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Investigating Barriers to Tuberculosis Evaluation in Uganda Using Geographic Information Systems

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Abstract. Reducing geographic barriers to tuberculosis (TB) care is a priority in high-burden countries where patients frequently initiate, but do not complete, the multi-day TB evaluation process. Using routine cross-sectional study from six primary-health clinics in rural Uganda from 2009 to 2012, we explored whether geographic barriers affect completion of TB evaluation among adults with unexplained chronic cough. We measured distance from home parish to health center and calculated individual travel time using a geographic information systems technique incorporating roads, land cover, and slope, and measured its association with completion of TB evaluation. In 264,511 patient encounters, 4,640 adults (1.8%) had sputum smear microscopy ordered; 2,783 (60%) completed TB evaluation. Median travel time was 68 minutes for patients with TB examination ordered compared with 60 minutes without ($P < 0.010$). Travel time differed between those who did and did not complete TB evaluation at only one of six clinics, whereas distance to care did not differ at any of them. Neither distance nor travel time predicted completion of TB evaluation in rural Uganda, although limited detail in road and village maps restricted full implementation of these mapping techniques. Better data are needed on geographic barriers to access clinics offering TB services to improve TB diagnosis.

INTRODUCTION

The Global Plan to Stop TB calls for tuberculosis (TB) diagnostic services to be "easily accessible, with no or minimal financial and geographic barriers to care" to achieve the targets of halving TB mortality and TB prevalence set for the 2015 Millennium Development Goals (MDG).[1] Unfortunately, many barriers remain. TB diagnostic algorithms requiring two or more sputum examinations over 2 or more days, with additional visits to receive results and to initiate treatment, remain the standard of care in sub-Saharan Africa and other high-burden regions. Furthermore, diagnostic centers in rural areas where the majority of the population resides are widely dispersed. Many patients initiate evaluation but do not complete it,[2,3] and as a result experience adverse outcomes.[4,5] Although the World Health Organization (WHO) has recently recommended that TB diagnostic algorithms be shortened to one day,[6,7] this change has not yet been widely adopted or promoted in countries where it could have the greatest impact, and additional data are needed on factors affecting initiation of therapy to inform public health policy.

A number of qualitative studies have highlighted the contribution of geography and extended travel times to failures to complete TB evaluation and initiate treatment,[8] but there is little quantitative information in this area. Geographic information systems (GIS) methods allow investigators to create digital representations of the landscape to enable estimation of the distance that patients travel, a technique that is complementary to information obtained from patient reports and more scalable for data collection on large populations.[9–13] In addition, newer techniques can be used to estimate travel time, which may be preferred for analyses of access to care because travel time varies among regions based on geography and mode of transportation.[12–17] Therefore, in this study, we used GIS to examine the relationship between the distance to care and patient travel time and the likelihood of completing TB evaluation in a multicenter study in rural Uganda. We hypothesized that geographic barriers, including distance and travel time, would be associated with failure to complete TB evaluation.

METHODS

Study design, setting, and population. We carried out a cross-sectional study of patients undergoing TB evaluation at government health facilities in Uganda. We examined routinely collected individual patient data on demographic characteristics and diagnostic services at six primary-health centers in six rural districts for the period January 2009 to January 2012. These six health centers were selected because they are located in a variety of different geographic areas of the country. The Ugandan government provides routine primary care, obstetric, and basic surgical services at these facilities without charge to patients. Each health center has an on-site laboratory that performs sputum smear microscopy for acid-fast bacilli (AFB), and participates in external quality-assurance activities overseen by the National TB Reference Laboratory.

The health centers are part of an infectious disease surveillance network in which clinic staff record clinical and demographic data, presenting symptoms, results of laboratory testing, and prescriptions for treatment of every clinical encounter on a standardized, one-page data collection form that is routinely entered into an electronic database, as previously described.[18,19] Demographic data include age,

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gender, and information about residence in one of 5,238 registered parishes,[20] the smallest administrative units in Uganda with an average population of 4,625 and a mean area of 38 km^2. In this analysis, we sampled all patients who presented to health centers with cough of more than 2 weeks' duration and underwent sputum examination as part of a TB diagnostic evaluation. We excluded those receiving follow-up monitoring and care for a previous diagnosis of TB.

Outcome variable. The primary outcome for the cross-sectional analysis was the completion of TB evaluation, which was treated as a dichotomous variable. In accordance with the International Standards for TB Care,[21] we defined TB evaluation as complete if a patient provided two or more sputum samples which were read and reported as negative for AFB, or if a patient provided one or more sputum samples showing AFB and initiated TB therapy.

Explanatory variables. We extracted data on participant gender, age, and date of clinic visit, and categorized the visits as occurring during the rainy season (March through May and September through November) or during the dry season (December through February and June through August). We assigned distance and travel time by matching the names of the patients' home parishes to those in a parish boundaries dataset for Uganda.[22] We used the Euclidean distance function in ArcMap 10 (Environmental Systems Research Institute [ESRI], Redlands, CA) to calculate the distance in a straight line from the centroid of the patient's home parish to the nearest clinic. We calculated travel time in minutes from the centroid of each patient's home parish to the nearest clinic by assembling a friction surface in ArcMap. We included data layers for elevation,[23] land cover,[24] roads,[25] rivers,[26] and bodies of water[26] at a 90 m by 90 m cell size. We calculated slope from the elevation data using the Spatial Analyst toolset in ArcMap. We assigned a time to cross each type of land cover, assuming mechanized transport use on roads and walking elsewhere, ranging from 1 minute/km over road surfaces; to 2 minutes/km in urban areas; to 24 minutes/km for areas with sparse shrub cover; to 36 minutes/km for croplands, forest and jungle; to 60 minutes/km over bodies of water, as previously described (Supplemental Table 1).[10,27] We multiplied ambulatory travel rates by a slope factor[27] to slow the travel speed as a function of the steepness of the terrain. We then assembled geographic raster layers into a single mosaic layer using ArcMap. We assigned the rate of travel time for each cell according to the fastest mode of travel available for that cell. We then calculated the path requiring the shortest travel time to the nearest clinic from the center of each parish using the cost-distance function in ArcMap.

Primary analyses. We compared median differences in participant age using the Wilcoxon rank sum test, differences in gender and season using the χ^2 test, and differences in median travel time using the Wilcoxon rank sum test. We evaluated bivariate associations between candidate covariates, including distance and travel time and the outcome variable, completing TB evaluation, and incorporated a random effect to account for clustering of data within health centers. We included candidate covariates with P value < 0.1 in the multivariate logistic regression model. We used Stata version 11 (StataCorp, College Station, TX) for all statistical analyses.

Sensitivity analyses. In addition to the review of patient encounter data, we also carried out patient interviews at all six sites with a convenience sample of patients who had been evaluated by a clinician and referred for sputum evaluation. The purpose of these interviews was to facilitate a sensitivity analysis exploring the validity of our GIS measures of travel time. We interviewed participants while they were waiting for sputum results, using a standardized script (see Online Supplement). Specifically, we asked each participant to provide the total time spent traveling and the mode of transportation used to travel to clinic that day.

We first compared GIS-estimated and patient-reported travel times using Kendall's tau test. We then described travel time differences between the two techniques by plotting the mean of the two measures against the percentage difference on the y axis, and calculating the mean differences and their 95% confidence limits using the Bland–Altman method.[28,29]

Finally, as an additional way of comparing the distance and travel time metrics with respect to the likelihood of patients attending health centers, we constructed a density function for patient visits per parish. We estimated the population per parish using the population map for Uganda produced by WorldPop.[30] We assessed the relationship between the total number of visits per parish with the population of each parish using negative binomial regression models. We compared a model that included distance as a covariate with one that included travel time using the Akaike information criterion (AIC).[31]

Human subjects' protection. The Makerere University School of Medicine Research Ethics Committee, the Uganda National Council for Science and Technology, and the University of California San Francisco Committee on Human Research approved the protocol. The committees waived the requirement for informed consent for the cross-sectional study on grounds that the study posed minimal risk. Participants interviewed at the clinics provided written informed consent with assistance from an interpreter. We previously presented these data in abstract form.[32]

RESULTS

Distance and travel time to clinic. There were 264,511 adult visits to the six clinics over the 3-year surveillance period. Geographic information was missing for 15,245 visits, including 12,374 for which the patient's home parish was not recorded and 2,871 for which we were unable to locate the reported parish on a map. This left 249,266 visits with complete geographic information. Figure 1 shows a map illustrating the travel times calculated using GIS for attendees of the Walukuba clinic as an example of the maps generated around each site. The median distance from home parish to clinic for all sites was 4.2 km (Interquartile range [IQR]: 1.4–9.2) for patients with a TB examination ordered ($N = 4,731$), compared with 3.2km (IQR: 1.4 – 7.2) for patients who did not have one ordered ($N = 244,535$, $P < 0.001$). Likewise, the median calculated travel time from home to clinic for all sites was 68 minutes (IQR: 29–125) for patients who had a TB examination ordered, compared with 60 minutes (IQR: 24–101) for patients who did not have one ordered ($P < 0.001$). Of the patients with a TB examination ordered, 3,512 (74%) lived within an estimated 2-hour travel radius of the clinic. Median calculated travel time from home parish varied substantially among the six clinics, from 28 minutes in a periurban area (Walukuba); to 61 minutes (Kihihi) and 77 minutes (Kamwezi) in mountainous southwest

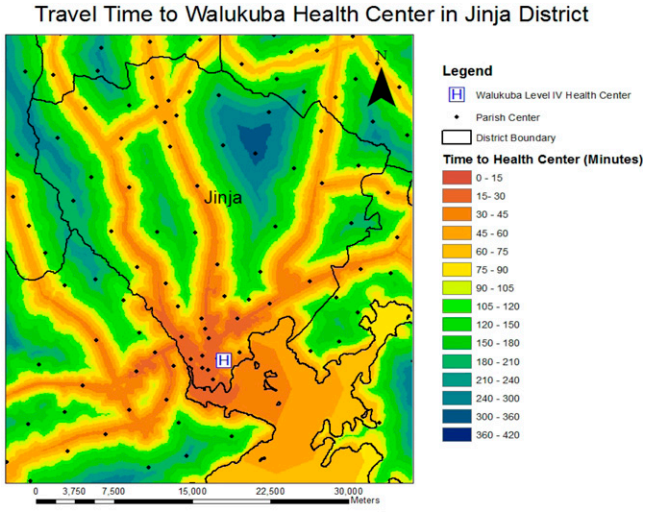

FIGURE 1. Map of estimated individual travel times to Walukuba health center. This map displays travel times for patients from the centers of parishes in Jinja District to Walukuba Level IV Health Centre as estimated using the geographic information system (GIS) modeling techniques.

TABLE 1

Bivariate associations between clinical and demographic characteristics and completion of TB evaluation status

Characteristic	Completed TB evaluation	Bivariate odds ratio	*P* value
N = 4,640	*N* = 2,783	(95% CI)	–
Gender*	–	0.59 (0.53–0.67)	< 0.001
Women (*N* = 2,414)	1,305 (54.1%)	–	–
Men (*N* = 2,225)	1,477 (66.4%)	–	–
Age (years)	–	–	< 0.001
15–35 (*N* = 2,226)	1,198 (53.8%)	Referent	–
36–49 (*N* = 1,198)	783 (64.0%)	1.52 (1.32–1.76)	–
> 50 (*N* = 1,190)	802 (67.4%)	1.77 (1.53–2.05)	–
Season	–	–	< 0.001
Rainy (*N* = 2,500)	1,412 (56.5%)	Referent	–
Dry (*N* = 2,140)	1,371 (64.1%)	1.37 (1.22–1.55)	–
Clinic	–	–	< 0.001
Kasambya (*N* = 618)	535 (86.6%)	4.31 (3.39–5.62)	–
Kihihi (*N* = 670)	523 (78.1%)	2.38 (1.90–2.98)	–
Aduku (*N* = 646)	485 (75.1%)	2.01 (1.61–2.51)	–
Nagongera (*N* = 914)	548 (60.0%)	Referent	–
Walukuba (*N* = 954)	383 (40.1%)	0.45 (0.37–0.54)	–
Kamwezi (*N* = 838)	309 (36.9%)	0.39 (0.32–0.47)	–

CI = confidence interval; TB = tuberculosis.
*One value missing.

Uganda; to 86 minutes adjacent to the Nile River (Aduku); to 64 minutes (Nagongera) and 126 minutes (Kasambya) in two less populated areas ($P < 0.001$).

Demographics and TB diagnoses. Clinicians ordered sputum examination in 4,731 patients. Ninety-one previously diagnosed TB patients returning for medication refills were excluded, leaving 4,640 patients included in our analysis (Figure 2). Of these 4,640, 2,783 (60.0%) completed TB evaluation (Table 1). As previously shown,[18] women were less likely to complete evaluation than men (odds ratio [OR]: 0.60, 95% confidence interval [CI]: 0.53–0.67, $P < 0.001$). Older patients were more likely to complete evaluation (OR: 1.20 for each additional decade of life, 95% CI: 1.15–1.24, $P < 0.001$). Although overall patients were more likely to complete their evaluation in the dry season than the wet season (OR: 1.37, 95% CI: 1.22–1.55), this effect was largely driven by the remote Kamwezi clinic (OR: 7.05 95% CI: 5.05–9.8). Patients were equally likely to complete evaluation in the dry and the rainy seasons at Kasambya, Nagongera, and Walukuba and modestly less likely to complete evaluation in the dry season at Aduku (OR: 0.63 95% CI: 0.44–0.92) and Kihihi (OR: 0.45 95% CI: 0.31–0.66). Human immunodeficiency virus (HIV) status was documented for 1,766 of 4,640 participants (38.1%). Among these, 605 of 1,766 (34.3%) participants were HIV positive. HIV-positive participants were less likely to complete their TB analysis than HIV-negative participants, but this effect did not remain significant when accounting for clustering by clinic site (OR: 0.75, 95% CI: 0.44–1.29).

Euclidean or "straight line" distance from home parish to clinic was not associated with likelihood of completing TB

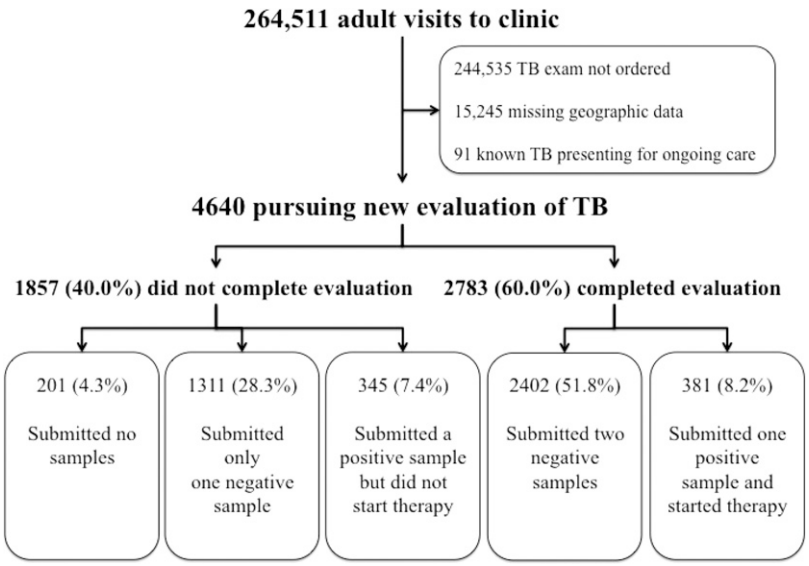

FIGURE 2. Flow diagram showing patient enrollment.

TABLE 2
Site-specific models for adjusted odds of completing TB evaluation as a function of each additional hour of GIS-predicted travel time

Clinic	District	Adjusted odds ratio*	95% Confidence interval	*P* value
Aduku	Apac	0.99	0.85–1.15	0.9
Kamwezi	Kabale	1.15	0.98–1.35	0.090
Kasambya	Mubende	1.28	1.05–1.56	0.016
Kihihi	Kanungu	0.91	0.77–1.07	0.2
Nagongera	Tororo	1.06	0.92–1.21	0.4
Walukuba	Jinja	0.91	0.71–1.17	0.5

GIS = geographic information system; TB = tuberculosis.
*Adjusted for age and sex.

evaluation. Similarly, at five of the six clinic sites, travel time from home parish to health center did not consistently differ between those who completed TB evaluation and those who did not (Table 2), even among those traveling for the longest time. At the sixth clinic, Kasambya, longer travel times were actually associated with a higher likelihood of completing evaluation (OR 1.3 for each additional hour of travel, 95% CI: 1.0–1.6, $P = 0.016$). Median travel time also did not differ between those who were TB positive ($N = 381$, 78.4 minutes) and those who completed TB evaluation with two negative samples ($N = 2{,}402$, 78.4 minutes, $P = 0.57$).

Comparison of patient-reported and GIS-estimated travel times. We approached 67 patients for interview at the clinic sites. Sixty-five (97%) agreed to the interview and 57 (85%) reported travel time and were included in further analysis (Supplemental Table 2). Twenty-six (46%) traveled to their chosen clinics using a motorized form of transport, including 24 (42%) by moped and two (4%) by shared taxi (*matatu*); 36 (63%) came by non-motorized transport, including 20 (35%) who walked and 13 (23%) who rode a bicycle. Three (5%) used multiple modes of transport and are included in the counts above, and one declined to disclose the method of travel. Although patient-reported and GIS-calculated travel times were associated by Kendall's tau test ($P = 0.045$), neither method provided consistently higher travel times. When we plotted the percent difference versus the mean using a modification of the Bland–Altman[28,29] method, the mean difference was 22.9% (95% limits of agreement −156 to +202%) (Figure 3). In a time-stratified analysis, we found that the difference between patient-reported and GIS-calculated travel times was proportional to the mean, such that precision decreased with increasing travel time from the clinic. The mean absolute difference between the measures was 30.3 minutes (IQR: 16.6–51.2) for travel times less than 1 hour ($N = 17$), 59.8 minutes (IQR: 23.8–88.2) for travel times between 1 and 2 hours ($N = 30$), and 129.1 minutes (IQR: 36.8–214.7) for travel times greater than 2 hours ($N = 10$). Limiting our analysis to those patients who traveled by mechanized transport ($N = 26$) did not improve agreement between the two measures (95% limits of agreement −195 to +197 minutes).

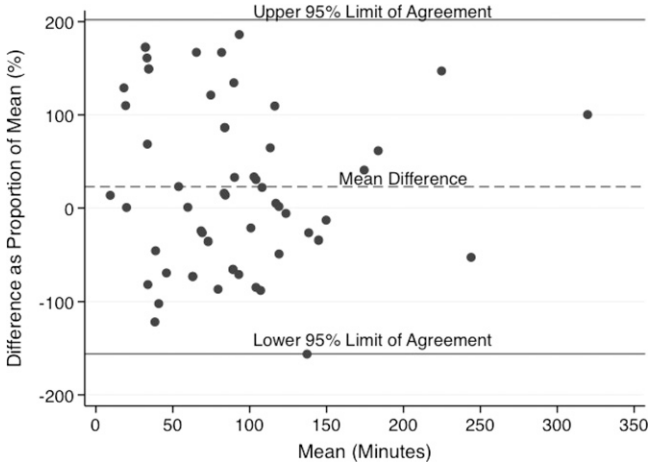

FIGURE 3. Bland–Altman plot comparing the differences in geographic information systems (GIS)-calculated and patient-reported travel times as a proportion of the mean.

Correlation of distance and travel time with density of patient visits. The model including distance was more predictive of visit density than was the model with estimated travel time (AIC 4957 for model including distance versus AIC 5275 for model including time). This indicates that the travel time estimate did not improve upon physical distance as a measure of accessibility.

DISCUSSION

Rigorously studying how geography acts as a barrier to TB evaluation is a critical but underutilized strategy for informing efforts to increase access to TB care in high-burden countries. Accessibility maps developed using GIS represent a novel and potentially useful tool to estimate the amount of time required to reach a diagnostic center. In rural Uganda, we found that patients who had a TB examination ordered travel further for care on average than patients who did not have a TB examination ordered. This likely reflects the restriction of TB diagnostic services to higher level clinics like these, whereas primary care services are available in facilities of any level. However, once patients reached a clinic to initiate TB evaluation, longer distance or travel times did not change the likelihood of completing the multiday process of evaluation and treatment initiation.

Our application of GIS in this study was limited by the lack of detail in publicly available, digitized maps of Uganda. Available "complete" digital road maps of Uganda omit many smaller roads and tracks, providing low resolution for modeling travel even when compared with maps of neighboring Kenya. In addition, we were only able to locate our patients to the center of their home parish because the majority of their villages could not be found on digitized maps or gazetteers with geolocations.[33] This meant that travel times were calculated from the center of parishes, which often may not correspond to an area on the road network, and this may have led to unrealistically high travel times being calculated in many cases. Improving the detail of digital spatial datasets of this region will increase the precision of the technique used here. In the absence of detailed maps, an alternative method would extend the use of mobile phone technology to allow patients to transmit the coordinates of their homes and/or their paths of travel rather than relying on maps of villages. Mobile phones have already been used in TB programs as platforms for data collection and to communicate with patients.[34–36]

Although neither travel time nor distance was associated with likelihood of completing TB evaluation at these primary health clinics in Uganda, other studies have found that increased travel time as measured by self-report is associated with delays both in seeking and delivering TB care.[8] In the

absence of more detailed individual covariates in our study, we propose several possible hypotheses for testing in future studies. One hypothesis is that patients traveling for a longer time period to access care may be wealthier or more motivated to complete evaluation than those traveling for a shorter period. Another hypothesis is that patients who have to travel for longer to reach clinic may delay seeking care, but may be more likely to complete evaluation once they reach the clinic because traveling back is relatively more costly and time consuming.

This study makes several new contributions to understanding the geographic accessibility of TB evaluation in Uganda. Although GIS is increasingly used to assess the accessibility of health services on the provincial[10,37,38] or national[12,13,39,40] level in sub-Saharan Africa, this is among the first analyses in this region to use GIS to investigate travel time for TB evaluation at a local level. This study also used a gridded travel-time surface that permitted travel off of the road network, in contrast to many accessibility studies done in developed countries that calculate travel over the road network.[41] This technique could be well suited to Uganda given our finding that half of patients traveled to clinic without using a mechanized form of transport, but would be improved with more precise detail about the patient locations. In our study, where the median distance from home parish to clinic was less than 4 km, our inability to locate patients more precisely than the parish center likely reduced our power to confirm or refute any association.

A limitation of our study is that GIS-predicted travel times did not correlate with those reported by patients, which may be due to the limitations in the travel time estimate discussed above. Socioeconomic status may be an unmeasured confounder because patients from different regions may have different levels of wealth, which may affect their access to transportation or their ability to take the time to seek care. An alternative explanation could be that patients traveled to clinic by multiple methods that entailed different transfer times not accounted for in our analysis. Alternatively, patients may not report travel times accurately, as shown in another study from a rural region of Uganda where travel time reported by patients attending an HIV clinic differed from the measured time of travel.[42] It is unknown whether these differences would persist if they were evaluated with more precise residential localization. Although we assigned travel speeds to various land surfaces based on values used in other studies,[10,27] they may not capture the actual travel times experienced by our patients. Attempts such as these to validate GIS estimates of travel time are important because of the goals set by health ministries to locate services within specified limits of travel time for their populations.[10,13]

A major focus of recent WHO TB diagnostic policy changes is on reducing diagnostic delays.[6,43,44] As these and future novel diagnostic strategies are implemented, it is important to assess their impact on multiple levels, including equity analyses of sub-populations by gender, socioeconomic status, and, as we argue here, geography.[45,46] Thus, future diagnostic implementation studies might consider using GIS estimations of travel time to assess access to new diagnostics. Improved availability of detailed spatial datasets from governments and researchers would greatly accelerate progress in this field.

In conclusion, we found that distance to care and patient travel time, as estimated by GIS, did not explain why nearly 40% of patients initiating TB evaluation at government health centers in rural Uganda did not complete their evaluation. In addition, large-scale application of the mapping technique used in our study is currently limited by lack of detail in publicly available road and village spatial datasets.

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