MEASURING THE PUBLIC HEALTH VALUE OF VACCINE BEYOND EFFICACY AND SAFETY

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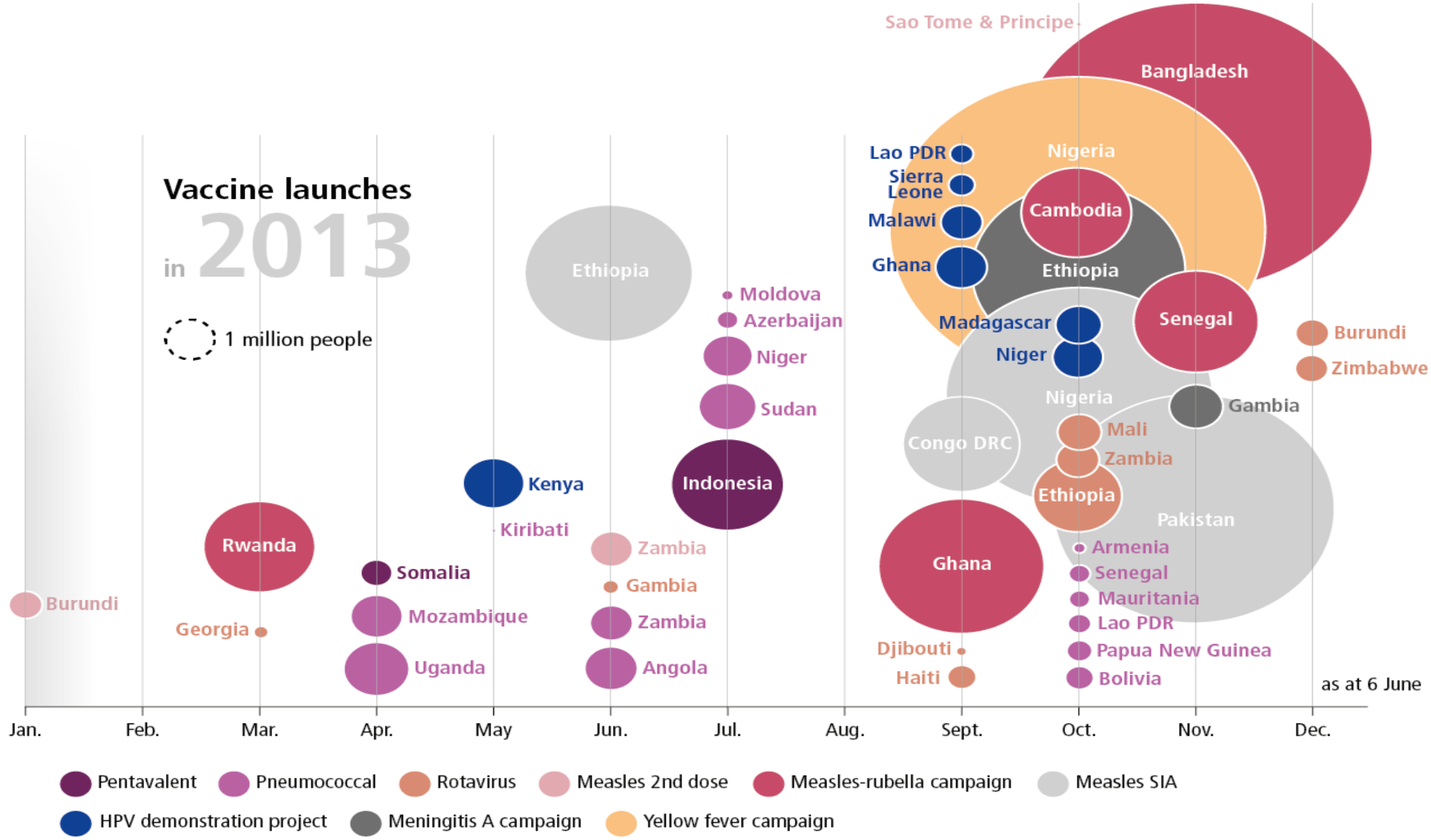
BURDEN CONCEPTS

Vaccine Launches 2013



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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

VACCINE EFFICACY AND PUBLIC HEALTH BURDEN MEASURES

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

- Number needed to vaccinate (NNV)
  = 100,000/VPDI/length of follow-up for VPDI

- Number prevented (nationally) (estimated!)
  = VPDI * (birth cohort/100,000) * years of follow-up for VPDI

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

VPDI, NNV and Cases prevented; VPDI per 100,000 CYO

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

Syndrome	Etiology confirmed				Clinical outcome			
	VE	VPDI	NNV	Cases prev.	VE	VPDI	NNV	Cases prev.
Gambia PCV radiological pneumonia	70%	140	357	216	37%	1300	38	2002
Indonesia, Hib, hospitalized meningitis	86%	16	3125	1516	22%	160	313	15,155
Kenya rotavirus, acute gastroenteritis	84%	3300	15	101,244	34%	19,000	3	582,920

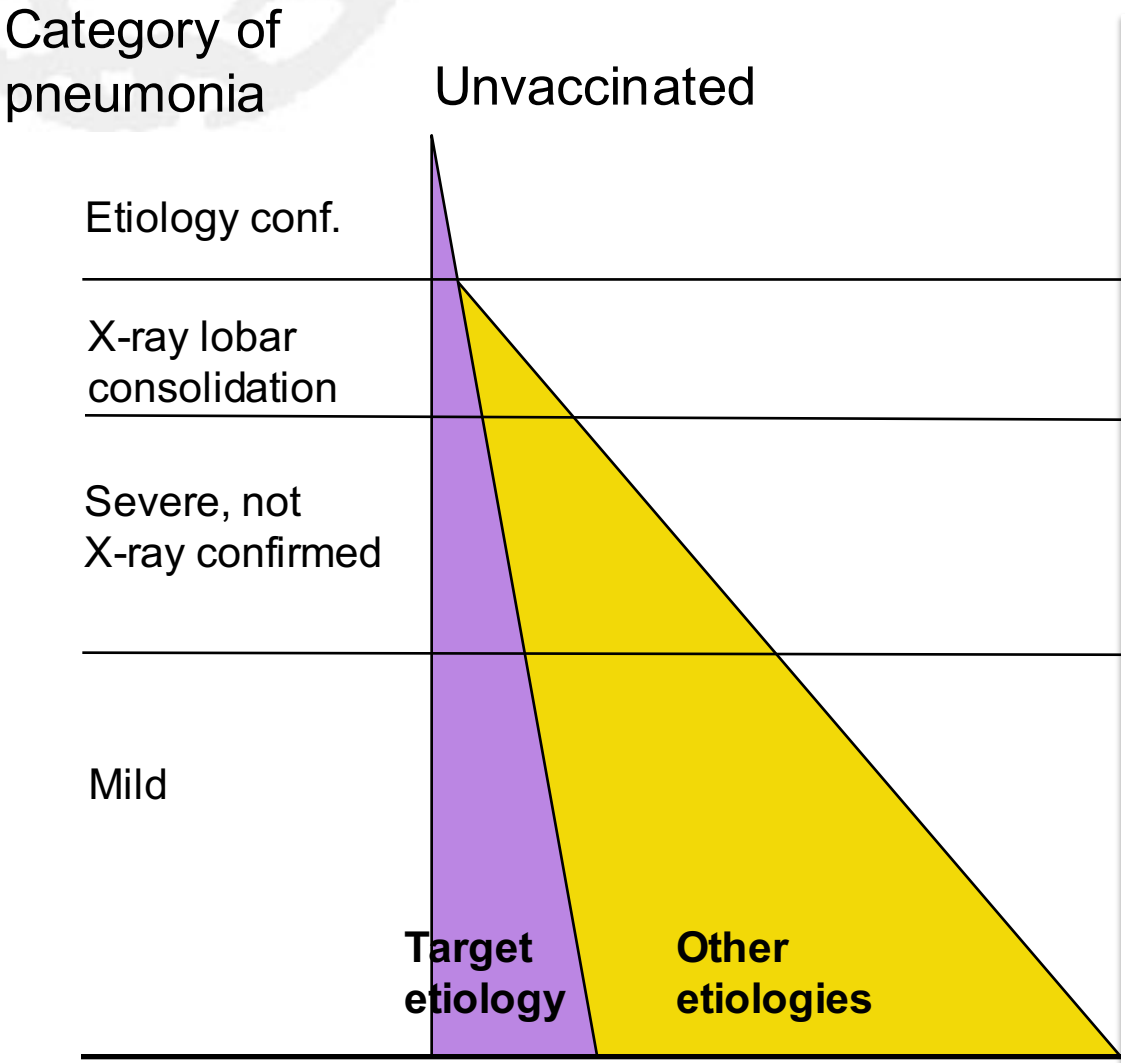
Measures useful outside of developing country settings: acute gastroenteritis (AGE)

Study	VE	VPDI	NNV	Cases prev.
Finland (Vaccine 2012;31:176-82)				
Confirmed inpatient AGE	80%	390	256	237
All cause inpatient AGE	54%	1070	93	651
Kenya (Vaccine 2012;30 Supp 1:A52-60)				
Confirmed severe	84%	3300	15	101,244
Community severe AGE*	34%	19,000	3	582,920

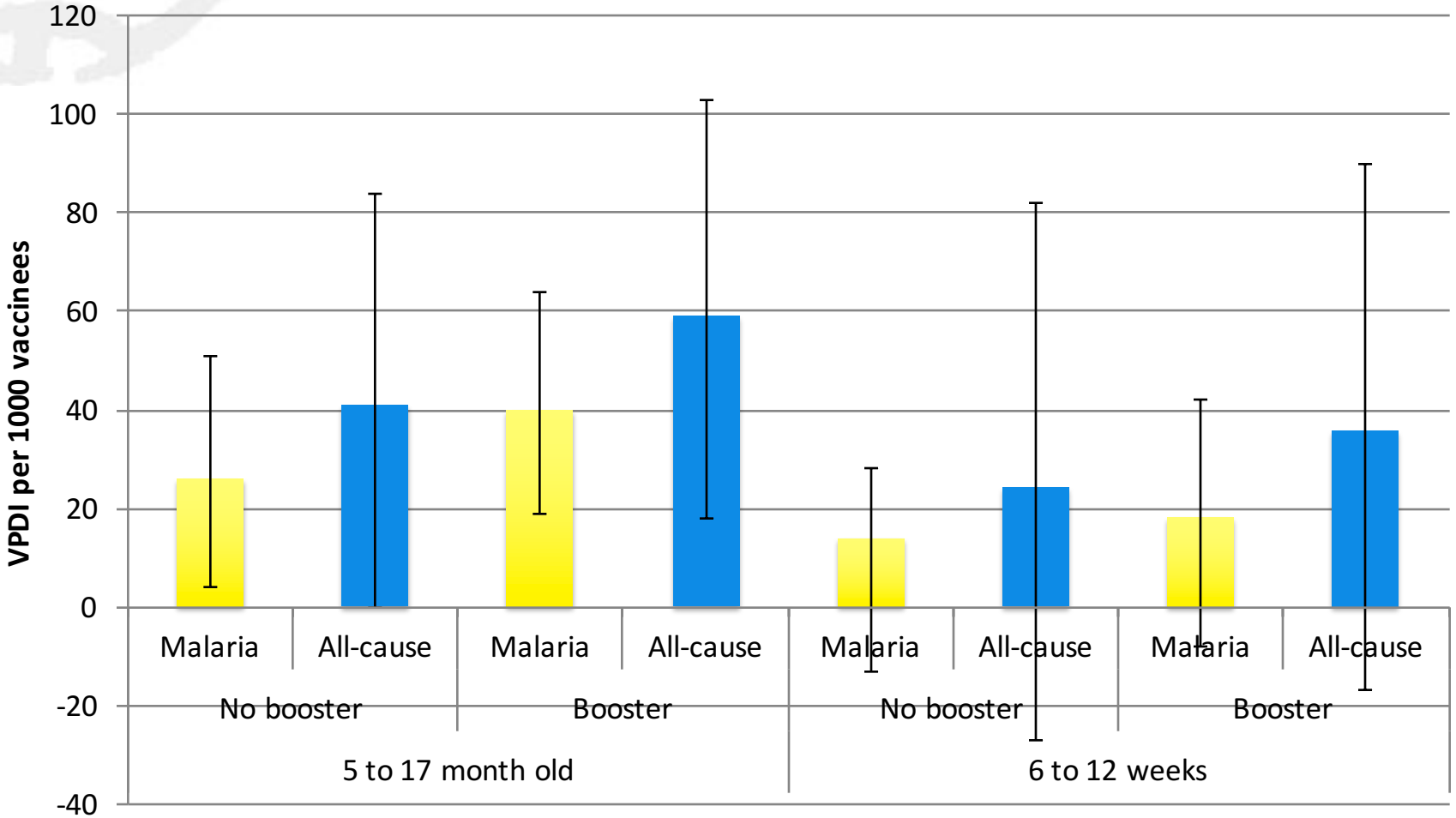
Public health impact can be greater in settings where vaccine efficacy is lower: acute gastroenteritis (AGE)

Study	VE	VPDI	NNV	Cases prev.
Severe rotavirus AGE (NEJM 2010;362:289-98)				
South Africa	77%	4200	24	46,284
Malawi	49%	6700	15	42,813
Severe rotavirus AGE (Lancet 2010;376:615-23)				
Vietnam	64%	2200	26	55,425
Bangladesh	43%	3500	16	192,950

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

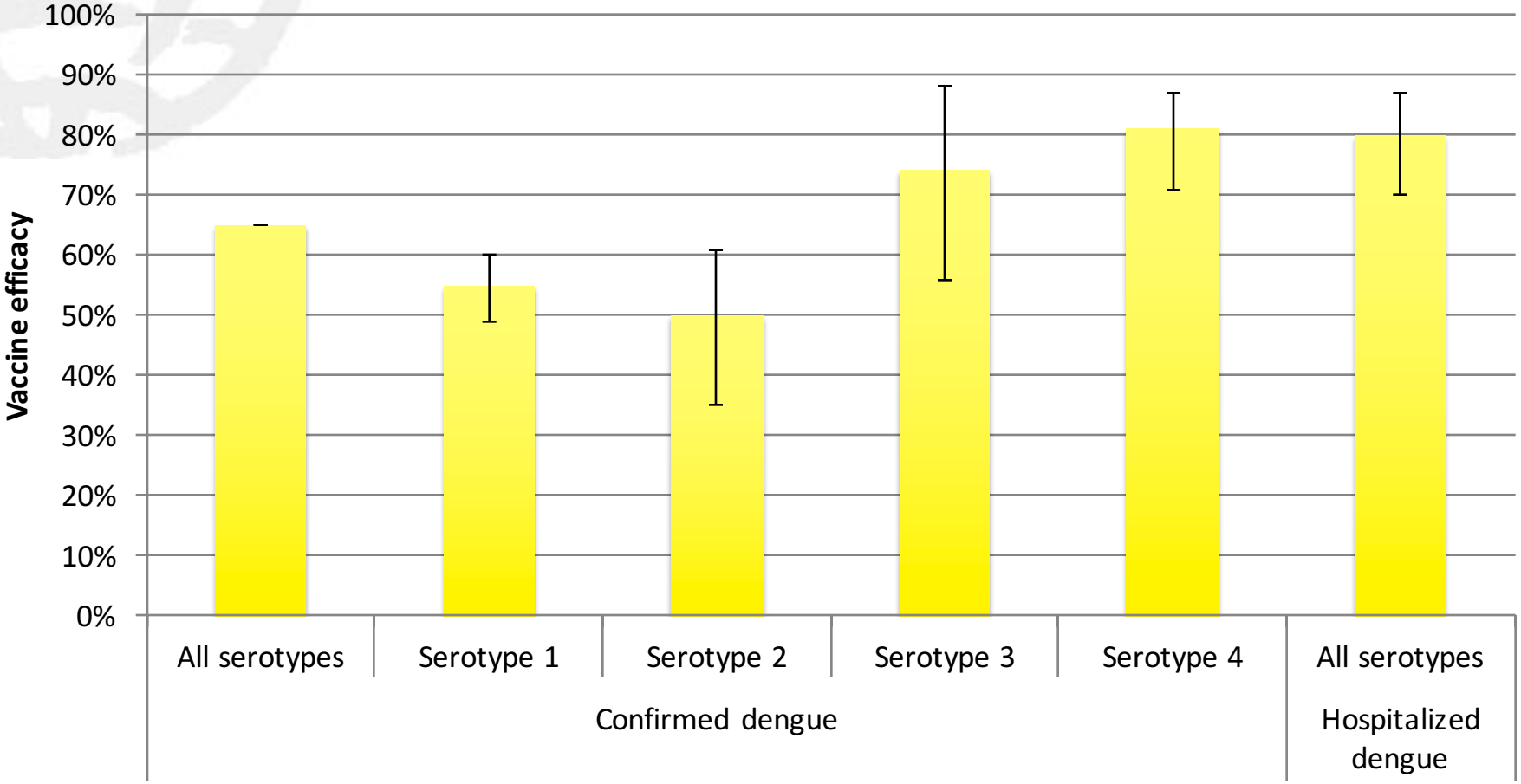


RTS,S VPDI against malaria-specific and all-cause hospitalization



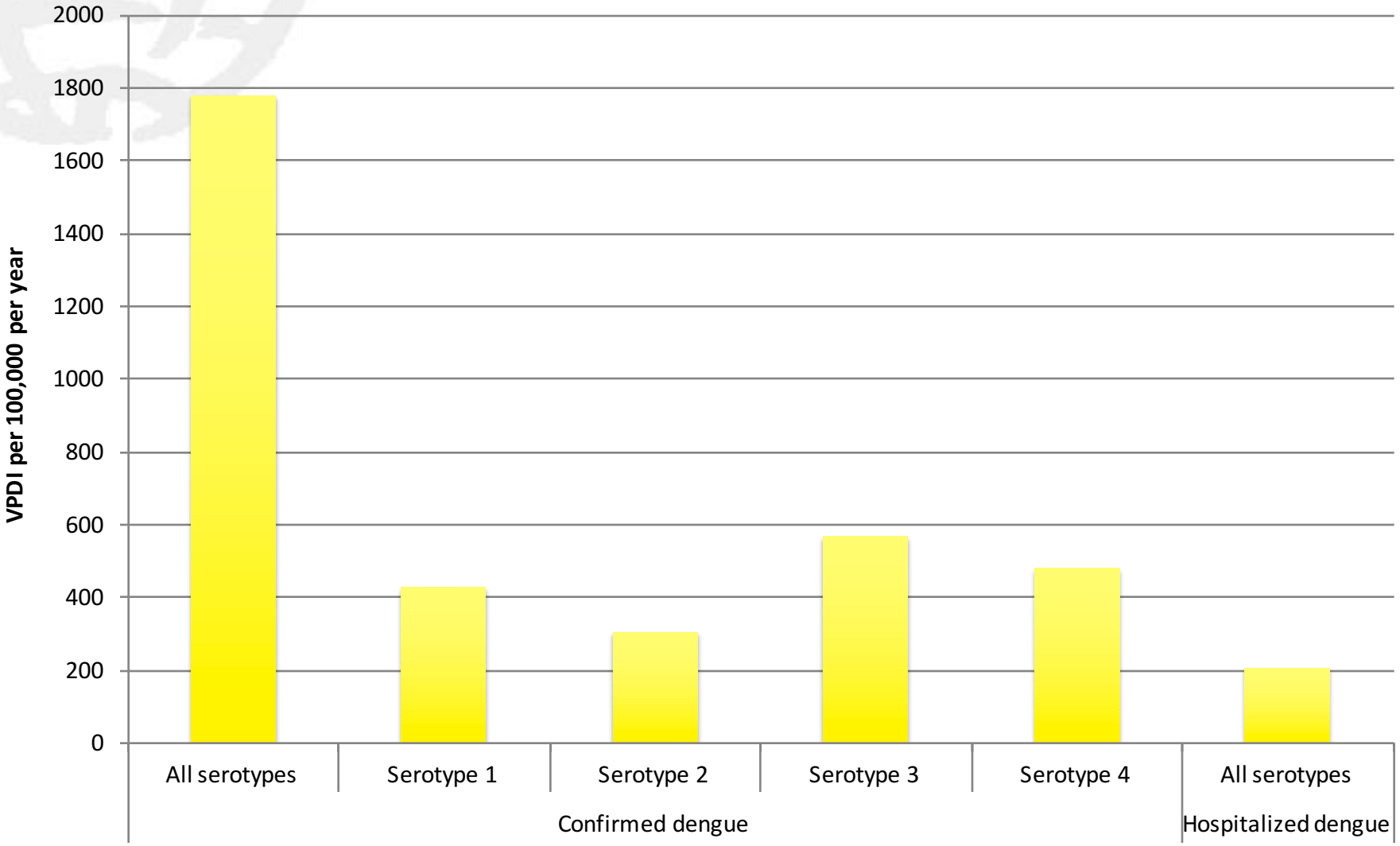
DENGUE

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

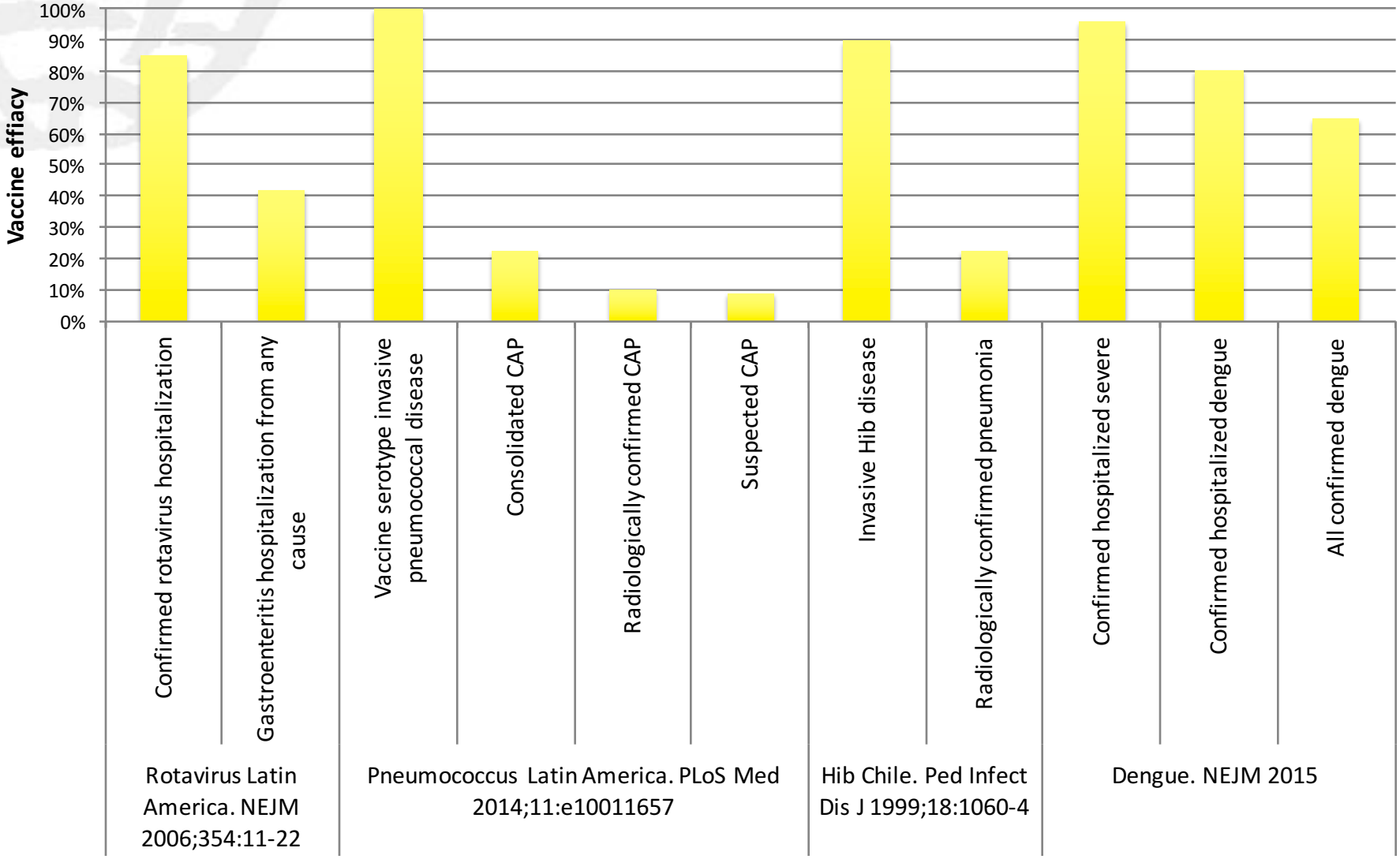


*All data based on 2 year VE estimates

Vaccine preventable disease incidence for confirmed dengue in Latin America

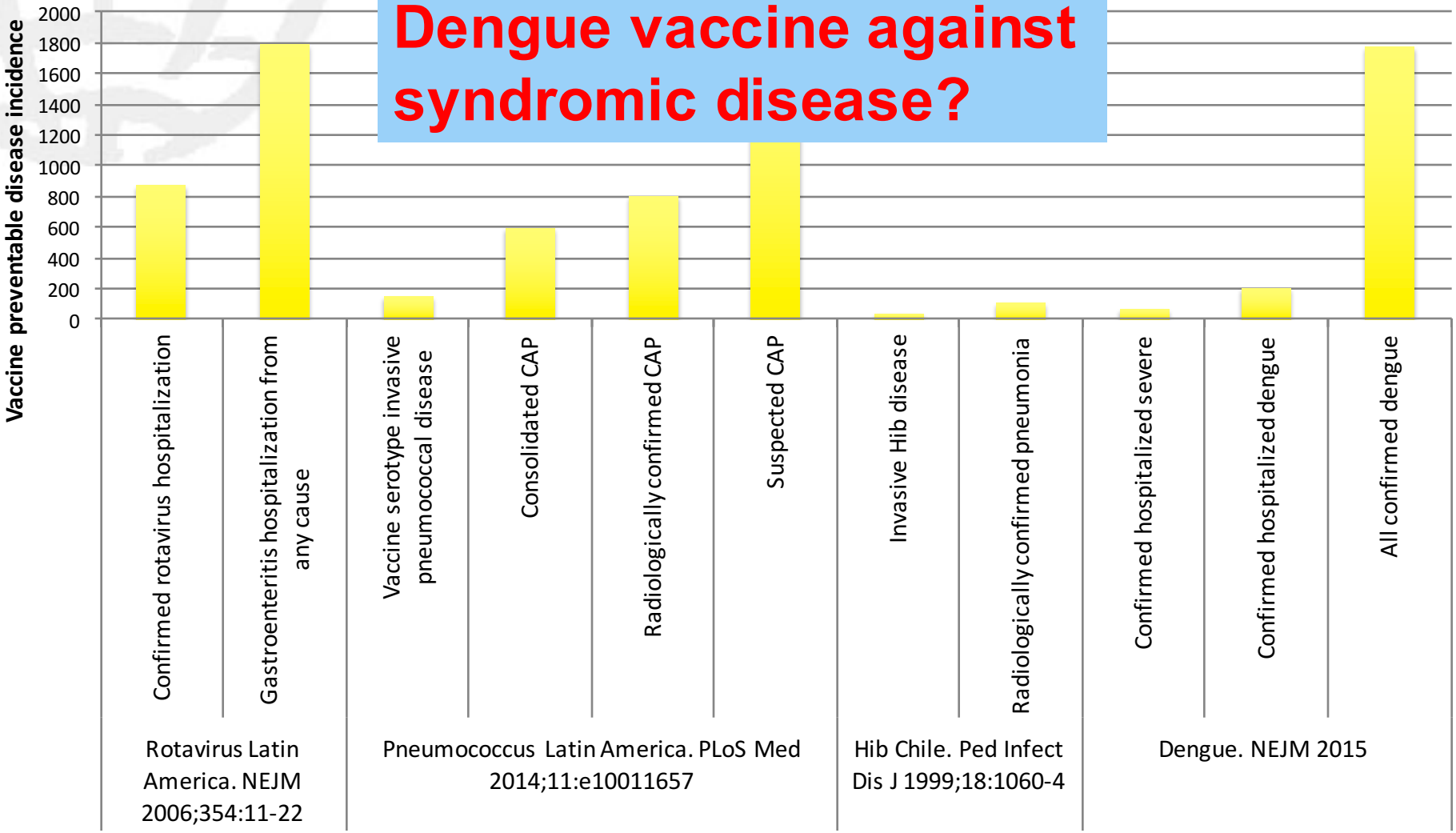


Vaccine efficacy for dengue compared to other vaccines studied and used in Latin America



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

Dengue vaccine against syndromic disease?



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	+	+	+	+++	+++

BEYOND VACCINES

H. pylori treatment and reduction in iron deficiency and anemia

- Design: Controlled, household-randomized trial
- Setting: 10 Alaska villages
- Subjects: All persons 7-11 years old with Hp+ and iron deficiency at enrollment
- Intervention: Triple therapy vs. nothing
- Follow-up: 40 months

JID 2009;199:652-60

Reductions in hematologic outcomes from Hp treatment

Outcome	Efficacy	Control prev. at 40 months	Prev. disease prevalence	NNT to prevent outcome at 40 mos
Iron deficiency	8%	58%	5%	21
Anemia	46%	21%	14%	7
Iron deficiency + anemia	75%	19%	15%	7

Effect of handwashing on child health: an RCT

- Design: Controlled, neighborhood-randomized trial
- Setting: 36 neighborhoods in Karachi, Pakistan
- Subjects: Children age <15 years in 600 intervention and 306 control households
- Intervention: Promotion of bactericidal or plain soap vs. no intervention
- Outcome: Diarrhea, impetigo, ARI
- Follow-up: Weekly for 1 year

Lancet 2005;366:225-33

Reductions in outcomes from antibacterial soap handwashing promotion

Outcome	Efficacy	Control incidence*	Intervention incidence*	PDI	NNT to prevent outcome at 1 year
Pneumonia (age <5 yr)	45%	228	125	104	0.96
Diarrhea	50%	104	213	109	0.92
Impetigo	36%	49	32	17	5.8

* Incidence per 100 person-years

SUMMARY

- Safety and efficacy just the start of assessing public health value of vaccine
- Burden is the foundation of decision making
  - Incidence
  - VPDI
  - NNV
  - Cases prevented
  - 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
- Methodology can be applied to any preventive/public health intervention