A Bayesian approach for estimating typhoid fever incidence from passive surveillance data

11th International Conference on Typhoid & Other Invasive Salmonelloses
March 26-28, 2018

Maile T. Phillips, M.S.
Yale School of Public Health
Advisor: Virginia E. Pitzer, ScD

The need for adjusted incidence estimates

- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence

The need for adjusted incidence estimates

- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence
- Facility-based laboratory-confirmed case estimates of typhoid are likely lower than actual number

The need for adjusted incidence estimates

- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence
- Facility-based laboratory-confirmed case estimates of typhoid are likely lower than actual number
  - ➢ Only a fraction of individuals with typhoid **seek care** at a healthcare facility

The need for adjusted incidence estimates

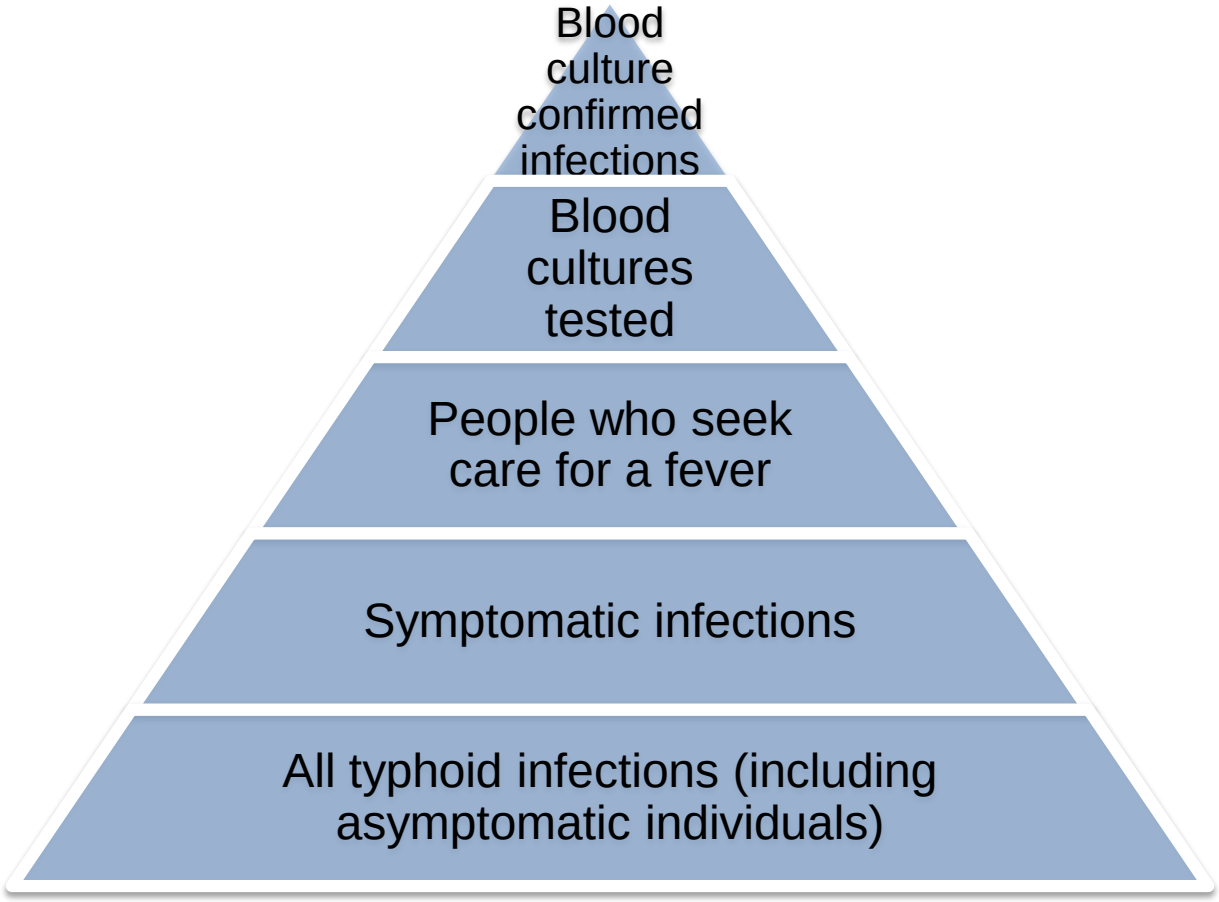
- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence
- Facility-based laboratory-confirmed case estimates of typhoid are likely lower than actual number
  - Only a fraction of individuals with typhoid **seek care** at a healthcare facility
  - Only a fraction of individuals with typhoid who seek care **receive a blood culture diagnostic test**

The need for adjusted incidence estimates

- Decision-making for typhoid control and prevention is based on crude estimates of typhoid incidence
- Facility-based laboratory-confirmed case estimates of typhoid are likely lower than actual number
  - Only a fraction of individuals with typhoid **seek care** at a healthcare facility
  - Only a fraction of individuals with typhoid who seek care **receive a blood culture diagnostic test**
  - Only a fraction of individuals with typhoid who receive a blood culture **test positive for typhoid**

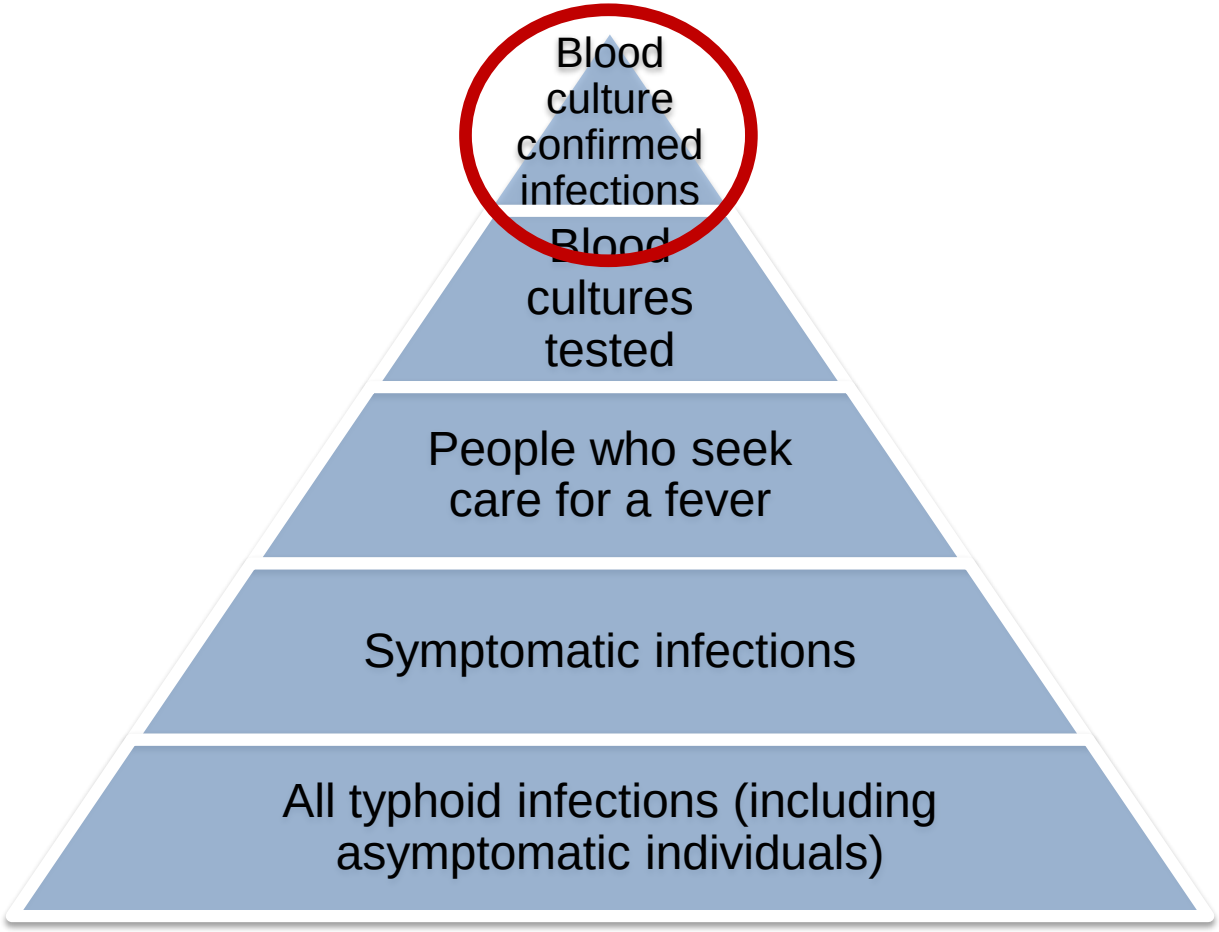
Typhoid Reporting Pyramid

Infections reported are only a fraction of the true number



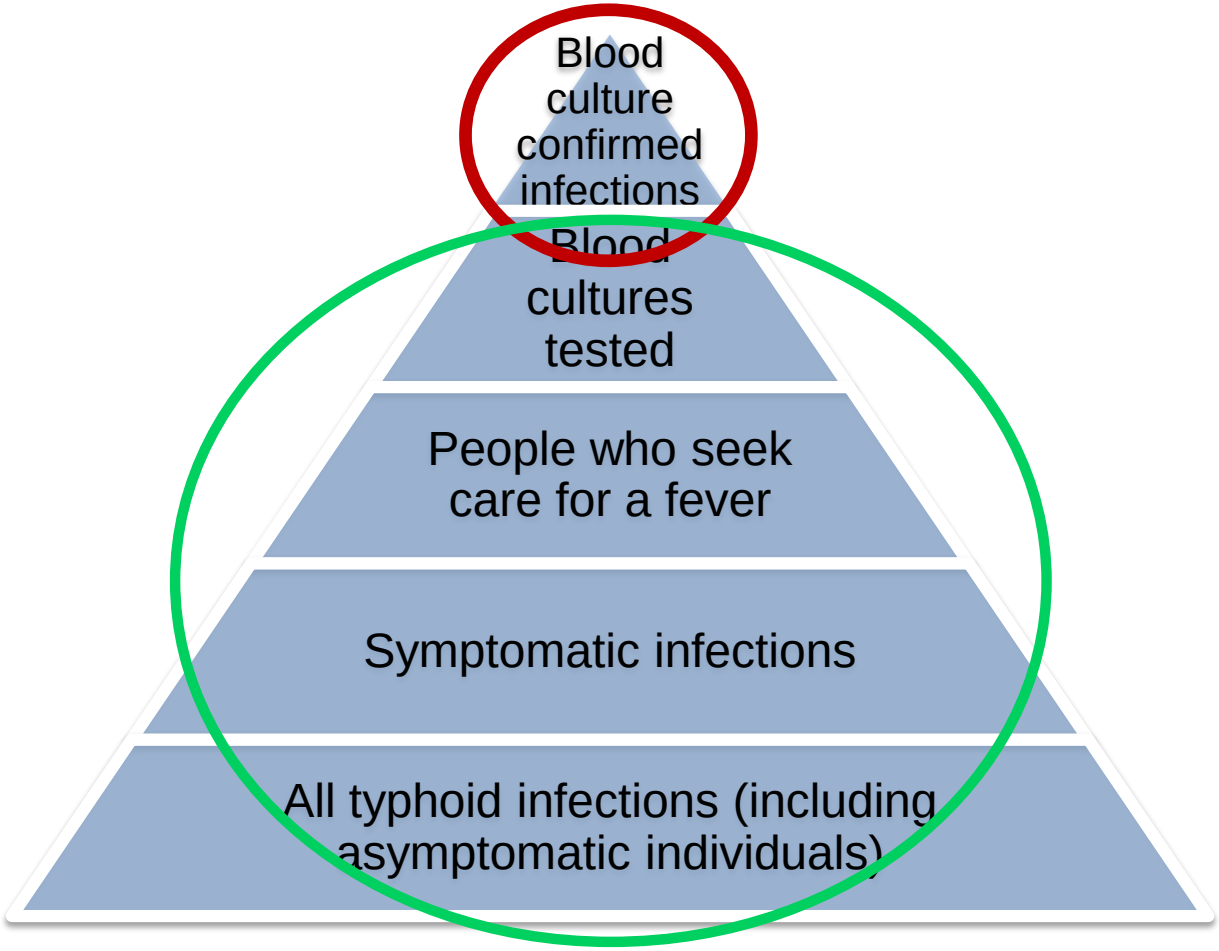
Typhoid Reporting Pyramid

Infections reported are only a fraction of the true number

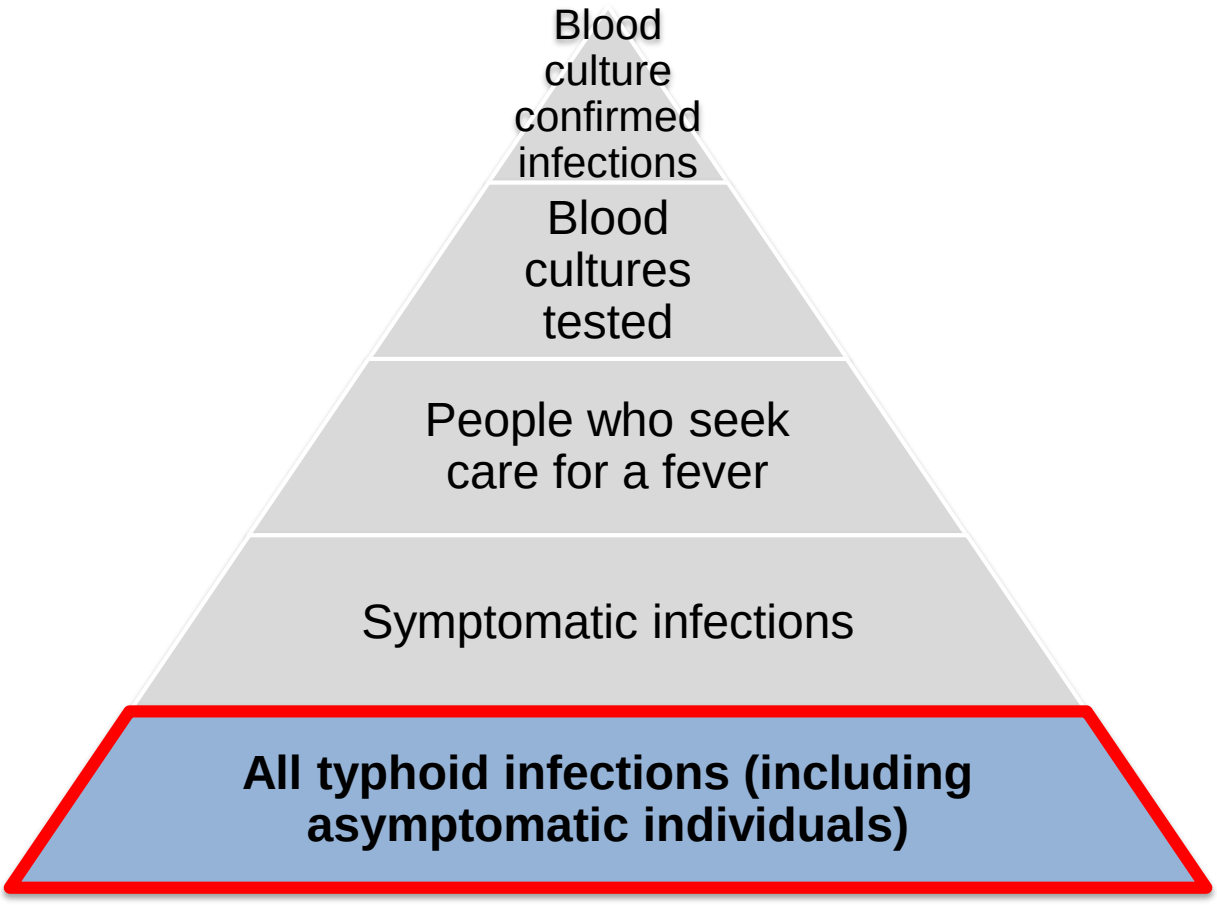


Typhoid Reporting Pyramid

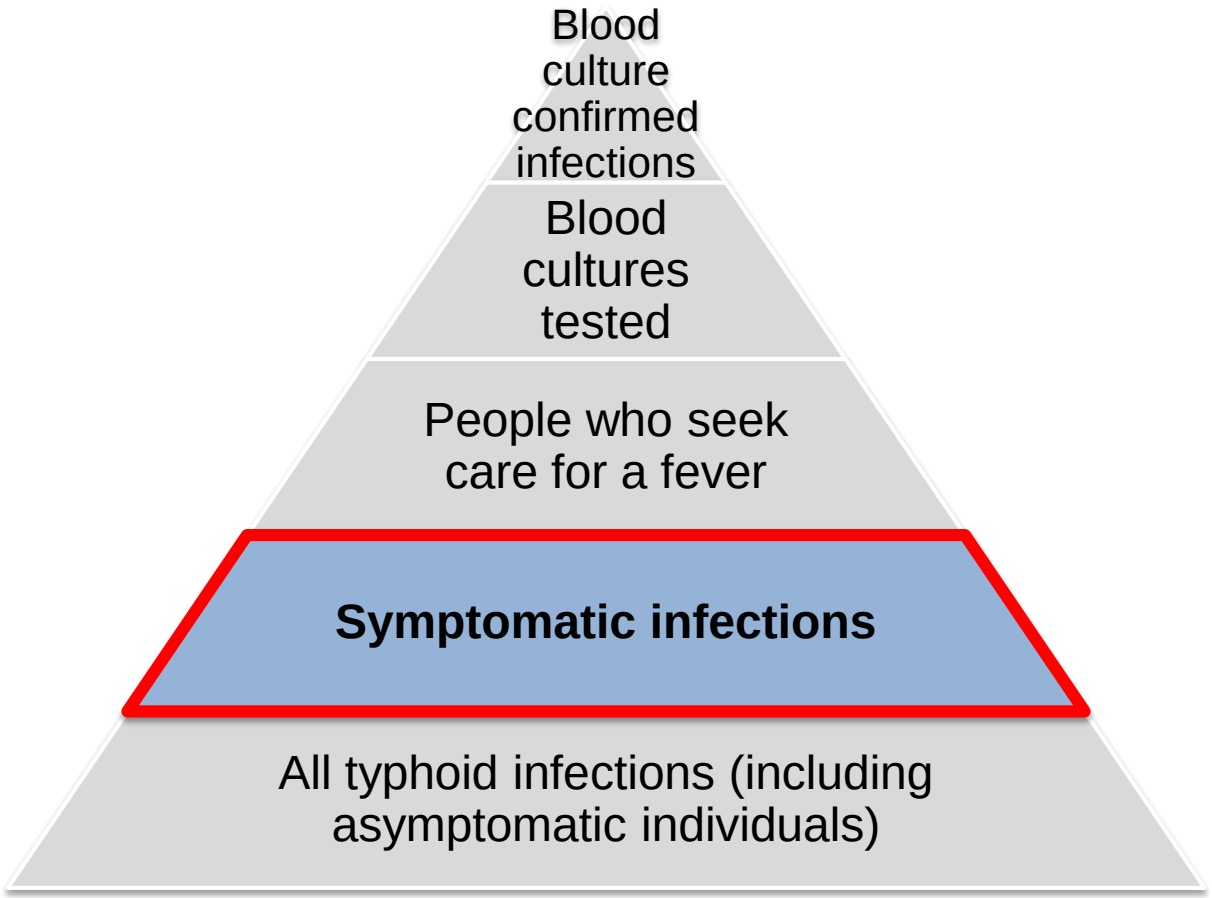
Infections reported are only a fraction of the true number



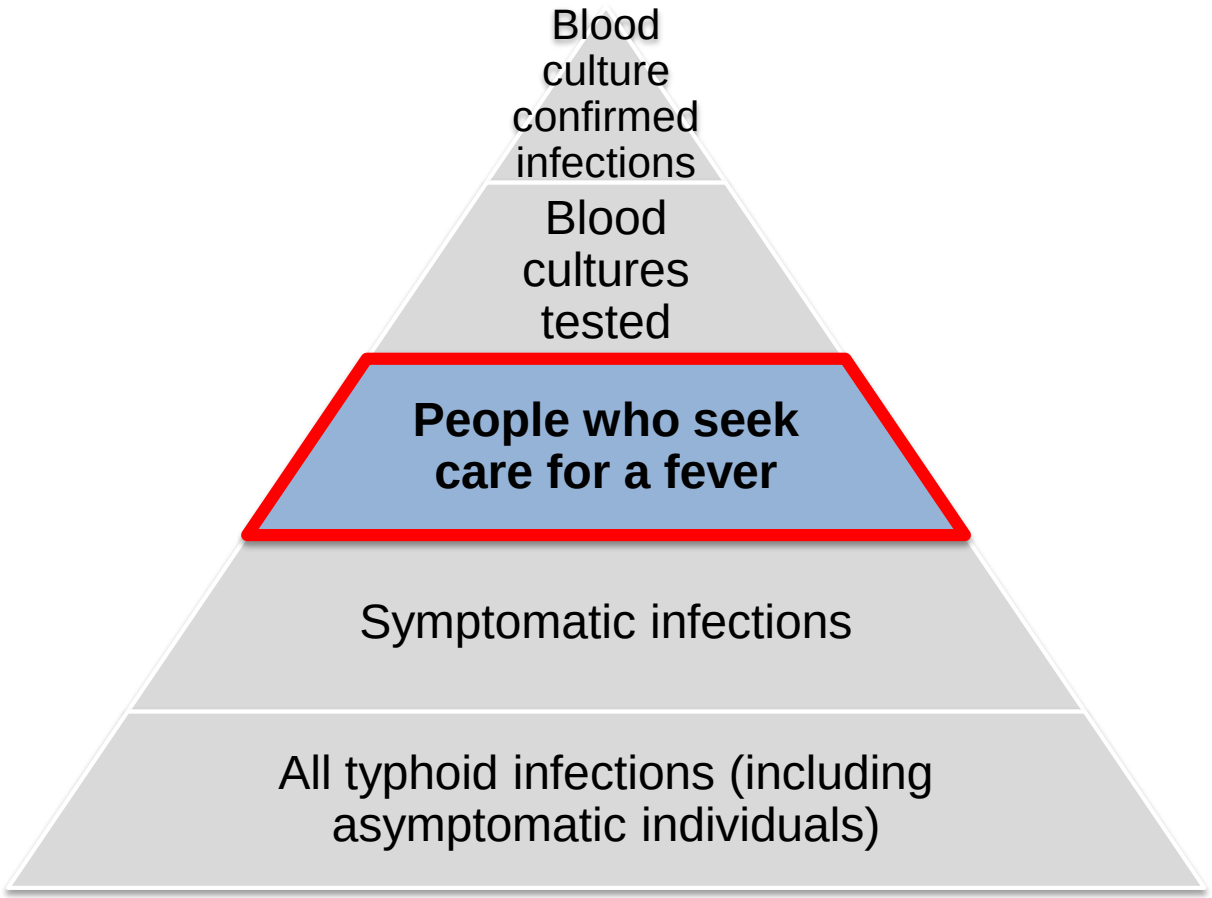
Typhoid Reporting Pyramid



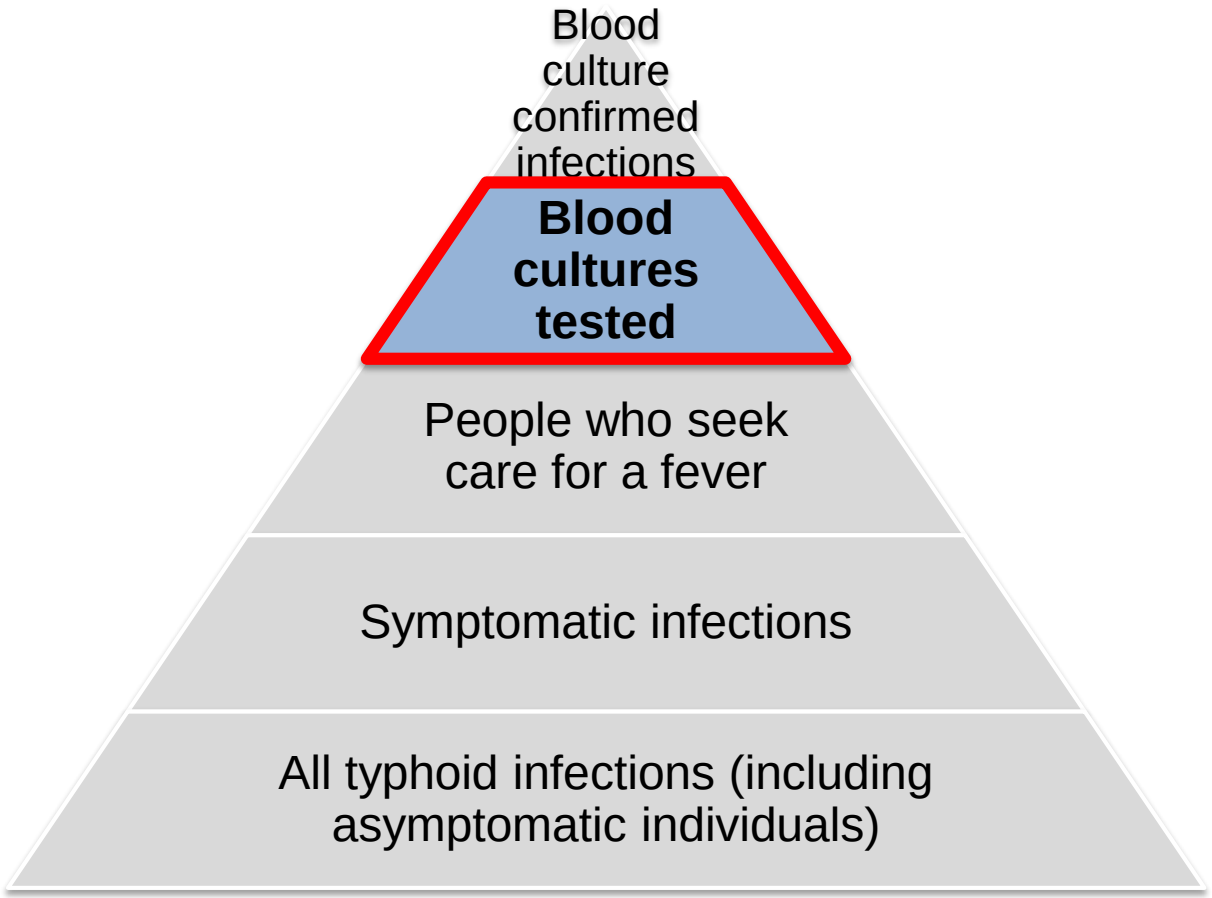
Typhoid Reporting Pyramid



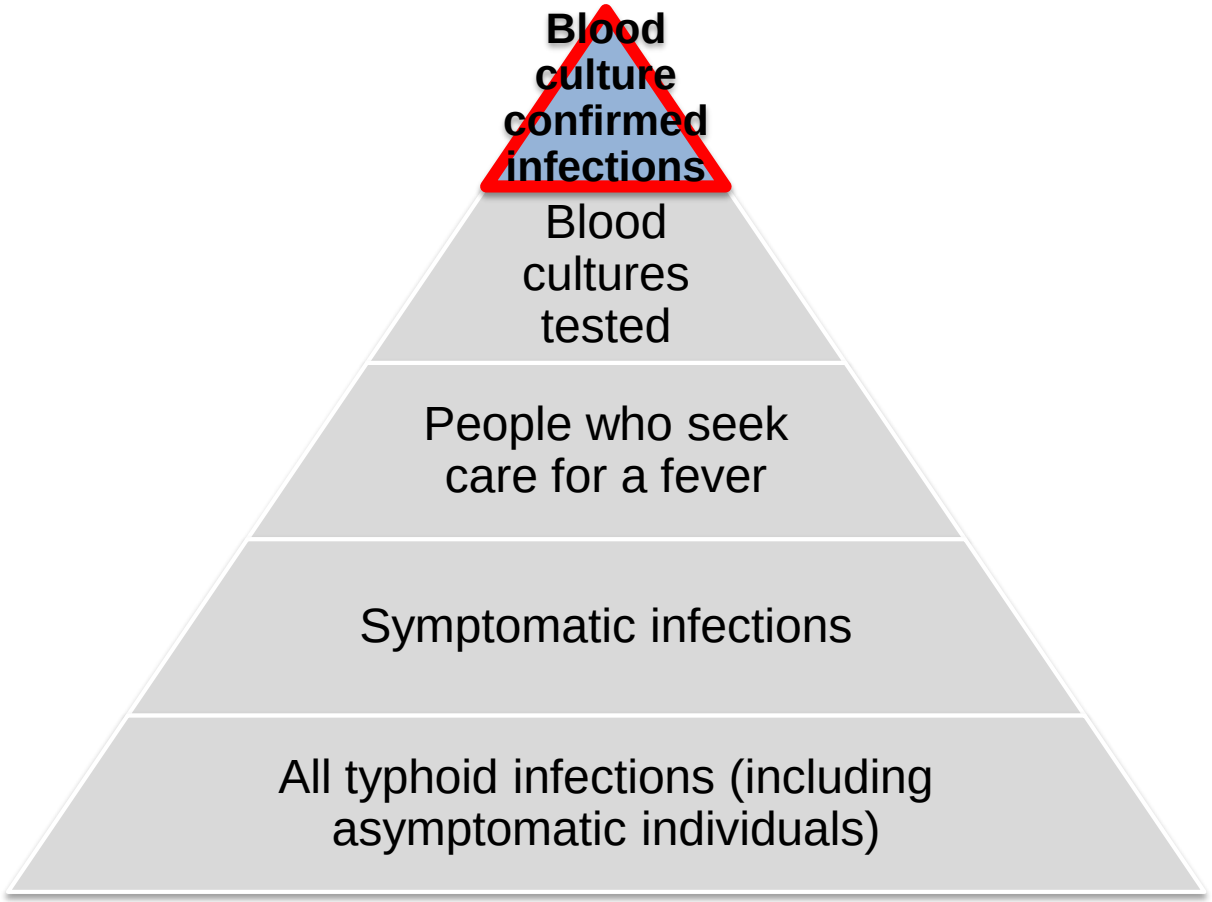
Typhoid Reporting Pyramid



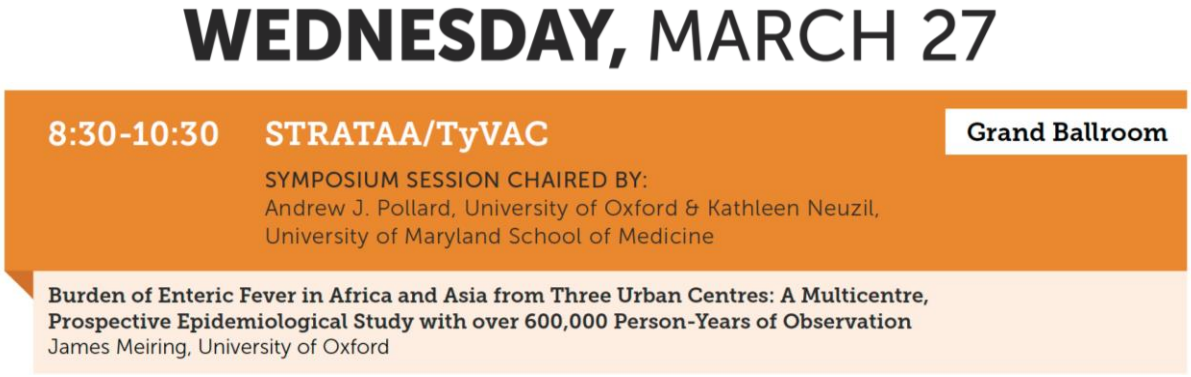
Typhoid Reporting Pyramid



Typhoid Reporting Pyramid



STRAtegic **T**yphoid alliance across **A**frica and **A**sia (STRATAA)



WEDNESDAY, MARCH 27

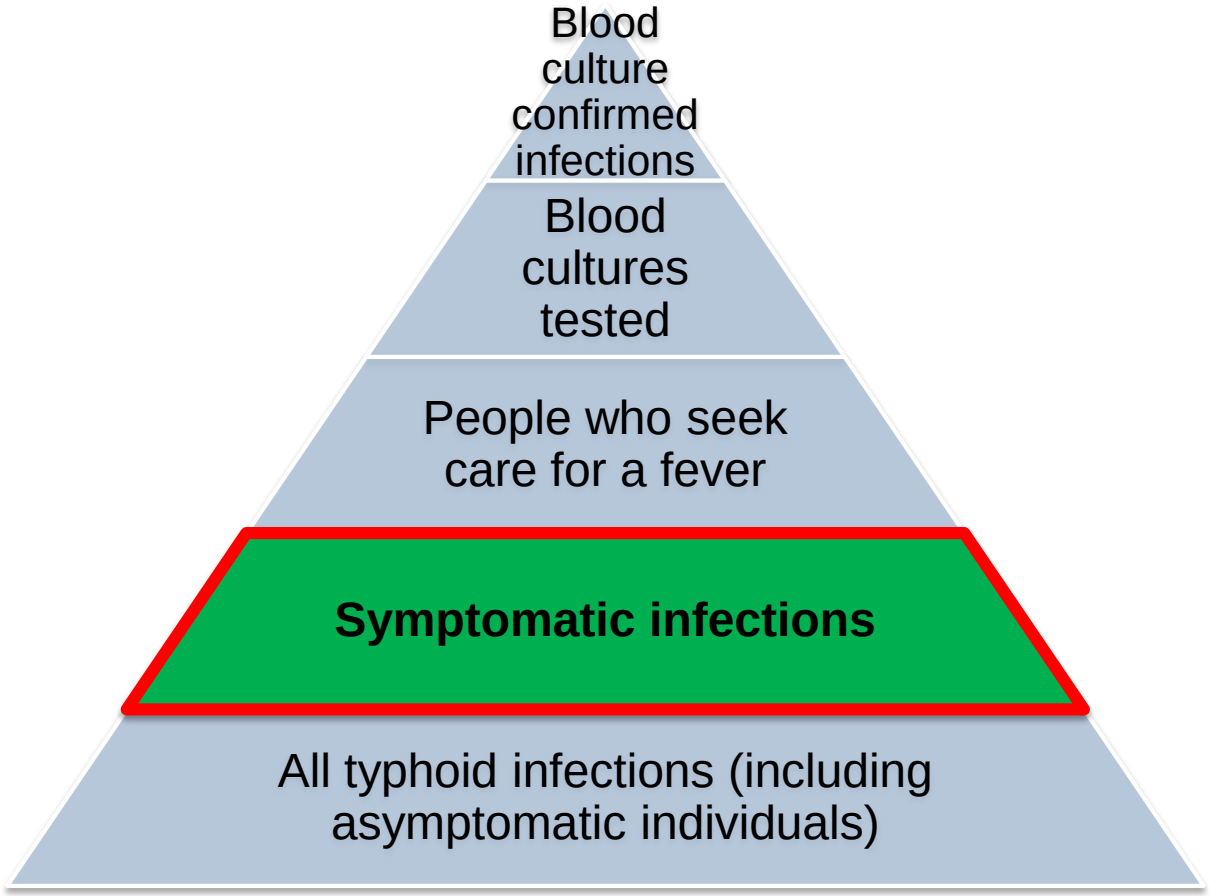
8:30-10:30 **STRATAA/TyVAC** — Grand Ballroom

SYMPOSIUM SESSION CHAIRED BY:
Andrew J. Pollard, University of Oxford & Kathleen Neuzil, University of Maryland School of Medicine

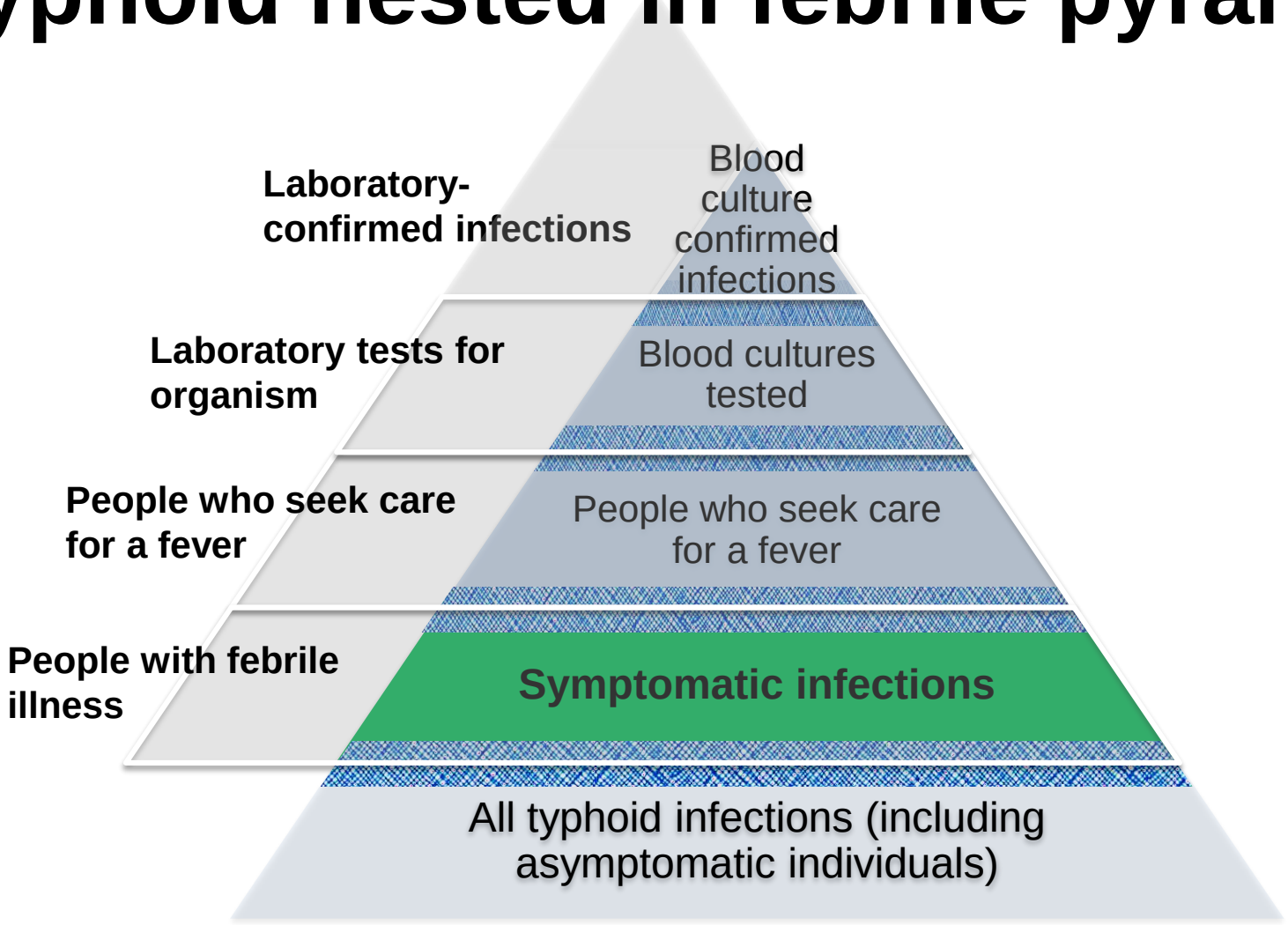
Burden of Enteric Fever in Africa and Asia from Three Urban Centres: A Multicentre, Prospective Epidemiological Study with over 600,000 Person-Years of Observation
James Meiring, University of Oxford

- A 2-year prospective epidemiological study
- 3 sites:
  - Dhaka, Bangladesh
  - Patan, Nepal
  - Blantyre, Malawi
- Passive surveillance, serosurveillance, and healthcare utilisation surveys nested within demographic census population

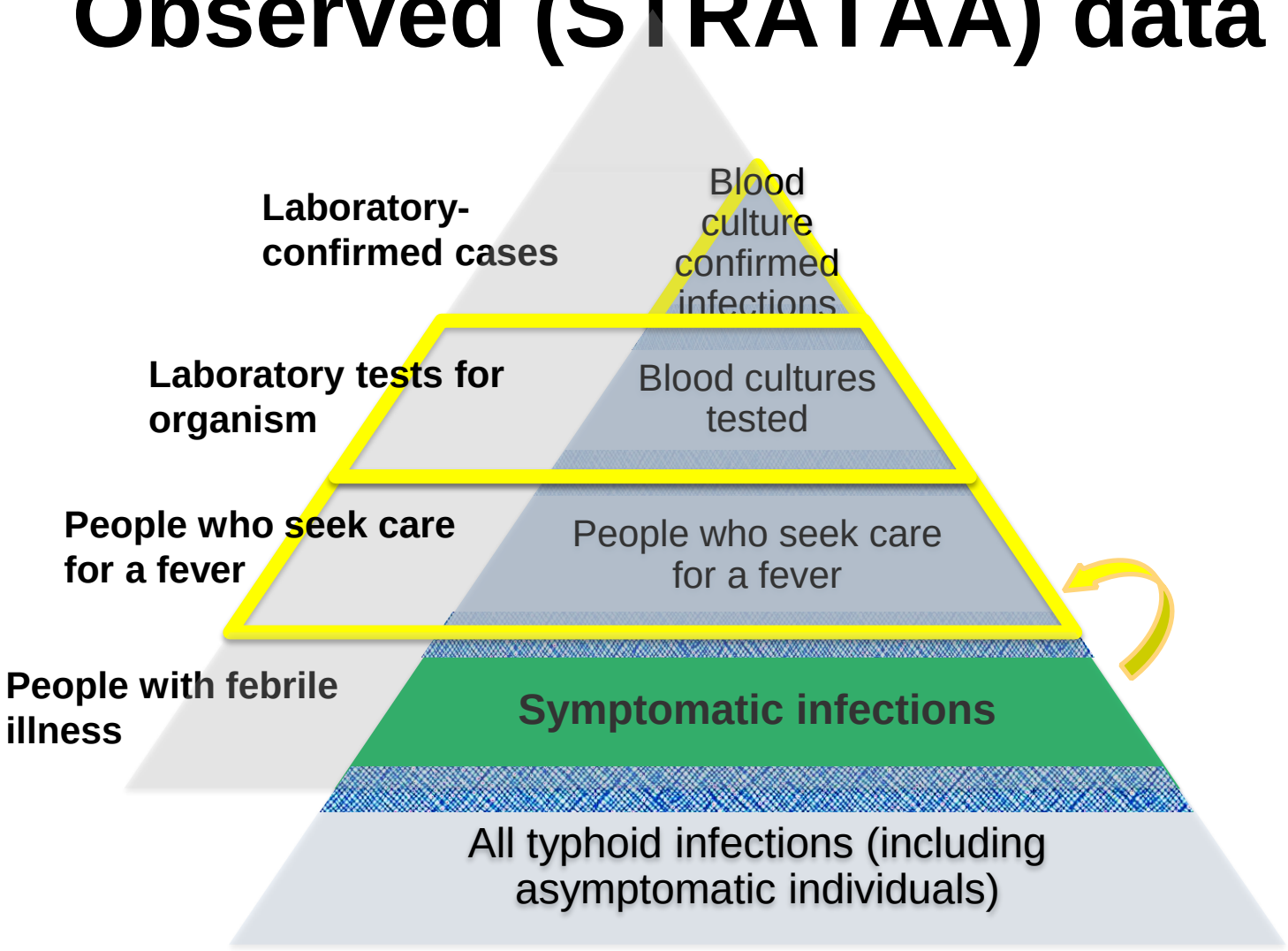
Estimating symptomatic typhoid infection incidence



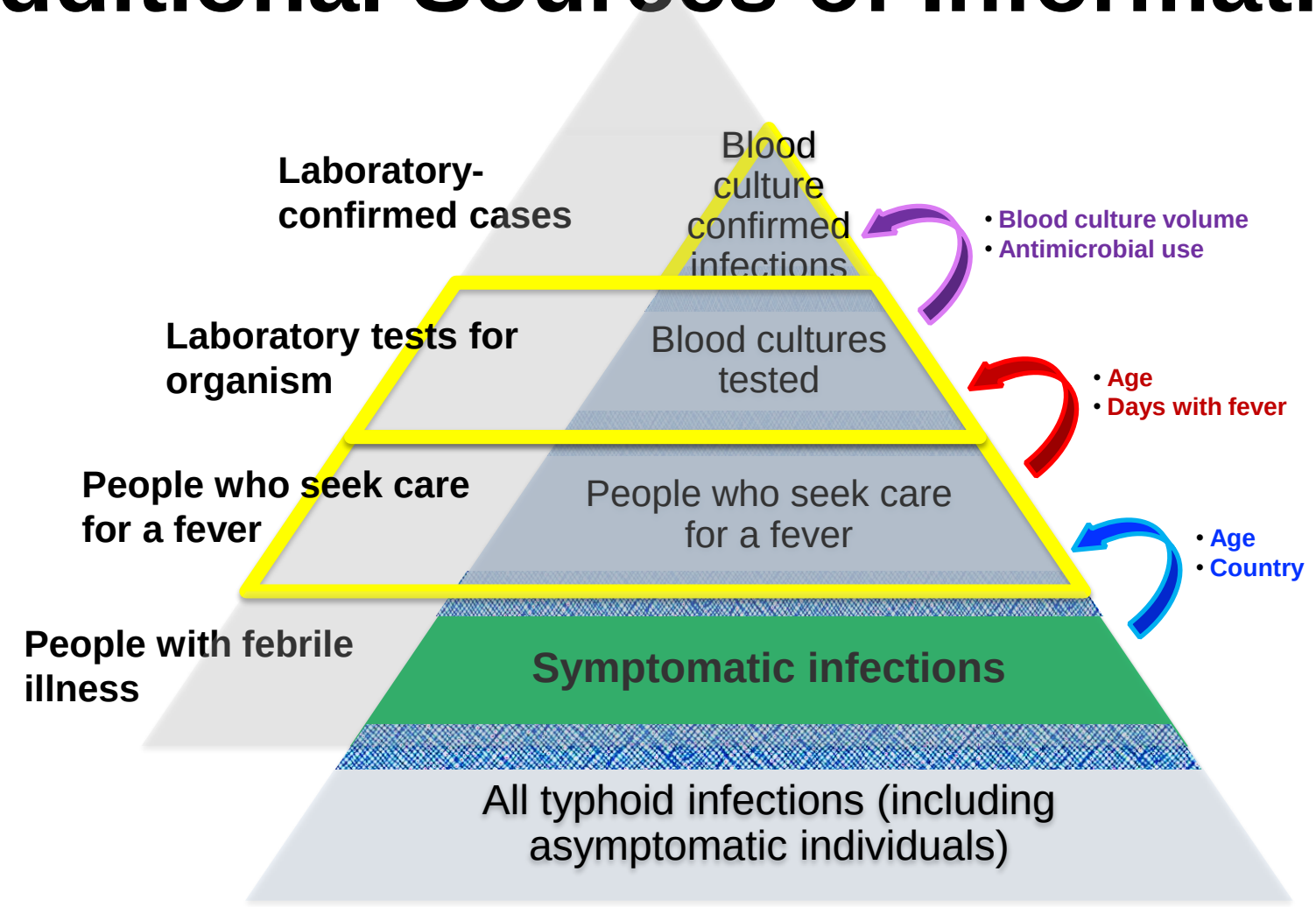
Typhoid nested in febrile pyramid



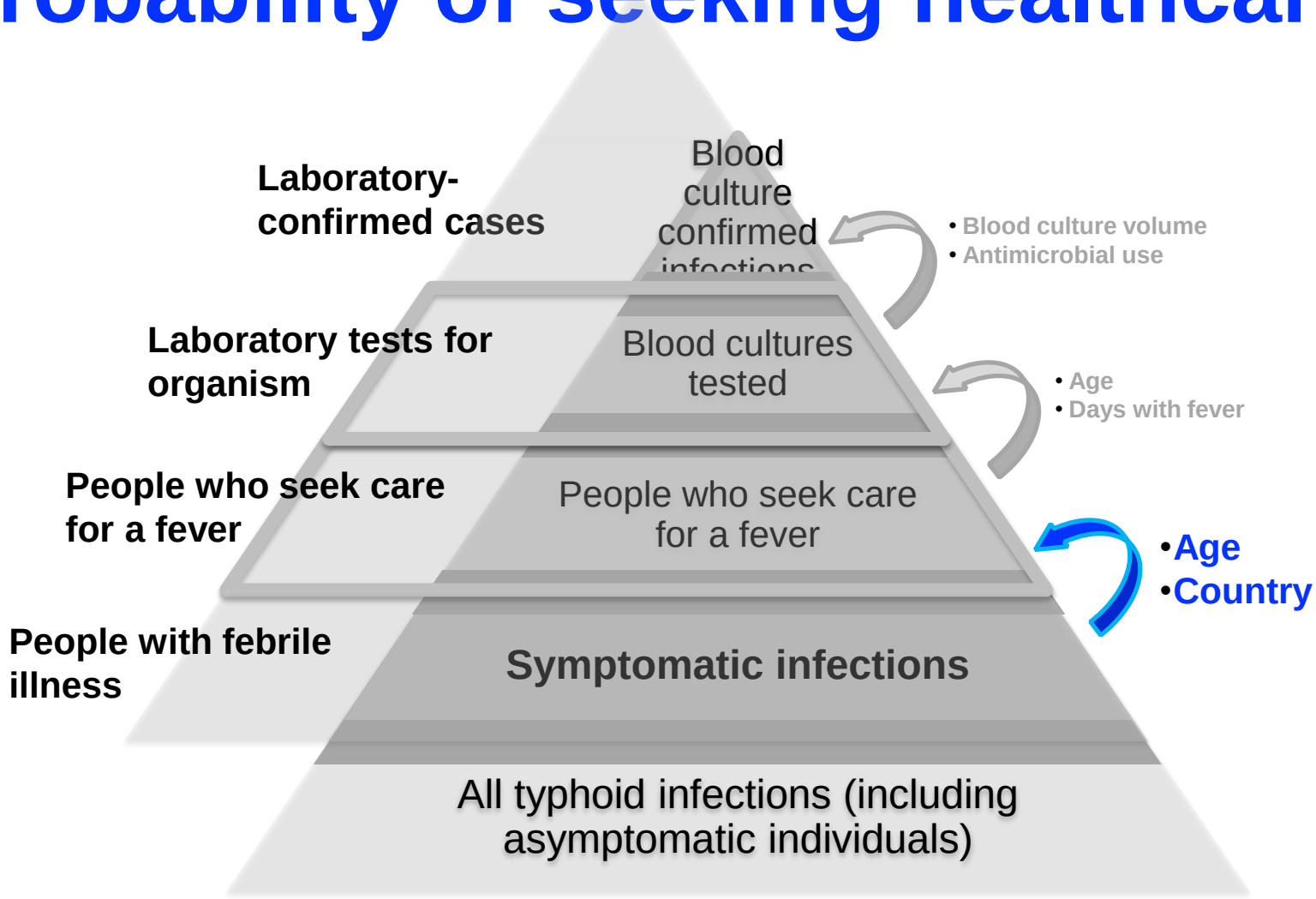
Observed (STRATAA) data



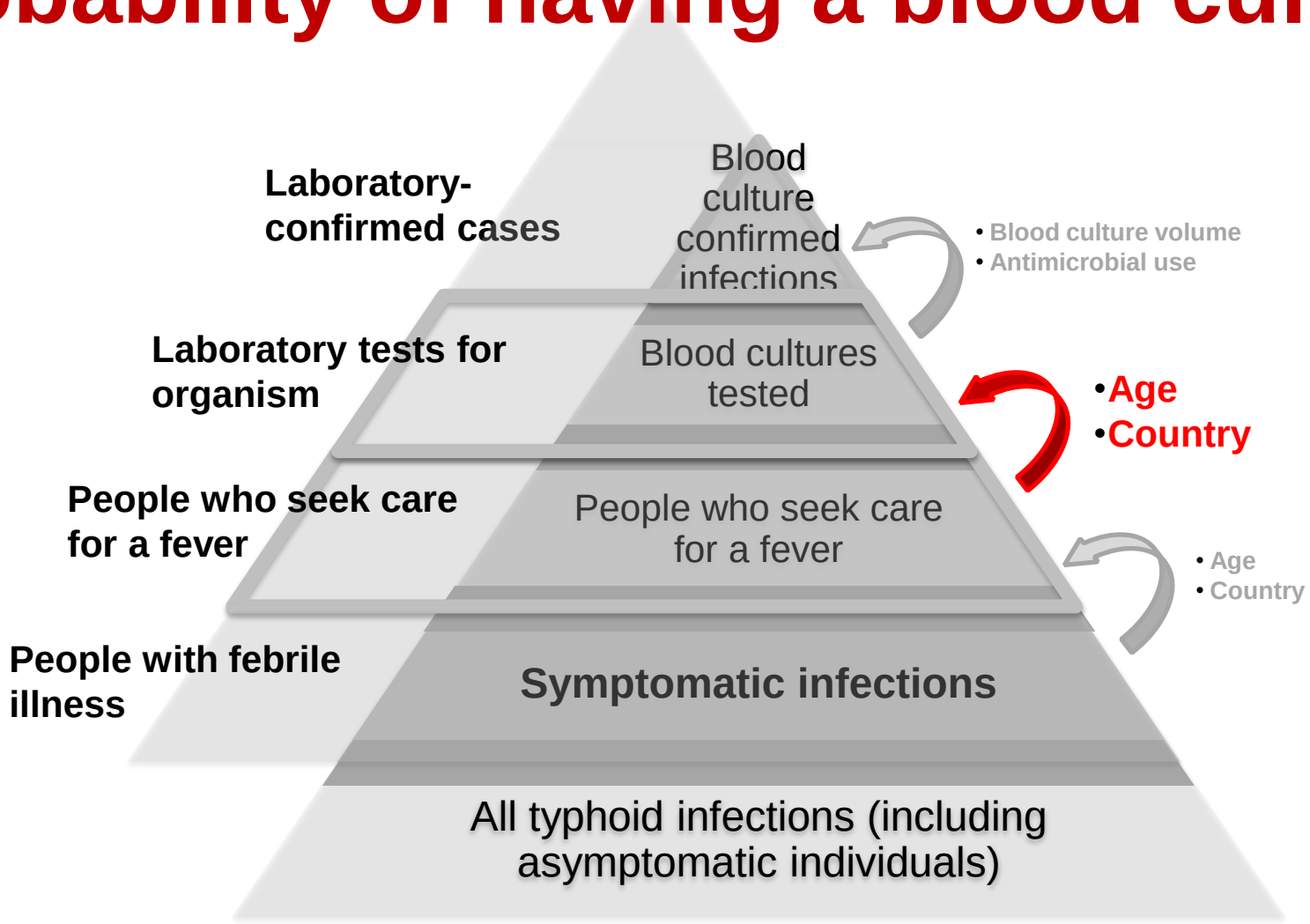
Additional Sources of Information



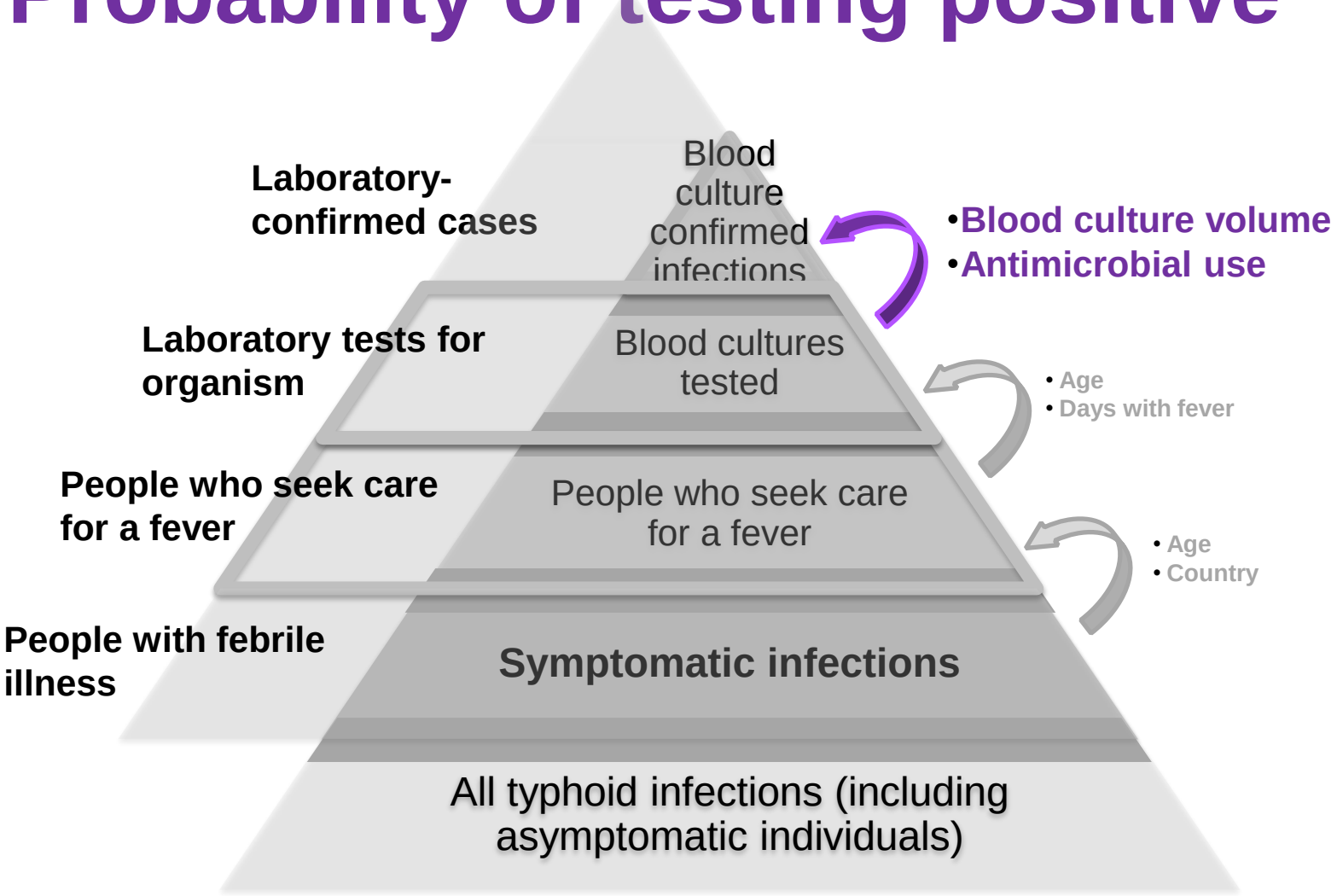
Probability of seeking healthcare



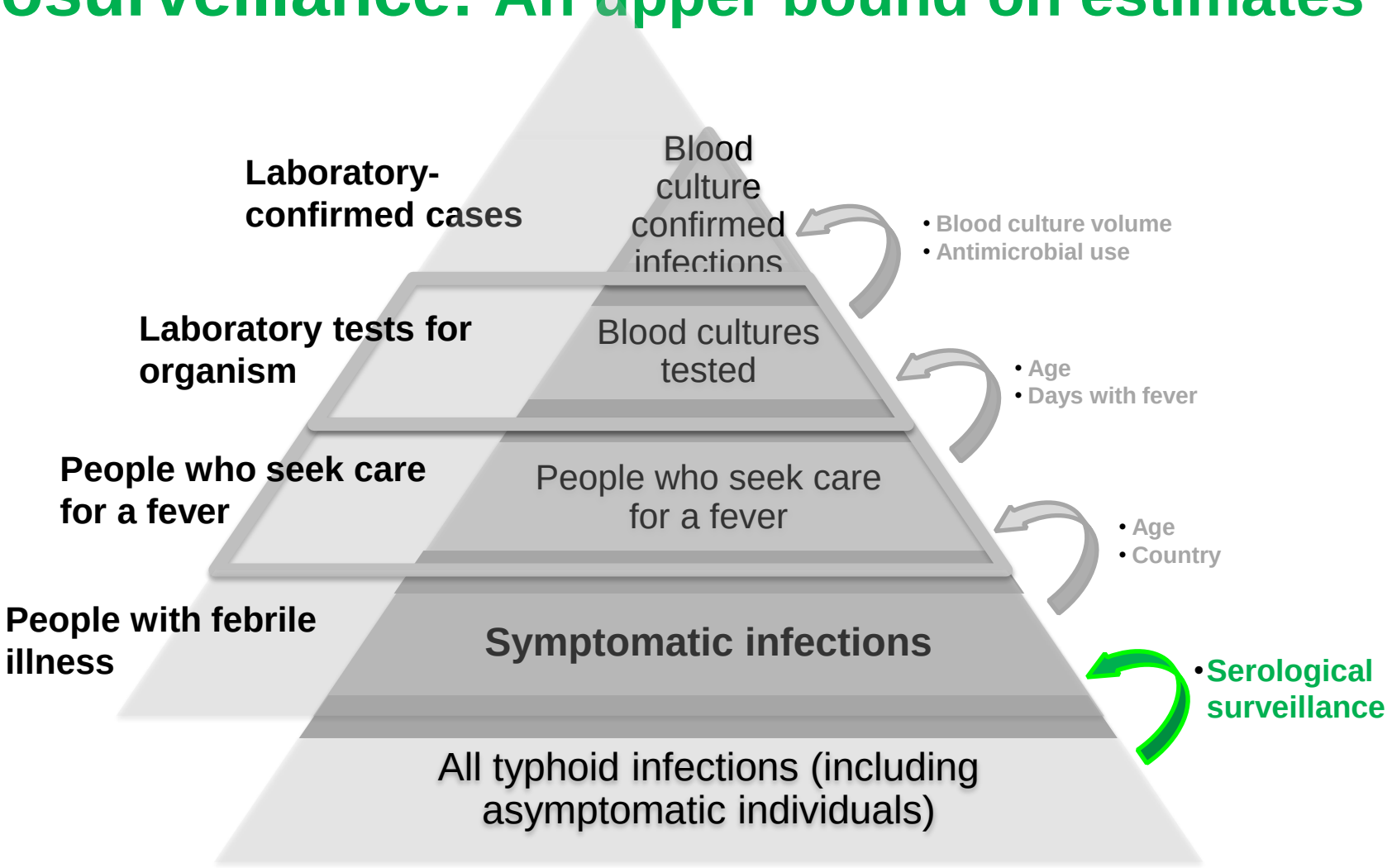
Probability of having a blood culture



Probability of testing positive



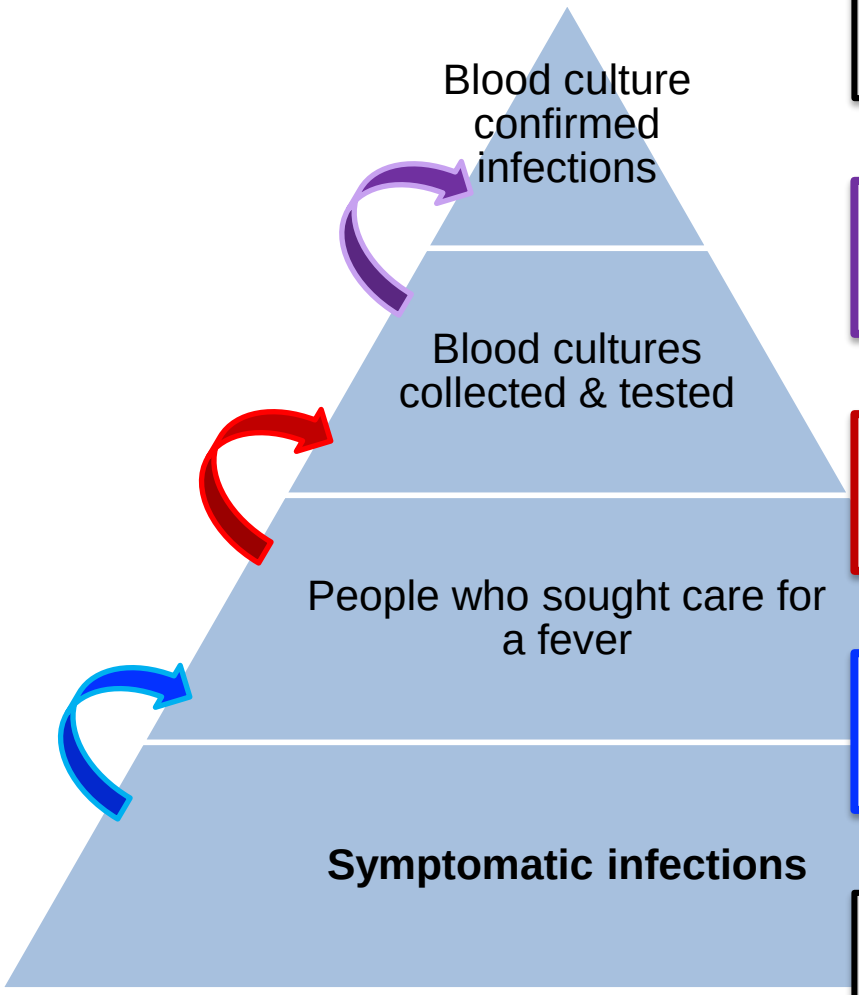
Serosurveillance: An upper bound on estimates



Bayesian inference

- Combines past experience with new data to form the current state of knowledge
- Quantifies uncertainty about estimates

Bayesian Framework



Blood culture (BC) positive infections
STRATAA passive surveillance

Probability of having positive BC result
STRATAA passive surveillance
Blood culture sensitivity by volume[1]

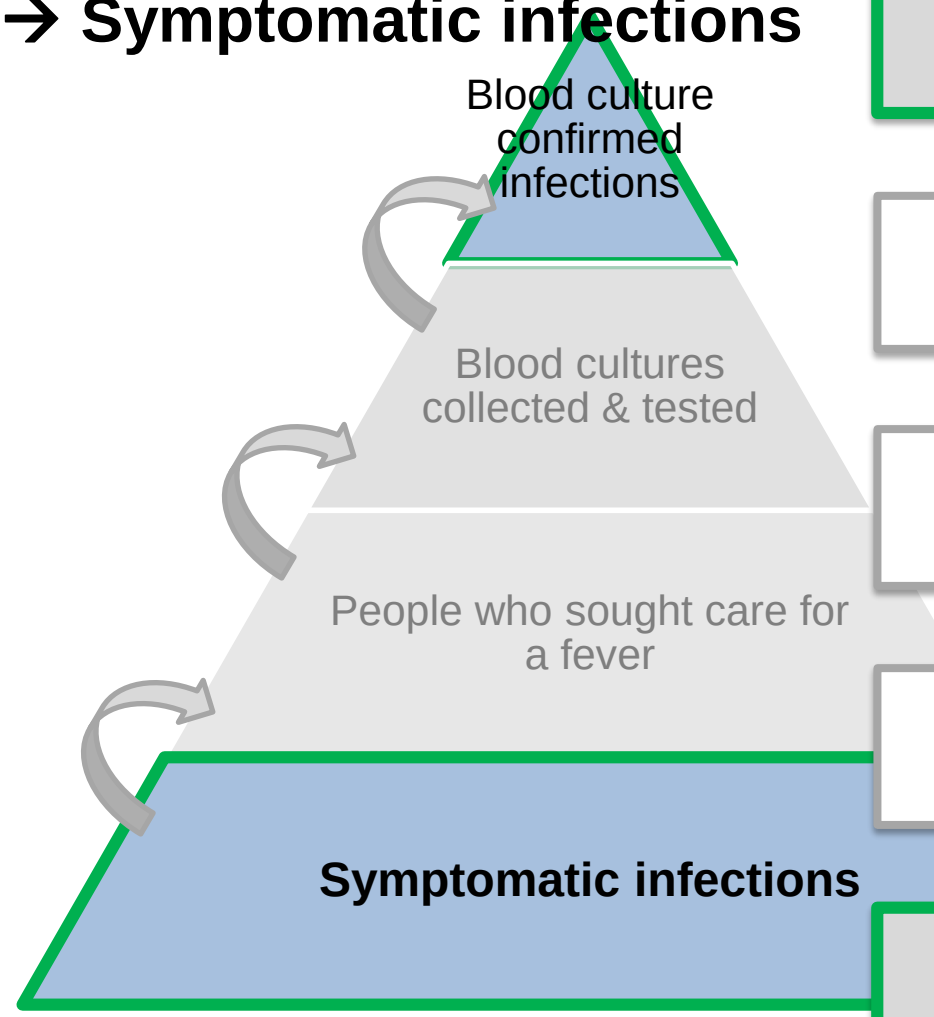
Probability of having BC drawn
STRATAA passive surveillance
Probability of blood culture by age

Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

"True" Symptomatic Infections

1. Antillón M et al. (2018). *JID 218* (supp 4).

Blood culture confirmed → Symptomatic infections



Blood culture (BC) positive infections
STRATAA passive surveillance

↓

Probability of having positive BC result
STRATAA passive surveillance
Blood culture sensitivity by volume[1]

↓

Probability of having BC drawn
STRATAA passive surveillance
Probability of blood culture by age[2]

↓

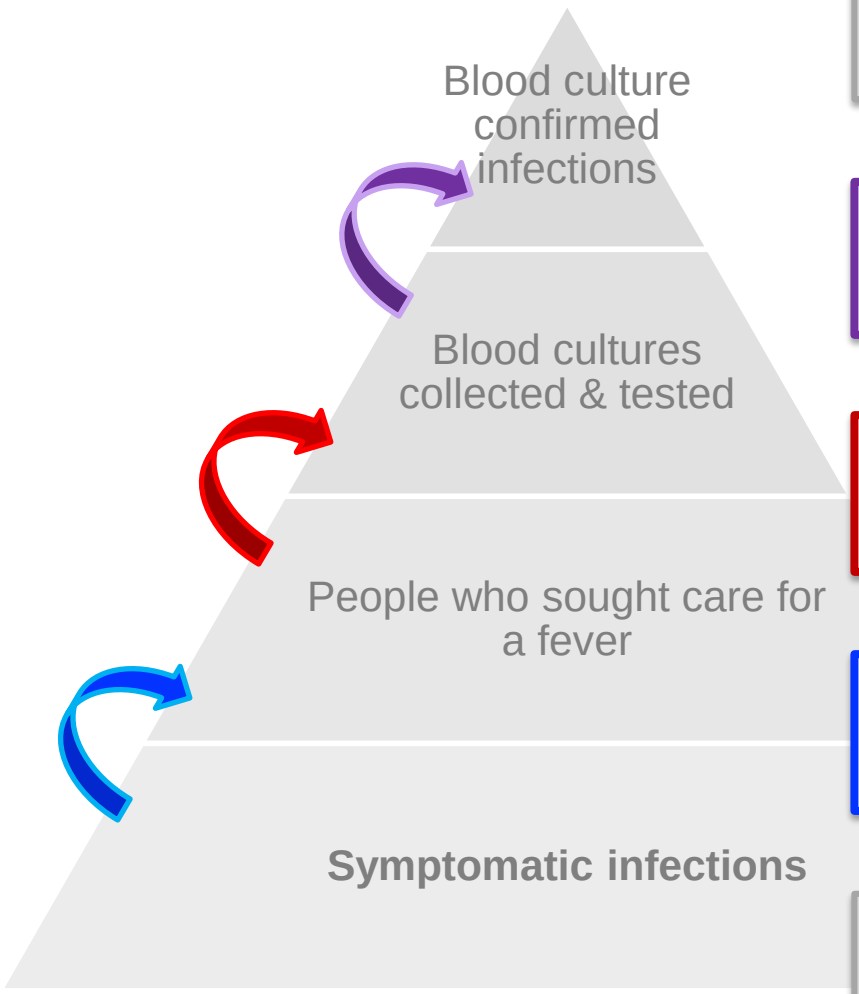
Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

↓

"True" symptomatic infections

1. Antillón M et al. (2018). *JID 218* (supp 4).

Intervening processes



Blood culture (BC) positive infections
STRATAA passive surveillance

Probability of having positive BC result
STRATAA passive surveillance
Blood culture sensitivity by volume[1]

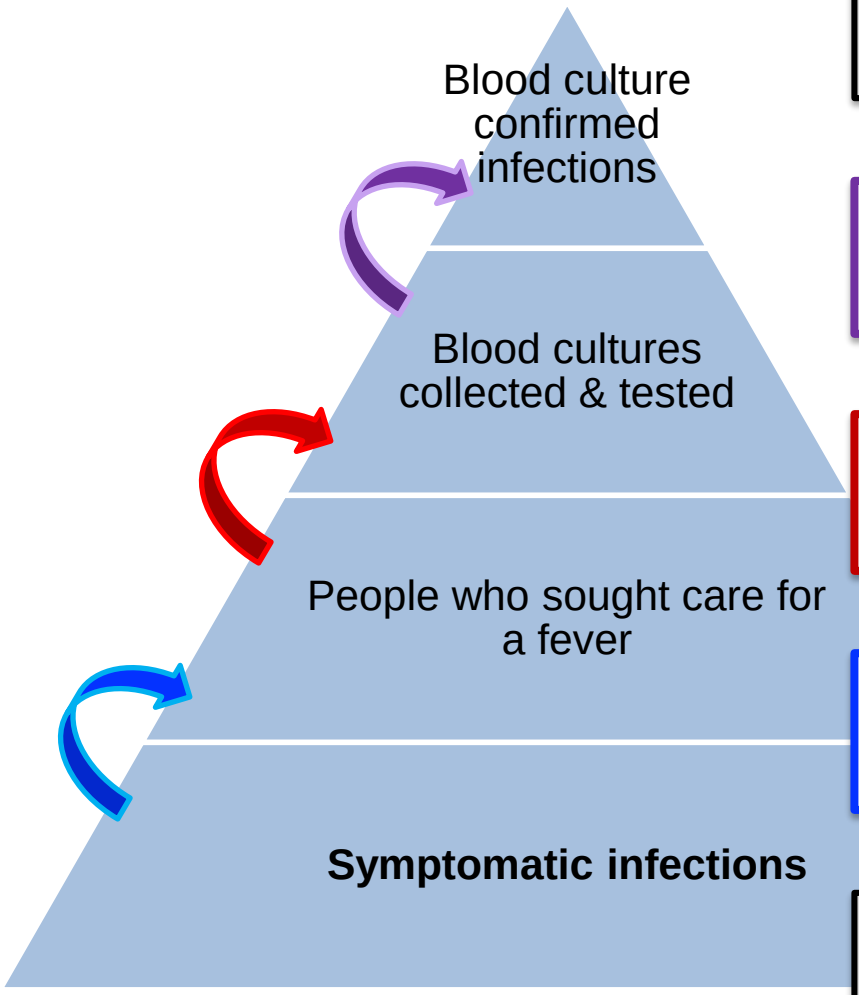
Probability of having BC drawn
STRATAA passive surveillance
Probability of blood culture by age[2]

Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

"True" Symptomatic Infections

1. Antillón M et al. (2018). *JID 218* (supp 4).

Bayesian Framework



Blood culture (BC) positive infections

STRATAA passive surveillance

Probability of having positive BC result

STRATAA passive surveillance

Blood culture sensitivity by volume[1]

Probability of having BC drawn

STRATAA passive surveillance

Probability of blood culture by age[2]

Probability of seeking healthcare

STRATAA Healthcare Utilisation Survey

"True" Symptomatic Infections

1. Antillón M et al. (2018). *JID 218* (supp 4).

All adjustment factors

		Age category			
	Country	<5	5-14	15+	all
Pr(BC positive | BC test)	Bangladesh	53%	53%	55%	53%
	Nepal	53%	53%	56%	54%
	Malawi	52%	53%	58%	54%
Pr(BC test | seek HC)	Bangladesh	82%	83%	84%	83%
	Nepal	65%	76%	82%	70%
	Malawi	39%	36%	20%	34%
Pr(seek HC)	Bangladesh	43%	32%	22%	30%
	Nepal	31%	15%	21%	24%
	Malawi	62%	53%	52%	56%

Lower probabilities — Higher probabilities

All adjustment factors

		Age category			
	Country	<5	5-14	15+	all
Pr(BC positive | BC test)	Bangladesh	53%	53%	55%	53%
	Nepal	53%	53%	56%	54%
	Malawi	52%	53%	58%	54%
Pr(BC test | seek HC)	Bangladesh	82%	83%	84%	83%
	Nepal	65%	76%	82%	70%
	Malawi	39%	36%	20%	34%
Pr(seek HC)	Bangladesh	43%	32%	22%	30%
	Nepal	31%	15%	21%	24%
	Malawi	62%	53%	52%	56%

about the same

Lower probabilities — Higher probabilities

All adjustment factors

		Age category			
	Country	<5	5-14	15+	all
Pr(BC positive | BC test)	Bangladesh	53%	53%	55%	53%
	Nepal	53%	53%	56%	54%
	Malawi	52%	53%	58%	54%
Pr(BC test | seek HC)	Bangladesh	82%	83%	84%	83%
	Nepal	65%	76%	82%	70%
	Malawi	39%	36%	20%	34%
Pr(seek HC)	Bangladesh	43%	32%	22%	30%
	Nepal	31%	15%	21%	24%
	Malawi	62%	53%	52%	56%

about the same

Malawi is lower

Lower probabilities — Higher probabilities

All adjustment factors

		Age category			
	Country	<5	5-14	15+	all
Pr(BC positive | BC test)	Bangladesh	53%	53%	55%	53%
	Nepal	53%	53%	56%	54%
	Malawi	52%	53%	58%	54%
Pr(BC test | seek HC)	Bangladesh	82%	83%	84%	83%
	Nepal	65%	76%	82%	70%
	Malawi	39%	36%	20%	34%
Pr(seek HC)	Bangladesh	43%	32%	22%	30%
	Nepal	31%	15%	21%	24%
	Malawi	62%	53%	52%	56%

about the same

Malawi is lower

Nepal is lower

Lower probabilities — Higher probabilities

All adjustment factors

		Age category			
	Country	<5	5-14	15+	all
Pr(BC positive | BC test)	Bangladesh	53%	53%	55%	53%
	Nepal	53%	53%	56%	54%
	Malawi	52%	53%	58%	54%
Pr(BC test | seek HC)	Bangladesh	82%	83%	84%	83%
	Nepal	65%	76%	82%	70%
	Malawi	39%	36%	20%	34%
Pr(seek HC)	Bangladesh	43%	32%	22%	30%
	Nepal	31%	15%	21%	24%
	Malawi	62%	53%	52%	56%

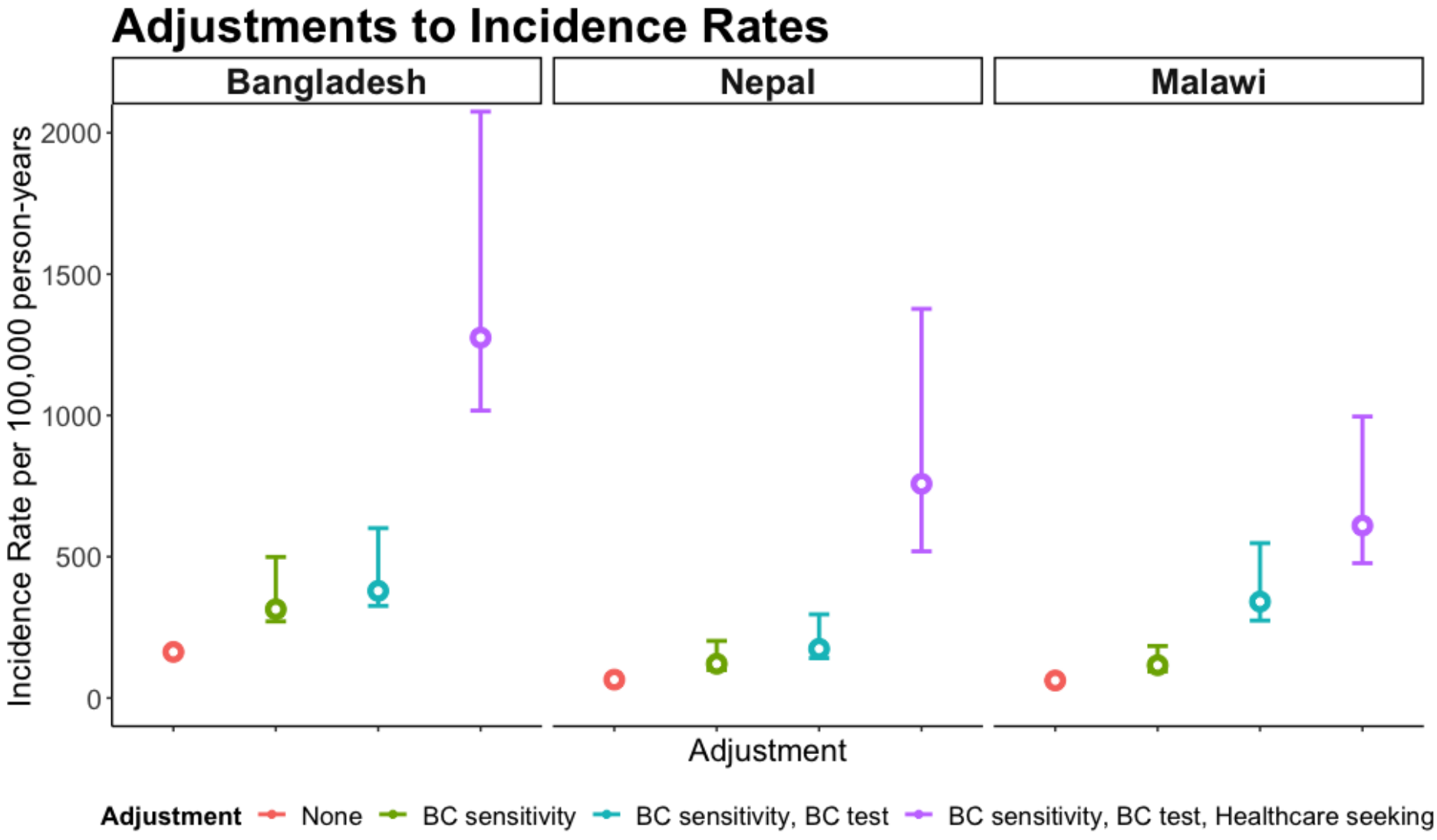
about the same

Malawi is lower

Nepal is lower

Malawi is higher

Lower probabilities — Higher probabilities



*BC = Blood Culture

Overall results

- 8- to 12-fold adjustments

	Crude rates*	Adjusted rates* (95% credible intervals)	Ratio (adj./obs.)
Bangladesh	163	1,275 (1,017-2,075)	7.8
Nepal	65	758 (519-1,377)	11.7
Malawi	62	610 (477-996)	9.8

*per 100,000 person-years

Overall results: **Bangladesh**

- Bangladesh has the highest crude incidence rates, but the lowest adjustment ratio

	Crude rates*	Adjusted rates* (95% credible intervals)	Ratio (adj./obs.)
Bangladesh	163	1,275 (1,017-2,075)	7.8
Nepal	65	758 (519-1,377)	11.7
Malawi	62	610 (477-996)	9.8

*per 100,000 person-years

Overall results: **Nepal**

- Nepal has the highest adjustment ratio

	Crude rates*	Adjusted rates* (95% credible intervals)	Ratio (adj./obs.)
Bangladesh	163	1,275 (1,017-2,075)	7.8
Nepal	65	758 (519-1,377)	11.7
Malawi	62	610 (477-996)	9.8

*per 100,000 person-years

Overall results: **Malawi**

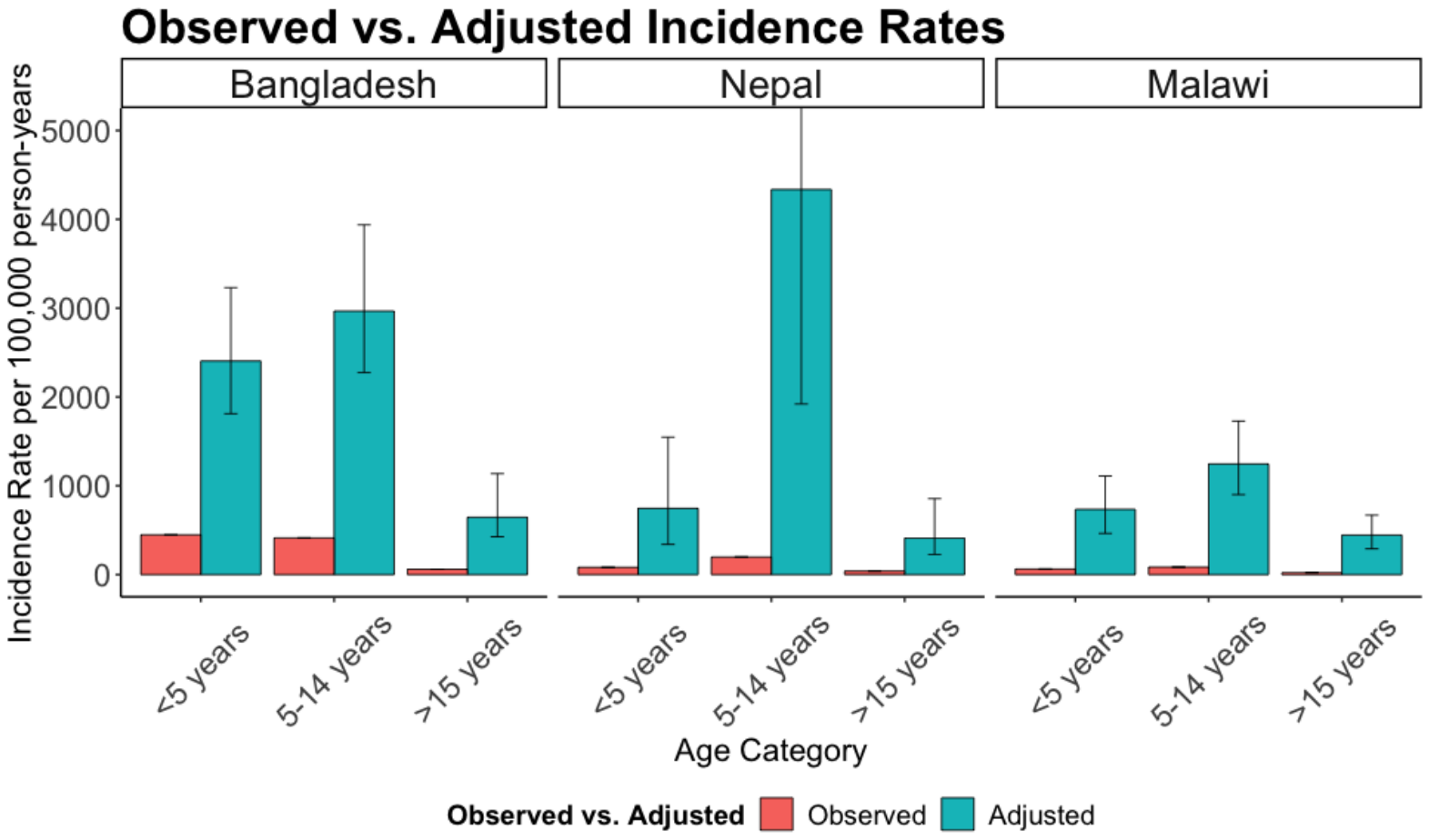
- Malawi is somewhere in between

	Crude rates*	Adjusted rates* (95% credible intervals)	Ratio (adj./obs.)
Bangladesh	163	1,275 (1,017-2,075)	7.8
Nepal	65	758 (519-1,377)	11.7
Malawi	62	610 (477-996)	9.8

*per 100,000 person-years

Adjusted rates vary by age

- *Adults (15+ years) had the lowest incidence rates*
- *Children 5-14 years had the highest incidence rates*



Implications

- Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population

Implications

- Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population
- Our model provides a method to estimate incidence while accounting for the reporting process
  - Improved understanding of intervening processes
  - Can be updated with additional information or contexts

Implications

- Passive surveillance of blood culture-confirmed results is a considerable underestimation of the true incidence of typhoid in the population
- Our model provides a method to estimate incidence while accounting for the reporting process
  - Improved understanding of intervening processes
  - Can be updated with additional information or contexts
- These upward-adjusted estimates can be used for analysis and/or decision-making for typhoid control

Acknowledgements

Oxford UK

Andrew Pollard, James Meiring, Merryn Voysey, Christoph J. Blohmke, Yama Ghulam Farooq, Jennifer Hill, Susan Tonks, Rachel Colin-Jones, Sarah Kelly, Olga Mazur, Nicola Smith, Sophie Temple

Dhaka, Bangladesh

John Clemens, Firdausi Qadri, Khalequzzaman Zaman, Arifuzzaman Khan, Farhana Khanam, Nirod Chandra Saha,

Blantyre, Malawi

Melita Gordon, Robert Heyderman, Tonney Nyirenda,

Chisomo Msefula, Deus Thindwa , Happy Chimphako Banda, Angeziwa Chunga Chirambo, Moses Kamzati, Tikhala Makhaza Jere, Clemens Masesa, Maurice Mbewe, Harrison Msuku, Patrick Munthali , Rose Nkhata , Eunice Kadzakumanja, Eve Kossam

Kathmandu, Nepal

Buddha Basnyat, Mila Shakya, Abhilasha Karkey, Sabina Dongol, Amit Aryja, Anup Adhikari, Maheshwar Ghimire , Pallavi Gurung, Archana,Maharjan

Cambridge, UK

Gordon Dougan, Zoe Dyson, Emily Lees, Ankur Mutreja, Derek Pickard, Stephen Reece

Ho Chi Minh, Vietnam

Stephen Baker, Thomas Darton, Christiane Dolocek, Tan Trinh Van, Nhu Tran Hoang, Tran Vu Thieu Nga

Melbourne, Australia

Sarah Dunstan, Kat Holt , Mike Inouye, Artika Nath, Louise Judd

New Haven, USA

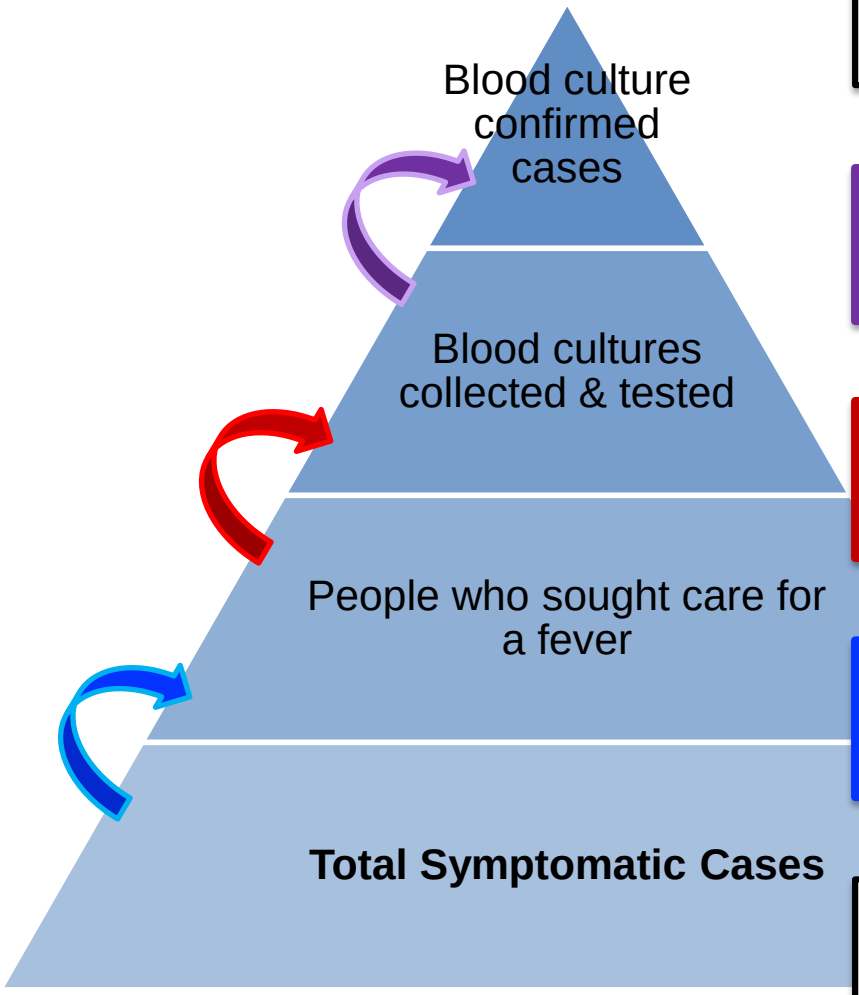
Virginia Pitzer, Maile Thayer Phillips, Yu-Han Kao, Neil Saad

Bayesian inference

- Bayesian inference combines past experience (prior) with new data (likelihood) to form the current state of knowledge (posterior)

$$posterior \propto \underbrace{likelihood}_{\text{Observed data}} \times \underbrace{prior}_{\text{Information from additional sources}}$$

Bayesian Framework



Blood culture (BC) positive infections
STRATAA passive surveillance

Probability of having positive BC result
STRATAA passive surveillance
Blood culture sensitivity by volume[1]

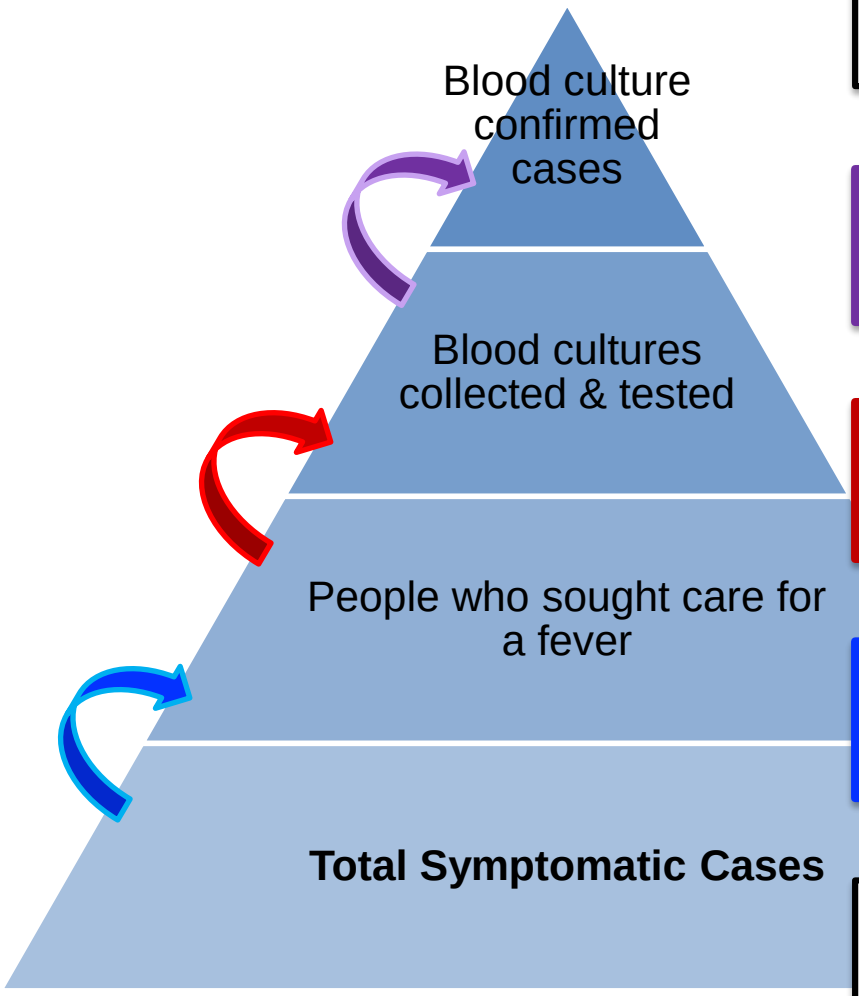
Probability of having BC drawn
STRATAA passive surveillance
Probability of blood culture by age[2]

Probability of seeking healthcare
STRATAA Healthcare Utilisation Survey

"True" Symptomatic Infections

1. Antillón M et al. (2018). *JID 218* (supp 4).

Bayesian Framework



$$N_{BC+} \sim Poisson(\lambda * p_{sens} * p_{BC} * p_{HC} | personyears)$$

$$p_{sens,i} = \exp(\gamma_0 + \gamma_1 * BCvol_i) * (1 - 0.34 * abx_i)$$

$$p_{BC} \sim Beta(\alpha_{BC}, \beta_{BC})$$

$$p_{HC} \sim Beta(\alpha_{HC}, \beta_{HC})$$

$$N_{true} \sim Poisson(\lambda | personyears)$$

*Non-informative priors unless otherwise specified