World Health Organization

Department of Immunization, Vaccines and Biologicals (IVB)

IVIR-AC – June 2024

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

MICROSOFT TEAMS - VIRTUAL MEETING

WHO HEADQUARTERS, GENEVA, SWITZERLAND

28 June 2024 – 1 July 2024

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)
28 June 2024 – 1 July 2024

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

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

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Current IVIR-AC – Advisory Committee Members

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**
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**
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William Moss, International Vaccine Access Center Johns Hopkins Bloomberg School of Public Health, **USA**
Patrick Munywoki, U.S. Centers for Disease Control and Prevention, Kenya, Nairobi, **Kenya**
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**
Xuan-Yi Wang, Research Scientist, Shanghai Medical College, Fudan University, **China**

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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)

World Health Organization

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)
28 June to 01 July 2024
Virtual Meeting
WHO HQ
Agenda

Day 1: Friday, 28 June 2024 (CEST)

Time CEST	Session	Purpose of the session, target outcomes and questions for IVIR-AC	Duration
13:30	**Welcome** K O'Brien	Update on global strategies and issues of relevance to WHO	**10 min**
13:40	**Introduction** S Silal, Chair P Lambach, Executive Secretary	Welcome, Objectives, Administrative information	**10 min**
13:50	**Revisiting the SAGE criterion for Rubella Vaccine Introduction** Background summary.*10 min.* N Crowcroft *Technical Presentation 10 min.* K Frey *Technical Presentation 10 min.* M Ferrari Discussion and preliminary IVIR-AC recommendations 40 min. IVIR-AC FPs: Meru Sheel, Allison Portnoy, Sun-Young Kim, Patrick Munywoki **SAGE Focal Points:** Shabir Madhi	**FOR DECISION** WHO SAGE policy recommends not introducing a Rubella-containing vaccine (RCV) unless immunization coverage has reached at least 80% for either the first dose of Measles-containing vaccine or in its last nationwide nonselective campaign. This is to avoid a potential risk of future increases in congenital rubella syndrome (CRS) due to a reduction in the force of infection leading to future increases in susceptible adults of childbearing age, also known as the paradoxical effect. IVIR-AC is being asked to review two studies that explore the risk of the paradoxical effect, comment on the methodology, make suggestions for any modifications or clarifications that are required, and comment on the needs for future related work	**1h 10 min**
15:00	**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	**10 min**
15:10	**Next steps** P Lambach, Executive Secretary	Follow-up from WHO Secretariat	**10 min**
15:20	**End of day**		

Day 2: Monday, 01 July 2024 (CEST)

Time CEST	Session	Purpose of the session, target outcomes and questions for IVIR-AC	Duration
12:00	**Opening** S Silal, Chair	Summary of the previous day and structure of the closed session	**10 min**
12:10	**Closed session**	Closed session discussion/finalization of recommendations among IVIR-AC focal points of the day's sessions	**50 min**

13:00	**Closing and Next Steps** S Silal, Chair P Lambach, Executive Secretary	Summary of the day's findings and follow-up from WHO Secretariat	**10 min**
13:10	**End of day**		

winAd hoc Meeting of the Advisory Committee on Immunization and Vaccines-Related Implementation Research (IVIR-AC)
Microsoft Teams
Venue VIRTUAL
28 June to 01 July 2024

Draft list of participants

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World Health Organization

Background information to the sessions

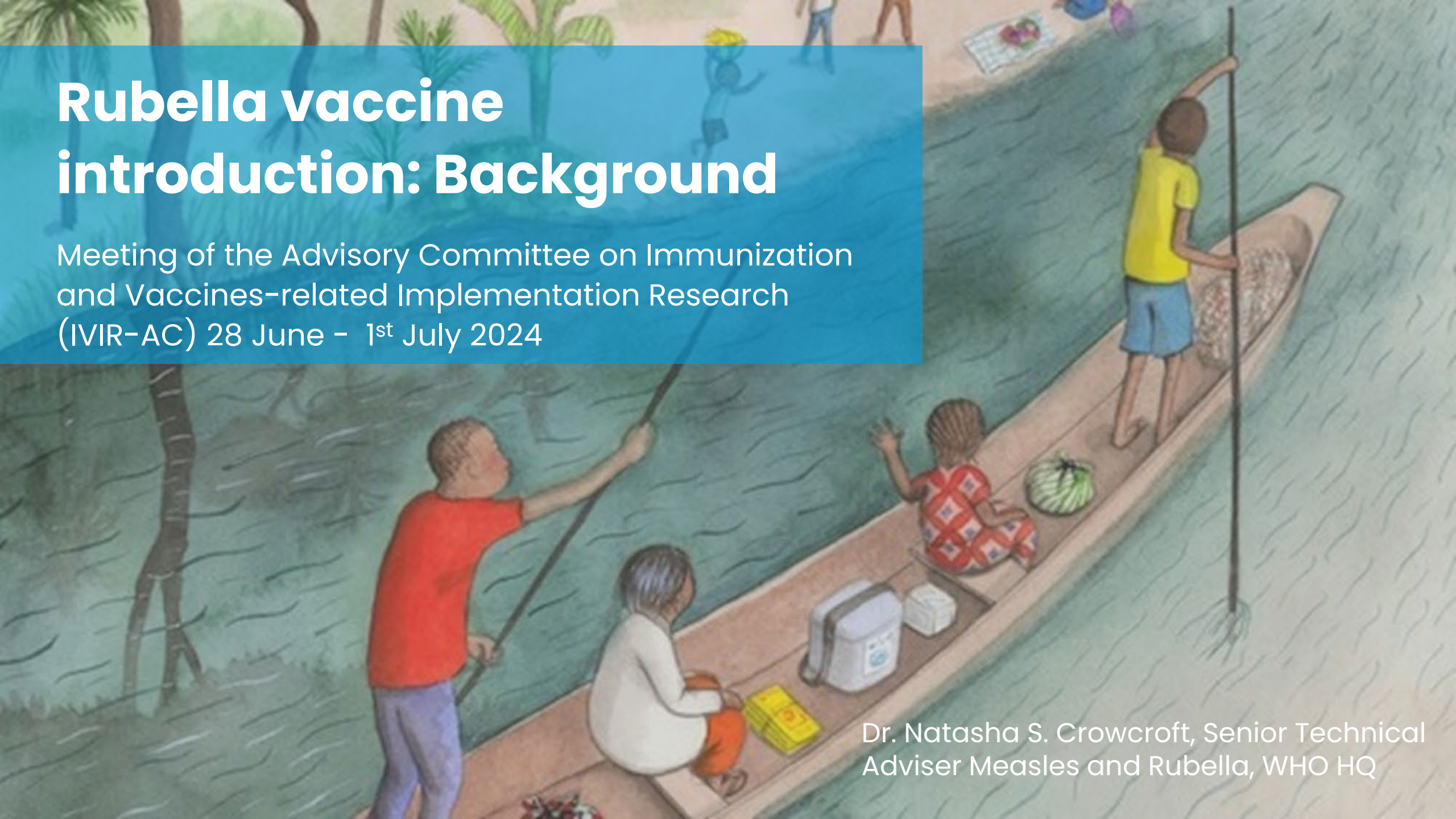
World Health Organization

Session

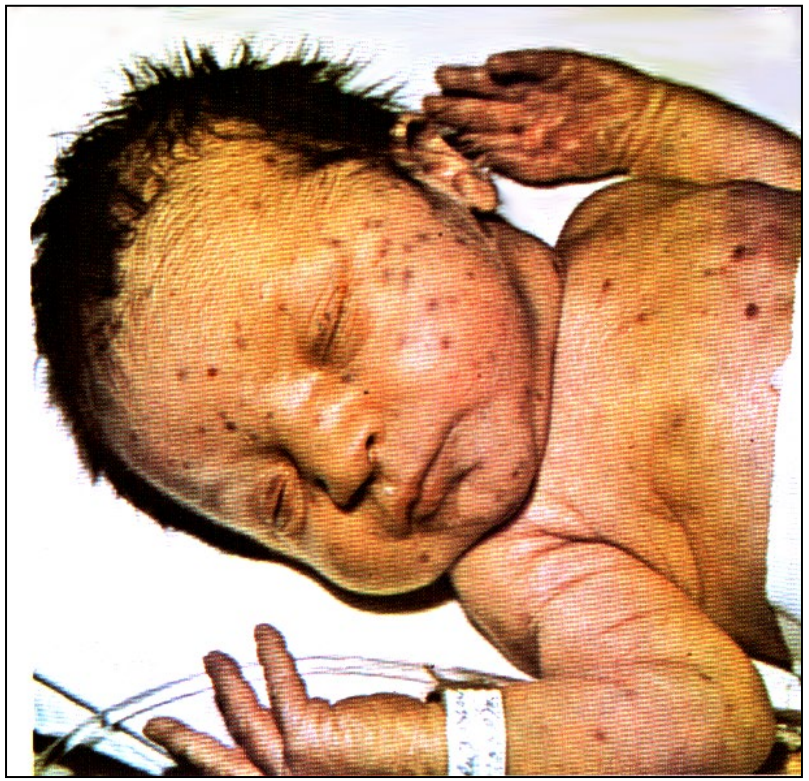
Revisiting the SAGE criterion for Rubella Vaccine Introduction

Rubella vaccine introduction: Background

Meeting of the Advisory Committee on Immunization and Vaccines-related Implementation Research (IVIR-AC) 28 June - 1st July 2024



Dr. Natasha S. Crowcroft, Senior Technical Adviser Measles and Rubella, WHO HQ



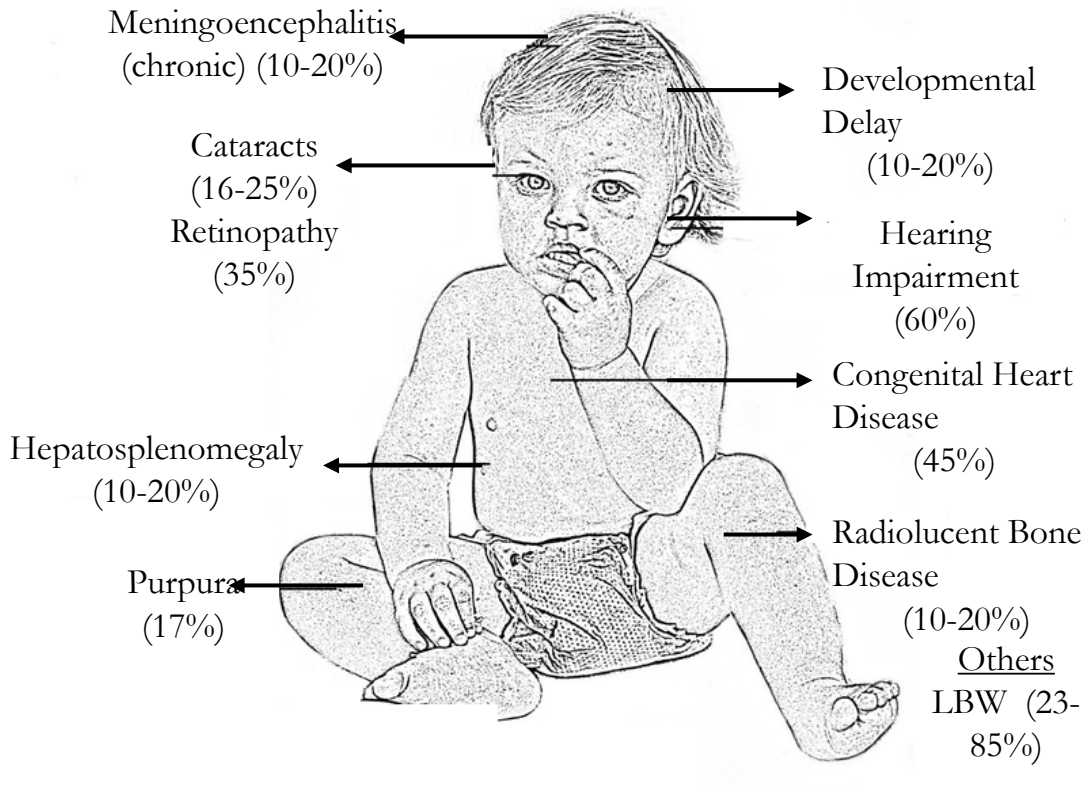
Dermal erythropoiesis (Blueberry muffin syndrome): An interference with the normal production of blood cells in the bone marrow

Outline

- Congenital Rubella Syndrome (CRS)
- WHO recommendations for Rubella Containing Vaccine (RCV) and RCV introduction
- Current programmatic context
- Request to IVIR AC

Congenital Rubella Syndrome

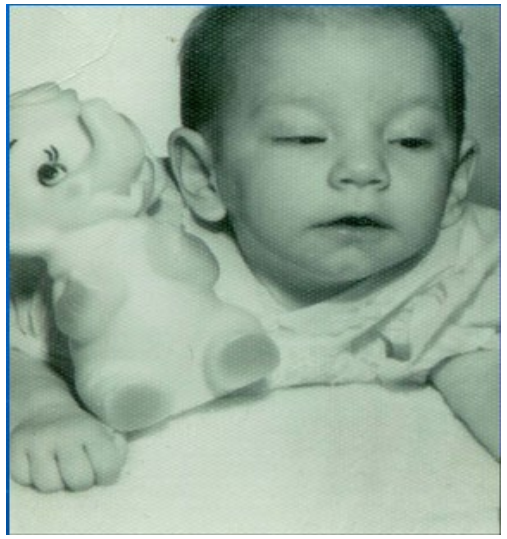
Weeks gestation	CRS
1–10	90%
11–12	33%
13–14	11%
15–16	24%
≥17	0%



Miller E. *Lancet* 1982; 2: 781-4.

Lifelong Disabilities of CRS

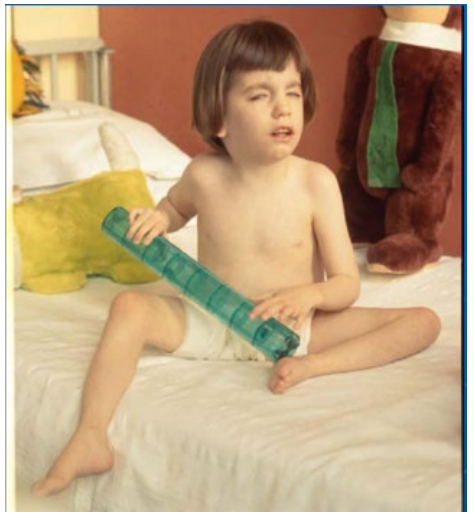
1966



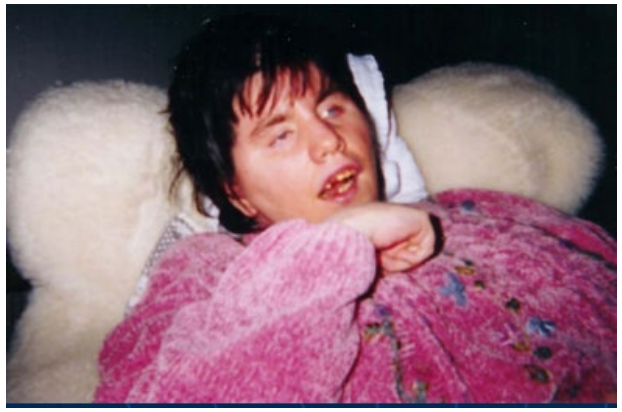
At ~5 years of age:

- Severe developmental delay
- Cataract
- Deafness

1970



CRS is largely now eliminated in high income countries, but thousands of CRS babies are born annually in countries yet to introduce rubella vaccine.



2005

Often the disease burden is not known to be due to the preventable rubella infection that occurred during pregnancy.

With acknowledgement of Dr. Louis Cooper who provided the photographs

WHO recommendations

Rubella Vaccine: 1 dose is 95% effective, conferring lifelong immunity; WHO recommends routine immunization of boys and girls in combination with measles

History of WHO recommendations for RCV introduction:

2000: Countries can introduce RCV if:

- They can achieve a nationwide coverage level of 80% or greater in their routine program

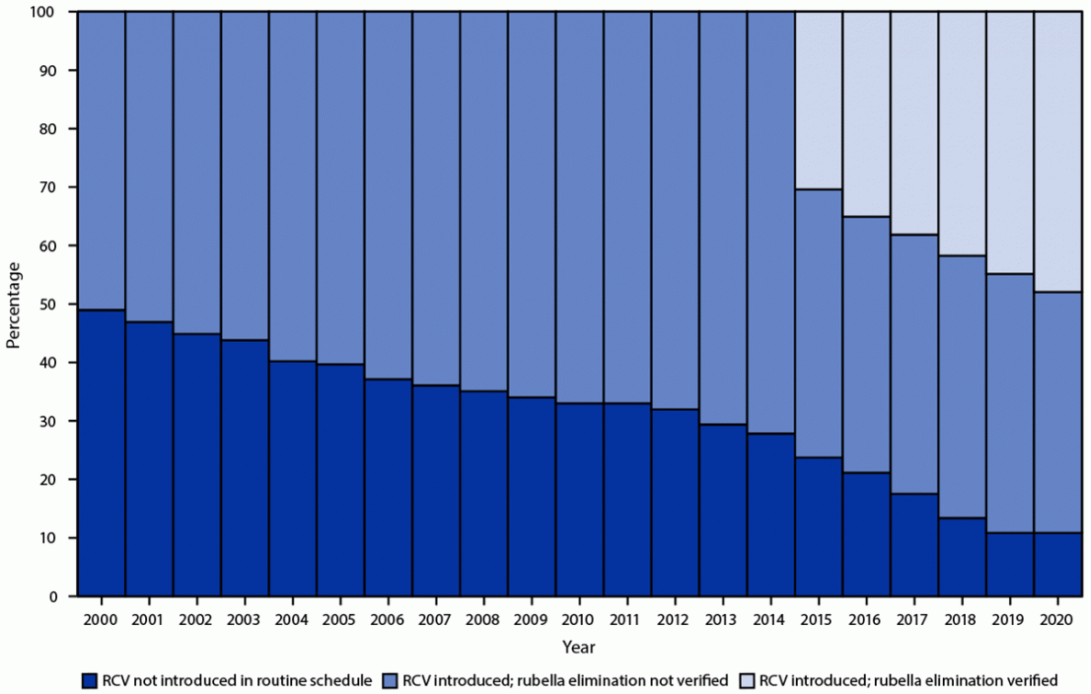
2010: Countries should introduce RCV if:

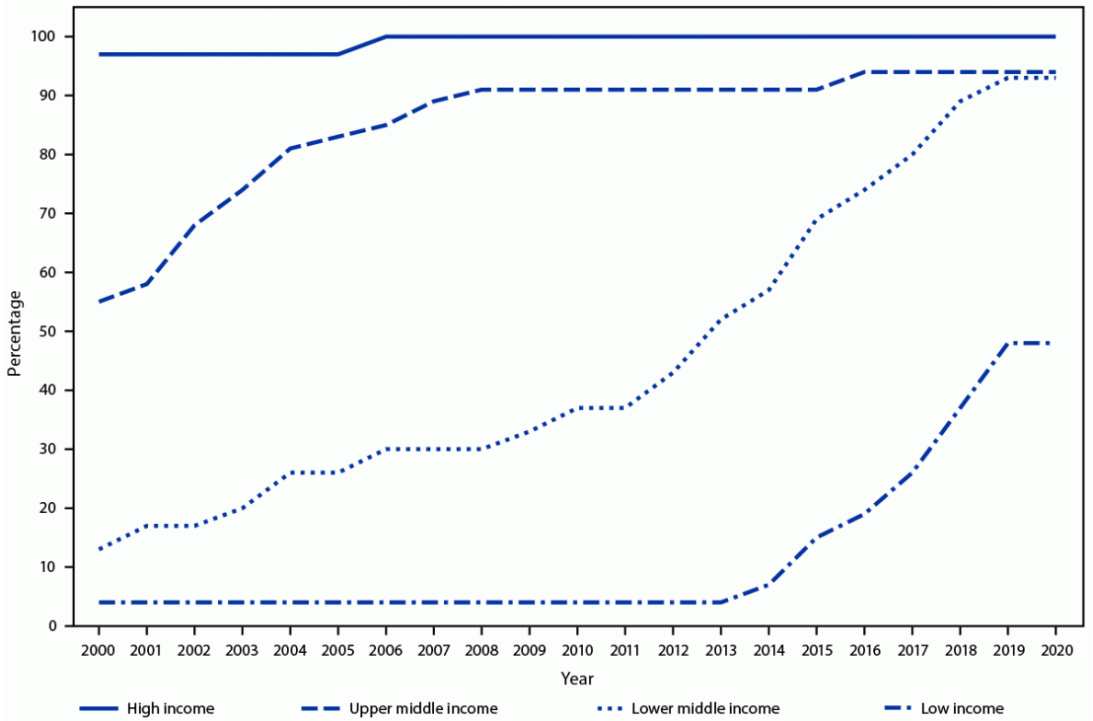
- They can achieve a nationwide coverage level of 80% or greater, through either routine immunization or campaigns, AND
- They conduct a wide age range campaign (1-14 years) prior to introduction

2020: 2010 requirements were upheld (Rubella Position Paper 2020)

Congenital Rubella Syndrome (CRS) cases fell from >100,000 per year to 32,000; Cases now occurring mainly in countries without rubella vaccine

Percentage of countries that have introduced rubella-containing vaccine in the routine immunization schedule and the percentage with verified rubella elimination, by year (first figure) and by World Bank income group (second figure) — worldwide, 2000–2020



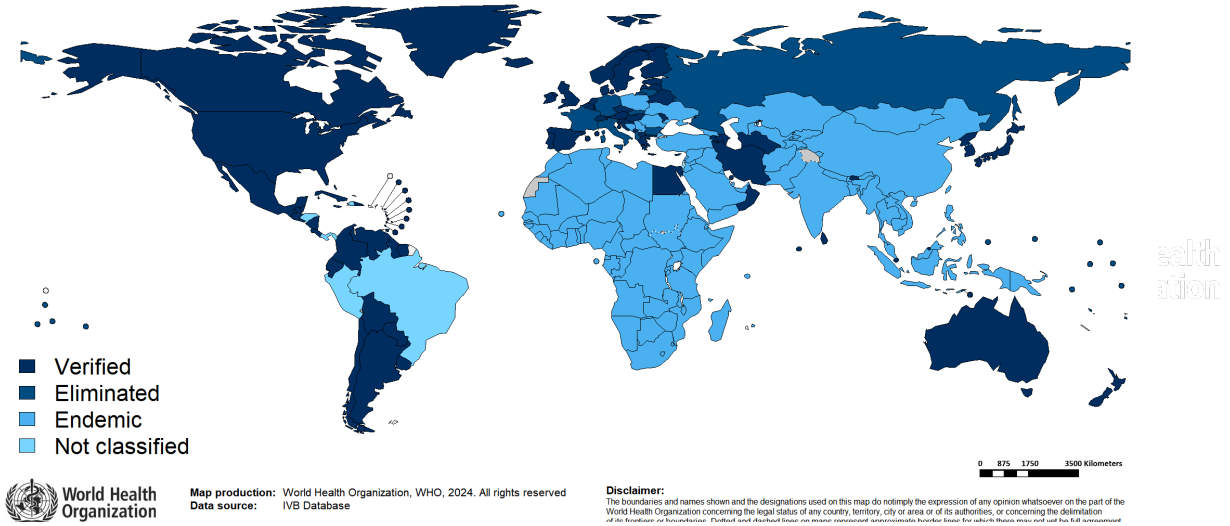


Zimmerman LA, Knapp JK, Antoni S, Grant GB, Reef SE. Progress Toward Rubella and Congenital Rubella Syndrome Control and Elimination — Worldwide, 2012–2020. MMWR Morb Mortal Wkly Rep 2022;71:196–201. DOI: http://dx.doi.org/10.15585/mmwr.mm7106a2external icon

Measles/rubella verification of elimination

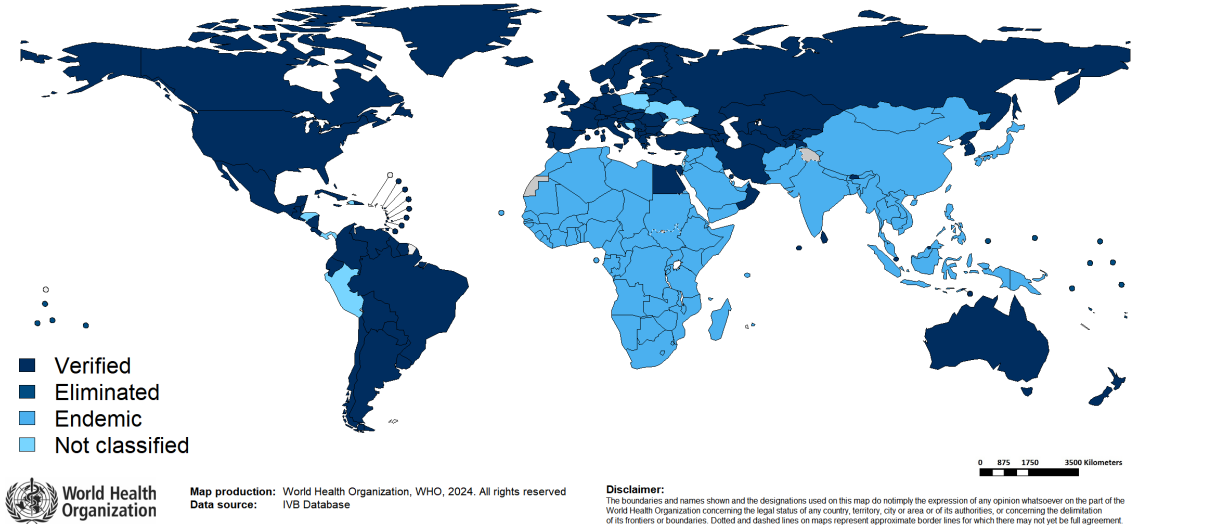
Measles

Region	Member States	Verified	% Verified	Eliminated	Endemic	Not classified
AFR	47	0	0	0	47	0
AMR	35	30	86	0	0	5
EMR	21	4	19	0	17	0
EUR	53	33	62	8	11	1
SEAR	11	5	45	0	6	0
WPR	27	6	22	13	8	0
GLOBAL	**194**	**78**	**40**	**21**	**89**	**6**



Rubella

Region	Member States	Verified	% Verified	Eliminated	Endemic	Not classified
AFR	47	0	0	0	47	0
AMR	35	31	89	0	0	4
EMR	21	4	19	0	17	0
EUR	53	49	92	0	0	4
SEAR	11	5	45	0	6	0
WPR	27	5	19	13	9	0
GLOBAL	**194**	**94**	**48**	**13**	**79**	**8**



Notes: Based on data available at WHO HQ as of 2024-06-10 . Terms used on this slide refer to the global framework for the verification of measles and rubella elimination. These terms might differ from those used by WHO Regional Offices.
Verified = Elimination verified by Regional Verification Commitee (RVC); Eliminated = Eliminated transmission but no RVC verification yet.

Current context has changed

Previous modelling was conducted under specific assumptions of R_0 and age-specific fertility rates

80% threshold to avoid future immunity gaps and outbreaks in older age groups - trading off prevention of current against potential future CRS

Changes to application of existing modelling methodologies include:

- New estimates of R_0
- Impact of demographic change
- Sub-national considerations

Accumulating **observational evidence** suggests robustness of elimination:

- Impact of wide age range introductory campaign highly effective at interrupting transmission
- >50% of countries have reached and sustained elimination
- None have lost elimination status despite drops in coverage (in contrast to measles)

Countries without RCV and anticipated date of introduction*

No.	Country	Anticipated date of introduction	Eligible	Survey from last SIA	MCV1 coverage
1	Mali	2024	Yes	>80%	70%
2	Sudan	2024	Yes	>80%	81%
3	South Africa	2024	Yes	NA	86%
4	Guinea-Bissau	2024	Yes	>80%	75%
5	Nigeria	2025	If approved by IRC	>80%	60%
6	DRC	2026	If approved by IRC	>80%	56%
7	Ethiopia	NA	TBD post 2025 campaign	>80%	56%
8	Chad	NA	TBD post 2024 campaign	71%	56%
9	Madagascar	NA	TBD post 2024 campaign	65%	44%
10	Afghanistan	NA	TBD post 2025 campaign	Pending	68%
11	Liberia	NA	TBD post 2024 campaign	Pending	79%
12	Niger	NA	TBD post 2025 campaign	Pending	65%
13	CAR	NA	TBD post 2025 campaign	Not Done	41%
14	Djibouti	NA	TBD post 2025 campaign	Not Done	50%
15	Guinea	NA	TBD post 2025 campaign	Not Done	47%
16	South Sudan	NA	Unknown	Not Done	72%
17	Somalia	NA	Unknown	Incomplete	46%
18	Equatorial Guinea	NA	Unknown	Not Done	53%
19	Gabon	NA	Unknown	Not Done	52%

*As of June 2024

Questions to be addressed by IVIR-AC

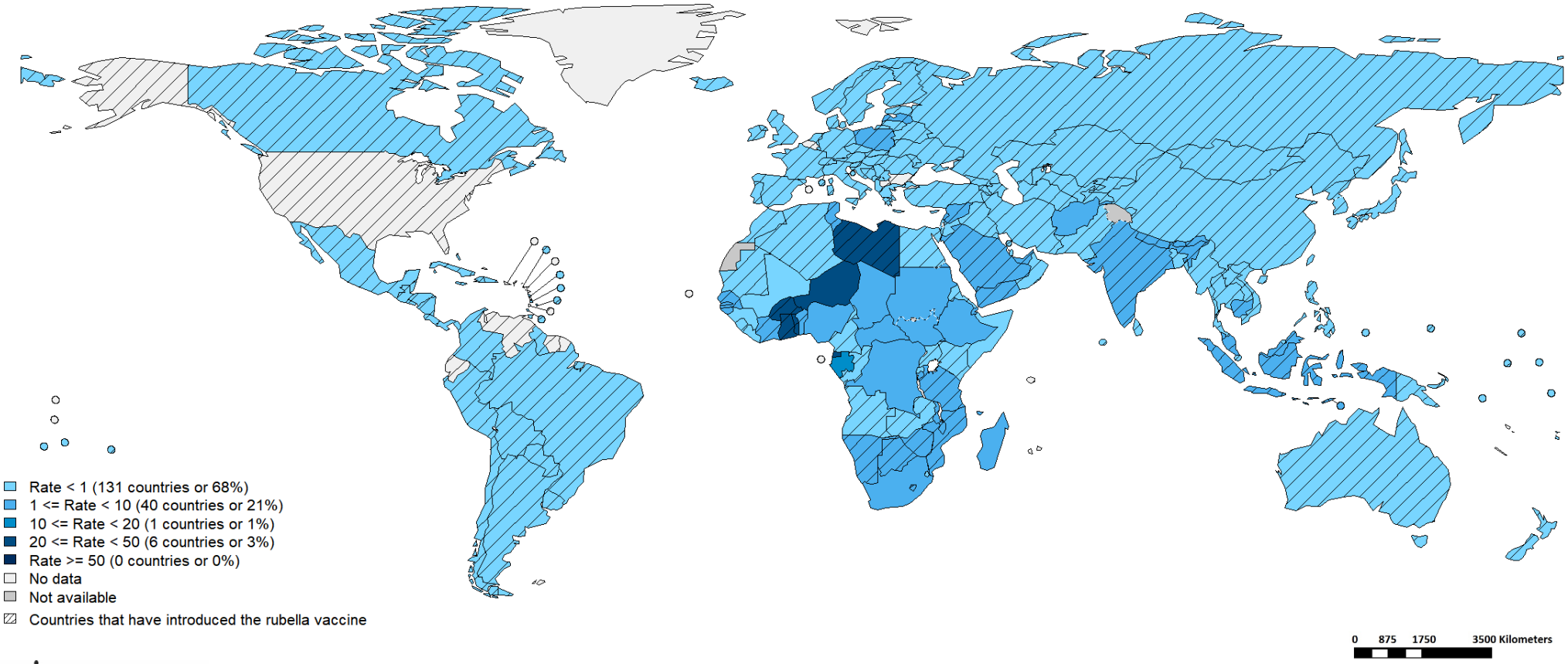
IVIR-AC is asked to review the modelling studies that have adapted established methodology to reassess the impact of RCV introduction versus status quo in the new context

IVIR-AC is requested to comment on the methodology and assumptions, make suggestions for any modifications or clarifications that are required, and comment on the need for future related work

Outcomes of this meeting will inform WHO SAGE as part of a package of evidence on RCV introduction to be reviewed in September 2024

Extra slides

Rubella Incidence Rate per Million (12M period)



Highest incidence rates

Country	Cases	Rate
Eq. Guinea	73	42.57
Togo	232	25.62
Burkina Faso	558	24.00
Ghana	720	21.10
Niger	562	20.66
Libya	140	20.32
Gabon	38	15.60
South Africa	555	9.19
Madagascar	260	8.57
Zimbabwe	118	7.08

Notes: Based on data received 2024-06 - Surveillance data from 2023-11 to 2024-04 - Incidence: Number of cases / population * 1,000,000 - Population data: World population prospects, 2019 revision

World Health Organization

Technical presentation 1

IDM INSTITUTE FOR DISEASE MODELING

Rubella vaccine introduction does not increase CRS burden

Kurt Frey

June 28, 2024

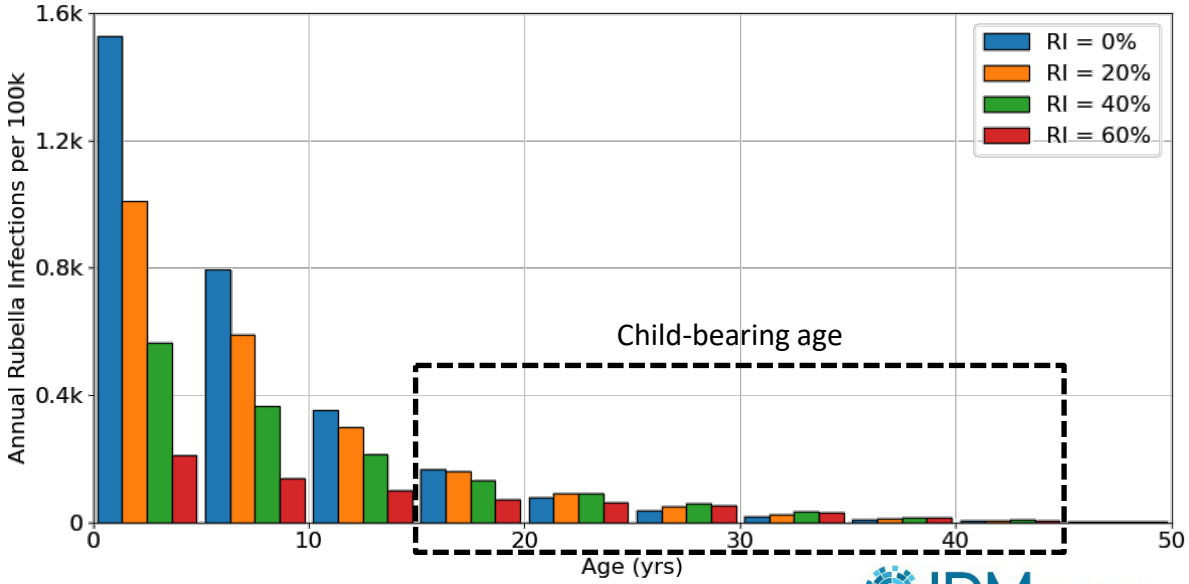
BILL & MELINDA GATES foundation

Average age-at-infection increases with vaccine coverage

Total rubella incidence (area under curve) and childhood incidence both decrease monotonically as vaccination coverage increases. Infection during childhood is mild or asymptomatic.

Incidence in some adult age groups may increase as the vaccination coverage increases.

Burden is calculated based on age-structured the incidence (model output) and the age-structured fertility rates (using data from the UN WPP).



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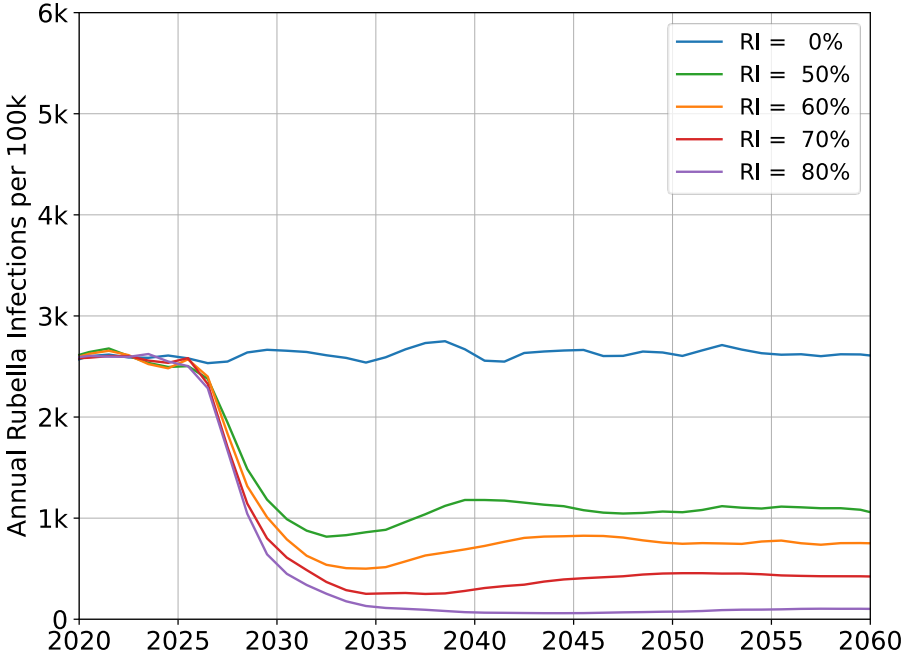
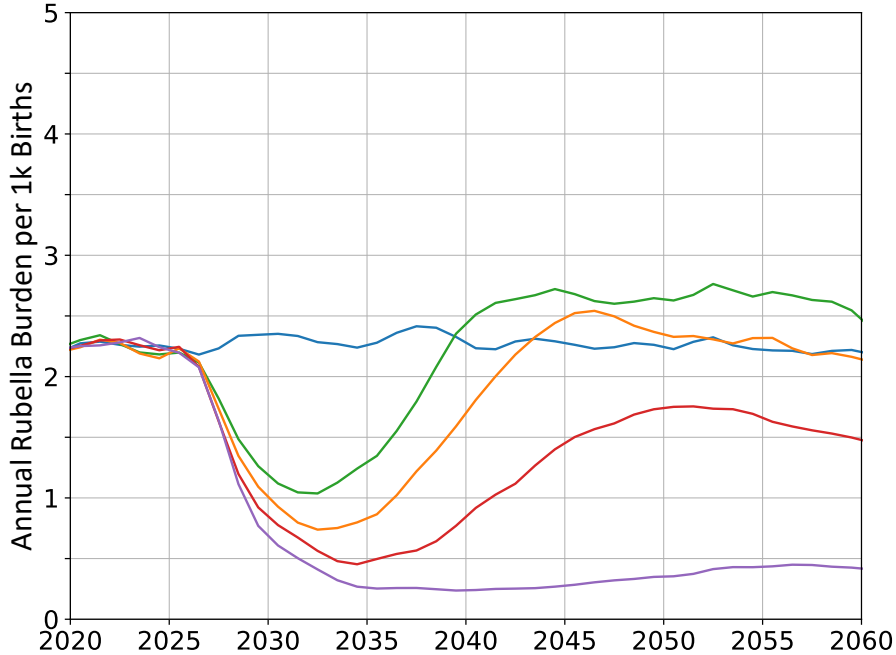
Disease equilibrium takes decades to establish

Transmission pre-vaccine is near equilibrium. The infection rate is at a new equilibrium within about 5 years, but the age distribution of cases continues to evolve for around 20 years.





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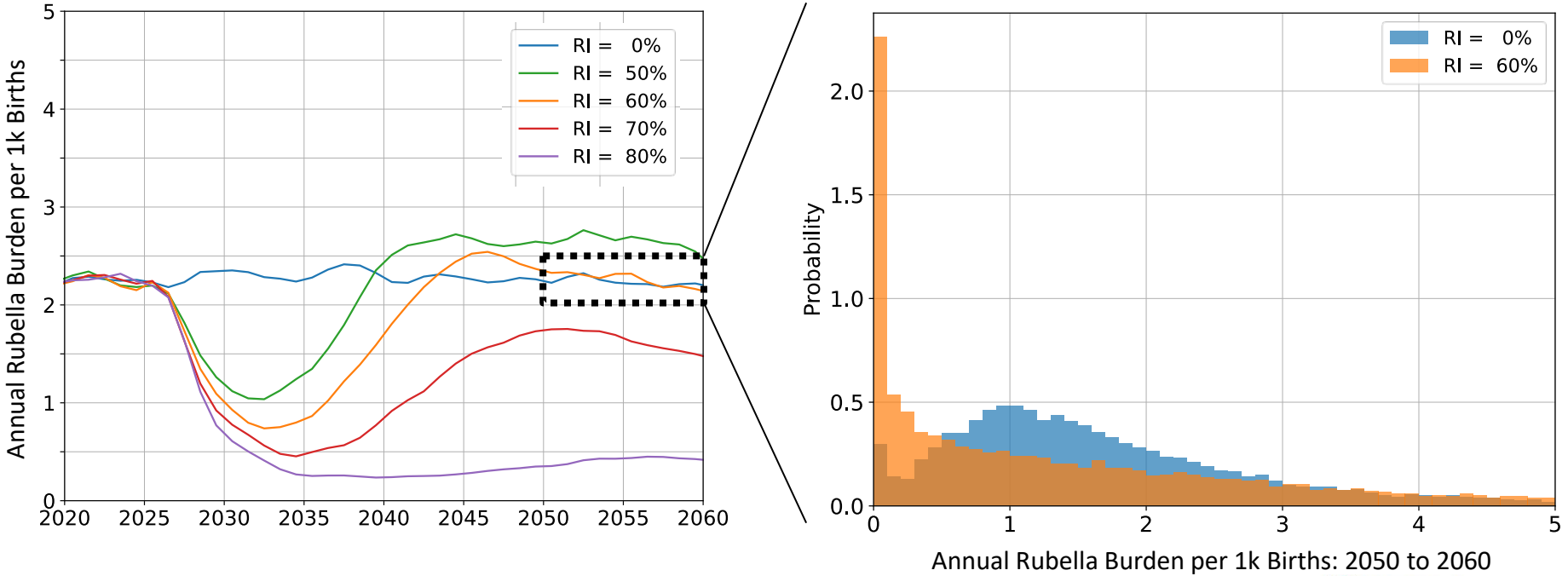
Vaccination leads to increased inter-year variability

Average yearly burden is equivalent for the period 2050 to 2060 in the scenarios with 0% and 60% coverage. However, both interruption and outbreaks are more common with vaccination.



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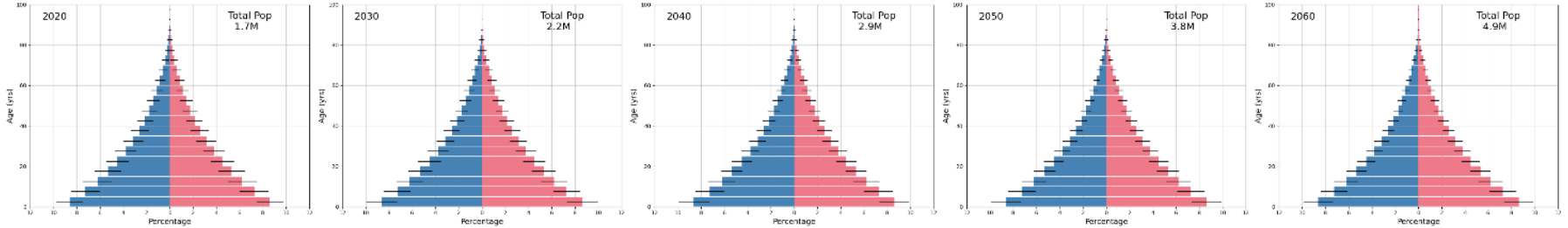
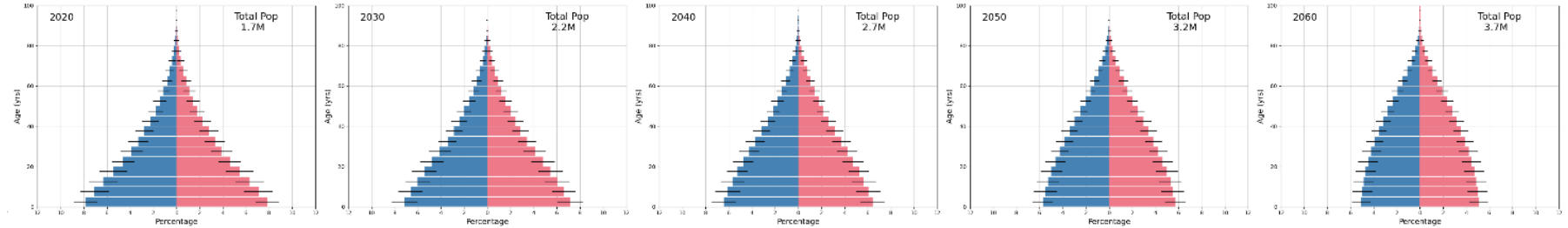
Demographics are never at steady-state

An equilibrium population pyramid is an approximation for modeling purposes.



Simulations leverage steady-state demographics (above) to clearly identify the time scales involved in vaccine introduction. Medium forward projections (below) are from UN WPP.

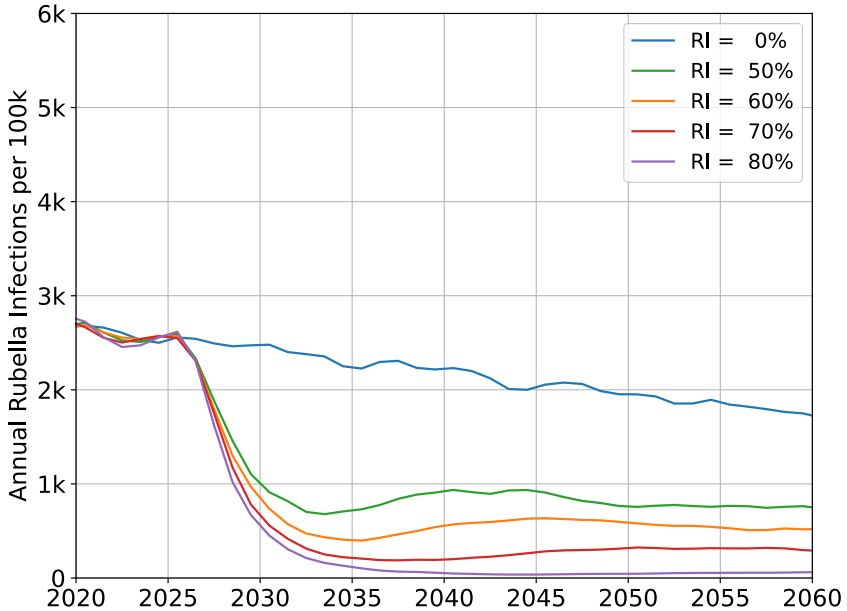


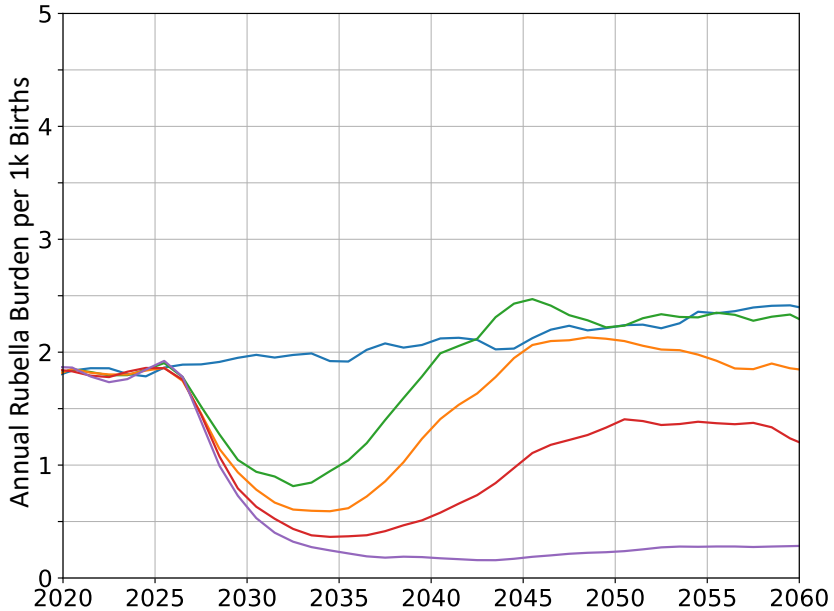
IDM INSTITUTE FOR DISEASE MODELING

Without vaccination, burden will increase

Declining fertility reduces transmission intensity but also increase baseline rates of CRS.

Disease control also become easier. Intermediate levels of RI not expected to reduce CRS using steady-state demography will achieve a significant reduction with declining fertility.





Rubella vaccine introduction does not increase CRS burden

- Vaccine introduction will lead to an immediate decrease in burden in all cases.
- Uncontrolled transmission (no vaccination) will lead to increased burden when fertility declines as part of a demographic transition.
- Incomplete vaccination may lead to resurgent burden of rubella, but that risk only exists more than 15 years post-introduction. It is associated with accumulation of susceptibility followed by outbreak.

  A wide age range campaign at the time of introduction, and periodic follow-up campaigns, greatly reduces susceptibility accumulation and the risk of outbreak.

World Health Organization

Technical presentation 2

Updated Risk Assessment for the Introduction of Rubella Containing Vaccine

Kurt Frey (IDM), Emilia Vynnycky (UKHSA), Amy Winter (U of Georgia), Matthew Ferrari (Penn State)

Outline

1. Results of sub-national modeling of CRS risk following rubella containing vaccine introduction in Nigeria
2. Proposal for simulation study to evaluate risk of CRS following vaccine introduction in 19 countries.

The impact of sub-national heterogeneities in demography and epidemiology on the introduction of rubella vaccination programs in Nigeria

Taishi Nakase, Tenley Brownwright, Oyeladun Okunromade, Abiodun Egwuenu, Oladipo Ogunbode, Bola Lawal, Kayode Akanbi, Gavin Grant, Orji Bassey, Melissa Coughlin, Bettina Bankamp, Ifedayo Adetifa, Jessica Metcalf, Matthew Ferrari

Published in Vaccine May 2024

Overview

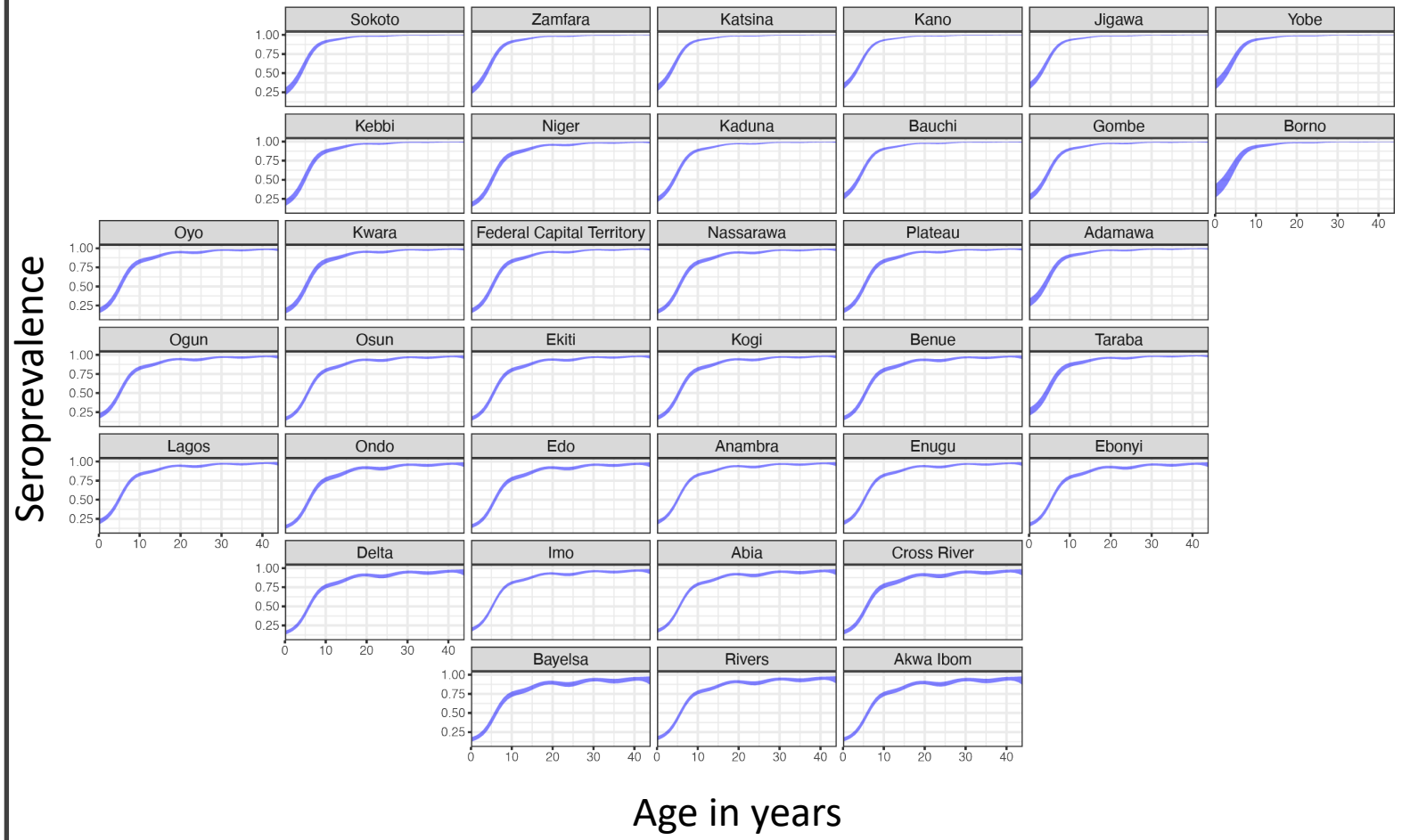
- Current 80% threshold is overly conservative relative to current rubella epidemiology and demographic rates
- Current MCV1 coverage is sufficient to achieve **net reduction** of CRS in Nigeria
  - Some low performing states could see increase in >10 years
- Catch-up and follow-up campaigns can prevent CRS increase even at current MCV1 coverage
- Current CRS burden in Nigeria is ~**3000 cases**. Introduction of RCV in Nigeria with wide age range catch-up campaign results in **11,000 CRS cases averted over 5 years.**

Data and Estimates of R0

NMS4 Project

- Sera collected from the 2018 Nigeria AIDS Indicator and Impact Survey (NAIIS)
  - >3000 clusters
  - 31,459 children under 15 y
  - 9737 women 15-45y
- Analyzed for tetanus, diphtheria, measles, and **rubella** specific antibodies with CDC protocol multiplex bead assay, jointly by US and Nigeria CDC

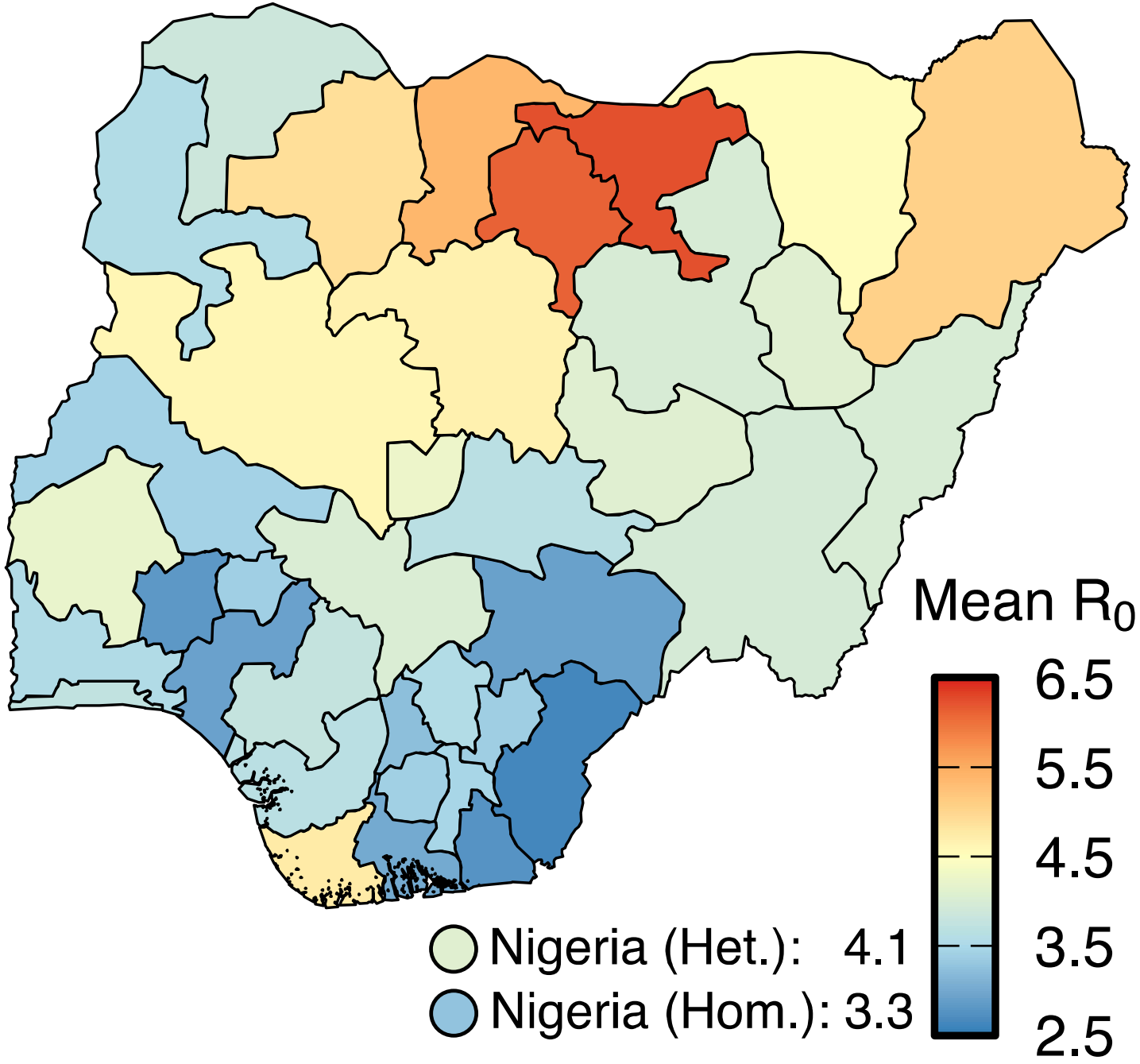
Rubella Seroprevalence



https://www.sciencedirect.com/science/article/pii/S0264410X24005899

Rubella in Nigeria

- Fitted a piecewise constant force of infection model with age classes:
  - [0,3) years
  - [3,15) years
  - [15,∞) years
- Assume structured mixing within 3 age-class model
- R_0 estimated as the dominant eigen value of the next generation matrix of 3-age class model



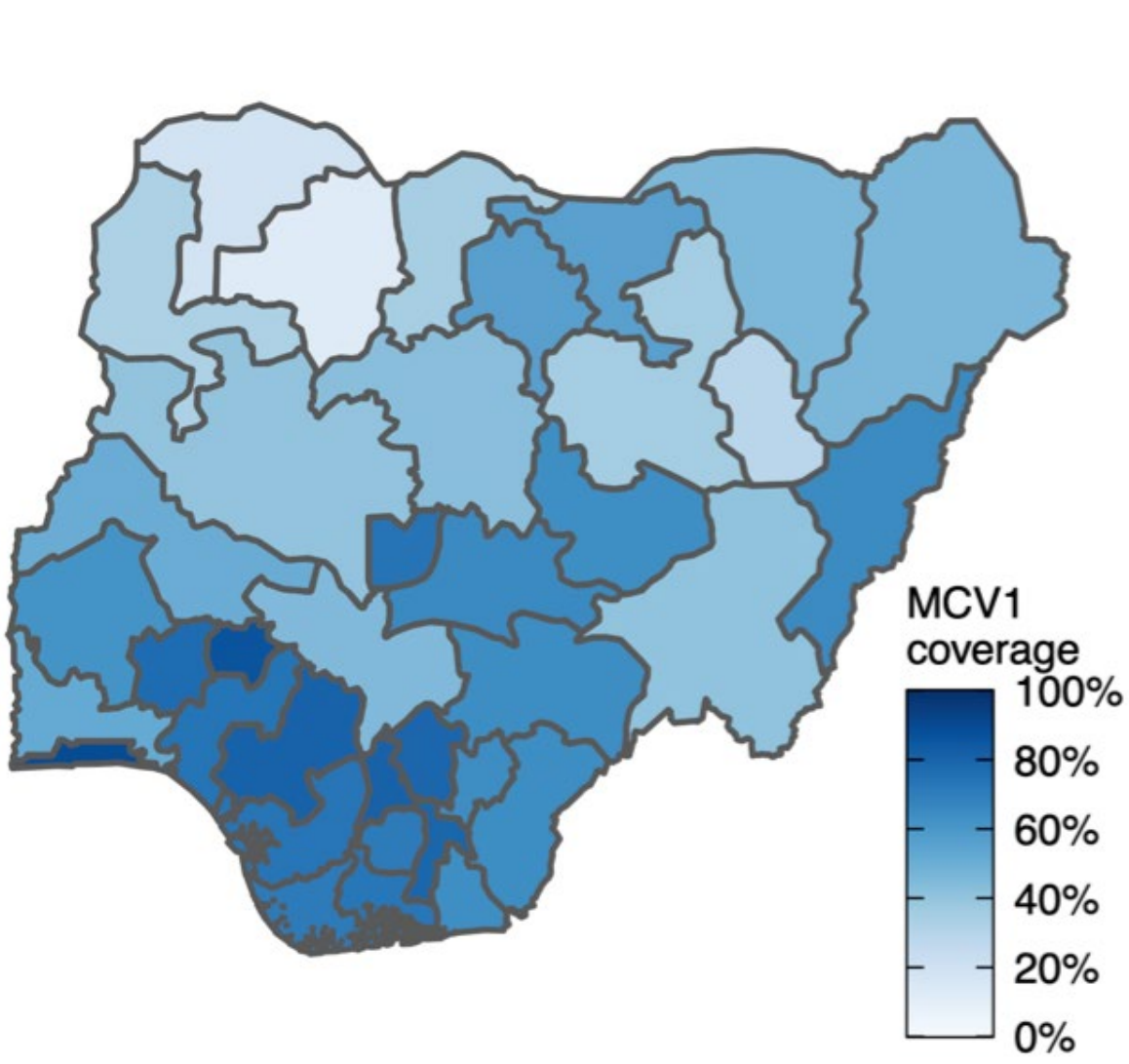
Consequences of Introduction

Naïve Simulation Nigeria

The simplest assumption is that we replace M-only vaccination with MR vaccination.

Current measles vaccination is heterogeneous in Nigeria (estimated from DHS) with some states >80%

The first results only assume routine vaccination to set a baseline (we will add campaigns)



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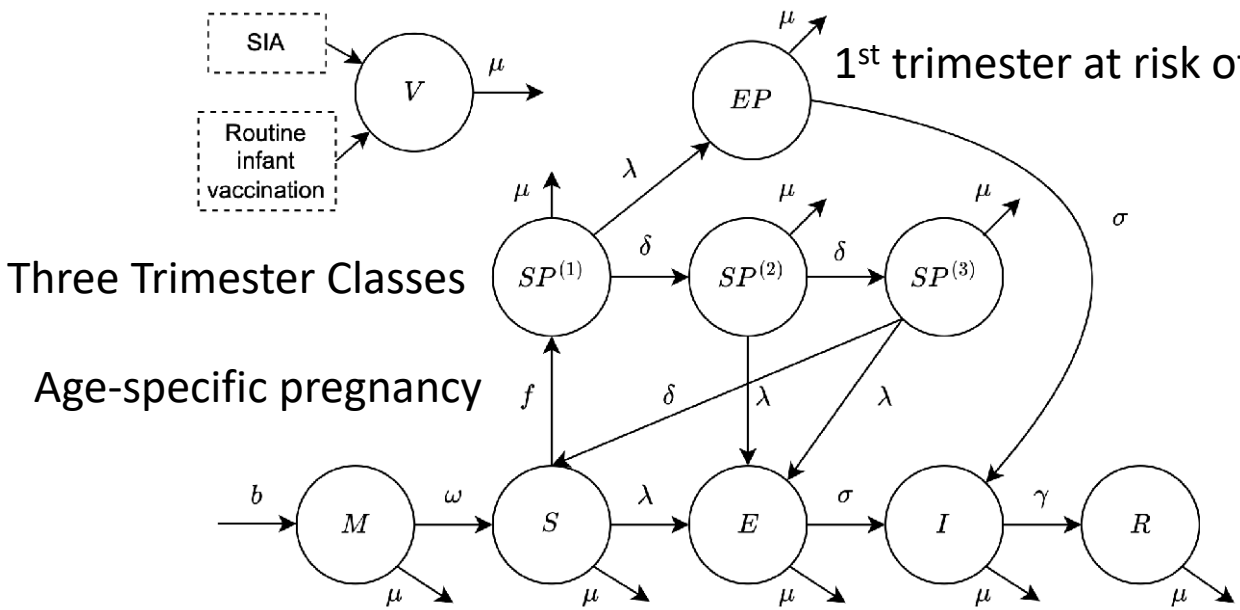
Flow Diagram for Deterministic Age-Structured Transmission Model

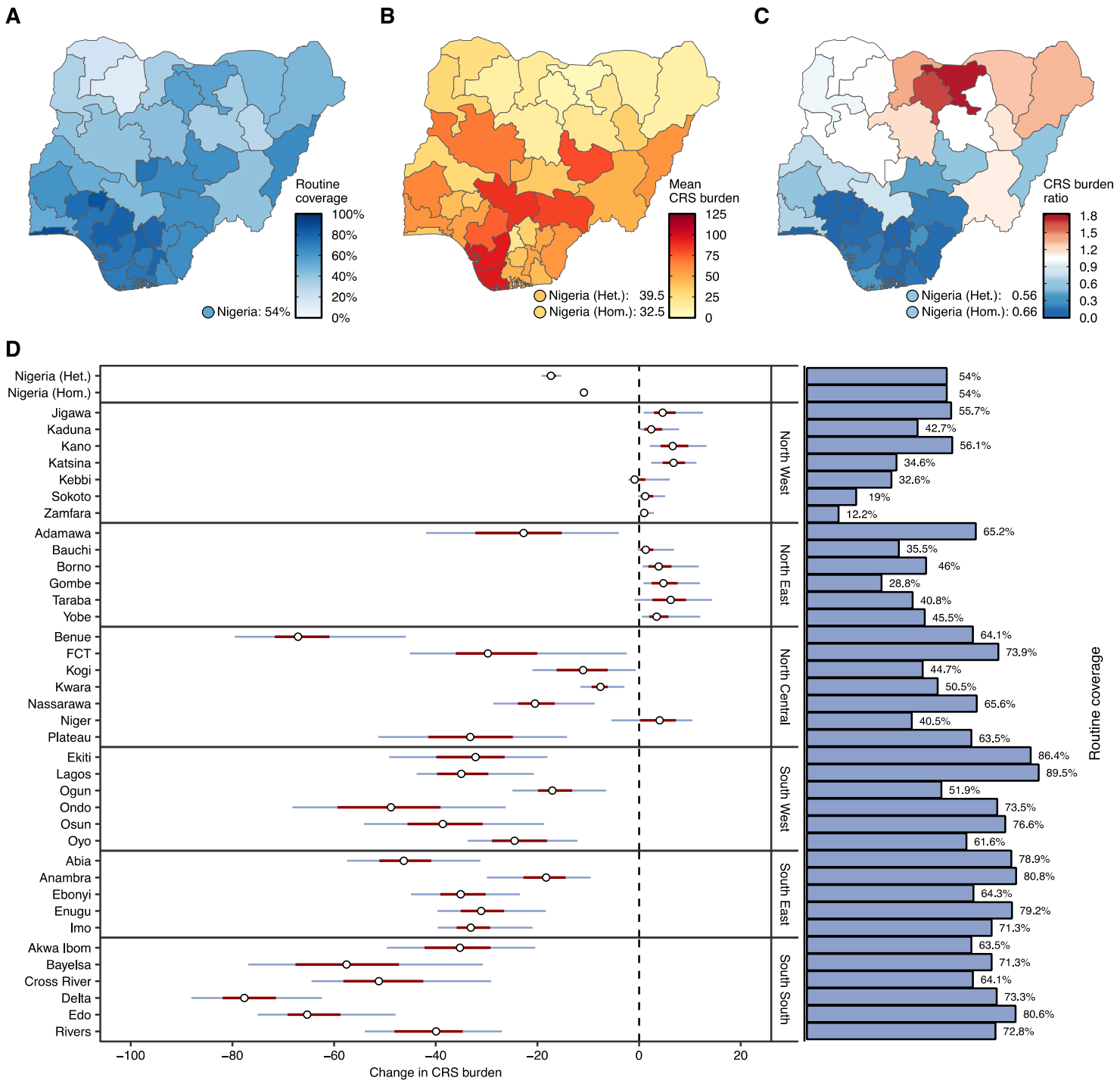


- Monthly age classes from 0-4 years
- Yearly age classes from 4-20 years
- 5-yearly age classes from 20-60 years
- 1 age class greater than 60 years
- Age-specific transmission matrix as estimated above; piecewise constant within groups [0-3), [3,15),[15, ∞) years

Heterogeneity in results reflect draws from posterior distribution of age-specific force of infection

Rubella introduction: Nigeria

- Much of Nigeria has lower coverage than 80% threshold
- In the absence of vaccination, south has higher CRS burden
- BUT, because of low R_0 in southern states, equilibrium CRS burden is predicted to decrease EVEN AT current vaccination coverage
- North would see increase in CRS given currently low coverage **over 30 years**



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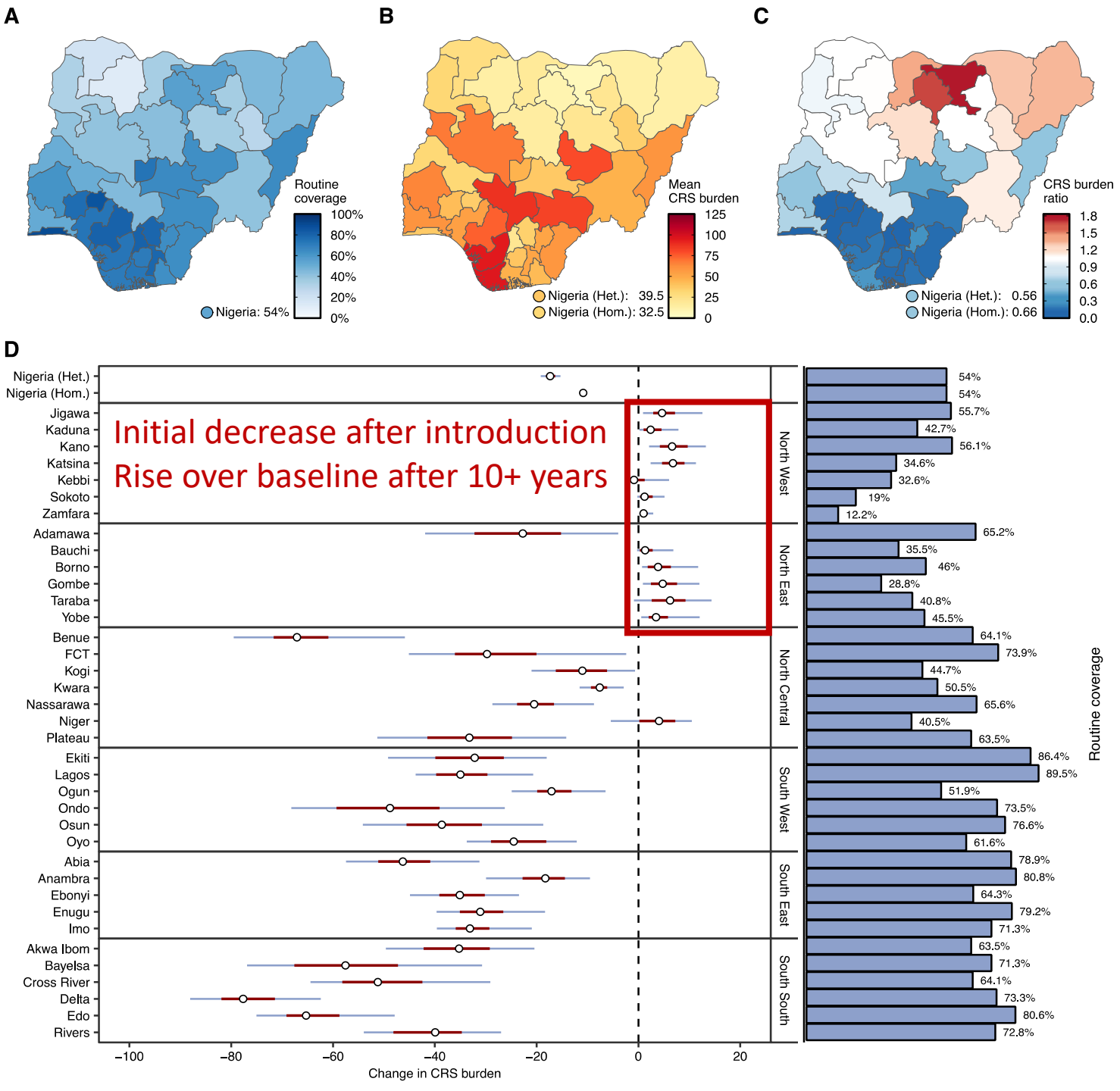

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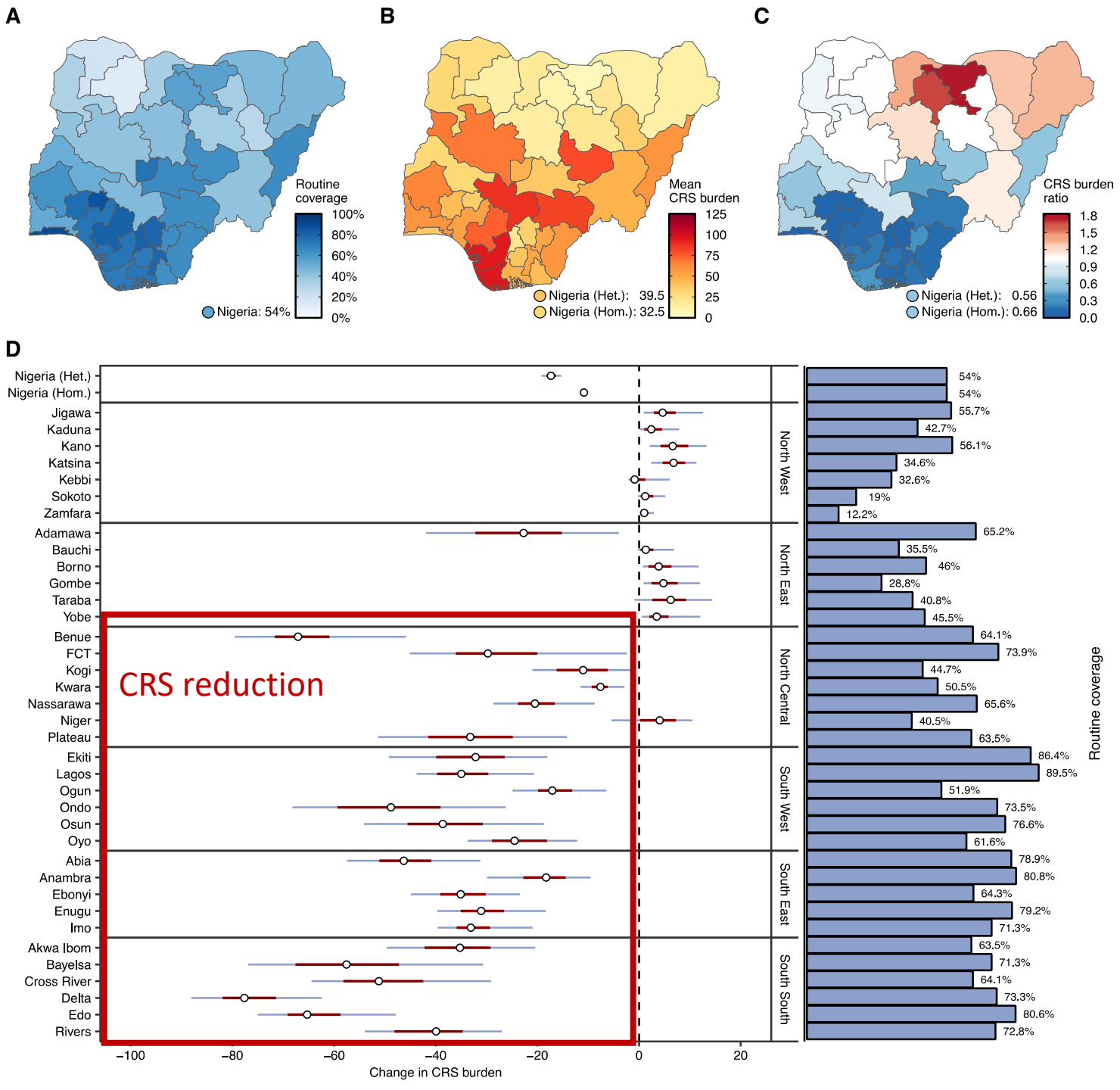

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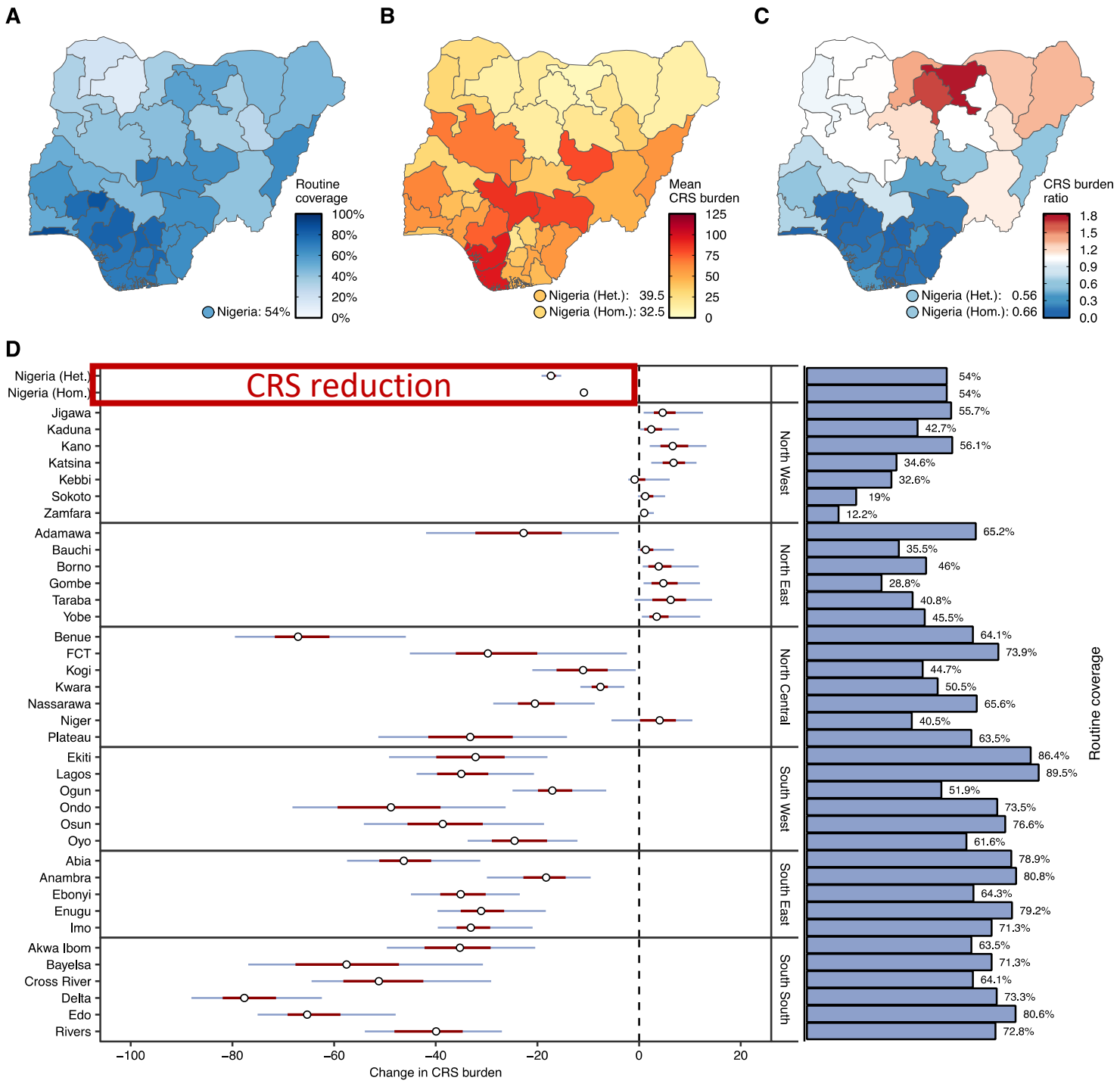
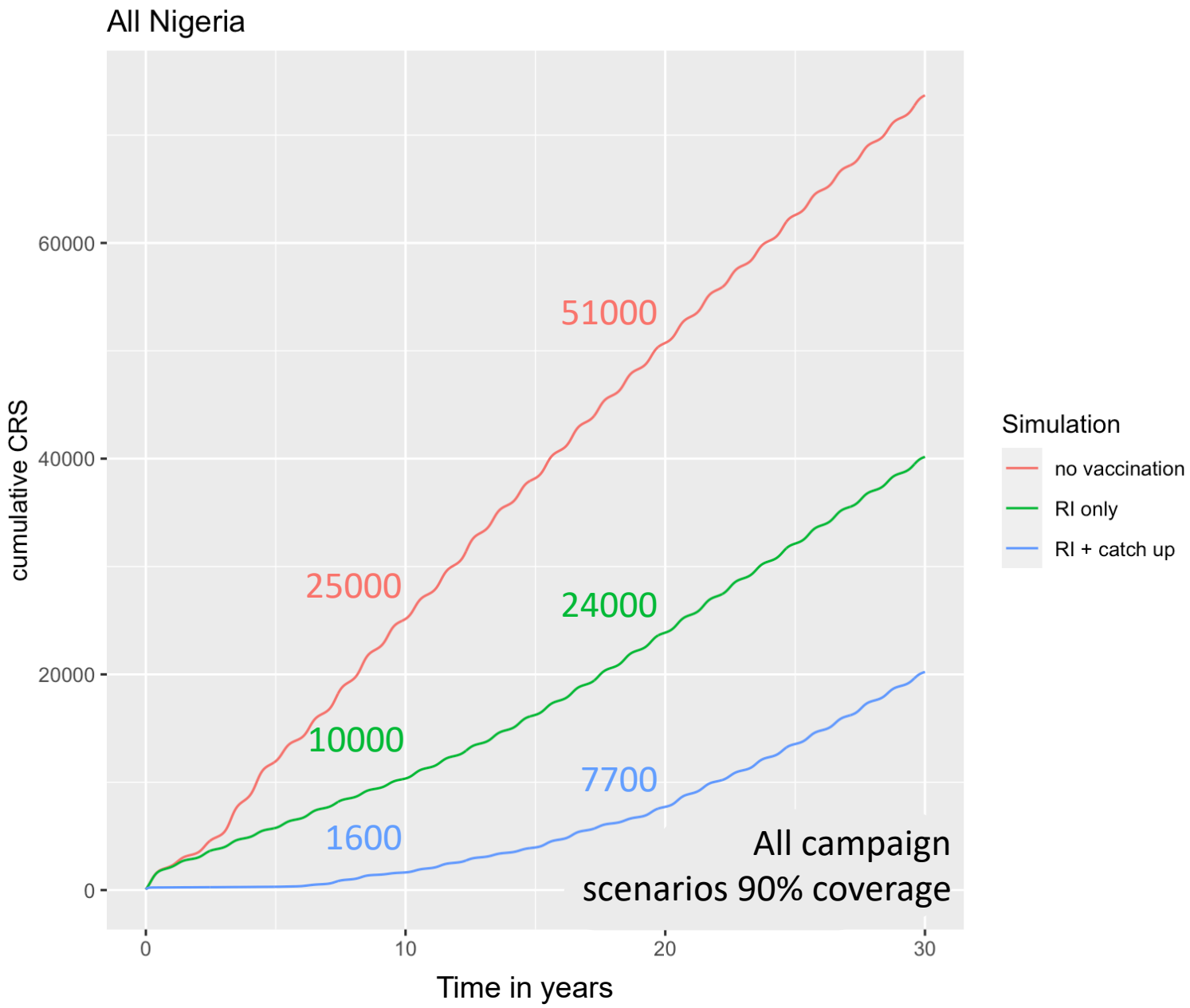


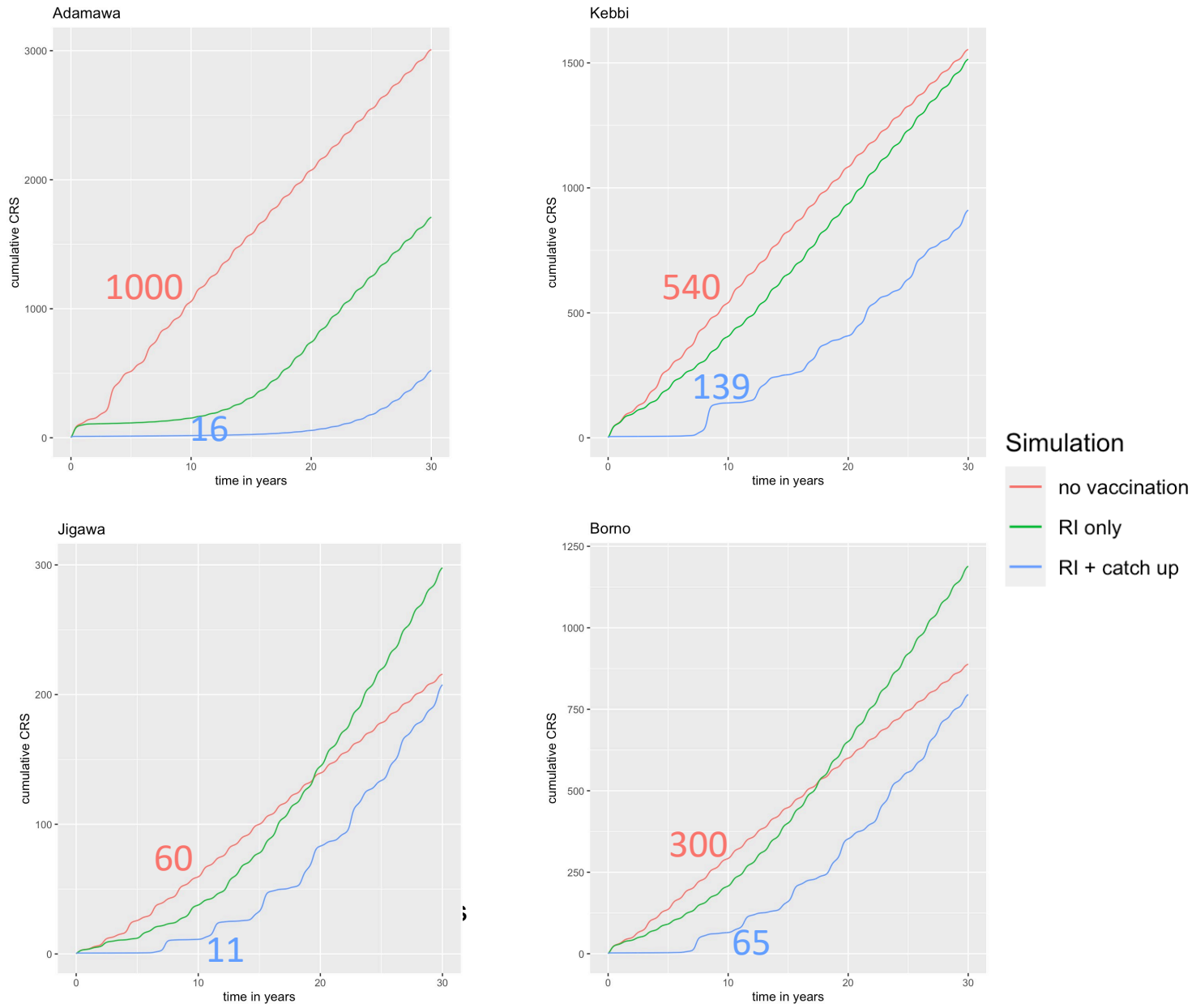
Initial short-term reduction: Nigeria

- In all scenarios, there is a large short-term reduction of CRS due to introduction (with or without catch-up campaign).
- For Nigeria we calculated the cumulative CRS cases over 30 years with and without vaccination
- With or without catch-up campaign there is a net reduction over 30 years



Initial short-term reduction: Nigeria

- Consider 4 northern states
- Adamawa and Kebbi see net benefit (positive CRS cases averted) over 30 years in all vaccination introduction scenarios
- Jigawa and Borno see net benefit over 30 years with introductory campaigns
  - Follow up campaigns or RI improvement lead to net benefit beyond 30 years



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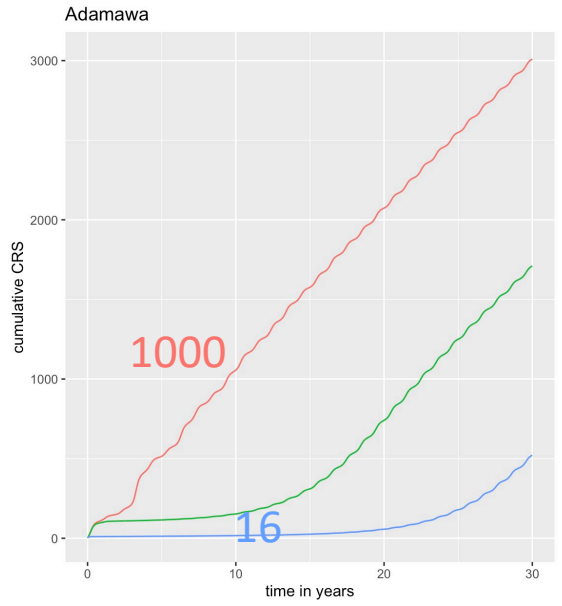
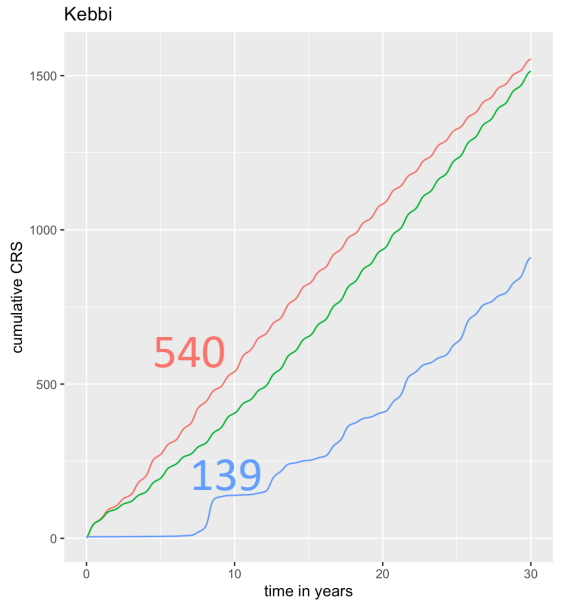
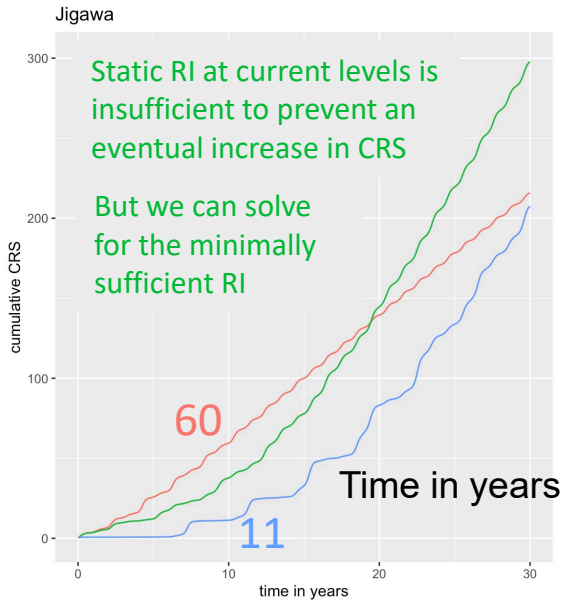
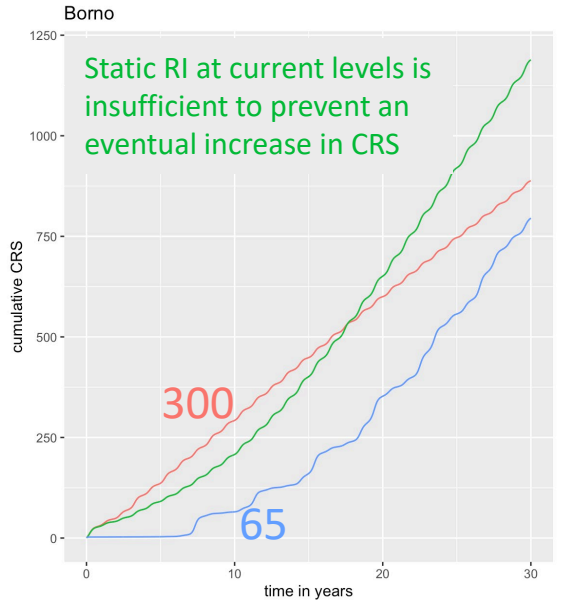
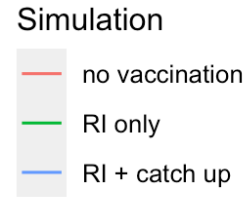










Increasing Vaccination Mitigates CRS Risk: Nigeria

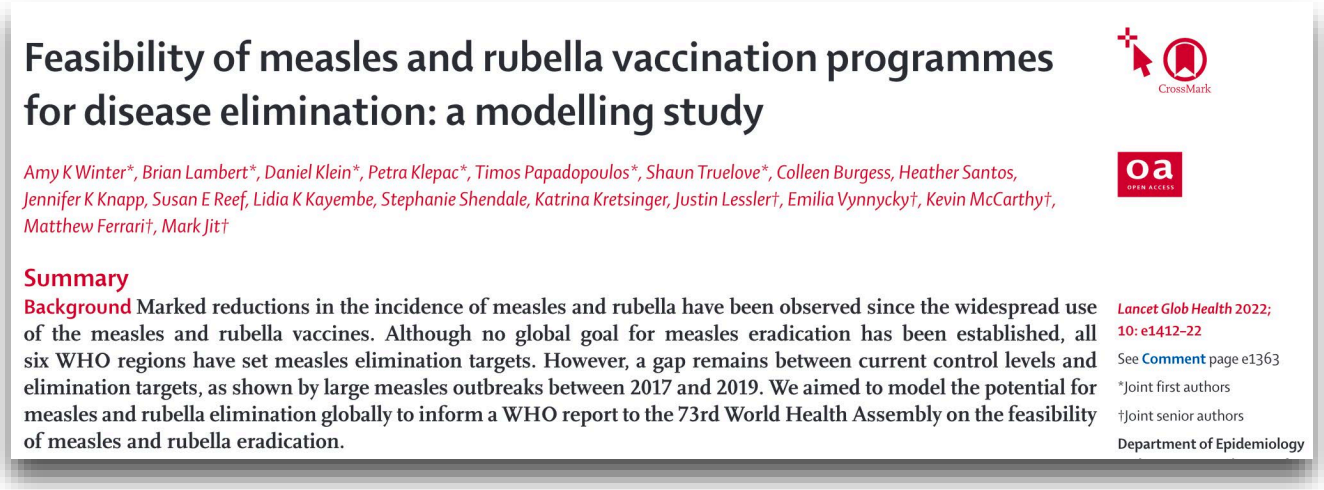
- Minimally sufficient coverage to avoid CRS increase is <80% ***in all states***
- We solve for the rate of RI increase (prior to CRS increase) necessary to avoid that increase in individual states. **In the absence of campaigns**:
  - 1% annual increase for 5 of 13 states
  - 2.5% annual increase in 5 of 13 states
  - 5% annual increase in 3 of 13 states
- Continued follow-up campaigns (using MR in measles SIAs) avoids increase ***in all 13 states***

Proposed Simulation Study of RCV introduction in 19 countries

Amy Winter, Emilia Vynnycky, Kurt Frey, Matthew Ferrari, M&RP RCV Introduction Task Team

Ensemble Projections from Two Models

- UGA – Amy Winter, Shaun Truelove, Justin Lessler, C. Jessica Metcalf
- UKHSA – Emilia Vynnycky, Timos Papadopoulos



Feasibility of measles and rubella vaccination programmes for disease elimination: a modelling study

Amy K Winter, Brian Lambert*, Daniel Klein*, Petra Klepac*, Timos Papadopoulos*, Shaun Truelove*, Colleen Burgess, Heather Santos, Jennifer K Knapp, Susan E Reef, Lidia K Kayembe, Stephanie Shendale, Katrina Kretsinger, Justin Lessler†, Emilia Vynnycky†, Kevin McCarthy†, Matthew Ferrari†, Mark Jit†*

Summary

Background Marked reductions in the incidence of measles and rubella have been observed since the widespread use of the measles and rubella vaccines. Although no global goal for measles eradication has been established, all six WHO regions have set measles elimination targets. However, a gap remains between current control levels and elimination targets, as shown by large measles outbreaks between 2017 and 2019. We aimed to model the potential for measles and rubella elimination globally to inform a WHO report to the 73rd World Health Assembly on the feasibility of measles and rubella eradication.

Lancet Glob Health 2022; 10: e1412–22

See Comment page e1363

*Joint first authors
†Joint senior authors
Department of Epidemiology

19 countries that had not introduced RCV as of 2024:
AFG, CAR, TCD, **COD**, DJI, ETH, GNQ, GAB, GIN, GNB, LBR, MLI, MDG, NER, **NGA**, SOM, RSA, SSD, SDN

Scenarios projected for 40 years following RCV introduction with future changes in population size and birth rates (consistent with Frey presentation)

14 proposed vaccination scenarios

- Baseline against which risk of CRS increase can be evaluated

Scenario	Routine Vaccination*	Catch-Up (6m-14y)	Follow-Up (9m-4y) Every 4 years
S1	None	None	
S2	MCV1 coverage	None	
S3	MCV1 coverage	90%	None
S4	MCV1 coverage	80%	
S5	MCV1 coverage	70%	
S6	MCV1 coverage	60%	
S7	MCV1 coverage	90%	90%
S8	MCV1 coverage	80%	
S9	MCV1 coverage	70%	
S10	MCV1 coverage	60%	
S11	MCV1 coverage	90%	60%
S12	MCV1 coverage	80%	
S13	MCV1 coverage	70%	
S14	MCV1 coverage	60%	

14 proposed vaccination scenarios

- Naïve introduction at current MCV1 coverage
- Assumes no introductory campaigns
- Strict test of 80% threshold

Scenario	Routine Vaccination*	Catch-Up (6m-14y)	Follow-Up (9m-4y) Every 4 years
S1	None	None	
S2	MCV1 coverage	None	
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S4	MCV1 coverage	80%	
S5	MCV1 coverage	70%	
S6	MCV1 coverage	60%	
S7	MCV1 coverage	90%	90%
S8	MCV1 coverage	80%	
S9	MCV1 coverage	70%	
S10	MCV1 coverage	60%	
S11	MCV1 coverage	90%	60%
S12	MCV1 coverage	80%	
S13	MCV1 coverage	70%	
S14	MCV1 coverage	60%	

*Mean WUENIC MCV1 pre-pandemic coverage from 2018-2019

14 proposed vaccination scenarios

- Introduction at current MCV1 coverage
- Coupled with a catch-up campaign
  - 4 levels of coverage to cover pessimistic to optimistic range
  - 60-90% coverage is consistent with the range of coverage from PCCS in 8 countries between 2001-2022

Scenario	Routine Vaccination*	Catch-Up (6m-14y)	Follow-Up (9m-4y) Every 4 years
S1	None	None	
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S6	MCV1 coverage	60%	
S7	MCV1 coverage	90%	90%
S8	MCV1 coverage	80%	
S9	MCV1 coverage	70%	
S10	MCV1 coverage	60%	
S11	MCV1 coverage	90%	60%
S12	MCV1 coverage	80%	
S13	MCV1 coverage	70%	
S14	MCV1 coverage	60%	

*Mean WUENIC MCV1 pre-pandemic coverage from 2018-2019

14 proposed vaccination scenarios

- Introduction at current MCV1 coverage
- Coupled with a catch-up campaign
  - At all 4 levels
- 2 levels of follow-up campaign coverage
  - Highest and lowest coverage levels
  - Regular schedule, every 4 years

Scenario	Routine Vaccination*	Catch-Up (6m-14y)	Follow-Up (9m-4y) Every 4 years
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S10	MCV1 coverage	60%	
S11	MCV1 coverage	90%	60%
S12	MCV1 coverage	80%	
S13	MCV1 coverage	70%	
S14	MCV1 coverage	60%	

*Mean WUENIC MCV1 pre-pandemic coverage from 2018-2019

Outcomes

1. **Annual and cumulative incidence of rubella infection**
2. **Annual and cumulative incidence of congenital rubella syndrome (CRS)**
3. Proportion of years with a rubella outbreak (defined as 5 infections per 100,000 population)
4. Effective reproductive number in each year (as a metric of outbreak risk)

Outcomes

1. Annual and cumulative incidence of rubella infection
2. Annual and cumulative incidence of congenital rubella syndrome (CRS)
3. **Proportion of years with a rubella outbreak (defined as 5 infections per 100,000 population)**
4. **Effective reproductive number in each year (as a metric of outbreak risk)**

Summary

- Simulation experiment using national-scale will explore a broader range of introduction scenarios than Nigeria and DRC case studies
- Two independent models allow comparison of consistent patterns:
  - Risk of exceeding baseline
  - Time to exceeding baseline
- Replicate the Nigeria and DRC case studies to identify biases that may arise from national scale

Thank You

Documents are organized in 3 sections: background and separately for the presentations of Kurt Frey and Matthew Ferrari. Within each they are ordered by relevance.

General Background Documents:

Background Document 1: *01_Knox1980.pdf*

Characterizes the essential features of a dynamic model for rubella transmission. Outcomes depicted in Figure 5, the application of universal childhood vaccination, are qualitatively in line with present models. (Figures 7 and 8 involve waning immunity and are not relevant; immunity to rubella virus is very long lasting.) Also note trajectory A in Figure 9: declining attrition (i.e., infectivity) leads to increasing burden.

Background Document 2: *02_Metcalf2012.pdf*

Profile of factors influencing rubella burden and estimates of the vaccination coverage needed to ensure burden reduction. Outcomes in Figure 2 demonstrate how *lower* transmission intensity (via lower R0 or lower birth rates) is associated with *higher* burden. Lower transmission intensity is associated with a greater average age at infection, and a greater probability of rubella infection occurring during pregnancy. Figure 3 illustrates how current WHO guidance (80%) is aligned with ensuring burden reduction even at very high infectivity (panel C; $R_0 = 12$).

Background Document 3: *03_LesslerMetfalf2013.pdf*

Estimates of R0 for a variety of countries in the African region; Figure 1 depicts the mean at 5.2. Note the 95th percentile estimate is for values below 7.0.

Panel D in figure 2 demonstrates very high confidence that current guidance for vaccine introduction (i.e., including a wide age range catch-up) will reduce burden for a wide variety of contexts. Here, columns are birth rate, rows are routine immunization coverage, and grid values are the R0 threshold above which CRS could increase. Colors correspond to the likelihood that a R0 value is above the threshold value in the grid (based on the distribution in Figure 1).

Background Document 4: *04_Papadopoulous2022.pdf*

Estimates of R0 for many countries based on seroprevalence data. Values are depicted as blue circles in Figure 1 (red circles are values estimated via an ML model trained on the blue circles).

Note the distribution of blue circles here is even lower than that presented in Document 3. Here, several countries in the African region have point estimates for R0 of rubella that is < 3.0.

Background Document 5: *05_Vynnycky2023.pdf*

Profile of the current global burden of rubella. As shown in Figure 2, countries that have introduced RCV have typically eliminated rubella. Only AFRO and EMRO have countries yet to introduce the vaccine.

Background Documents for Presentation by Kurt Frey

Background Document 6: *06_Frey2024.pdf*

Pre-print currently under review and source for the technical presentation "Implications of different levels of routine coverage, demography, and wide age-range RCV introduction catch-up campaign on the risk of increasing CRS burden."

Background Document 7: *07_Cheng2021.pdf*

Earlier work using the same model applied in Document 6, applied to examine rubella transmission in the provinces of the Democratic Republic of the Congo.

Background Document 8: *08_ Cheng2021_supplement.pdf*

Supplementary material with technical details for Document 7.

Background Documents for Presentation by Matthew Ferrari

Background Document 9: *09_Nakase2024.pdf*

Source for the technical presentation "Implications of sub-national heterogeneity in R0 and routine immunization coverage for RCV introduction in Nigeria".

Background Document 10: 10_*Nakase2024_supplement.pdf*

Supplementary material with technical details for Document 8.

Background Document 10: 10_*Proposed Research Plan.pdf*

Describes proposed plan for simulation of rubella introduction scenarios in 19 countries that had yet to introduce rubella containing vaccine as of start of 2024. Text describes rationale, outcomes, and proposed scenarios. Summaries of the two rubella models that will be used are included.

Background articles for the Session

1. Knox EG. Strategy for rubella vaccination. *Int J Epidemiol*. 1980;9(1):13-23. doi:10.1093/ije/9.1.13
2. Metcalf CJ, Lessler J, Klepac P, Cutts F, Grenfell BT. Impact of birth rate, seasonality and transmission rate on minimum levels of coverage needed for rubella vaccination. *Epidemiol Infect*. 2012;140(12):2290-2301. doi:10.1017/S0950268812000131
3. Lessler J, Metcalf CJ. Balancing evidence and uncertainty when considering rubella vaccine introduction. PLoS One. 2013;8(7):e67639. Published 2013 Jul 5. doi:10.1371/journal.pone.0067639
4. Papadopoulos T, Vynnycky E. Estimates of the basic reproduction number for rubella using seroprevalence data and indicator-based approaches. *PLoS Comput Biol*. 2022;18(3):e1008858. Published 2022 Mar 3. doi:10.1371/journal.pcbi.1008858
5. Vynnycky E, Knapp JK, Papadopoulos T, et al. Estimates of the global burden of Congenital Rubella Syndrome, 1996-2019. *Int J Infect Dis*. 2023;137:149-156. doi:10.1016/j.ijid.2023.09.003
6. Frey K. Congenital Rubella Syndrome Does Not Increase with Introduction of Rubella-Containing Vaccine. *Vaccines*. 2024; 12(7):811. https://doi.org/10.3390/vaccines12070811
7. Cheng A, Frey K, Mwamba GN, McCarthy KA, Hoff NA, Rimoin AW. Examination of scenarios introducing rubella vaccine in the Democratic Republic of the Congo [published correction appears in Vaccine X. 2022 Sep 16;12:100215. doi: 10.1016/j.jvacx.2022.100215]. *Vaccine X*. 2021;9:100127. Published 2021 Nov 12. doi:10.1016/j.jvacx.2021.100127
8. Supplementary material for Document for #7
9. Nakase T, Brownwright T, Okunromade O, et al. The impact of sub-national heterogeneities in demography and epidemiology on the introduction of rubella vaccination programs in Nigeria. *Vaccine*. Published online May 28, 2024. doi:10.1016/j.vaccine.2024.05.030
10. Supplementary material for Document for #9

Proposed Research Plan: The impact of rubella containing vaccine introduction in 19 countries.

Summary: We will use 2 previously published country-scale models to simulate rubella virus transmission and CRS incidence in the 19 countries (AFG, CAR, TCD, COD, DJI, ETH, GNQ, GAB, GIN, GNB, LBR, MLI, MDG, NER, NGA, SOM, RSA, SSD, SDN) that had not yet introduced rubella containing vaccine (RCV) at the start of 2024 under alternative scenarios of RCV introduction.

For each we will use the existing models (see below) simulated forward with and without (S1 below) RCV introduction. We will use 2024 as the initial year and assume introduction (with or without catch-up campaign) in 2024. Results should be interpreted in terms of time since introduction year rather than explicit predictions of calendar years (e.g. analysis could be rescaled to year 2024 == year 0 without loss of generality). We will run all scenarios for all countries for 40 years.

For each country and scenario we will quantify:

1. Annual and cumulative incidence of rubella infection
2. Annual and cumulative incidence of congenital rubella syndrome (CRS)
3. Proportion of years with a rubella outbreak (defined as 5 infections per 100,000 population)
4. Effective reproductive number in each year (as a metric of outbreak risk)
5. Mean and 95% CI annual proportion of women aged 15-49 years who are susceptible (# susceptible women aged 15-49 yr / # 15-49 year old women)
6. Mean and 95% CI annual proportion of the susceptible population that's made up by 15-49 women (# susceptible women aged 15-49 yrs / # susceptible all ages, genders)

Outcomes 1-2 reflect the expected future disease burden. Outcome 3 reflects the annual risk of a rubella outbreak. Outcomes 4-5 reflect the population at risk for CRS pregnancies if a rubella outbreak occurs.

Models: We will use two models from the current Vaccine Impact Modelling Consortium portfolio that were developed by project leads Emilia Vynnycky and Amy Winter respectively. Both are age-structured, dynamic SIR-type models. Model details are summarized below.

Scenarios: We propose to run 14 scenarios with span a range of assumptions about routine immunization, catch-up and follow-up campaigns. The list of scenarios is described in the Table 1 below.

S1 reflects the baseline, no-vaccination setting and will give the annual CRS incidence against future changes and paradoxical increases will be quantified.

S2 reflects the impact of the introduction of routine (RI) rubella containing vaccination only. Here we assume measle-only vaccine is replaced with MR vaccine and coverage is then projected as current MCV1 coverage. We assume no annual increase in MCV1 coverage and no second dose of RCV. Nakase et al (2024) has previously shown that any annual increase in RCV1 coverage will result in a net reduction in CRS in all years.

S3-6 reflect a range of scenarios for the impact of optimistic (90%) to pessimistic (60%) coverage of introductory catch-up campaigns. We chose 60% as the lower bound scenario here as it is lower than the minimum coverage (67%; Madagascar in 2007) from recent measles post-campaign coverage surveys in countries that have not yet introduced RCV.

S7-14 reflect the scenarios in S3-6 with optimistic (90%) and pessimistic (60%) coverage of follow-up campaigns.

Table 1. Proposed rubella vaccination scenarios

Scenario #	Scenario Description
S1	No vaccination
S2	RI only (per mean WUENIC MCV coverage 2018-2019)
S3	RI with catch-up campaign (6m-14y) with coverage 90%
S4	RI with catch-up campaign (6m-14y) with coverage 80%
S5	RI with catch-up campaign (6m-14y) with coverage 70%
S6	RI with catch-up campaign (6m-14y) with coverage 60%
S7	RI with catch-up campaign (6m-14y) with coverage 90% PLUS follow-ups (9m-4y) every 4 years at 90%
s8	RI with catch-up campaign (6m-14y) with coverage 80% PLUS follow-ups (9m-4y) every 4 years at 90%
S9	RI with catch-up campaign (6m-14y) with coverage 70% PLUS follow-ups (9m-4y) every 4 years at 90%
S10	RI with catch-up campaign (6m-14y) with coverage 60% PLUS follow-ups (9m-4y) every 4 years at 90%
S11	RI with catch-up campaign (6m-14y) with coverage 90% PLUS follow-ups (9m-4y) every 4 years at 60%
S12	RI with catch-up campaign (6m-14y) with coverage 80% PLUS follow-ups (9m-4y) every 4 years at 60%
S13	RI with catch-up campaign (6m-14y) with coverage 70% PLUS follow-ups (9m-4y) every 4 years at 60%
S14	RI with catch-up campaign (6m-14y) with coverage 60% PLUS follow-ups (9m-4y) every 4 years at 60%

Summary of the UKHSA rubella model used for VIMC

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General assumptions

The rubella model used for VIMC is an age and sex-structured, deterministic, compartmental model of the transmission dynamics of rubella, based on previous publications [1-4]. The supplement to reference [4] provides the model's equations and further details; the paper and supplement are included for reference. The population is stratified into those with maternal immunity (lasting 6 months), susceptible, pre-infectious (infected but not yet infectious), infectious and immune, using annual age bands and a "Realistic Age Structure"[5]. Country-specific birth and age-specific death rates in previous VIMC runs were fixed at 2010 levels and calculated from UN population survival data for 2010-15 [6] respectively.

Force of infection

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

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

The effective contact rate differs between <13 and ≥13 year olds, with its relative size based on contact survey data [7]. β_1 and β_2 are calculated from the average force of infection in <13 and ≥13 year olds, estimated from age-stratified rubella seroprevalence data, which had been collected before rubella containing vaccine (RCV) was introduced [2]. Seroprevalence data were available for 40 of the countries modelled for VIMC (see [4] for further details of the available data). For countries lacking seroprevalence data, we used data from countries in the same WHO region [2, 3]. Confidence intervals (CI) on the force of infection were calculated using 1000 bootstrap-derived-seroprevalence datasets [2, 3]. The vaccine doses for VIMC runs were assumed to be correlated, with 100% of those vaccinated previously being vaccinated in SIAs, where possible and 50% of those who have received RCV1 receiving RCV2, where possible.

CRS incidence

Country-specific numbers of congenital rubella syndrome (CRS) cases in year *y* were calculated by summing the number of CRS cases born each day to women aged 15-49 years. As assumed elsewhere [1-3, 8], infection during the first 16 weeks of pregnancy carries a 65% risk of the newborn having CRS. The number of CRS deaths in year *y* was calculated by multiplying the number of CRS cases born in year *y* by the assumed case fatality rate (30%). The latter was assumed to have a plausible range of 10-50%, consistent with the number of DALYs for cases in year *y* was calculated by multiplying the number of CRS cases in year *y* by the corresponding DALY [9], which was based on the country-specific World Bank Income group for 2017 [10]. Both the DALYs and the assigned World Bank income group remained fixed over time. As rubella infections are mild, rubella-specific deaths are not included and people with rubella infection are assumed to die at the general all-cause, age and sex-specific mortality rate.

Range of values

Confidence intervals on the outputs for each setting were calculated as the 95% range of the outputs obtained by running the model using 200 combinations of 5 randomly-sampled parameters. The parameters were the pre-vaccination force of infection which was used to calculate the contact parameters (see above), the risk of a child being born with CRS if his/her mother had been infected during pregnancy, the CRS-related case-fatality rate, the vaccine coverage and the vaccine efficacy.

The pre-vaccination force of infection was sampled from 1000 bootstrap-derived force of infection estimates, obtained by fitting catalytic models to bootstrap-derived seroprevalence data for that setting, or, if that setting lacked seroprevalence data, from bootstrap-derived force of infection estimates from countries in the same WHO region as the country of interest [2, 3].

The remaining parameters were randomly sampled from distributions reflecting their plausible range, as implied by published studies, wherever possible[92]. For example, the CRS-related mortality was sampled from the uniform distribution in the range 10-50%, consistent with estimates from 3 studies in Vietnam, Greece and Panama, in which the 95% confidence intervals were 20-51%, 12-50% and 15-40% respectively[11-13]. The risk of a child being born with CRS to a mother infected in the first 16 weeks of pregnancy was sampled from the Gamma distribution with shape and scale parameters 37 and 56 respectively. This assumption leads to a median and 95% range of 65% and 47-88% respectively for this risk, consistent with estimates from several studies[14-16]. Further details about the basis for this range can be found in the supplement to [4]. The sampling was conducted assuming that the parameters were independent.

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University of Georgia (UGA): rubella model, national level mode

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The UGA rubella transmission model is a discrete-time, stochastic, age-structured, compartmental model, building from previous work describing rubella dynamics.[1,2] The key feature of the model is a matrix that at every time-step defines transitions from each combination of epidemiological stage (maternally immune 'M', susceptible 'S', infected 'I', recovered 'R', and vaccinated 'V', taken to indicate those effectively vaccinated) and age group (1 month age groups up to 20 years old, then 1 year age groups up to 100 years old) to every other possible combination of epidemiological stage and age group. The discrete time-step was set to roughly two weeks (i.e., 24 time-steps in a year), the approximate generation time of rubella.

Humans are born either directly into the 'susceptible' class or move there as passively acquired 'maternal immunity' wanes over the first year of life. As individuals age, they can be exposed to either vaccination which, if successful, moves them permanently into the 'vaccinated' class, or to natural infection, moving them to 'infected' for a time-step (or rubella generation) then permanently into the 'recovered' class. In addition to these epidemiological transitions, there are demographic transitions including births, deaths, and aging.

Demographic parameters (population size, crude birth rates, and age-specific death rates) were supplied by the Vaccine Impact Modelling Consortium, and vaccination coverages were time- and country-specific, as defined by the scenarios described above. We further adjusted vaccination coverage based on the assumptions that repeated vaccination activities are not completely independent, and that a portion of the population may always remain inaccessible to vaccination campaigns. We assumed the age- and time-specific proportion inaccessible corresponded to WUENIC diphtheria, tetanus, and pertussis (DTP) routine vaccination rates.[3] Duration of maternal immunity[4] and vaccine efficacy[5] were assumed from published literature and are constant across time and country. The annual introduction of infected individuals scaled with the median population size of each country, ranging from 24 to 0.006, and was set to trigger an outbreak if the size of the susceptible population was large enough to induce transmission, but small enough not to alone surpass elimination thresholds.

Country-specific transmission to individuals in age group *a* from individuals in age group *j* for each time-step *t* is defined by the mean transmission from individuals in age group *j* to age group *a*, and the magnitude of seasonal fluctuations (assumed 0.15[1] and constant over time and country), estimated by rescaling population-adjusted age-contact rates (time constant and country-specific[6]) to reflect the assumed basic reproductive number (R_0) of rubella. R_0 distributions were country-specific and estimated by fitting a dampened exponential model[7] with likelihood-based Markov chain Monte Carlo algorithm to published rubella immunoglobulin G (IgG) seroprevalence data. Model parameters (i.e., R_0) were fit to empirical data, however the transmission model is not directly fit to data. Model uncertainty includes process uncertainty for all epidemiological and demographic transitions and uncertainty on the value of R_0.

Age- and time-specific CRS cases were estimated from each country's model output by multiplying the age-specific number of susceptible individuals, the sex ratio of the population, the age-specific fertility

rate, the probability of becoming infected over 16-week period, and finally the probability of CRS following rubella infection during the first 16 weeks of pregnancy (estimated 0.59 [8-9, 10-12]). Fetal and child deaths were estimated from the number of CRS cases as mean estimated 9.3 per 100 live births, and mean estimated 1.4 per 100 live births, respectively.[13]

The model incorporates parameter uncertainty (i.e., country-specific rubella basic reproductive number, gestational age-specific CRS risk, and age-specific CRS death rates) and uncertainty of stochastic processes for every epidemiologic and demographic transition in the model. The model was validated to capture demographic changes and intra-annual rubella transmission.[1,14]

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