Kim Mulholland

Barriers to the introduction of new vaccines into Asia - 2015

Outline

- The current state of new vaccine introduction in Asia
- Cost issues
- Safety issues
- Concerns regarding burden of disease
- Concerns regarding vaccine effectiveness
- Advocacy and advertising
- The way forward

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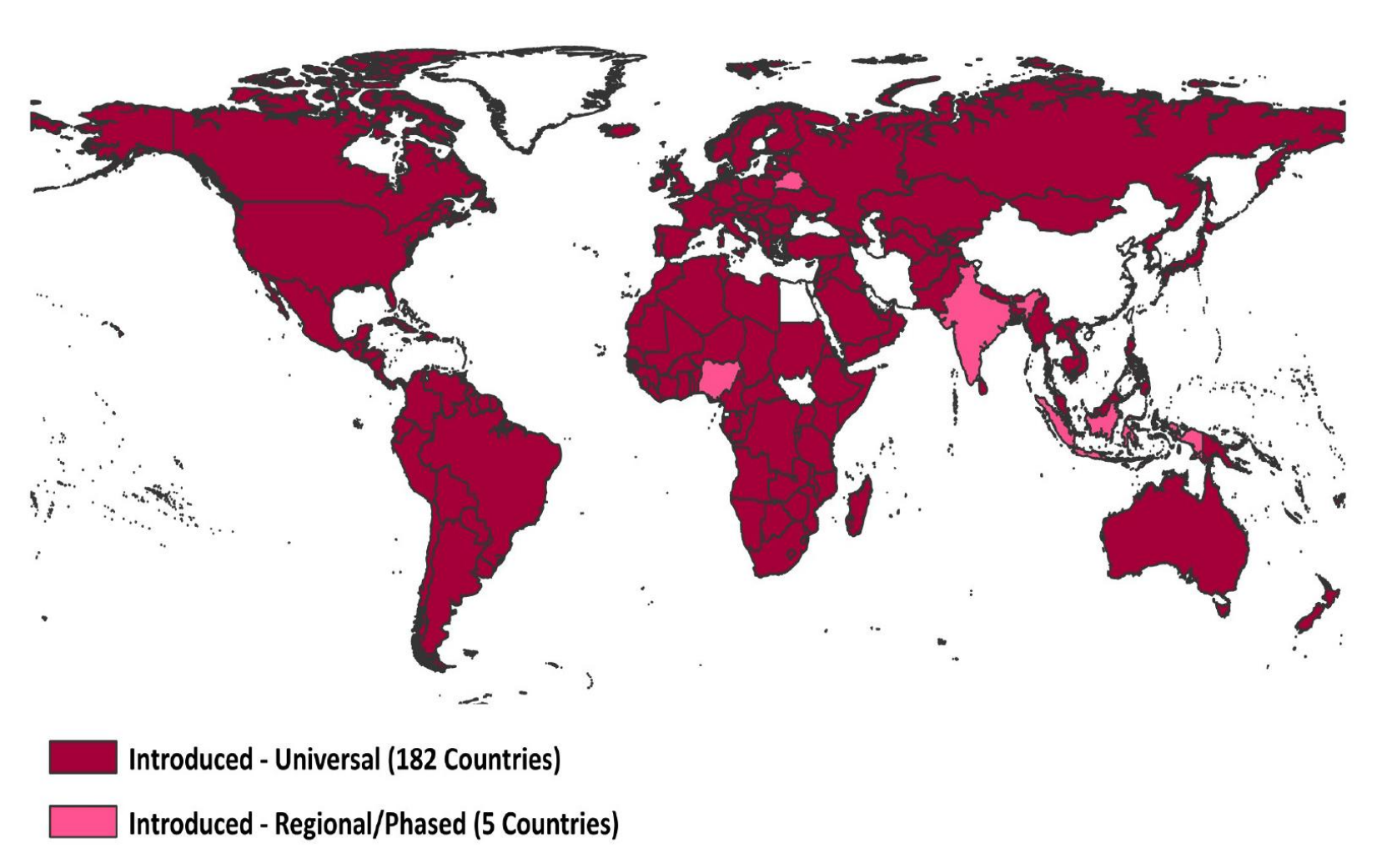
New vaccine introduction in Asia – by 2014 (thanks to WHO)

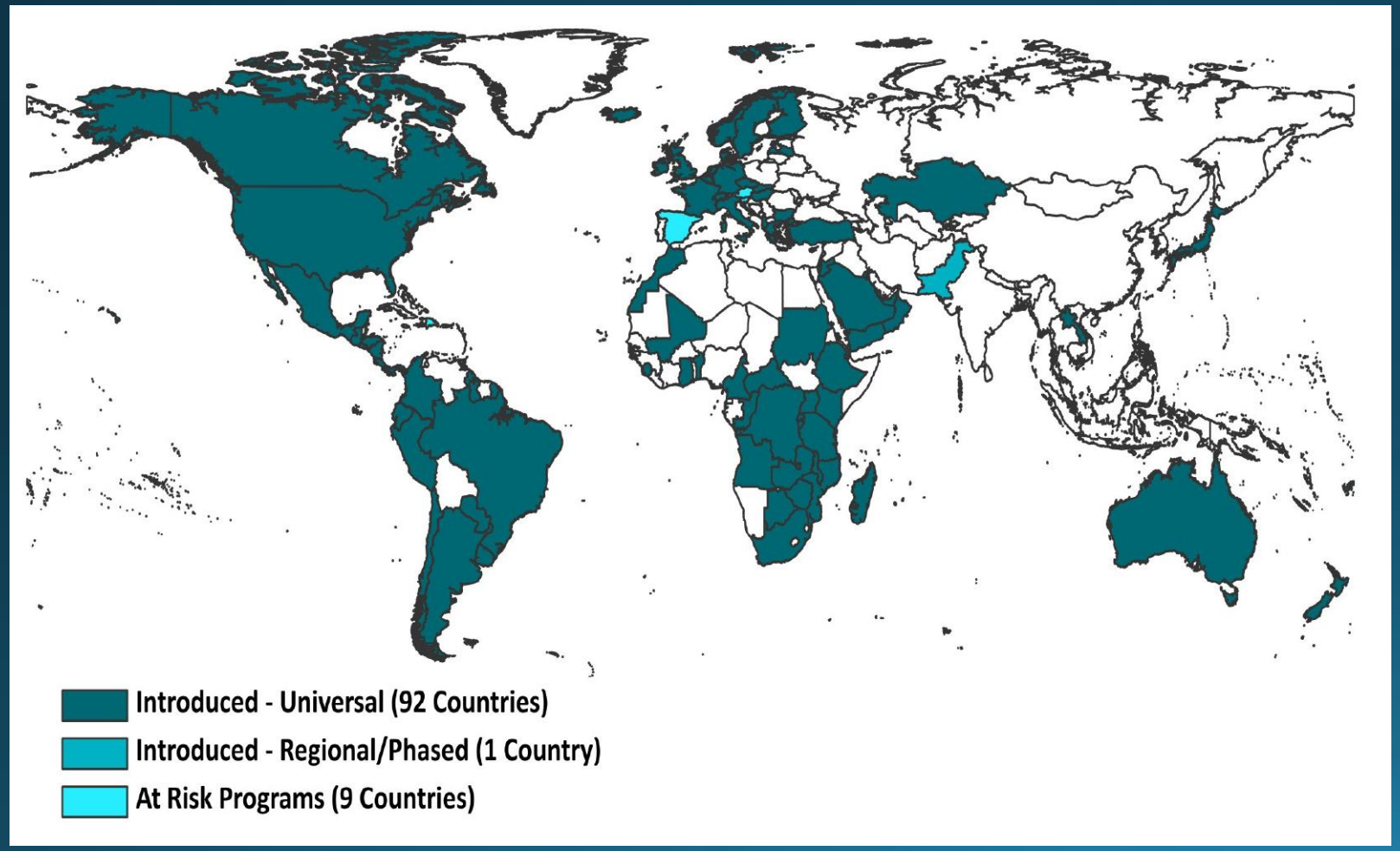
	Hepatitis B	Hib	PCV	Rotavirus	HPV
SEARO	Indonesia Thailand Maldives Bhutan India Bangladesh Nepal Sri Lanka Myanmar, N Korea Timor Leste ALL	Bangladesh Nepal Sri Lanka North Korea Indonesia (India) Maldives Myanmar Timor Leste All but Thailand	Bangladesh Nepal India for 2017?	Thailand (one province only)	Bhutan
WPRO	Most WPRO countries ALL	Malaysia, Mongolia All Pacific states Cambodia, Lao, VN Japan, Korea, Sing. Philippine, Vanuatu All but China, HK	French/US states Hong Kong, Macau Singapore (Medisave) Japan, Fiji, Kiribati, Laos, PNG, Philippines (two provinces)	French/US island states Fiji Philippines (part)	French/US island states Malaysia, Singapore (Medisave) ~~Japan~~, Brunei Fiji, Vanuatu Cook Is, N Caledon

Hib vaccine use - 2013



Data from Vaccine Information and Management System, IVAC, Johns Hopkins University

Pneumococcal conjugate vaccine use - 2013



Data from Vaccine Information and Management System, IVAC, Johns Hopkins University

Partial introductions and demonstration projects

- Hib –
  - Partial introduction – India, Indonesia (complete in 2014)
- PCV –
  - Pilot evaluation – Mongolia (2016)
  - Partial introduction – Philippines (2014)
- Rotavirus –
  - Partial introduction – Philippines
- HPV –
  - Pilot introductions – Mongolia, Kiribati, Laos, Philippines

- ***All these vaccines are widely available in the private sector throughout Asia for very high prices***

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Cost issues

- GAVI eligible countries
  - SEARO – Indonesia, Maldives, Bhutan, India, Bangladesh, Nepal, Sri Lanka, Myanmar, N Korea, Timor Leste
  - WPRO – Cambodia, Laos, Vietnam, PNG, Solomons, Kiribati
- LMI countries – Pacific states, Philippines
- Increasing effort within GAVI to develop mechanisms for LMI countries to have access to new vaccines

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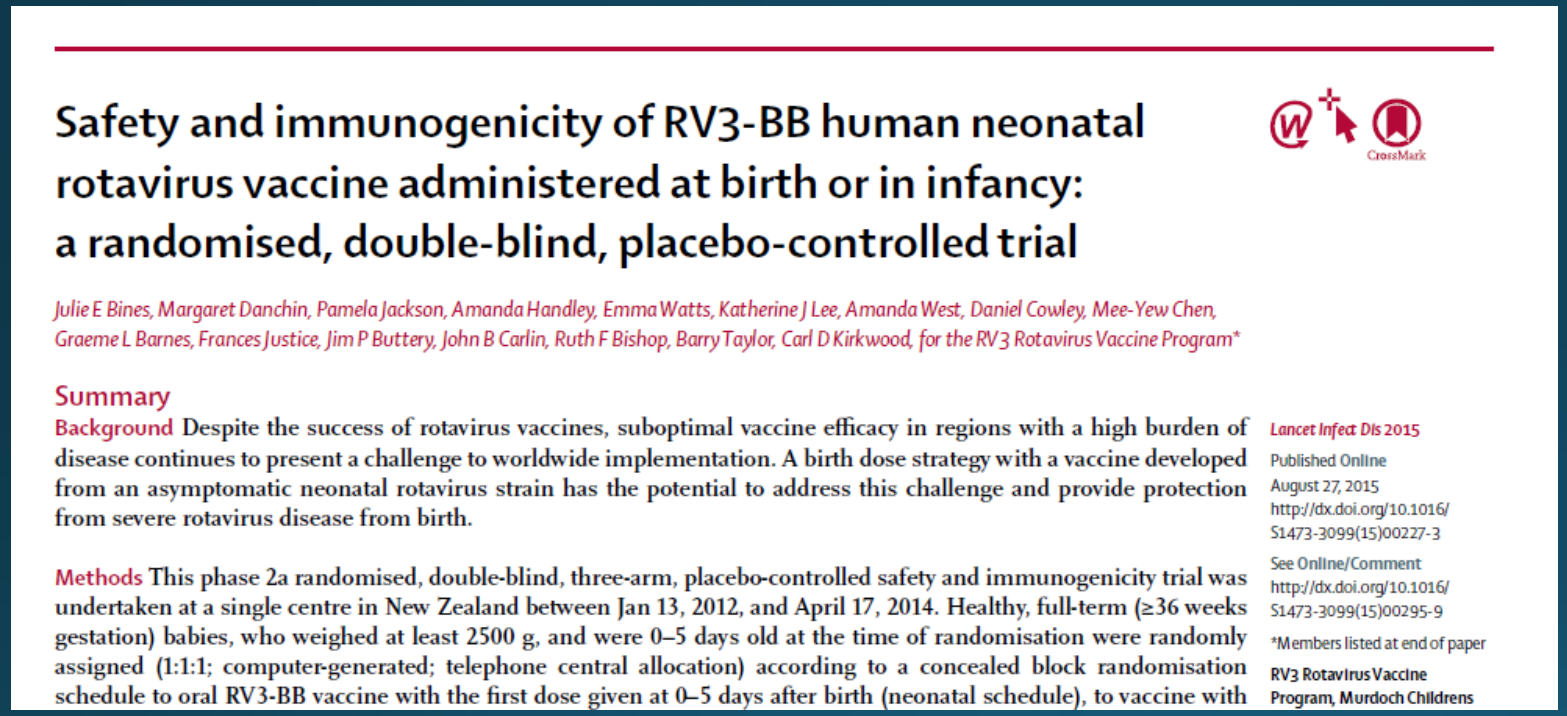
Safety issues

- Increasing awareness of vaccine safety issues
  - RV vaccine and intussusception
  - Sudden death following pentavalent – no proven association
  - Sudden death following HPV – no proven association
- Emerging data on the relative effectiveness of aP and wP vaccines
- The strange phenomenon of HANS in Japan

New neonatal rotavirus vaccine



Safety and immunogenicity of RV3-BB human neonatal rotavirus vaccine administered at birth or in infancy: a randomised, double-blind, placebo-controlled trial

*Julie E Bines, Margaret Danchin, Pamela Jackson, Amanda Handley, Emma Watts, Katherine J Lee, Amanda West, Daniel Cowley, Mee-Yew Chen, Graeme L Barnes, Frances Justice, Jim P Buttery, John B Carlin, Ruth F Bishop, Barry Taylor, Carl D Kirkwood, for the RV3 Rotavirus Vaccine Program**

Summary

Background Despite the success of rotavirus vaccines, suboptimal vaccine efficacy in regions with a high burden of disease continues to present a challenge to worldwide implementation. A birth dose strategy with a vaccine developed from an asymptomatic neonatal rotavirus strain has the potential to address this challenge and provide protection from severe rotavirus disease from birth.

Methods This phase 2a randomised, double-blind, three-arm, placebo-controlled safety and immunogenicity trial was undertaken at a single centre in New Zealand between Jan 13, 2012, and April 17, 2014. Healthy, full-term (≥36 weeks gestation) babies, who weighed at least 2500 g, and were 0–5 days old at the time of randomisation were randomly assigned (1:1:1; computer-generated; telephone central allocation) according to a concealed block randomisation schedule to oral RV3-BB vaccine with the first dose given at 0–5 days after birth (neonatal schedule), to vaccine with

Lancet Infect Dis 2015

Published Online
August 27, 2015
http://dx.doi.org/10.1016/S1473-3099(15)00227-3

See Online/Comment
http://dx.doi.org/10.1016/S1473-3099(15)00295-9

*Members listed at end of paper

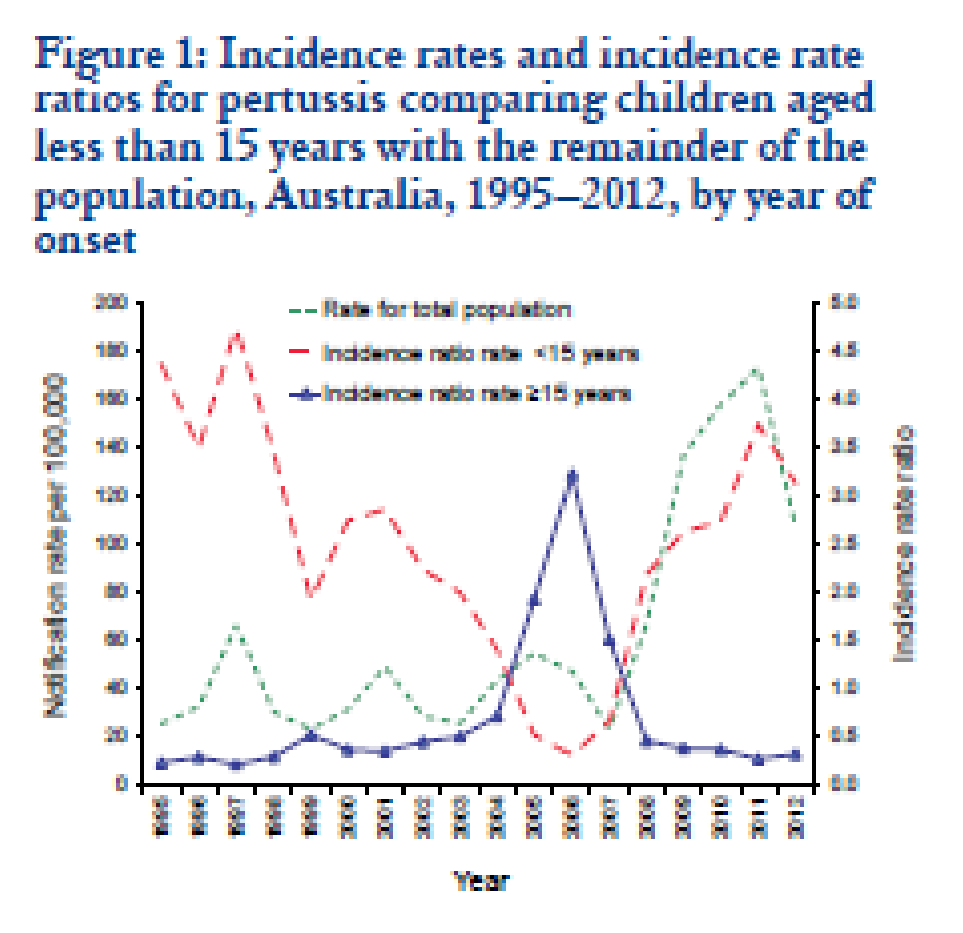
RV3 Rotavirus Vaccine Program, Murdoch Childrens

RV3 vaccine manufactured by BioFarma Indonesia
0, 8, 15 weeks similar to 8, 15, 24 weeks in New Zealand
Phase 2b trial underway in Yogjakarta, Indonesia

The strange public interpretations of AEFIs

- Consider the following:
- "If the birth cohort of 25 million were immunised (with pentavalent vaccine), 1/8000-10,000 would die of AEFI, so 3125 children would die from AEFI. To save 350 lives from Hib disease, 3125 children would die from the adverse effects of the vaccine."
  - Indian Journal of Medical Ethics, Vol X No. 3, July-September 2013
- Grossly misleading – AEFI is not a diagnosis, or a cause of death

Pertussis vaccines – new developments



- Similar experience in Australia, UK, US
- Increased disease over past 15 years
- Young adults + young infants
- Now increased cases in 2-5 years group

Pertussis vaccines – new developments

- New studies show that immune response of aP is very different to that of wP
- Vaccine efficacy after 3 doses of aP vaccine:
  - 1st year – 83.5%
  - 2nd year – 70.7%
  - 3rd year – 59.2%

Duration of Protection After First Dose of Acellular Pertussis Vaccine in Infants
Helen E. Quinn, Thomas L. Snelling, Kristine K. Macartney and Peter B. McIntyre
Pediatrics 2014;133;e513; originally published online February 10, 2014;
DOI: 10.1542/peds.2013-3181

- Pertussis hospitalizations and deaths, Australia 2006-2013

0-6 mths	1832	10
6 mths-4 years	557	0
5-9 years	113	0
10-64 years	1,166	0
65 years+	740	1

Commun Dis Intell 2014;38(3):E179-194.

Strategies to control infant pertussis mortality

- Cocoon strategy – successful in some settings where compliance is very good (eg. Chile)
- More boosters
  - Australia, US – 2m, 4m, 6m, 18m, 4y, adolescent
  - Effectiveness of boosters seems short
- Maternal immunization
  - Recommended in US, UK, Australia
  - Effectiveness in UK >90%
- Re-introduction of wP vaccines
  - Studies looking at wP for dose 1 under consideration

HPV in Japan - Human papillomavirus vaccination Associated with Neuropathic Syndrome (HANS)

思春期に打つワクチンであることが事態をややこしくしている

WEDGE REPORT

エビデンス無視で作り出される"薬害"

子宮頸がんワクチン再開できず 日本が世界に広げる薬害騒動

世界からも懸念が示されている日本の子宮頸がんワクチン騒動。その内容はあまりに非科学的だ。専門家も記者も政治家も、ワクチンのせいにする方がリスクはなく、世間も正義の味方と見てくれる。

文・村中璃子 Riko Muranaka、Wedge編集部

口に出せなくなった大多数の医師たちの考え

Source – Dr Riko Nakamura

HPV vaccine in Japan - HANS

- Pain, fatigue, neuro-psychiatric symptoms
- Autonomic dysfunction
- Pseudo-seizures (normal EEG)
- Declining cognitive function
  - Eg. Inability to manage Chinese characters

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- *“The focus is the central nerve in the brain. Basically, adjuvants are the only possible cause. When they are highly active, they go beyond the blood-brain barrier like a tsunami. Microglia in the brain become active and the entire immune system goes wrong.”*
- *Professor from the Institute of Medical Science, Tokyo Medical University), President of the Japan College of Fibromyalgia Investigation (JCFI).*

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Hib in Asia

- No new developments
- China likely to introduce Hib soon
  - Private sector paradox – private sector market creates situation where powerful groups have a vested interest in status quo

Pneumonia burden in Asia

- General agreement that pneumonia is the top cause of post-neonatal child death in Asia
- Very few actual studies of causes of child death in Asia
- Models of pneumonia numbers by cause, etc, now lack credibility
- Gates Foundation now investing in studies to actually determine the causes of child death – SE Asia excluded


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Will confusion about pneumonia and pneumococcal burden impede PCV use in Asia?

- Most major Asian countries have indicated their readiness to introduce PCVs
  - Pakistan, Bangladesh, Nepal, Laos have introduced
  - India, Sri Lanka, Philippines, Vietnam, PNG have plans
  - Indonesia involved in development of new pneumococcal vaccine
- Mongolia will undertake a PCV impact study in Ulaanbaatar
- Formal impact evaluation studies underway in Fiji, Laos, Nepal, Pakistan, Bangladesh

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Vaccine effectiveness

- Rotavirus
  - Slowness of rotavirus vaccine introduction hard to explain
  - Efficacy of vaccines ↓ in higher mortality settings
- PCV and Hib
  - Effectiveness tied up with disease burden and the fraction of pneumonia cases that can be affected by the vaccine
  - The potential for serotype replacement is a major threat to PCV effectiveness
    - Already signs of emerging serotype replacement with PCV13 in UK, US

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Advocacy and advertising

- Traditional role of UNICEF – very cautious about new vaccine advocacy
- Role of "champions" – can be overstated
- Advocacy groups have been perceived as tied to industry
- Wary of above, Asian countries are looking for "evidence" but unsure what evidence is needed
- Large scale private sector use in Asian countries appears to be a barrier to national introduction

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The way forward

- New vaccine introduction in Asia must be:
  - Evidence based, owned and wanted by countries
- Key role of WHO
  - Regional meetings and interaction
  - Promoting regional research as needed
  - Provide sober interpretation of published modelled data
- Role of research community
  - Undertake research that is needed
  - Minimize role of industry
  - Generate MUCH better data on mortality and causes of death
- Role of industry
  - Work as colleagues of the public sector
  - Move away from the notion of vaccines as products to be peddled

Thanks…

- Thanks to Dr Riko Nakamura for information on the HPV vaccine introduction in Japan
- Thanks to Dr Kim Fox, Dr Nyambat Batmunkh, Dr James Heffelfinger at WPRO/WHO