Community-level variation in TB testing history: analysis of a prevalence survey in Blantyre, Malawi

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Abstract

Setting

Equitable access to tuberculosis testing is vital for achieving global diagnosis and treatment targets, but access to diagnostic services is often worse in poorer communities. The SCALE survey estimated TB prevalence in Blantyre city, Malawi, and recorded previous engagement with TB services.

Objective

To explore local variation in prevalence of ever-testing for TB in Blantyre and investigate potential socio-economic drivers.

Design

We fit a mixed effects model to self-reported prior TB testing from survey participants across 72 neighbourhood clusters, adjusted for sex, age and HIV status and with cluster-level random intercepts. We then evaluated to what extent cluster-level variation was explained by two alternate poverty indicators.

Results

We observed substantial variation between clusters in previous TB testing, with little correlation between neighbouring clusters. Participants in poorer households had, on average, lower odds of previous testing, yet adjusting for poverty did not explain the cluster-level variation.

Conclusion

Despite a decade of increased active case finding efforts, access to TB testing is inconsistent across the population of Blantyre. This likely reflects health inequities that also apply to TB testing in many other settings, and motivates collection and analysis of TB testing data to identify the drivers behind these inequities.

Background

Tuberculosis (TB) was second only to COVID-19 as an infectious cause of death in 2021, with 1.6 million deaths globally. In the same year, an estimated 42% of people who developed TB disease did not receive care, equivalent to 1.5 million people [1]. Providing equitable access to testing services is vital for reaching End TB goals [2,3].

Sub-optimal performance and high cost of available diagnostic tests present a major challenge to timely diagnosis and treatment, with testing difficult to decentralise and often requiring multiple clinic visits. This leads to high direct and indirect costs of care-seeking [4,5] prior to diagnosis, compounded by difficulties accessing primary care. Socio-economically vulnerable populations may face further barriers, motivating a re-focus of interventions to target these groups [6]. In Malawi, previous studies suggest that underdiagnosis may be higher in peripheral, informal neighbourhoods that are often the least affluent [7–10].

TB testing in Malawi is primarily delivered through primary healthcare centres, where sputum from symptomatic individuals is tested with Xpert [11]. In urban areas like Blantyre, community-wide active case-finding by mobile digital X-ray vans and door-to-door symptom screening was introduced following a 2013-14 national survey showing ~1% of urban adults with undiagnosed infectious TB [7,12]. The WHO further recommends routine screening for TB among people living with HIV (PLHIV) and close contacts of TB cases[13]. TB testing data are not routinely reported to WHO (as done for HIV), nor included in national surveys[7]. As such, little is known about how testing varies by demographic characteristics or geographic location.

The Sustainable Community-wide Active case-finding for Lung hEalth (SCALE) study[14] conducted a city-wide TB prevalence survey (using symptom screening, digital chest radiography and bacteriological sputum tests) in 72 neighbourhoods of Blantyre, including questions about previous TB testing. We investigated variation in TB testing unexplained by individual characteristics which may instead reflect structural factors[6]. If the neighbourhood-level pattern of testing history correlates with our previous estimates of underdiagnosis[8], this measure could provide an alternative to costly surveys for identifying under-served populations to benefit from targeted interventions.

Methods

Study Design

The SCALE TB prevalence survey estimated the prevalence of pulmonary TB disease in urban Blantyre, Malawi, by interviewing and screening 15,897 out of 20,899 eligible adults living across 72 neighbourhood clusters (See Feasey et al.[14] for further detail). 20% of participants were randomly invited to complete an extended survey, capturing previous experience with TB testing. Participants were asked whether they had ever given sputum for examination or undergone a chest x-ray (CXR) and, if so, the most recent date. Our primary outcome was defined as “ever-testing” for TB, i.e. whether the participant answered “yes” regarding either sputum or CXR.

Baseline model

We fitted a Bayesian logistic regression model to ever-testing, adjusting for age group (18-24, 25-34, 35-44, 45-54 and ≥ 55 years), sex and HIV status. *Supplementary Materials B* describes how HIV status was defined from self-reported and measured survey outcomes. Independent and identically-distributed (IID) random intercepts were fitted across clusters to account for correlation between individuals in the same neighbourhood. See *Supplementary Materials C* for the full model specification.

Evidence of interaction between age and sex was assessed graphically and then formally by the significance of an interaction term in the baseline model, defined by exclusion of zero from 95% credible intervals of the posterior distribution of coefficients. Model fit and convergence was assessed by Rubin-Gelman $\hat{R}$ statistics, inspecting trace plots and through plots of posterior predictive distributions[15,16].

Evidence of residual spatial autocorrelation between clusters was assessed by comparing Moran's I statistic calculated across the fitted random intercepts to 999 monte-carlo simulations under the assumption of spatial independence [17]. Neighbours were defined by proximity of the nearest cluster centroids, as opposed to shared borders.

Explaining residual heterogeneity

The structure of variation in the fitted random effects was explored across neighbouring clusters and with respect to two measures of poverty at the household level:

- **Self-assessed wealth**
  Survey participants were asked to position themselves on a six-step scale of wealth using a question and figure from the National Integrated Household Survey (NHIS) [18] (*"Imagine six steps, where on the bottom, the first step, stand the poorest people, and on the highest step, the sixth, stand the rich. SHOW THE PICTURE OF THE STEPS. On which step are you today?"*; *Supplementary figure S2*).
- **Proxy Means Test poverty score**
  A household-level proxy means test (PMT) based on assets, food security, head of household education and sleeping conditions was also included in the survey. A composite score was constructed with higher values reflecting higher probability of the household living below the poverty line of $2/day (as in the NHIS). This score was negated and categorised into six quantiles to align with self-assessed wealth.

These two measures were assumed to capture much of the same information. They were added in turn to the baseline model to evaluate whether either better explained cluster-level variation. Their relative impacts on model fit were compared with respect to the leave-one-out cross-validation information criterion (LOOIC)[19] and estimated standard deviation of cluster-level random intercepts.

Sensitivity analyses

Primary results are based on a complete case analysis. A sensitivity analysis with imputation of missing HIV status is described in *Supplementary Materials D*.

Results

Testing history by individual

20,555 residents were enumerated across 7175 sampled households, of whom 15,897 (76%) responded to the primary and 2738 (17%) the extended survey (*Supplementary Figure S3*). Of 2,590 respondents with complete data (95%) (*Supplementary Materials C*), 414 (15.9%) reported previous investigation for TB: 257/414 (62%) had submitted sputum; 262/414 (63%) had CXR and 105/414 (25%) reported both.

248 (60.0%) of those reporting ever-testing did not give a test date. Where a date was given, this varied from less than a month to over twenty years prior to the survey (median 7.0 months). Stratifying by type, median time since last test was shorter for CXR than sputum (6.4 vs 9.8 months, respectively). See *Supplementary Table S1* for further detail on recency of testing.

Reported TB testing history was similar amongst men and women and more common among older people (*Table 1*). A substantial difference was observed between HIV-negative and HIV-positive individuals undergoing antiretroviral therapy (ART) (295/2,292, 12.9% vs 116/292, 39.7%), with HIV-positive individuals *not* on ART in-between (8/37, 21.6%). Due to the small size of the latter group, all PLHIV were combined for analysis regardless of ART use.

Most respondents self-identified at moderate wealth rather than most/least wealthy. TB testing appeared more common among residents of more affluent households (according to both PMT and self-assessed wealth; *Table 1*).

Table 1: *The distribution of key characteristics across the surveyed population, with the percentage reporting previous testing for TB (by sputum sample or CXR).*

Variable	Value	Frequency	Ever tested for TB? N(%)
Sex	Female	1,664	258 (15.5)
	Male	1,074	175 (16.3)
Age group (years)	18-24	1,028	63 (6.1)
	25-34	761	93 (12.2)
	35-44	475	121 (25.5)
	45-54	230	72 (31.3)
	≥55	241	84 (34.9)
	Missing	3	0 (0)
Ever tested for HIV	Yes	2347	406 (17.3)
	No	391	27 (6.9)
	Missing	0	0 (-)
HIV status	Positive ART	292	116 (39.7)

	Positive untreated	37	8 (21.6)
	Negative	2,292	295 (12.9)
	Missing	117	14 (12)
Wealth quantile	1 (poorest)	418	47 (11.2)
	2	469	75 (16)
	3	476	67 (14.1)
	4	454	78 (17.2)
	5	462	88 (19)
	6 (richest)	430	73 (17)
	Missing	29	5 (17.2)
Self-assessed wealth	1 (poorest)	184	25 (13.6)
	2	654	82 (12.5)
	3	1,216	201 (16.5)
	4	541	103 (19)
	5	86	14 (16.3)
	6 (richest)	28	3 (10.7)
	Missing	29	5 (17.2)

Testing history by neighbourhood

An average of 15% of respondents per survey cluster reported previous TB testing (range 0% to 27.5%) (*Figure 1 (A)*). Stratifying by type of investigation, greater variability was observed between clusters in the proportion reporting CXR than sputum collection (*Figure 1 (B)*).

[Figure 1]

Figure 1: (A) *Percentage prevalence of self-reported TB testing history (by sputum sample or CXR) across the 72 survey clusters. Locations of TB clinics are indicated in black.* ***(B)*** *Distribution of observed cluster percentages by type of test (any, sputum or X-ray).*

Poverty by cluster

The distribution of scores from the proxy means test was bimodal, since higher education of the head of household substantially reduced the odds of the household living below the poverty line in the underlying model (Figure 2 (A)). Nevertheless, cluster means of PMT scores and self-assessed wealth show broad agreement (Figure 2 (B)).

[Figure 2]

Figure 2: (A) *The distribution of calculated poverty scores from the proxy means test for each level of self-assessed wealth (1 = poorest, 6 = richest).* ***(B)*** *A scatter plot to illustrate the correlation between mean values per cluster of self-assessed wealth and PMT score. Note that less negative scores from the PMT reflect greater poverty.*

A higher percentage of respondents self-identified at the lowest level of wealth (7%; 95% binomial CI [6, 8]) than had PMT score greater than 0 (i.e. below the poverty line) (5%; 95% CI [4, 6]). Visually, self-assessed wealth appeared more similar between neighbouring clusters than PMT score (see *Supplementary Figure S4*).

Baseline model fit

Differing age trends by sex were evident with respect to previous TB testing (*Supplementary Figure S5*). An interaction term added to the baseline model resulted in a small decrease in LOOIC (2043 (SD 61.8) vs 2048 (61.6)).

The baseline fit demonstrated that older age was associated with greater odds of ever-testing, with a larger effect size for men than women (OR for age ≥ 55 vs 18-24 years = 4.0 [2.33, 6.67] for women; 9.3 [5.50, 15.41] for men) (*Figure 3 (A)*). Greater odds among PLHIV were also evident (OR for PLHIV: 2.72 [2.04, 3.60], versus HIV-negative people). Including unknown HIV as an additional estimated factor level in sensitivity analyses had negligible impact on the OR for PLHIV (2.7 [2.03-3.55]).

[Figure 3]

Figure 3: (A) *Fixed effect estimates from baseline model fit; a log-odds ratio greater than 1 indicates a higher chance of having been tested relative to the baseline for that variable* ***(B)*** *Variation across clusters in the cluster-level random effect (posterior mean); blue and red indicate where testing prevalence in the cluster is generally higher or lower than expected, respectively, having adjusted for each respondent's age, sex and HIV status.* ***(C)*** *Posterior standard deviation (SD) of the cluster-level random effect.*

Cluster-level random effects demonstrated residual heterogeneity between clusters after accounting for individual characteristics (posterior SD 0.3 [0.08 - 0.51]) (*Figure 3 (B)*). Some clusters stood out in contrast to their neighbours in the city's centre-north and north-east, with no clear pattern overall.

Explaining residual heterogeneity

Wealth with respect to PMT score was associated with a borderline-significant positive trend: the most affluent quantile were estimated to have significantly higher odds of ever-testing than the poorest quantile (*Table 2; Supplementary Figure S6 (A)*). Odds were also significantly higher among those who self-identified at the 3rd/4th steps of wealth, relative again to the poorest.

Table 2: *Comparison of fixed effect estimates from models incorporating poverty through two different metrics: quantiles of PMT poverty score (predicted probability of living on < $2/day), and self-assessed wealth on a six-point scale. Including PMT poverty score yielded the greater reduction in the leave-one-out information criterion (LOOIC).*

Variable	Estimate	Change in LOOIC from baseline
PMT score quantile: 2	1.4 (1.01-2.00)	-5.4

3	1.2 (0.86-1.76)	
4	1.9 (1.39-2.69)	
5	1.8 (1.33-2.60)	
6 (richest)	1.7 (1.21-2.83)	
Self-assessed wealth: 2	1.1 (0.74-1.73)	-1.3
3	1.6 (1.11-2.47)	
4	1.8 (1.21-2.83)	
5	1.5 (0.81-2.78)	
6 (richest)	1.1 (0.34-2.99)	

Despite significant coefficients of both poverty indicators, neither improved the overall fit of the model (*Table 2*). Moreover, neither explained cluster-level variation to a greater extent than the baseline model, shown by negligible impact on the estimated SD of the random intercept (*Supplementary Figure S6 (B)*). Multiple imputation of unknown HIV status and the two poverty variables had negligible impact on estimated coefficients compared to the presented complete case analysis (*Supplementary figures S7 and S8*).

Comparison with prevalence-to-notification ratios

The cluster-level residuals from either the baseline or poverty-adjusted models showed no visible association with previously estimated prevalence-to-case-notification ratios (*Supplementary figure S9*), although these were limited by low numbers of prevalent TB cases.

Discussion

Questionnaire data from a pre-intervention survey for undiagnosed infectious TB in Blantyre, Malawi, indicates that 16.0% (95% CI [14.6%, 17.4%]) of adults reported having ever submitted sputum or undergone chest x-ray, likely to represent previous TB testing. By comparison, 85.7% of participants reported at least one previous HIV test. Even among the oldest participants (55 years and older) only 34.9% reported ever-testing for TB. The observed divergence between older men and women with respect to ever-testing was unexpected and may warrant further investigation; this could reflect different age patterns of health service engagement by sex (e.g. women's use of maternity/child services), or the under-representation of certain age groups of men in the survey sample. It could also be that the expansion of testing in recent years has reached younger people more than older, therefore testing among older people reflects more historical rather than current biases in access. Most reported TB testing was recent, likely reflecting the scale-up of TB case-finding efforts by the National TB and HIV Programmes over the last decade, with decentralisation of testing and treatment and more intensive, systematic screening in outpatient attendees, people living with HIV, and prisoners [20].

Reported testing rates varied substantially between neighbourhood clusters, after adjusting for individual age, sex and HIV status. The poorest individuals in all neighbourhoods were least likely to have previously tested for TB, yet this did not explain the residual cluster-level variation. This could reflect the complexity of barriers to accessing and engaging with testing *within* clusters as opposed to between[6]. The way in which behaviours may vary for those in extreme poverty across the city should be investigated further. In this analysis we did not incorporate the locations of TB diagnostic facilities, for example; previous work found this to be a risk factor for TB case fatality among patients notified at the central hospital in Blantyre [21].

Estimated urban prevalence of adult (> 15 years) pulmonary TB was 452 (312-593) per 100,000 nationally and 1,014 (486-1,542) in Malawi's 2013-14 prevalence survey[7,12], but had fallen substantially by SCALE's 2019-20 pre-intervention survey to 180 per 100,000 in Blantyre [14]. The 2013-14 survey qualified Malawi as a high disease burden country, with urban areas conditionally recommended for general population active case-finding by WHO. A systematic review [22] discussed the potential importance of intensively-delivered active case-finding, yet our analysis suggests that its reach may have been inconsistent between otherwise-comparable communities. The low prevalence of ever-testing supports monitoring self-reported TB testing data - as successfully done with HIV regionally - to identify and target under-served communities as we work towards EndTB targets.

Guidelines recommend screening for TB on every healthcare encounter with the WHO "4 Symptom Screen"[23], however, in practice, coverage is likely to be substantially lower. Among people without HIV, only those reporting symptoms progress to CXR or sputum examination[24], which reduces numbers needing to test but has lower sensitivity than systematic, non-symptom-based screening[25]. This likely contributes to the high proportion of Blantyre's adult residents who have never been investigated but unlikely fully explains the heterogeneity seen in this study, considering the lower coverage of testing for the poorest in any given cluster. National TB programmes should monitor TB testing coverage to ensure consistent representation of all population groups. As with case notifications, coverage of TB testing could be mapped to identify under-testing prospectively if geospatial data were collected for each tested patient [9].

Limitations

The underlying SCALE prevalence survey had suboptimal participation, notably for working-age men. This may have biased the estimates presented, for instance underestimating the role of poverty if the poorest men were also least likely to have participated and least likely tested for TB. Post-stratification to adjust for this required cluster-level, age-sex-stratified estimates of HIV prevalence, which were not available. Our definition of ever-testing also includes misclassification from individuals having submitted sputum or undergone CXR unrelated to TB. CXR has not - until recently - been widely available in Blantyre, accessible only through hospital referral. Since 2019, the Blantyre District Health Office introduced digital CXR via community-based mobile TB screening and a number of small studies of CXR in health facilities have been conducted to investigate impact on TB diagnosis yield [26,27]. We therefore assume that TB diagnosis would be the most likely reason for CXR in Blantyre.

Conclusions

Despite decades of emphasis on TB case-finding and revision of global guidance to support community-based active case-finding and chest-x-ray-based screening, few studies have

investigated population patterns of TB testing as a marker of programmatic reach. To our knowledge, this is the first analysis of TB testing history measured from a city-wide survey. Although Blantyre has experienced a generalised HIV epidemic and extremely high TB burden, only a small proportion of residents reported having ever been tested for TB. Neighbourhood-level variation in testing was not explained by demographics, HIV positivity or household-level poverty, suggesting that access to healthcare provision remains a persistent barrier to TB diagnosis. Behavioural drivers - opportunity, individual motivation and capacity - may contribute to this variability. As TB epidemics in Africa decline and concentrate in vulnerable groups, analysis of TB testing data can inform improvement of access, acceptability and equity in provision of TB services.

Ethical statement

Approval for the SCALE trial (registered trial: ISRCTN11400592) was granted by the LSHTM Research Ethics Committee (Ref: 16228) and by the University of Malawi College of Medicine Research and Ethics Committee (Ref: P.12/18/2556). Informed consent was obtained for all survey participants.

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First author Emily S. Nightingale is a research fellow in statistical modelling at the London School of Hygiene and Tropical Medicine. Her research primarily focuses on the spatial epidemiology of infectious diseases, with work on leishmaniasis, TB and COVID-19.

Availability of data and materials

All data and code used in this analysis are accessible via the following repository: https://github.com/esnightingale/tb-testing-history.

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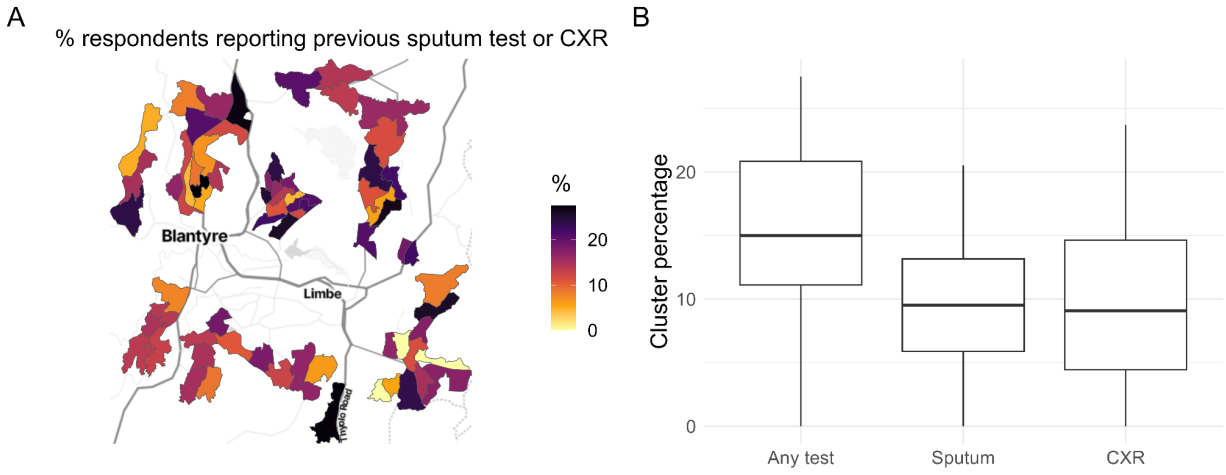
Figures



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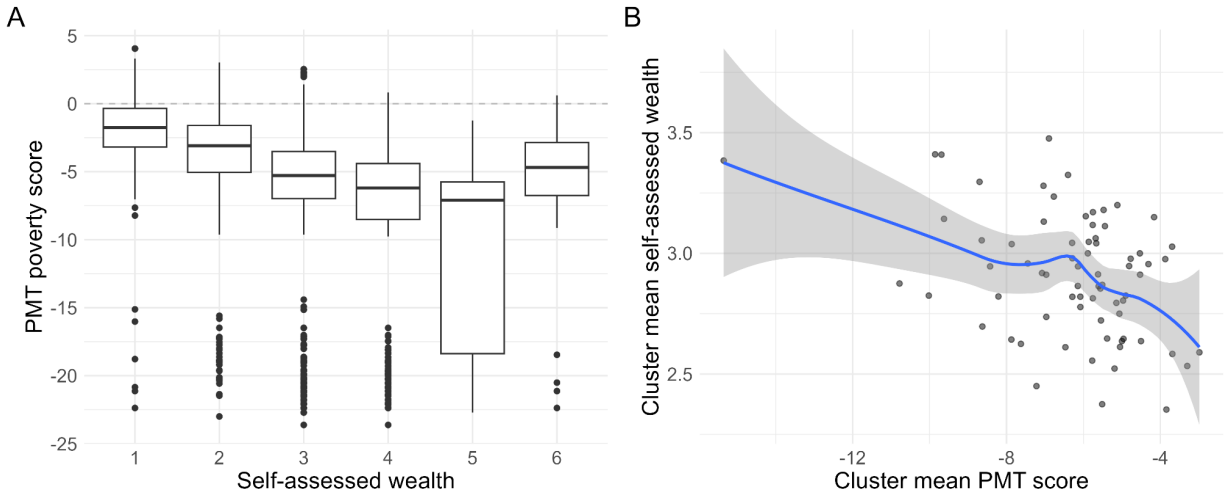

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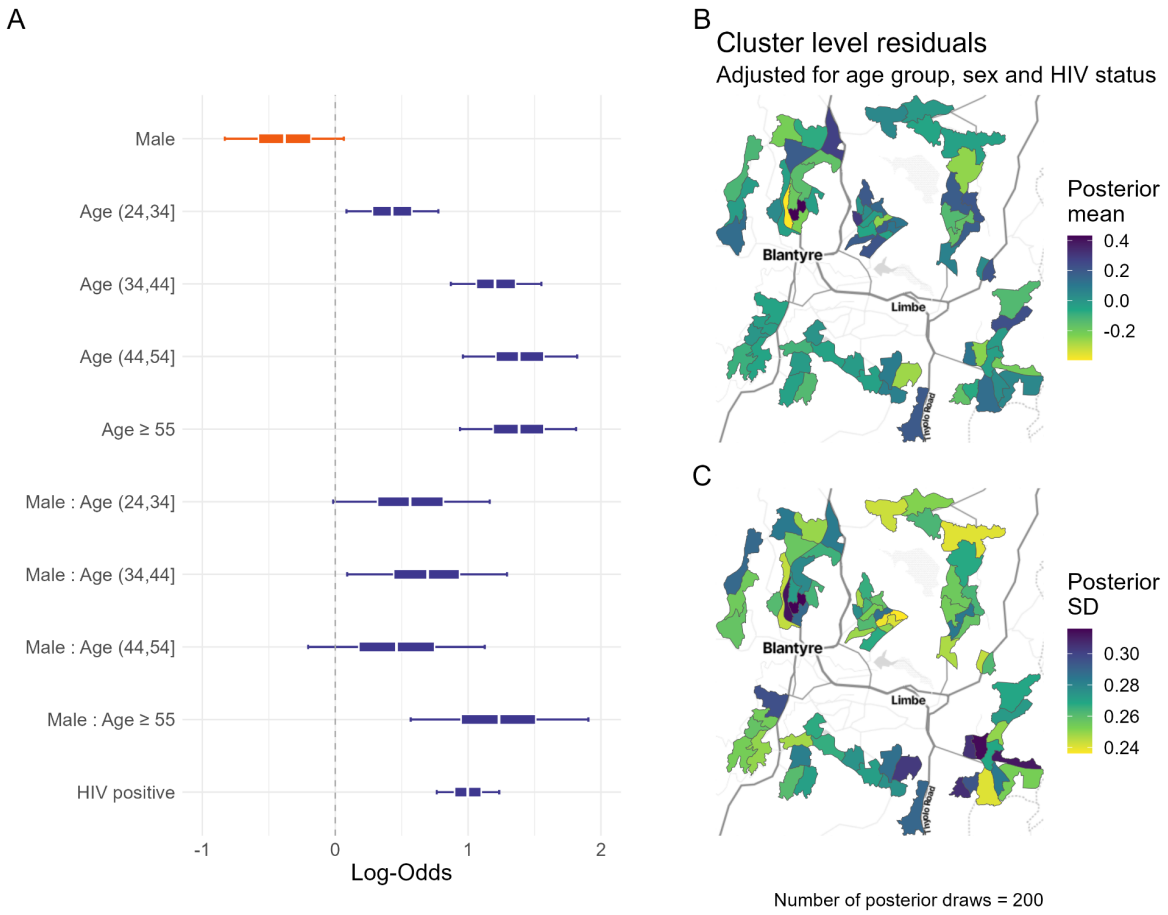

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