“New” Pneumonia?: 2012 and beyond

Daniel Feikin, MD
International Vaccine Access Center
Johns Hopkins School of Public Health

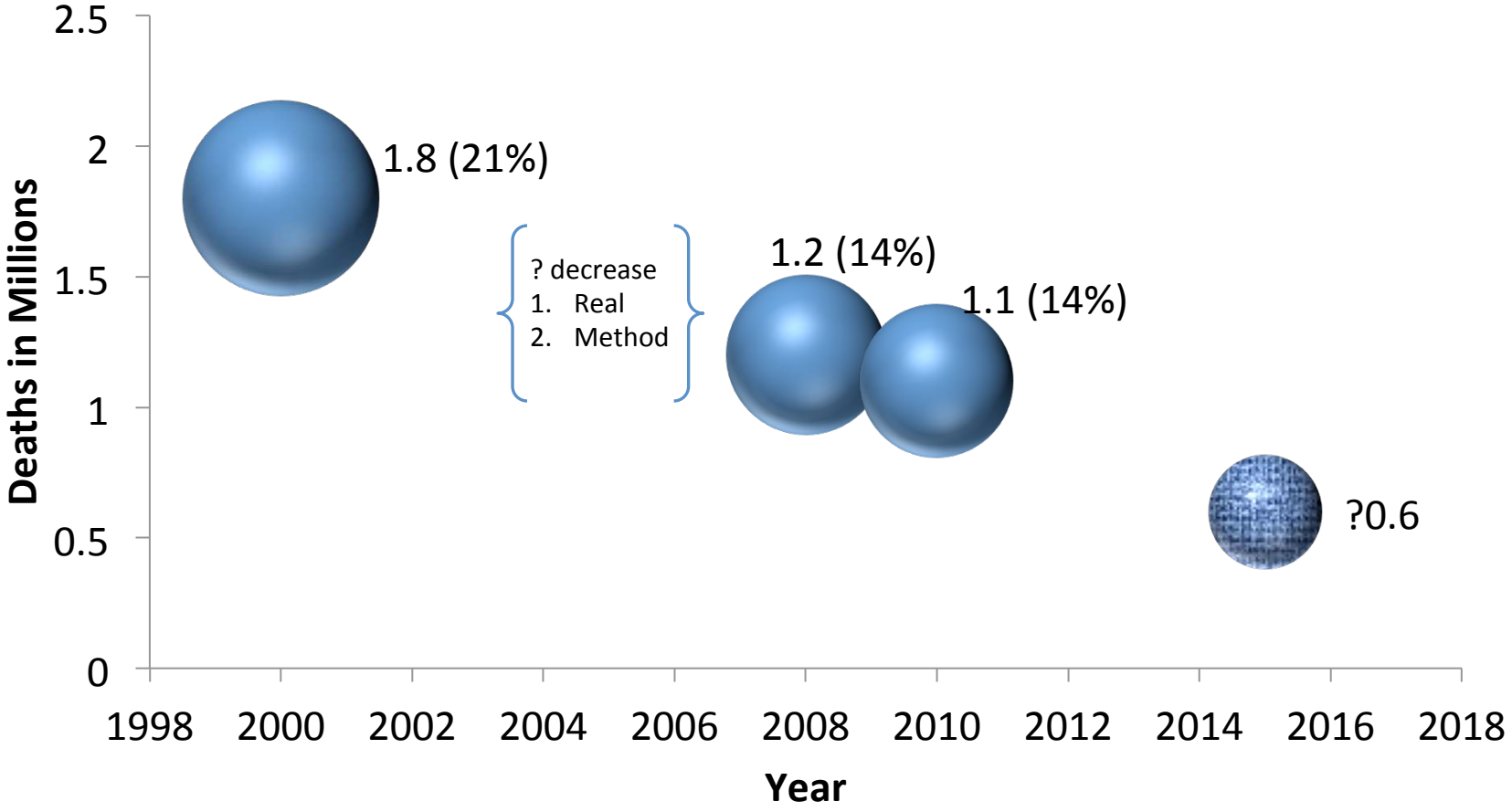
Outline of talk

- Pneumonia burden
- Pneumonia diagnostics
- Pneumonia etiology
- Pneumonia as part of fever algorithm

How much pneumonia in children?

- 0.29 episodes per child year based on community-based studies (Rudan, Bull WHO, 2004)
- 151 million episodes per year
- About a quarter of these are severe pneumonia (Hair N, personal communication)

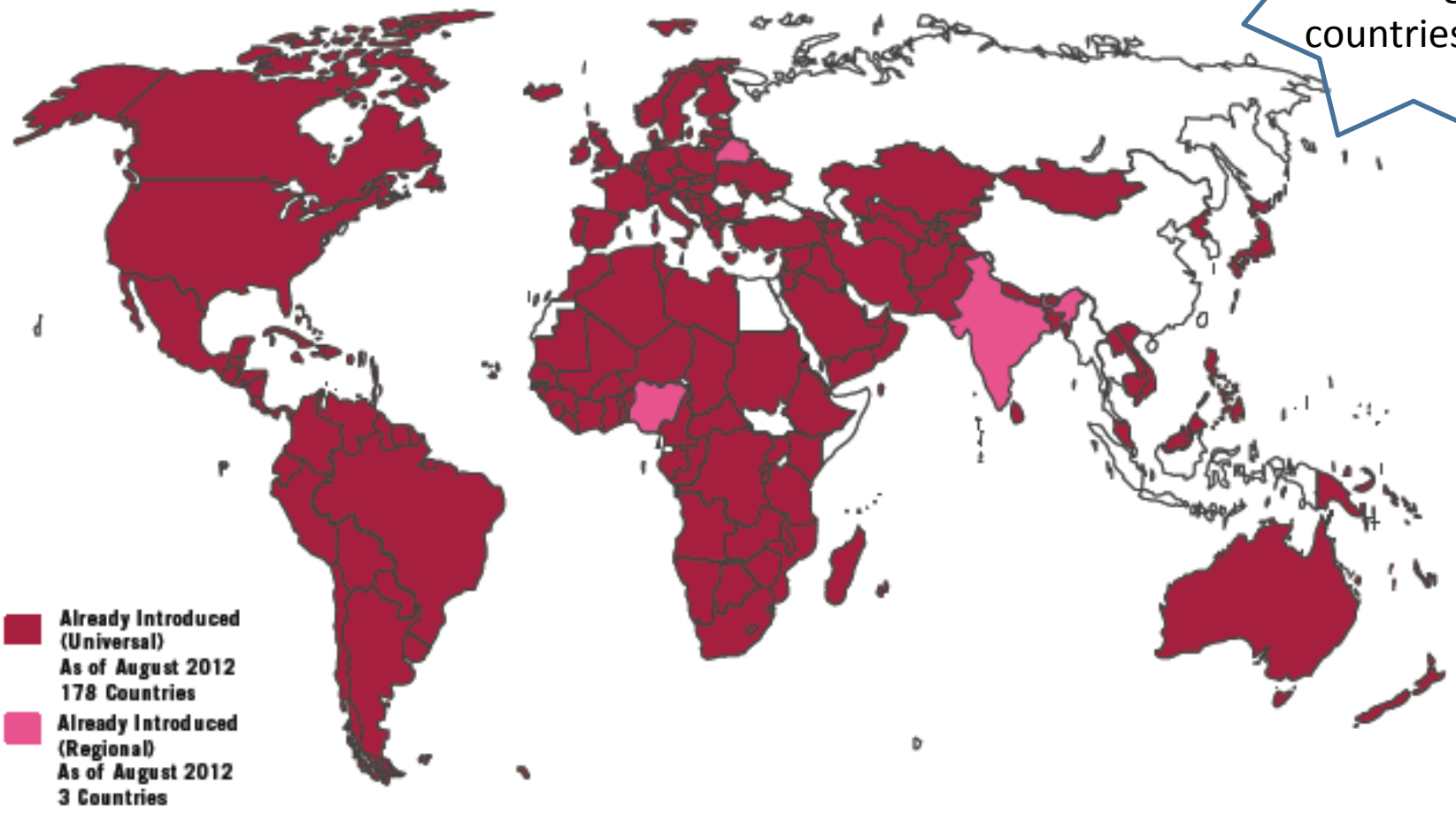
Global pneumonia deaths in children < 5 years old (WHO CHERG)



Black, R, Lancet 1993; Black R, Lancet 2010; Liu L, Lancet 2012.

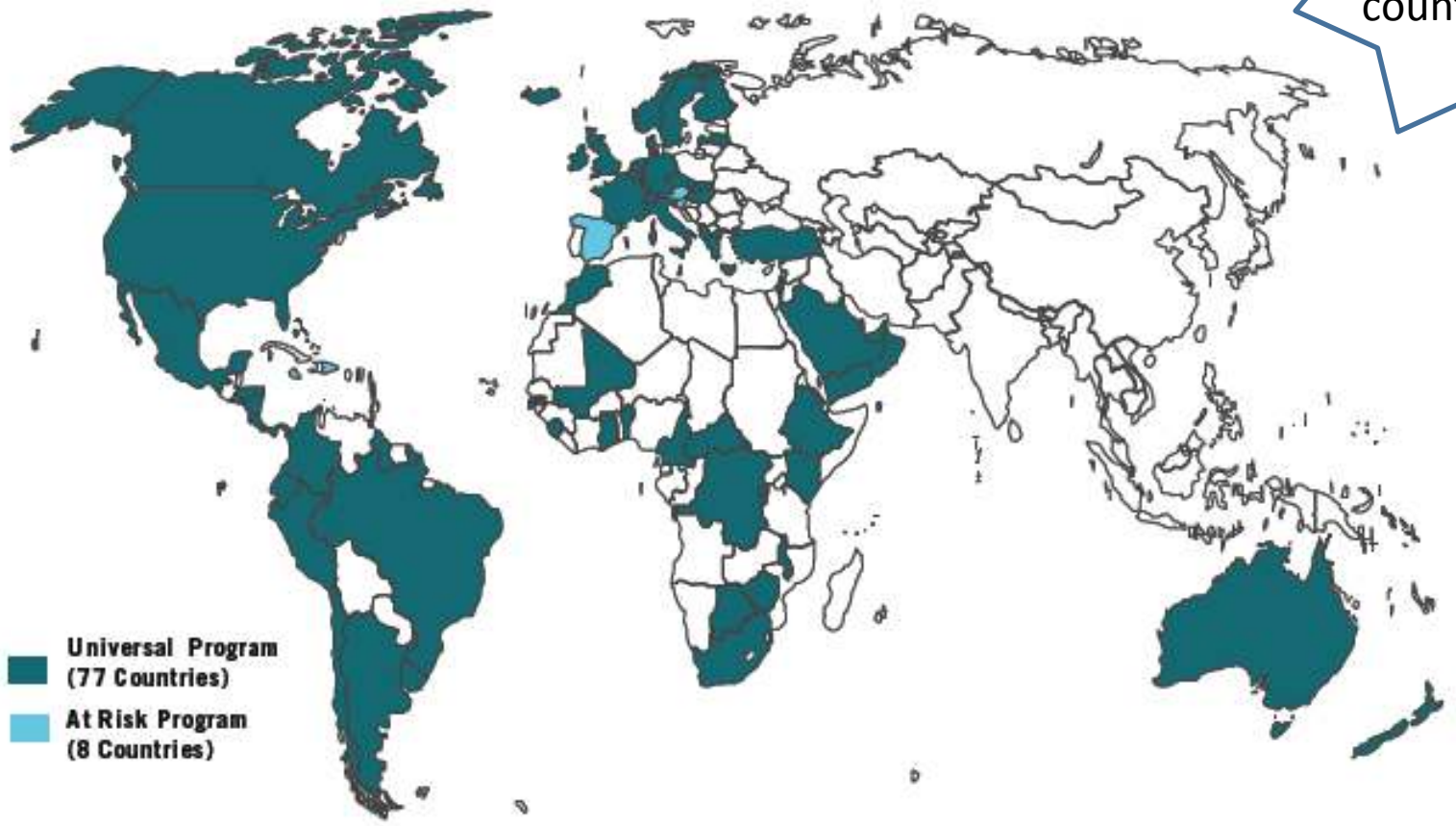
Hib vaccine use – August 2012

68 / 73
GAVI-eligible
countries



Pneumococcal conjugate vaccine use – August 2012

18 / 73 GAVI-eligible countries



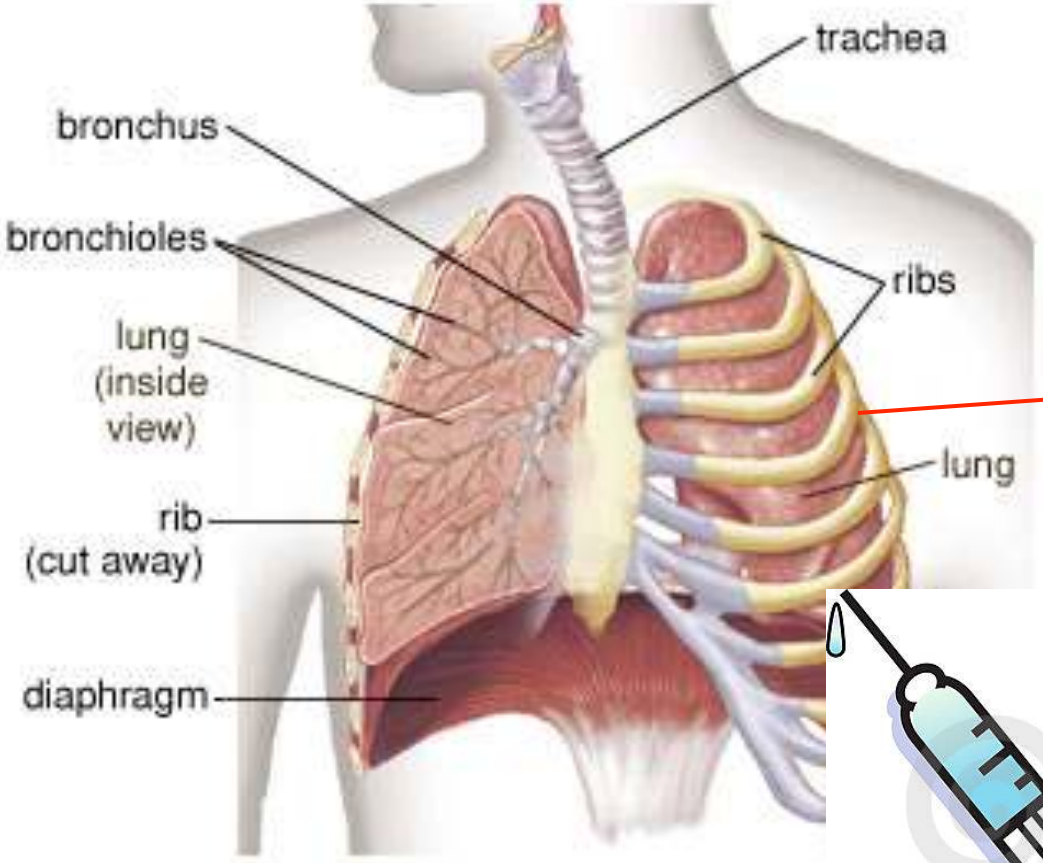
A brief history of pneumonia diagnostics

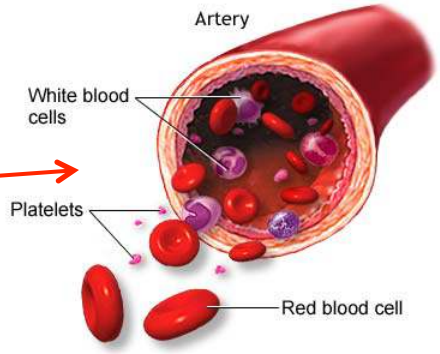
The present

The past

The future

Pneumonia diagnostics – the past

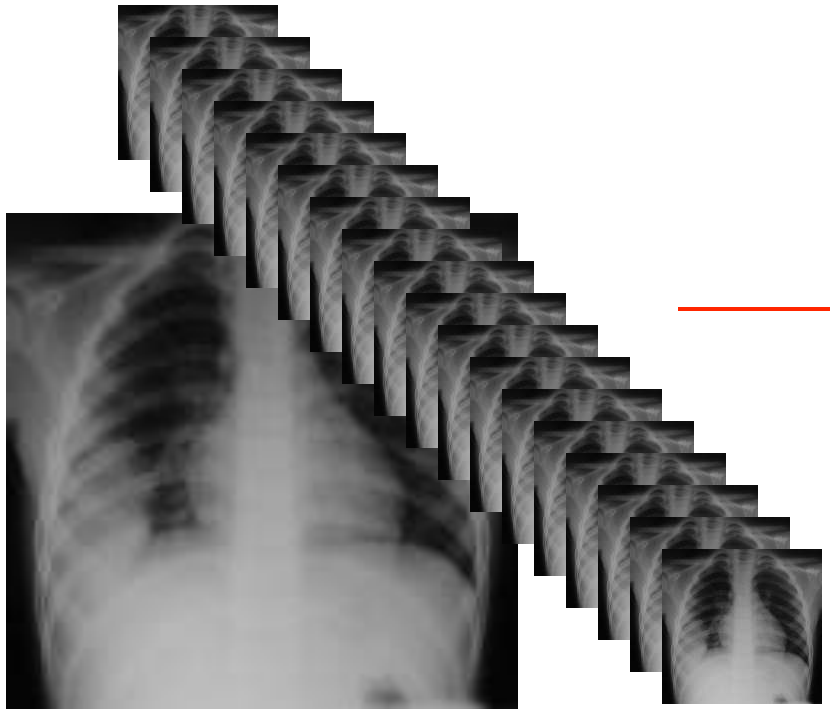


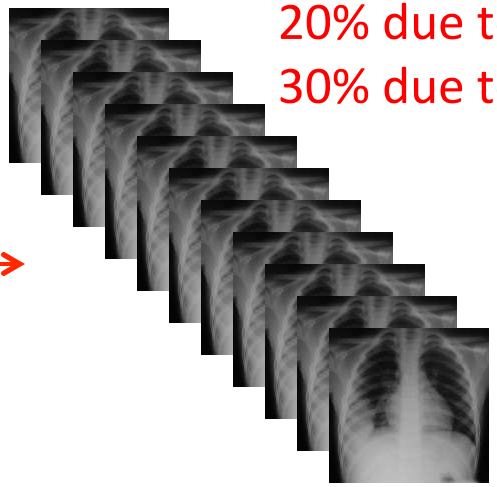


10-15% bacterial pneumonia is bacteremic

50% get diagnosis with lung aspirate

Pneumonia diagnostics – the past



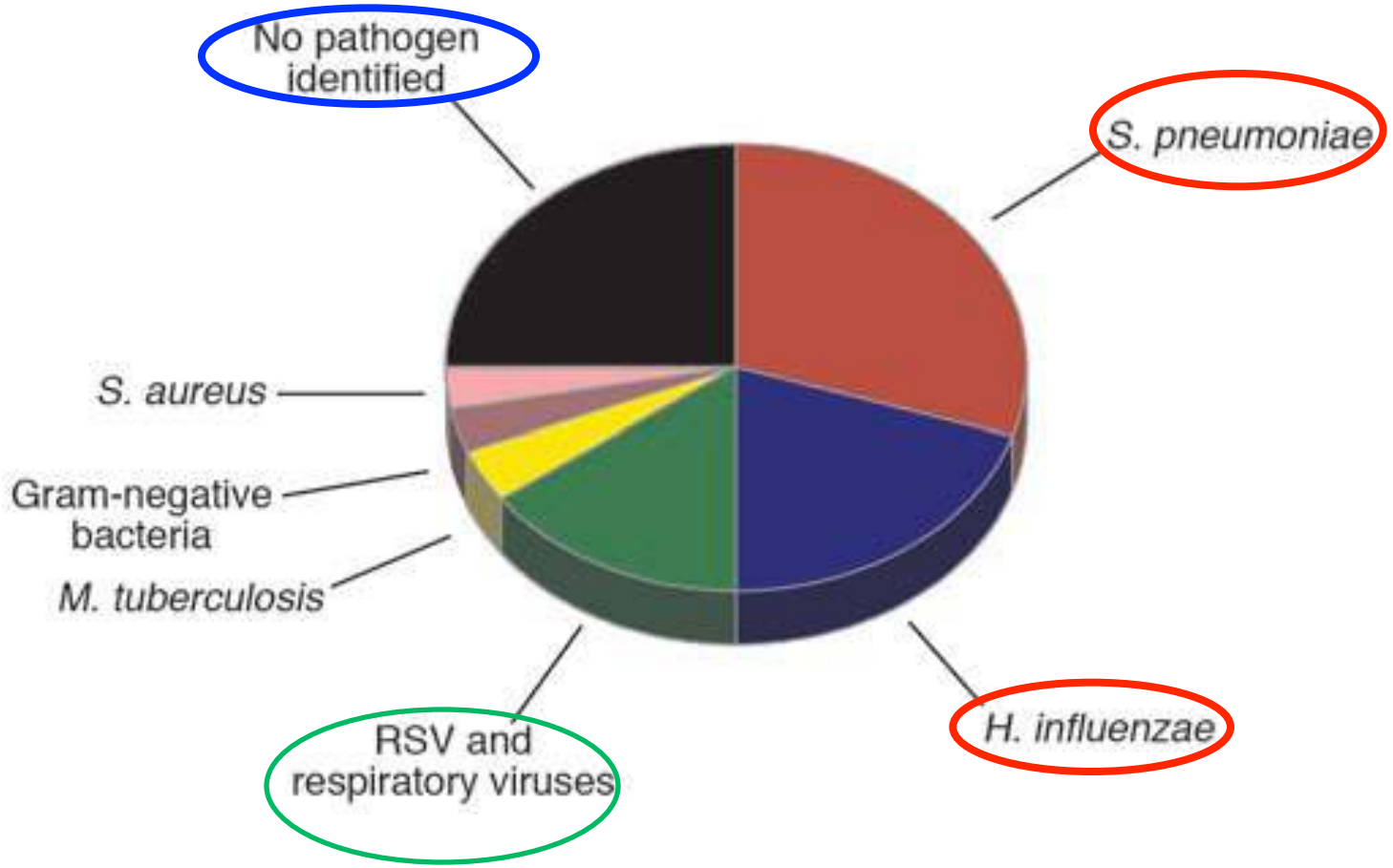


20% due to Hib
30% due to Pneumo

Causes of severe pneumonia

HIV negative children in developing countries

1995-2005

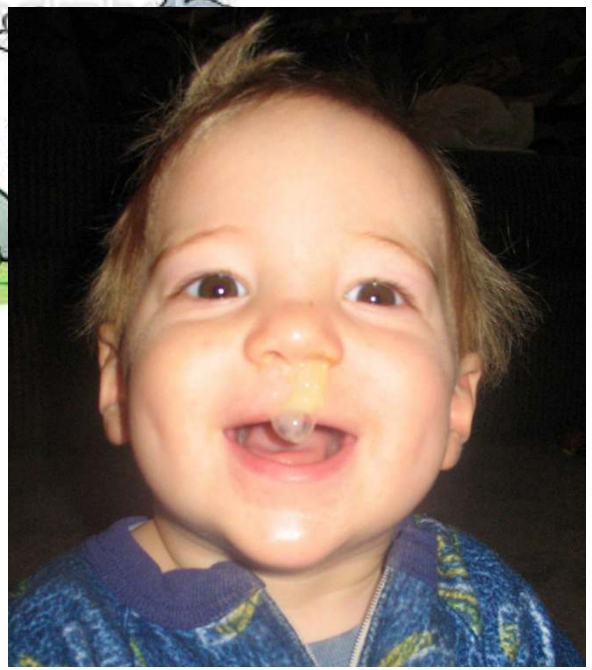


Scott et al. J Clin Invest 2008;118:1291-1300

Pneumonia diagnostics – the present

Viruses

Bacteria



The Pneumonia Etiology Research for Child Health (PERCH) Project

PERCH Sites

*** PERCH coordinating centre**

PERCH CASES: inclusion criteria

Target = ~4,000 cases

- Age 28 days to 59 months
- Lives in defined catchment area
- Admitted to hospital
- **Meets WHO criteria for severe or very severe pneumonia**

PERCH CONTROLS: inclusion criteria

Target = ~4,000 controls

- Age 28 days to 59 months
- Lives in same catchment area as PERCH cases
- Recruited from home
- **No evidence of pneumonia**

PERCH Specimen Testing

Body Fluid	Laboratory Analyses
Acute blood	Blood culture; l*ytA* pneumococcal PCR Archived for serology and possible other testing
Convalescent blood	Archived for serological testing
NP rayon swab	Bacterial culture for pneumococcus (and serotyping if applicable)
Throat rayon and NP flocked swabs	PCR for respiratory pathogens Archived for future testing
Induced Sputum	Microscopy and bacterial culture; Mycobacterial microscopy, culture PCR for respiratory pathogens
Lung Aspirate (at select sites)	Microscopy and bacterial culture; M.tb microscopy, culture PCR for respiratory pathogens
Pleural Fluid	Microscopy and bacterial culture; Protein and glucose testing M.tb microscopy, culture; PCR for respiratory pathogens Antigen detection (pneumococcus)
Gastric Aspirate	Mycobacterial microscopy and culture
Urine	Storage for future testing (antigens; biomarkers)
Lung Tissue (from post mortem needle biopsy, at select sites)	Histology ; Gram Stain and bacterial / mycobacterial culture, PCR for respiratory pathogens

WHO clinical guidelines for classification and treatment of pneumonia

ASSESS AND CLASSIFY THE SICK CHILD AGE 2 MONTHS UP TO 5 YEARS

ASSESS | CLASSIFY | IDENTIFY TREATMENT

ASK THE MOTHER WHAT THE CHILD'S PROBLEMS ARE

- Determine if this is an initial or follow-up visit for this problem.
  - If follow-up visit, use the follow-up instructions on *TREAT THE CHILD* chart.
  - If initial visit, assess the child as follows:

CHECK FOR GENERAL DANGER SIGNS

ASK:	*LOOK:*
• Is the child able to drink or breastfeed? • Does the child vomit everything? • Has the child had convulsions?	• See if the child is lethargic or unconscious.

A child with any general danger sign needs *URGENT* attention; complete the assessment and

USE ALL BOXES THAT MATCH THE CHILD'S SYMPTOMS AND PROBLEMS TO CLASSIFY THE ILLNESS.

THEN ASK ABOUT MAIN SYMPTOMS:
Does the child have cough or difficult breathing?

IF YES, ASK:
- For how long?

LOOK, LISTEN, FEEL:
- Count the breaths in one minute.
- Look for chest indrawing.
- Look and listen for stridor.

CHILD MUST BE CALM

Classify COUGH or DIFFICULT BREATHING

If the child is:	Fast breathing is:
2 months up to 12 months	50 breaths per minute or more
12 months up to 5 years	40 breaths per minute or more

SIGNS	CLASSIFY AS	TREATMENT (Urgent pre-referral treatments are in bold print.)
• Any general danger sign or • Chest indrawing or • Stridor in calm child.	SEVERE PNEUMONIA OR VERY SEVERE DISEASE	➢***Give first dose of an appropriate antibiotic.*** ➢***Refer URGENTLY to hospital.****
• Fast breathing.	PNEUMONIA	➢***Give an appropriate antibiotic for 5 days.*** ➢Soothe the throat and relieve the cough with a safe remedy. ➢Advise mother when to return immediately. ➢Follow-up in 2 days.
No signs of pneumonia or very severe disease.	NO PNEUMONIA: COUGH OR COLD	➢If coughing more than 30 days, refer for assessment. ➢Soothe the throat and relieve the cough with a safe remedy. ➢Advise mother when to return immediately. ➢Follow-up in 5 days if not improving.

WHO guidelines for pneumonia

- Developed in the 1970-1980's
- Designed for first point of contact at peripheral health facility
- Premised on high sensitivity, specificity less important
- Early referral and treatment with antibiotics for bacterial pneumonia
- 24% reduction in mortality from pneumonia case management (Sazawal, Lancet 2003)

Fever absent IMCI pneumonia algorithm Low sensitivity

Table 2. Clinical signs in 200 paediatric outpatients presenting with a cough, with or without crepitations

Clinical sign	With crepitations ($n = 67$)		Without crepitations ($n = 133$)	
	No. with this clinical sign present = true positive	No. with this clinical sign absent = false negative	No. with this clinical sign present = false positive	No. with this clinical sign absent = true negative
Respirations > 40/min	60 (90)[a]	7 (10)	55 (41)	78 (59)
Respirations > 50/min	48 (72)	19 (28)	25 (19)	108 (81)
Rapid respiration[b]	52 (78)	15 (22)	36 (27)	97 (73)
Breathless (as stated by the mother)	43 (64)	24 (36)	31 (23)	102 (77)
Respirations > 50 or breathless	62 (93)	5 (7)	49 (37)	84 (63)
Temperature > 37.5 °C	35 (52)	32 (48)	52 (39)	81 (61)

[a] Figures in parentheses are percentages.
[b] Under 12 months old = respiration > 50/min. Aged 12 months or more = respiration > 40/min.

Shann F, Bull WHO, 1984. Technical bases WHO, WHO/ARI/91.20.

Fever absent IMCI pneumonia algorithm – Low PPV

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (1996) 90, 658–662

Clinical overlap between malaria and severe pneumonia in African children in hospital

Michael English[1,2], Jeanine Punt[1], Isaiah Mwangi[1], Kieran McHugh[3] and Kevin Marsh[1,2] *[1]Clinical Research Centre, KEMRI Kilifi Unit, P.O. Box 428, Kilifi, Kenya; [2]Nuffield Department of Clinical Medicine and [3]Department of Radiology, John Radcliffe Hospital, Headington, Oxford, OX3 9DU, UK*

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (1993) 87, 662–665

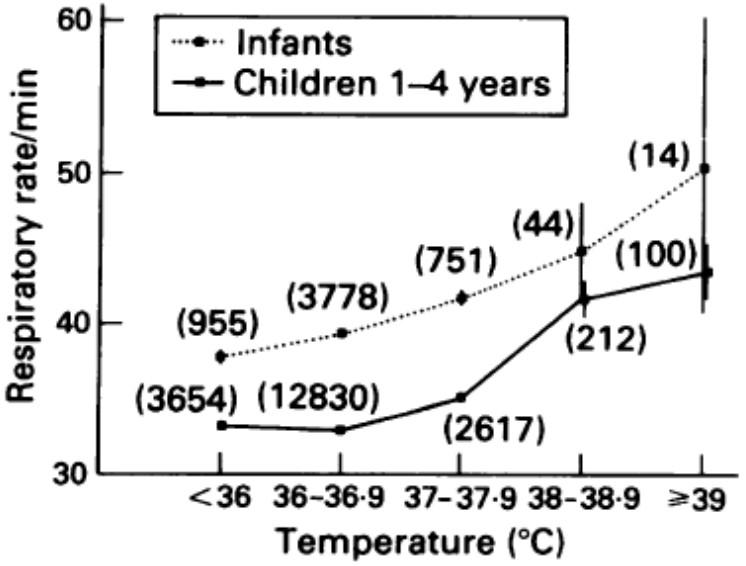
Overlap in the clinical features of pneumonia and malaria in African children

T. J. D. O'Dempsey[1], T. F. McArdle[1], B. E. Laurence[1], A. C. Lamont[2], J. E. Todd[1] and B. M. Greenwood[1] *[1]Medical Research Council Laboratories, P.O. Box 273, Banjul, The Gambia; [2]Department of Paediatric Radiology, Leicester Royal Infirmary, Leicester, UK*

Fever ≠ Pneumonia

Fever can elevate Respiratory Rate

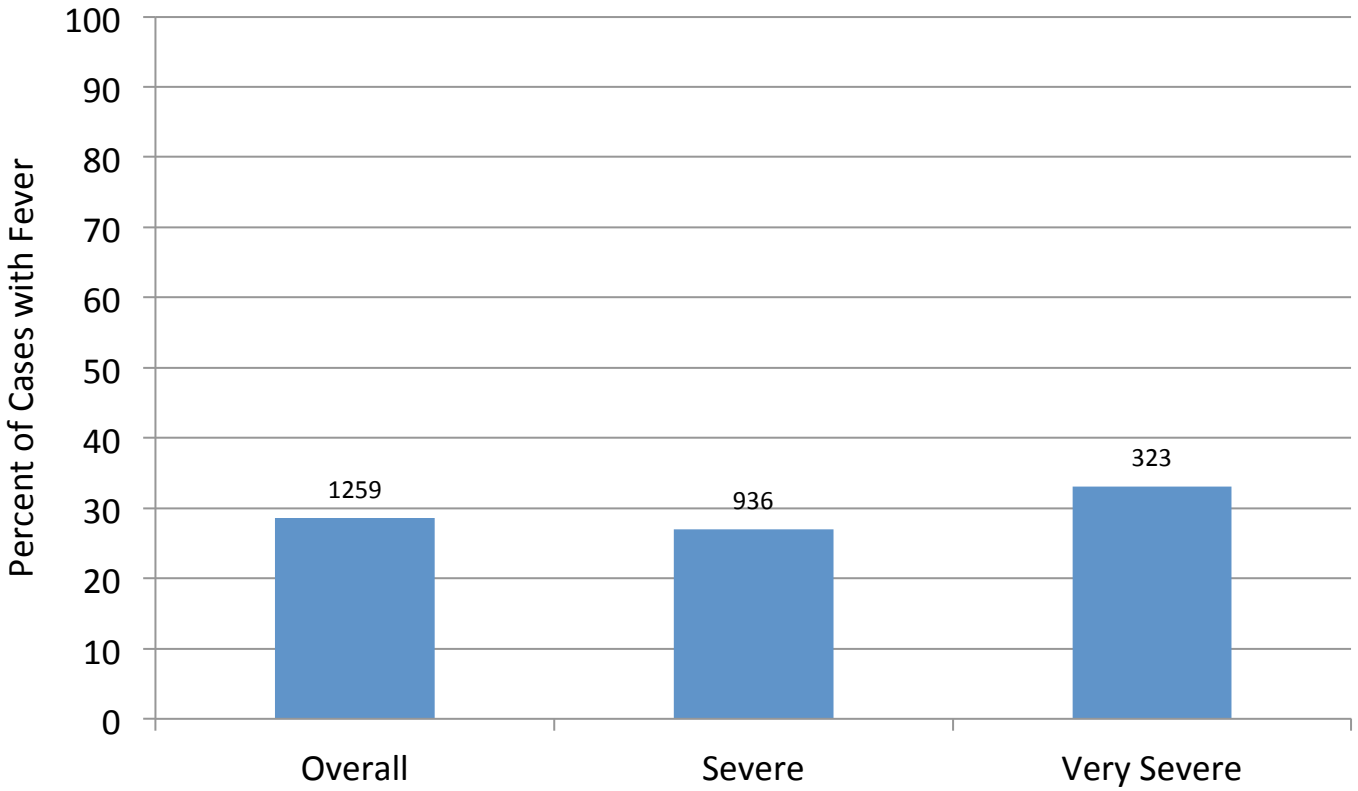
- Fever can lead to elevated RR, independent of ARI
- About 4 bpm per degree centigrade of fever (O'Dempsey, Arch Dis Child, 93)



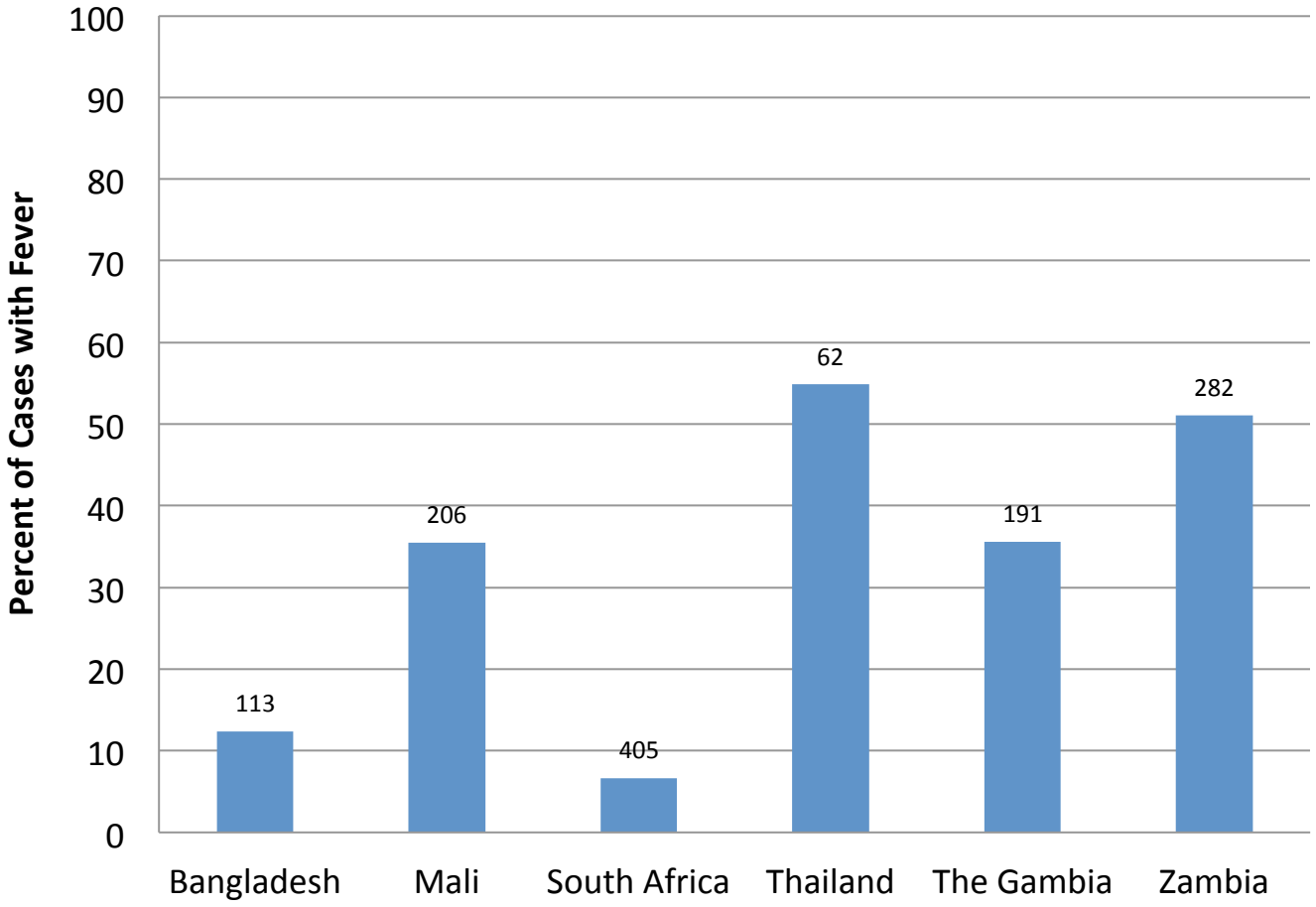
Relationships between respiratory rate and temperature in young Gambian children. Vertical bars represent 95% confidence intervals of the mean, and numbers of observations for each point are shown in parentheses.

Campbell H, Arch Dis Child 1992

Fever (T ≥38.0 ° C) Upon Admission of PERCH cases



Fever (T ≥38.0 ° C) Upon Admission of PERCH cases



Role of pneumonia in fever algorithm

OPEN ACCESS Freely available online

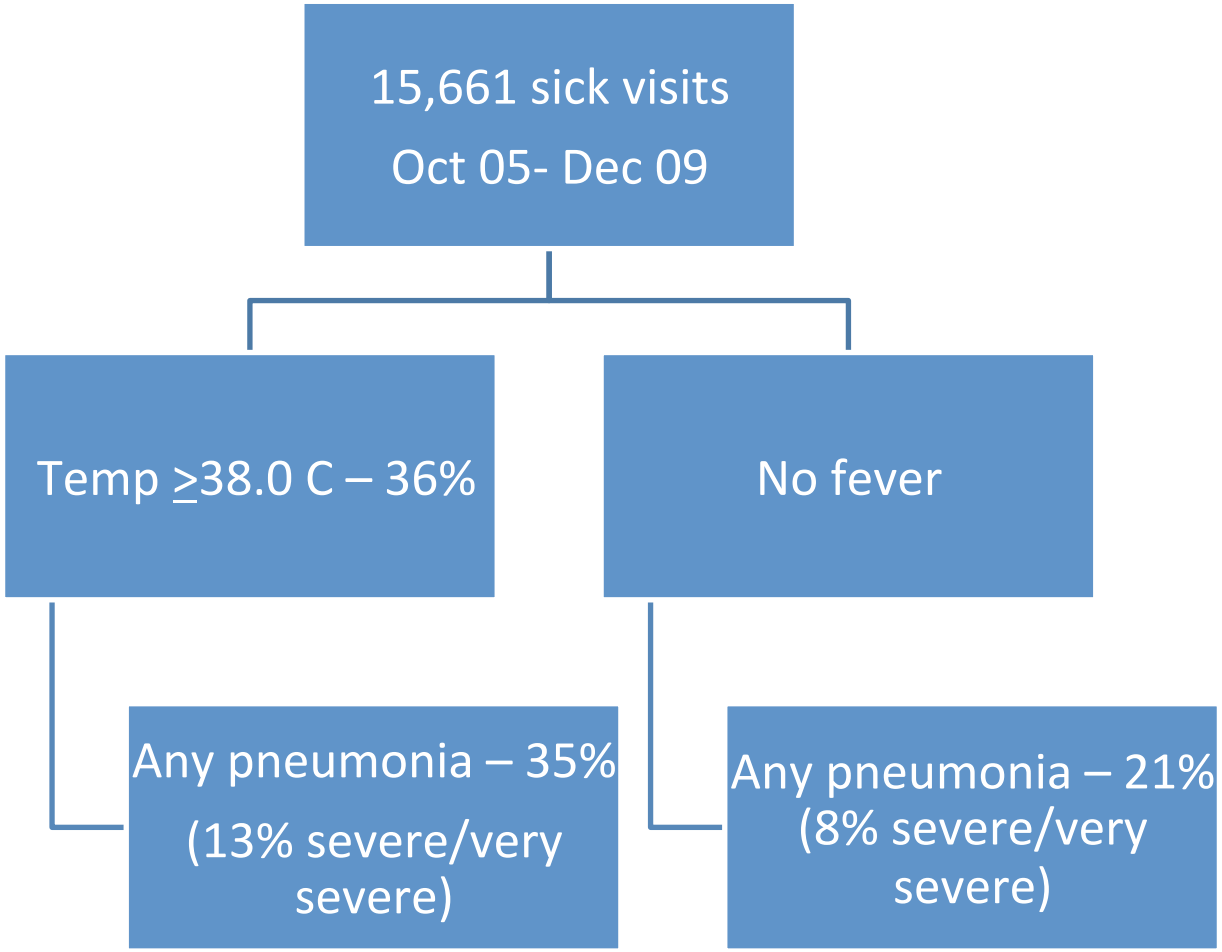
PLoS one

The Burden of Common Infectious Disease Syndromes at the Clinic and Household Level from Population-Based Surveillance in Rural and Urban Kenya

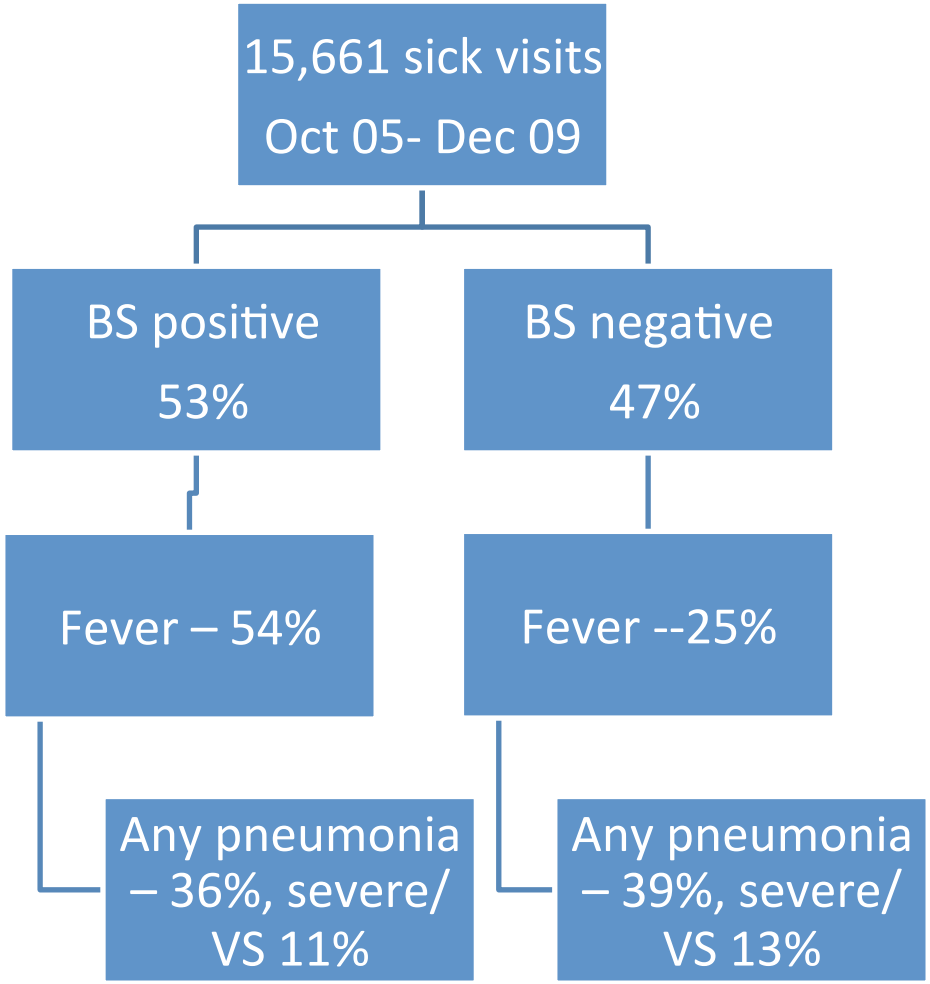
Daniel R. Feikin[1,2]*, Beatrice Olack[1,2], Godfrey M. Bigogo[1,2], Allan Audi[1,2], Leonard Cosmas[1,2], Barrack Aura[1,2], Heather Burke[1,2], M. Kariuki Njenga[1,2], John Williamson[2], Robert F. Breiman[1,2]

1 International Emerging Infections Program-Kenya, Centers for Disease Control and Prevention-Nairobi and Kisumu, Nairobi and Kisumu, Kenya, **2** Kenya Medical Research Institute/CDC Public Health and Research Collaboration, Kisumu and Nairobi, Kenya

Role of pneumonia in fever algorithm



Role of pneumonia in fever algorithm



Pneumonia in fever algorithm

- Sensitivity of fever for pneumonia ~30%
- Positive predictive value of fever for pneumonia ~35-40%
- Pneumonia is not a febrile illness

Questions to consider

- Should another sign/symptom be added to fever algorithm for pneumonia treatment
  - Chest indrawing, tachypnea
- Do RDTs change the role of pneumonia in a fever algorithm?
  - It's always been there. % with pneumonia increase as malaria declines, but not counts
  - Pneumonia can occur in RDT positive or negative kids

THANK YOU