Estimating the impact and cost-effectiveness of RSV interventions on infant health

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Background

Respiratory syncytial virus (RSV) has a large morbidity and mortality burden

RSV interventions under development

- RSV maternal vaccines
- RSV monoclonal antibodies (mAbs)

RSV interventions, once available, are expected to be included in Gavi, the Vaccine Alliance's portfolio
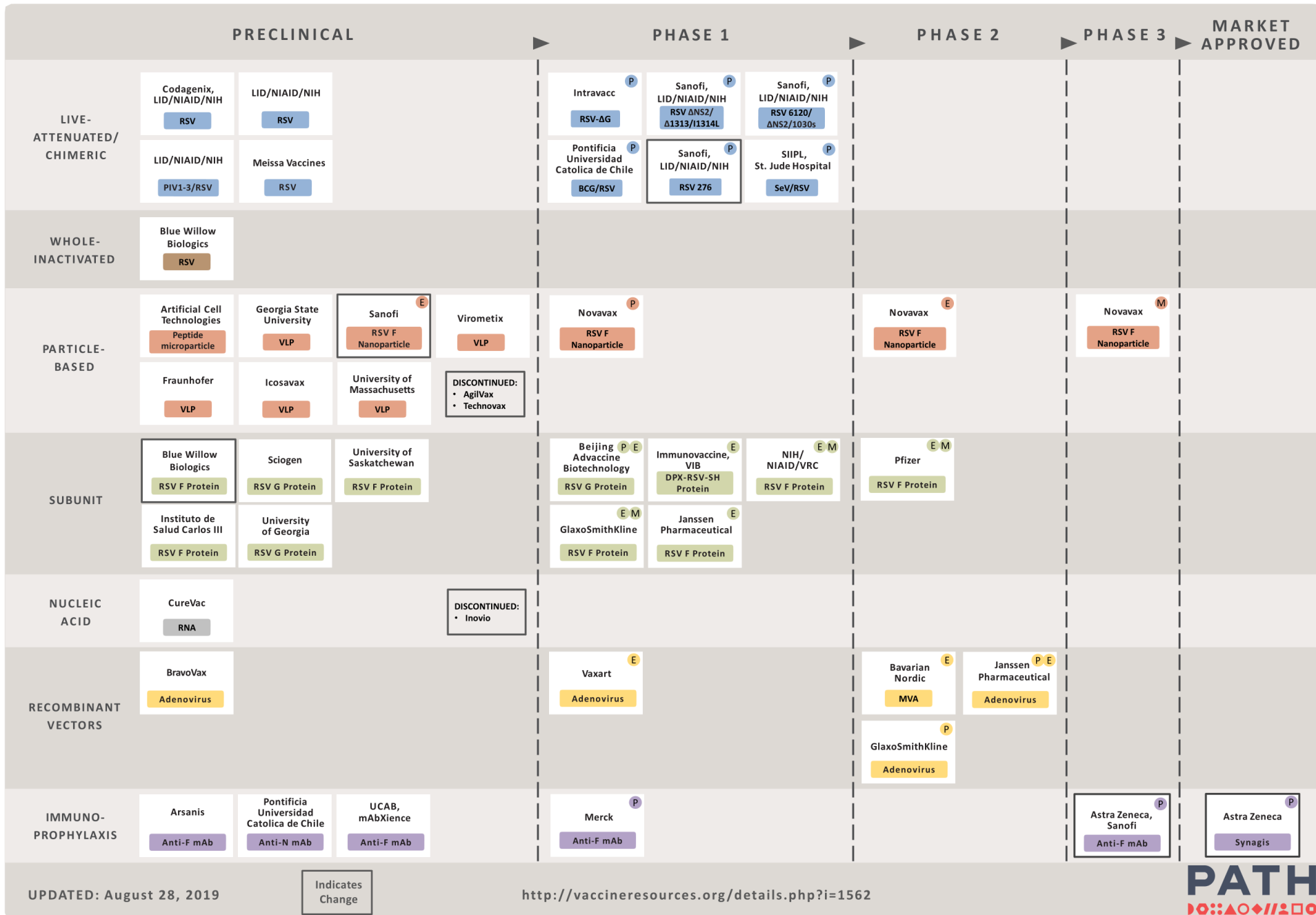
Interventions are anticipated to be available in non-Gavi low- and middle-income countries (LMICs)

Impact and cost-effectiveness modelling can inform the value of RSV interventions for global and country decision makers

RSV Vaccine and mAb Snapshot

TARGET INDICATION: **P** =PEDIATRIC **M** =MATERNAL **E** =ELDERLY

	PRECLINICAL				PHASE 1			PHASE 2	PHASE 3	MARKET APPROVED
LIVE-ATTENUATED/ CHIMERIC	Codagenix, LID/NIAID/NIH — RSV	LID/NIAID/NIH — RSV			Intravacc — RSV-ΔG (P)	Sanofi, LID/NIAID/NIH — RSV ΔNS2/Δ1313/I1314L (P)	Sanofi, LID/NIAID/NIH — RSV 6120/ΔNS2/1030s (P)			
	LID/NIAID/NIH — PIV1-3/RSV	Meissa Vaccines — RSV			Pontificia Universidad Catolica de Chile — BCG/RSV (P)	Sanofi, LID/NIAID/NIH — RSV 276 (P)	SIIPL, St. Jude Hospital — SeV/RSV (P)			
WHOLE-INACTIVATED	Blue Willow Biologics — RSV									
PARTICLE-BASED	Artificial Cell Technologies — Peptide microparticle	Georgia State University — VLP	Sanofi — RSV F Nanoparticle (E)	Virometix — VLP	Novavax — RSV F Nanoparticle (P)			Novavax — RSV F Nanoparticle (E)	Novavax — RSV F Nanoparticle (M)	
	Fraunhofer — VLP	Icosavax — VLP	University of Massachusetts — VLP	DISCONTINUED: • AgilVax • Technovax						
SUBUNIT	Blue Willow Biologics — RSV F Protein	Sciogen — RSV G Protein	University of Saskatchewan — RSV F Protein		Beijing Advaccine Biotechnology — RSV G Protein (P E)	Immunovaccine, VIB — DPX-RSV-SH Protein (E)	NIH/NIAID/VRC — RSV F Protein (E M)	Pfizer — RSV F Protein (E M)		
	Instituto de Salud Carlos III — RSV F Protein	University of Georgia — RSV G Protein			GlaxoSmithKline — RSV F Protein (E M)	Janssen Pharmaceutical — RSV F Protein (E)				
NUCLEIC ACID	CureVac — RNA			DISCONTINUED: • Inovio						
RECOMBINANT VECTORS	BravoVax — Adenovirus				Vaxart — Adenovirus (E)			Bavarian Nordic — MVA (E)	Janssen Pharmaceutical — Adenovirus (P E)	
								GlaxoSmithKline — Adenovirus (P)		
IMMUNO-PROPHYLAXIS	Arsanis — Anti-F mAb	Pontificia Universidad Catolica de Chile — Anti-N mAb	UCAB, mAbXience — Anti-F mAb		Merck — Anti-F mAb (P)				Astra Zeneca, Sanofi — Anti-F mAb (P)	Astra Zeneca — Synagis (P)

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Objective

Estimate the impact and cost-effectiveness of using RSV maternal immunization and/or mAbs to protect young infants from severe RSV disease across LMICs

- Highlight results from Asia

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Methods overview

Static population-based cohort model

Examine benefits of RSV maternal vaccine or mAb to impact newborn health

- Explore vaccine efficacy against RSV end points
- Explore vaccine efficacy against all cause LRTI, as demonstrated in recent trial

Comparator is no intervention

Key outcomes include averted cases, hospitalizations, deaths, DALYs, cost/DALY

Includes 131 LMICs

Time period: 2030-2039

Assumes national introduction in all countries in 2030

Perspective: Health system perspective, though excludes Gavi subsidy for eligible countries

Costs presented in 2016 USD

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Key data inputs and assumptions

Inputs	Vaccine	mAb	Sources
Efficacy against RSV (%)	Cases (41%); Hospitalizations (42%); Deaths (60%)	Cases (60%); Hospitalizations (60%); Deaths (70%)	PREPARE Phase 3 trial (expanded results), expert opinion
Duration of protection against RSV	3-months	6-months	PREPARE Phase 3 trial (expanded results), expert opinion
Efficacy against all lower respiratory tract infections (LRTI)	Cases (25%); Hospitalizations (25%); Deaths (39%)	Cases (25%); Hospitalizations (25%); Deaths (39%)	PREPARE Phase 3 trial (expanded results), expert opinion
Duration of protection against all LRTI	6-months	6-months	PREPARE Phase 3 trial (expanded results), expert opinion
Vaccination window	24-36 weeks of gestation for maternal vaccine	Not applicable	Expert opinion
Intervention coverage	Derived from antenatal care coverage *(Range in 40%-96%, in year 2030)*	BCG coverage *(Range in 74%-99%, in year 2030)*	Demographic and Health Surveys

Key data inputs and assumptions

Inputs	Value	Source
Disease burden (RSV-acute lower respiratory infection [ALRI])	Global, regional, and national level estimates	Shi et al., 2017 (Lancet)
Disease burden (all cause-ALRI)	National level estimates	IHME, GBD 2017
Intervention pricing	$3 per dose in Gavi countries $5 per dose in non-Gavi countries	Assumed
Intervention delivery costs for maternal vaccine and mAb	$0.63 (low-income country); $1.73 (middle-income country)	Immunization Delivery Cost Catalogue (ICAN)

RSV burden averted, (2030-2039)

- **A maternal RSV vaccine is projected to avert millions of RSV cases and hospitalizations; more than 130k deaths.**
- **Approximately half of the projected impact of a maternal RSV vaccine is in Asia.**

Maternal RSV vaccine — bar chart of Averted burden, Millions for All LMICs and Asian LMICs across Non-severe cases, Severe cases, Hospitalizations, and Deaths.
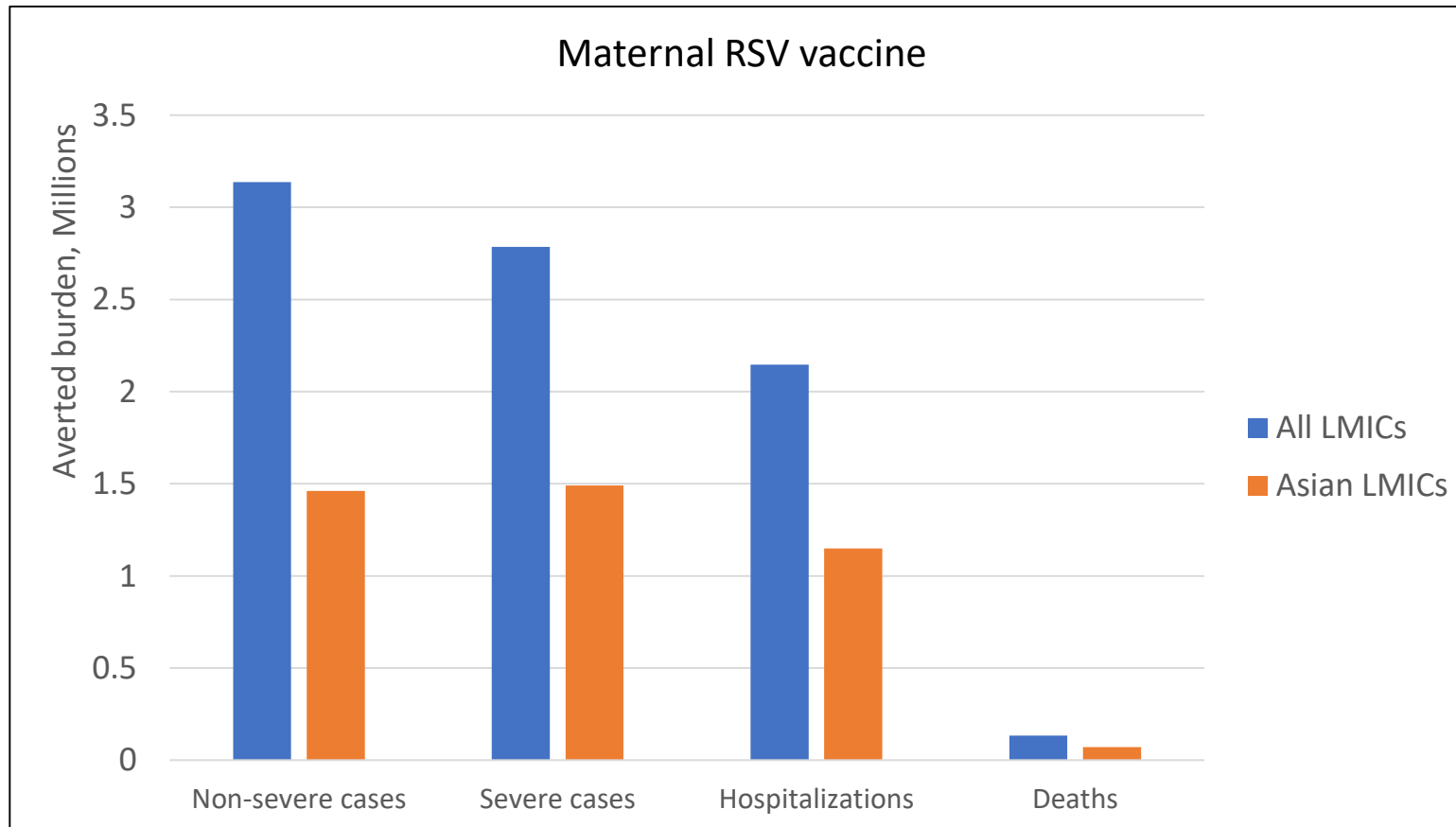
RSV burden averted, (2030-2039)

- **A mAb is projected to avert millions of RSV cases, hospitalizations, and nearly 300k deaths.**
- **Approximately half of the projected impact is in Asia.**

RSV monoclonal antibodies
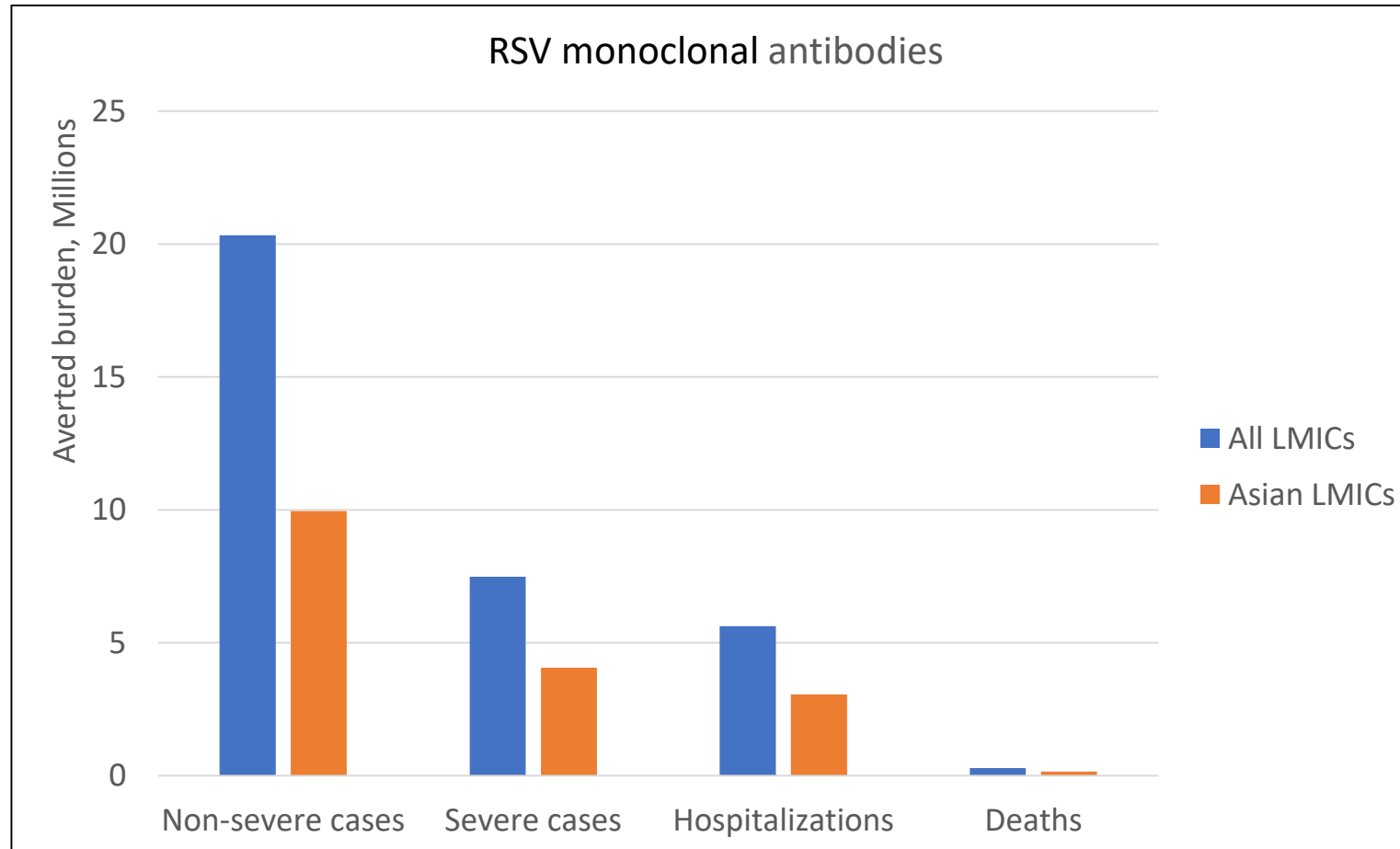
RSV burden averted, (2030-2039)

A mAb could be more than two times as impactful on RSV disease as a maternal vaccine due to higher expected coverage, efficacy and longer duration of protection.
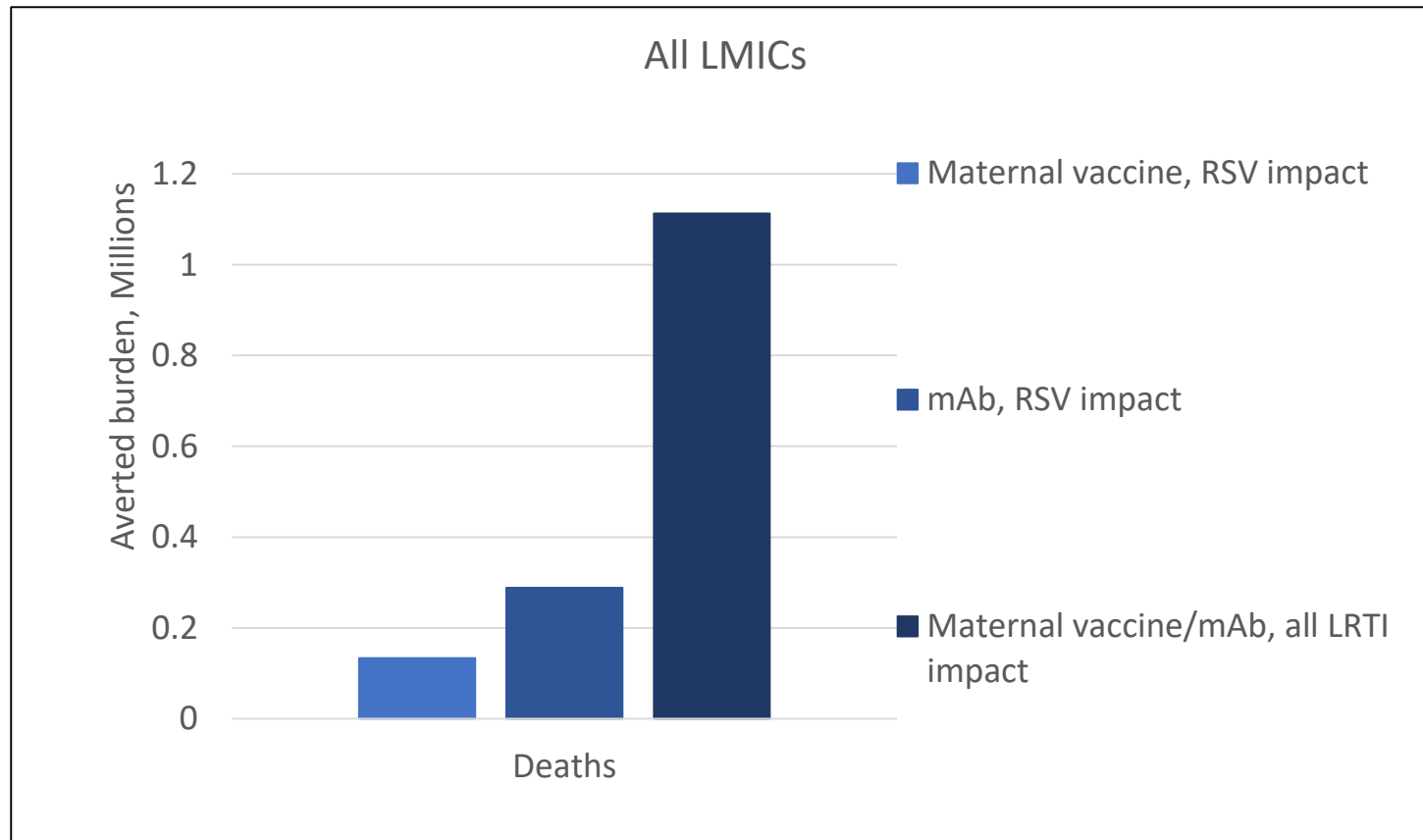

All LMICs

Averted burden, Millions

Legend: Maternal vaccine, mAb

Categories: Non-severe cases, Severe cases, Hospitalizations, Deaths
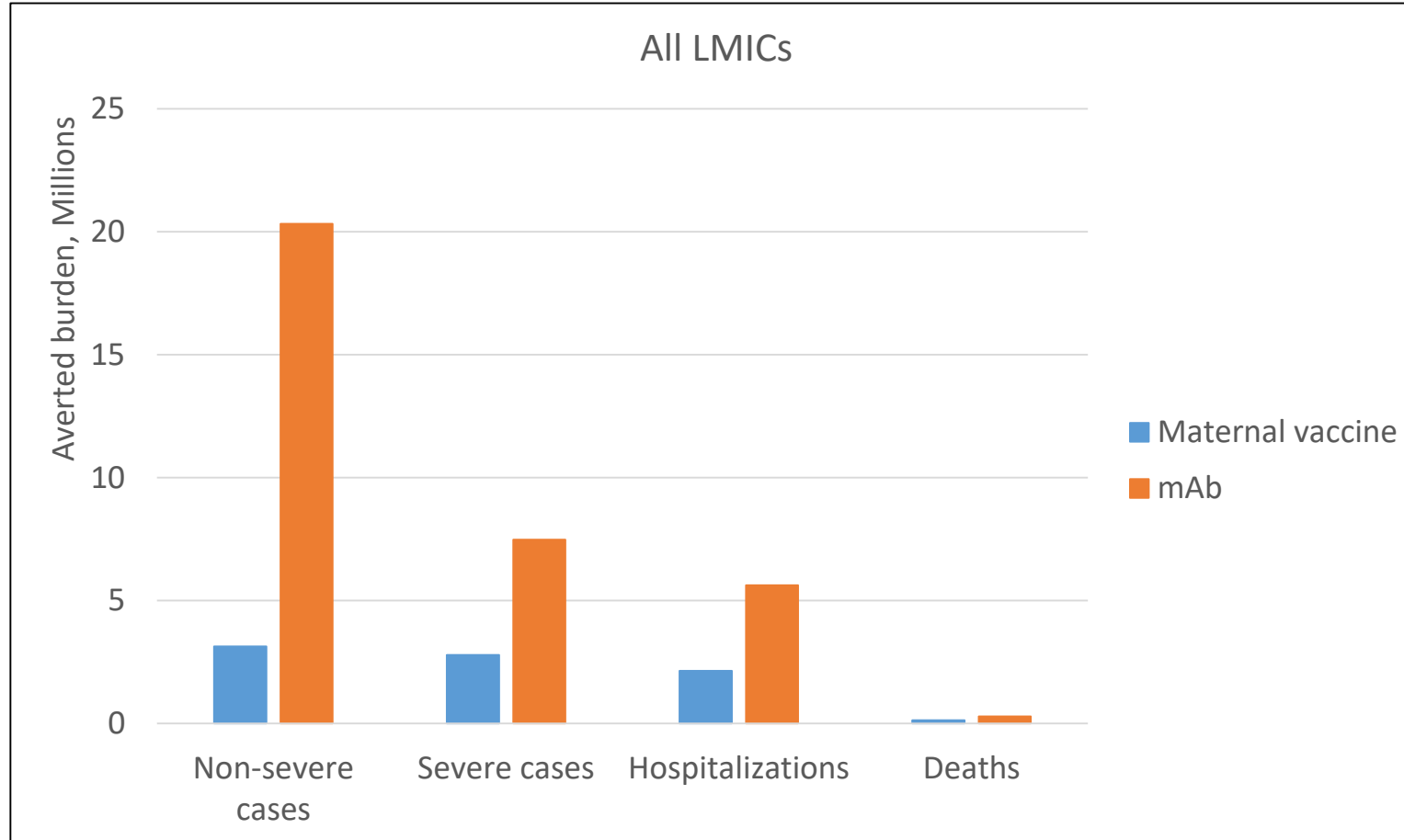
All cause LRTI burden averted, (2030-2039)

Maternal RSV vaccines and mAbs have been shown to avert substantial all cause LRTI burden—millions of severe cases, hospitalizations and deaths.
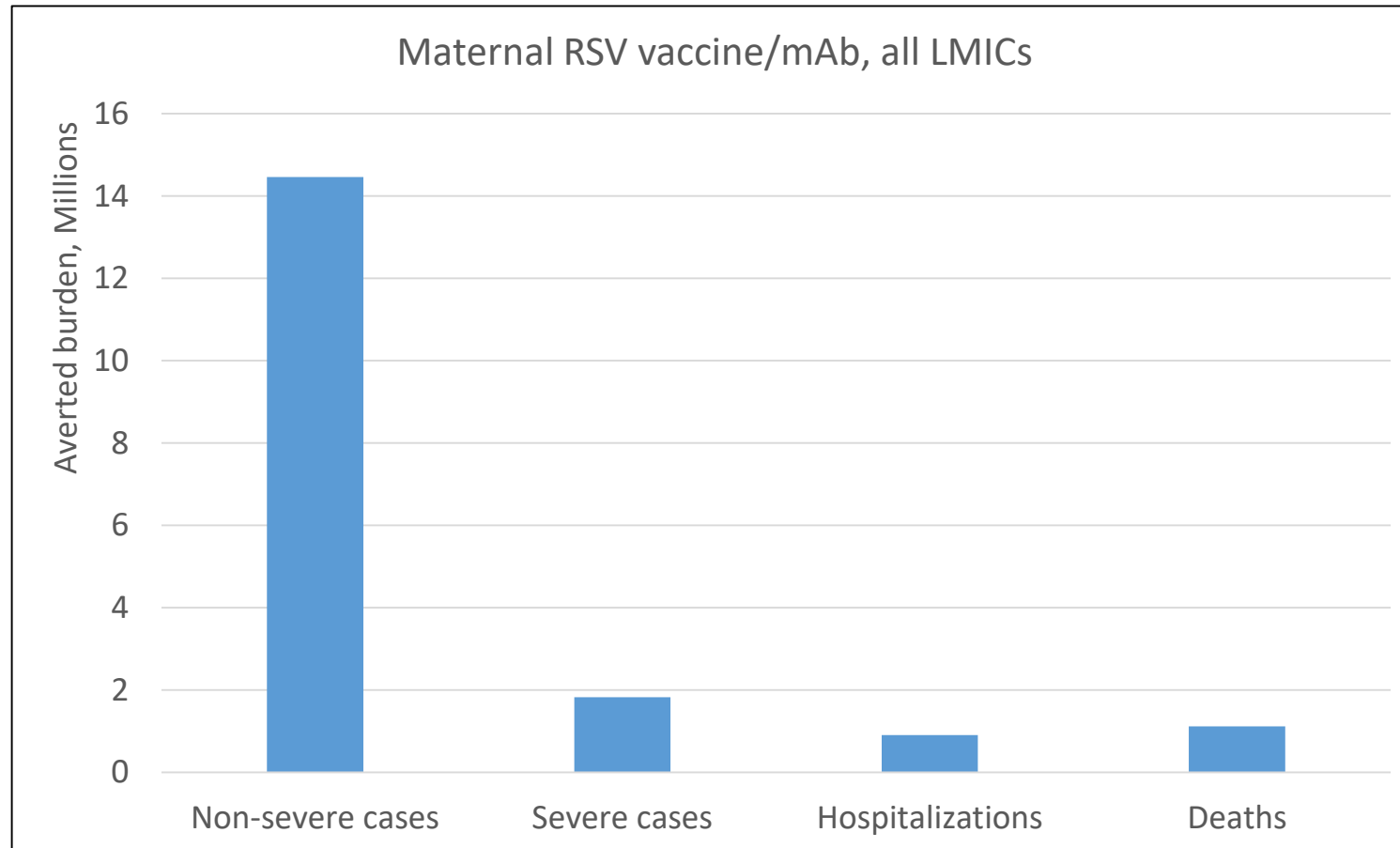
RSV and all LRTI deaths averted, (2030-2039)

- **All LRTI mortality impact may be much larger than RSV mortality impact!**
- **All LRTI mortality impact demonstrated by maternal vaccine and mAbs.**
  - If maternal vaccines and mAbs perform similarly against all LRTI mortality, overall health impact may be similar between the interventions.

All LMICs

Averted burden, Millions — Deaths

Legend:
- Maternal vaccine, RSV impact
- mAb, RSV impact
- Maternal vaccine/mAb, all LRTI impact

Context on cost effectiveness interpretation

Historically, income per capita thresholds were used to determine cost effectiveness at the country level

- < 1X income per capita was highly cost effective

- < 3X income per capita was cost effective

- > 3X income per capita was not cost effective

Historical thresholds are no longer recommended

Country specific thresholds are recommended but often do not exist in practice

In the absence of a country specific threshold, new (interim?) norms seem to be evolving ~ 0.5X – 1X income per capita

- For example, a cost per disability-adjusted life-year (DALY) of 0.5X income per capita would likely be viewed by many as cost effective.

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Incremental cost effectiveness ratios per DALY (discounted)

Intervention	Gavi countries	Non-Gavi countries	Countries in Asia
Maternal vaccine (impact on RSV)	1,042	1,626	1,275
mAb (impact on RSV)	296	579	422
Maternal vaccine or mAb (impact on all cause LRTI)	89	733	697

Results exclude any co-financing to Gavi-eligible countries.

Percent of countries where RSV interventions are likely to be cost effective

Intervention	Gavi countries	Non-Gavi countries
Maternal vaccine *(impact on RSV)*	NA; Gavi co-financing excluded	88%
mAb *(impact on RSV)*	NA; Gavi co-financing excluded	100%
Maternal vaccine or monoclonal antibody *(impact on all cause LRTI)*	NA; Gavi co-financing excluded	100%

*Assumes cost effectiveness threshold < 50% GDP p.c.

Key limitations

Knowledge and awareness of RSV disease burden is still growing.

The age distribution of all-cause LRTI is not well established in the model.

mAb efficacy and duration of protection are not yet firmly established.

Intervention prices are uncertain, and not differentiated by product.

- Some anticipate that mAb prices will be higher.

Country specific cost effectiveness thresholds are not known, so a conservative (but uniform) threshold is applied.

Photo: M. Dorgabekova

Conclusions

RSV interventions are in development and expected to be available in the coming years.

RSV interventions are projected to be highly impactful, with as much as 50% of the potential impact in Asia.

A mAb is projected to avert more <u>RSV disease</u> than a maternal vaccine due to higher coverage, efficacy, and a longer duration of protection.

Interventions have already demonstrated ability to avert substantial all-cause LRTI.

- All-cause LRTI reductions could be substantially larger than RSV reductions alone.
- Maternal vaccines and mAbs could have similar overall health impact.

RSV interventions are likely to be cost effective in most LMICs, including in Asia, though much depends on intervention pricing.

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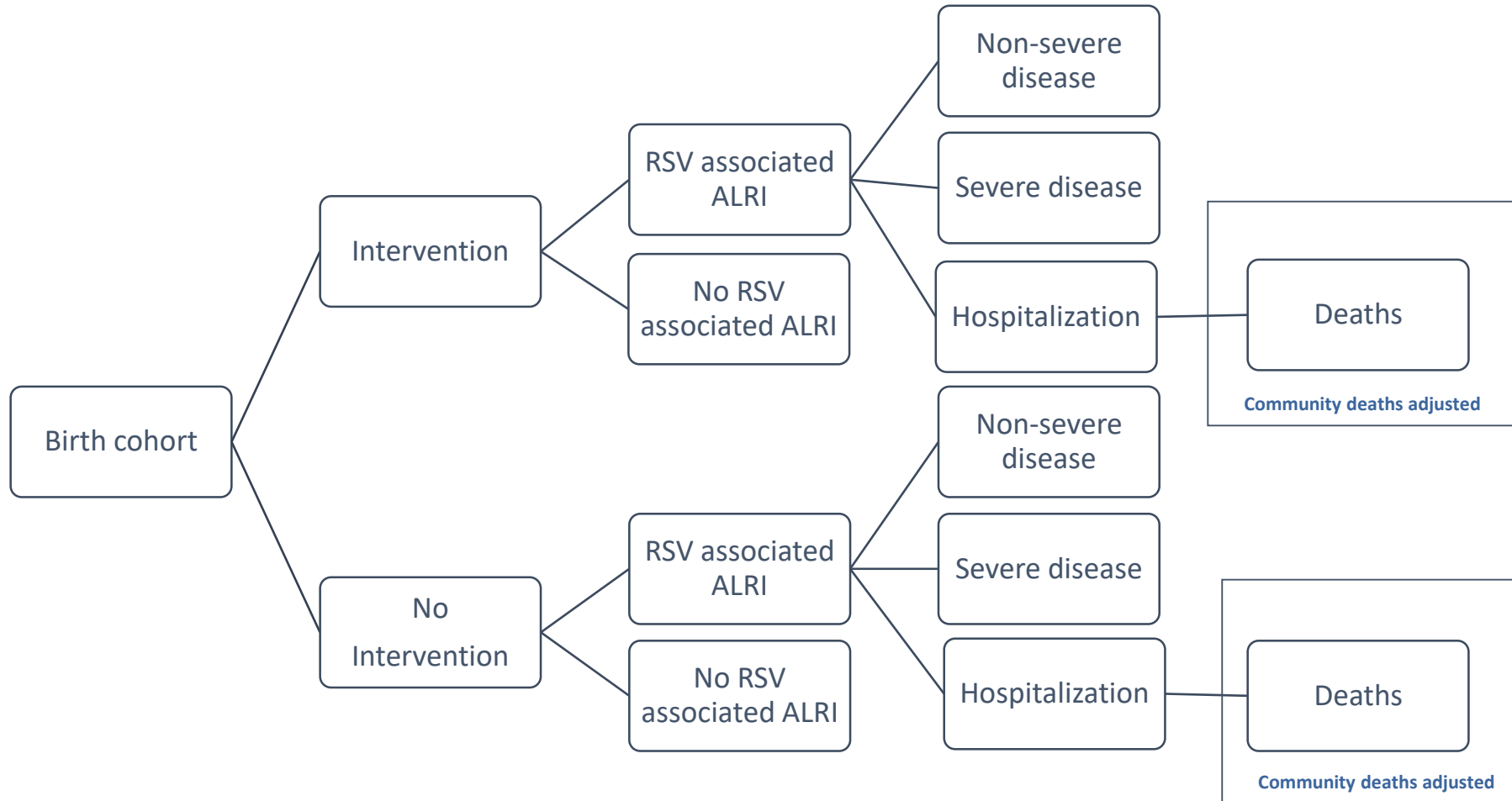# For more information contact:

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Backup slides

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Model structure

Birth cohort
- Intervention
  - RSV associated ALRI
    - Non-severe disease
    - Severe disease
    - Hospitalization → Deaths — **Community deaths adjusted**
  - No RSV associated ALRI
- No Intervention
  - RSV associated ALRI
    - Non-severe disease
    - Severe disease
    - Hospitalization → Deaths — **Community deaths adjusted**
  - No RSV associated ALRI

This schematic is specific to scenarios examining RSV end points. The model for LRTI endpoints is similar.

RSV burden <6 months of age, without vaccination (2030-2039)

Country group	Non-sev. Cases	Severe cases	Hosp. Adm.	Total deaths
All countries (N=131)	41,946,625	15,282,497	11,489,765	504,963
Asia (N=28)	17,521,126	7,116,824	5,350,607	235,153

All cause LRTI burden <6 months of age, without vaccination (2030-2039)

Country group	Non-sev. Cases	Severe cases	Hosp. Adm.	Total deaths
All countries (N=131)	70,451,672	8,885,796	4,395,313	3,700,737
Asia (N=28)	35,546,669	4,483,364	2,228,191	1,425,864

Data inputs and assumptions

Inputs	Value	Source
Treatment cost	Total cost per episode for managing severe pneumonia in LMIC: Outpatients $53; Inpatient $250	Zhang et al., 2016
Duration of illness	Severe illness: 10 days Non-severe illness: 5 days	Hall et al., 2011
Length of hospital stay	Length of hospital stay for severe pneumonia in LMICs: 6.4 days	Zhang et al., 2016
Health care seeking	Health seeking for children (<5) with pneumonia	WHO database
DALY weight	Severe ALRI: 0.21 Non-severe ALRI: 0.053	GBD 2010
DALY discount rate	3%	Assumed
Population	• UN population estimates (medium variant) • Adjusted for still births • Assumed uniform age distribution across months	UN Pop 2019 Lawn et.al., 2016
Life expectancy at birth	• By country, year	UN POP projections, 2019

Data inputs and assumptions – disease burden

Inputs	Value	Source
Incidence of RSV-ALRI	• Country specific incidence for 0-5 years for envelope • Developing country estimate by narrow age band for case distribution by age • Rescaled to match country specific incidence envelope	Shi et.al., 2017
Incidence of severe RSV-ALRI; hospitalization; case fatality rate	• Developing country estimates with uniform age distribution	Shi et.al., 2017
RSV-ALRI mortality	• Hospital deaths *2.2 (adjusted for community deaths) *0.9 (adjusted for influenza activities)	Shi et. al., 2017
Incidence of LRTI	• Country specific • By ages- early neonates (0-7days), post neonates (7-28days), late neonates (1-12 months). Burden for post neonates uniformly distributed across ages by month.	GBD 2017
Incidence of severe LRTI	• 11.5% of all incidence resulting in severe cases	Assumed (based on the estimates used in Rudan et al., 2013)
Hospital admission for LRTI	• 40% of all severe cases resulting in hospital admission	Assumption
Mortality due to LRTI	• Country specific, early neonates, post neonates, late neonates. Burden for post neonates uniformly distributed across ages by month.	GBD 2017
Age distribution of LRTI burden	• Assumes uniform distribution of burden across months by age	Assumption

Projected RSV burden averted <6 months of age, (2030-2039)

	Country group	Non-sev. Cases	Severe cases	Hosp. Adm.	Total deaths
Maternal Vaccine	All countries (N=131)	3,136,827 (7%)*	2,785,082 (18%)	2,146,635 (19%)	133,646 (26%)
	Asia (N=28)	1,461,770 (8%)	1,490,606 (21%)	1,148,903 (21%)	71,529 (30%)

*% of burden averted

Projected RSV burden averted <6 months of age, (2030-2039)

Monoclonal antibody

| Country group	Non-sev. Cases	Severe cases	Hosp. Adm.	Total deaths
All countries (N=131)	20,328,954 (48%)*	7,483,101 (49%)	5,625,983 (49%)	288,465 (57%)
Asia (N=28)	9,952,740 (57%)	4,063,751 (57%)	3,055,230 (57%)	156,653 (57%)

*% of burden averted

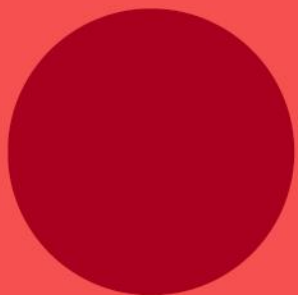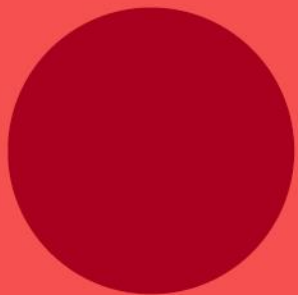# All cause LRTI burden averted <6 months of age, (2030-2039)

Maternal Vaccine or mAb

Country group	Non-sev. Cases	Severe cases	Hosp. Adm.	Total deaths
All countries (N=131)	14,462,195 (21%)*	1,824,061 (21%)	903,089 (21%)	1,112,802 (30%)
Asia (N=28)	7,265,971 (20%)	916,429 (20%)	455,809 (20%)	428,599 (30%)

*% of burden averted

Projected RSV burden averted <6 months of age, (2030-2039)

mAb, all LMICs
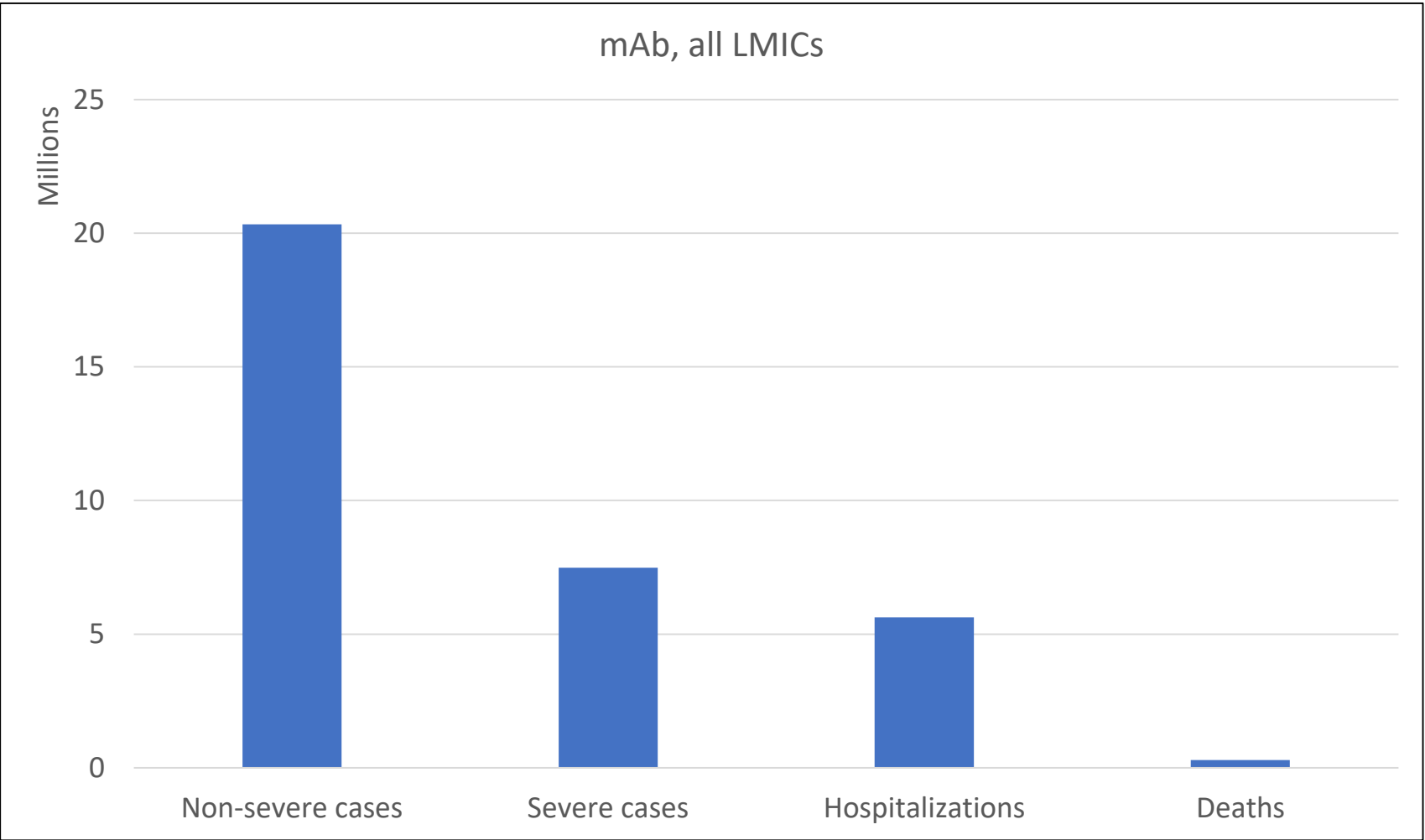
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