Drug-resistant tuberculosis patient care journeys in South Africa: a pilot study using routine laboratory data

J. Hill,[1] L. Dickson-Hall,[2] A. D. Grant,[1,3] C. Grundy,[4] J. Black,[5,6] K. Kielmann,[7] K. Mlisana,[8] L. Mitrani,[2] M. Loveday,[9,10] M. Moshabela,[11] S. Le Roux,[2] W. Jassat,[12] M. Nicol,[2,13,14] H. Cox[2,14]

[1]TB Centre, London School of Hygiene & Tropical Medicine (LSHTM), London, UK; [2]Division of Medical Microbiology, University of Cape Town, Cape Town, [3]Africa Health Research Institute, School of Nursing and Public Health, University of KwaZulu-Natal and School of Public Health, University of the Witwatersrand, Johannesburg, South Africa; [4]Department of Infectious Disease Epidemiology, LSHTM, London, UK; [5]Livingstone Hospital, Eastern Cape Department of Health, Port Elizabeth, [6]Department of Medicine, University of Cape Town, Cape Town, South Africa; [7]Institute for Global Health and Development, Queen Margaret University, Edinburgh, UK; [8]Department of Medical Microbiology, University of KwaZulu-Natal, Durban, [9]Health Systems Research Unit, South African Medical Research Council, Cape Town, [10]Centre for the AIDS Programme of Research in South Africa (CAPRISA), University of KwaZulu-Natal, Durban, [11]School of Nursing and Public Health, University of KwaZulu-Natal, Durban, [12]School of Public Health, University of the Western Cape, Cape Town, [13]National Health Laboratory Service, Johannesburg, [14]Institute of Infectious Disease and Molecular Medicine and Wellcome Centre for Infectious Diseases in Africa, University of Cape Town, Cape Town, South Africa

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SETTING: Thirteen districts in Eastern Cape (EC), KwaZulu-Natal (KZN) and Western Cape (WC) Provinces, South Africa.

OBJECTIVE: To pilot a methodology for describing and visualising healthcare journeys among drug-resistant tuberculosis (DR-TB) patients using routine laboratory records.

DESIGN: Laboratory records were obtained for 195 patients with laboratory-detected rifampicin-resistant TB (RR-TB) during July–September 2016. Health facility visits identified from these data were plotted to visualise patient healthcare journeys. Data were verified by facility visits.

RESULTS: In the 9 months after the index RR-TB sample was collected, patients visited a mean of 2.3 health facilities (95% CI 2.1–2.6), with 9% visiting ≥4 facilities. The median distance travelled by patients from rural areas (116 km, interquartile range [IQR] 50–290) was greater than for urban patients (51 km, IQR 9–140). A median of 21% of patient's time was spent under the care of primary healthcare facilities: this was respectively 6%, 37% and 39% in KZN, EC and WC. Journey patterns were generally similar within districts. Some reflected a semi-centralised model of care where patients were referred to regional hospitals; other journeys showed greater involvement of primary care.

CONCLUSION: Routine laboratory data can be used to explore DR-TB patient healthcare journeys and show how the use of healthcare services for DR-TB varies in different settings.

KEY WORDS: tuberculosis; MDR-TB; mapping; GIS; health systems; routine data; patient-focused

SOUTH AFRICA CONTRIBUTES 10% of the total global burden of notified drug-resistant tuberculosis (DR-TB, defined as resistance to at least rifampicin, and including multi- and extensively DR-TB), with 16 733 patients diagnosed in 2017.[1] While a large number of patients are diagnosed nationally, only 64% were estimated to have started second-line treatment in 2013.[2] Treatment outcomes are poor, with only 55% treatment success among those starting treatment in 2015.[1]

In response to the large burden of DR-TB in South Africa, a national policy to decentralise DR-TB services was launched in 2011.[3] Both the conventional 18–24 month and the shortened 9–12 month DR-TB regimens are arduous and associated with significant adverse events.[4,5] Patients taking these regimens require monthly monitoring with laboratory tests to identify drug toxicities and determine treatment response.[5] Hospital admissions are also burdensome for patients and providers, and efforts to reduce this burden through community-based models of care have been described.[6–10] Decentralised care has been reported to achieve similar or better outcomes than centralised treatment programmes[11,12] while being more acceptable to patients and reducing provider costs.[13,14] Ambulatory-based models of care are recommended by the World Health Organization (WHO).[5]

Since 2011, different models of decentralised DR-TB care have emerged across South Africa based on different interpretations of the policy and the varying contexts within which care is delivered.[15,16] Published analyses of patient pathways have recently highlighted the mismatch between health service provision and the preferences of drug-susceptible TB patients seeking care.[17,18] Examining where DR-TB patients access care and tracing their journeys between health facilities may help us understand better variations in the implementation of decentralised care in different settings. As part of a broader health systems research project investigating how health systems may be optimised to deliver high-quality, patient-centred, decentralised care for DR-TB, we aimed to pilot a methodology that utilises routine laboratory data to describe and visualise patient pathways through healthcare services.

METHODS

This was a descriptive pilot study aiming to assess whether routine laboratory data could be used to construct DR-TB patient healthcare journeys in South Africa. The pilot study was conducted in 13 districts across three of the nine South African provinces: Eastern Cape (EC), KwaZulu-Natal (KZN) and Western Cape (WC). These were chosen based on key informant interviews with local and national TB programme staff (unpublished), suggesting variations in the implementation of decentralised care, as well as to include both rural and urban areas.

Participants

Patients with a new diagnosis of rifampicin-resistant tuberculosis (RR-TB) where the diagnostic specimen was collected during July–September 2016 at a health facility in one of the study districts were eligible. New diagnoses were defined as a diagnostic RR-TB result with no previous such results during the preceding 6 months. A random sample of 15 patients was selected (using a random number generator) from a list of patients generated from the laboratory data for each district. This sample size was chosen for pragmatic reasons in order to be able to verify the patient journeys derived from laboratory data. Patients were excluded if discordant results indicated drug-susceptible TB, or if no subsequent laboratory records could be matched to the patient (i.e., no health care journey could be constructed). In these circumstances, replacement patients were randomly selected.

Data sources

All laboratory data were obtained from the National Health Laboratory Service (NHLS), which provides laboratory services for government health services, including all TB services, in South Africa.[19] Along with the list of all RR-TB patients diagnosed between July

and September 2016 from the 13 districts, raw data comprising all laboratory records linked to the randomly selected patients during a 9-month follow-up period, beginning when the index RR-TB specimen was collected, were obtained from the NHLS central data warehouse. These laboratory data provided information on all laboratory testing, including TB-related testing, adverse event monitoring and human immunodeficiency virus (HIV) related tests. As there is no unique patient identifier consistently captured at healthcare visits, an automated linking algorithm was applied by the NHLS to identify different healthcare visits by the same patient. To identify specimens missed by the linking algorithm, the online NHLS database was then manually searched for the same follow-up period using name and date of birth variations, hospital folder numbers and facility names.

Facility names were extracted from laboratory records, along with facility type and location. Facility type was categorised as either: primary care; secondary hospital (district and regional hospitals, including those containing DR-TB units); and tertiary hospital (also including DR-TB units); TB hospital; or TB Centre of Excellence hospital (one of which is designated in each province). In addition to NHLS geographic coordinates for health facilities, the South African District Health Management Information System (DHMIS) and the healthsites.org.za resource were used to confirm facility location. If no coordinates could be found, we collected new spatial data from online sources.

Rural/urban categorisation was obtained from two different sources.[20,21] In order to verify patient care journeys, we visited all health facilities identified by laboratory records, searched for and, if located, reviewed medical records for all participants. We then compared these to healthcare journeys constructed using laboratory records, to detect discordance, or missing visits.

Data analysis

Unique combinations of facility name and collection date were extracted from laboratory data, and placed in chronological order for each patient. Records of different health facilities at which samples were collected, on different days, formed patient healthcare journeys. We then described and visualised these journeys.

Spatial data were analysed and maps produced in ArcGIS v10.5.1 (ESRI, Redlands, CA, USA). Descriptive statistics were analysed in Stata v13.1 (StataCorp, College Station, TX, USA). Patient time bar charts were produced using Excel 2016 (Microsoft, Seattle, WA, USA). We assumed that a health facility was responsible for patient care until the patient provided a laboratory specimen at a new health facility. We assumed that patients remained in the care of the last recorded health facility for 14 days, or until the end of the follow-up period, whichever was earlier.
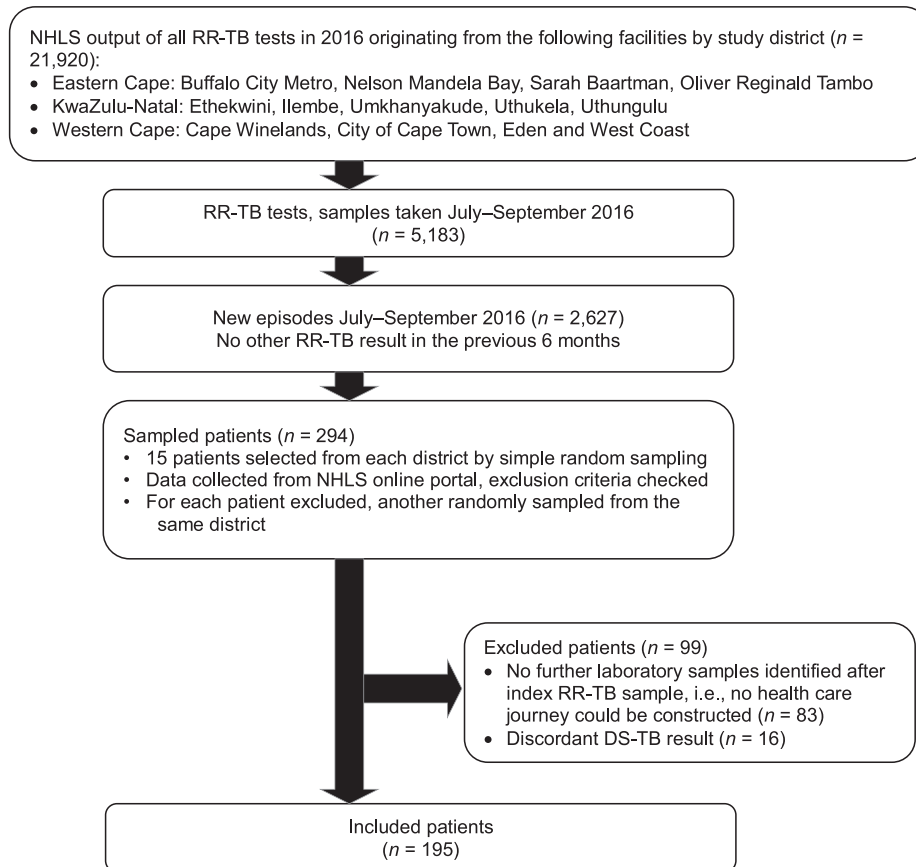
Figure 1 Diagram illustrating the eligibility, sampling and exclusion process. NHLS = National Health Laboratory Service; RR-TB = rifampicin-resistant tuberculosis; DS-TB = drug-susceptible TB.

Ethical approval

Ethical approval for the study was provided by the University of Cape Town, Cape Town, South Africa (350/2016), and the London School of Hygiene & Tropical Medicine, London, UK (11680); research approval was obtained in each province (EC_2016RP30_232, KZ_2016RP51_466, WC_2016RP45_978).

RESULTS

Characteristics of study participants

The study sample included 195 participants from 13 districts in three provinces (Figure 1). Patients were followed for a median of 248 days (interquartile range [IQR] 176–267) within the 9-month period, based on our definition of remaining in care. Among the sample, 120 (61%) were male, and the median age was 35 years (IQR 28–44; Table).

Validation of laboratory data with clinical record review

Clinical records were located for 76% of patients (149/195). All facility visits identified using laboratory data for these patients were confirmed in clinical records. Additional facility visits were identified in facility records for 16% (24/149) of these patients.

For the majority of these patients, this was an additional single health facility visit, predominantly unrelated to their TB care.

Healthcare visits and distance travelled

Patients visited a mean of 2.3 different health facilities (95% confidence interval [CI] 2.1–2.6), with a mean of 12.2 health facility visits recorded per patient (95%CI 11.7–12.7) over the 9-month follow-up period. Results from univariate analysis by sub-group are given in the Table. While the mean number of unique facilities visited varied little by the factors assessed, the proportion of patients who visited four or more facilities varied considerably; more patients from KZN visited at least four facilities.

Of the 25 patients who remained at a single facility for all recorded health facility visits, 13 were diagnosed in WC. Patients from WC also switched facilities less than those from the other two provinces. Healthcare visits were similar across age, sex and multi/extensively DR-TB subgroups. As the treatment initiation date cannot be inferred from laboratory data alone, it is unclear whether different health facilities were visited as part of the diagnostic process, initiation of treatment or for treatment monitoring.

Table   Characteristics of participants and univariate results

	n	Number of unique facilities visited*			Number of transfers between facilities*			Total distance travelled, km		Proportion of time spent in primary care, %	
		Mean	(95% CI)	≥4 %	Mean	(95% CI)	≥4 %	Median	[IQR]	Median	[IQR]
All	195	2.4	(2.2–2.6)	9	2.3	(2.1–2.6)	21	66	[15–207]	21	[2–60]
Sex											
Female	75	2.4	(2.1–2.8)	9	2.2	(1.9–2.5)	15	77	[29–243]	20	[0–55]
Male	120	2.4	(2.1–2.6)	8	2.4	(2.2–2.7)	24	64	[9–176]	23	[6–69]
Age, years											
0–19	10	2.5	(1.6–3.7)	10	2.2	(1.4–3.3)	20	104	[51–290]	6	[0–34]
20–29	46	2.5	(2.1–3)	20	2.5	(2.1–3)	26	98	[23–293]	20	[4–66]
30–39	61	2.3	(1.9–2.7)	5	2.3	(2–2.8)	18	62	[5–206]	18	[1–60]
40–49	51	2.4	(2–2.8)	6	2.3	(1.9–2.8)	22	74	[15–206]	31	[8–72]
≥50	27	2.3	(1.8–3)	4	2.1	(1.6–2.7)	15	42	[17–110]	23	[0–48]
Province											
Eastern Cape	60	2.4	(2.1–2.9)	8	2.8	(2.4–3.2)	28	76	[19–266]	37	[17–70]
KwaZulu-Natal	75	2.5	(2.1–2.9)	11	2.4	(2.1–2.8)	21	92	[47–216]	6	[0–19]
Western Cape	60	2.2	(1.8–2.6)	7	1.8	(1.4–2.1)	12	36	[2–172]	39	[16–91]
Place of residence											
Urban	121	2.4	(2.1–2.7)	7	2.4	(2.2–2.7)	21	51	[9–140]	23	[7–60]
Rural	74	2.4	(2–2.8)	11	2.2	(1.9–2.5)	19	116	[50–290]	11	[0–60]
Type of resistance											
First-line drug[†]	124	2.3	(2.1–2.6)	7	2.2	(2–2.5)	19	81	[12–205]	22	[2–60]
Second-line drug[‡]	48	2.5	(2.1–3)	13	2.7	(2.3–3.2)	27	76	[18–220]	22	[4–53]
Missing	23	2.3	(1.7–3)	9	2	(1.5–2.7)	17	33	[10–60]	14	[0–85]

* Poisson distributions used to calculate means and CIs for count variables.
[†] Rifampicin, isoniazid, pyrazinamide, ethambutol.
[‡] Fluoroquinolones, aminoglycosides, bedaquiline, delamanid, linezolid, ethionamide, cycloserine/terizidone, clofazimine, para-aminosalicylic acid.
CI = confidence interval; IQR = interquartile range.

The median cumulative distance travelled between facilities over the follow-up period was 66 km (IQR 15–207). The median distance travelled was greater for patients from rural areas (116 km, IQR 50–290) than for those from urban areas (51 km, IQR 9–140). Figure 2 shows these data disaggregated by province. The difference in distance travelled between rural and urban patients was
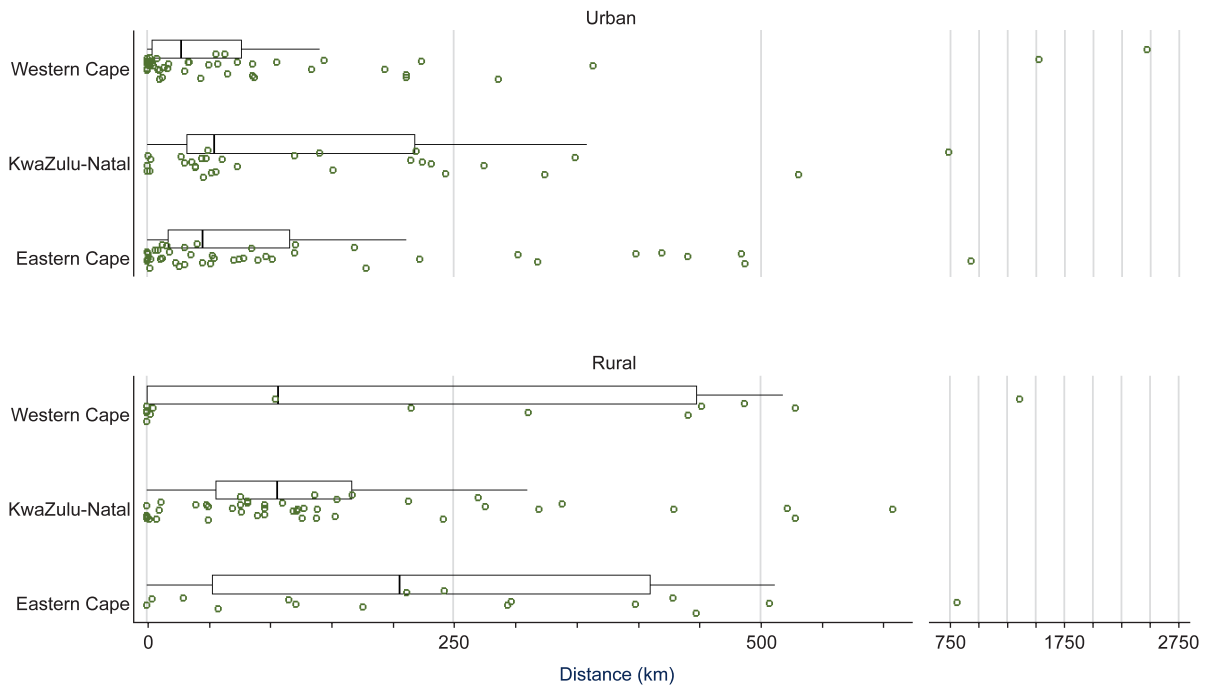
Figure 2   Distances travelled by patients from urban and rural areas, disaggregated by province, with box and whisker plots denominating the median (central bar), interquartile range (box ends), and adjacent values (whisker, largest/smallest values within 1.5 times interquartile range of the upper and lower quartiles). Each point represents a single patient. The horizontal scale is broken and condensed at right to show outliers.
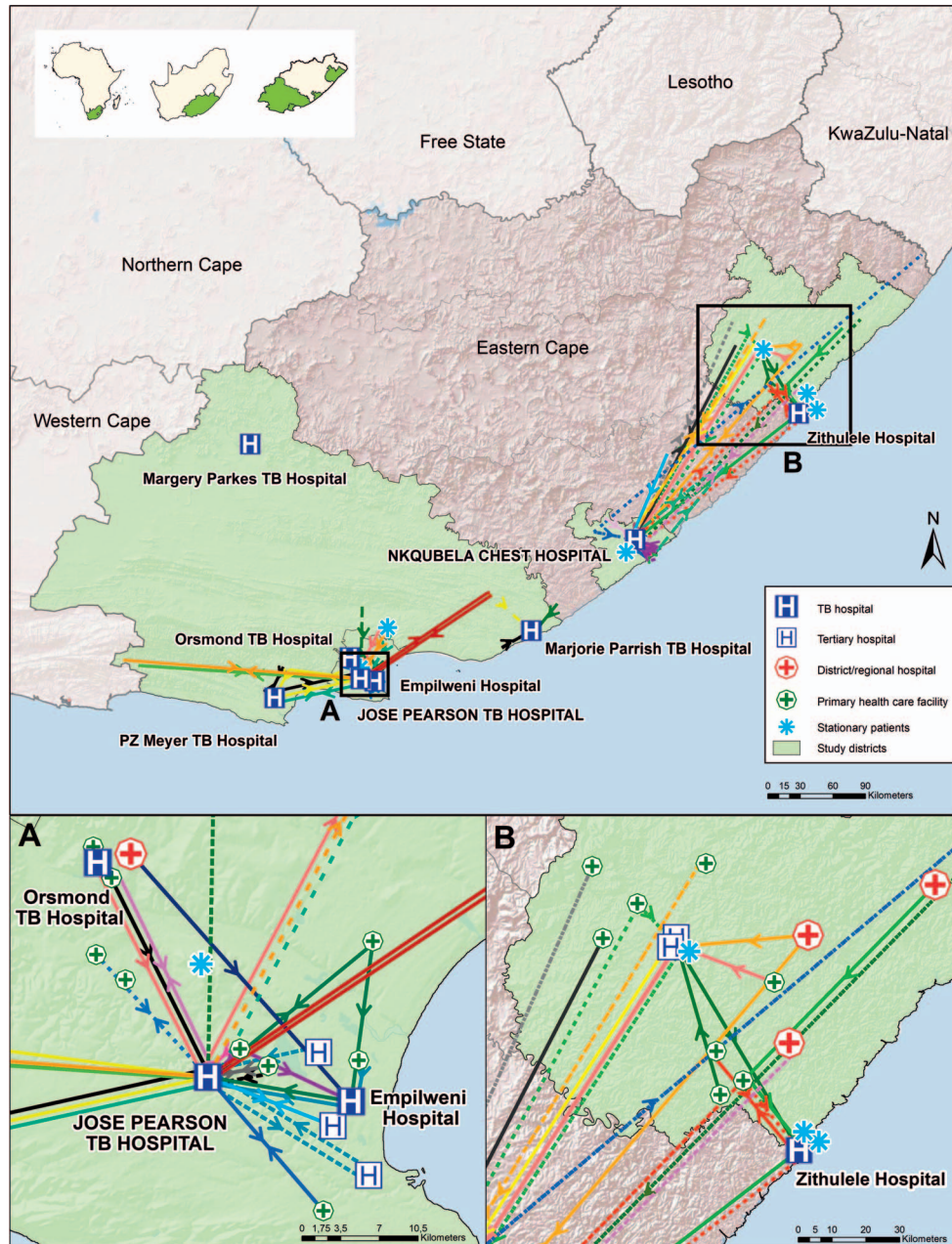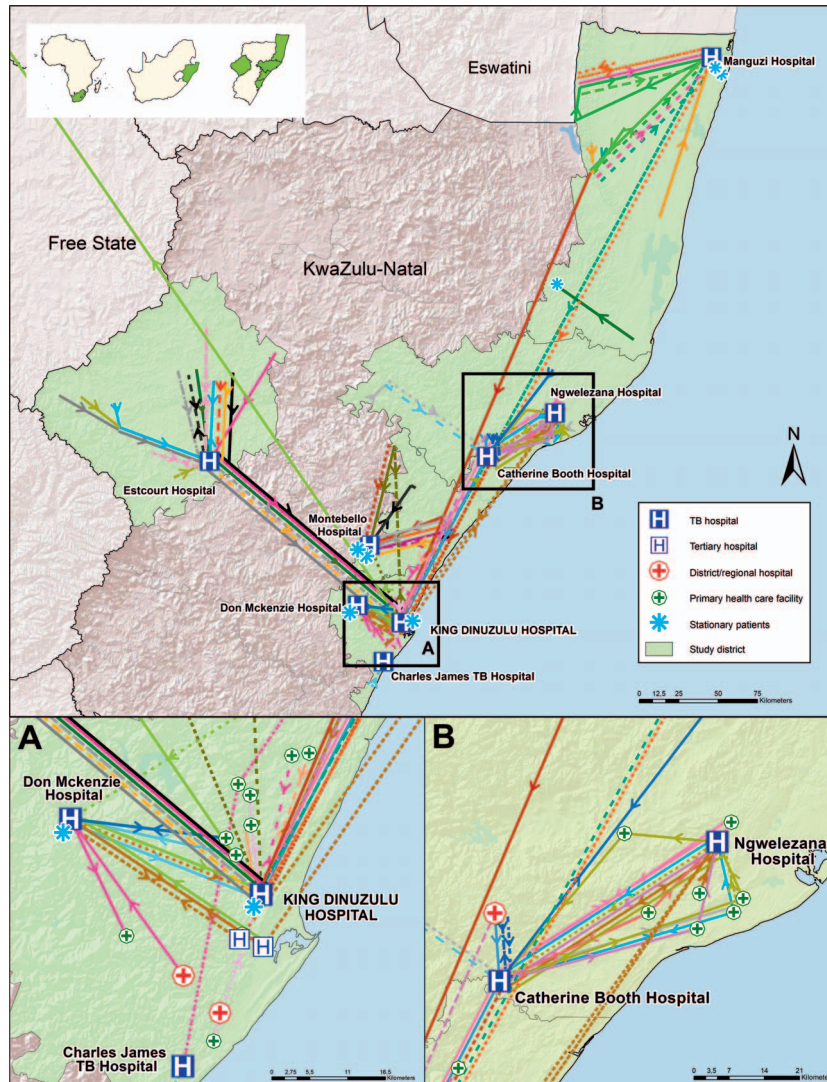
Figure 3 Patients' health care journeys in Eastern Cape Province. **A)** Detail of patients' journeys in Buffalo City Metro district (Port Elizabeth). **B)** Detail of patients' journeys in Oliver Reginald Tambo District. In all maps, individual patients are represented by differently coloured/styled lines, with arrows indicating the direction of travel; those who were diagnosed and treated at a single facility are represented by blue stars instead of coloured lines ('stationary patients' in the legend). COE hospital names are in capitals. Health facilities that are most frequently visited by patients are labelled by name. TB = tuberculosis; COE = Centre of Excellence.

more pronounced in EC and in WC than in KZN. Although some patients travelled extraordinary distances during the follow-up period (max: 2,598 km), chart review revealed that these patients had been transferred across provinces.

Mapping patient health care journeys

Figures representing individual patient journeys (Figures 3–5) show how patterns of care emerge when DR-TB patient healthcare journeys are viewed together. In EC, patients from rural areas travelled to

and from two centralised DR-TB units to obtain care—a quasi-centralised model. In KZN a 'hub and spoke' pattern emerged, with most patient journeys focused around regional 'hub' hospitals, some patients referred to centralised units, and some decentralised to lower level hospitals or clinics. In WC, patient journeys in urban areas reflected largely decentralised care utilising primary care facilities, compared to more rural areas where patients travelled to TB hospitals.

Figure 4   Patients' health care journeys in KwaZulu-Natal Province. **A)** Detail of patients' journeys in Ethekwini District (Durban). **B)** Detail of patients' journeys in Uthungulu District. COE hospital names are in capitals. TB = tuberculosis; COE = Centre of Excellence.

Time spent at lower levels of care

The median proportion of time in care that was spent under primary care was 21% (IQR 2–60). Patients from KZN spent a median of 6% of the duration of their healthcare journey under primary care (IQR 0–19), lower than either EC or WC patients (median, 37%; IQR 17–70 and median, 39%; IQR 16–91, respectively).

Time spent in different levels of care is charted in Figure 6. In WC, patients were mostly diagnosed and treated at primary care facilities, with a subgroup of patients referred to TB hospitals and then back to primary care. In EC, most patients also started their healthcare journeys in primary care, however there was greater use of centralised units. Journeys of patients from KZN demonstrated low utilisation of primary care facilities, but greater use of TB hospitals in each region.

DISCUSSION

This pilot study demonstrates how routine laboratory data can be used to describe and visualise DR-TB patient journeys through the healthcare system in South Africa. In this setting, decentralisation of DR-TB care aims to provide care at lower levels of the health system, both to improve treatment access and to deliver patient-centred care.[3] The patient journeys described here can be used to identify differences in patterns of care in order to explore variations in the implementation of decentralised care and generate hypotheses regarding the health system or patient features which may impact implementation. This methodology is comparable to that of Clouse et al., who used centrally collated NHLS laboratory data to map HIV patient encounters with the health system.[22] As DR-TB treatment generates comparably more laboratory data, we are able to construct a more
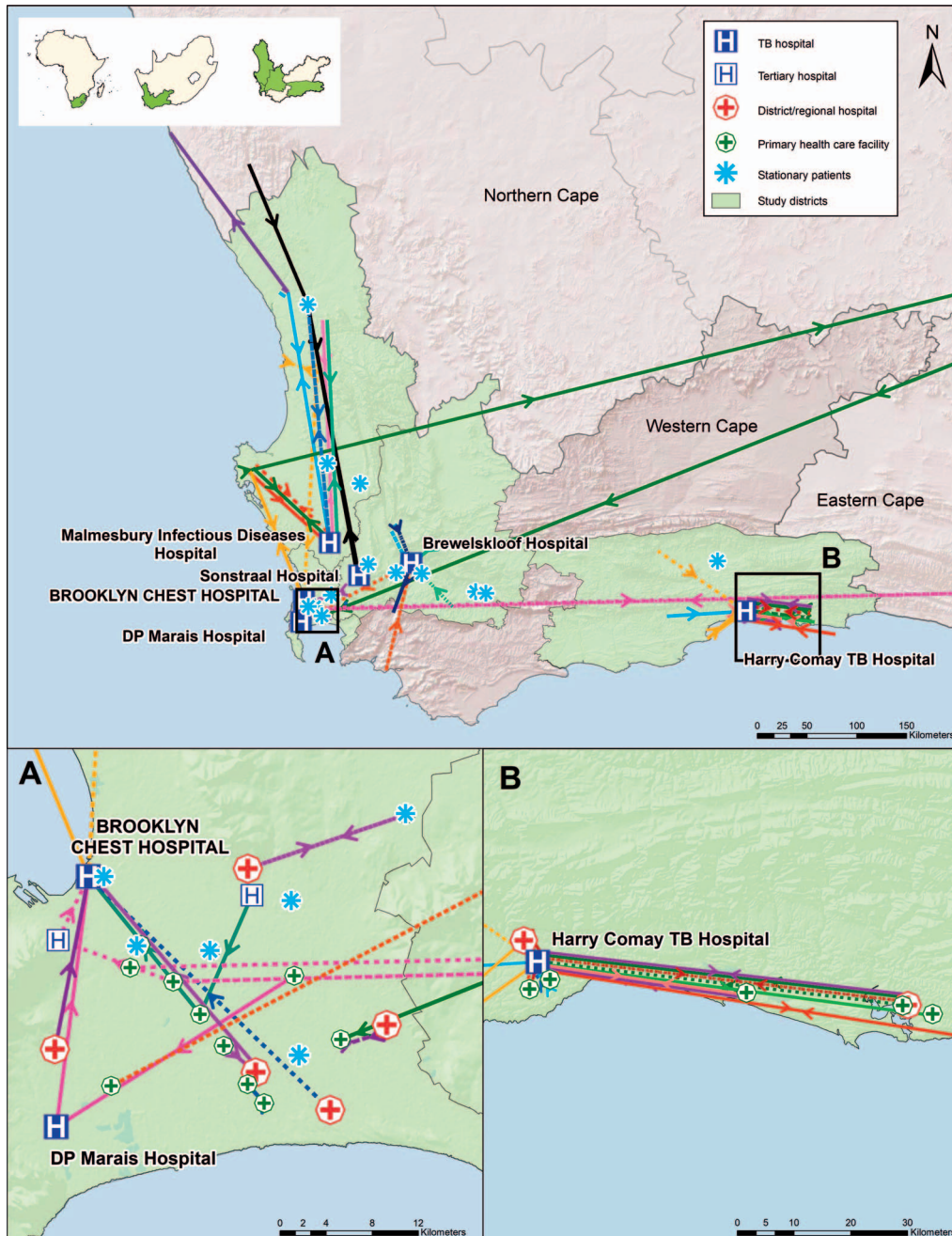
Figure 5   Patients' health care journeys in Western Cape Province. **A)** Detail of patients' journeys in City of Cape Town district. **B)** Detail of patients' journeys in Eden District. COE hospital names are in capitals. TB = tuberculosis; COE = Centre of Excellence.

granular picture of encounters over a longer period. In Thailand, mapping has been used to understand DR-TB patient journeys, albeit on a much smaller scale and focused on infectious spread during the pre-treatment period.[23] In comparison, we have focused on patient journeys to obtain an understanding of patterns of care.

While this was a pilot study and the sample was not intended to be representative, the quantitative results suggest that patient journeys may differ according to the province in which the patient lives, whereas results were similar across other subgroups.

This could reflect different models of care in each province, or other provincial-level differences. For example, these data suggest that DR-TB care has been decentralised to primary healthcare level in WC (fewer facilities, fewer switches between facilities and more time spent in primary care), which is consistent with the >400 decentralised facilities reported there.[15,16] Conversely, rural patients travelled larger distances in this study. Challenges in access to care in rural areas in South Africa are well documented, consistent with our findings.[24,25]

More meaningful insights were derived from visu-
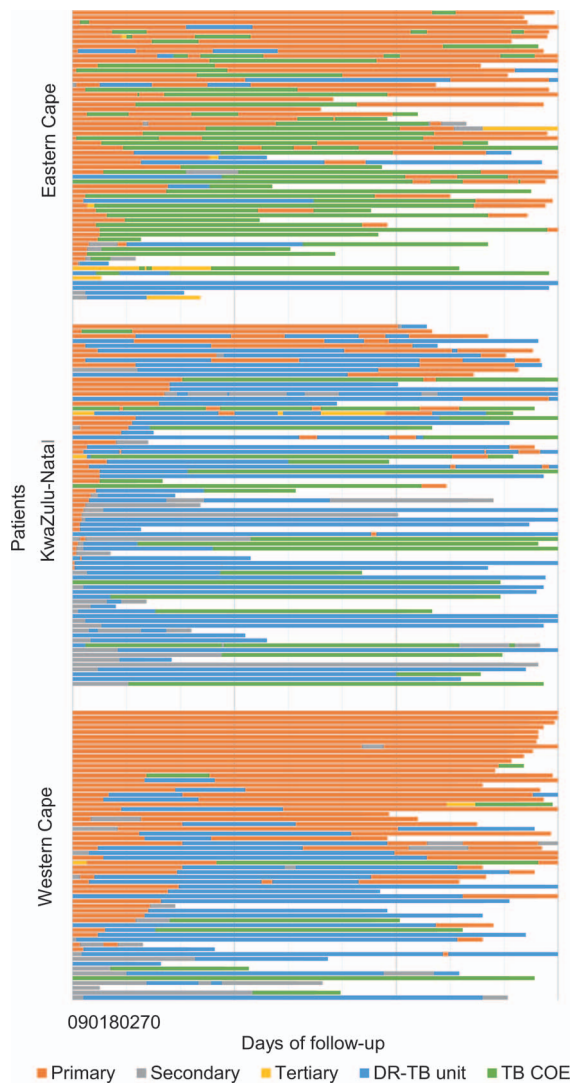
Figure 6 Bar chart of patient journeys during the follow-up period, showing consecutive changes in level of care, by province. Each patient is represented by one horizontal bar, with the date the diagnostic sample was taken for each patient represented as day 0. Orange: primary health care facilities. Grey: secondary hospitals. Yellow: tertiary hospitals. Blue: centralised DR-TB units. Green: TB COE hospitals. DR-TB = drug-resistant TB; COE = Centre of Excellence; TB = tuberculosis.

alisations of individual patient journeys. There were clear differences in the implementation of decentralised DR-TB care between provinces, identifiable as different patterns emerging in maps of patient health care journeys. The maps of patient journeys in the WC showing highly decentralised care within clinics in the City of Cape Town compared with the long distances travelled by rural patients suggest that models of care differ between the City of Cape Town and rural districts. In EC, the maps showed patients being referred back and forth between peripheral and centralised sites, a reality corroborated by analysis of patient journeys over time which showed periods of time spent in primary care facilities, interspersed with care in TB Centres of Excellence.

Our methodology has several limitations that would be apparent even if the methodology were to be applied on a larger scale using more representative data. First, the method requires linkage of laboratory tests to the same individual across episodes of care in different health facilities. We achieved this using manual matching. However, there are a variety of algorithmic techniques that could be utilised.[26] Our method also requires accurate spatial data for health facilities. In the NHLS data, only half the named facilities had useable geographic coordinates. The introduction of unique identifiers and improvements to the recording of spatial data by the NHLS, which are both underway, will make NHLS data an increasingly valuable tool for programmatic analysis of patient journeys. Second, a visit would only be recorded on the laboratory information system if a specimen was submitted; 16% of facility visits were missed based on the clinical record review, predominantly as there were no laboratory specimens taken. Third, there is no reliable way to identify from laboratory metadata whether a patient is admitted or treated as an outpatient, or what the treatment outcome was. As patient home addresses are not reliably captured by the laboratory database, we are unable to determine how close to home a patient received care. Our analysis of time spent in different levels of care is also limited by approximating the date on which care was transferred. Finally, since we excluded participants who had only one laboratory result, we did not capture care for patients who died early or were lost to follow-up.

The methodology and results of this study should be interpreted in the context of a range of factors, including geography, health system capacity, population density and DR-TB burden. Given the wide variation in these factors,[25,27] implementation of decentralised DR-TB care in South Africa is likely to vary and local adaptation to the needs of patients and communities in different areas would be appropriate. These contextualising factors have also been recognised in related research (for example, patient pathway analysis) in South Africa and internationally.[18]

Routine laboratory records provide an important source of data for research into health systems and responses to the TB epidemic. This study pilots a methodology for the use of routine laboratory records to reconstruct DR-TB patient health care journeys, and the results highlight different patterns emerging from the implementation of decentralised care for DR-TB in selected districts in South Africa. These patterns provide a starting point for understanding the varying responses of the health system to implementation of a policy of decentralised care and the complex healthcare journeys for some patients.

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RÉSUMÉ

CONTEXTE : Treize districts des provinces du Cap Est (EC), du KwaZulu-Natal (KZN) et du Cap Ouest (WC), Afrique du Sud.

OBJECTIF : Piloter une méthode de description et de visualisation du parcours de soins des patients atteints de tuberculose pharmacorésistante (DR-TB) grâce à des dossiers de laboratoire de routine.

SCHÉMA : Les dossiers des laboratoires ont été obtenus pour 195 patients ayant eu une TB résistante à la rifampicine (RR-TB), détectée par le laboratoire de juillet à septembre 2016. Les consultations identifiées à partir de ces données ont été localisées afin de visualiser le parcours de soins. Les données ont été vérifiées grâce à des visites dans les structures de soins.

RÉSULTATS : Au cours des 9 mois suivant le recueil de l'échantillon RR-TB index, les patients se sont rendus dans une moyenne de 2,3 structures de santé (IC95% 2,1–2,6), et 9% sont allés dans ≥4 structures. La distance médiane couverte par les patients des zones rurales (116 km, intervalle interquartile [IQR] 50–290) a été plus élevé que pour les patients urbains (51 km, IQR 9–140). Une médiane de 21% du temps des patients a été passée dans des structures de soins de santé primaires ; 6%, 37% et 39% dans les provinces du KZN, du EC et du WC, respectivement. Les profils de parcours ont été généralement similaires dans les différents districts. Dans certains cas, le modèle de soins était semi centralisé et les patients ont été référés à des hôpitaux régionaux ; d'autres parcours ont mis en évidence une plus grande implication des soins de santé primaires.

CONCLUSION : Les données de laboratoire de routine peuvent être utilisées pour explorer les parcours de soins de patients DR-TB et illustrer la façon dont l'utilisation des services de soins de santé de la DR-TB varie en fonction du contexte.

RESUMEN

MARCO DE REFERENCIA: Trece distritos en las provincias del Cabo Oriental (EC), KwaZulu-Natal (KZN) y el Cabo Occidental (WC) en Suráfrica.

OBJETIVO: Realizar el ensayo preliminar de un método para describir y visualizar el itinerario asistencial de los pacientes con tuberculosis farmacorresistente (DR-TB), a partir de los registros corrientes de laboratorio.

MÉTODO: Se obtuvieron los registros de laboratorio de 195 pacientes con TB resistente a rifampicina (RR-TB) detectada en el laboratorio de julio a septiembre del 2016. Se trazaron en gráficos las consultas al establecimiento de salud a partir de estos datos, con el fin de visualizar los itinerarios asistenciales de los pacientes. Los datos se verificaron con las citas al centro asistencial.

RESULTADOS: En los 9 meses posteriores a la fecha de recogida de la muestra inicial RR-TB, los pacientes acudieron en promedio a 2,3 centros de atención (IC95% 2,1–2,6) y 9% consultaron cuatro centros o más. La mediana de la distancia recorrida por los pacientes de zonas rurales (116 km; amplitud intercuartílica [IQR] 50–290) fue mayor que la distancia recorrida por los pacientes urbanos (51 km; AIC 9–140 km). En promedio, 21% del tiempo de atención de los pacientes transcurrió en establecimientos de atención primaria; esta proporción fue 6% en KZN, 37% en el EC y 39% en el WC. El perfil de los itinerarios fue equivalente en cada distrito. En algunos casos se observó un modelo de atención semicentralizada, en el cual los pacientes se remitían a hospitales regionales; otros itinerarios revelaron una mayor participación de la atención primaria.

CONCLUSIÓN: Los datos corrientes del laboratorio se pueden utilizar con el fin de evaluar los itinerarios asistenciales de los pacientes con DR-TB y reflejan las diferencias en la utilización de los servicios de salud por este tipo de TB en los diversos entornos.