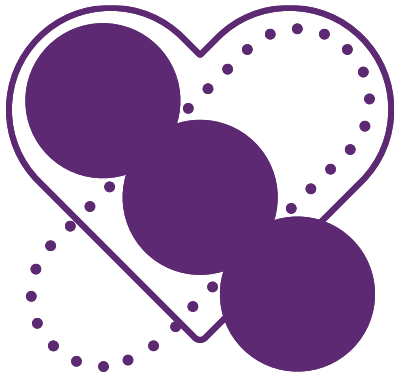

Strep A Vaccine Global Consortium

https://savac.ivi.int/

Introduction

- **Group A Streptococcus (Strep A)**
  - A wide spectrum of clinical manifestations – pharyngitis, skin infections, acute rheumatic fever (ARF), and rheumatic heart disease (RHD), etc.
  - Currently no vaccine available against Strep A infections
  - Lack of standardized surveillance programs and economic evaluations
  - Available studies being disproportionately lower in low-income countries than in high-income countries

- **Traditional investment case**
  - Literature review on existing cost-effectiveness analysis (CEA)
  - Estimating the economic burden of Strep A infections
  - Carrying out the cost-effectiveness analysis for a hypothetical Strep A vaccine at the global-level

Methods – Economic burden estimation 1

- **Initial literature search by the TKI team to identify any costs associated with Strep A**
- **Existing costs reported in various formats – manually reviewed and categorized them into:**
  - Direct medical costs (DMC)
  - Direct non-medical costs (DNMC)
  - Indirect costs (IC)
- **Insufficient number of existing studies**
  - By income group (as classified by the World Bank): significantly lower number of studies available in non-high-income countries
  - By disease manifestation: disproportionately low number or absence of economic burden data for multiple disease manifestations
- **Disease outcomes for economic burden estimation**
  - Pharyngitis, ARF, RHD, severe RHD, invasive infections, impetigo, and cellulitis

Methods – Economic burden estimation 2

- **Creating adjustment factors to overcome related data insufficiency**
  - WHO-CHOICE unit cost database
    - Patient type (inpatient, outpatient), Facility type (primary-, secondary-, and tertiary-level)
  - Healthcare big data hub system
    - Frequency of visits, duration of bed-days, number of inpatients / outpatients
    - 10-year period to account for variability
    - The number of outpatient visits / inpatient bed-days per episode
  - GDP per capita
- **Productivity loss due to death**
  - Premature death from RHD and invasive infections
  - The weighted average age of death based on IHME
    - RHD, Invasive infections (pneumococcus and meningococcal meningitis)
  - Multiplying productivity years lost by minimum wage (discounted at the rate of 3%)
- **Sensitivity analysis**
  - A large degree of uncertainty on input parameters
  - Probabilistic multivariate sensitivity analysis
  - Monte Carlo simulation – estimate 95% confidence intervals

Methods – Cost-effectiveness analysis 1

- **A static cohort model and 6 vaccination scenarios set up by the TKI team**
  - Pharyngitis, RHD, invasive infections, impetigo, and cellulitis

Scenario	Assumption
1	Vaccine adoption year (country-specific), coverage rate (country-specific Hib3), full efficacy for 10 years
2	Vaccine adoption year (country-specific), coverage rate (country-specific Hib3), linear waning over 20 years
3	Vaccine adoption year (2022), coverage rate (50%), full efficacy for 10 years
4	Vaccine adoption year (2022), coverage rate (50%), linear waning over 20 years
5	Vaccine adoption year (country-specific), coverage rate (50%), full efficacy for 10 years
6	Vaccine adoption year (country-specific), coverage rate (50%), linear waning over 20 years

- Initial vaccination coverage rate: 10% of the peak coverage rates
- Annual uptake rate of 10% since the year of vaccine introduction

Methods – Cost-effectiveness analysis 2

- **WHO preferred product characteristics (PPC) for a Strep A vaccine**
  - Pharyngitis (80%), RHD (50%), invasive infections (70%), impetigo (80%), cellulitis (70%)

Item	Assumption
Geographical presentation	World Bank income groups (HIC, UMIC, LMIC, LIC)
Vaccine doses	3 doses
Vaccination strategies	Routine at birth; routine at 5 years of age
Cost per fully vaccinated person	$0 - $300
Discounting	3% discounting for costs and health outcomes (default); 0% discounting for health outcomes (sensitivity analysis)
Wastage factor during vaccination campaigns	10% (default); 5% and 20% (sensitivity analysis)
Economic burden	Point estimates (default); 95% confidence intervals (sensitivity analysis); societal perspective
Cost-effectiveness threshold	1 x GDP per capita (default); health opportunity costs (conservative)

- **Sensitivity analyses – univariate, as well as multivariate sensitivity analyses**

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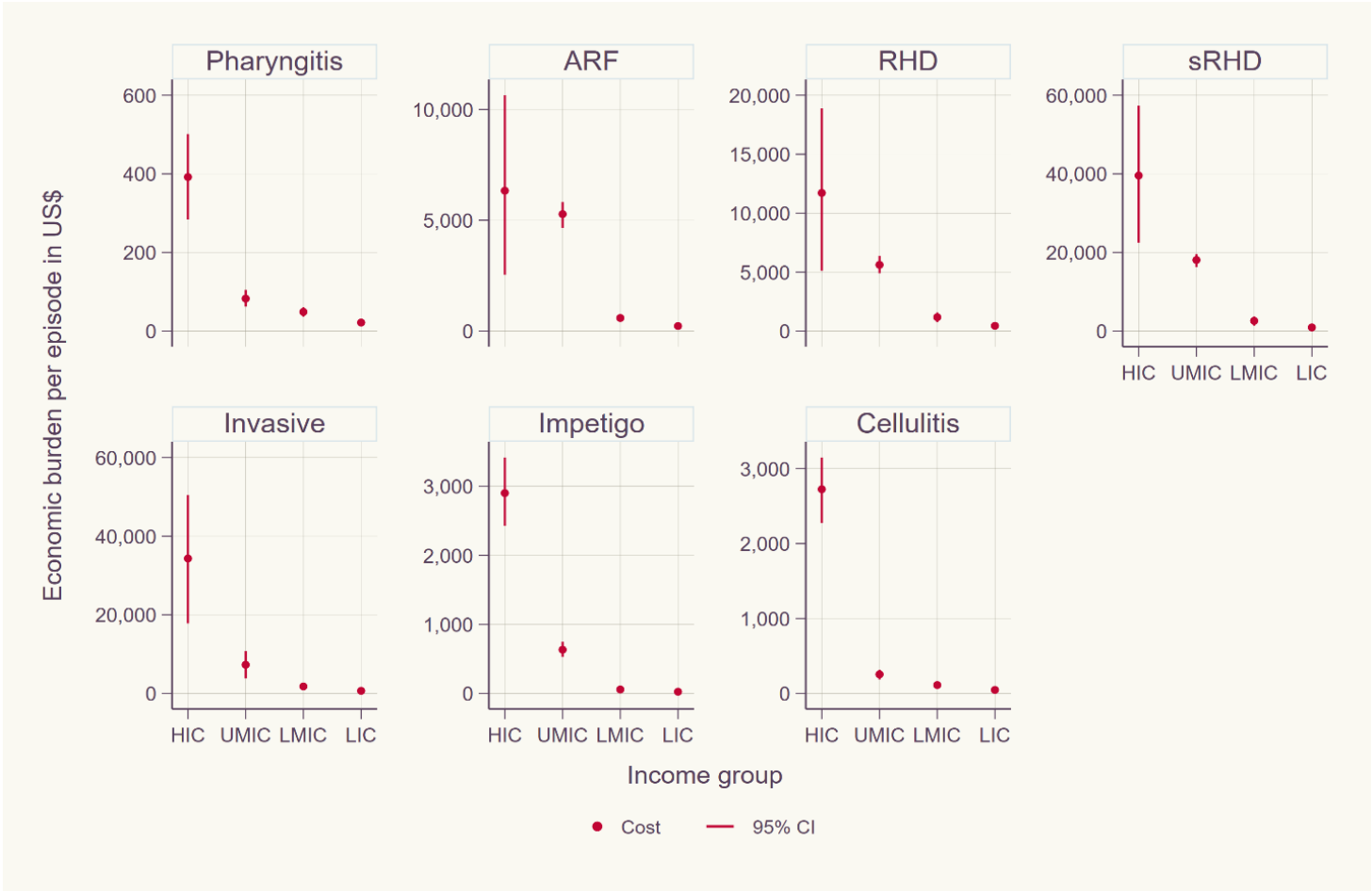
Results – Economic burden per episode by income group

- Overall, economic burden being higher in HIC than in LIC / for more severe illnesses than for mild infections
- $22 - $392 for pharyngitis, $231 - $6,332 for ARF, $449 - $11,717 for RHD, $949 - $39,560 for severe RHD, $662 - $34,330 for invasive infections, $25 - $2,903 for impetigo, and $47 - $2,725 for cellulitis



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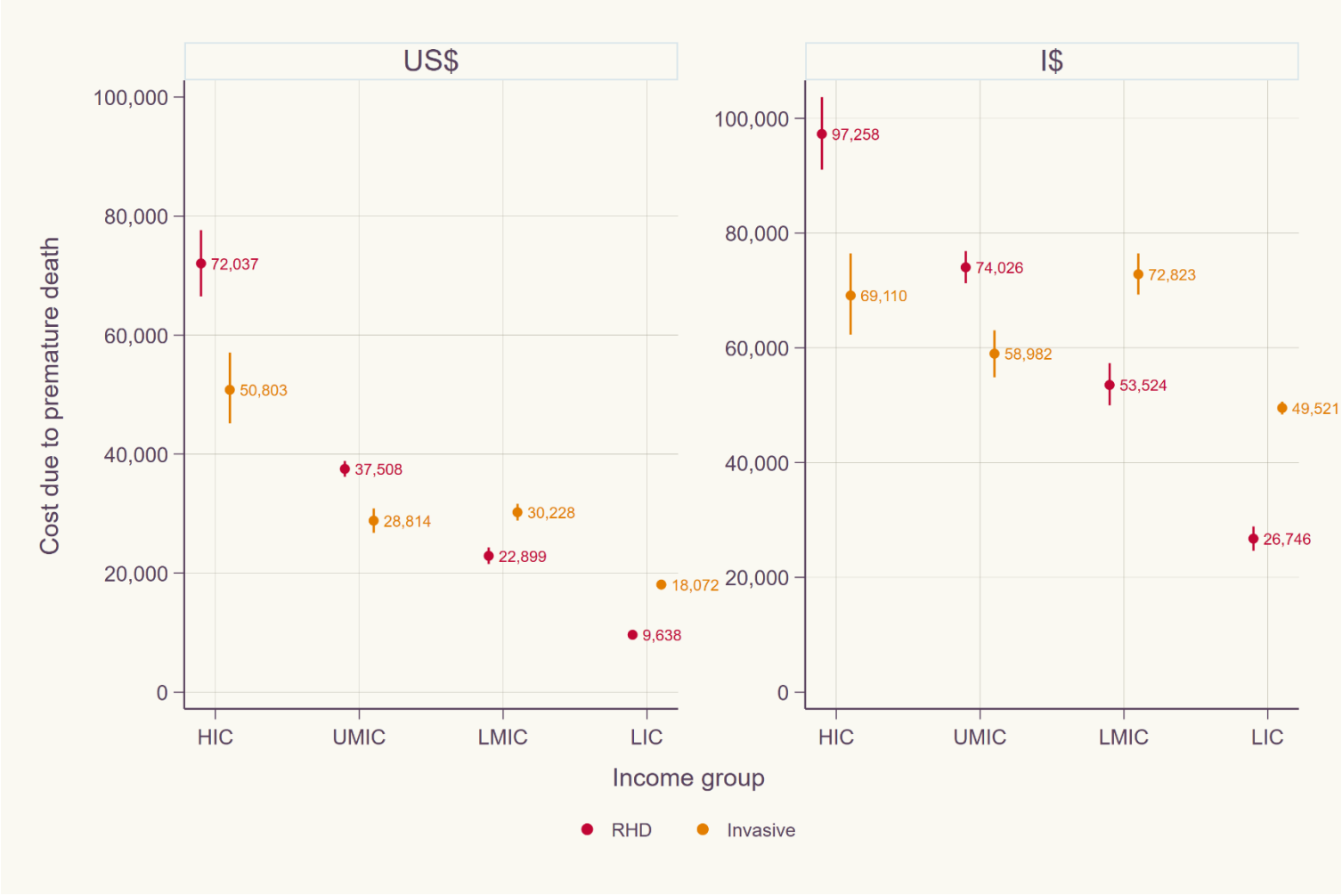
Results – Productivity loss due to premature death

- Productivity years lost being the lowest in HIC
- Cost due to early death being the greatest in HIC and the lowest in LIC
- Higher income level in the higher-income groups than lower-income groups



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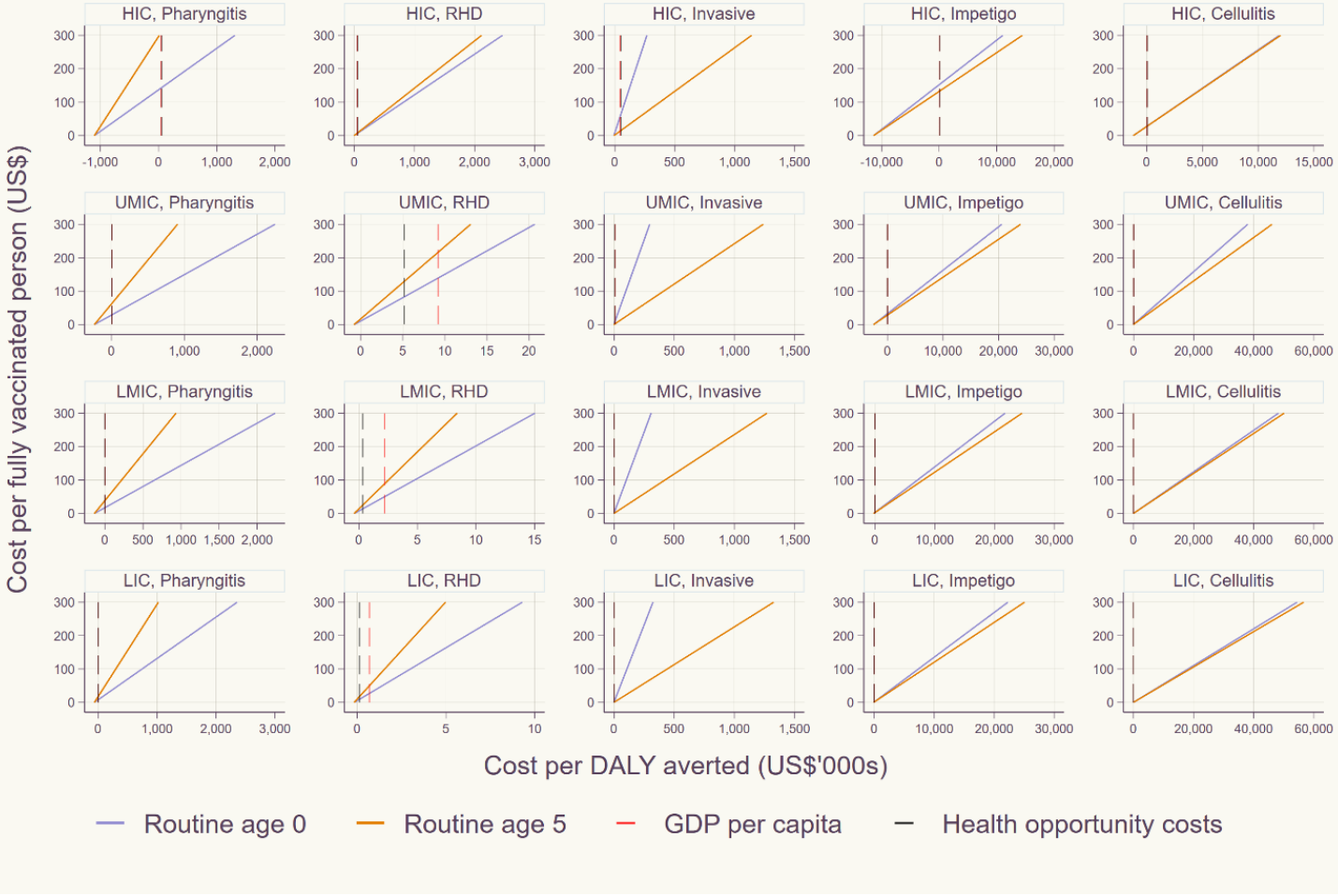
Results – Incremental cost-effectiveness ratios (ICERs)

- 5-yo routine vaccination for pharyngitis and RHD
- Infant routine vaccination for invasive infections
- Marginal differences between the two vaccination strategies for skin infections



Incremental cost-effectiveness ratios by income group under scenario 1.

Interventions are considered to be cost-effective if the total cost per fully vaccinated person is located on the left side of varying threshold costs per DALY averted.

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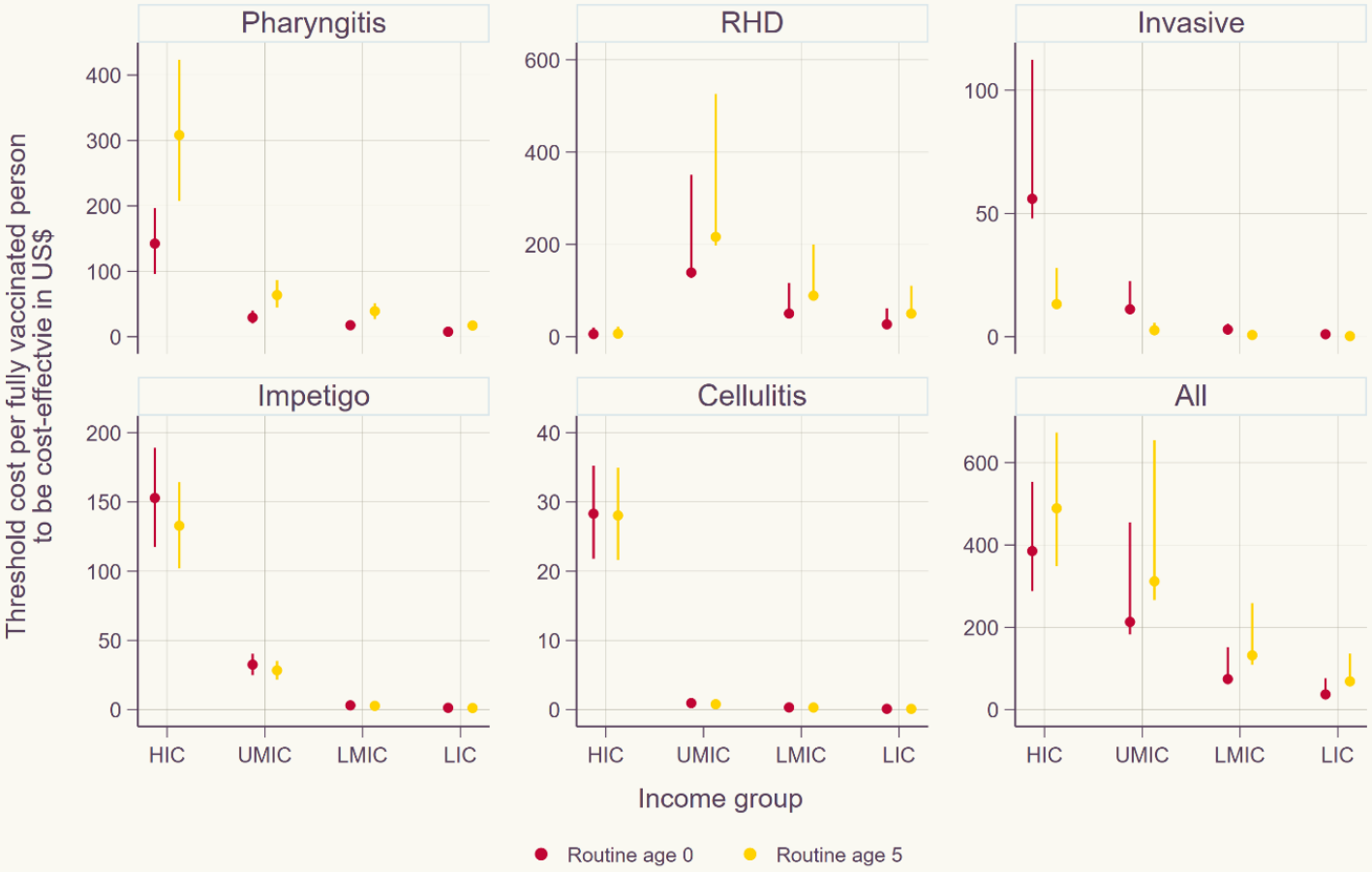
Results – Maximum cost per fully vaccinated person

- At the threshold of 1 x GDP per capita
- Pharyngitis ($8-$308), RHD ($6 - $216), Invasive infections ($0.2 - $56), Impetigo ($1 - $153), Cellulitis ($0.1 - $28), All ($37 - $489)



Threshold cost per fully vaccinated person to be cost-effective by income group under scenario 1.

Lower bounds are for the least favorable scenario: 20% wastage rate, lower bound of economic burden, and 3% discounting of health outcomes. Upper bounds are based on the most favorable scenario: 5% wastage rate, upper bound of economic burden, and 0% discounting of health outcomes. Scales on the Y-axes vary.

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Findings, limitations, and future research needs

- **Substantial economic burden for Strep A infections**
- **Cost-effective if a threshold cost per fully vaccinated person is properly set**
- **Sensitive to vaccine characteristics**
  - Efficacy, waning, duration of protection, etc.
  - Absence of Strep A vaccines – WHO preferred product characteristics
  - Updates required as clinical trials for potential vaccine candidates advance
- **Scarcity of existing studies on both economic and disease burden for multiple disease outcomes caused by Strep A**
- **Future research needs**
  - Increase a number of primary data points such as surveillance programs, and field-based economic burden studies
  - Lack of evidence in LMICs and LICs

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Thank you!

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