“Typhoid Control and Elimination Efforts in Samoa in the Shadow of COVID-19”

Samoa Typhoid Fever Control Program

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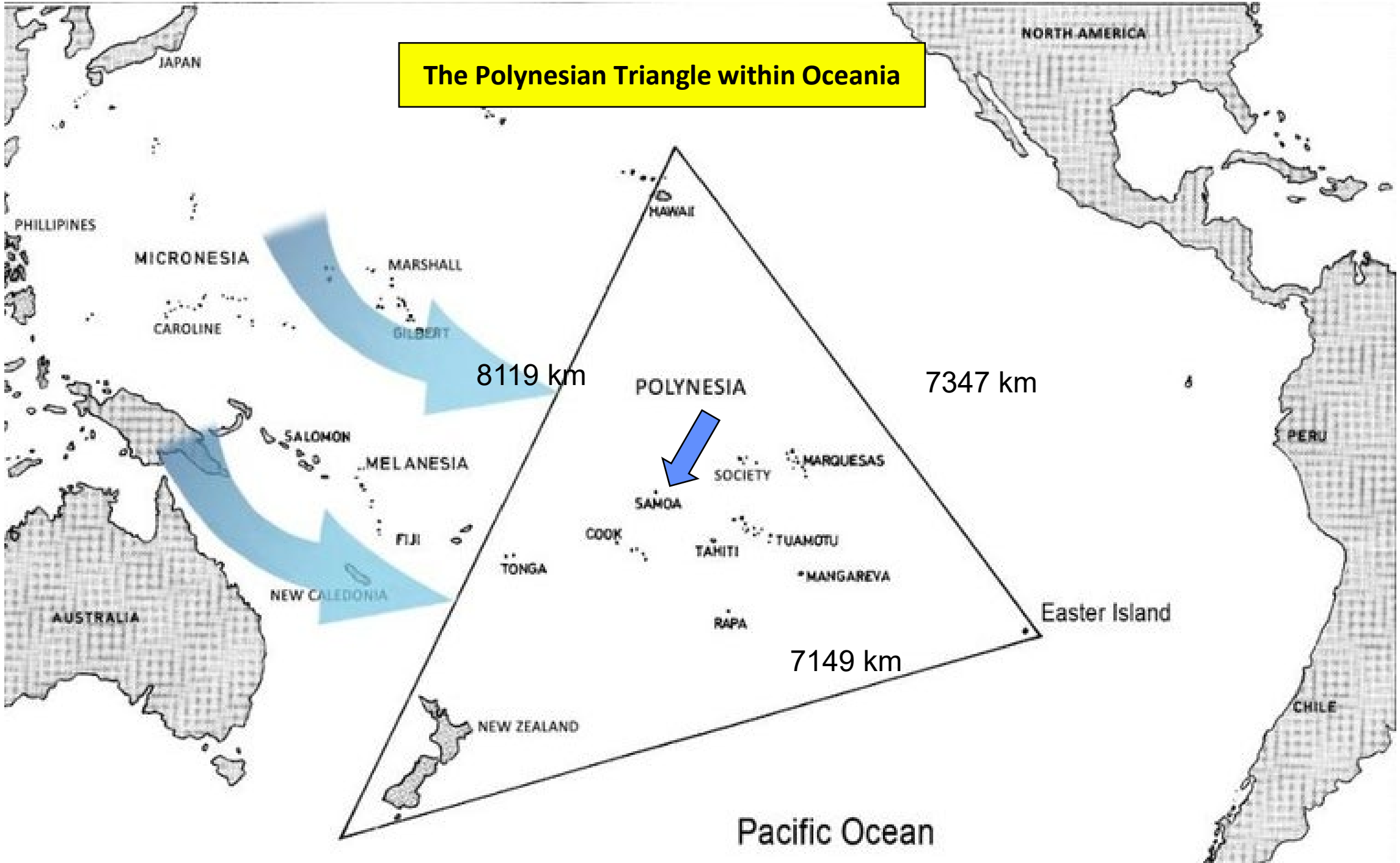

The Polynesian Triangle within Oceania
JAPAN
NORTH AMERICA
PHILLIPINES
MICRONESIA
MARSHALL
CAROLINE
GILBERT
HAWAII
8119 km
POLYNESIA
7347 km
SALOMON
MELANESIA
SOCIETY
MARQUESAS
PERU
SAMOA
COOK
TUAMOTU
FIJI
TAHITI
TONGA
MANGAREVA
NEW CALEDONIA
AUSTRALIA
RAPA
Easter Island
7149 km
NEW ZEALAND
CHILE
Pacific Ocean

Epidemiological Model of Typhoid Fever and its Use in the Planning of Antityphoid Immunization and Sanitation Programmes

B. CVJETANOVIĆ, B. GRAB & K. UEMURA

***Bull. Wld. Hlth Org.* 1971; 45:53-75**

Used demographic and disease burden data from Samoa (1960s) for the model to predict the impact from use of vaccine and sanitation interventions.

Population: ~150,000;

Annual crude typhoid incidence: 72/100,000

Predicted that high coverage with an effective vaccine would have a strong impact

Samoa – MM Levine WHO typhoid consultancy, 2013

- In 2012, the Samoan gov't became deeply concerned about endemic typhoid
- 2013 – Gov't of Samoa & WHO invited MM Levine to Samoa as a WHO Consultant to design a Samoa Typhoid Fever Control Program
- A plan for a Samoa Typhoid Fever Control Program was crafted.
- Initial external funding came from the BMGF

3 Phases of the Samoa Typhoid Fever Control Program

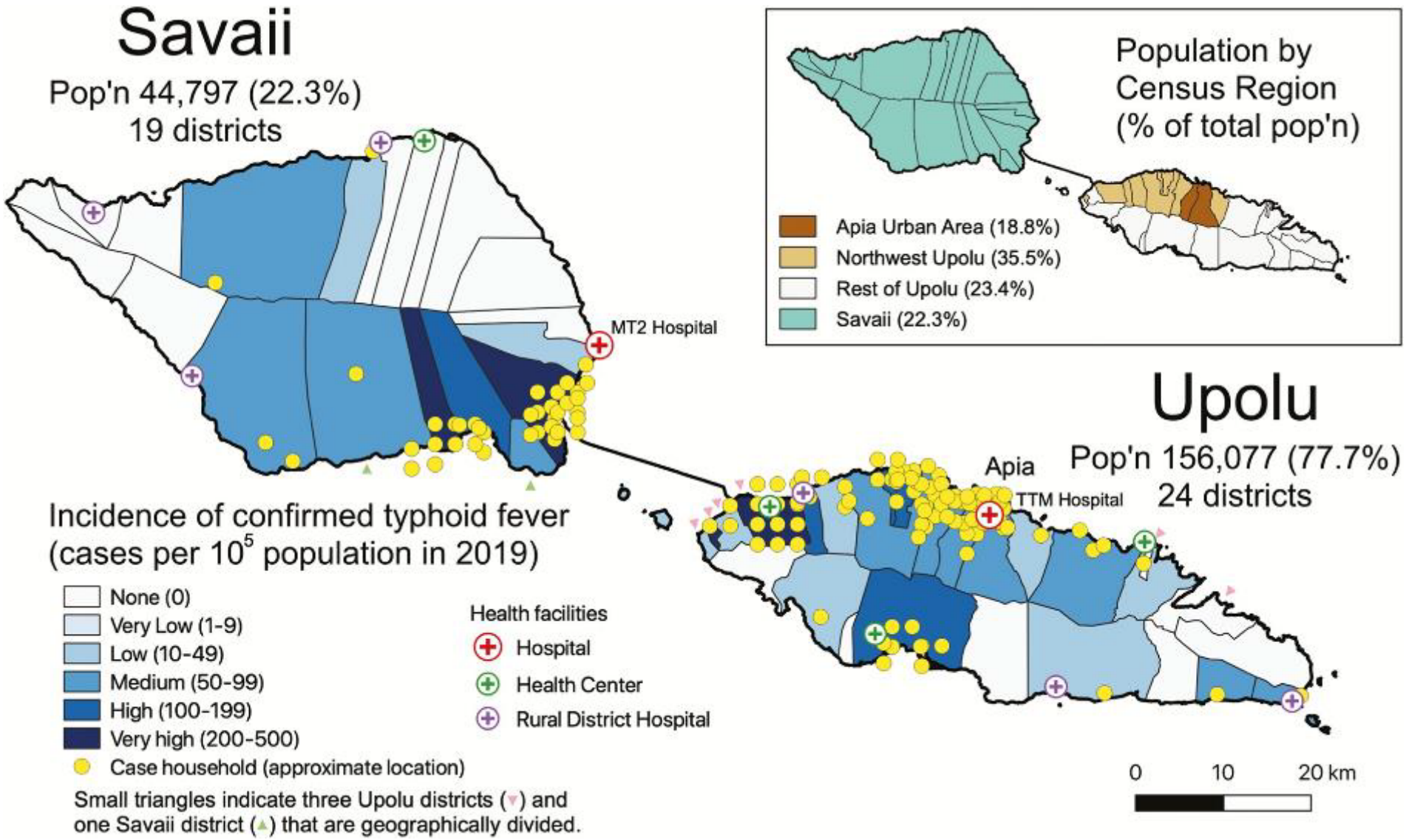
- **Preparatory Phase** (~24 months)
  - Strengthen clinical microbiology
  - Create epidemiologic investigation capability
- **Original Attack Phase Plan** (~3 years)
  - **Mass vaccination with Typbar-TCV of all Samoans 1-45 yrs of age**
  - **Routine toddler vaccination (Typbar-TCV, age 12 mos)**
  - **Ty21a live oral vaccine for persons > 45 years of age**
- **Consolidation Phase** (3-5 yrs)
  - Enhanced surveillance for residual cases
  - Environmental microbiology to detect *S*. Typhi in wastewater & sewage
  - **Intensive search to find all chronic carriers**
  - **Rx of chronic carriers** (Samoan strains are ciprofloxacin-sensitive)

Samoa Typhoid Epidemiologic SWAT Team activities

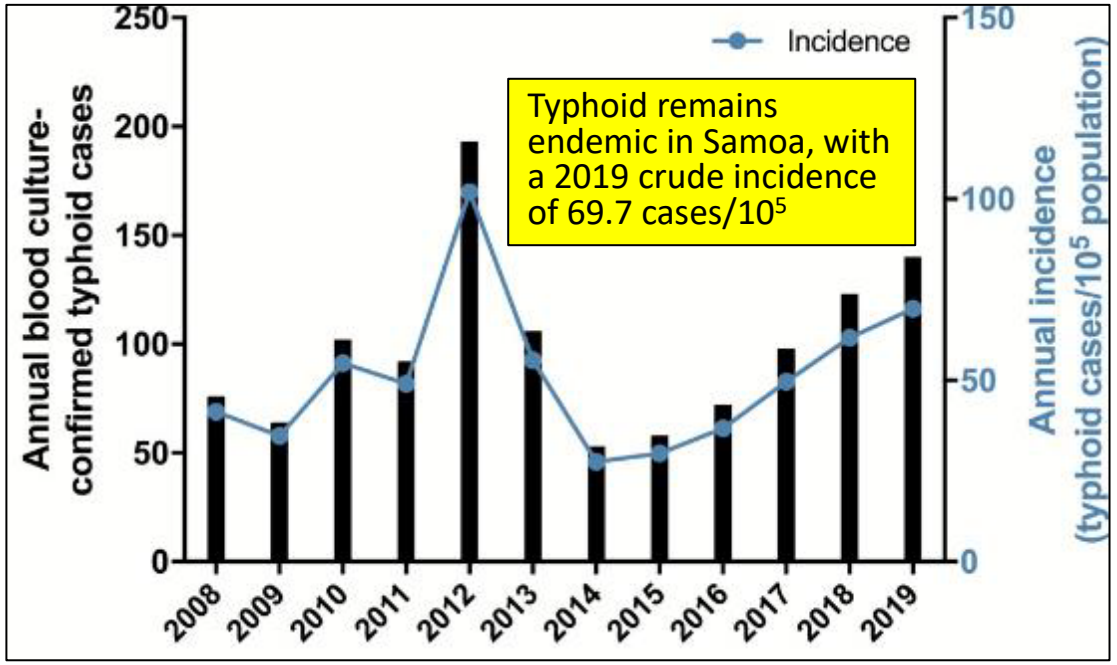
Expeditiously visit household (or school or workplace) of every confirmed typhoid case

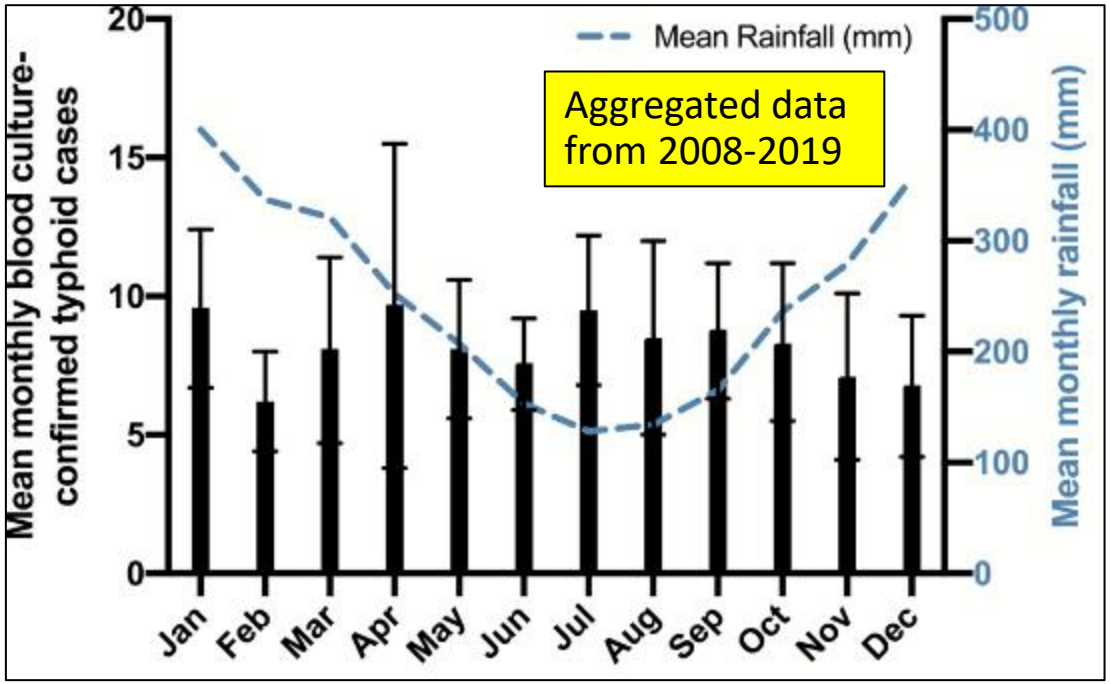
- Epidemiologic investigation, questionnaire
- **Determine water source & sanitation facility**
- **3 stool cultures** from all contacts
- **Detect subclinical acute & chronic infections**
- Serum from all adult contacts for **Vi serology**
- **RUQ ultrasound of adult contacts** to find gallstones using hand-held POCUS device
- Place **Moore swabs in septic tank** (or latrines) **and in intakes of untreated piped river water**
- MDU performs whole genome sequencing of *S.* Typhi isolates within 3 weeks

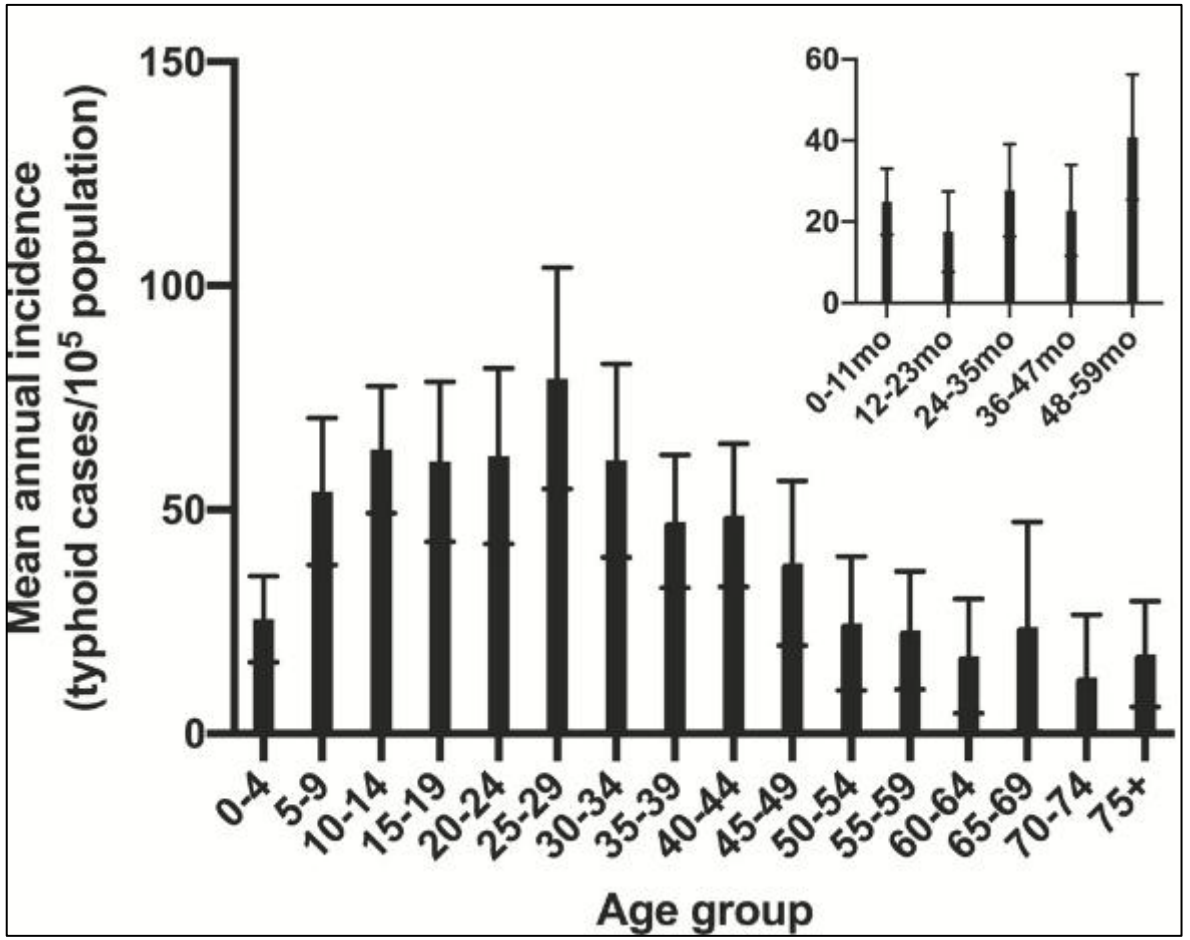
Typhoid in Samoa by Island and Region



Sikorski, et al. 2020 *Clin Infect Dis* 71(Suppl 2):S120–S126 (PMID: 32725232)







Typhoid incidence is low among young children < 5 years, increases steadily from ages 5-24 yrs, peaks in ages 25-29 yrs, and then declines.

Sikorski, et al. 2020 *Clin Infect Dis* 71(Suppl 2):S120–S126 (PMID: 32725232)

Savaii typhoid case clusters, June 19 – August 19, 2019

SALELAVALU

SALELOLOGA

SATUPAITEA

FAMILY I (SATUPAITEA/SALELOLOGA)
1. 21 yo M, BC+ on June 19, 2019
2. 13 yo M, BC+ on July 5, 2019
3. 17 yo F, BC+ on July 30, 2019
4. 18 yo M, BC+ on Aug 7, 2019

FAMILY O (SALELOLOGA/SALELAVALU)
1. 14 yo M, BC+ on June 22, 2019; he was ill while visiting family on Upolu in mid-June 2019
2. 1 yo M, BC+ on July 17, 2019
3. 9 yo F, BC+ on July 18, 2019
4. 17 yo F, BC+ on July 22, 2019

FAMILY P (SALELOLOGA)
1. 15 yo M, BC+ on July 23, 2019
2. 14 yo M, BC+ on Aug 1, 2019

FAMILY S (SALELAVALU)
1. 36 yo M, BC+ on June 27, 2019
2. 15 yo, F, BC+ on Aug 15, 2019

NON-FAMILY CASES (SALELAVALU)
1.7 yo F, BC+ on July 29, 2019
2.9 yo M, BC+ on Aug 1, 2019

→

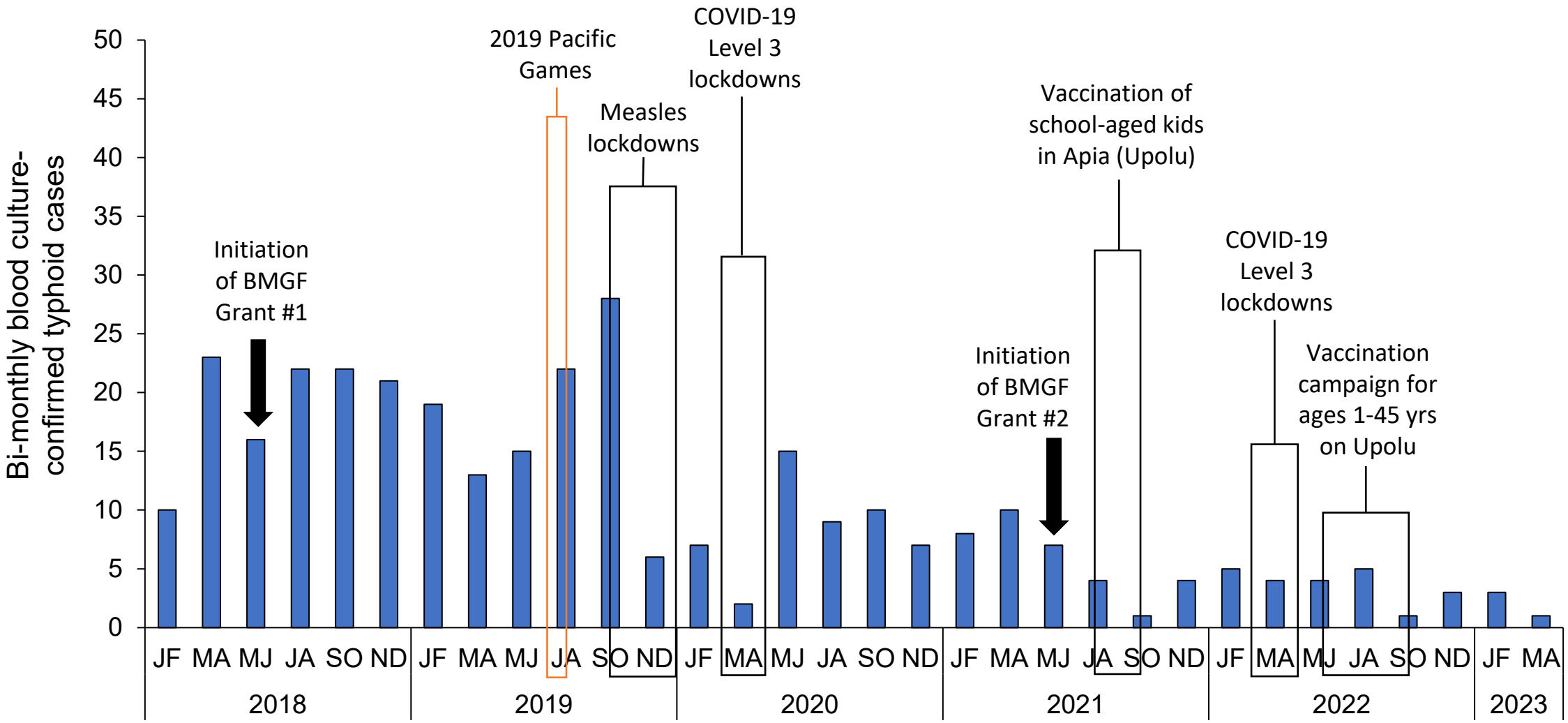
FAMILY F/O (VAILELE, UPOLU) (relatives of family O)
1. 1 yo M, BC+ on July 11, 2019; his 14 yo M uncle from Savaii, while ill with fever and malaise, visited these relatives on Upolu in June 2019
2. 23 yo M, BC+ on Aug 19, 2019. Father of the 1 yo M Upolu case; he visited Savaii during the 2nd week of Aug 2019

Rationale for vaccination against typhoid in Samoa

Even if a remediable mode of amplified transmission cannot be detected in Samoa, the susceptibility of Samoans to typhoid fever can be greatly diminished by the use of vaccines:

- Vi-TT for all Samoans age 1 to 45 yrs
- Vi-TT for all toddlers age 12 mos
- Ty21a live oral vaccine for persons age > 45 years (doesn't stimulate Vi antibodies)

Total blood culture-confirmed typhoid fever cases (all ages) by 2-month intervals, on Upolu, January 2018 through April 2023



Definitions of CONTROL and ELIMINATION of TF in Samoa

- **CONTROL** - <5 autochthonous cases/10^5/yr
  - Initially in priority target age groups (0-19 yrs; 20-45 yrs)
  - Ultimately in all ages (including >45 years)
- **ELIMINATION** - 0 autochthonous cases/10^5/yr
  - Systematic search for chronic typhoid carriers in Samoans >45 years
    - RUQ POCUS, stool cultures, Vi serology
    - Rx with 4 wks of oral ciprofloxacin or 2 weeks of i.v. ampicillin
    - Monitor all chronic carriers annually; health education

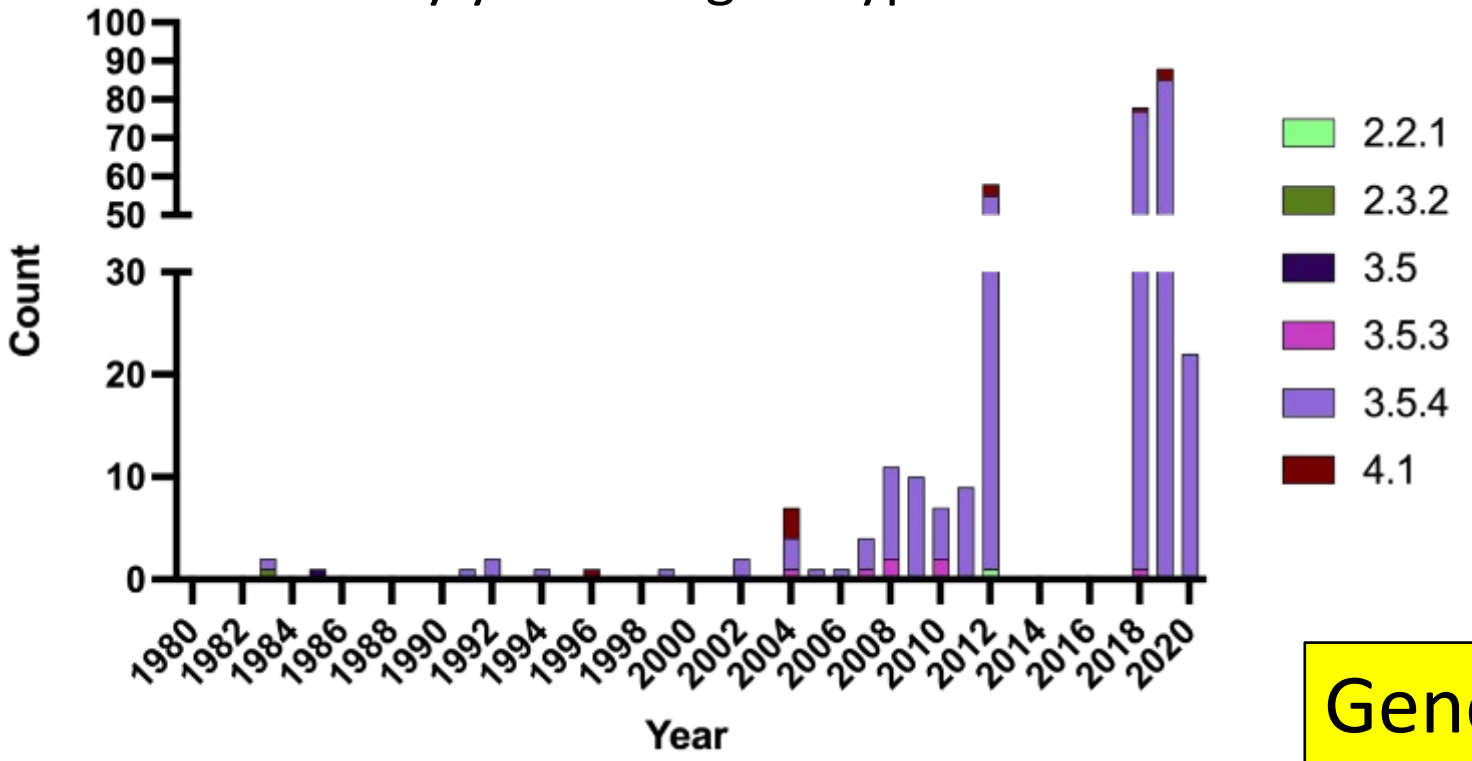
Annual Total Typhoid Cases among Upolu Residents, by Age Group and Year

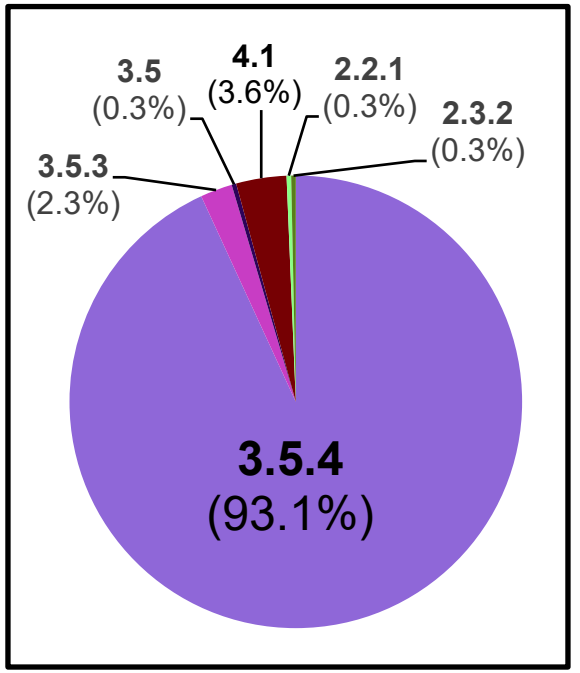
	All ages		0-4 yrs		5-19 yrs		20-45 yrs		>45 yrs	
Year	Cases	Inc/10^5	Cases	Inc/10^5	Cases	Inc/10^5	Cases	Inc/10^5	Cases	Inc/10^5
2018	114	73.1	6	28.8	44	83.0	49	98.4	15	46.7
2019	103	65.5	9	42.8	39	72.9	39	77.6	16	49.4
2020	50	31.5	7	33.0	18	33.3	19	37.4	6	18.3
2021	34	21.2	3	14.0	13	23.8	15	29.3	3	9.1
2022	22	13.6	0	0	7	12.7	13	25.1	2	6.0
2023*	4	2.4	0	0	0	0	4	7.7	0	0

* January through April

What *S.* Typhi genotypes are in Samoa?

306 Samoan *S.* Typhi from 1983-2020, by year and genotype





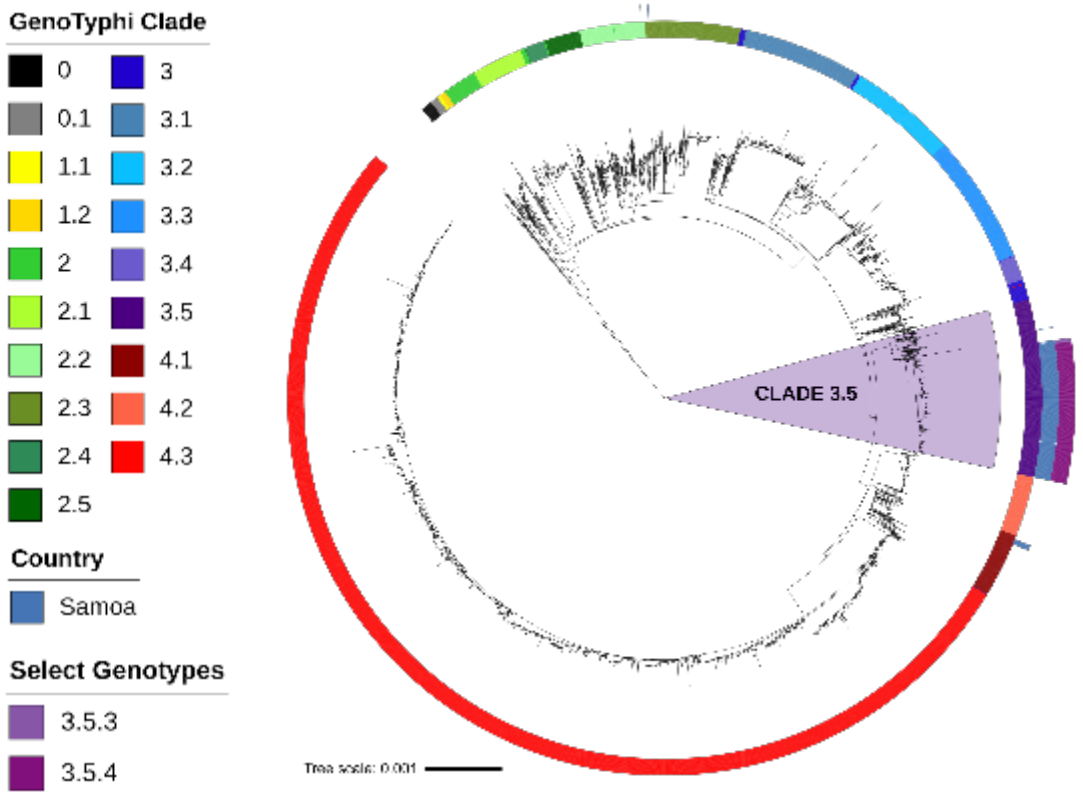
Genotypes 3.5.4/3.5.3 comprise 95.4% (292/306)

Sikorski et al., *mBio.* 2022 (5):e0192022. PMID: 36094088

Dyson & Holt, *J Infect Dis*. 2021;224(12 Suppl 2):S775-S780. PMID: 34453548

How do Samoan *S.* Typhi genotypes compare globally?

306 Samoan *S.* Typhi from 1983-2020
versus 4,934 global *S.* Typhi



Maximum-likelihood phylogeny

Genotype 3.5.3 is nested within genotype 3.5.4

Genotype	Samoa	Non-Samoa
3.5.4	285	1*
3.5.3	7	1*
4.1	11	137
2.2.1	1	19
2.3.2	1	49
3.5	1	92
Others	0	4,635
Subtotals	306	4,934
Total N	5240	

**Australian isolations of unknown travel origin*

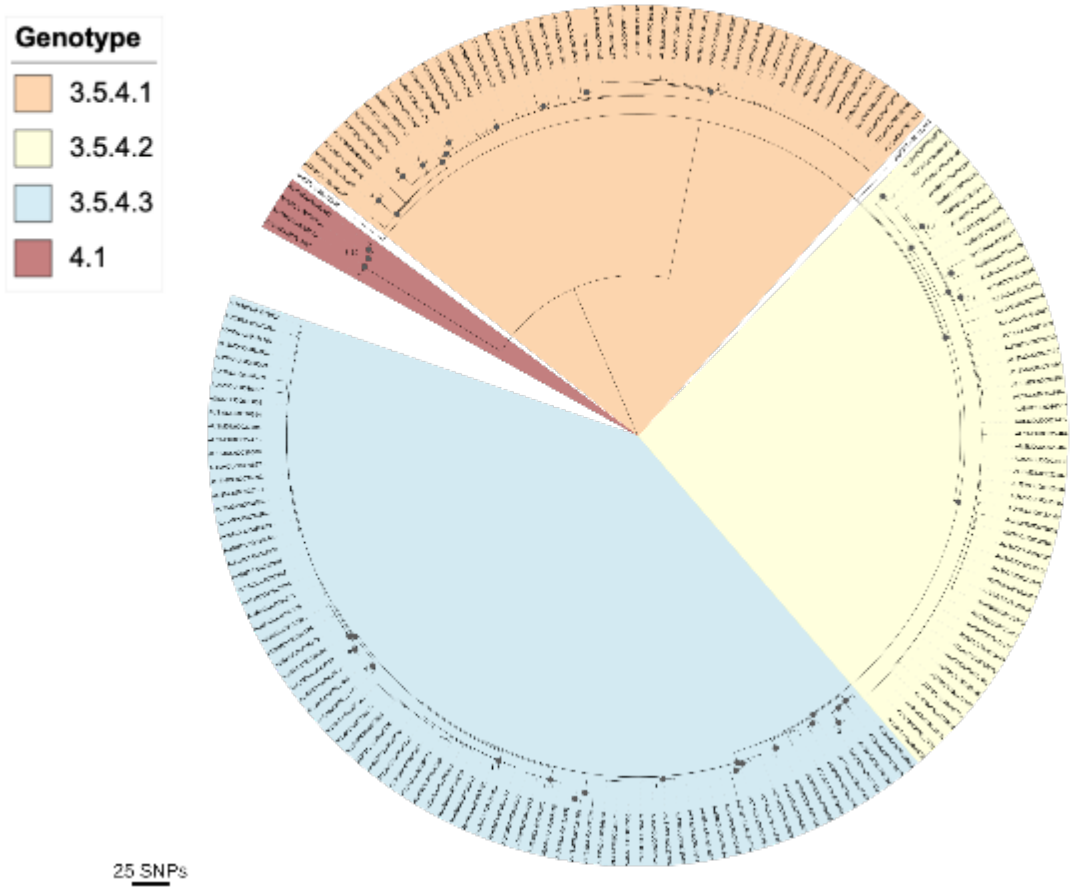
Genotypes 3.5.4/3.5.3 are essentially exclusive to Samoa

Sikorski et al., *mBio.* 2022 (5):e0192022. PMID: 36094088
Dyson & Holt, *J Infect Dis*. 2021;224(12 Suppl 2):S775-S780. PMID: 34453548

Special Acknowledgement: Corin Yeats, PhD and Jason Sahl, PhD

Sub-lineages for epidemiologic analysis

186 Samoan *S.* Typhi from 2018-2020



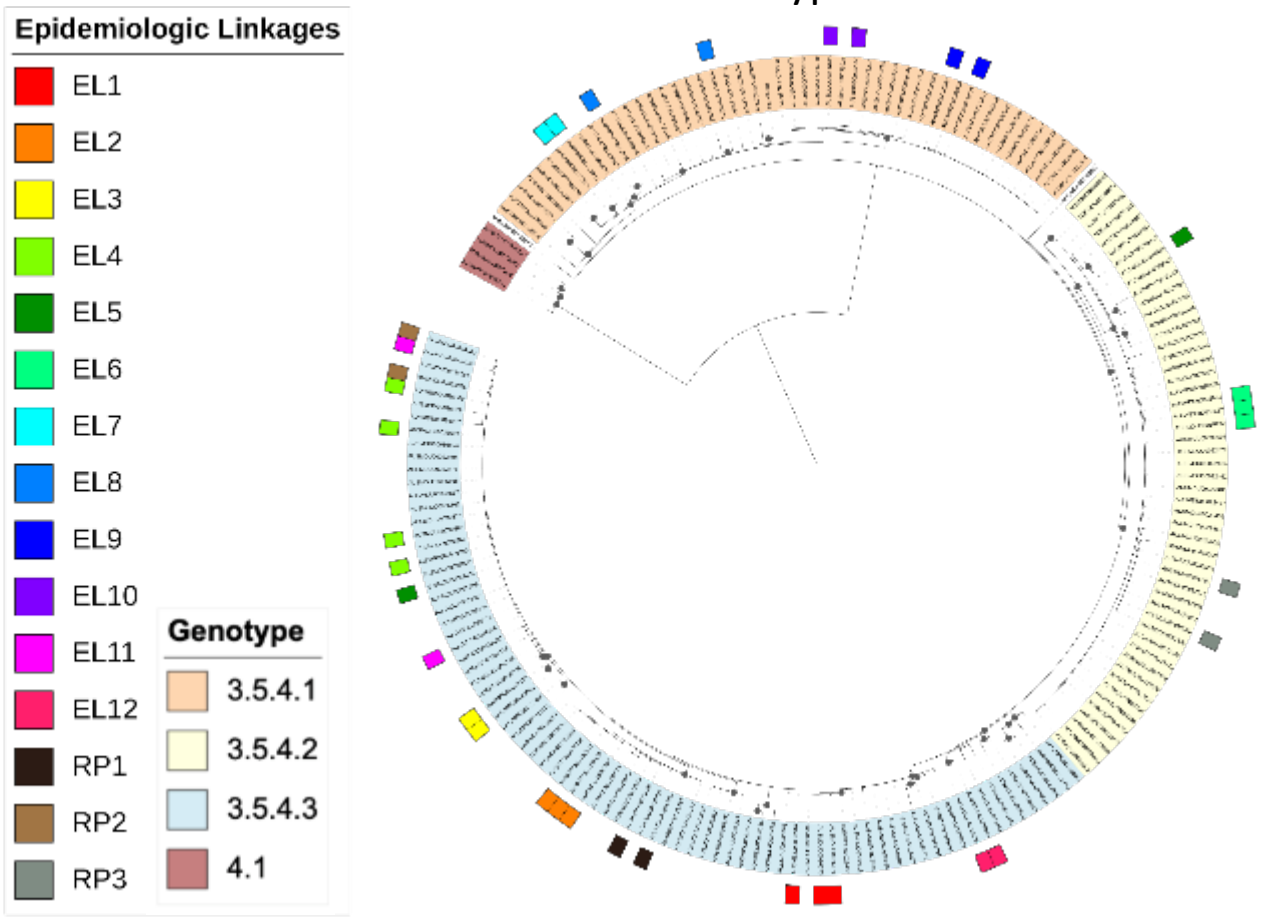
Maximum-likelihood phylogeny

- Molecular subtyping by genotype and sub-lineage
- **Hypothesis**: similar isolates represent a network or chain of infection via a common vehicle and/or source

Sikorski et al., *PLoS Negl Trop Dis.* 2022 Oct 17;16(10):e0010348. PMID: 36251704

WGS and epidemiologic linkages of infections

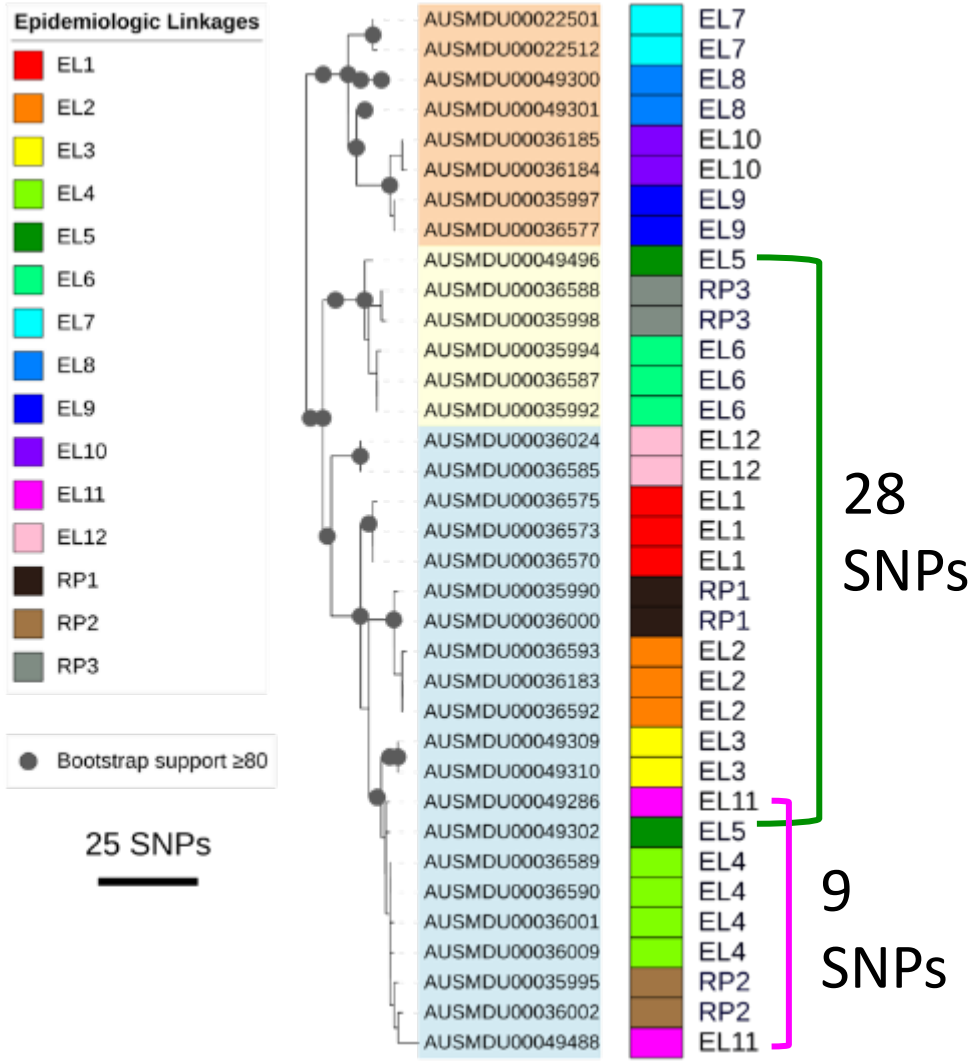
186 Samoan *S.* Typhi from 2018-2020



- **Epidemiologic linkages**, e.g.
  - Familial contact; same or different household
  - Known recent gathering
  - Repeat positive culture after 1 month
- **Dataset**: 12 examples of epidemiologic linkages (EL) and 3 repeat positive (RP) cultures from same individual ~1 month apart

Sikorski et al., *PLoS Negl Trop Dis.* 2022 Oct 17;16(10):e0010348. PMID: 36251704

Epidemiologic linkages are supported by SNP cutoffs



Phylogeny supports 10/12 epidemiologic linkages with 0-3 SNP differences

EL5: different sub-lineages, 28 SNPs
EL11: same sub-lineage, 9 SNPs

SNP cutoff is not defined for *S.* Typhi

- ≤10 for *S. enterica* (Burnsed, 2019)
- ≤4 for *S.* Typhi (Schürch, 2018)

1-3 SNPs separate repeat positives cultures from same individual ~1 month apart

Sikorski et al., *PLoS Negl Trop Dis.* 2022 Oct 17;16(10):e0010348. PMID: 36251704

Burnsed, et al. *Epidemiol Infect.* **2019**; 157:e11
Schürch, et al. *Clin Microbiol Infect.* **2018**; 24:350-354

Genomic epidemiology during Consolidation Phase

- Unique genotypes (3.5.4/3.5.3) permit monitoring for importation
- Validated WGS framework and SNP typing to compare relatedness:

Isolate Source*	Epidemiologic Tool
Sparse cases	-Blood culture surveillance (central and peripheral)
Asymptomatic shedders (“carriers”)	-Household “SWAT team” investigations -Village-level POCUS surveys for carriers
Environment	-Moore swabs in septic tanks, sewers, and waterways

*Culture-based methods required


A sunset on typhoid in Samoa? Stay tuned…