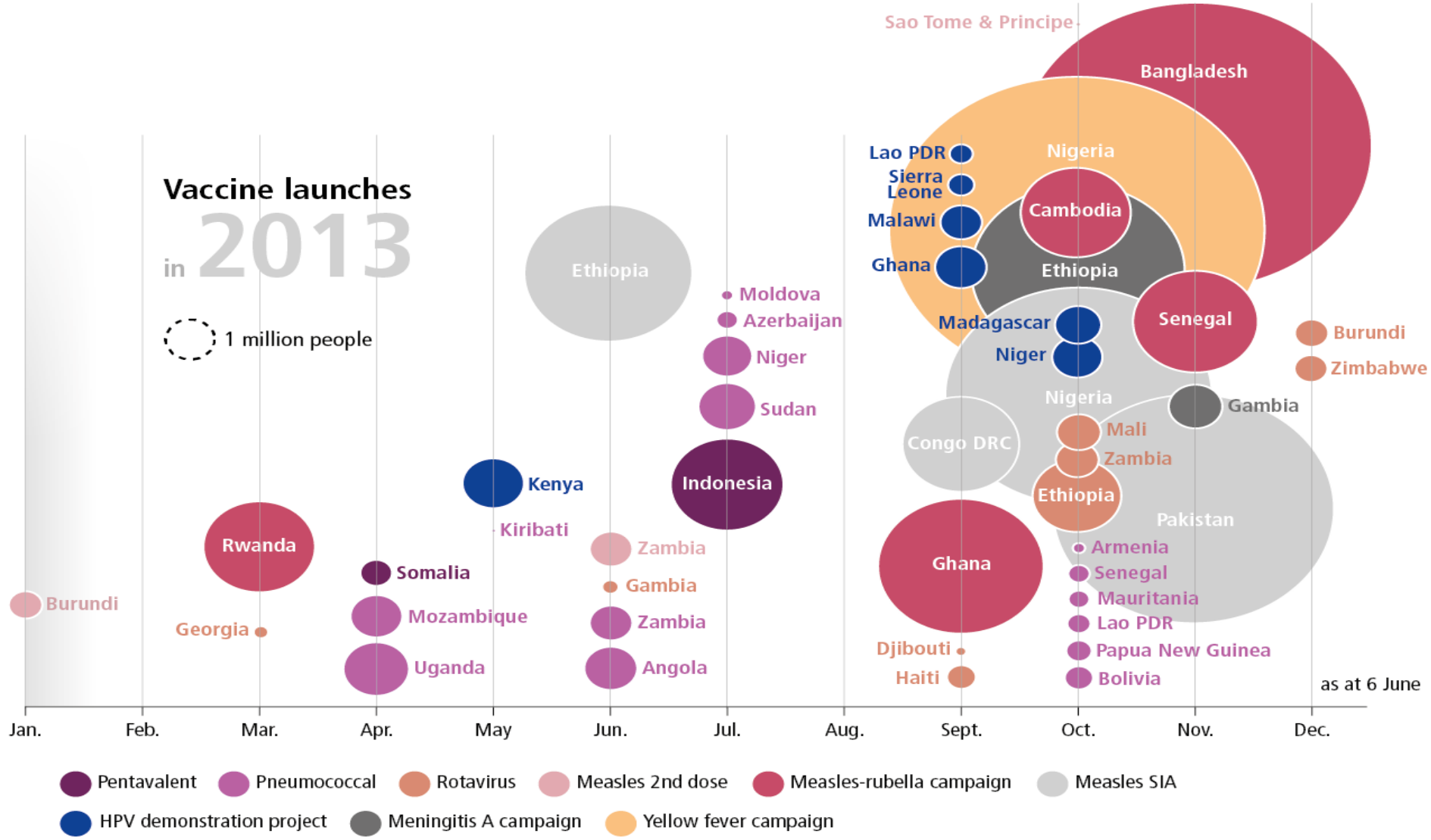
ASSESSING THE VALUE OF VACCINE BEYOND EFFICACY AND SAFETY

Bradford D. Gessner, MD
Agence de Médecine Preventive

First Regional Dengue Symposium
Rio de Janeiro, Brasil
November 3-4, 2015

BURDEN CONCEPTS

Vaccine Launches 2013



ELSEVIER

Social Science & Medicine 65 (2007) 1751–1764

SOCIAL SCIENCE & MEDICINE

www.elsevier.com/locate/socscimed

What influences government adoption of vaccines in developing countries? A policy process analysis

Syarifah Liza Munira[a,*], Scott A. Fritzen[b]

"Disease burden has been consistently mentioned by policymakers in countries to be the number one factor in setting priorities for vaccines to be introduced into immunization programs; the higher the burden, the more attractive a potential addition to the immunization regime of the country would be."

Burden measure limitations

- Poor diagnostics: non-bacteremic Hib/Sp, typhoid
- Causal etiology gone at time of presentation: flu/viral ARI pathogens precipitating bacterial ARI
- Pathogen present but not causal: flu
- Lack of testing, poor specimen transport systems: all etiologies
- Limited health care access: all etiologies

Definition of measures

- Vaccine effectiveness/efficacy (VE)

  = 1 – (Incidence[vaccinated] ÷ Incidence[unvaccinated])

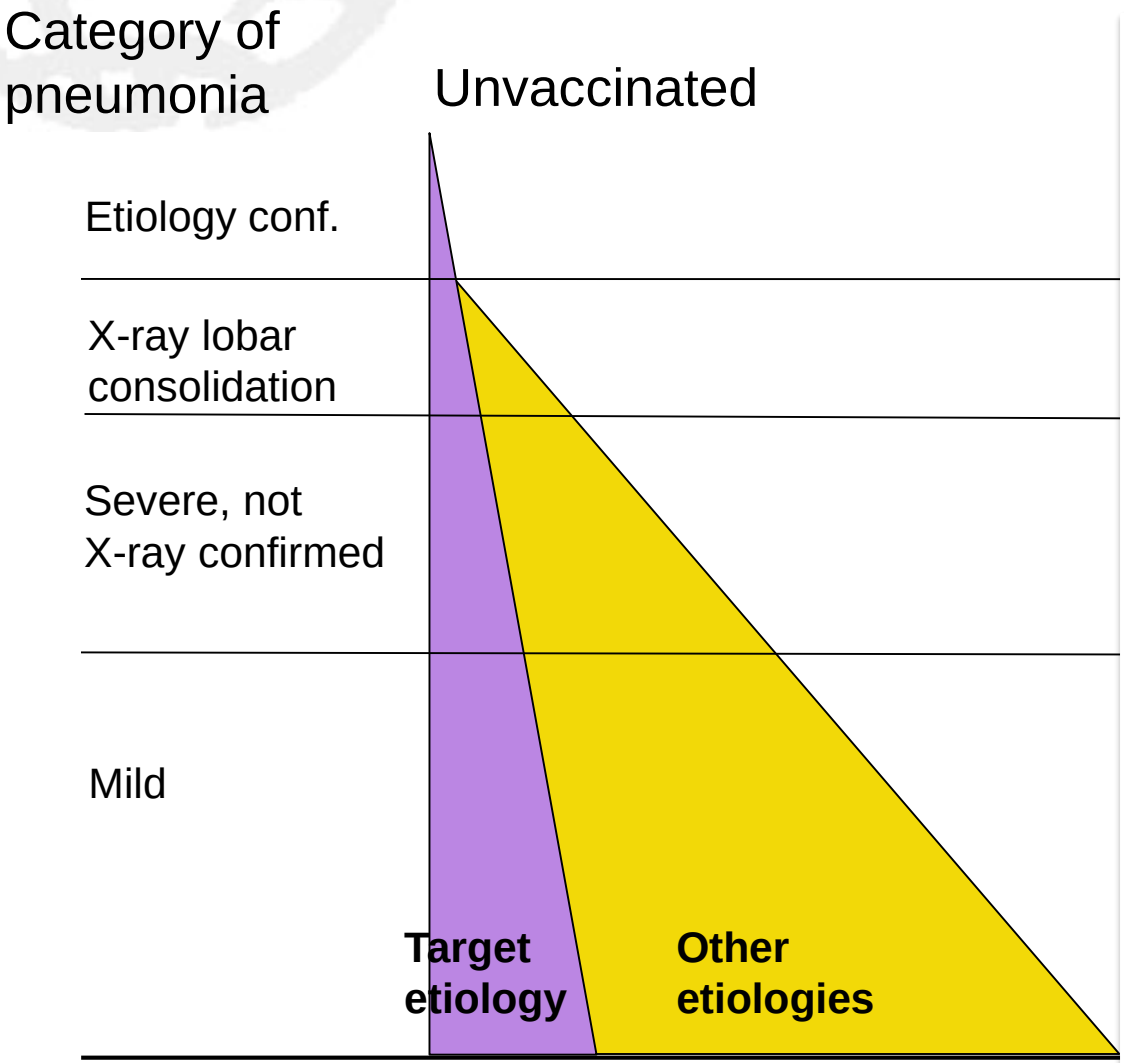
- Vaccine preventable disease incidence (VPDI)

  = Incidence[unvaccinated] – Incidence[vaccinated]

  = Incidence[unvaccinated] X VE

Feikin, Scott, Gessner. Use of vaccines as probes to define disease burden. Lancet 2015;383:1762-70

Impact of vaccine against pneumonia categories of pneumonia (Lancet 2014;383:1762-70)



VACCINE EFFICACY AND PREVENTABLE DISEASE INCIDENCE EXAMPLES

Examples of vaccine preventable disease incidence (VPDI) use; VPDI per 100,000 CYO

	Syndrome	Etiology confirmed		Clinical outcome	
		VE	VPDI	VE	VPDI
Gambia, PCV	Radiological pneumonia	70%	140	37%	1300
Indonesia, Hib	Hospitalized meningitis	86%	16	22%	160
Kenya, rotavirus	AGE* (conf in hosp vs. all cause in comm)	84%	3300	34%	19,000

* AGE = acute gastroenteritis

Lancet 2005;365:1139-46; Lancet 2005;365:43-52; Vaccine 2012;30 (suppl 1):A52-60

Vaccine preventable disease incidence (VPDI) is useful outside of developing country settings

Study	Vaccine efficacy	VPDI (per 1000 CYO)	Reference
Finland			Vaccine 2012;31:176-82
Confirmed inpatient AGE*	80%	3.9	
All cause inpatient AGE*	54%	10.7	
Kenya			Vaccine 2012;30 Supp 1:A52-60
Confirmed severe	84%	33	
Community severe AGE*	34%	190	

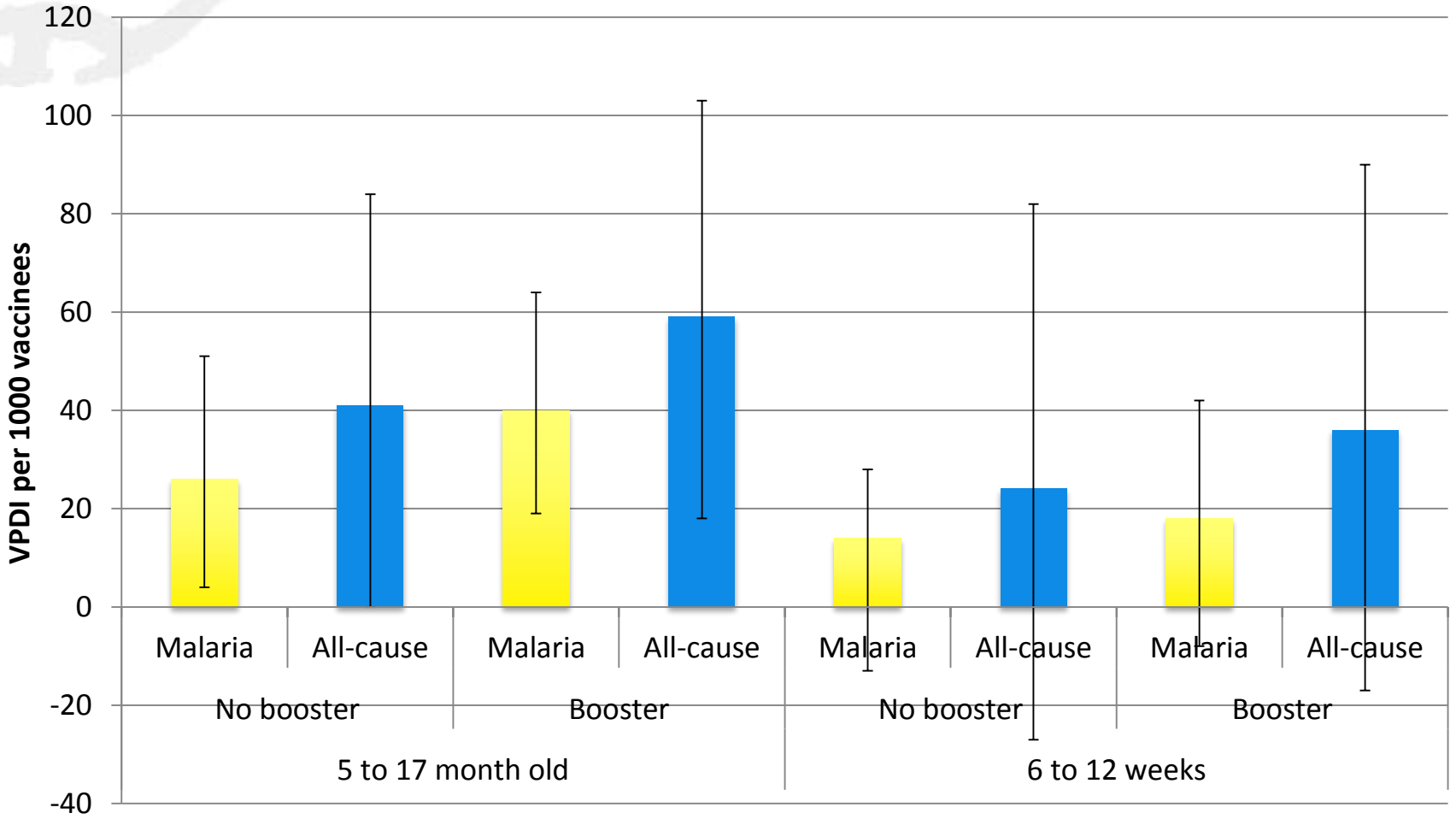
* AGE = acute gastroenteritis

Public health impact can be greater in settings where vaccine efficacy is lower

Study	VE	VPDI (per 100,000 CYO)	Ref
Severe rotavirus AGE*			NEJM 2010;362:289-98
South Africa	77%	4200	
Malawi	49%	6700	
Severe rotavirus AGE*			Lancet 2010;376:615-23
Vietnam	64%	2200	
Bangladesh	43%	3500	

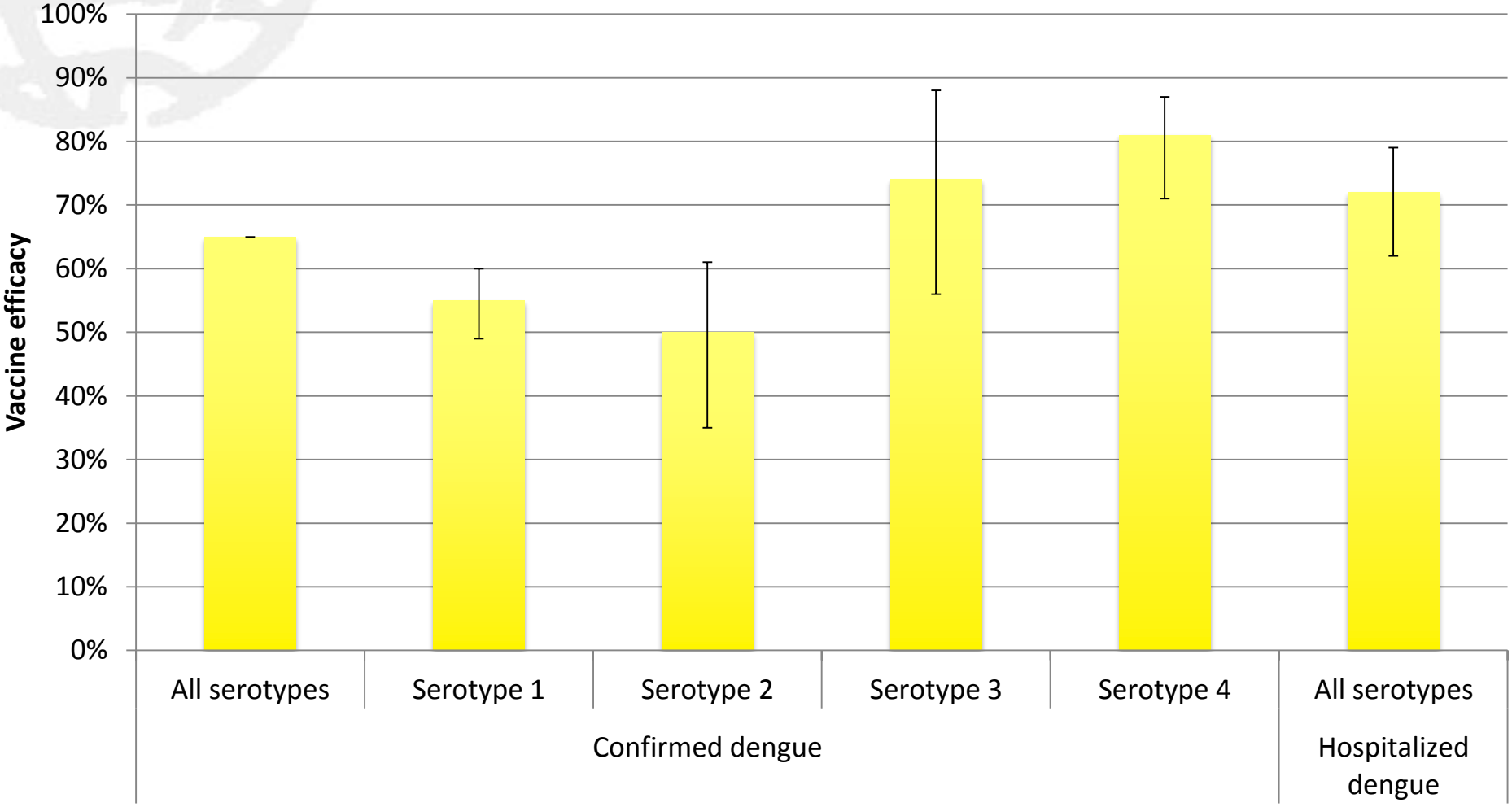
* AGE = acute gastroenteritis

RTS,S VPDI against malaria-specific and all-cause hospitalization

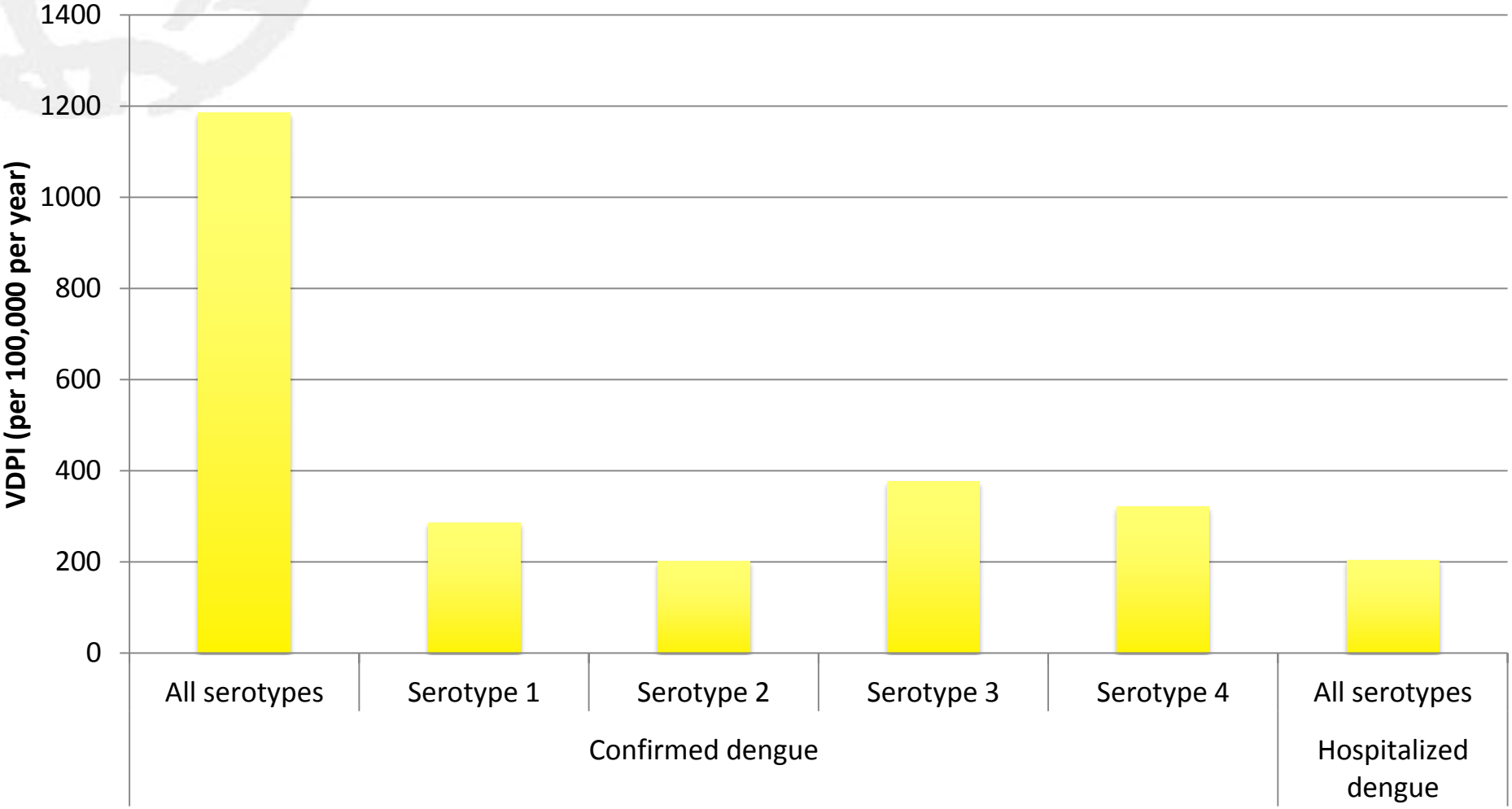


DENGUE

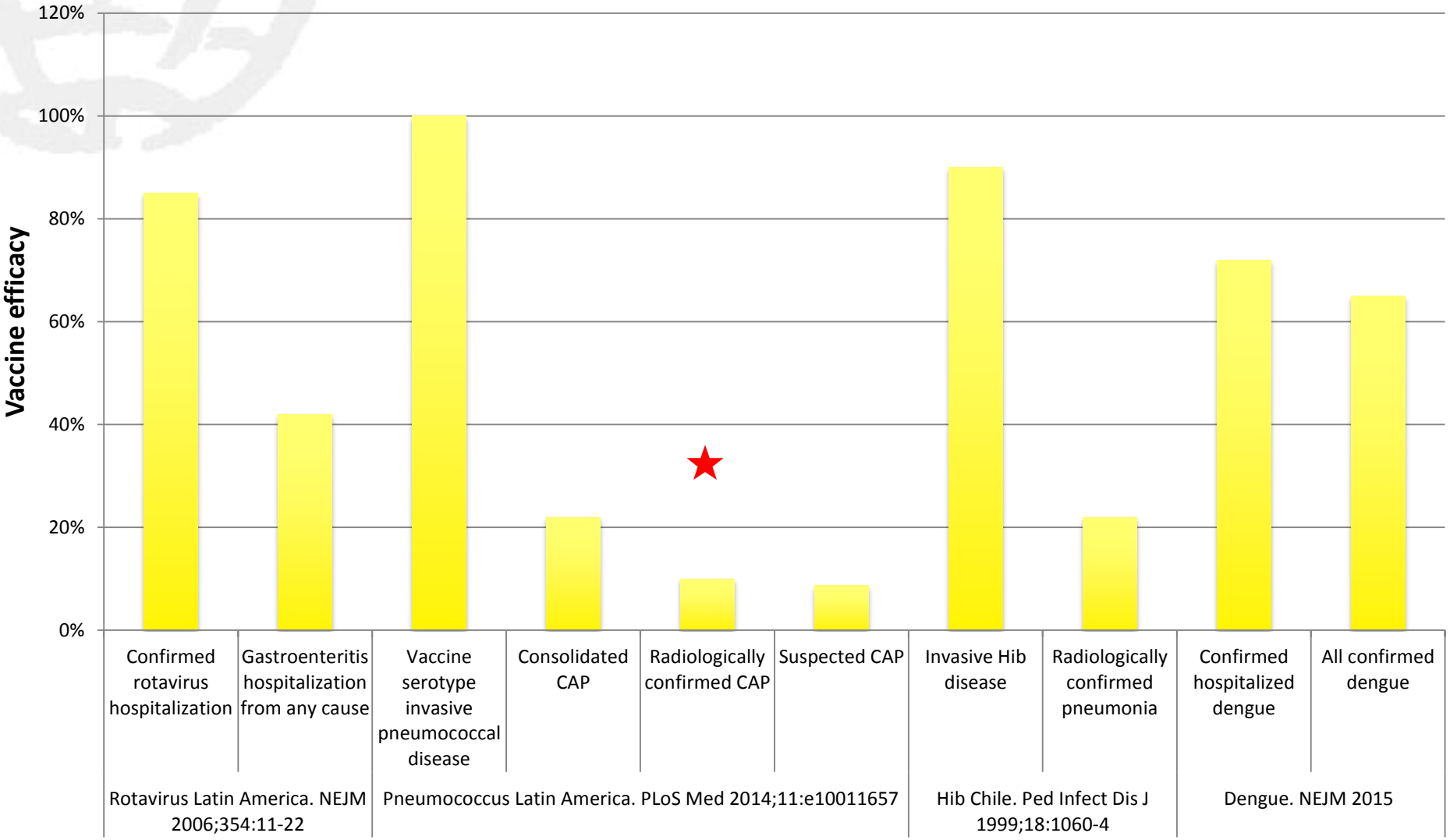
Vaccine efficacy against confirmed dengue in children 9-16 years of age in Latin America



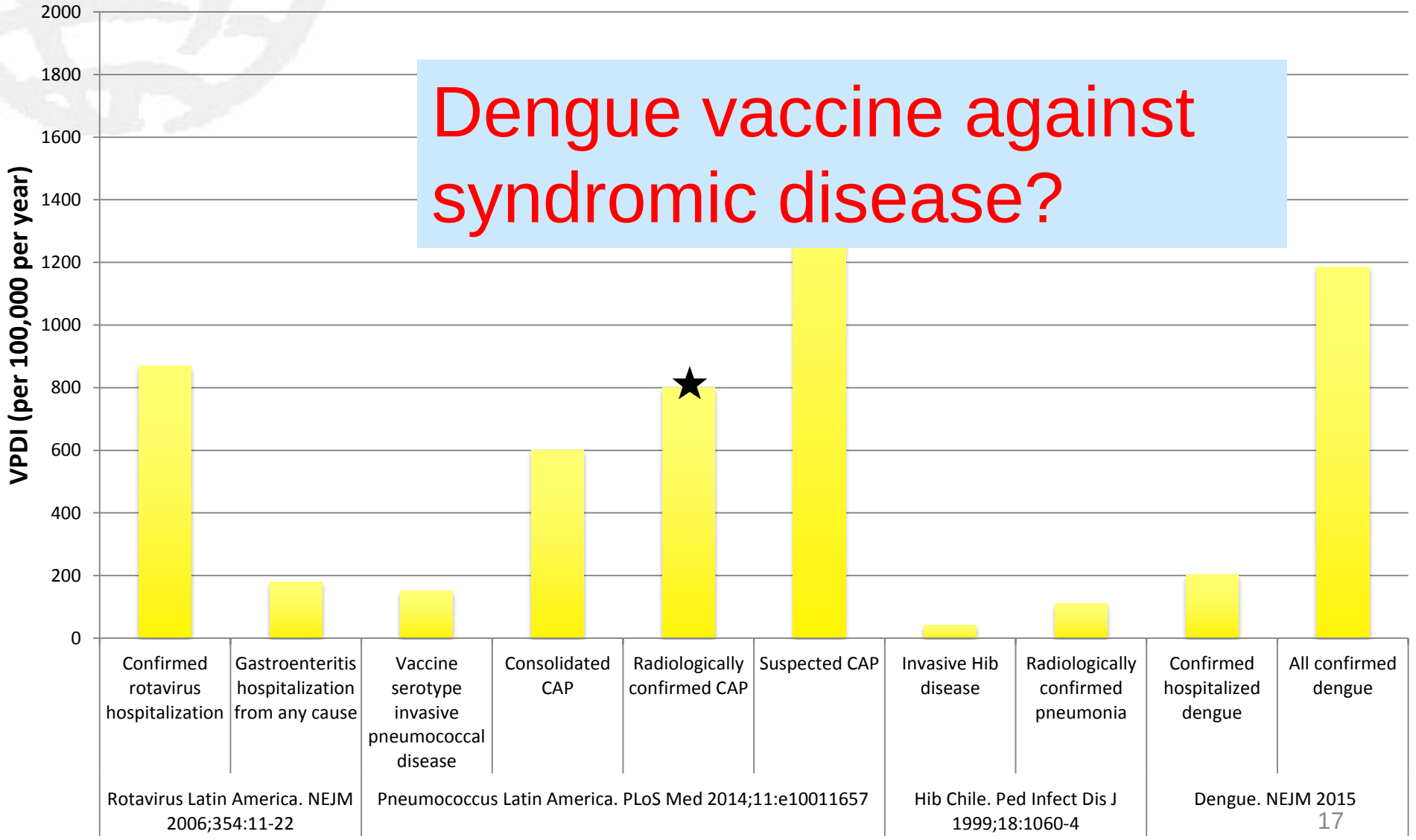
Vaccine preventable disease incidence (VPDI) for confirmed dengue in children age 9-16 years in Latin America



Vaccine efficacy for dengue compared to other vaccines studied and used in Latin America



Vaccine preventable disease incidence (VPDI) for dengue compared to other vaccines studied and used in Latin America



BEYOND BURDEN

Age distribution

	Sp	Hib	Rotavirus	Malaria	DENGUE
<5 year disease	++++	++++	++++	++++	++/+++
<5 year severity/sequelae	++++	--	--	++++	+
5+ year disease	++/+++	+	--	++++	++++
5+ year severity/sequelae	+++	+	--	+	+

Sequelae/mortality

	Sp/Hib meningitis	Sp/Hib pneumonia	Rotavirus	Malaria	DENGUE
Cognitive (MR, dev delay, learning disability, language)	++++	--	--	+++	--
Sensory (hearing, vision)	++++	--	--	--	--
Physical (CP, seizures)	++++	--	--	+++	+
Stunting	?	?	+	+++	--
Case fatality ratio	++++	+++	+	++	+

E.g., in US, big cost driver for Hib was long-term care and institutionalization for meningitis sequelae

Indirect/replacement/rebound effects

	Sp	Hib	Rotavirus	Malaria	DENGUE
Indirect	+++	++++	++	--	?
Replacement	+++	+ (so far)	--	--	?
Rebound	-/+ (without booster)	+ (without booster in some settings)	--	+++ (depends on transmission)	?

Work in different directions:

- Indirect effects can greatly increase immunization efficiency and public health value
- Replacement can completely negate immunization efficiency
- Rebound shifts disease to older age; generally beneficial

Immunization program issues

	Sp	Hib	Rotavirus	Malaria	DENGUE
Fits with current childhood schedule	+++	+++	+++	--	+
Duration of immunity (with booster)	+++	+++	Less relevant	-/+	??
Variable geographic distribution within affected countries	--	--	--	++	+++

Health system impact

	Sp	Hib	Rotavirus	Malaria	DENGUE
Outbreak potential	+	--	--	+	+++
May overwhelm clinical resources	+	--	++	++	+++
Requires other intensive + expensive interventions	+	+	++	+++	+++
Increasing incidence in absence of vaccine	--	--	--	--	+++
Political dimension	+	+	+	++	+++

SUMMARY

- Safety and efficacy just the start of assessing public health value of vaccine
- Burden is the foundation of decision making
  - Incidence
  - VPDI
  - Sequelae
  - Mortality
- Other key issues
  - Vaccine characteristics
  - Programmatic concerns
  - Health system impact
- All of these features contribute to models estimating public health value of vaccine

QUESTIONS

- How can VPDI inform decision-making on dengue vaccine?
- What data exist on vaccine impact against clinical outcomes (e.g., fever hospitalization) and how will this alter public health value estimate of vaccine?
- What are the appropriate public health outcomes for dengue vaccine?
  - Severe confirmed disease
  - Clinical confirmed disease
  - Fever hospitalization or clinic visit
  - Outbreak control
- How important is health system impact compared to sequelae/mortality?
- How important are programmatic concerns?
- What additional studies are needed to
  - Decide on vaccine use
  - Determine scope of vaccine use (age groups/geography)
  - Refine schedule
  - Assess impact post introduction