vaccines-related Implementation Research Advisory Committee (IVIR-AC), the Malaria Policy Advisory Group (MPAG), and the Strategic Advisory Group of Experts on Immunization (SAGE), and is developed, implemented and evaluated in consultation with modelling teams, and independent experts convened by WHO.

As part of the preparatory phase, WHO convened the first technical consultation on 16–18 December 2024 to define key questions, parameters, scenarios, and timelines for the M3CPI modelling exercise, and to align methodologies across participating modelling teams. After a thorough review process, following the steps proposed by the WHO IVIR-AC endorsed *guidelines for multi-model comparisons of the impact of infectious disease interventions*,[2] two models were selected to contribute to the M3CPI analysis: *malariasimulation* by Imperial College London (ICL) and *OpenMalaria* by the Swiss Tropical and Public Health Institute (STPH). The modeling methodology was further defined through a series of planning meetings involving the modeling teams and WHO secretariat. On 3–4 June 2025, a second consultation was held to review the methodology, assess progress on the cost database, evaluate pilot results, and discuss analytical challenges in synthesizing the results from both models along with proposed solutions. The meeting also addressed communication strategies, explored future analytical needs, and finalized the project timeline and next steps. Outputs from this initial phase will form the foundation for a potential second phase, contingent on available funding and sustained stakeholder engagement.

Meeting objectives

1. Review progress in the analysis performed by ICL and STPH involved in the M3CPI based on the analysis of pilot settings taken as test case parametrized by both models at the administrative level 1 (admin-1) sites, based on historical prevalence and historical intervention effects;
2. Review emerging issues and solutions proposed on defining parameters of malaria

[1] Guiding principles for prioritizing malaria interventions in resource-constrained country contexts to achieve maximum impact. Geneva: World Health Organization; 2024. https://doi.org/10.2471/B09044
[2] den Boon, S., Jit, M., Brisson, M. et al. Guidelines for multi-model comparisons of the impact of infectious disease interventions. BMC Med 17, 163 (2019). https://doi.org/10.1186/s12916-019-1403-9

transmission, epidemiological outcomes and economic outcomes, including cost-effectiveness, that will inform the completion of the analysis;
3. Review plans and timelines to complete the work including for presentation to the IVIR-AC in September 2025, to the WHO technical consultation on M3CPI in October 2025 and to the joint section of MPAG and SAGE in November 2025; and
4. Review and agree on how the main outputs of the analysis will be presented at the conclusion of the modelling to work together across modelling groups.

Methodology of M3CPI

Summary of presentation

A multi-model approach, using the *malariasimulation* and *OpenMalaria* models, is applied to simulate and identify cost-effective prioritization of malaria interventions based on contextual characteristics of sub-Saharan Africa, from an analysis of approximatively 600 administrative level 1 (admin-1) sites of 43 countries. A diverse set of scenarios will be simulated to provide the flexibility needed to address both broad strategic questions and highly specific policy decisions. Recommendations will be generated using these two independent and structurally distinct models, to support WHO global guidance for malaria control. This analysis will specifically answer the following questions:

1. How to prioritize malaria interventions within a specific setting based on some contextual characteristics?
2. To what extent do uncertainties in the model structure, parameterization, and input data (e.g., malaria transmission, disease epidemiology and cost estimates) affect prioritization of malaria interventions?
3. Can we identify generalizable patterns (archetypes), to inform WHO guidance on intervention prioritization in resource-constrained settings?

However, this analysis will not guide malaria intervention prioritization for specific country or sub-national analysis and will not have in-depth alignment between models. The findings will inform WHO prioritization guidance but not specific country recommendations.

The following modelling steps were proposed:

1. Reproduce historical interventions and burden
   - Similar data types and sources were used to parameterize the history in two models: (a) seasonality of malaria transmission, (b) vector composition and behavior, (c) population age distribution, (d) history of interventions deployed, and (e) history of malaria burden.

2. Run 24 combinations of interventions starting with 'business-as-usual (BAU)', to predict future impact
   - Interventions considered in the models include:
     a. insecticide-treated nets (ITNs) (0%, current and 80% usage),
     b. indoor residual spraying (IRS) (0% and current level),
     c. chemoprevention (seasonal malaria chemoprevention [SMC] or perennial malaria chemoprevention [PMC]) (0% and current/ high),

    d. vaccine (0% and coverage based on three doses of Diphtheria, Tetanus, and Pertussis (DTP) vaccine and for the fourth dose based on the second dose of Measles and Rubella (MR) vaccine data),
    e. case management (treatment and diagnosis) (constant at current level).
  - The models will project health outcomes, including malaria cases averted, malaria deaths averted and disability-adjusted life years (DALYs) averted, over both short-term and long-term horizons. These projections will be disaggregated by age groups: 0-5 years, 5-15 years, 15 years and older.

3. Add cost estimates of malaria interventions as an input to the models for the economic analysis
   - Cost estimates will be from a systematic review led by WHO.

4. Conduct cost-effectiveness analysis and intervention pathways identification (scaling up/ down at different budget levels) across a large sample of realistic and generalizable settings
   - For each setting, the model will first run the BAU scenario. The next most cost-effective strategy, defined as having an incremental cost-effectiveness ratio (ICER) below the established threshold compared to the BAU, will then be selected. Strategies with ICERs exceeding the threshold will be excluded. As the budget increases or decreases, the model will identify subsequent optimal strategies based on their ICERs.

5. Categorize each sampled setting into archetypes based on the decision rule that triggers a change in the preferred strategy
   - Uncertainty in contextual characteristics will be addressed through simulations based on analyses of realistic settings, incorporating factors such as infection history, intervention efficacy, and geographic features. These simulations will then be aggregated into representative archetypes.

6. Generalize policy-relevant patterns to inform WHO's GPP
   - WHO's GPP will be updated based on the findings from this analysis, reflecting resource constraints while maintaining a generalized approach without country-specific tailoring for local decision-making.

Summary of discussions

1. Simulations in the models

   430,000 simulations = 600 settings X 24 intervention combinations X 30 uncertainty/stochastic runs

   The '600 settings' represent distinct admin-1 settings across sub-Saharan Africa. Specific countries or regions were intentionally not named, as the objective of this exercise is to capture the heterogeneity in sub-Saharan Africa and to identify decision rules that vary according to contextual characteristics. Ultimately, these diverse settings will be grouped into representative archetypes to inform broader insights.

2. Assumptions on intervention coverage change

   For chemoprevention and vaccine, if they are already implemented and reached a high coverage in a setting, there will not be further 'scaling up' in coverage, i.e., the intervention can either be dropped or maintained at the current coverage level.

   For ITNs, the coverage can still be increased to cover more population in the site rather than the number of areas being protected.

   For case management (treatment and diagnosis), the assumption is keeping its coverage constant at the current level.

3. Impact of constant case management level on the cost-effectiveness analysis

   The number of cases treated – and consequently, the cost of treatment – will vary depending on the intervention strategy implemented. Maintaining a constant level of case management refers to sustaining the same treatment coverage or probability of receiving care, based on the average coverage levels reported between 2020 and 2022 in the *World Malaria Report*.[3] This assumption implies that access to treatment in both the public and private sectors remains unchanged.

4. Relationship between diagnosis and treatment in the models

   Diagnosis is factored into the cost estimates of case management together with treatment, but not explicitly into the impact assessment.

5. Number of SMC rounds in the models

   In the models, the deployment of the SMC rounds is determined by rainfall patterns at the admin-1 site, according to WHO criteria. The default assumption is four rounds per year. However, in areas with a historical precedent of five rounds, the model retains five to avoid underestimating impact.

   There was a suggestion to explore scenarios with reduced SMC rounds, reflecting potential policy shifts in some countries. While this adjustment is feasible within the models, it would require assumptions about the impact of fewer cycles on effectiveness.

6. Seasonality representativeness in the model

   The factors contributing to seasonality are not defined in the model yet. Variables such as rainfall or clinical incidence may influence the patterns. The model is not intended to precisely replicate the observed seasonality, but rather to explore a range of seasonal patterns. While the modeling exercise aims to be as comprehensive as possible, it does not attempt to cover every possible combination of parameters.

[3] World malaria report 2024: addressing inequity in the global malaria response. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2024

7. Climate change assumptions

   The impact of climate change was assumed to be consistent across all interventions in the analysis. However, the resulting archetypes will reflect varying seasonality patterns, which may offer valuable insights into how climate-related effects differ by context. It was also noted that large-scale funding cuts could potentially overshadow short-term impact of climate change, significantly influencing the observed outcomes.

8. Harmonization between models

   The two models try to harmonize on:

   - the effort to reproduce the history of the same settings using a shared set of parameters;
   - the types of interventions to be modeled;
   - the types of study outcomes; and
   - the overall process for conducting and presenting the analysis.

   However, each team handles uncertainty differently – whether through model structure and/or model parameter assumptions. The goal of this multi-model comparison is to observe how conclusions vary based on different and independent modeling structures and approaches.

9. Consideration of including new interventions in the analysis

   A question was raised regarding the inclusion of new interventions or tools, especially as programs increasingly face decisions about adopting them. It was concluded that new interventions, such as novel antimalarial medicines (e.g., ganaplacide-lumefantrine, anticipated for registration in 2027) or alternative delivery strategies (e.g., multiple first-line therapies), will not be incorporated into the models as 'intervention strategies.' The potential impact and associated costs of these innovations remain highly speculative and would introduce significant additional uncertainty into the analysis. Given current financial constraints, it is unlikely that malaria case management will expand in the short-term (next three years) to include new medicines or innovative delivery approaches, as both would require substantial increases in funding. Therefore new interventions will not be included in the phase of the M3CPI project and potentially a consideration for a future phase of the project.

Conclusions

The M3CPI methodology leverages a robust multi-model approach to simulate and evaluate the cost-effectiveness of malaria interventions across diverse settings in sub-Saharan Africa. The discussion reaffirmed the value of using two independent and structurally distinct models to enhance the reliability and generalizability of findings, while acknowledging differences in how uncertainty is handled. Key assumptions, such as fixed case management coverage and context-specific intervention scaling, were

clarified, and the rationale for excluding new or speculative interventions was agreed upon. Although the models are not designed for country-specific guidance, they aim to identify generalizable patterns that can inform WHO's GPP.

Costs of malaria control interventions and costing methodology of M3CPI

Summary of presentation

A malaria intervention cost database will be updated by July 2025 led by WHO. It will compile primary cost data from the provider (health system) perspective, with a focus on settings endemic for *Plasmodium falciparum*. Data sources will include an ongoing systematic literature review, covering both published and grey literature for the period September 2018 to April 2025, as well as websites and databases of relevant stakeholders.

Cost breakdowns will be extracted following the structure used in the previous review by Conteh et al. (2021),[4] and expanded where additional detail is available. As part of the systematic review process, titles and abstracts are currently being screened independently by two WHO reviewers.

Summary of discussion

1. Cost requirements for modeling

   To support the modeling work, cost data by intervention type and delivery strategy will be required. This includes distinguishing between mass campaigns and routine distribution for net delivery.

   The following specific cost elements are needed:

   a. Cost per net delivered, disaggregated by net type and/or delivery strategy
   b. Cost per person, household, or building reached through IRS
   c. Cost per child per cycle of SMC
   d. Cost per dose of PMC
   e. Cost per vaccine dose delivered
   f. Cost of treating non-severe malaria cases in the public sector (including diagnostics, medicines, and outpatient care)
   g. Cost of treating severe malaria cases in the public sector (including diagnostics, medicines, and inpatient care)

   The modeling teams will assess the uncertainty in cost estimates across studies and will construct cost distribution for each intervention. To enable this, a comprehensive list of cost data from all available studies will be necessary. Moreover, further discussion is needed to ensure a smooth transition between the outputs of the costing team and the inputs required by the modeling teams for analysis.

[4] Conteh L, Shuford K, Agboraw E, Kont M, Kolaczinski J, Patouillard E. Costs and Cost-Effectiveness of Malaria Control Interventions: A Systematic Literature Review. Value Health. 2021 Aug;24(8):1213-1222. doi: 10.1016/j.jval.2021.01.013. Epub 2021 May 18.

2. Consideration of using costing tools

   The costing team will compile unit costs for all interventions, including cost ingredients where available. While there was discussion around using existing costing tools to estimate intervention costs based on these ingredients, given time constraints and the anticipated availability of cost data in the published and grey literature, the team has decided that intervention costs will be extracted directly from published and grey literature rather than generated through costing tools.

3. Costing methodology and limitations in this M3CPI exercise

   Costs will be estimated for each intervention strategy, but not at the archetype level. To address uncertainty in unit costs, sensitivity analyses will be conducted. It is planned to sample a distribution of costs to account for uncertainty. It is also possible to consider using defined 'low' and 'high' bound cost scenarios to explore whether prioritization outcomes would differ under varying cost assumptions.

   Given that the objective of this exercise is to inform the WHO global guidance and the analysis is focusing on summarizing archetypes rather than tailoring results to highly context-specific scenarios, the models will not address all cost-related factors, such as country-specific programmatic costs or economies of scale. Additionally, the cost database will be drawn from multiple countries, inherently reflecting a range of economic contexts and scales. As such, the diversity in the data provides a broad representation of cost structures without the need to model scale effects directly.

   The proposed approach for costing net distribution links the number of nets distributed in a country to the resulting usage levels. This reflects a non-linear relationship between usage and cost – higher usage levels incur disproportionately higher costs, as it becomes increasingly expensive to drive usage upward. However, this approach differs from how countries typically budget for nets as discussed in the meeting. In practice, countries often allocate funds based on full population coverage plus a buffer, regardless of the actual usage achieved.

4. Contingency Planning

   It was noted in the meeting that a backup plan is needed in case a distribution of intervention costs cannot be derived because of limited data points. However, this point was only briefly mentioned, and no in-depth discussion has taken place on potential alternatives.

Conclusions

The discussion on the costs of malaria control interventions and the M3CPI costing methodology highlighted the importance of robust, intervention-specific cost data to support modeling efforts. While the team will rely on published sources rather than costing tools due to time constraints, a comprehensive database is being developed to capture cost variations across settings. Key methodological decisions, such as focusing on intervention-level rather than archetype-level costs and addressing uncertainty

through sensitivity analyses, reflect the pragmatic scope of this exercise. Although some limitations remain, particularly regarding scale effects and country-specific costs, the approach is designed to ensure consistency and relevance for informing global guidance. Contingency planning for data gaps was acknowledged but requires further elaboration.

M3CPI results from pilot settings

Summary of presentation

Context-specific factors were drawn from admin-1 data already integrated into each modeling group's architecture. These include vector species composition and bionomics, rainfall seasonality, historical intervention coverage and usage, and population demographics. These factors influence intervention prioritization and will inform the definition of archetypes used to summarize modeling results.

For each admin-1 site, intervention combinations were generated for ITNs, IRS, PMC or SMC (depending on malaria transmission patterns), and vaccines. The BAU scenario reflects average coverage levels from 2020 to 2022, based on the *World Malaria Report* data.[5] If an intervention is dropped, its coverage is reduced to 0%; if added or scaled up, coverage increases to 80%.

Multiple model iterations are conducted for each site and intervention combination to capture epidemiological uncertainty arising from model structure, stochastic variation, and parameter assumptions. Both short- and long-term impacts will be assessed through a series of simulations.

A total of 24 intervention combinations were modeled, producing results for current coverage levels as well as scale-up and scale-down scenarios. Comparative outputs were generated using two independent models with different structures.

Next steps include:

1. Conducting an in-depth review of pilot results to assess alignment between models and identify key differences in malaria morbidity and mortality outcomes.
2. Incorporating costing data, starting with placeholder values and later integrating full cost uncertainty once the cost database is available.
3. Estimating cost-effective prioritization, generating cost-effectiveness planes, and identifying frontier solutions.
4. Aggregating results into representative archetypes and summarizing findings in a clear and communicable format.

[5] World malaria report 2024: addressing inequity in the global malaria response. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2024

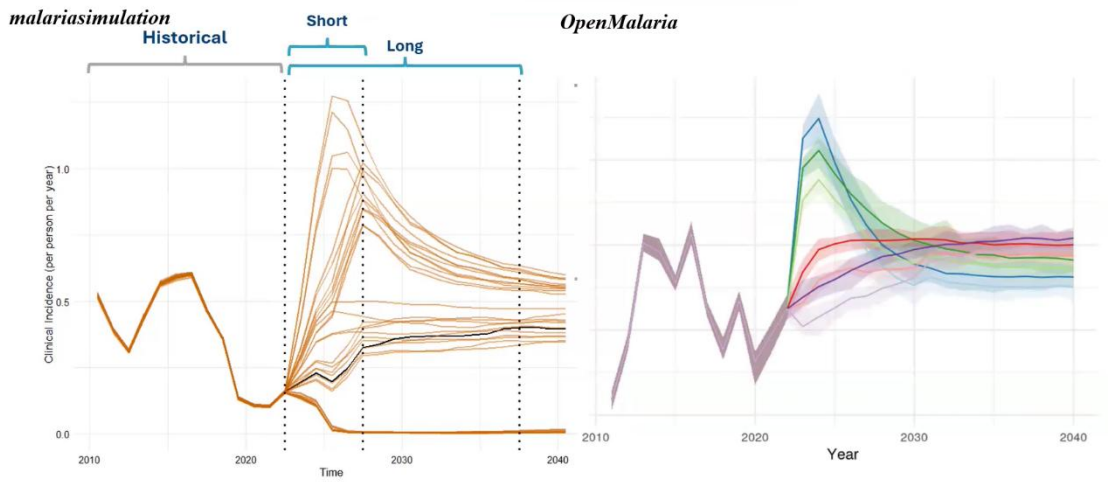

Fig. 1. Illustrative example of projected impacts through 2040 for various intervention combinations at a single site by the *malariasimulation* and *OpenMalaria* models

Conclusions

The pilot results demonstrate the feasibility of modeling 24 intervention combinations per site and incorporating key contextual factors, capturing both epidemiological variability and strategic trade-offs. The next steps – integrating cost data, conducting cost-effectiveness analyses, and aggregating findings into archetypes and synthesizing the results from both independent models as an input for MPAG/SAGE deliberations and global recommendations – will be critical for translating complex model outputs into actionable guidance.

Emerging issues and solutions to inform completion of M3CPI analysis

Summary of discussion

1. Definition of 'scaling down'

   Scaling down refers to reducing overall spending by decreasing the number of interventions implemented, without introducing any new interventions.

2. Definition of BAU as the starting point

   In the reference BAU scenario, the models currently generate intervention combinations based on the coverage levels estimated by the *Malaria Atlas Project* averaged across 2020-2022 period.[6]

3. Consideration for aligning the modeling exercise with WHO guidelines
   a. Geographic exclusivity of SMC and PMC:

[6] Weiss DJ, et al. Mapping the global prevalence, incidence, and mortality of Plasmodium falciparum and Plasmodium vivax malaria, 2000-22: a spatial and temporal modelling study. Lancet. 2025 Mar 22;405(10483):979-990. doi: 10.1016/S0140-6736(25)00038-8. Epub 2025 Mar 5.

SMC and PMC should not be implemented in the same geographical areas, as this is already fully aligned with WHO guidelines and country policies.

b. Sequential use of IRS and ITN:
The continuation or suspension of IRS will only be considered in areas where it has already been implemented. No option for de-novo introduction or scaling-up of IRS will be considered.

4. Consideration of trade-off scenarios between case management and preventive measures

A question was raised during the meeting regarding the need to model a specific trade-off scenario between case management and ITNs. Specifically, this would involve exploring ITN coverage levels between 0% and the current baseline. However, the topic was not discussed in detail during the meeting and would require substantial deliberation to define and justify such a scenario.

The modeling teams acknowledged that while incorporating this scenario is technically feasible, it would be challenging and resource-intensive. Given these constraints, it is proposed that this scenario not be included at the current stage of the modeling exercise.

5. Time horizon in cost-effectiveness analysis

The time horizon is one of the uncertainties incorporated into the sensitivity analysis. The current analysis considers both 5-year and 15-year time horizons, with results generated by integrating outcomes across both timeframes. However, there is debate about the appropriate duration for cost-effectiveness analysis.

The modeling teams emphasized the importance of evaluating both short- and long-term horizons. While short-term projections can be volatile – especially following abrupt intervention changes – longer horizons help smooth out these transitory effects and better reflect sustained impacts. To address this, the teams proposed exploring multiple timeframes, aligned with the 3-year mass distribution cycle. Suggested windows include 3, 6, 9, and 15 years.

Concerns were raised about the 15-year horizon, particularly due to the anticipated introduction of new tools and interventions. Long-term impact from modeling without accounting for these innovations could mislead stakeholders.

6. Timing of archetype definition

The timing of defining archetypes was discussed, with the proposed approach being to define them after the modeling runs. This strategy is intended to ensure that all possible scenarios are explored and captured comprehensively.

Some concerns were raised during the meeting about this approach, particularly the risk that emergent archetypes might produce results that appear to contradict existing WHO guidelines or lack statistical robustness. In response, the modeling teams clarified that archetypes can be either predefined or derived from model outputs, depending on the specific objectives and context of the analysis.

After consideration, the group agreed to proceed with the original proposal: archetypes will be defined based on the outputs of the modeling process, allowing for a more flexible and data-driven approach.

7. Delivery strategies considered in the models

   The models currently include only one delivery strategy per intervention: mass campaigns for ITNs and age-based distribution for vaccines. While incorporating multiple delivery strategies is technically feasible, it would significantly increase complexity, requiring more simulations (and thus more time and resources) and detailed cost data, which may not be readily available.

   Key points from the discussion include:

   - Programmatic relevance: There is a suggestion on exploring scenarios such as phasing out IRS or shifting ITN distribution from mass campaigns to continuous channels. However, these raise concerns due to limited data and lack of WHO or donor guidance.
   - Continuous ITN distribution: There is currently no country using continuous ITN distribution as an alternative to campaigns. Due to insufficient data on its impact and cost, modeling this strategy would be speculative.
   - Modeling priorities: To ensure the WHO's GPP guidance document remains clear and actionable, the models should focus on essential and well-supported strategies. Including every possible delivery method is not necessary or practical.

8. Using averages and ranges to simplify intervention strategy assumptions

   To account for different intervention types and delivery strategies without introducing excessive complexity, one practical approach is to use average values with uncertainty bounds or defined ranges (e.g., low and high) for both coverage and costs. This method can also be applied to impact and cost data for mixed intervention strategies, allowing for more flexible and interpretable modeling inputs.

9. Maintaining strategic flexibility and high-level guidance

   While current financial resource constraints are a reality, the modeling exercise and WHO's GPP should not be confined to 'scaling down' scenarios only. With the potential emergence of new technologies, and changes in funding allocations from domestic and international sources, there may be opportunities for 'scaling up' in the future. Therefore, the modeling exercise should avoid focusing too narrowly on operational strategies that are highly context- or demographic-specific. Instead, it should aim to provide high-level guidance on broad intervention prioritization.

   The current phase of the modeling exercise should remain high-level, offering global recommendations on prioritization. A second phase can incorporate greater contextual complexity once a clearer understanding of broad prioritization patterns

emerges from this initial analysis.

Importantly, the WHO's GPP should clearly articulate the rationale for prioritization, grounded in ICERs.

10. Limitations

The WHO's GPP offers high-level principles for selecting combinations of malaria interventions. However, it is not feasible to capture every nuanced change in intervention usage across diverse settings. This limitation also applies to the current modeling exercise, which cannot simulate all possible scenarios, such as dynamic coverage patterns or real-world variations in intervention effectiveness.

This exercise does not account for minor fluctuations in intervention coverage, as such variations are difficult to represent accurately in models or to summarize meaningfully in guidance. Similarly, partial reductions in coverage are not explicitly modeled. However, since the analysis identifies which interventions could be removed to achieve cost savings, a linear approximation could be used to interpret these findings as indicative of potential coverage reductions for those interventions.

Rather than focusing on binary decisions, such as full removal or introduction of an intervention, the emphasis should be on communicating findings clearly and with appropriate caution.

The timing of coverage changes in the model varies by intervention type. For ITNs, coverage declines gradually as nets are phased out. In contrast, stopping SMC is modeled as an immediate halt at the point when a round would have occurred. When introducing new interventions like SMC or vaccines, the model assumes an immediate uptake to the target coverage level.

It is also important to note that the real-world effectiveness of interventions may be lower than the efficacy assumed in the model, which is typically based on clinical trial data. This assumption is applied uniformly across all interventions.

11. Model comparison strategy

The current plan for model comparison involves aligning both models using the transmission parameters and history of infection at admin-1 sites, with most of the variables already harmonized. The analysis of emerging archetypes are conducted based on the key drivers influencing the choice of one strategy over another. Once both models have completed their runs, the resulting solutions will be collected and analyzed to determine whether the same drivers emerge across models. Differences in outcomes within the same archetype will be treated as an additional dimension of uncertainty, visualized in the Sankey diagram. If the models yield slightly different results, this will be reflected as varying probabilities in the diagram. If the drivers of models differ, the same archetypes can still be used to represent both models. Further analysis will then explore whether the results differ between models for each archetype. The methodology of model comparison will be written up as a section of the M3CPI analysis plan.

Based on the WHO multi-model comparisons guide,[7] WHO will provide further guidance on how model comparisons should be communicated to the writing team responsible for updating the GPP, how to synthesize findings across models, and how to address and resolve discrepancies.

Conclusions

The meeting addressed several key methodological and strategic considerations essential for finalizing the M3CPI analysis. Alignment with WHO guidelines was reinforced, particularly regarding intervention exclusivity and sequencing. While some complex trade-off scenarios and alternative delivery strategies were discussed, it was agreed that these would not be included in the current phase due to feasibility constraints. The group supported a flexible, output-driven approach to defining archetypes and emphasized the importance of maintaining high-level guidance that remains adaptable to future innovations. Simplified assumptions using averages and ranges were endorsed to balance realism with model manageability. Limitations in modeling real-world variability were acknowledged, and a structured plan for model comparison will have to be developed, with WHO guidance to support harmonization and interpretation of results across models.

Options for presenting and communicating the main outputs and conclusions of M3CPI

Summary of presentation

In developing and interpreting various modeling scenarios, it is essential to incorporate uncertainty and translate complex outputs into actionable guidance. The cost-effectiveness frontier is a key tool in this process, helping to identify both the next best steps under changing budget constraints and how current strategies compare to modeled optimal solutions. However, the full sequence of solutions along the frontier can become overly complex, making them difficult to visualize, communicate, and implement, especially when uncertainty is factored in.

To improve clarity and feasibility, additional rules have been introduced:

- Interventions not currently in use cannot be newly introduced; and
- Interventions that have been removed cannot be reintroduced.

While these rules simplify communication and support operationalization, they may exclude more cost-effective alternatives to current strategies.

Each admin-1 site will generate multiple potential solutions due to the sampling of uncertainties. These uncertainties will be explicitly communicated in the results.

Archetypes are defined as groupings of individual sites that share common characteristics. By aggregating solutions from all sites within an archetype, a broader set of potential strategies is produced. The aim is to define archetypes with minimal

[7] den Boon, S., Jit, M., Brisson, M. et al. Guidelines for multi-model comparisons of the impact of infectious disease interventions. BMC Med 17, 163 (2019). https://doi.org/10.1186/s12916-019-1403-9

internal variability, allowing for the development of meaningful and actionable guidance. It is equally important to clearly communicate the uncertainty associated with each archetype.

To reflect the diversity of settings and challenges across sub-Saharan Africa, key contextual factors will be sampled. These will be used to group settings into a small number of practical archetypes, enabling the resulting guidance to be relevant and not overly generalized. While pre-defining archetypes is possible, the modeling team recommends defining archetype variables and boundaries after analyzing model results. This approach ensures that groupings are evidence-based and support clear prioritization.

An illustrative example of a de-prioritization pathway at an admin-1 site was presented in a Sankey diagram (Fig. 2). Each archetype will be associated with a unique set of solutions and a corresponding diagram. An interactive format, such as dropdown menus to select archetype characteristics, was proposed to facilitate exploration of outputs across archetypes. Depending on how the archetypes are ultimately defined, the interactive tool will allow users to select criteria that best illustrate the archetype they wish to explore, along with the direction of prioritization from the outset. For example, users can specify direction of prioritization (prioritization or de-prioritization), transmission intensity (low, medium, or high), and seasonality (seasonal or perennial). This flexibility will enable tailored exploration of intervention strategies across diverse contexts. The presentation format will be refined based on feedback from this meeting and further clarification of the intended users, to ensure that uncertainty is communicated transparently and responsibly in the final guidance.

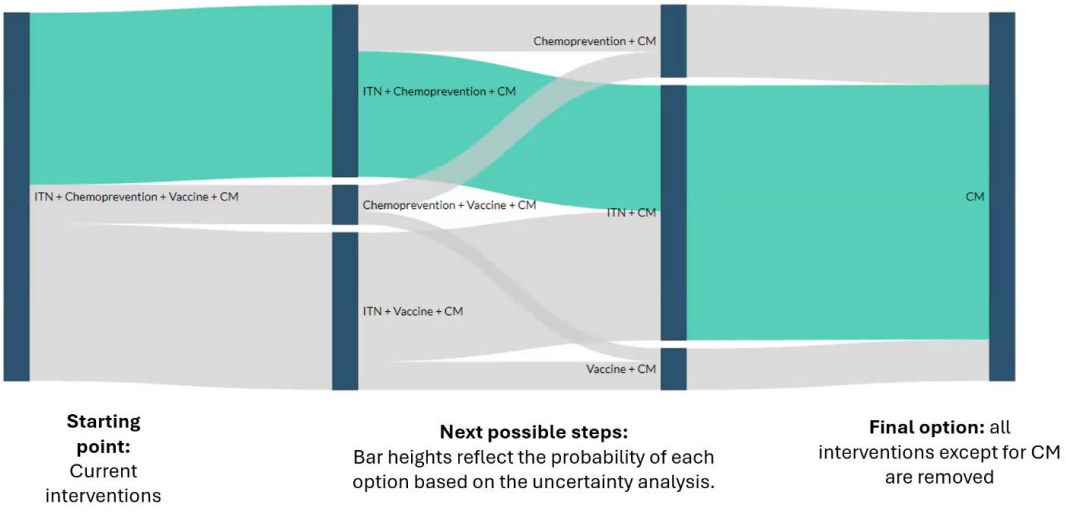

Fig. 2. Sankey diagram showing a hypothetical example of a de-prioritization pathway at an administrative level 1 site. Blue vertical bars represent the sequential steps in the de-prioritization process, which progress from left to right and can be halted at any point depending on budget constraints. Bar heights indicate the probability of each option based on uncertainty analysis – taller bars represent more likely options, while shorter bars indicate less likely ones. The first blue vertical bar reflects the starting point, based on historical intervention strategies. Green flow highlights the most probable pathway through the sequence of decisions. The text labels refer to

sections of the blue vertical bars, not to the flow.

Summary of discussion

1. Feedback on Sankey diagram for prioritization pathway

   Meeting participants generally found the Sankey diagram to be a valuable tool for communicating with the team responsible for drafting the WHO's GPP. The visualization clearly illustrates the prioritization pathway. However, it was emphasized that the interactive tool visualizing the optimal options in a Sankey diagram should not be used in communications with national program managers, as it may lead to misinterpretation or misuse.

   To improve visualization, it was suggested to incorporate interactive features, such as displaying the actual probability numbers of intervention strategies when hovering over a bar. Additionally, the diagram should specify the type of chemoprevention being considered, as SMC and PMC differ in both impact and cost, and are relevant to different archetypes.

   There was also a suggestion to allow users to input specific cost estimates without uncertainty. However, it was clarified that the purpose of this exercise is not to create a country-level decision-making tool, but rather to inform WHO global guidance. Moreover, uncertainties are already incorporated and visualized within the Sankey diagram.

   Another recommendation was to include cost and impact drivers in the diagram, if they can be distinguished from the modeling exercise. However, this presents challenges: cost and impact are interdependent, as total cost is the product of unit cost and intervention coverage, and the ICER is a relative measure derived from ranges of both cost and impact. As such, it may be difficult to quantitatively isolate cost and impact drivers across all pathways. Nonetheless, this is an area that modeling teams could explore qualitatively.

2. Target audience of M3CPI results

   This modeling exercise is designed to generate evidence on cost-effective strategies to support the revision of WHO's GPP. The output will be a high-level, concise document aimed at informing global recommendations.

   It is essential that the findings are communicated clearly and accurately to the primary audience – namely, the WHO GMP team responsible for revising the GPP and translating the results into high-level policy recommendations. In addition, technical advisory groups such as IVIR-AC, MPAG and SAGE, who possess a certain level of familiarity with modeling, are also key stakeholders.

   While national malaria control programs and funders may eventually use the results, they are expected to do so through the lens of the WHO's GPP and be aware of the caveats of the generalizable M3CPI results. These stakeholders should contextualize the findings before applying them, rather than relying directly on the reports or outputs from this modeling exercise.

3. Key elements for communicating modeling findings

The advantages and limitations of this modeling exercise should be clearly highlighted in the communication package. Unlike the current WHO's GPP, which does not address combinations of interventions or incorporate cost considerations, this modeling effort fills those critical gaps. Modeling is the only viable approach to explore these dimensions in a structured and transparent manner, and the use of multiple models enhances the robustness and credibility of the predictions.

It is also important to emphasize that this exercise is not intended to provide country-specific recommendations on how to allocate interventions. Instead, it aims to inform global guidance by identifying cost-effective strategies across different archetypes.

Key assumptions and sources of uncertainty should be transparently communicated. These include differences in model structures (which is also a strength of the exercise), the use of archetypes, the spatial scale of the models, underlying data sources, interpretation approaches, how coverage levels are modeled, and the range of delivery strategies considered.

The communication package should focus on archetypes rather than specific interventions. For example, it should guide what types of settings should consider when prioritizing malaria interventions. The interpretation of findings should remain flexible and not be limited to simply adding or removing a single intervention. Countries may choose to implement intervention A in one area and intervention B in another, even if the latter is a second-best option for that archetype, depending on contextual factors such as donor support and operational feasibility.

4. Defining and communicating archetypes

The resulting archetypes should reflect meaningful differences in outcome pathways and key contextual characteristics that WHO aims to address, such as transmission intensity, seasonality, and income level. If income level is included as a criterion in defining archetypes, the cost-effectiveness thresholds should be adjusted accordingly to reflect economic context.

The modeling teams have already compiled a comprehensive list of potential archetype-defining variables. Archetypes will be developed using a combination of qualitative exploration and quantitative statistical clustering based on these drivers.

The number of archetypes will be determined by the modeling results. Regardless of the final number, results for all archetypes should be presented and reported. Each archetype should be accompanied by interpretation notes and caveats to ensure consistency and clarity in communication.

High-level, generalizable patterns should be drawn from the prioritization pathways within each archetype. While some archetypes may yield robust and consistent results, others may be more sensitive to cost assumptions. In such cases, limitations should be clearly communicated, and users should be advised to interpret recommendations with caution.

The modeling teams will synthesize these findings and present them in the third technical consultation in October 2025. Refinement and improvement will be

discussed during the consultation.

Finally, there was feedback on the term ‘archetypes’ itself, suggesting that a more intuitive or appropriate term should be explored.

5. Modeling outcomes

   A concern was raised about the potential for overly complex communication if too many outcomes are presented. Currently, the minimum set of outcomes includes malaria cases averted and malaria deaths averted, though malaria direct mortality estimates are generally more uncertain in the models and derived from severe malaria estimates, and DALYs averted will be calculated based on the predicted number of deaths. To assess the robustness of the findings, the modeling teams will run all relevant outcomes, at a minimum including incidence and deaths, and evaluate whether the results remain consistent across these measures.

6. Publication strategy

   The first publication of this work should be the WHO’s GPP, with the full report of the modeling exercise included as reference. Ultimately, the findings should also be published in a peer-reviewed journal, which could be aligned to be just after the WHO’s GPP, in coordination between the modeling groups, the journal and WHO. However, it is important to ensure that the results are not misinterpreted or misused by countries. Clear communication and contextual framing will be essential to prevent unintended applications of the findings outside the scope of the exercise.

Conclusions

The meeting underscored the importance of presenting M3CPI results in a clear, structured, and policy-relevant manner. Archetypes will serve as the foundation for summarizing findings, with their definitions grounded in model outputs and contextual characteristics. The interactive Sankey diagrams were endorsed for internal use to illustrate prioritization pathways, while communication to external audiences will focus on high-level, interpretable guidance. Emphasis was placed on transparently conveying uncertainty, assumptions, and limitations, and ensuring that outputs support WHO’s GPP revision without being misapplied at the country level. A phased publication strategy was proposed, beginning with the GPP and followed by peer-reviewed dissemination.

Needs of additional modelling work beyond M3CPI

Given the tight timeline and the complexity involved in modeling the cost-effectiveness of malaria intervention combinations, additional work could be considered for a second phase – pending the availability of funding. Potential areas for expansion include:

1. Estimating total malaria mortality, including indirect mortality
2. Assessing the combined impact of interventions such as SMC and ITNs
3. Evaluating multiple delivery strategies for interventions

4. Incorporating greater contextual complexity
5. Analyzing the distribution of spending across interventions and settings
6. Exploring trade-offs between efficiency and equity
7. Identifying interactions between interventions, potentially by focusing on specific archetypes to better understand the conceptual framework and inform simplification rules
8. Extending the time horizon of the analysis to capture cost-effectiveness of new interventions and long-term effects

These additions would enhance the comprehensiveness and policy relevance of the modeling work.

Project timeline

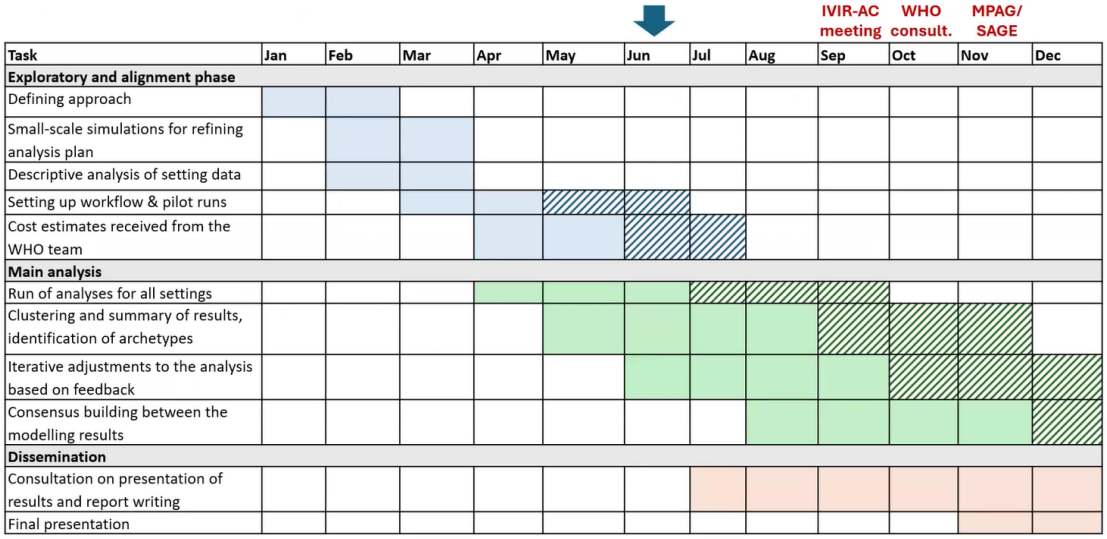

Fig. 3. Revised project timeline as proposed at the end of the meeting. Solid-colored cells indicate the original plan, while dashed cells represent the updated timeline.

Given that no major changes to the modeling methodology were raised during the meeting, the modeling teams confirmed they can proceed with the agreed workplan. However, due to an expected delay in receiving cost estimates from the WHO costing team, the modeling work will be postponed by approximately two months.

To address this delay, an in-depth discussion was held to explore ways to streamline the systematic review process – currently conducted by two independent reviewers – while maintaining sufficient rigor. The group agreed that additional manpower is essential to accelerate progress and meet project deadlines. The Gates Foundation (GF) is likely to provide financial support for this purpose. However, to avoid delays associated with issuing new contracts, any additional personnel should come from existing teams.

STPH may reallocate a new part-time staff member to support the review. PATH and CHAI, both of which have experience in malaria budgeting and costing, may also be able to contribute to data extraction activities.

Three potential adjustments to the systematic review process were proposed, with the possibility of implementing any combination of them also being considered:

1. Single screening round: Shift from dual independent screening to a single reviewer per article to reduce time, accepting a trade-off in methodological rigor.
2. Early termination of screening: Conclude screening after a pre-agreed number of relevant articles have been reviewed, using COVIDENCE's machine learning functionality to prioritize the most promising studies. This would allow for a timely batch of cost data but may limit the comprehensiveness of cost distribution.
3. Parallel review process: Bring in two to three additional reviewers to support full-text review and data extraction in parallel with ongoing title and abstract screening. This would maintain the standard two-reviewer approach while increasing efficiency.

Further discussions will be needed to finalize the approach and ensure that cost estimates are available by early July 2025.

In the interim, the modeling teams will continue working with dummy cost data to test and refine the models. It was noted that adding more personnel to the modeling teams at this stage would not accelerate progress.

Key milestones and deliverables include:

- September 2025: Methodology approach and communication plan will be presented to IVIR-AC for review and feedback.
- October 2025: Final results will be shared at the third WHO technical consultation, where the group will work collaboratively to finalize conclusions.
- November 2025: The final report will be submitted for consideration by MPAG and SAGE.
- February 2026: The WHO' will be finalized and published, ensuring alignment with the timelines of Global Fund's Eighth Replenishment (GC8), as country allocation letters will be sent early March 2026. The drafting process is expected to take 4–6 weeks.

Conclusions

The second WHO technical consultation on M3CPI reaffirmed the value of a multi-model approach to inform strategic malaria intervention planning. The consultation validated the use of two independent models (*malariasimulation* and *OpenMalaria*) to simulate intervention impacts across diverse settings in sub-Saharan Africa. This approach enhances the robustness and generalizability of findings, despite differences in how uncertainty is handled.

Participants confirmed key methodological assumptions, including fixed case management coverage, context-specific intervention scaling-up and suspensions, and the exclusion of new tools under development. The costing methodology was reviewed and endorsed, with consensus on using published and grey literature to build a comprehensive intervention cost database. While limitations such as the inability to model scale effects and/or country-specific costs were acknowledged, the approach was deemed appropriate for informing global guidance.

Preliminary results from pilot settings demonstrated the feasibility of modeling 24

intervention combinations across diverse contexts, capturing both short- and long-term impacts through 2040. The group supported a flexible, output-driven approach to defining archetypes after modeling runs, allowing for comprehensive scenario exploration. Simplified assumptions using averages and uncertainty ranges were endorsed to balance realism with model manageability.

The group also emphasized that the intention of the M3CPI project is not to guide country-level decision making on the optimal mix of malaria interventions. For that, customized analyses would be required taking into consideration local data, evidence and involvement of local decision makers. The analysis plan will be updated based on the discussion during the meeting, including a section on model comparison to harmonize outputs and interpret differences across models.

Looking ahead, participants identified several areas for potential expansion in a second phase of M3CPI, including modeling indirect malaria mortality, evaluating synergies between interventions and cost-effectiveness of multiple delivery strategies, exploring efficiency-equity trade-offs, and extending the time horizon to capture long-term effects. These additions would enhance the comprehensiveness and policy relevance of the modeling work.

The group proposed streamlining the process of systematic review on malaria intervention costs and increasing number of experts to complete the development of the cost database to facilitate the completion of M3CPI project towards the end of 2025. This will allow time for updating GPP to inform country applications to GC8 in March 2026.

The meeting concluded with a shared commitment to completing simulations, finalizing the cost database, and synthesizing findings into actionable archetypes from both independent models. These outputs will inform the WHO's GPP revision MPAG/SAGE deliberations and global recommendations, and supporting evidence-based decision-making in resource-constrained settings.

Next steps

Further coordination is needed between the WHO costing team and the modeling teams to finalize the details of the cost estimates and to determine whether additional manpower is available to support the systematic review process.

Based on the discussions during the meeting, the modeling teams will revise the analysis plan, including a section of model comparison, and proceed with the analysis as agreed. WHO will review the revised analysis plan to ensure the revision will be aligned with the conclusions from this technical consultation and with the WHO multi-model comparison guide.

Annex 1: Meeting agenda

Global **Malaria** Programme

World Health Organization

WHO Technical Consultation to Review Progress on Malaria Multi-Model Comparison of Priority Interventions

3-4 June 2025, virtual meeting from WHO room D45044, Geneva (CET)

Chairperson: Dr Sheetal SILAL
Rapporteur: Dr Karene Hoi Ting YEUNG

AGENDA

Tuesday, 3 June 2025		
11:00 – 11:10	Welcome and introduction of participants	Chairperson
11:10 – 11:20	Opening remarks, M3CPI in changing international context	Vasee Moorthy
11:20 – 11:40	Methods of malaria multi-model comparison of priority interventions	Monica Golumbeanu
11:40 – 12:00	Discussion	
12:00 – 12:05	Progress on compilation of malaria costing database	Karene Yeung
12:05 – 12:20	Discussion on cost analysis	Kathy Leung (discussant)
12:20 – 12:40	Results from pilot settings Results from pilot settings	Tom Brewer
12:40 – 13:00	Discussion	
13:00 – 13:30	Break	
13:30 – 14:00	Review emerging issues and solutions to inform completion of analysis • parameters of malaria transmission • epidemiological outcomes, including effectiveness and impact • economic inputs and outcomes, including cost-effectiveness • others	Emilie Pothin & Peter Winskill
14:00 – 15:00	Discussion	Tom Smith (discussant)
	End of day 1	

Wednesday, 4 June 2025		
11:00 – 11:10	Recap of Day 1	Rapporteur
11:10 – 11:30	Discussion on unresolved emerging issues	
11:30 – 12:00	Options for presentation and communication of main outputs and conclusions of the M3CPI analysis	Emilie Pothin & Peter Winskill
12:30 – 13:00	Discussion	William Moss (discussant)
13:00 – 13:30	Break	
13:30 – 13:45	De-prioritization pathway: emerging scenarios and demands from multiple stakeholders in relation to planned M3CPI analysis	Peter Winskill
13:45 – 14:00	Discussion on need for additional modelling work, beyond M3CPI	
14:00 – 14:20	Review timelines to complete the M3CPI: IVIR-AC in September, WHO consultation in October and MPAG/SAGE in November	Monica Golumbeanu
14:20 – 14:55	Discussion	
14:55 – 15:00	Concluding remarks and next steps	Vasee Moorthy
	End of the meeting	

Annex 2: List of participants

Global **Malaria** Programme

WHO Technical Consultation to Review Progress on Malaria Multi-Model Comparison of Priority Interventions

3-4 June 2025, Virtual meeting, WHO room D45044, Geneva (CET)

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Some of the documents related to this session are currently confidential and not available for public access.

World Health Organization

Session 10: Additional seasonal doses of malaria vaccine (7 doses vs. 5 doses)

Session 11: 3 doses vs. 4 doses of malaria vaccine in perennial settings

Modelling the public health impact and cost-effectiveness of malaria vaccine dose schedules: background document to support IVIR-AC review

July 2025

Background and aims

WHO recommends the use of malaria vaccines for the prevention of *P. falciparum* malaria in children living in malaria-endemic areas, prioritizing areas of moderate and high transmission.[1] Malaria vaccines should be provided in a four-dose schedule starting from 5 months of age (with a minimum interval of four weeks between doses 1-3 and fourth dose given 6–18 months after the third dose to prolong protection). A fifth dose may be given in areas of highly seasonal transmission or where malaria risk remains high during the third year of life or beyond.

In 2025, two topics will be brought to the Strategic Advisory Group of Experts on Immunization (SAGE) and the Malaria Policy Advisory Group (MPAG) regarding the consideration of alternative dose schedules in the recommendation:

Topic #1: Malaria vaccine 3 versus 4 doses schedule in perennial (year-round) transmission settings
Specific policy questions:

- Is a 3-dose schedule of malaria vaccine safe and effective?
- Should a 3-dose malaria vaccine schedule be considered as an alternative option to a 4-dose schedule in some context?
- If recommended as an alternative option, are there specific epidemiological settings and/or implementation scenarios where a 3-dose schedule could be considered?

Topic #2: Additional annual malaria vaccine doses in areas of moderate or high, highly seasonal malaria transmission
Specific policy question:

- In areas of highly seasonal malaria transmission, should annual pre-season malaria vaccine doses provided to children until 5 years of age be considered as an option to reduce malaria burden?

To support the SAGE and MPAG evidence review, modelling is being conducted to estimate the public health impact and cost effectiveness of the different dose schedules being considered in comparison to the currently recommended dose schedules. This modelling builds on previous analyses and incorporates data available from a number of recent malaria vaccine studies.

Mathematical models to evaluate malaria vaccines were first developed in 2015, examining the addition of the RTS,S/AS01 malaria vaccine to existing malaria control interventions and treatment, following the conclusion of the Phase 3 trial. These models were developed by multiple groups and used harmonized inputs drawing on data from the RTS,S/AS01 Phase 3 clinical trials and malaria disease burden studies. Subsequently, these modelling analyses were updated in 2021 by two of the groups (Swiss Tropical Public Health Institute and Imperial College) to estimate impact and cost-effectiveness using data from the RTS,S/AS01 Phase 3 clinical trials, as well as additional evidence from the Malaria Vaccine Implementation Programme (MVIP). The models included previously modelled and validated disease and vaccine parameters (from the 2015 analysis), with assumptions and cost of delivery estimates from the MVIP.

In 2023, further modelling on the public health impact and cost-effectiveness of the R21/Matrix-M malaria vaccine (R21) was conducted by Imperial College. The modelling was informed by data from the R21 Phase 2b study in Burkina Faso that evaluated seasonal vaccination, and were validated against vaccine efficacy data from 5 the five study sites in the R21 Phase 3 trial.

All models predicted a substantial additional public health impact and high cost-effectiveness of a 4-dose schedule of RTS,S and R21 compared with no vaccination, across a wide range of transmission settings (results are summarized in Penny et al[2] and Schmidt et al[3]). Further details on public health impact and cost-effectiveness modelling are described in the 2021 Full evidence report on the RTS,S/AS01 malaria vaccine[4] and its Annex 9[5] and the 2023 Full evidence report on the R21/Matrix-M malaria vaccine.[6] Both models have been previously reviewed by IVIR-AC in 2015 and 2024 as part of the WHO recommendation processes for RTS,S and R21.

Modelling for Topic 1

To estimate the comparative impact of a 3-dose and 4-dose schedule, modelling has been conducted that incorporates the data from a case control study (embedded within the MVIP), which evaluates vaccine effectiveness against severe malaria of 3 doses vs. 4 doses. Moreover, further model calibration and validation can also be conducted with additional data available since the previous 2023 modelling analyses: 46-months of follow-up from the MVIP and 2-years of follow-up from the R21 Phase 3 trial. Also of interest is the potential impact and cost-effectiveness of different dose allocation strategies.

The aims of modelling of 3-doses vs. 4-doses of malaria vaccine are:

- To estimate the potential public health impact and cost-effectiveness of a 3-dose vs. 4-dose malaria vaccine schedule
- To estimate the potential public health impact of different vaccine allocation strategies, such as vaccinating fewer children with 4-doses or more children with 3 doses

Modelling estimates will be based on the previously used *OpenMalaria* model (The Kids Research Institute, formerly Swiss Tropical Public Health Institute) and the *malariasimulation* model (Imperial College).

Modelling for Topic 2

To estimate the impact of additional pre-season doses up to 5 years of age (up to 7 doses total), modelling has been conducted that builds on previous analysis of RTS,S seasonal vaccination, incorporating further data on additional doses from the extended 2 year follow-up of the Phase 3b trial.

The aims of modelling additional seasonal doses of malaria vaccine are:

- To estimate the public health impact and cost-effectiveness of a 7-dose schedule vs. a 5-dose schedule when administered in a seasonal or hybrid approach
- To estimate the public health impact and cost-effectiveness of different dose allocation strategies, such as vaccinating fewer children with 6 or 7 doses or more children with a 5-dose schedule

Modelling will be based on the previously used *malariasimulation* model (Imperial), and analysis will be conducted by PATH.

References

[1] Malaria vaccine: WHO position paper. Weekly Epidemiologicl Record, 13 May 2024. https://www.who.int/publications/i/item/who-wer-9919-225-248

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[3] Schmidt et al, 2024. The public health impact and cost-effectiveness of the R21/Matrix-M malaria vaccine: a mathematical modelling study. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00816-2/fulltext

[4] Full evidence report on the RTS,S/AS01 malaria vaccine, 2021. https://zenodo.org/records/6394605

[5] Modelled public health impact and cost effectiveness estimates of RTS,S/AS01 malaria vaccine in perennial and seasonal settings (August 2021) https://zenodo.org/record/6395841%20

[6] Full evidence report on the R21/Matrix-M malaria vaccine, 2023. https://zenodo.org/records/10908560