Ashish Bavdekar

Temsunaro Rongsen-Chandola

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Jacob John

Gagandeep Kang

Surveillance for Enteric Fever in India

Background

- A cohort study in 1995 reported typhoid rates in excess 2/ 1000 child-years in young children in urban Delhi
- One in four children in these settings were likely to develop typhoid fever by the age of 20.
- India produces the only WHO prequalified conjugate typhoid vaccine with > 80% vaccine efficacy

Age groups	Delhi 1995	Kolkata 2006	Santiago 1977	Dong Thap 1995
0-4	2730	1293	358	89
5-9	1390	610	272	531
10-14	860	610	333	429
15-19	860	58[$]	283	153

NTAGI concerns

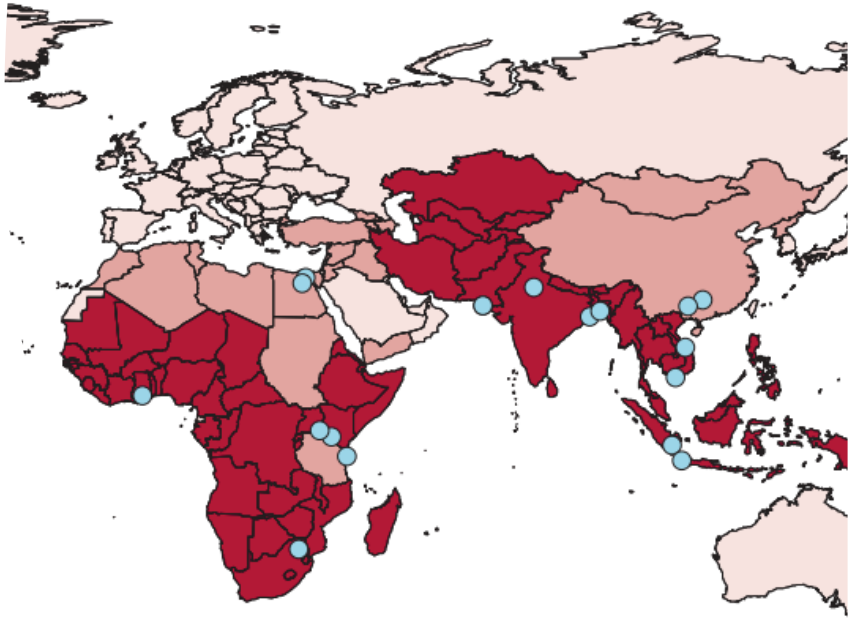
MINUTES OF THE MEETING OF THE NATIONAL TECHNICAL ADVISORY GROUP ON IMMUNIZATION
1:45 pm-2:30 pm, Friday, 9 December 2016
Nirman Bhawan, New Delhi

Representative contemporary data

- Secular trends
- Heterogeneity

Understanding the epidemiology

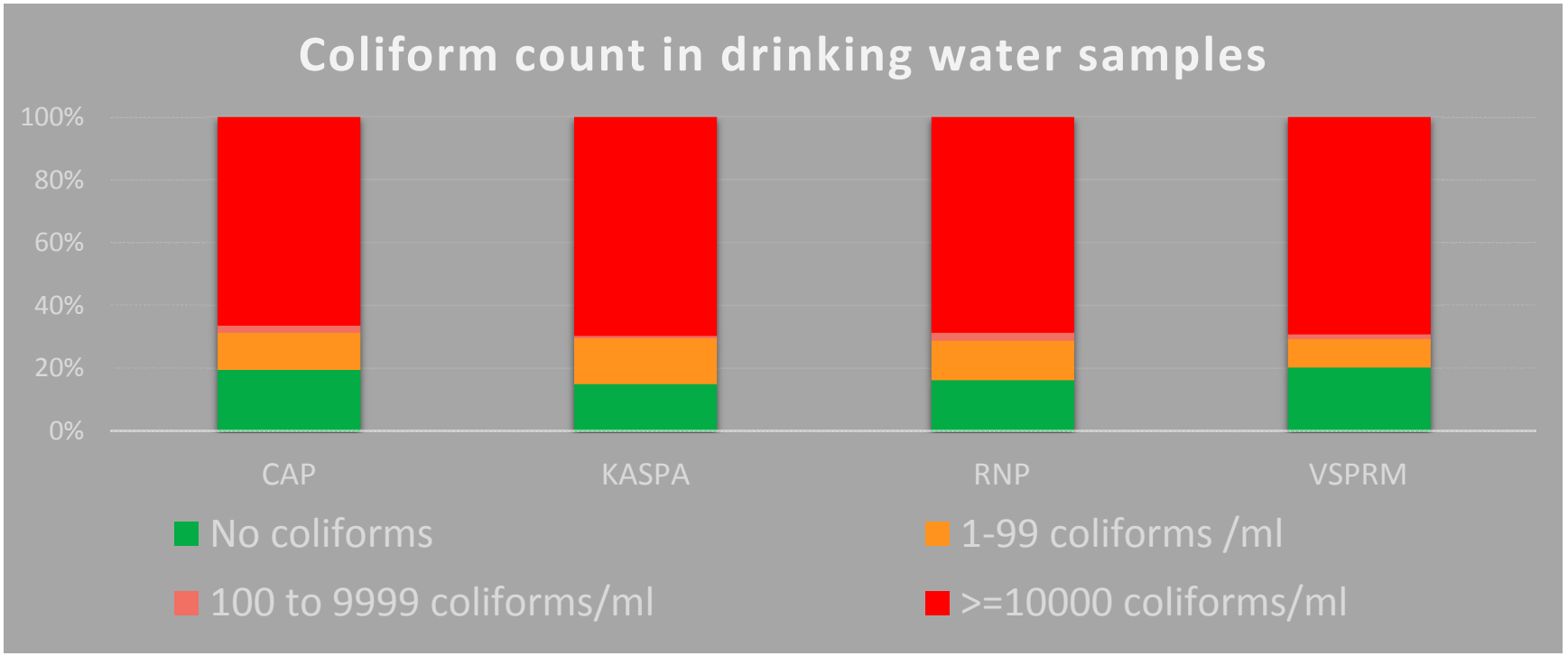
- Transmission dynamics
- Age distribution
- Predictors of severity

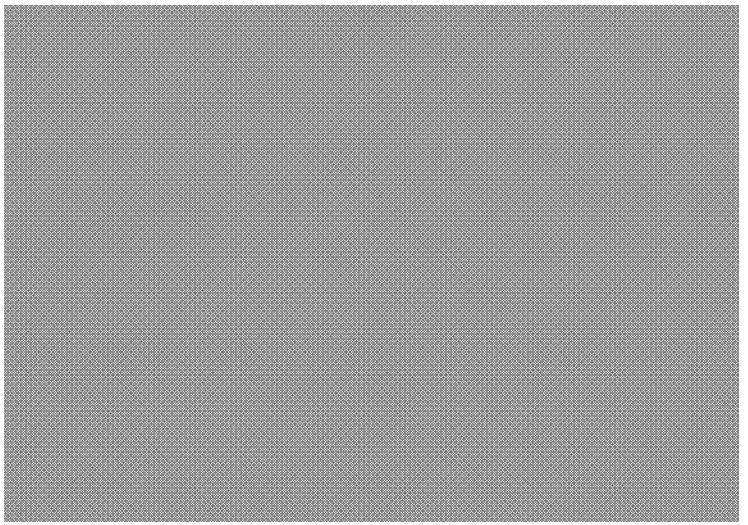


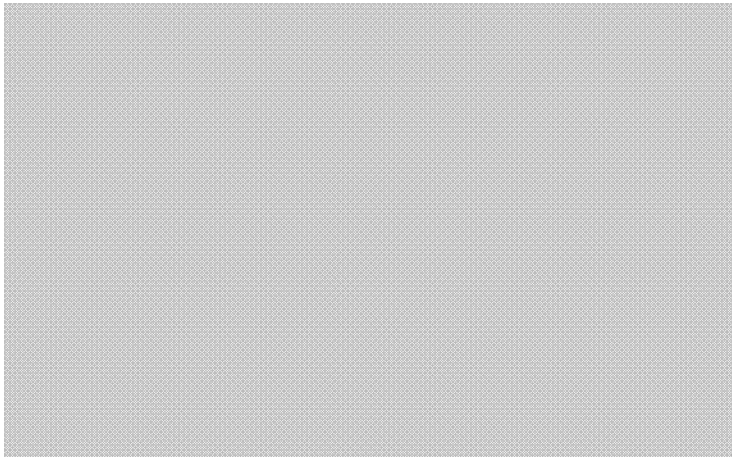
Mogasale 2014

Secular trends

- Secular trends suggest decline or heterogeneity
  - Lower S. typhi isolation & complications in tertiary care settings in the last couple of decades
- Are improvements in economic indices, access to healthcare and WASH leading us towards elimination?

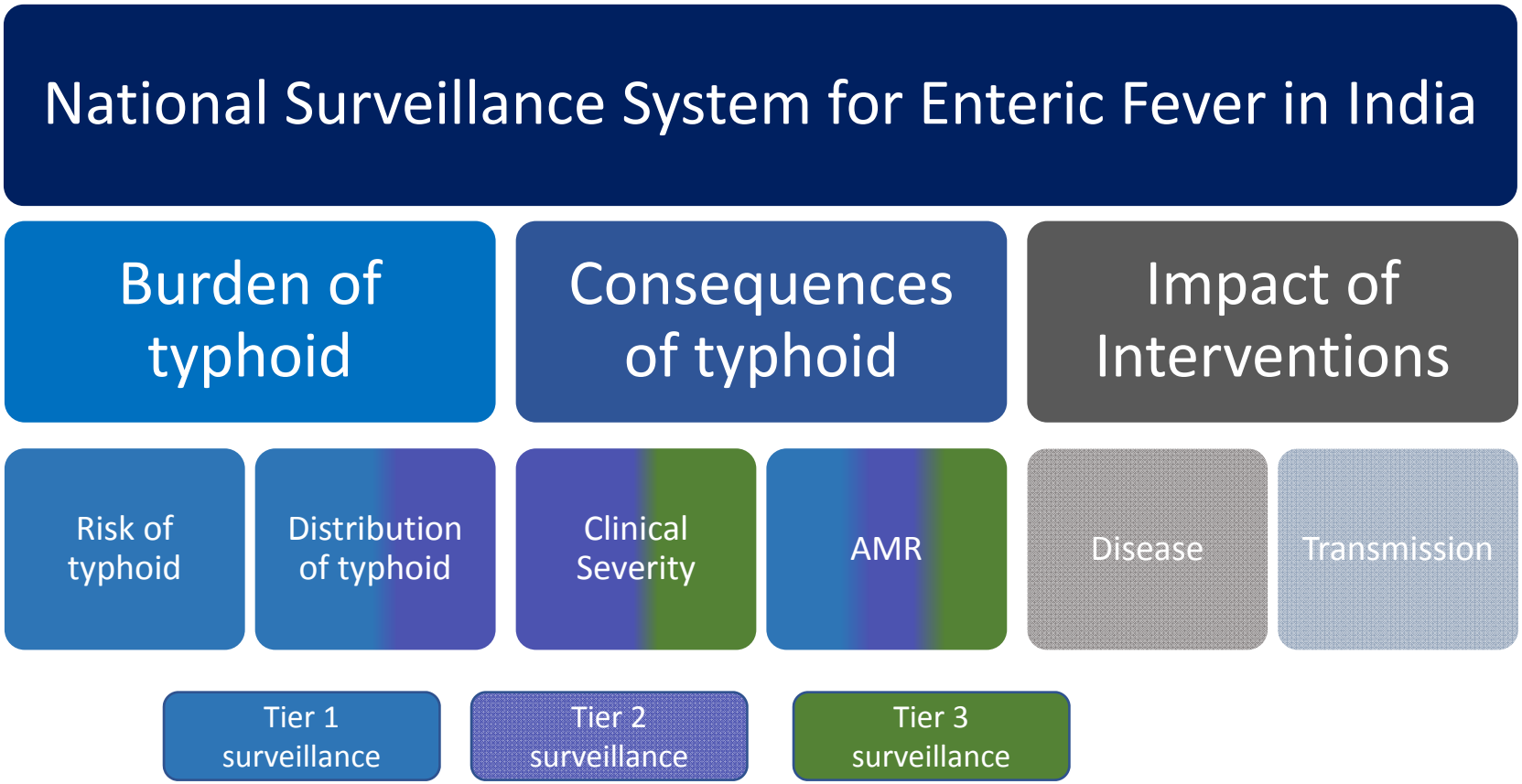







07.09.2017 12:38

Overview of SEFI



Objectives of SEFI

Tier 1

- Estimate the *incidence of typhoid fever* in children between 6 months and 15 years in India using an active surveillance approach.

Tier 2

- Estimate the incidence of *severe typhoid fever* in all ages using a hybrid approach combining hospitalization and healthcare utilization data.

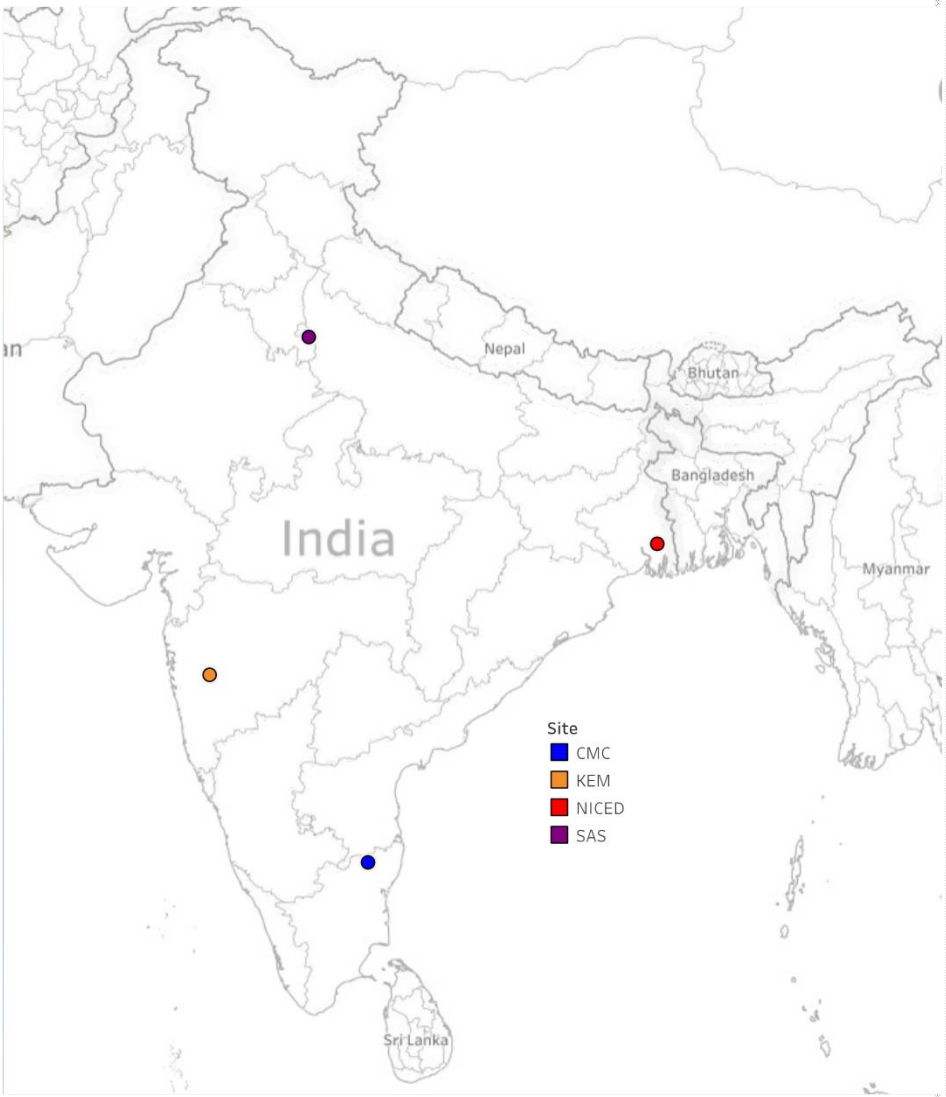
- Monitor patterns of antimicrobial use and antimicrobial resistance in patients with typhoid fever.
- Estimate cost and consequence of typhoid fever in different healthcare settings in India.

Tier 1 Community Surveillance

Age-stratified incidence of culture-confirmed typhoid fever in 6m - 15-year-old children in four sites across India

Characterize the study population in terms of key risk factors

- Population density
- WASH parameters
- Demographics & socio-economic profile
- Vaccine coverage



Surveillance sites

Delhi
- Urban cohort
- North India

Kolkata
- Urban cohort
- Eastern India

Vellore
- Semi-urban cohort
- Southern India

Pune
- Rural cohort
- Western India

Methods

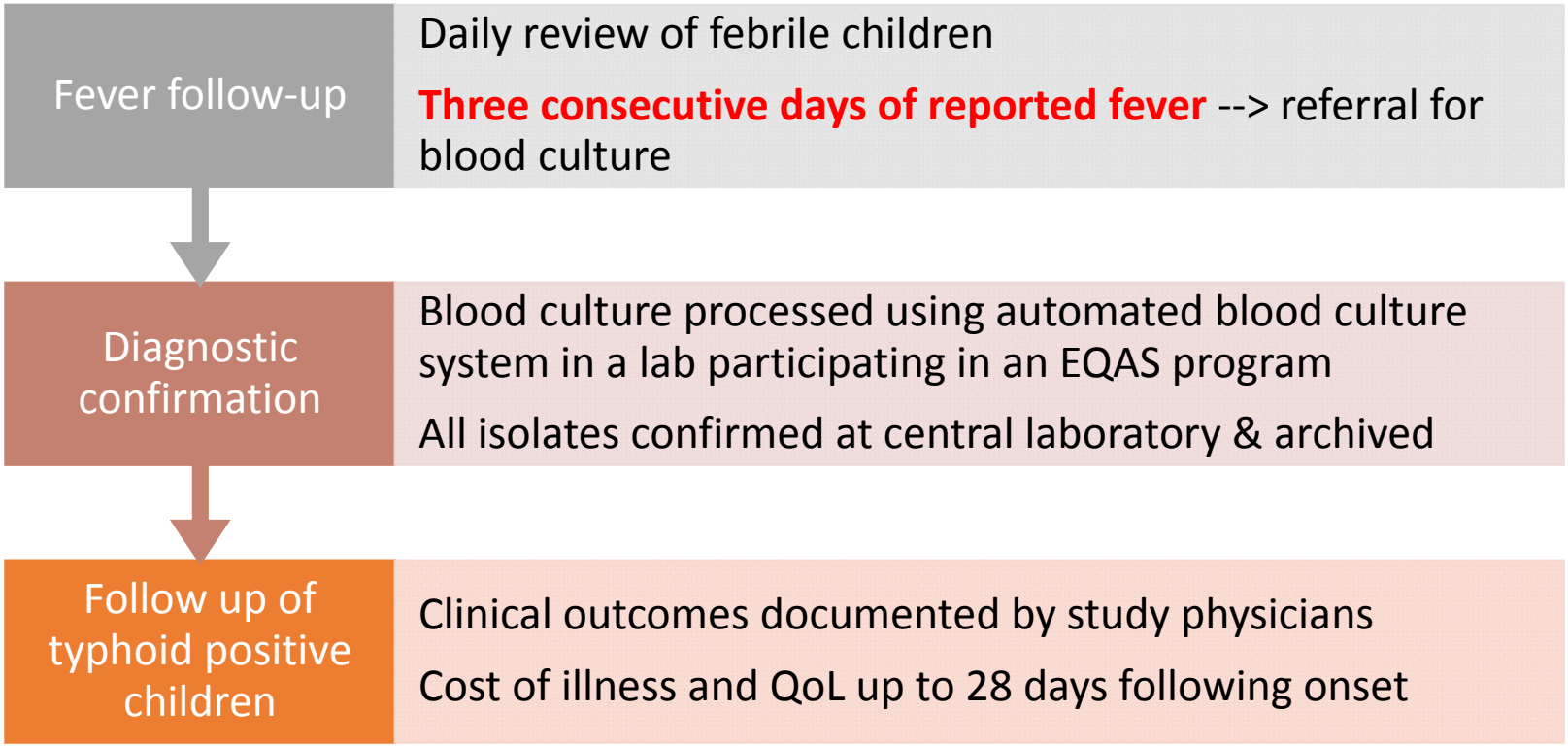
Recruitment

- Children between 6 months and 14 year
- 6000 eligible children per site
- Follow up for 24 months

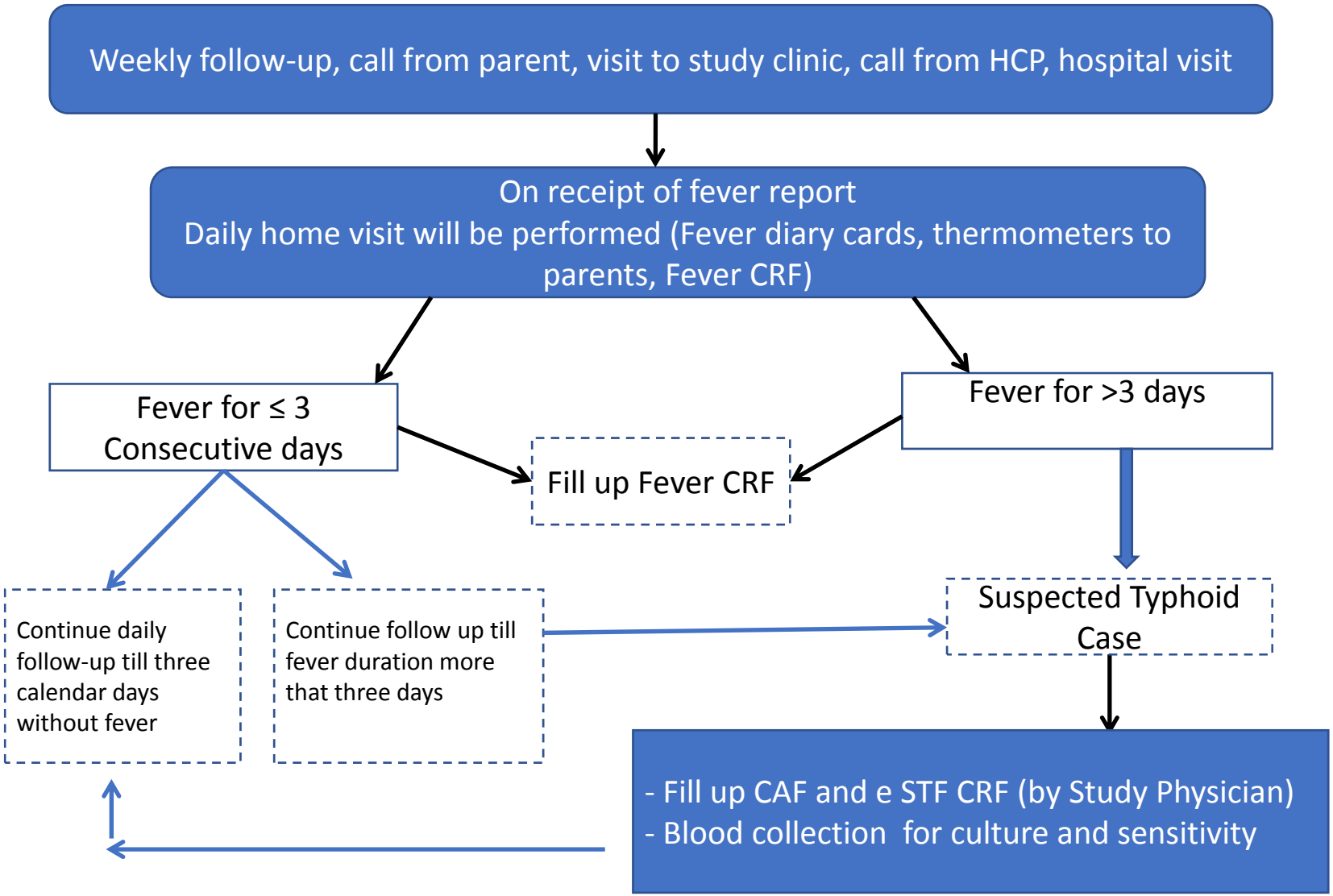
Surveillance for fever

- Weekly surveillance contact
  - In-person interviews (or) telephonic
- Parents encouraged to report fever & to visit study clinics
- HCFs report febrile illness in participants

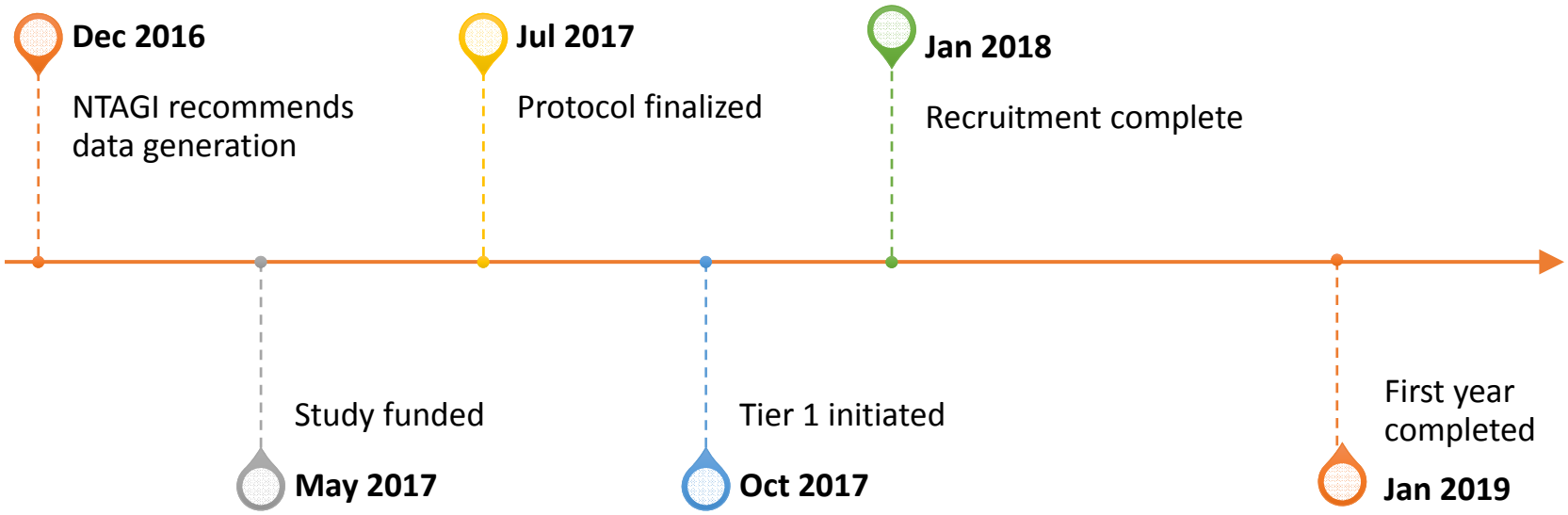
Methods


Fever follow-up
Daily review of febrile children
Three consecutive days of reported fever --> referral for blood culture
Diagnostic confirmation
Blood culture processed using automated blood culture system in a lab participating in an EQAS program
All isolates confirmed at central laboratory & archived
Follow up of typhoid positive children
Clinical outcomes documented by study physicians
Cost of illness and QoL up to 28 days following onset

Fever surveillance



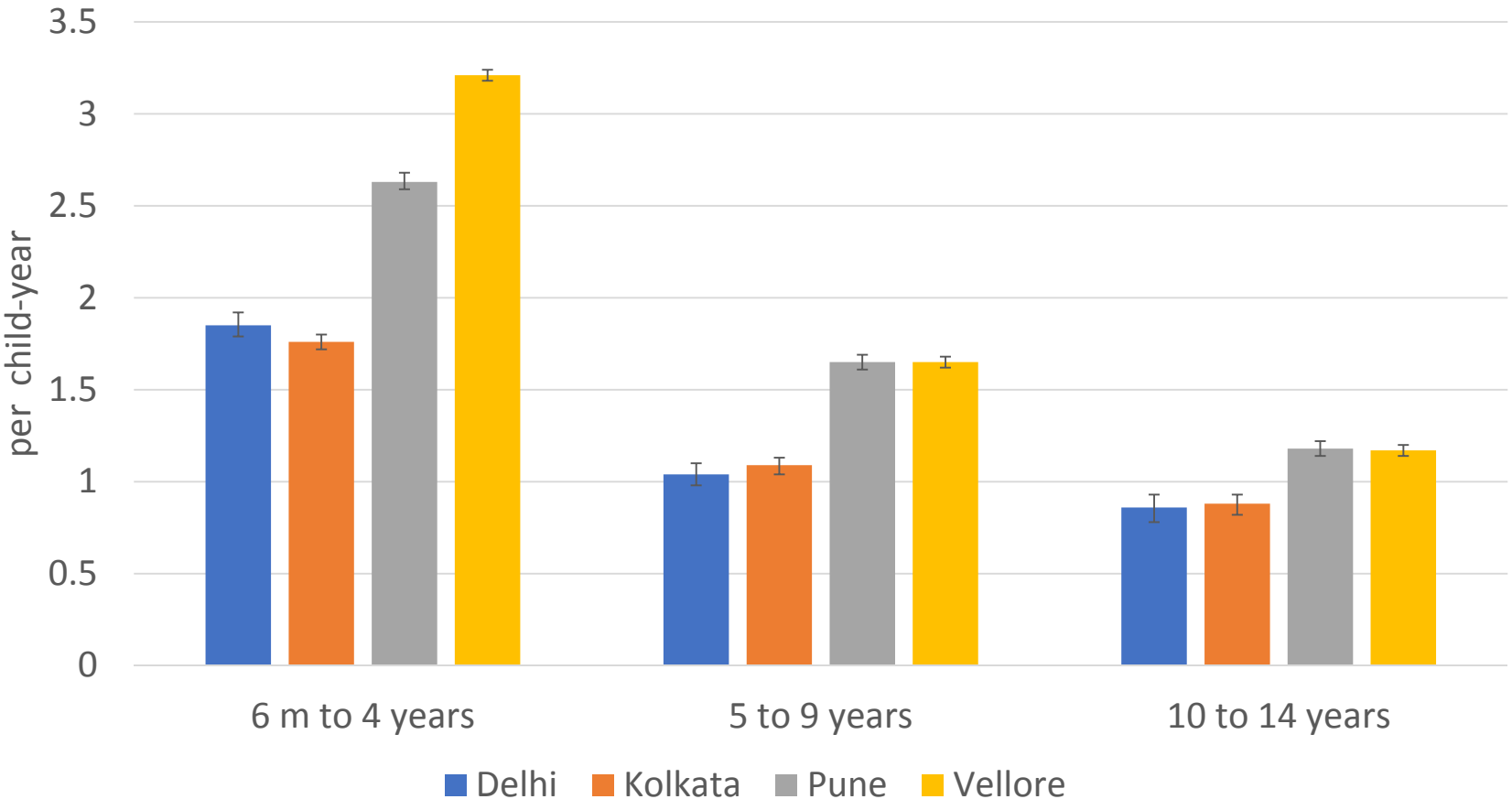
A work in progress



Summary findings (Jan 31, 2019)

	DELHI (URBAN)	KOLKATA (URBAN)	PUNE (RURAL)	VELLORE (SEMI-URBAN)	CUMULATIVE
Enrolled	6,000	6,017	6,004	6,041	**24,062**
Child years F/U	6,290	6,997	6,977	7,546	**27,810**
Fever episodes	7,761	8,392	12,591	14,477	**43,221**

Incidence of fever (per child-year)



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Child years F/U	6,290	6,997	6,977	7,546	**27,810**
Fever episodes	7,761	8,392	12,591	14,477	**43,221**
Eligible for B/C	1,700	1,522	2,324	2,627	8,173
B/C performed	1,285 (76%)	1,234 (81%)	2187 (94%)	2,376 (90%)	7,082 (87%)
S. typhi	21	50	2	56	129
S. paratyphi A	6	6	2	0	14

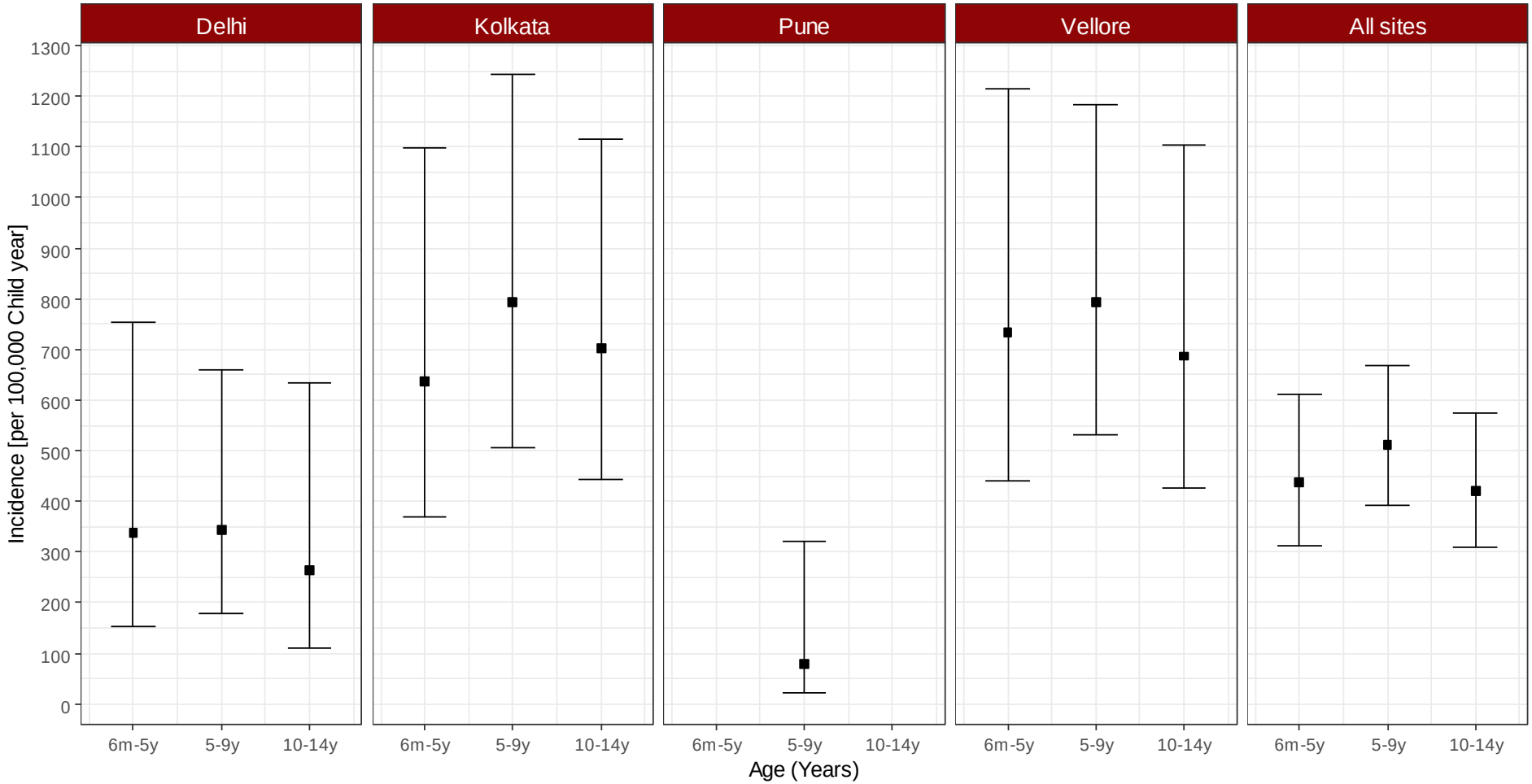
Patient characteristics

Site	Delhi	Kolkata	Pune	Vellore
Typhoid cases	**20**	**50**	**2**	**56**
Gender Male N(%)	9 (43)	28 (56)	1 (50)	29 (52)
Mean age in years (range)	7.1 (1.4-14.8)	7.8(1.4-14.1)	9.3(9.2-9.4)	7.5(1.4-13.9)
Mean temperature (^{0}F)	102.3	103.3	100.0	102.4
Mean duration of fever in days (range)	10.2(3-19)	10.2(4-27)	5.5(5-6)	8.9(4-14)
Hospitalizations	2	11	1	3
Mean duration of hospitalization in days (range)	8 (7-9)	5.9 (2-11)	5(5-5)	6.3(5-7)

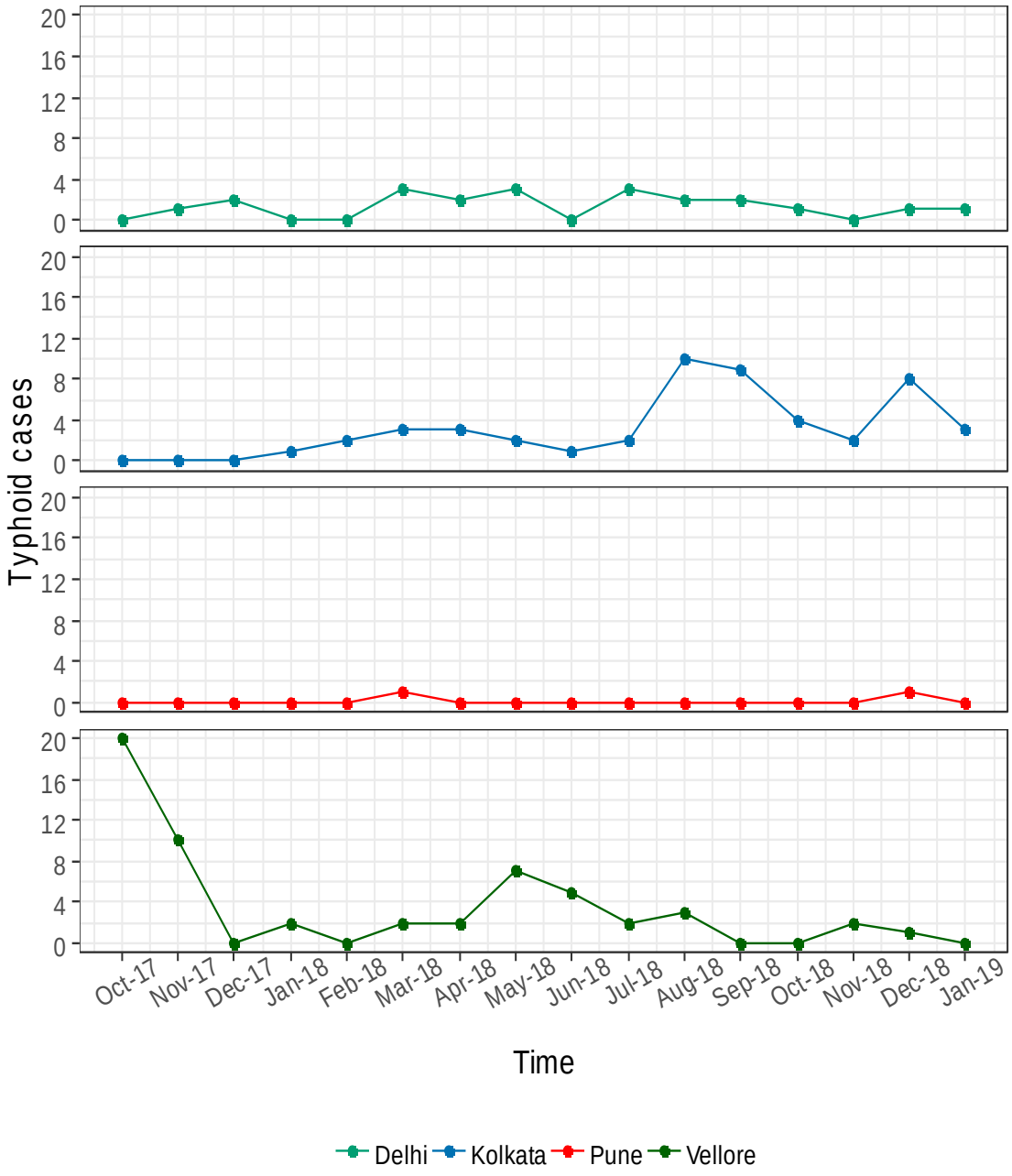
Incidence of typhoid fever (100,000 child-years)

	Delhi 20	Kolkata 50	Pune 2	Vellore 56	Overall 128
0.5 to < 5	338 152 - 752	637 370-1098	0	733 442-1215	437 312-612
5 to <10	343 179 - 660	793 506-1243	80 20-321	794 532-1185	513 393-669
10 to 15	264 110 - 635	702 443-1115	0	687 427-1105	421 309-574
Overall	318 205-493	714 542-943	29 7-115	742 571-964	460 387-547

Incidence of typhoid fever (per 100,000 child-years)

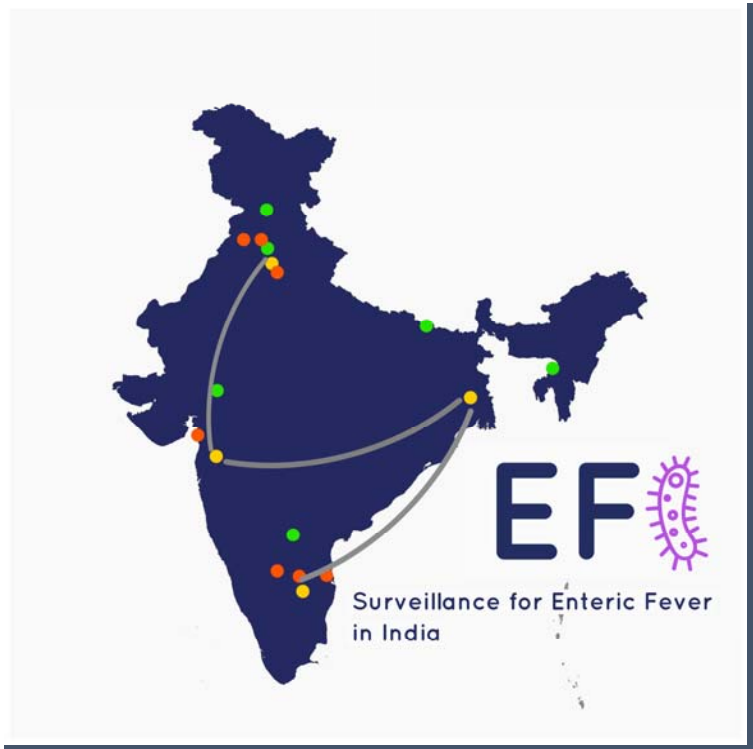


Time trends in typhoid detection across sites



Summary

- High burden in children in urban areas
- Lower incidence in rural Pune
- Variable incidence over time in each location
- Mean age of typhoid patients 7.5 years
- Youngest case 1.4 years old
- Associated morbidity is non-trivial
- Burden in less densely populated rural areas needs further characterization



Thank you

SAS, Delhi	KEMHRC, Pune	NICED, Kolkata	CMC, Vellore	Coordination
• Temsunaro RC • Alok Arya • Nidhi Goyal • Bireshwar Sinha	• Ashish Bavdekar • Ankita S • Sanjay Juvekar	• Shanta Dutta • Suman Kanungo • Jayanta Saha	• Jacob John • Manikandan S • Chella Sindhu • Prabhakar Moses • Winsley Rose	• Gagandeep Kang • Swathi Krishna • Venkat R Mohan • Balaji V • Karthik R

BILL & MELINDA GATES foundation

Additional slides

Person-years of follow-up (Jan 31, 2019)

Age	Delhi	Kolkata	Pune	Vellore	Cumulative
6 m to < 5 years	1775	2039	1917	2048	**7799**
5 to <10 years	2622	2396	2494	3022	**10534**
10 to 15 years	1893	2562	2566	2476	**9487**
Overall	**6290**	**6997**	**6977**	**7546**	**27810**

Incidence of typhoid fever per 100,000 child year excluding the outbreak (Vellore Oct-Nov 2017)

	Delhi **20**	**Kolkata** **50**	**Pune** **2**	**Vellore** **26**	**Overall** **98**
0.5 to < 5	338 152 - 752	637.48 370-1098	0	321 144-715	329 222-487
5 to <10	343 179 - 660	793.12 506-1243	80 20-321	340 177-654	384 281-526
10 to 15	264.17 110 - 635	702.59 443-1115	0	500 277-902	369 263-516
Overall	318 205-493	714.61 542-943	29 7-115	387 264-569	363 298-443

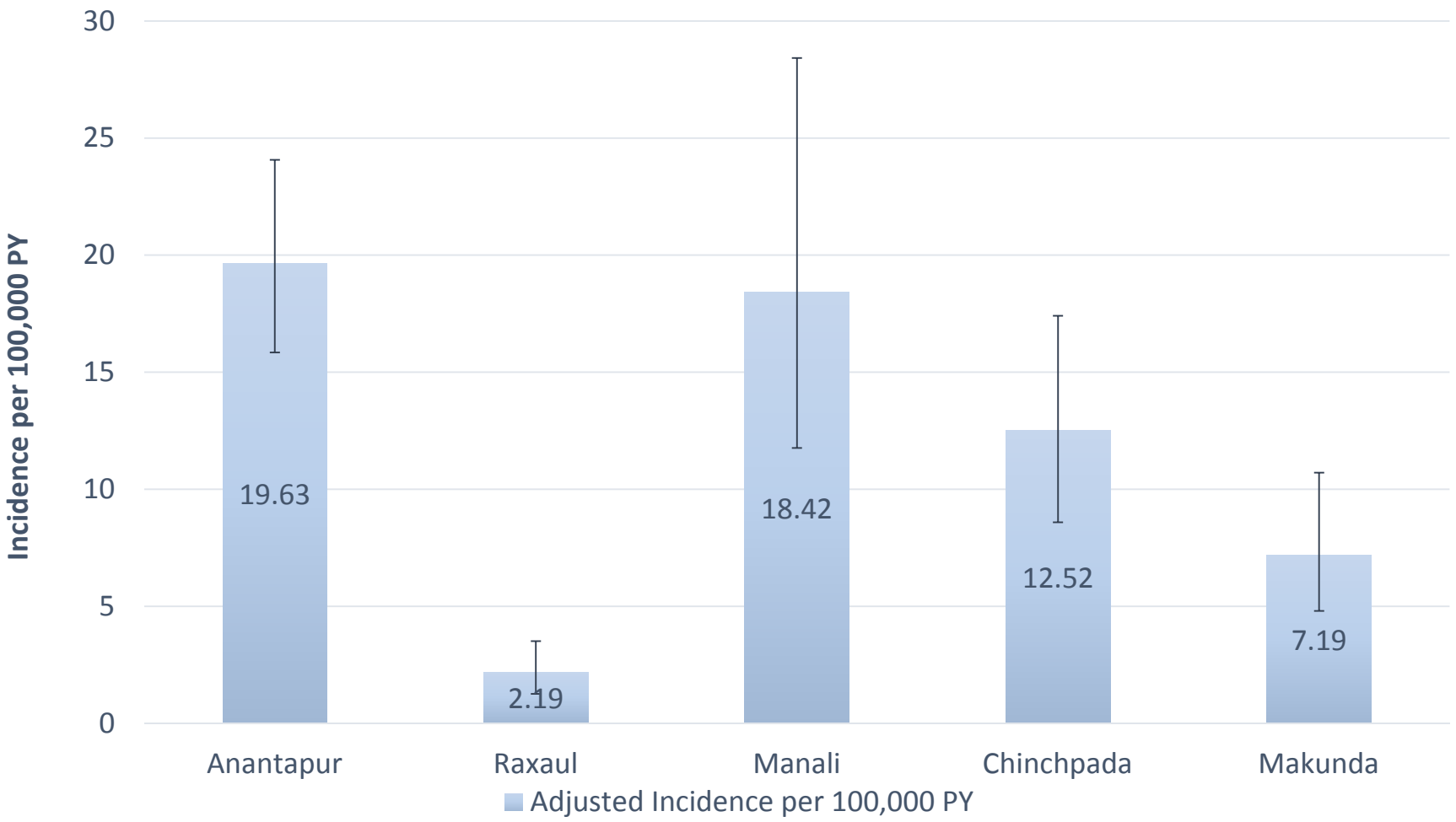
HCUS-adjusted incidence of hospitalized typhoid

	ANANTAPUR	CHANDIGARH	RAXAUL	MANALI	CHINCHPADA	MAKUNDA
Projected population in 2018	4,81,505	1,40,199	7,61,152	1,20,720	3,05,998	3,77,243
Number of days of surveillance	340	268	331	323	298	318
Blood culture confirmed S. typhi	17	53	4	5	3	8
Crude incidence per 100,000	3.79	51.52	0.58	4.68	1.20	2.44
AFI hospitalization in HCUS recall	383	223	343	59	594	180
HCUS AFI @ Study Facility	74	84	91	15	57	61
Adjustment factor	0.19	0.38	0.27	0.25	0.10	0.34
Adjusted Incidence / 100,000	19.63	136.78	2.19	18.42	12.52	7.19
Adjusting for severity	**167**	**1163**	**18**	**156**	**106**	**61**

Laboratory surveillance (Jan 31, 2019)

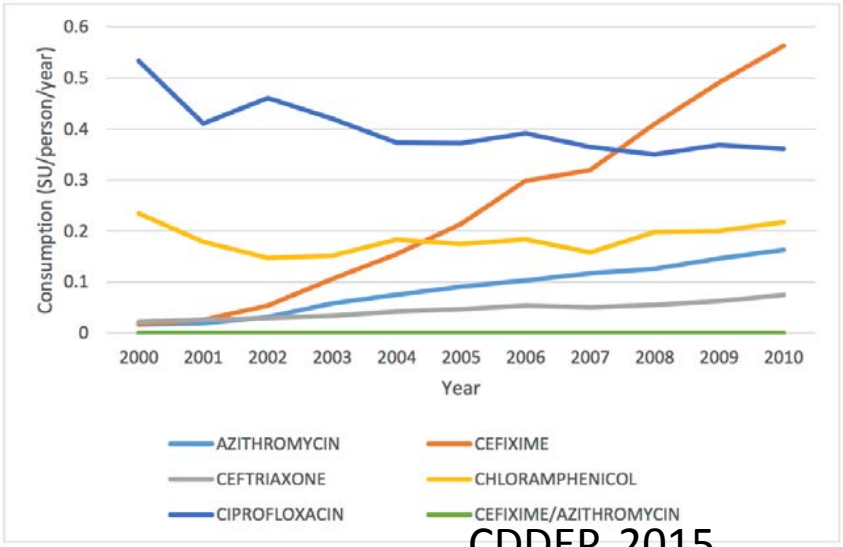
	AIIMS	CMC V	PGIMER	TNMC	ST JOHNS	CMC L	CNBC	KKCTH	TOTAL
Blood culture performed	28475	63535	40400	9538	14300	6296	12042	7488	1,82,074
S typhi	50	139	124	35	98	118	228	91	883
(OP+IP)	0.18%	0.22%	0.31%	0.37%	0.69%	1.87%	1.89%	1.22%	0.48%
S paratyphi	10	27	53	3	29	23	26	21	192
(OP+IP)	0.04%	0.04%	0.13%	0.03%	0.20%	0.37%	0.22%	0.28%	0.11%
Others (OP+IP)	1851	5582	7213	684	1879	656	940	532	19,337
Recruited enteric fever (IP)	26	64	37	40	100	92	67	66	492
Ileal perforations	12	3	-	0	12	5	14	1	47

HCUS-adjusted incidence of hospitalized typhoid @ rural sites



Role of antibiotics

- Improvements in economic conditions & declining drug prices
  - Antibiotic use in the community has increased rapidly
- Antibiotic use may result in decreased sensitivity of culture-based surveillance systems
- Emerging AMR may cause an unmasking or rebound



CDDEP, 2015