Insights into Drug Resistance Tuberculosis in Ghana / West Africa

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INTEGRI PROCEDAMUS

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Background Information AboatGhana

- WHO estimates for Ghana:
- TB incidence of 133 per 1
- Part of the 30 high TB/HIV
  2021
- Estimated P% of new TB
  TB = 1.9%
- Estimated P% of previous
  with MDR/RR-TB = 3.6%
- More than 20% of TB is caused by
  Mycobacterium africanum (L5 and L6)

- BPaL and BPaLM rolled out in Ghana – since
  3
- all regions of Ghana currently
- old regimen have gradually been
  PaL & BPaLM
- loped for recording all adverse
  ating MDR cases
- d by the FDA

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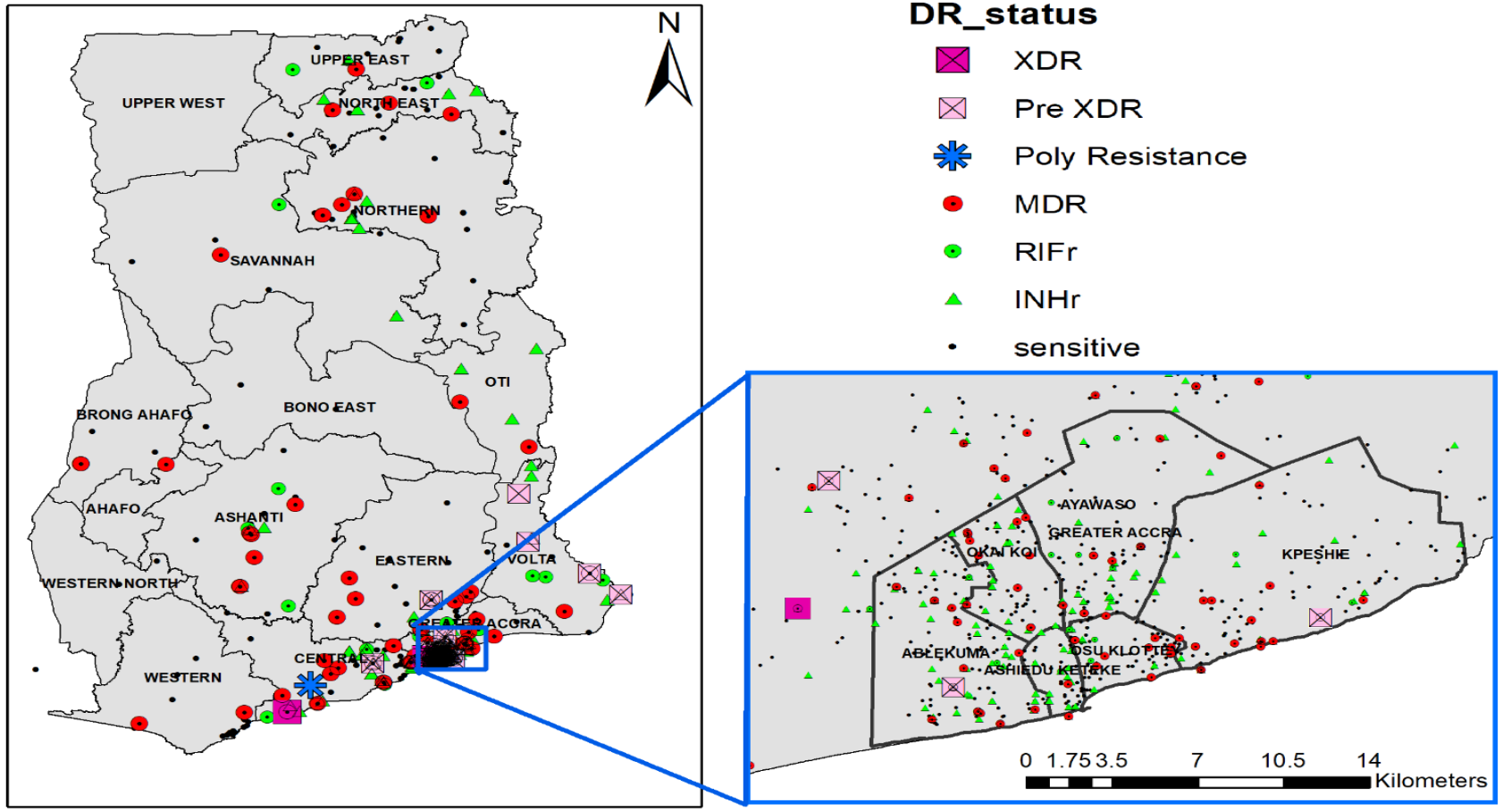
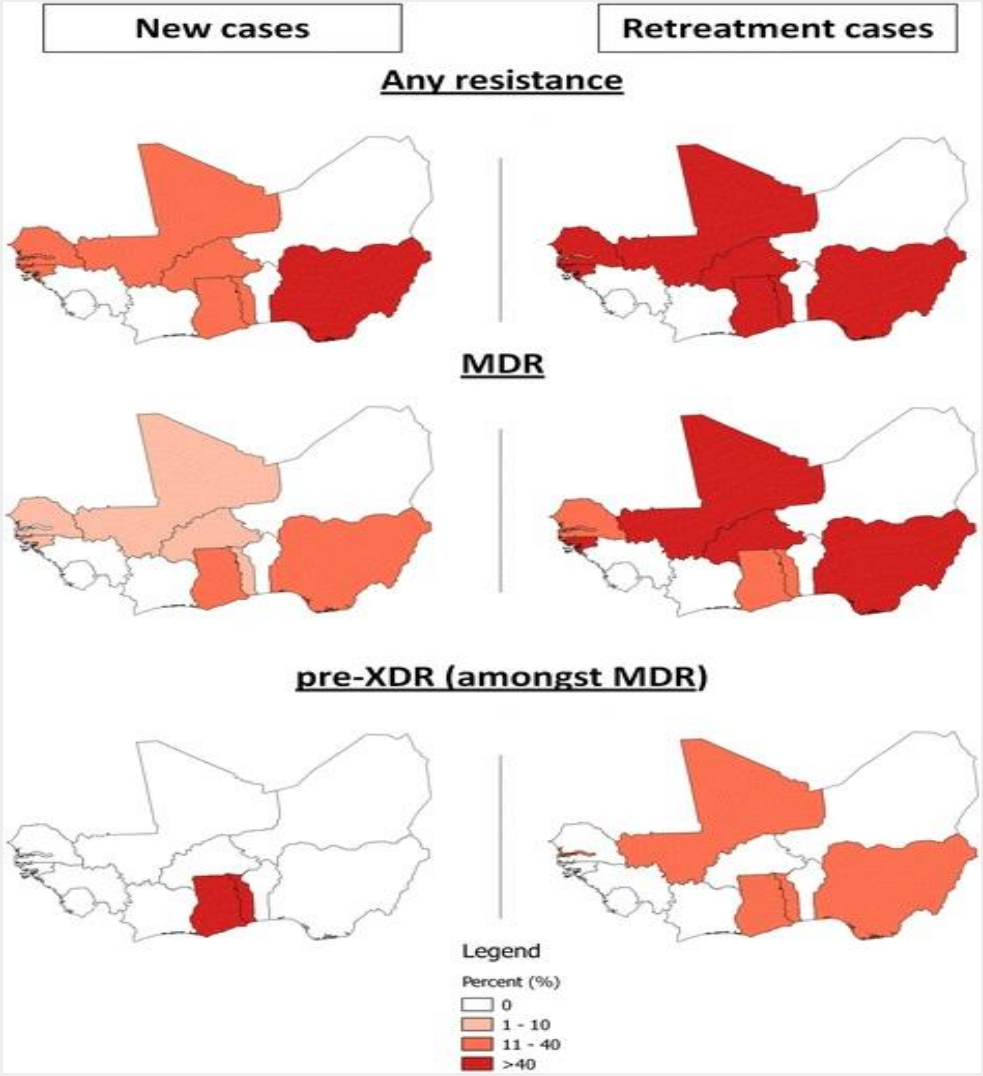
Spread of DR-TB across Ghana



Accra metropolitan asembly

The Emerging Threat of DR-TB in West Africa

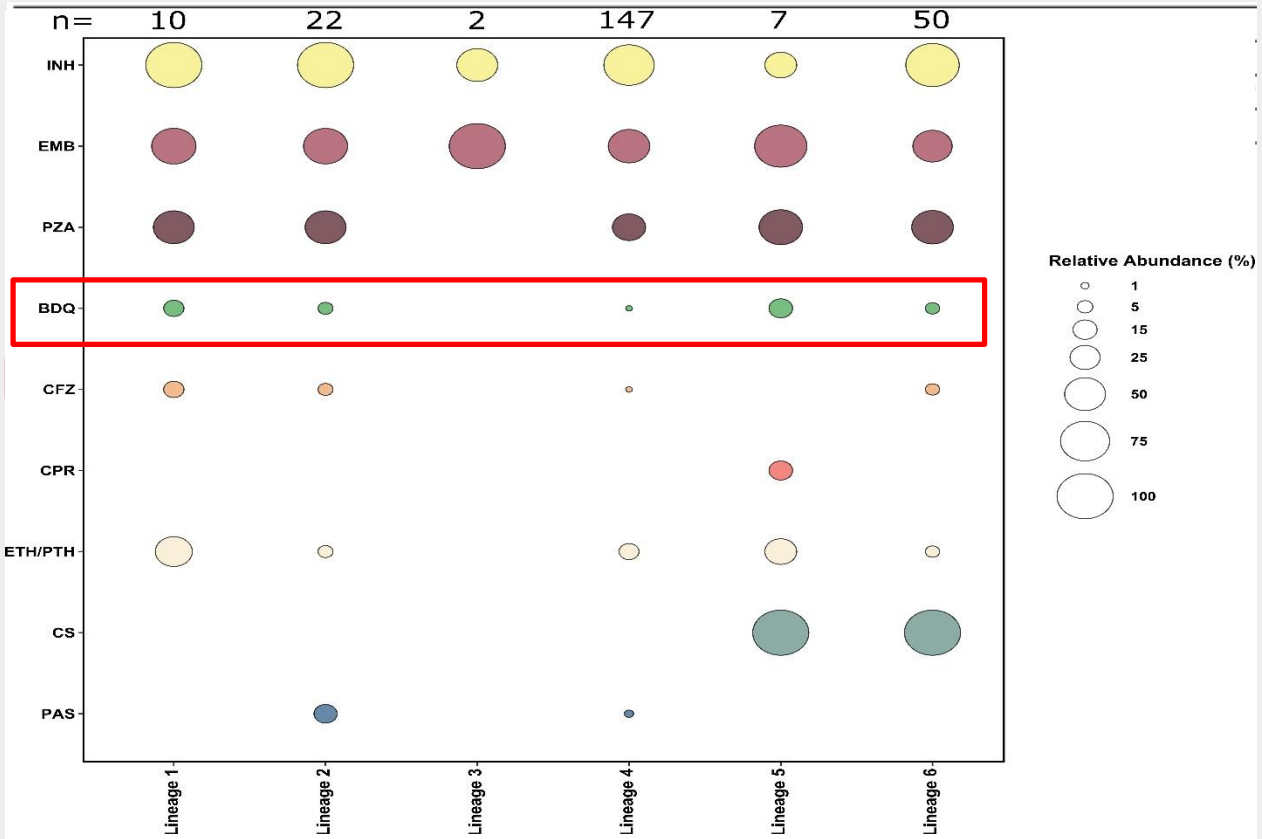
DR-TB in WANETAM study sites



Gehre et al

Blankson et al

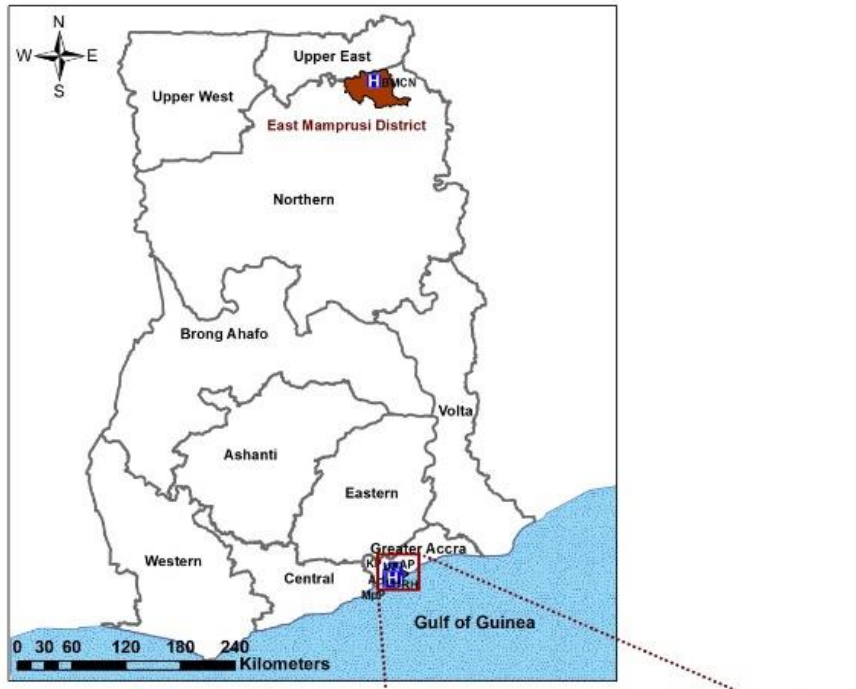
Second-line DR in West Africa

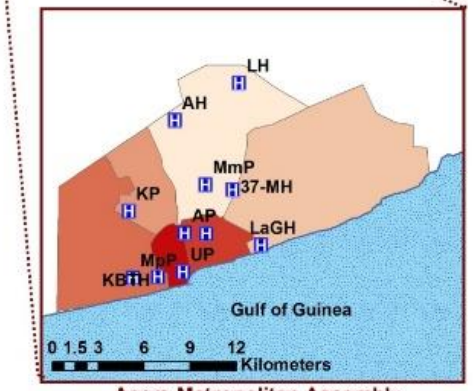


- Resistance prevalence:
  - INH= 82% (*n* = 196)
  - EMB= 53% (*n* = 126)
  - PZA= 39% (*n* = 92)
- 5 strains were resistant to BDQ/clofazimine (CFZ) based on mutations in ***Rv0678***

Distribution of Drug resistance among MTBC Isolates

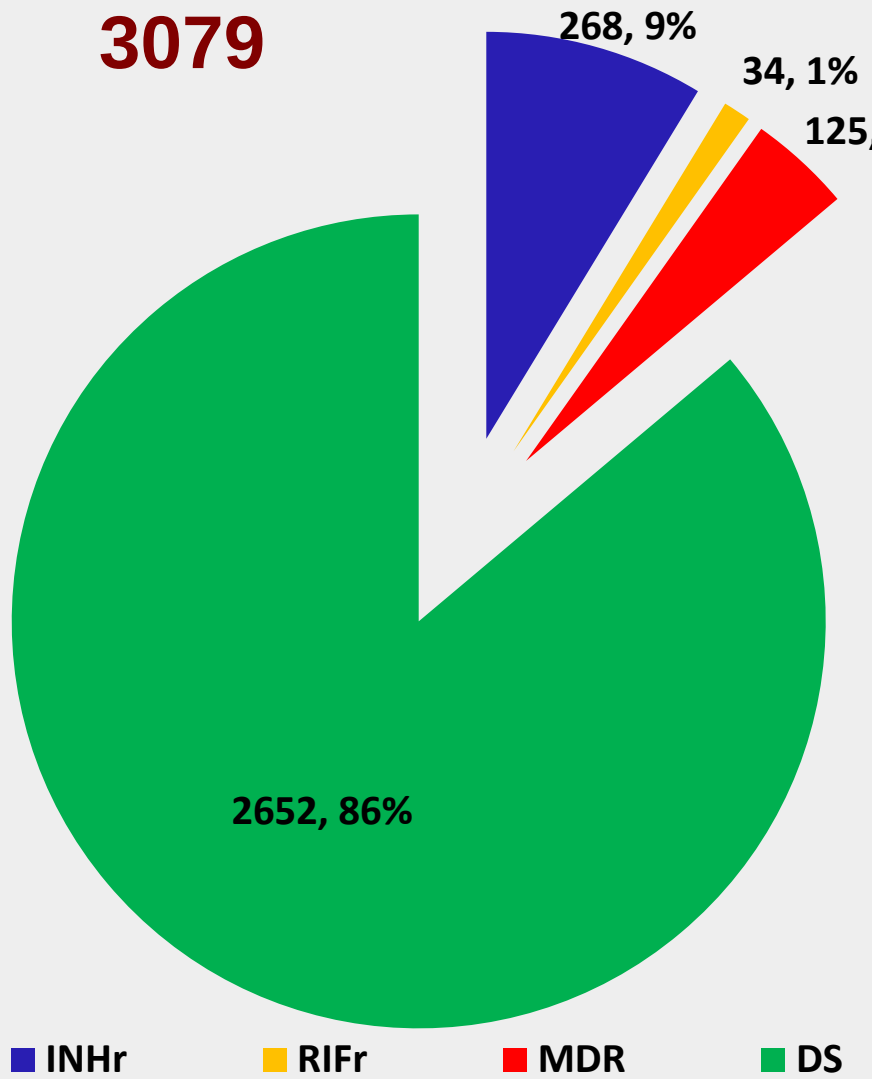
Urban vs Rural Setting





Accra Metropolitan Assembly

Legend
- Location of health facilities
- Regional_Boundary
- Sea



- 14% of the isolates were resistant to at least one of the drugs tested
- Approximately 4% MDR-TB cases

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Drug resistant conferring and compensatory mutations

RIF Resistance Isolates

Target	Mutation	Number	Other mutations
rpoB	Q432P	1;1.5%	
	Q432P & I491S	1;1.5%	
	Q432K	1;1.5%	
	D435V	11;16.7%	
	D435Y	1;1.5%	
	S441L	1;1.5%	
	H445R	3;4.5%	
	H445C	2;3.0%	
	H445D	4;6.1%	
	H445Y	6;9.1%	
	S450L	**32;48.5 %**	*1: rpoB* S388L, *1: rpoB* Q409R*, *rpoC* ;2:G332R, 3:V483G
rpoC	G332R	2;3.0%	*rpoB*; S450L
	V483G	3;4.5%	*rpoB*; S450L

INH Resistant Isolates

Target	Mutation	Number
inhApro	-8T/C	7;3.5%
	-15C/T	28;14.6%
	-17G/C	1;0.5%
katG	S315T & I317V	1;0.5%
	S315T	**142;70.3%**
inhA	G204D*	16;7.2%
	V78A	1;0.5%
ahpCpro	-54C/T	1;0.5%
	-88G/A*	2;1.0%
	-142G/A*	1;0.5%
ndh	V117I*	2;1.0%

* Represents Novel mutations

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DR and resistance conferring mutations are driven by specific MTBC genotypes

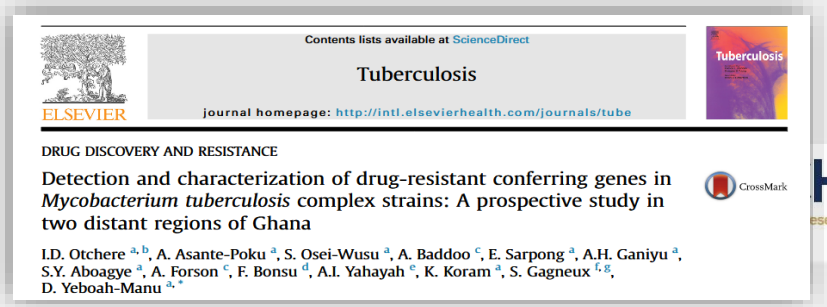
Association of drug resistance with Specific MTBC genotypes

Resistance	Cameroon (806)	Ghana (195)	OR	95% CI	p-value
INH	54 (6.7%)	43 (22.1%)*	0.25	0.16–0.40	0.0000
RIF	19 (2.4%)	12 (6.2%)*	0.37	0.17–0.85	0.0103
MDR	13 (1.6%)	9 (4.6%)*	0.34	0.13–0.91	0.0240
ANY	60 (7.4%)	46 (23.6%)*	0.26	0.17–0.41	0.0000
	MAF WA 1 (165)	Ghana (195)			
INH	25 (15.2%)	43 (22.1%)	0.63	0.35–1.12	0.1059
RIF	10 (6.1%)	12 (6.2%)	0.98	0.37–2.56	0.9998
MDR	10 (6.1%)	9 (4.6%)	1.33	0.47–3.81	0.6384
ANY	25 (15.2%)	46 (23.6%)*	0.58	0.32–1.02	0.0472
	MAF WA 2 (107)	Ghana (195)			
INH	6 (5.6%)	43 (22.1%)*	0.21	0.07–0.52	0.0001
RIF	1 (0.9%)	12 (6.2%)*	0.144	0.00–1.00	0.0372
MDR	1 (0.9%)	9 (4.6%)	0.19	0.00–1.45	0.1040
ANY	6 (5.6%)	46 (23.6%)*	0.19	0.06–0.48	0.0000

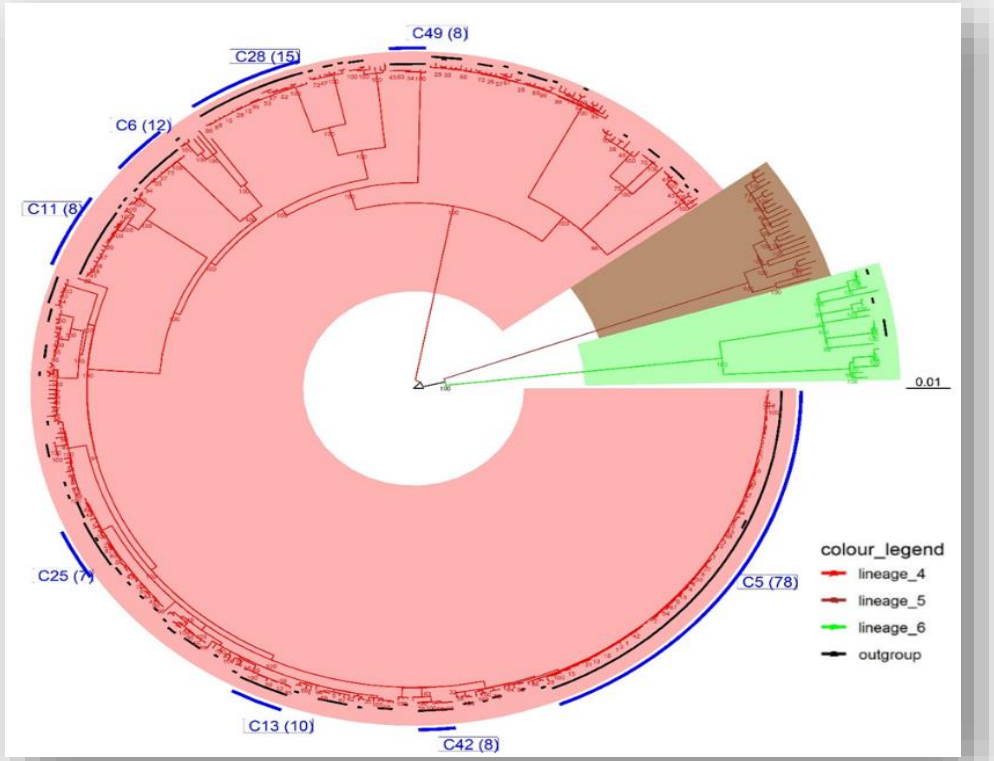
MAF WA 1: *M. africanum* West Africa 1 (Lineage 5).
MAF WA 2: *M. africanum* West Africa 2 (Lineage 6).
* Significantly higher.

- **Bedaquilin-resistance?**
  - *Rv0678:* No mutation seen
  - *atpG*: Y220S (L5-specific)
  - *atpH:* Q40K (2 isolates) & E351D (2 isolates).
  - *pepQ*: G96R (1 isolate)
  - *Rv1979c*: L14R (3 isolates), A50T (2 isolates) & D286G (5 isolates)
- **Pretomanid resistance?**
  - *fbiA*: I208V (1 isolate)
  - *fbiB/C* : No mutation
  - *fgb1*: K270M (5 isolates)
  - *ddn*: D113N (L5)

Ghana genotype of L4 causing about 13% of TB in Ghana is associated with drug resistance

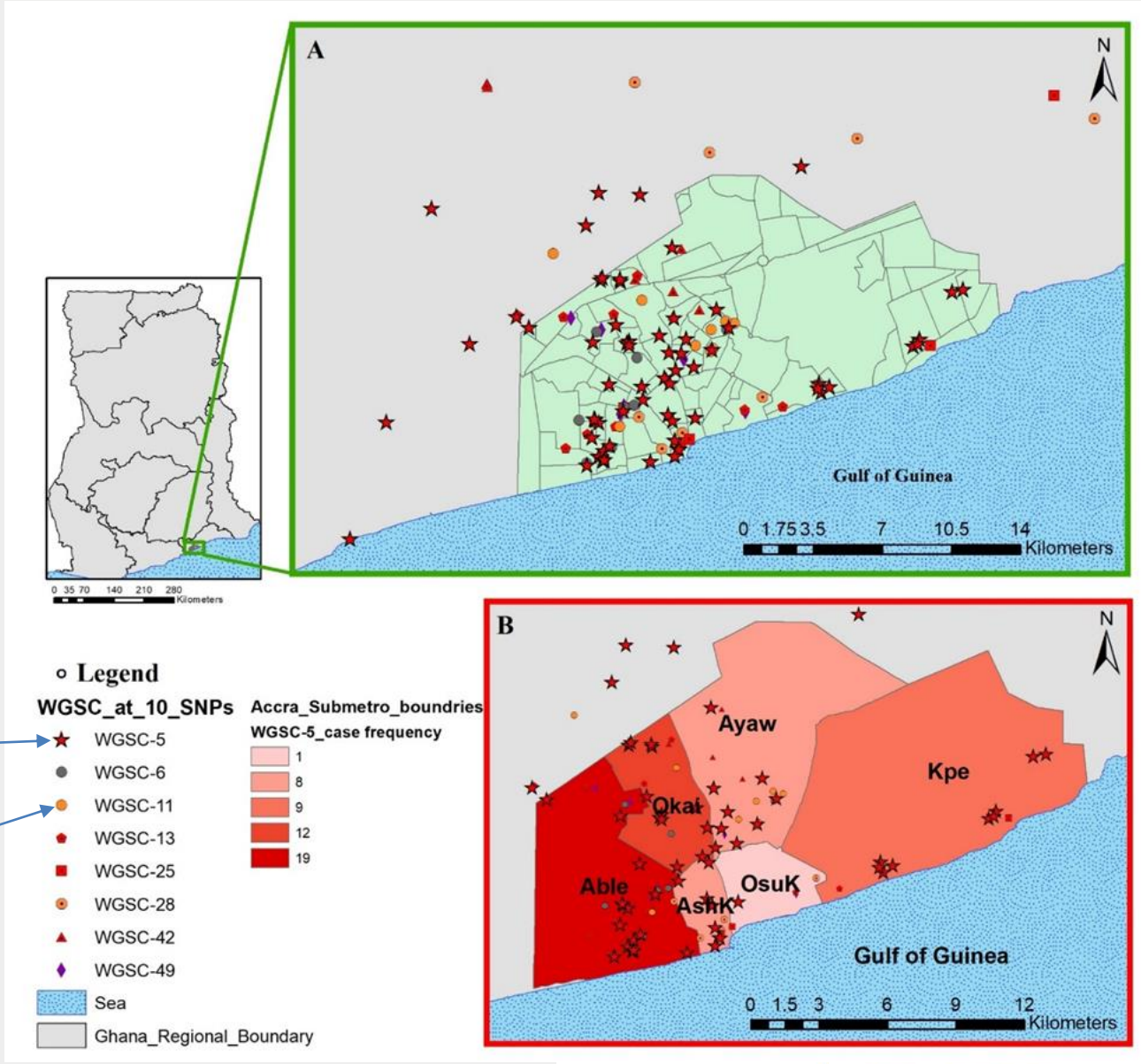


Hotspots of recent TB transmission in Accra, Ghana



Largest recent transmission cluster predominantly in Ablekuma sub-district

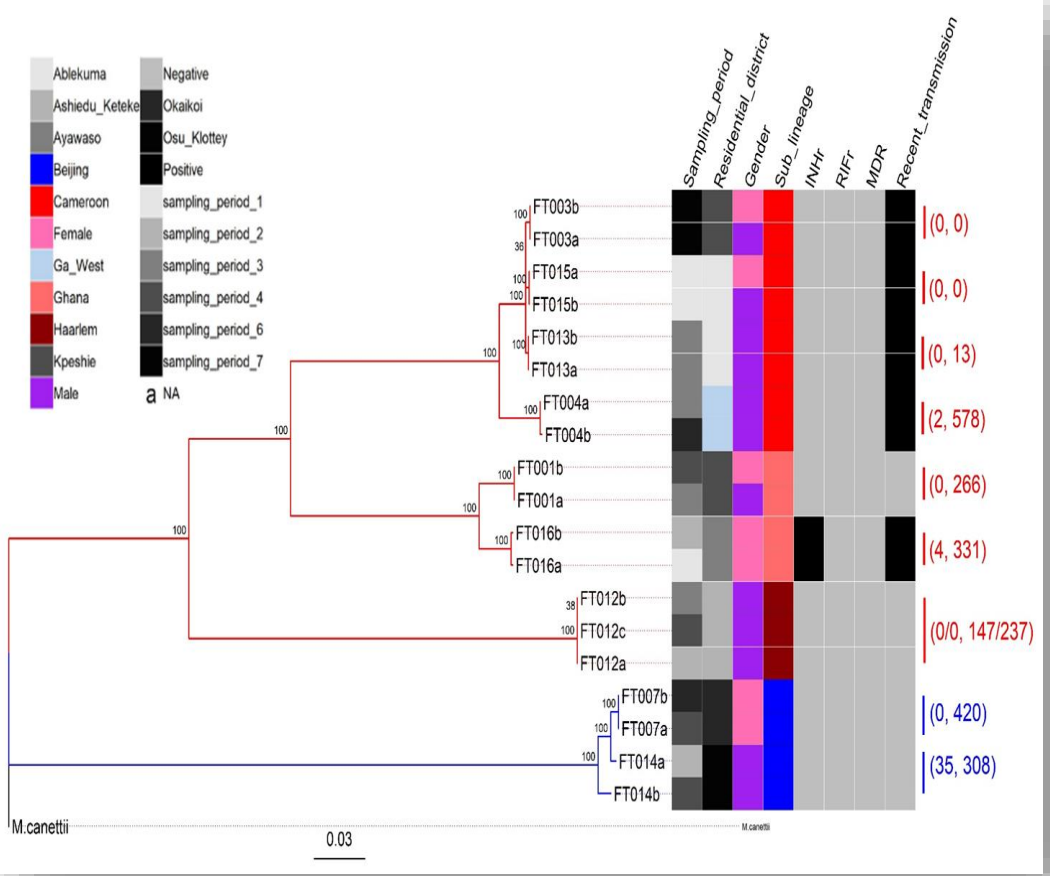
Isoniazid transmitting cluster predominantly in Ayawaso sub-district



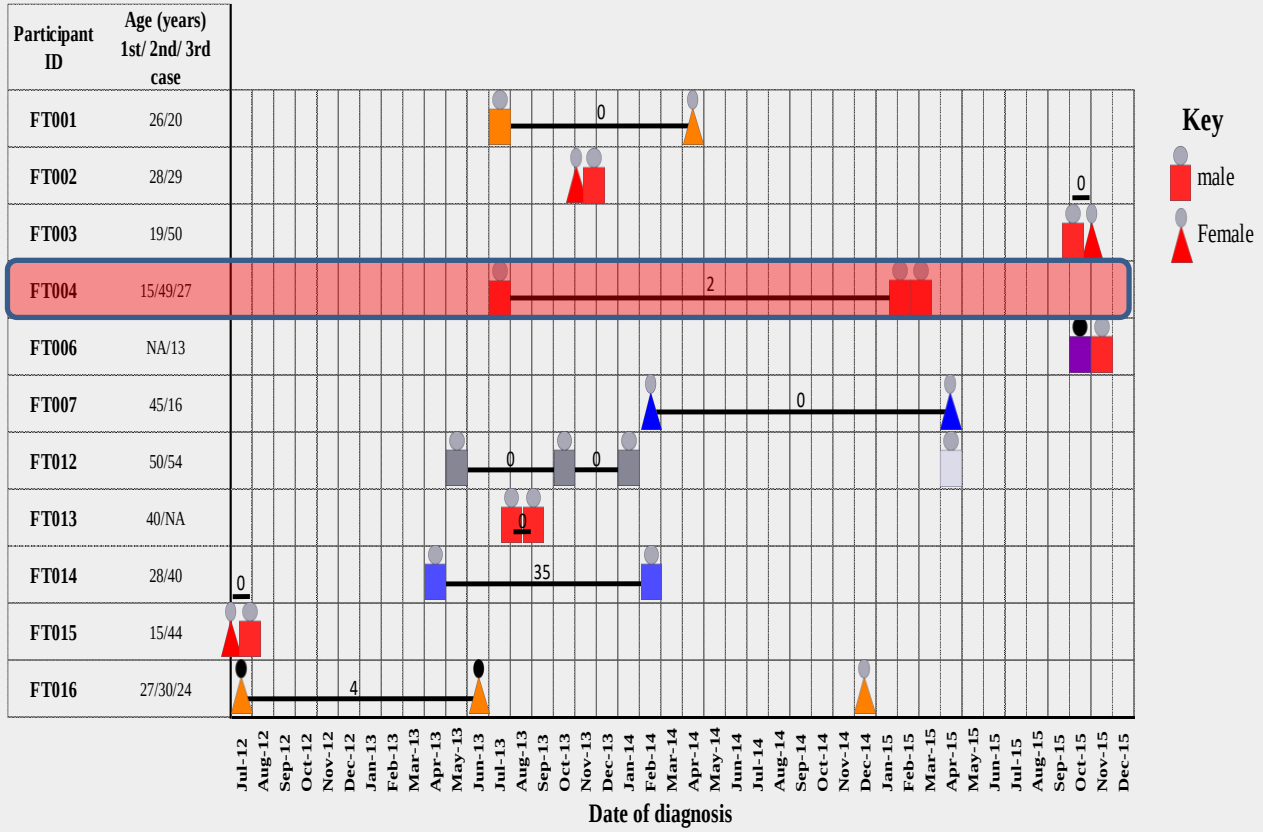
Using genomics to support both diagnosis and epidemiology

Asare P…Yeboah-Manu D. (2020). Frontiers in Medicine

Evidence of Household Recent TB Transmission



Phylogenetic reconstruction showing the genomic relationship between 19 MTBC isolates from 9 households

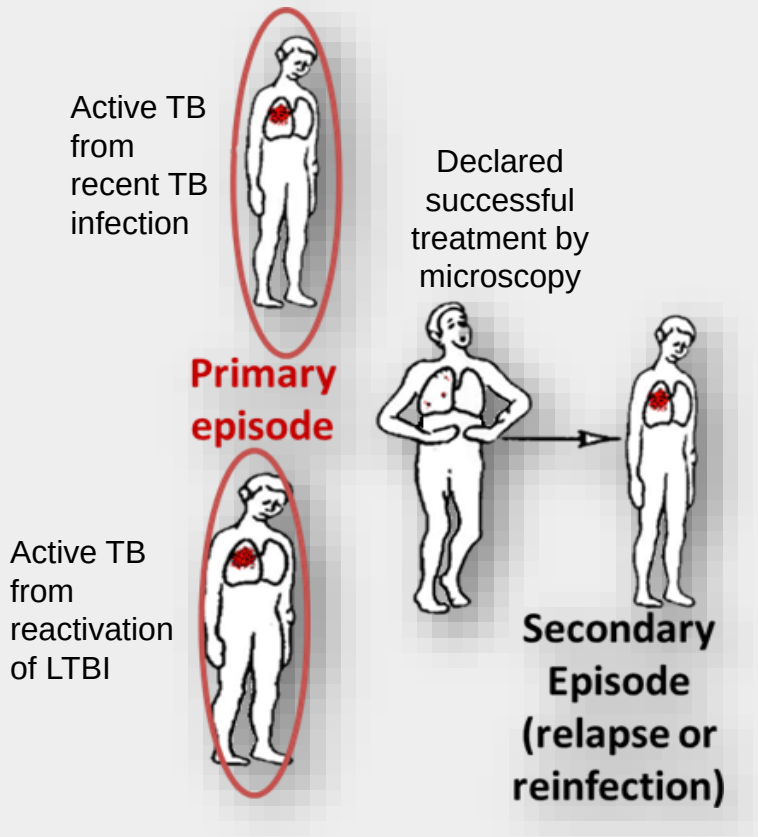


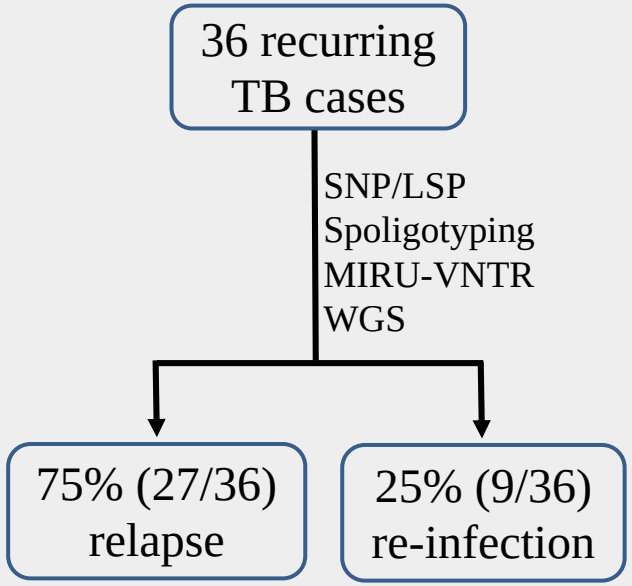
Time till event of household related tuberculosis cases

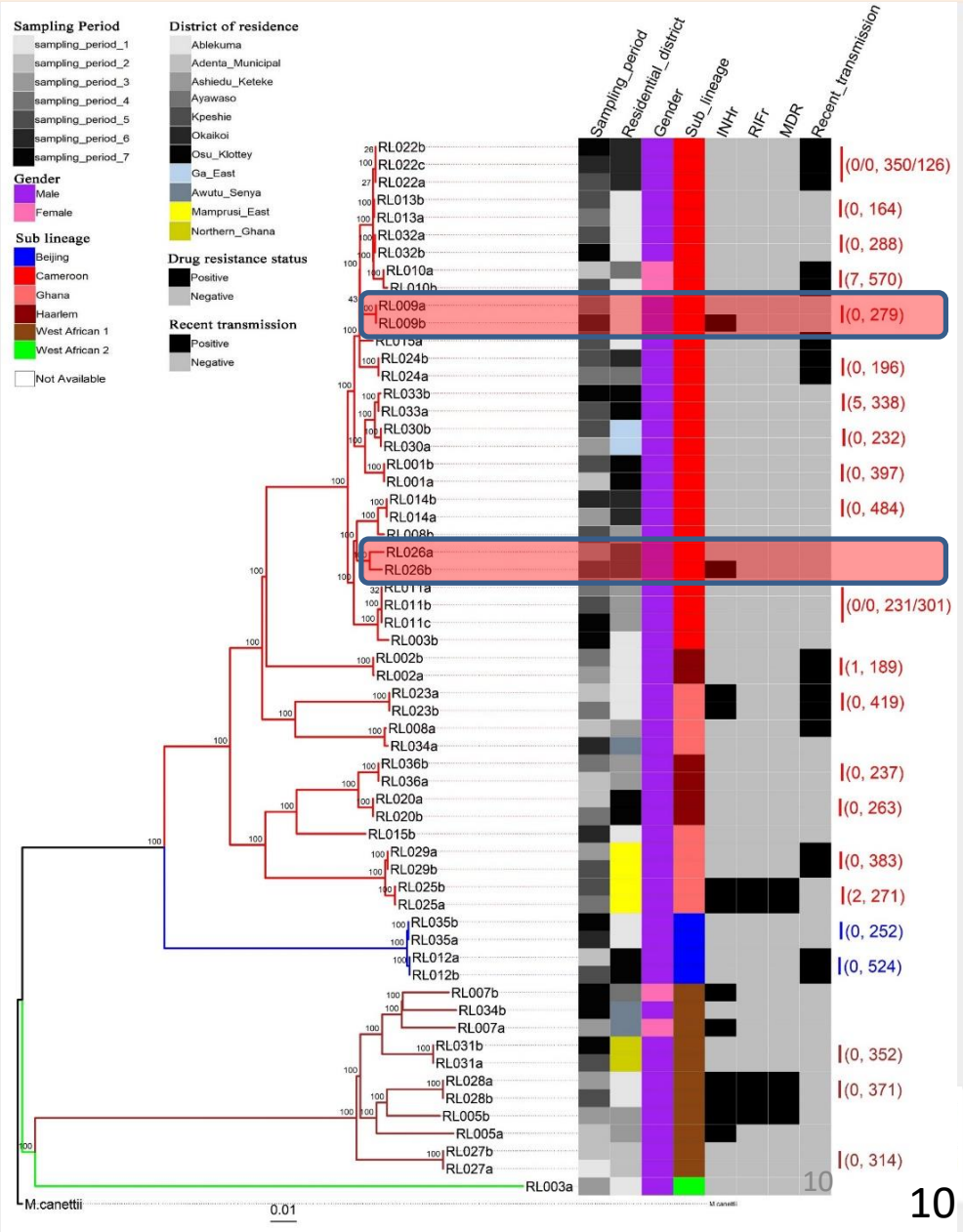
Need for contact screening

Asare …. Yeboah-Manu, 2021, *Int J Infect Dis*

Delineating the Occurrence of Recurrent TB in Ghana







Patients with recurring TB are largely due to relapse (inadequate treatment) of previous infection

Asare …. Yeboah-Manu, 2021, *Int J Infect Dis*

Community Engagement

Educating Market women on TB

Student Engagement on TB/DR-TB

Explaining TB in Local Language (Twi) on National TV

Free Health Screening at identified hotspots of transmission

Education on TB during the free health screening

MDR Survivor shared her story to sensitize others of TB

Take Home Message

- Lineage diversity is very important ==>Geography
- Evidence of Community and household spread
- Intensify public education to improve early case reporting
- Observed relapse rate calls for measures to improve compliance and treatment monitoring

THANK YOU