Modelling Report: SEAR M&R Elimination Timeline

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Contributors

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Background

The objective of this analysis was to assess the impact of five vaccination scenarios on the probability of measles and rubella elimination in six countries. The **six countries** of interest are Bangladesh, India, Myanmar, Indonesia, Nepal, and Thailand. The **time frame** of interest is 2022 to 2040. The **five vaccination scenarios** represent a range of routine coverage over time and range of campaign coverage, timing, and age targets. The vaccination scenarios, detailed in the supplement below, are summarize here:

- Baseline: Routine immunization MRCV1 and MRCV2 coverage remain stagnant from 2022 onwards at highest coverage achieved in last three years (2019,2020,2021) as per WUNEIC estimates.
- Scenario 1: Intensified with immunity gap closure in adults (up to 40 years) and children (assuming all adults beyond 40 years are protected by natural immunity during pre-vaccination era)
- Scenario 2: Intensified with immunity gap closure in children under five years of age only
- Scenario 3: Sub optimal implementation of scenario 1 by 15%
- Scenario 4: Sub optimal implementation of scenario 2 by 15%

Two national level **transmission models** were used to simulate the vaccination scenarios for each disease. The four established models have previously been used to generate future projections of the impact of Gavi the Vaccine Alliance's investments as part of the Vaccine Impact Modelling Consortium; they include measles models Dynamic Measles Immunisation Calculation Engine (DynaMICE) and Pennsylvania State University (PSU), and rubella models University of Georgia (UGA), and UK Health Security Agency (UKHSA). For every combination of vaccination scenario and country, each model was used to generate 200 simulations of disease-specific transmission over time.

The **outcome of interest** is the probability of elimination. We defined "elimination" as an annual incidence of 5 infections per one million people or less; although in practice we view the "elimination" threshold as a **necessary condition for elimination** during which transmission would be fragile and likely to be interrupted in the absence of continued importation. This differs from the programmatic definition of elimination, or the event of elimination, which is defined as zero endemic cases for at least 12 months. We also note that our threshold is based on infections rather than observed clinical cases.

Rubella Results

Achieving the conditions necessary for rubella elimination is highly probable under these vaccination scenarios.

Given these vaccination scenarios, rubella elimination is highly likely in all six countries by 2025. **Figure 1** shows the probability that conditions for rubella elimination have been achieved by a given year for each country, scenario, and model. The probability that elimination is achieved by a given year is calculated as the proportion of 200 simulations in which the incidence (i.e., infections per one million population) was less than or equal to 5 for any year between 2022 and the given year. The UGA model showed a delay in elimination in Indonesia in the baseline scenario and the UKHSA model showed a slightly lower probability of elimination for all vaccination scenarios in Myanmar (Figure 1). The continued, albeit limited, rubella transmission in the model simulations can also be viewed by the annually estimated mean number of Congenital Rubella Syndrome (CRS) cases for these specific scenarios and countries in **Figure 2**. The UGA model estimates a mean of over 200 CRS cases in Indonesia 2022-2040 in the baseline vaccination scenario. The UKHSA model estimates a mean between 166-421 CRS cases in Myanmar 2022-2040 across all vaccination scenarios, with the lowest number of CRS cases in scenarios 1 and 3. The population-weighted regional probability of rubella elimination for both models and all vaccination scenarios was 1.00 by 2025. Despite these findings, there is need for continued vigilance to surveil rubella and CRS cases and rapidly respond to sporadic outbreaks after country elimination is achieved due to risk of infected importations.

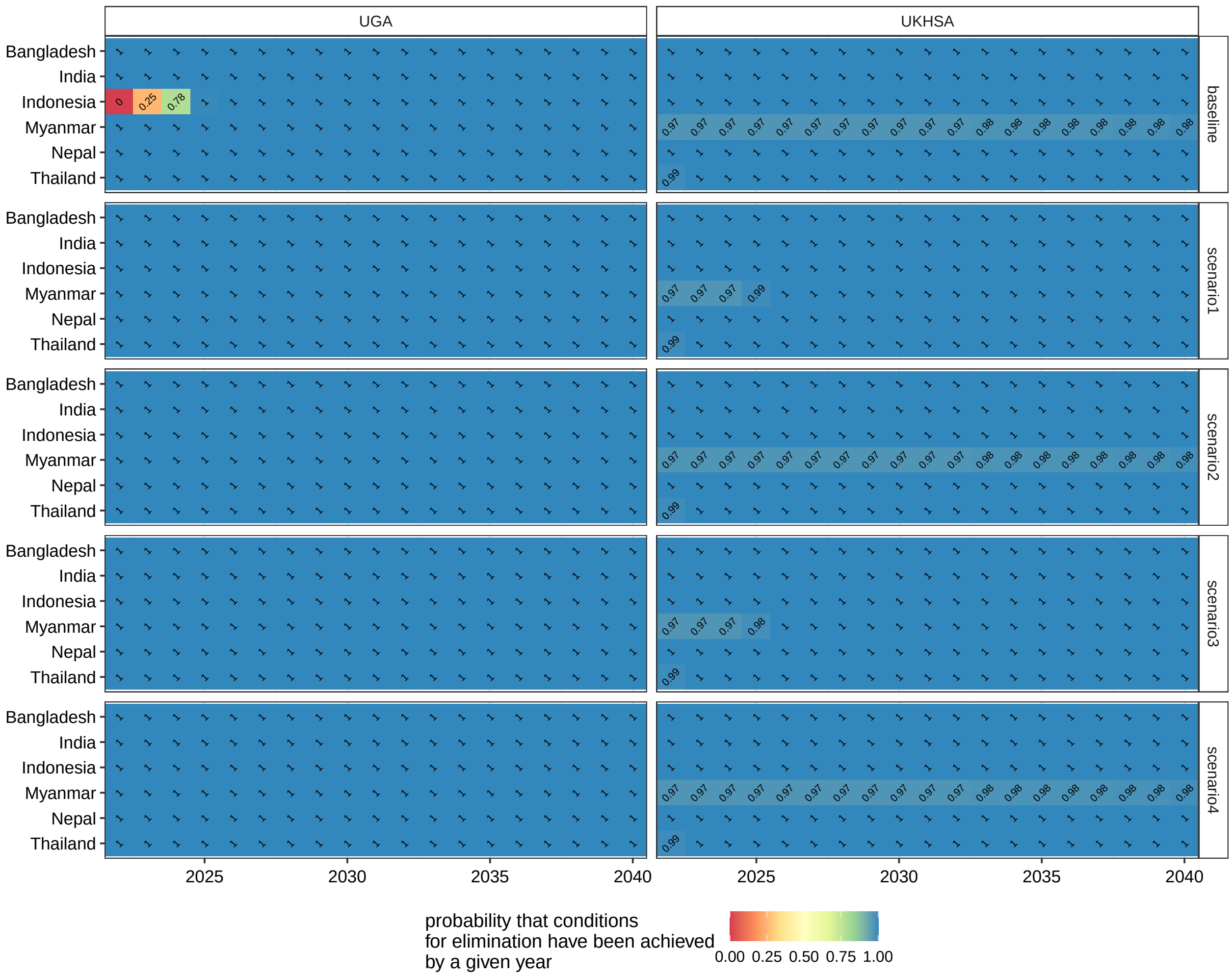


Figure 1: Probability that the conditions for rubella elimination (<= 5 infections per one million population) have been achieved by a given year (x-axis) for each country (y-axis), scenario (panel rows), and model (panel columns)

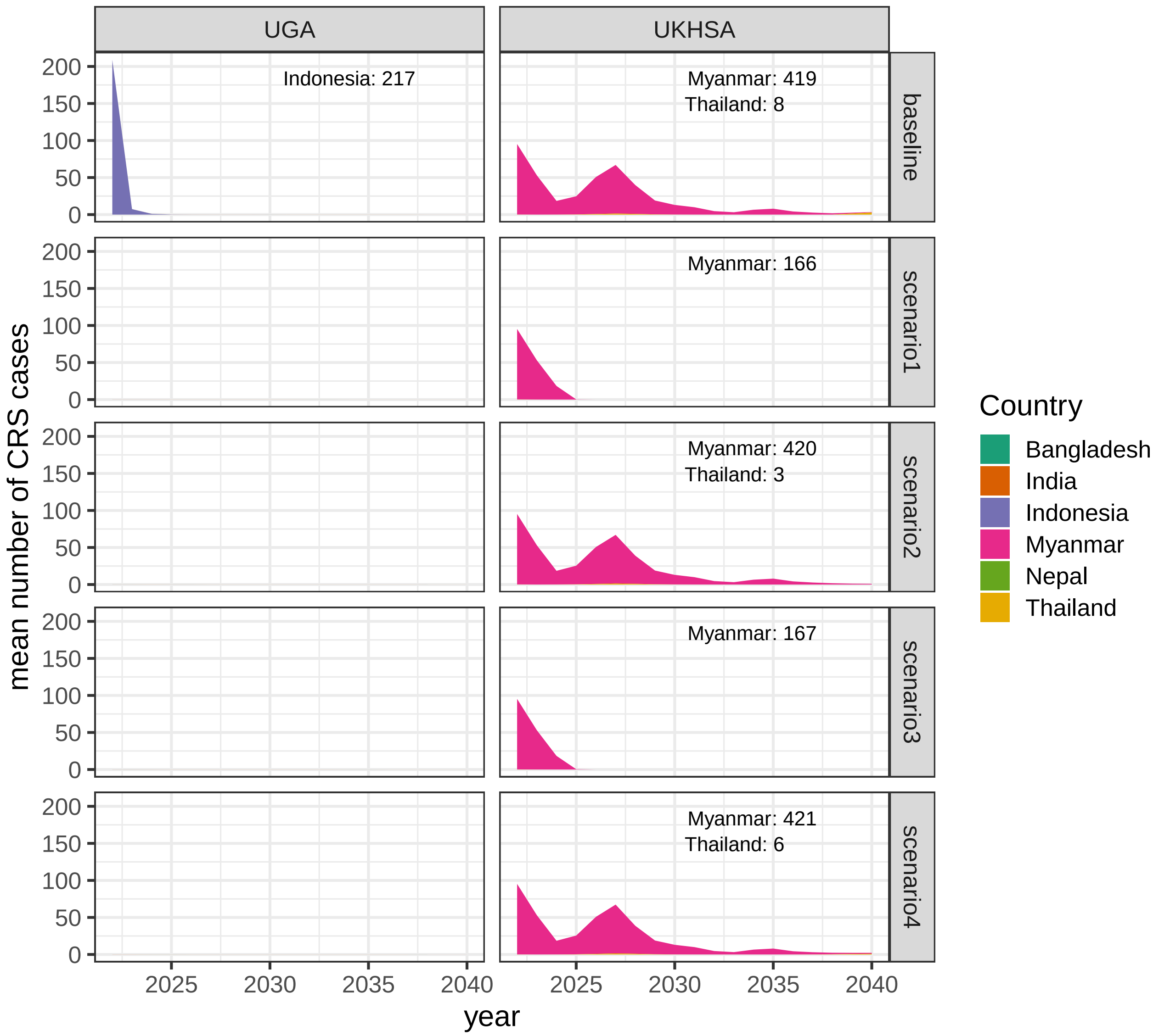


Figure 2: Annually estimated mean number of CRS cases (2022 - 2040) for each scenario (panel rows), model (panel columns), and country (colors)

Measles Results

Achieving the conditions necessary for measles elimination is probable under these vaccination scenarios.

Figure 3 displays the annually estimated mean number of measles infections (2022 - 2040) for each scenario, model, and country. Both measles models (DynaMice & PSU) showed similar trends and magnitude of measles infections by scenario, country, and time. We find that scenarios 1 and 3 tend to have the fewest number of infections (which included child and adult SIAs), followed by scenarios 2 and 4 (which included child SIAs only), and then baseline. The exception is Myanmar which have the fewest number of infections in the baseline scenario. **Figure 4** displays the probability of achieving conditions for measles elimination each year by country, model, and scenario. The annual probability of achieving conditions for elimination is calculated as the year-specific proportion of 200 simulations in which the incidence (i.e., infections per one million population) was less than or equal to 5. Consistent across models (and congruent with Figure 3 results) we find that in Bangladesh, India, and Nepal, scenarios 3 and 1 tended to have the highest 2022-2040 mean probability of elimination, followed by scenarios 2 and 4, and then finally the baseline scenario. In Indonesia both models found that scenarios 3 and 1 had highest 2022-2040 mean probability of elimination, followed by baseline, and then scenarios 2 and 4. And in Myanmar, the baseline vaccination scenario actually had the highest 2022-2040 mean probability of elimination in both models; this is the result of the faster increase in routine MR1 and MR2 in the baseline scenario compared to the other vaccination scenario (see supplement for vaccination scenario details).

The two measles models differ, however, on when and how often measles incidence in each country drops below the elimination threshold of 5 infections per one million population. Figure 4 shows large differences in the magnitude and range in the probability of elimination between the two measles models. The DynaMice model output has an overall higher probability of elimination in all countries and vaccination scenarios, and smaller differences across vaccination scenarios. These model output differences are primarily the result of how the models incorporate vaccination coverage (see supplement for more details). **Figure 5** shows the probability that conditions for measles elimination have been achieved by a given year for each country, scenario, and model. The probability that elimination is achieved by a given year is calculated as the proportion of 200 simulations in which the incidence (i.e., infections per one million population) was less than or equal to 5 for any year between 2022 and the given year. This figure is helpful to understand the year by which measles elimination could be achieved under these vaccination scenarios. Here we also see a higher probability elimination is achieved by a given year in the DynaMice model compared to the PSU model, though by 2025 both models estimate a probability of elimination greater than 60% by 2025 across all vaccination scenarios and countries. The population-weighted regional probability that the conditions for measles elimination have been achieved are displayed in **Figure 6**. We find that by 2025, the regional probability of elimination ranges from 0.94 to 0.95 in the DynaMice model and 0.76 to 0.83 in the PSU model. Given that measles is highly transmissible and the likely continuous importation pressure from other regions of the world, planning and investment for sustainable control strategies will be crucial to maintaining elimination once achieved.

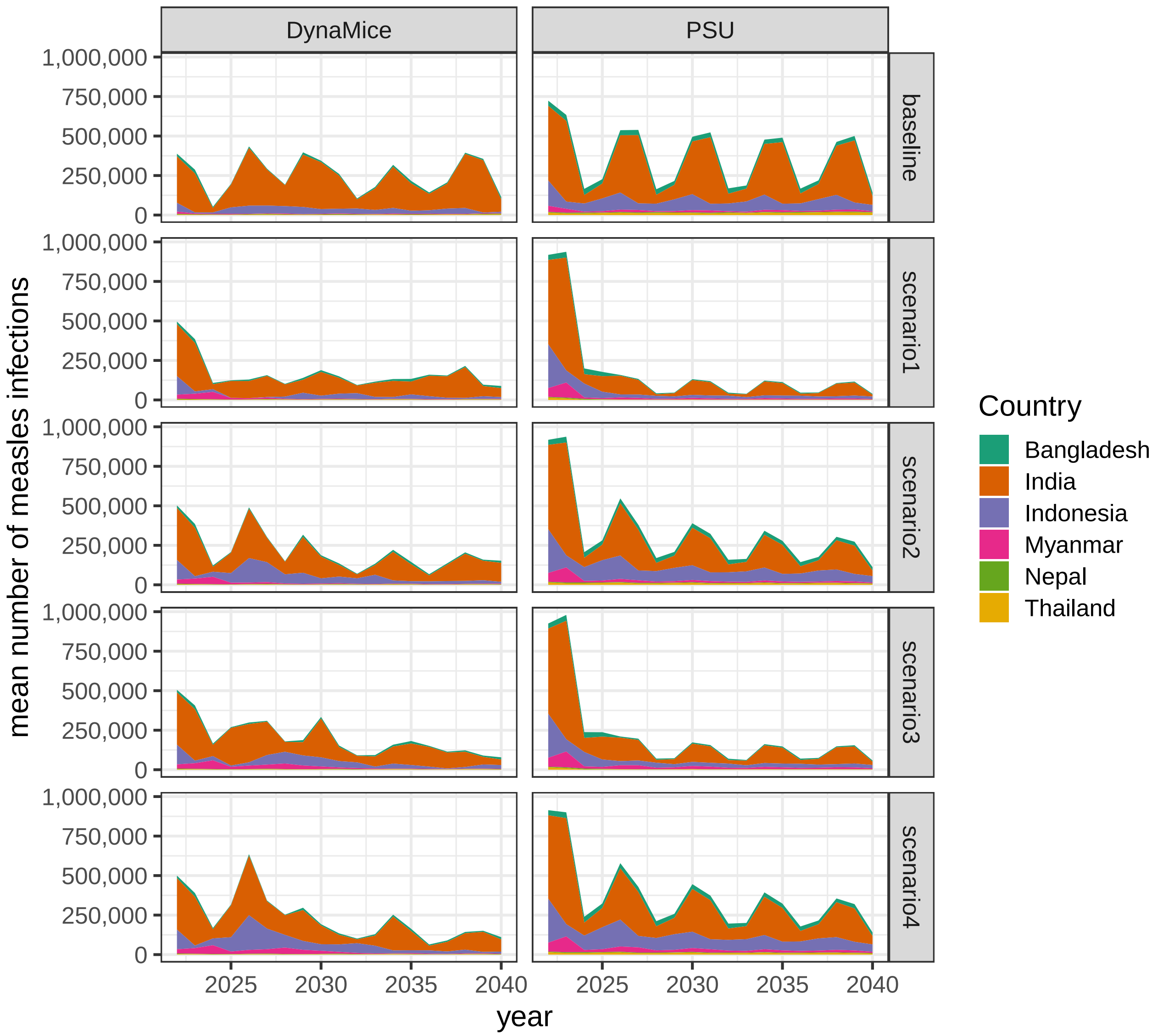


Figure 3: Annually estimated mean number of measles infections (2022 - 2040) for each scenario (panel rows), model (panel columns), and country (colors)

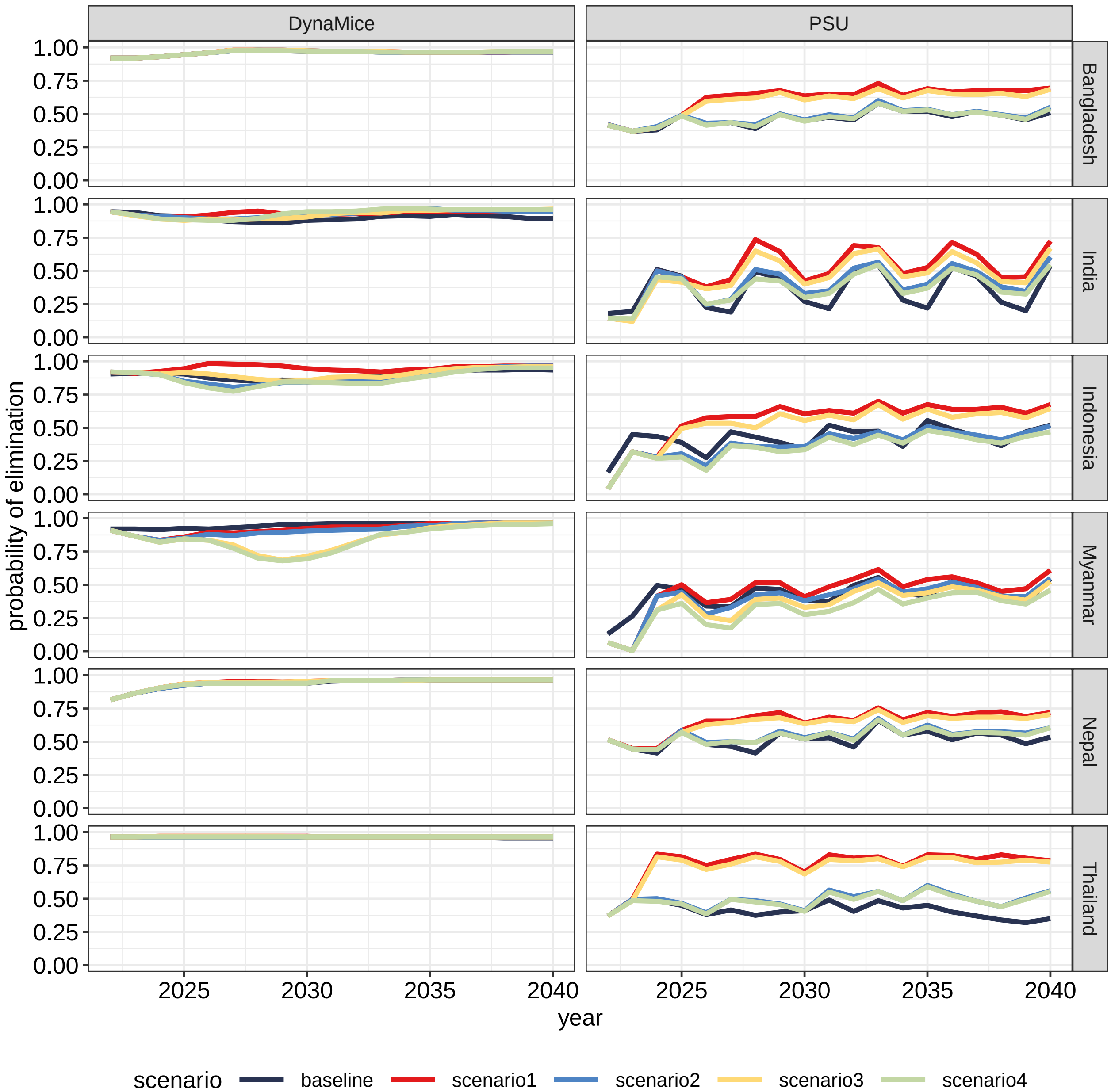


Figure 4: Annually estimated mean probability of achieving conditions for measles elimination (<= 5 infections per one million population) (2022 - 2040) for each country (panel rows), model (panel columns) and scenario (line colors)

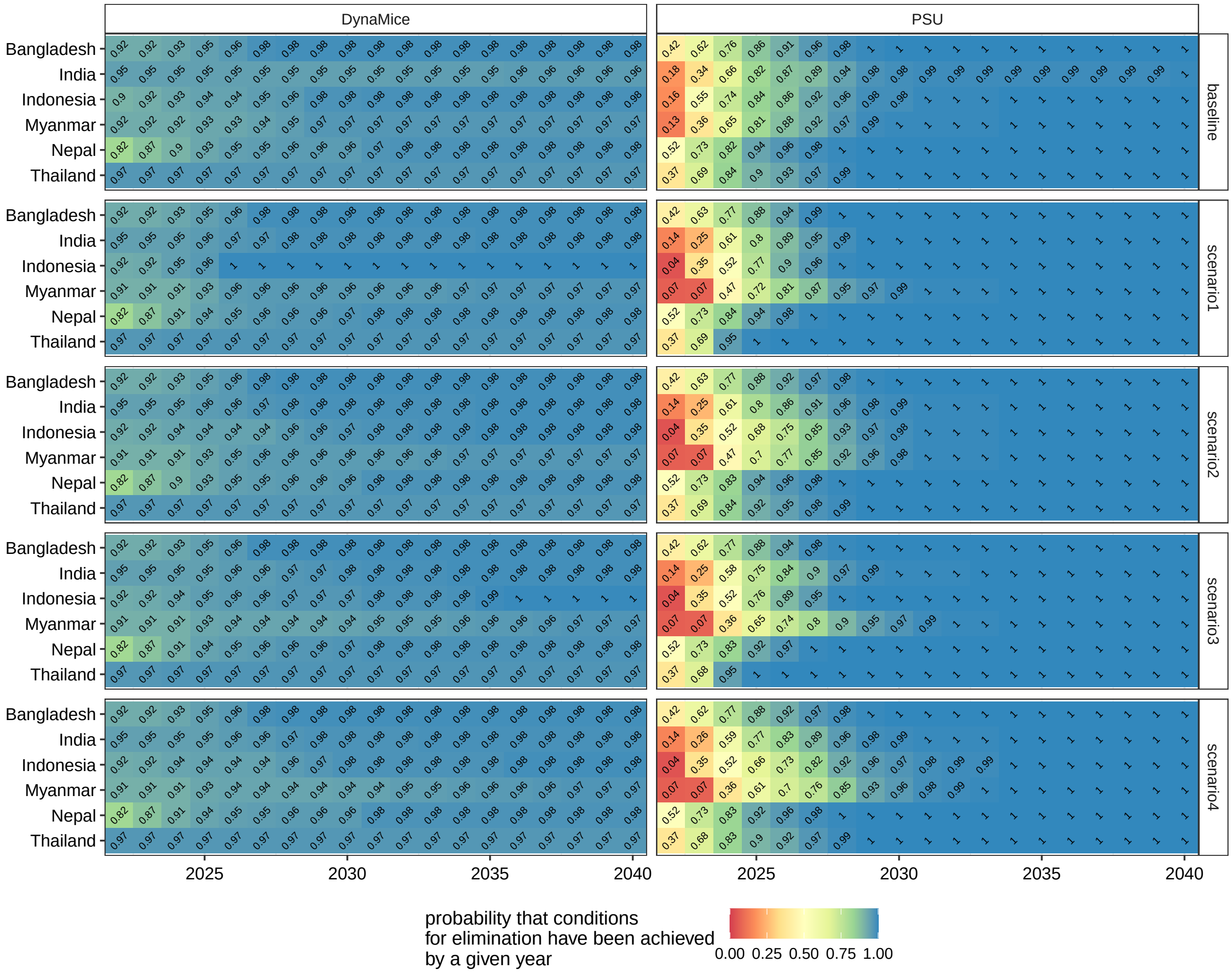


Figure 5: Probability that the conditions for measles elimination (<= 5 infections per one million population) have been achieved by a given year (x-axis) for each country (y-axis), scenario (panel rows), and model (panel columns)

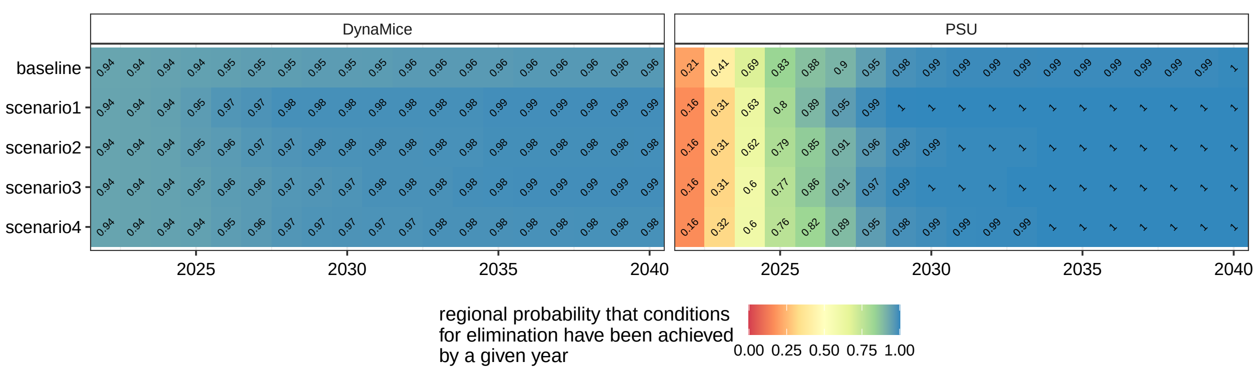
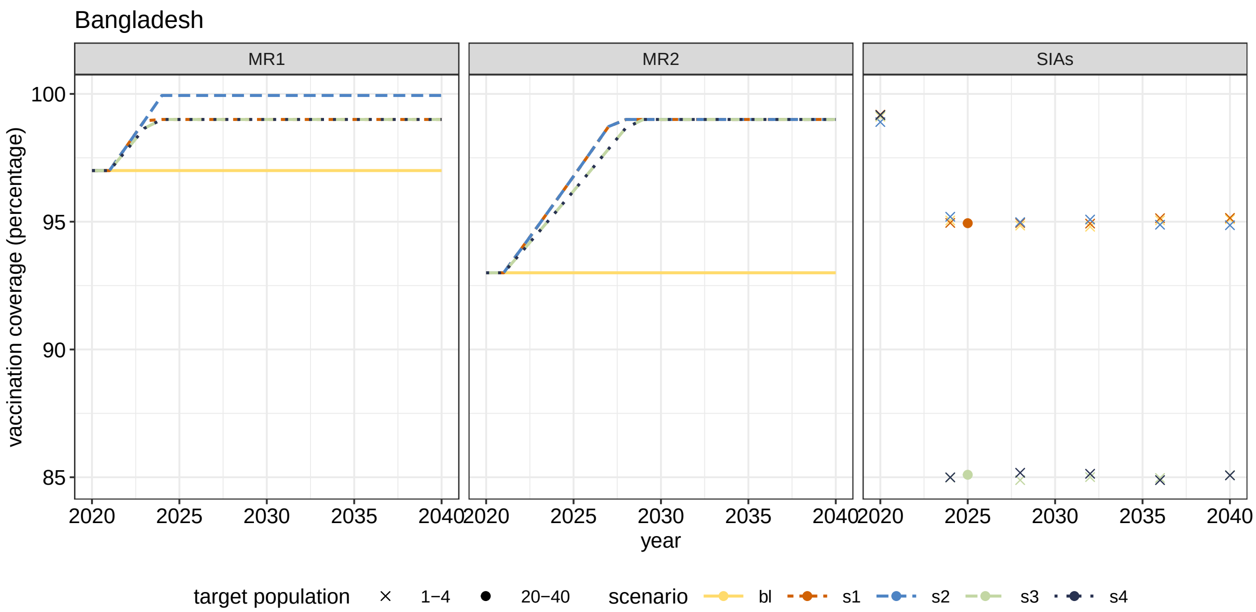


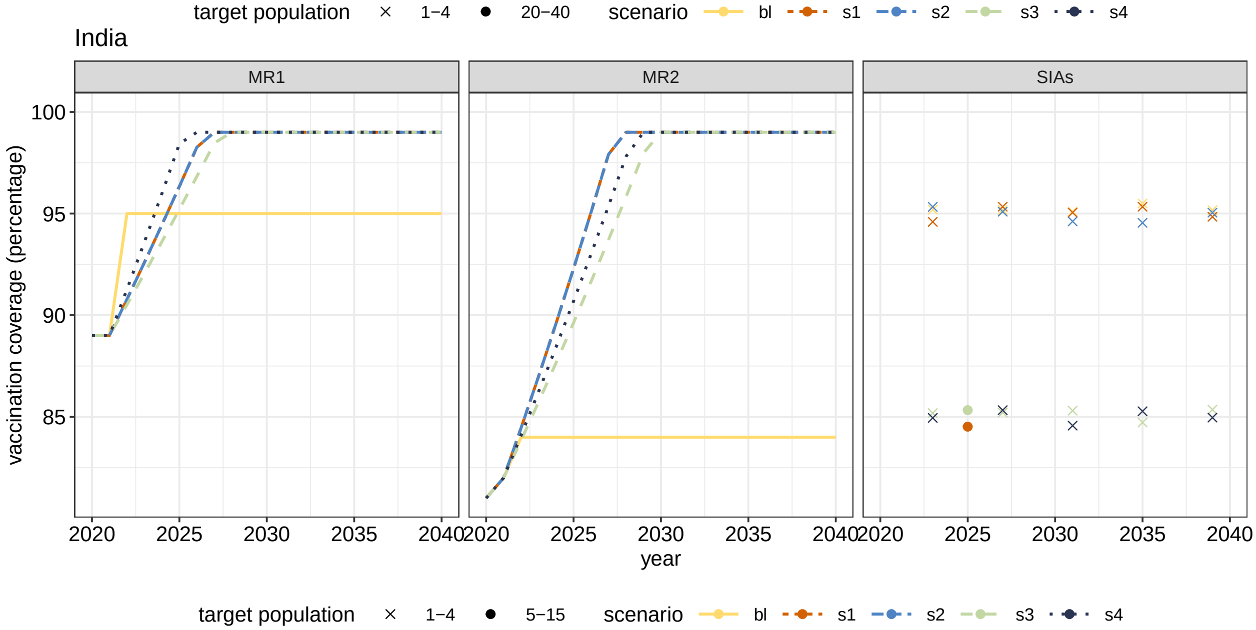
Figure 6: Regional probability that the conditions for measles elimination (<= 5 infections per one million population) have been achieved by a given year (x-axis) for each scenario (y-axis) and model (panel columns)

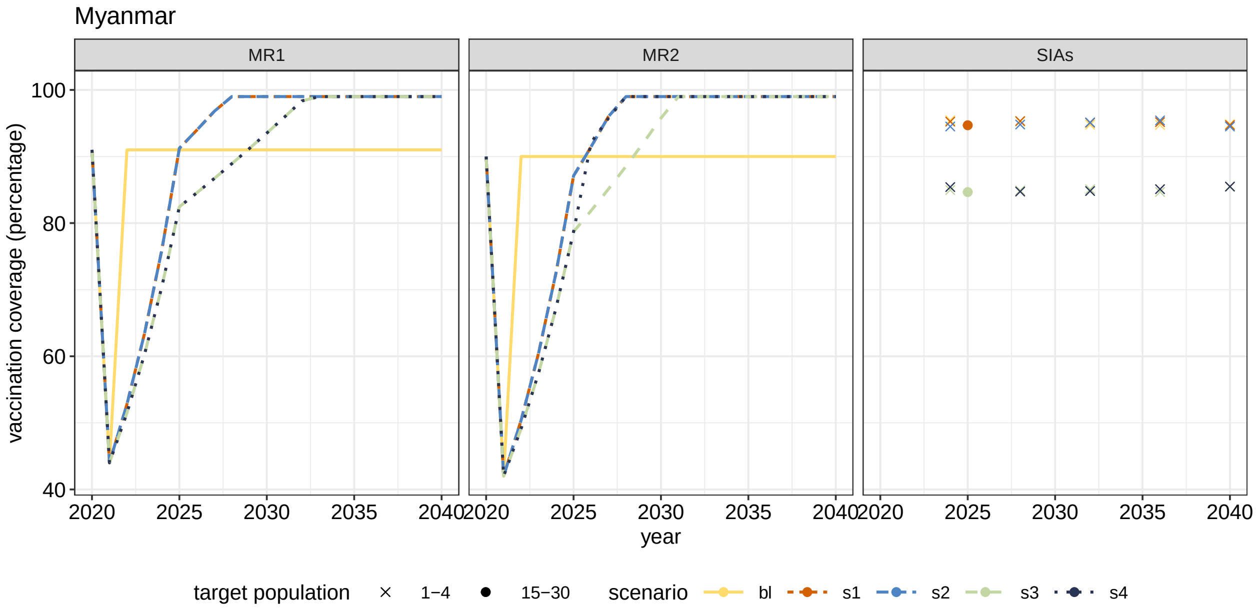
Supplemental Information

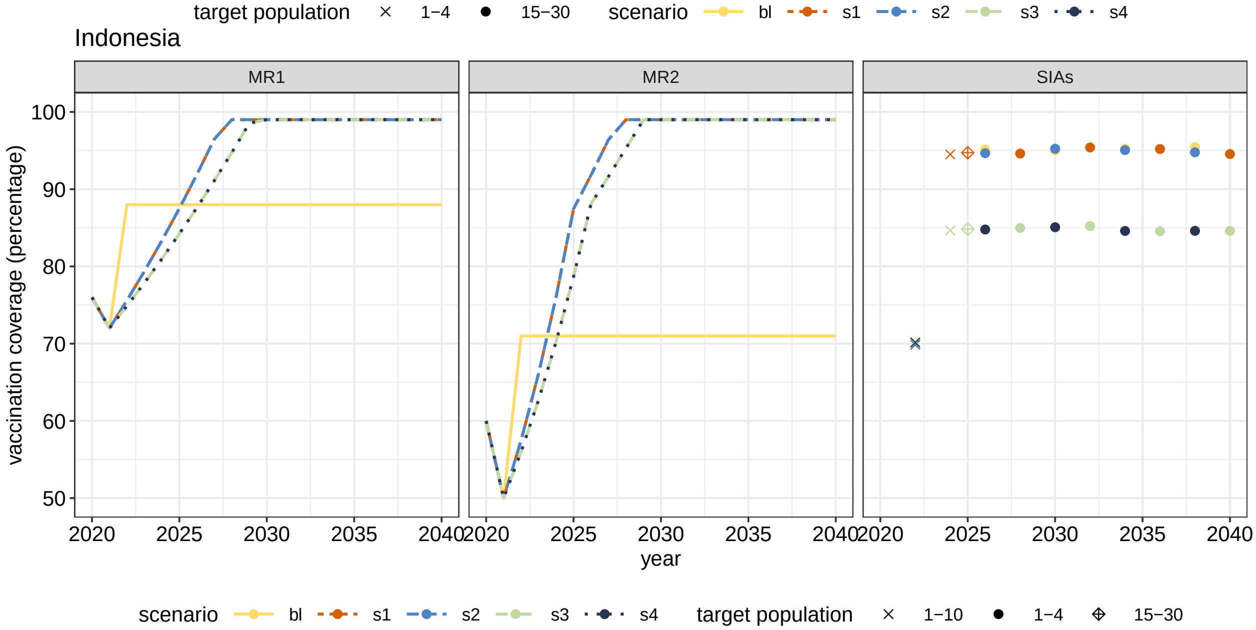
Vaccination Scenarios

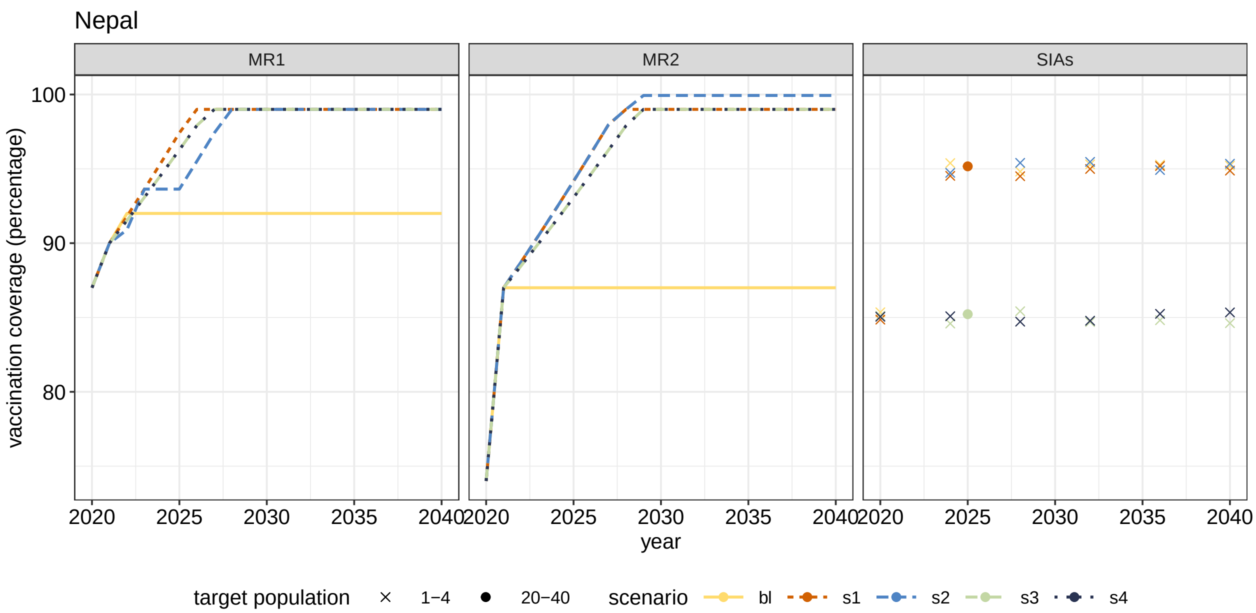
Measles and rubella vaccination scenarios are the same after rubella introduction which occurred prior to 2020 in all six countries of interest. The following displays MR vaccination per dose (i.e., MR1, MR2, campaign) in the columns, country in the rows, and vaccination scenarios represented by different colors.

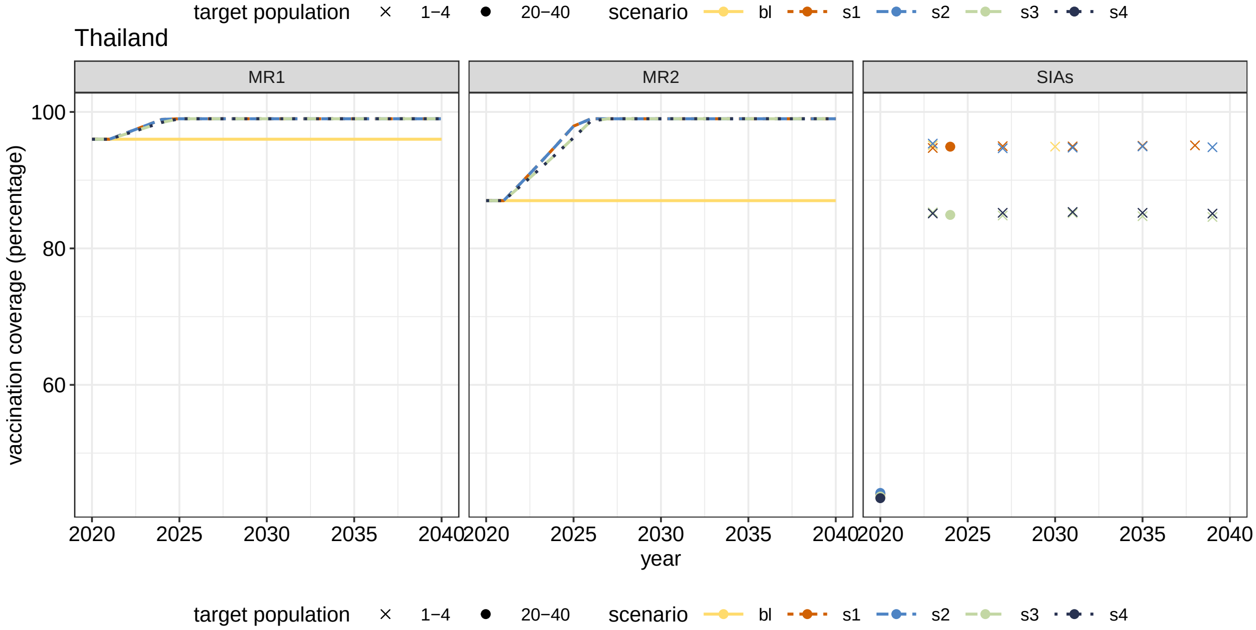





Myanmar
MR1
MR2
SIAs
vaccination coverage (percentage)
100
80
60
40
2020
2025
2030
2035
2040
year
target population
1−4
15−30
scenario
bl
s1
s2
s3
s4


Indonesia
MR1
MR2
SIAs
vaccination coverage (percentage)
100
90
80
70
60
50
2020
2025
2030
2035
2040
year
scenario
bl
s1
s2
s3
s4
target population
1−10
1−4
15−30





Understanding Differences in Measles Models

Differences in national measles model outputs are primarily the result of how the models incorporate vaccination coverage. The DynaMice model uses a more direct translation of coverage to impact than the PSU model. Taking into account age-specific vaccine effectiveness and dose correlations, vaccination coverage proportionately reduces the number of susceptibles in the DynaMice model, which is then translated into impact using a mass-action SIR-type model with age-dependent mixing. The PSU model fits a logistic relationship between the annual attack rate and the proportion of the susceptible population in each country independently. The estimated slope and intercept determine the speed at which measles cases respond to increases in the proportion of the population susceptible (i.e., coverage). For example, a steep slope indicates that the probability of infection increases quickly with a small increase in the proportion of the population susceptible (i.e. a large outbreak is likely after a small disruption). A shallow slope means that a large reduction in coverage (i.e., a large increase in susceptibles) would be necessary to generate a large and immediate outbreak. The shape of this function is fit to the annual measles time series from 1980 to 2019. As a result of these differences, the DynaMice model is more sensitive to vaccination changes close to the herd immunity threshold, is more likely to reduce to zero cases and stay low until the accumulation of susceptible individuals reaches herd immunity, at which time is likely to simulate a faster increase in the number of cases. This has a particular impact in countries with high vaccination coverage but continuing transmission in which the DynaMice model is more likely to predict elimination than the PSU model.

Despite these model differences, the trends in cases are consistent across models and the magnitude of cases are relatively similar in the two different scenarios.