Meningitis Research Foundation

Neonatal Sepsis in sub-Saharan Africa

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[4]KEMRI-Welllcome Trust Research Programme

I have no conflicts of interest to declare

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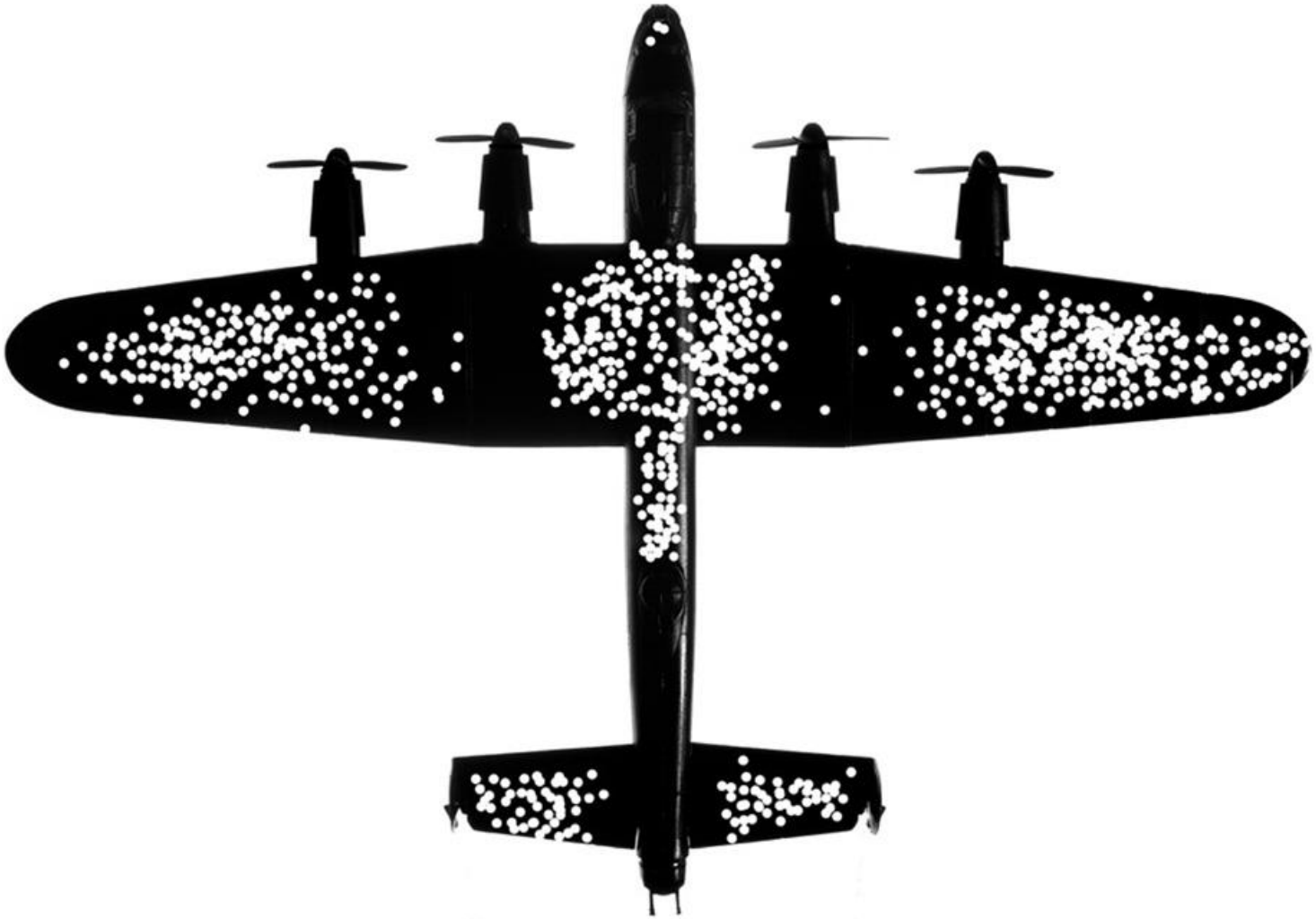
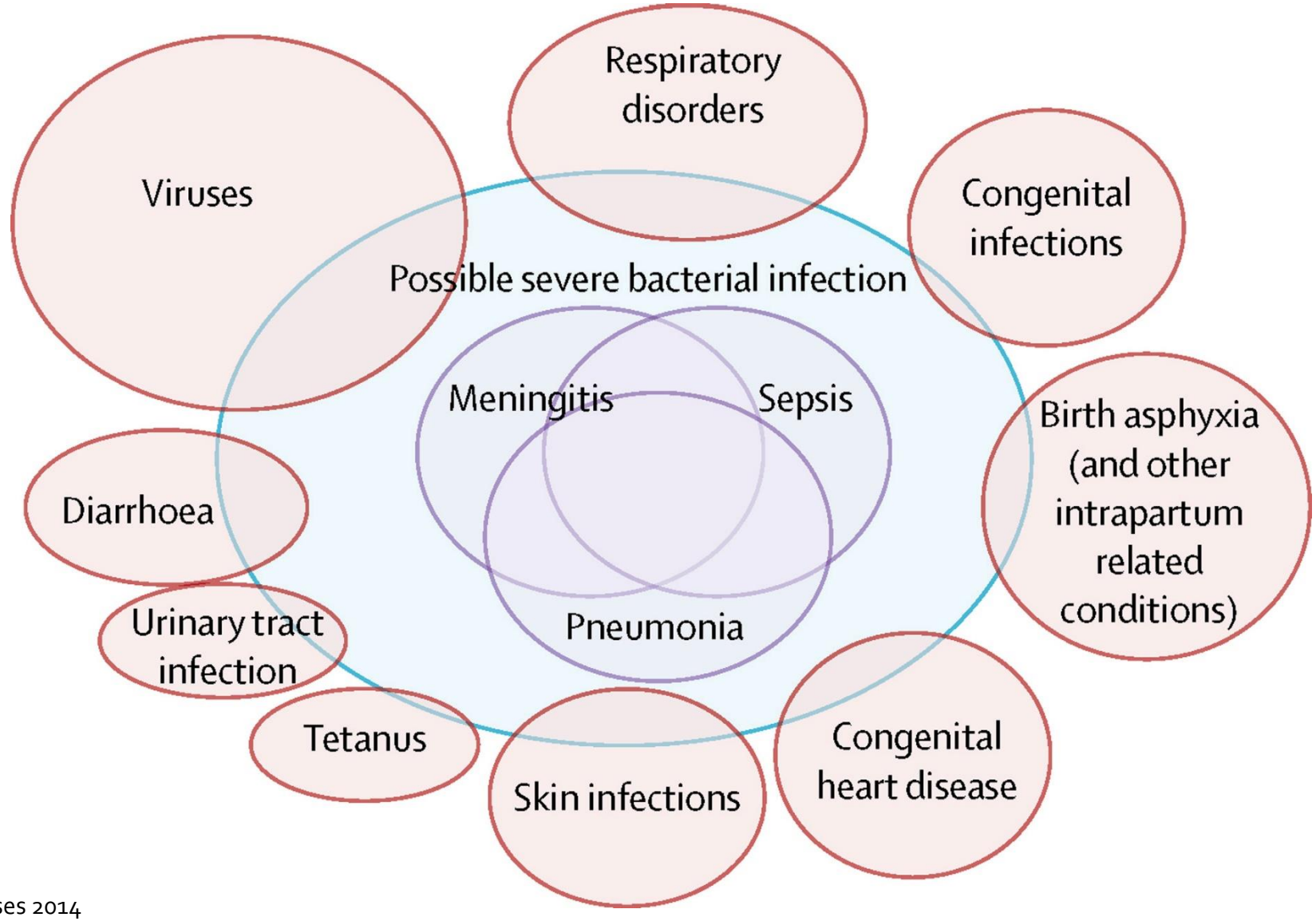
World War II Centre for Naval Analysis - warplanes



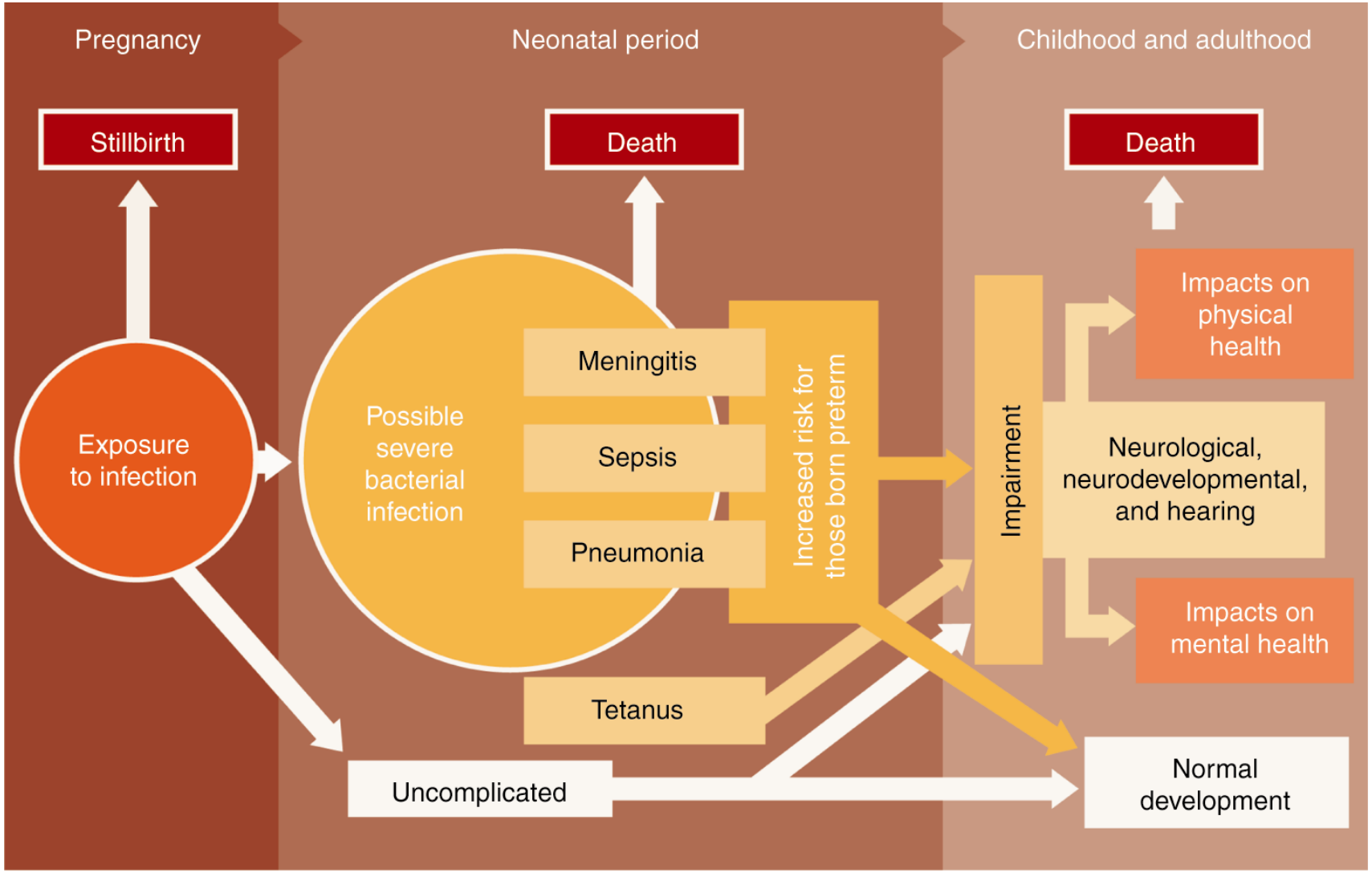
Strengthen the planes where the bullets are causing most damage

Neonatal sepsis – the diagnosis



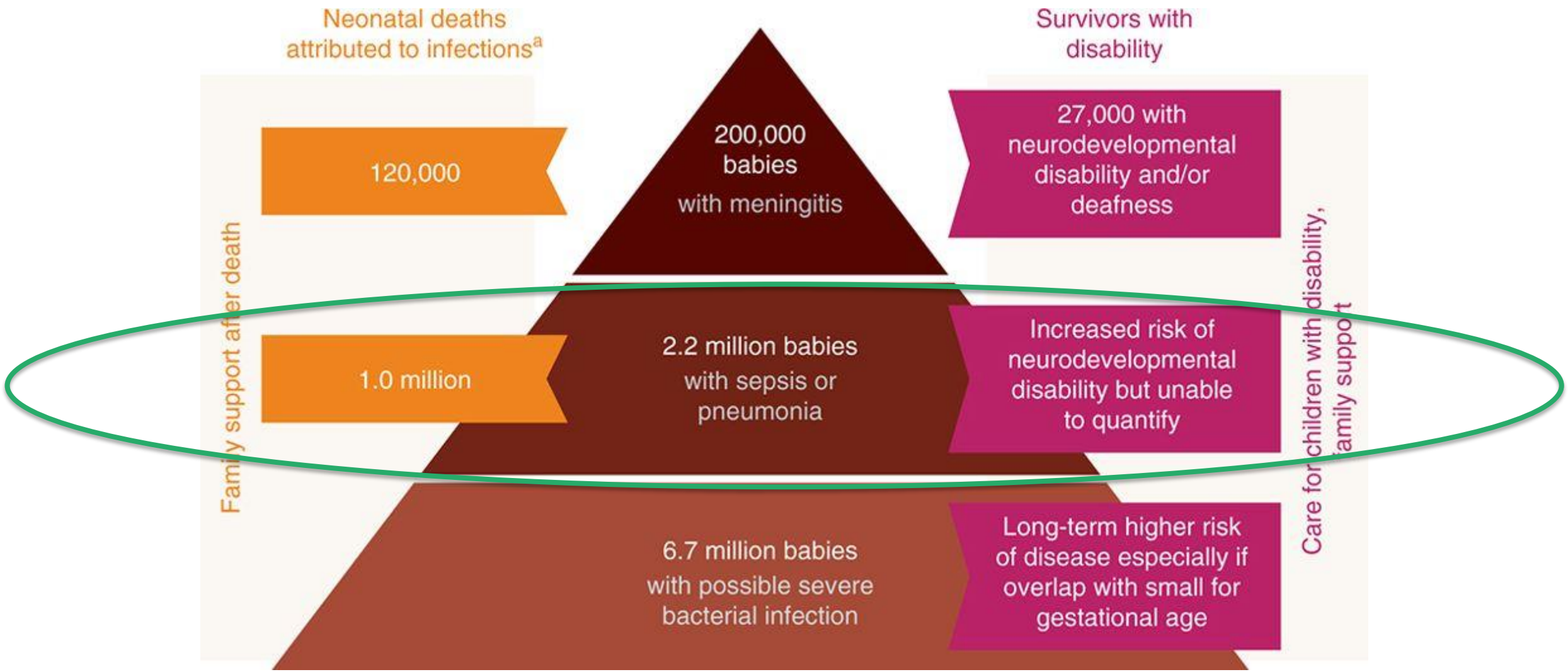
Seale et al Lancet Infectious Diseases 2014

Neonatal sepsis – morbidity



Seale et al Paediatric Research 2013

Neonatal sepsis – compartmental model estimates

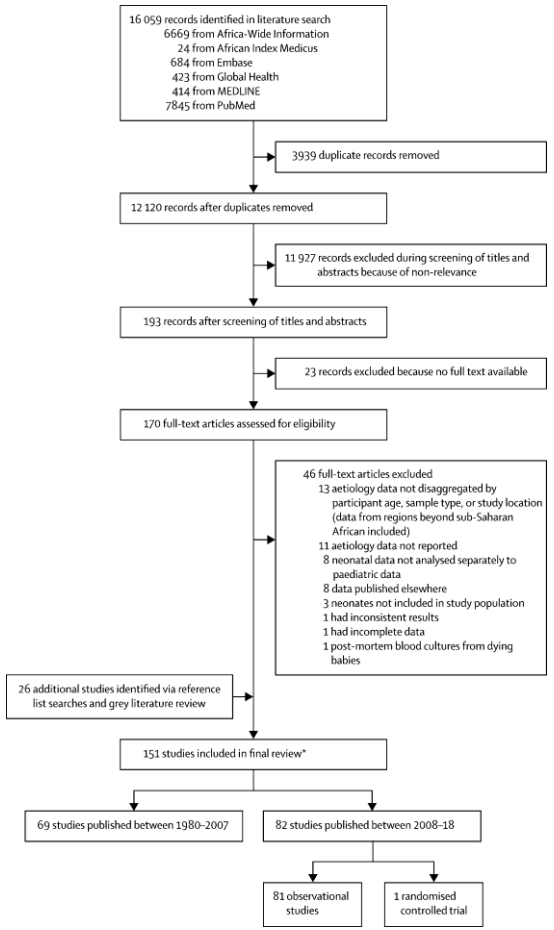


Seale et al Paediatric Research 2013

Neonatal sepsis – population incidence based estimates

3·0 million cases of neonatal sepsis based on these data – none from sub-Saharan Africa

Neonatal sepsis – the aetiology



- 151 studies
- (82 since 2008)
- 84534 neonates
- 26 countries
- Almost all in hospital

- Staphylococcus aureus 25% (21–29)
- Klebsiella spp 21% (16–27)
- Escherichia coli 10% (8–10)

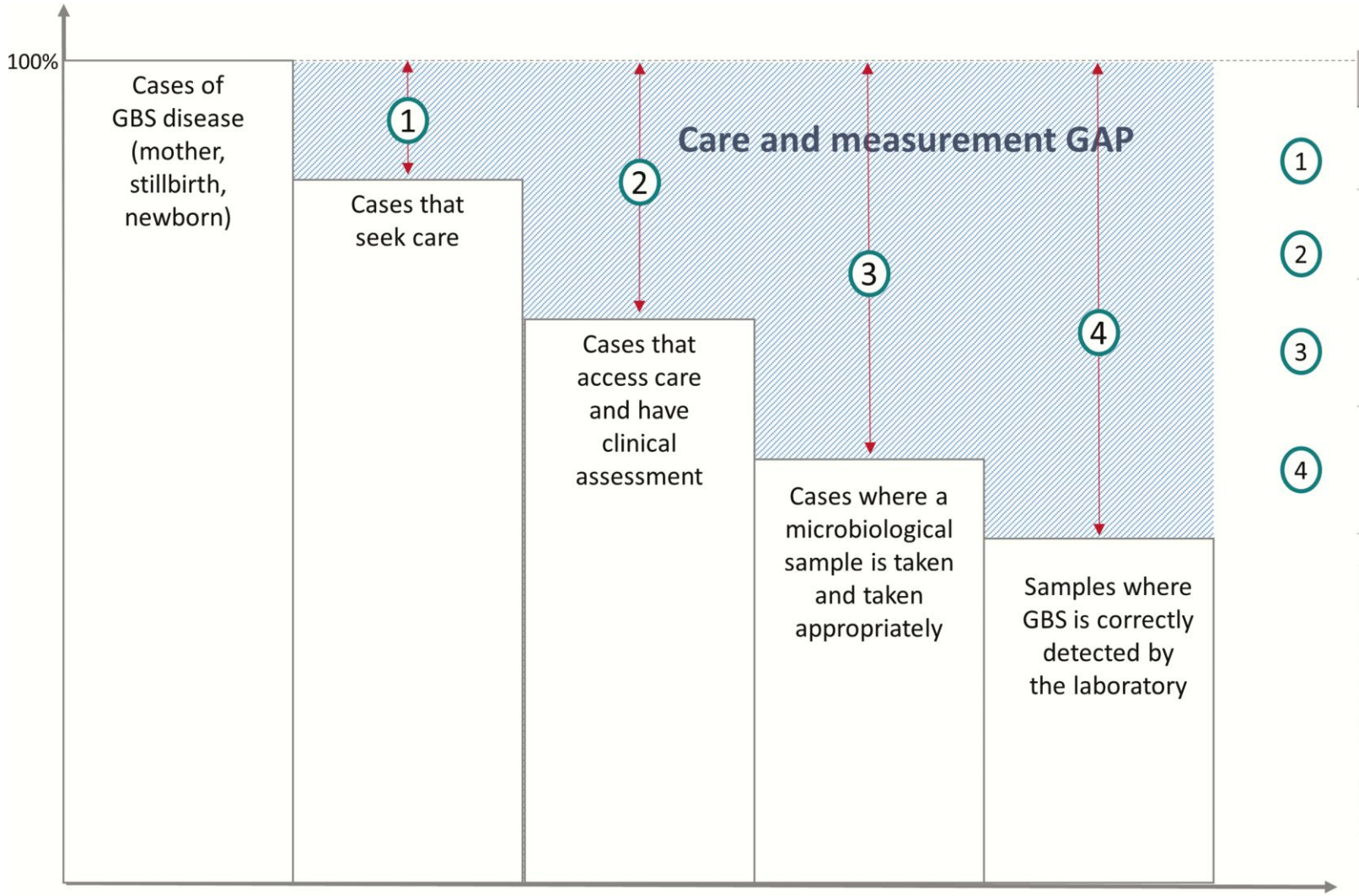
	1980–2007		2008–18	
	Number of isolates	Proportion (95% CI)	Number of isolates	Proportion (95% CI)
Bacteraemia or sepsis				
Gram-positive				
Staphylococcus aureus	912	0·25 (0·19–0·31)	2080	0·25 (0·21–0·29)
Streptococcus pyogenes	75	0·04 (0·02–0·08)	117	0·04 (0·02–0·07)
Group B streptococci	213	0·07 (0·03–0·12)	342	0·06 (0·03–0·10)
Group D streptococci or enterococcus	139	0·05 (0·03–0·07)	449	0·05 (0·04–0·07)
Streptococcus pneumoniae	72	0·04 (0·02–0·08)	114	0·02 (0·01–0·04)
Viridians streptococci	7	0·01 (0–0·05)	71	0·03 (0·01–0·05)
Other *Streptococcus* species	63	0·03 (0·01–0·05)	209	0·05 (0·03–0·07)
Other or unspecified Gram-positives	86	0·04 (0·01–0·08)	155	0·06 (0·03–0·09)
Gram-negative				
Klebsiella species	644	0·15 (0·11–0·20)	1730	0·21 (0·16–0·27)
Escherichia coli	377	0·10 (0·08–0·13)	856	0·10 (0·08–0·13)
Pseudomonas species	146	0·04 (0·02–0·05)	189	0·03 (0·02–0·04)
Enterobacter species	270	0·08 (0·03–0·13)	263	0·04 (0·03–0·05)
Serratia species	0	..	129	0·03 (0·01–0·07)
Proteus species	54	0·02 (0·01–0·04)	126	0·03 (0·02–0·04)
Salmonella species	162	0·03 (0·02–0·05)	176	0·04 (0·02–0·06)
Citrobacter species	61	0·04 (0·01–0·07)	122	0·02 (0·02–0·04)
Haemophilus influenzae	11	0·01 (0–0·02)	10	0·01 (0–0·03)
Neisseria meningitidis	0	..	17	0·03 (0–0·08)
Acinetobacter species	94	0·05 (0·02–0·07)	299	0·05 (0·03–0·07)
Other or unspecified Gram-negatives	522	0·20 (0·14–0·27)	508	0·10 (0·06–0·14)
Other pathogens	14	0·05 (0·02–0·07)	9	0·02 (0·01–0·04)
Meningitis				

Okomo U et al. Lancet Infect Dis 2019

World War II Centre for Naval Analysis - warplanes

Abraham Wald: those that return to base are those that survive
Strengthening needed where the bullet holes aren't seen

Neonatal sepsis – the example of Group B Streptococcus

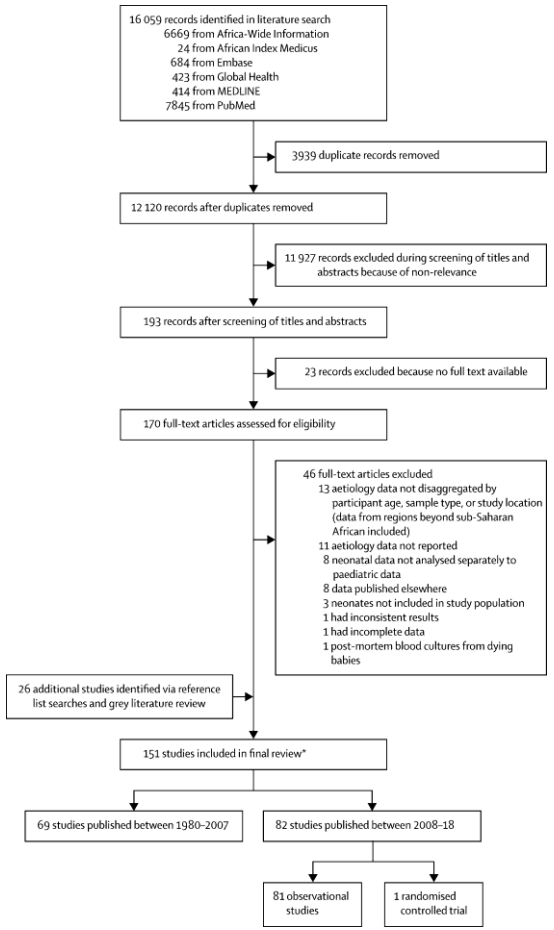


Lower case ascertainment	
1	Lack of access to care
2	Poor quality of care and lack of clinical assessment
3	Failure to take appropriate samples due to lack of protocols, skilled personnel or supplies
4	Poor quality of laboratory methods to support pathogen detection e.g. automated blood cultures

Case ascertainment in low income contexts may be lower at every stage leading to more biased data, often with inconsistent reporting in published literature

Lawn et al CID 2017

Neonatal sepsis – the aetiology



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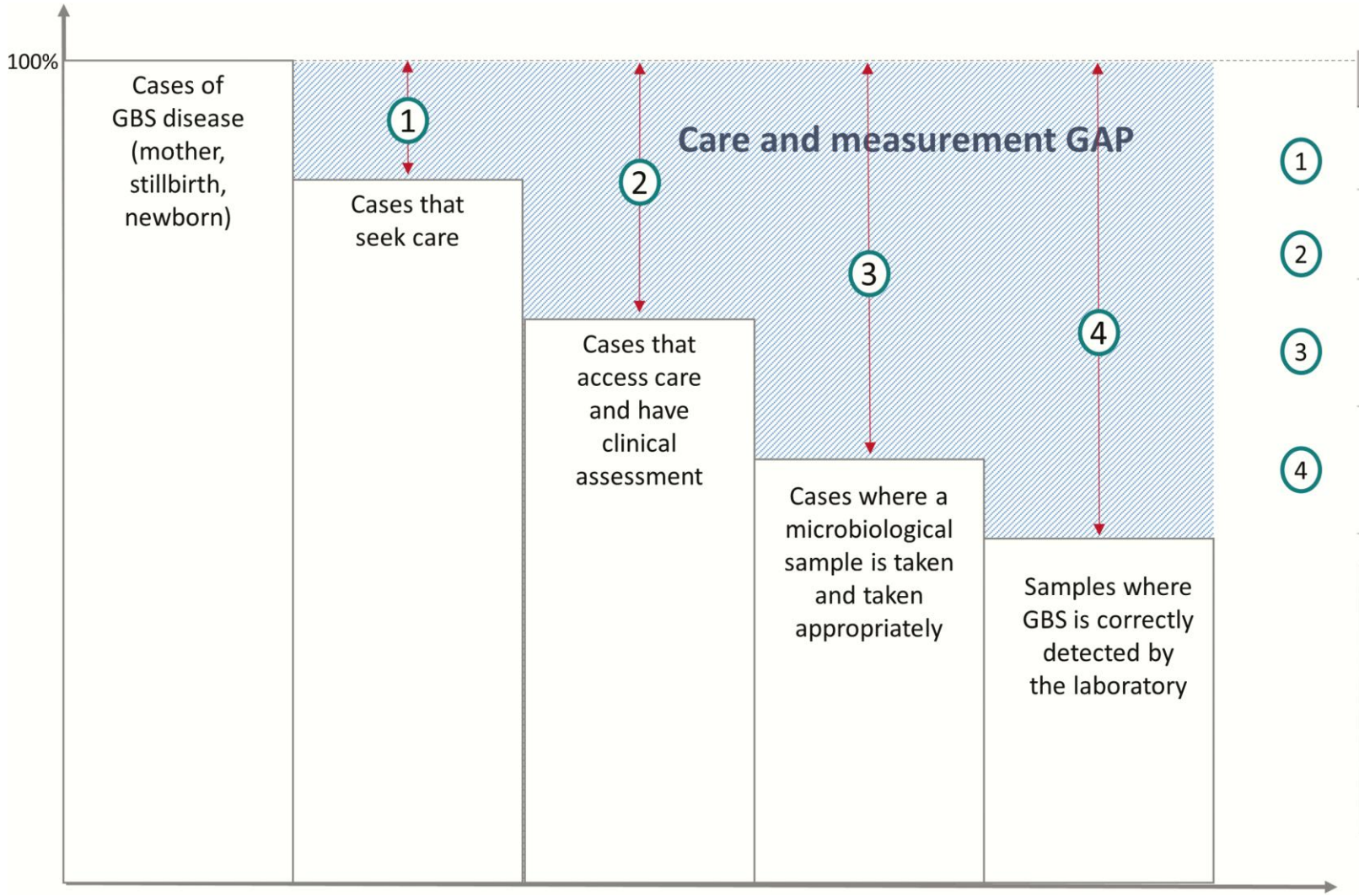
Meningitis				

Late onset pathogens and typically associated with hospital outbreaks

Neonatal sepsis – what are we missing



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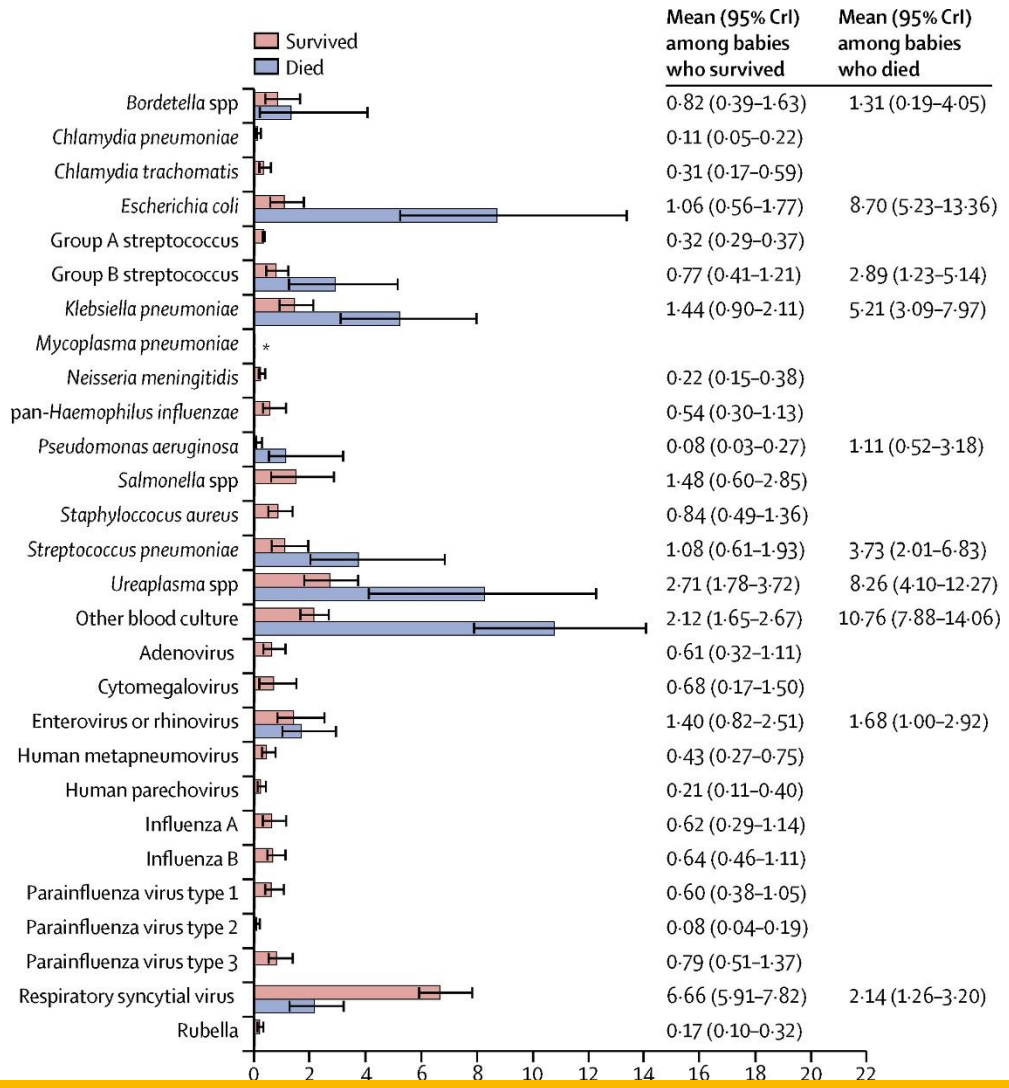
Early-onset, high mortality, difficult to sample, difficult to detect in the lab

Neonatal sepsis – what does this mean?

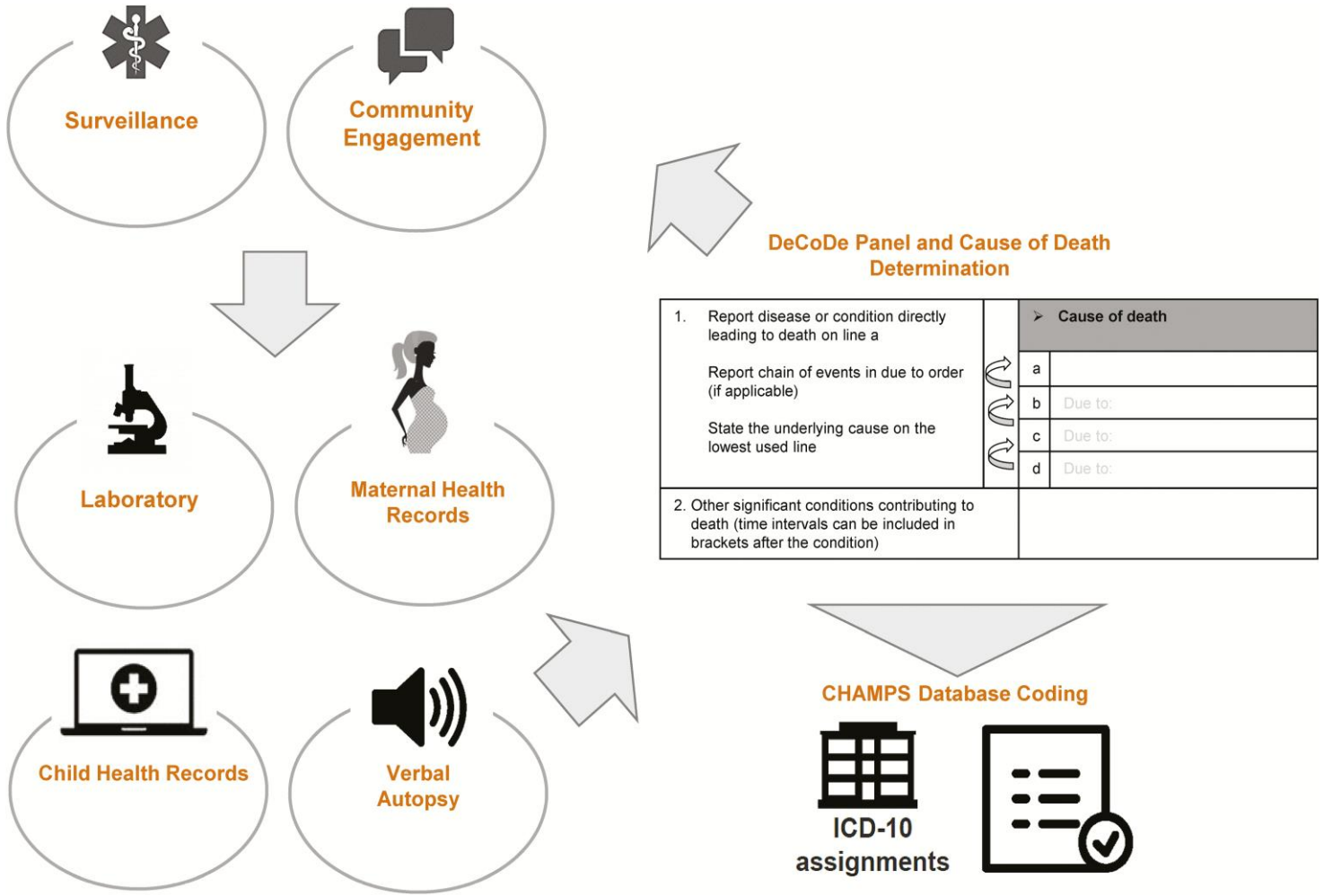
ANISA:
A robust, large, community based investigation of neonatal sepsis in South Asia



	Mean (95% CrI) among babies who survived	Mean (95% CrI) among babies who died
Bordetella spp	0·82 (0·39–1·63)	1·31 (0·19–4·05)
Chlamydia pneumoniae	0·11 (0·05–0·22)	
Chlamydia trachomatis	0·31 (0·17–0·59)	
Escherichia coli	1·06 (0·56–1·77)	8·70 (5·23–13·36)
Group A streptococcus	0·32 (0·29–0·37)	
Group B streptococcus	0·77 (0·41–1·21)	2·89 (1·23–5·14)
Klebsiella pneumoniae	1·44 (0·90–2·11)	5·21 (3·09–7·97)
Mycoplasma pneumoniae	*	
Neisseria meningitidis	0·22 (0·15–0·38)	
pan-*Haemophilus influenzae*	0·54 (0·30–1·13)	
Pseudomonas aeruginosa	0·08 (0·03–0·27)	1·11 (0·52–3·18)
Salmonella spp	1·48 (0·60–2·85)	
Staphyloccocus aureus	0·84 (0·49–1·36)	
Streptococcus pneumoniae	1·08 (0·61–1·93)	3·73 (2·01–6·83)
Ureaplasma spp	2·71 (1·78–3·72)	8·26 (4·10–12·27)
Other blood culture	2·12 (1·65–2·67)	10·76 (7·88–14·06)
Adenovirus	0·61 (0·32–1·11)	
Cytomegalovirus	0·68 (0·17–1·50)	
Enterovirus or rhinovirus	1·40 (0·82–2·51)	1·68 (1·00–2·92)
Human metapneumovirus	0·43 (0·27–0·75)	
Human parechovirus	0·21 (0·11–0·40)	
Influenza A	0·62 (0·29–1·14)	
Influenza B	0·64 (0·46–1·11)	
Parainfluenza virus type 1	0·60 (0·38–1·05)	
Parainfluenza virus type 2	0·08 (0·04–0·19)	
Parainfluenza virus type 3	0·79 (0·51–1·37)	
Respiratory syncytial virus	6·66 (5·91–7·82)	2·14 (1·26–3·20)
Rubella	0·17 (0·10–0·32)	

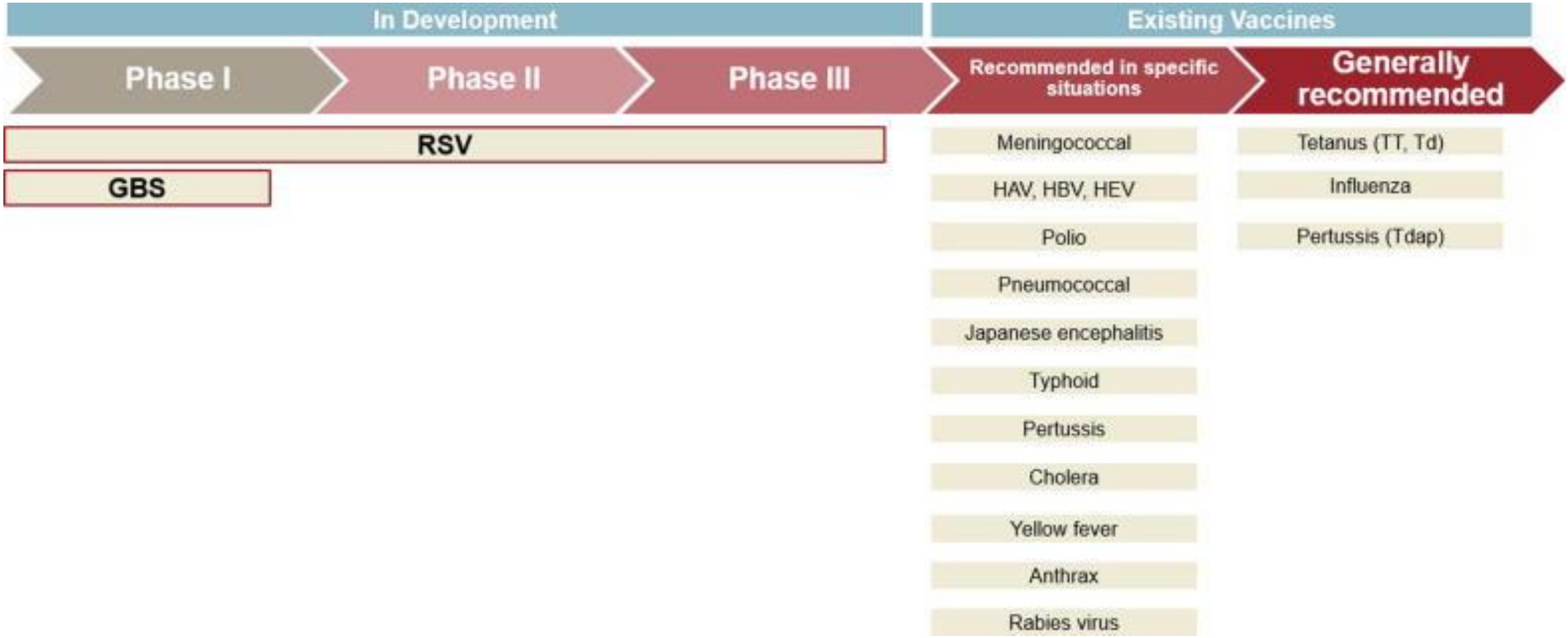
Even the most robust observational study will be limited by survivor bias

Neonatal sepsis – we need to look at alternatives



Study design – include those that don't survive

Neonatal sepsis – we need to look at alternatives



Study design – an intervention to prevent the deaths

World War II Centre for Naval Analysis - warplanes

The analysis informed design of planes through the Vietnam War and is considered to have substantially reduced casualties.

Thank you

All those whose work is included here.

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