Loss to follow-up among patients diagnosed with spinal tuberculosis at a tertiary hospital in Western Cape Province, South Africa: A retrospective cohort study

T N Mann,[1,2] BSc, BSc (Med) Hons, MPhil, PhD; **J H Davis,**[1] MB ChB, MMed, FC Orth (SA); **R Dyers,**[2,3] MB ChB, MSc, MMed, FCPHM (SA)

[1] *Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*

[2] *Division of Health Systems and Public Health, Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*

[3] *Western Cape Government: Health, Cape Town, South Africa*

Corresponding author: *T N Mann (theresa.mann@gmail.com)*

Background. Patients diagnosed with spinal tuberculosis (TB) at a major tertiary hospital in Western Cape Province, South Africa, are required to attend regular follow-up at the hospital's outpatient spine clinic and to remain on TB treatment for at least 9 months. This follow-up and lengthy treatment is intended to allow for specialist monitoring of TB treatment response and early identification of secondary complications, and to reduce the risk of recurrence. However, little is known about adherence to these recommendations.

Objectives. The main objectives were to describe (*i*) loss to spine clinic follow-up (LTFU), and (*ii*) TB treatment duration among patients diagnosed with spinal TB at the hospital. Secondary objectives were to investigate (*i*) the association between LTFU and treatment duration, and (*ii*) factors associated with LTFU.

Methods. This retrospective cohort study included 173 adults diagnosed with spinal TB between 2012 and 2015 and investigated follow-up within 2 years from diagnosis. Clinical, demographic and appointment data were obtained from hospital records and a dataset provided by the provincial Department of Health. LTFU was presented as frequency (%) and as a survival analysis. TB treatment duration was reported as frequency <9 months or ≥9 months, and the association between LTFU and <9 months of treatment was investigated using relative risk (RR) with 95% confidence intervals (CIs). Univariate associations between explanatory variables and LTFU were investigated using simple logistic regression analysis.

Results. Patients had a median (interquartile range) age of 36 (29 - 48) years and included 98 females (57%) and 151 individuals (87%) residing <50 km from the hospital. Primary outcomes were that 129 patients (75%) were LTFU within 2 years of diagnosis and 45 (30%) completed <9 months of treatment. The RR of <9 months of treatment was 1.62 (95% CI 1.39 - 1.88) among those LTFU compared with those retained in follow-up. LTFU was not associated with any of the clinical or demographic variables investigated.

Conclusions. Three-quarters of the patients did not complete follow-up at the tertiary hospital spine clinic, and almost one in three received <9 months of TB treatment. Remaining in spine clinic follow-up was significantly associated with receiving at least the minimum duration of TB treatment. However, LTFU could not be predicted from routine clinical and demographic information and is likely to be related to factors not accounted for in the current analysis.

S Afr Med J 2020;110(4):284-290. https://doi.org/10.7196/SAMJ.2020.v110i4.14179

Spinal tuberculosis (TB) accounts for ~2 - 4% of all tuberculosis cases and is the most common form of musculoskeletal TB.[1,2] The condition involves gradual destruction of one or more spinal vertebrae following haematogenous spread of *Mycobacterium tuberculosis* from a primary focus and typically manifests as gradually worsening back pain, with or without constitutional symptoms.[3-6] Progression of the disease is associated with significant morbidity, with previous reports suggesting spinal deformity in 16 - 77% of cases and neurological deficits due to compression of the spinal cord in 33 - 73%.[4-7] Early diagnosis and adequate TB treatment are key factors in optimising outcomes.[5]

Western Cape Province, South Africa (SA), has one of the highest burdens of TB worldwide, with 681 notified cases per 100 000 population and an HIV co-infection rate of 38.5% in 2015.[8] In this setting, spinal TB is comparatively common, with at least 393 cases seen at tertiary hospitals in the province between 2012 and 2015 and an estimated incidence of 1.22 - 2.57 cases per 100 000 over this period.[7] Drug-resistant spinal TB was established in 9% of cases.[7] While health policy specifically addressing spinal TB is currently lacking, established practice in the province has been to refer patients with suspected spinal TB to specialist orthopaedic services for diagnosis, including an in-theatre spine biopsy.[3,7] TB treatment is typically initiated in hospital and then continued at a local primary healthcare clinic upon discharge. Patients are treated with a combination preparation of rifampicin, isoniazid, ethambutol and pyrazinamide throughout the course of treatment, although this approach is informed by clinical experience rather than controlled trials.[3]

The appropriate length of treatment for spinal TB remains a contentious issue, as discussed in detail elsewhere.[3,9-11] Although certain studies have suggested that 6 months of treatment is effective, most treating orthopaedic specialists continue to report at least 9 - 12 months of treatment.[9,11] Furthermore, advanced imaging over the course of treatment has suggested substantial variation in

the time to apparent clinical cure in spinal TB, with most patients showing unresolved spinal lesions at 9 months of treatment.[12-14] In the absence of convincing evidence for shorter regimens, orthopaedic specialists in the Western Cape have continued to prescribe a minimum of 9 months of treatment for patients with spinal TB, based on clinical experience and historical teaching.[3,10,15] Furthermore, the established standard of care has been for patients to attend follow-up at the tertiary hospital's outpatient spine clinic every 3 - 4 months over the course of treatment, over and above monthly visits to their local primary healthcare clinic.

In the current high-burden, resource-limited setting, routine advanced imaging to assess clinical cure in spinal TB is not feasible. However, serial follow-up at the spine clinic allows for monitoring of treatment response using clinical improvement, the erythrocyte sedimentation rate (ESR) and signs of healing on a spine radiograph.[10,15] While these measures cannot reliably establish clinical cure, they are used to assess for a trend of healing. Furthermore, the visits are used to ensure that patients complete the extended period of treatment and to monitor for any progression of deformity or late neurological changes. After the minimum 9 months of treatment, the decision to terminate or continue TB treatment is made on an individual level based on the clinical judgement of the specialist.[10] Treatment is stopped by the specialist providing the patient with a letter to the clinic to this effect, and patients are typically requested to attend one final spine clinic visit 3 months post treatment to ascertain whether there has been any recurrence of symptoms or notable increase in the ESR.

In the event of drug-resistant spinal TB, an appropriate regimen and duration are determined by infectious disease specialists. However, patients with drug resistance attend follow-up at both the spine clinic and the infectious diseases clinic and are monitored using the same measures as used in drug-sensitive spinal TB. The decision to terminate treatment is made in collaboration with infectious disease specialists, based on clinical judgement.

It is envisaged that spine clinic follow-up plays an important role in providing adequate care for patients with spinal TB. While necessary treatment duration is likely to vary between individuals, extended treatment serves to err on the side of caution in the absence of a marker of clinical cure. Specialist follow-up facilitates clinical monitoring and may help to ensure completion of extended treatment, whereas patients lost to follow-up may stop treatment prematurely, potentially increasing the risk of recurrence, further pathology and a renewed burden on the health system. However, there are several factors that may impact on patient willingness and ability to attend spine clinic follow-up, including the lengthy follow-up period, the time and expense of travel to the hospital, the discomfort of travel for this particular patient group, and the concurrent monthly local clinic visits.

Although spine clinic follow-up and extended treatment for spinal TB is a longstanding practice in the current setting, little is known about adherence to this follow-up or about treatment duration in practice. Previous TB-related studies have reported on continuity of care between hospital-diagnosed TB cases and primary care,[16-19] loss to follow-up from TB treatment at primary healthcare level[20-23] and adherence to TB treatment.[24-28] However, there appears to be little existing literature addressing tertiary hospital follow-up as part of care for a TB episode. Previous studies investigating hospital-based follow-up in orthopaedics have for the most part focused on trauma follow-up in a developed country setting, including well-resourced clinical trials.[29-34] Although Dunn *et al.*[15] alluded to poor compliance with tertiary hospital follow-up among spinal TB patients in the Western Cape, this concern fell beyond the main objective of the present study and was not subsequently investigated.

Objectives

The main objectives of the present study were to describe (*i*) loss to spine clinic follow-up (LTFU), and (*ii*) TB treatment duration among patients diagnosed with spinal TB at a major tertiary hospital in the Western Cape. Secondary objectives were to investigate (*i*) the association between LTFU and treatment duration, and (*ii*) baseline variables associated with LTFU. It was envisaged that insight into the extent of LTFU among patients with spinal TB and the relevant risk factors could help to inform health systems strengthening for the treatment of this severe TB disease as well as other conditions requiring tertiary hospital follow-up.

Methods

Study design and population

A retrospective cohort study was conducted, with all adults (age ≥15 years) diagnosed at a single tertiary hospital between 1 January 2012 and 31 December 2015 systematically selected for inclusion. These patients formed part of a larger, finite population of 319 adults diagnosed with spinal TB at tertiary hospitals in the Western Cape over the 4-year period, with further details of case identification and diagnosis described elsewhere.[7] This lengthy study period and systematic inclusion of patients was necessary, given the comparatively low incidence of spinal TB.[7] The follow-up period was 2 years from diagnosis to allow for 9 - 18 months of treatment plus the standard post-treatment assessment.

Exclusion criteria for the study were management by a specialty other than orthopaedic spinal services, moving away upon inpatient discharge, or death within 5 months of inpatient discharge. Patients managed by other specialties or who moved away upon discharge were never scheduled for spine clinic follow-up and therefore could not be evaluated for the primary outcome. Patients who died shortly after discharge were excluded on the basis that they did not contribute insight into follow-up or the relationship between follow-up and treatment duration. Finally, cases in which it was unclear from the available data whether the patient was discharged or LTFU were also excluded, as these patients could not be reliably assigned to an outcome category. Characteristics of patients for whom discharge/LTFU were unclear were presented separately.

Setting

The study took place at a major tertiary referral hospital serving approximately half the Western Cape, including a portion of the City of Cape Town Metro and certain rural districts, a catchment area of at least 3.4 million people.[35] The hospital provided the only public health sector specialist spine services in its catchment area, resulting in a considerable burden on service provision and considerable travelling distance for certain referral areas.

Data collection

Clinical and demographic data as well as details of TB treatment and appointments attended were accessed from a combination of hospital sources and a health dataset obtained from the Western Cape Department of Health. Hospital sources included patient medical records, whereas the dataset included routine information from the patient administration system, pharmacy records and the Electronic Tuberculosis Register (ETR.net) or Electronic Drug Resistant Tuberculosis Register. The time period for the dataset was 1 January 2012 - 31 December 2017. Finally, distance from the

hospital was taken as the shortest distance by road between the patient's area of residence and the hospital according to Google Maps[30,34] and reported as both a continuous variable and a categorical variable, < or ≥50 km. All study data were captured by a single investigator using custom-designed electronic data capture forms in order to optimise data quality and consistency.

Loss to follow-up

The definition of loss to follow-up may have a large impact on study findings and should be kept consistent between studies wherever possible.[36,37] However, existing definitions such as loss to follow-up from TB treatment[38] and loss to follow-up in orthopaedic trauma[29,31,32,34] were not suitable for the current context. The following definition was therefore developed, based on the expected frequency of visits.[36] Loss to spine clinic follow-up (LTFU) among patients with spinal TB was defined as absence from the spine clinic for at least 6 months (180 days), including at least one missed appointment. This definition detected patients who were not monitored at the clinic as frequently as required and was approximately equivalent to two missed visits.

To determine LTFU, time between appointments was screened for periods of ≥6 months. Periods of ≥6 months were subsequently investigated for missed appointments, as identified from the patient administration system or the follow-up plan documented in the medical record. The date of LTFU was recorded as the date of the missed appointment for patients with scheduled appointments[36] and the hospital inpatient discharge date when no spine clinic appointment had been booked. Data capture included whether patients LTFU returned to the spine clinic within 2 years of diagnosis. Patients who were not LTFU were described as having been retained in spine clinic follow-up. This group included patients who were discharged from the spine clinic and patients who remained in spine clinic follow-up 2 years after diagnosis. The duration of follow-up was calculated from the date of the magnetic resonance imaging scan, the first step in formal diagnosis of spinal TB, to LTFU or spine clinic discharge as applicable.

Treatment duration

Treatment duration was calculated as the difference between the start and termination of treatment dates and categorised as <9 months or ≥9 months of TB treatment. The start and termination of TB treatment were determined based on the best available evidence, according to the following hierarchy: medical records, pharmacy records or the ETR.net. Additional treatment data extracted included whether or not TB treatment was terminated by an orthopaedic specialist and treatment outcome recorded in the ETR.net.

Data analysis

Categorical variables were presented as frequency (%), whereas continuous data with a non-parametric distribution were reported as medians and interquartile ranges (IQRs). Primary outcomes LTFU and treatment duration <9 months were presented as frequency. Furthermore, LTFU was also presented as a Kaplan-Meier survival analysis of all included patients. Patients discharged from the spine clinic were censored from survival analyses at discharge, and follow-up was limited to 2 years from diagnosis for all patients.

The association between LTFU and <9 months of TB treatment was investigated by calculating the relative risk (RR) and associated 95% confidence intervals (CIs). In addition, a separate survival analysis was presented for patients completing <9 months and ≥9 months of TB treatment, and survival curves were compared using a log-rank test. Univariate relationships between explanatory variables and LTFU were investigated using a χ^2 test or Fisher's exact test for categorical variables and simple logistic regression analysis for continuous variables. Explanatory variables associated with LTFU at $p \leq 0.20$ were eligible for inclusion in the logistic regression model to predict LTFU and were reported as crude and adjusted odds ratios with 95% CIs. All statistical analyses were performed in Graphpad Prism version 6.00 (GraphPad Software Inc., USA) or Stata version 15 (StataCorp, USA) with significance accepted at $p<0.05$. Reporting of study findings was guided by the STROBE checklist for observational studies.[39]

Ethical considerations

The study was approved by the Health Research Ethics Committee of Stellenbosch University (ref. no. N15/07/062), the Provincial Health Research Committee (ref. no. WC_201801_014) and the management of the hospital.

Results

Patient characteristics

Of 199 adult patients diagnosed with spinal TB at the hospital between 2012 and 2015, 26 were excluded from further analysis, as described in Fig. 1. The remaining 173 patients were included in the LTFU analysis, with the characteristics of included patients presented in Table 1. The 7 patients with discharge/LTFU unclear had a median (IQR) age of 35 (22 - 58) years and comprised 4 males and 3 females, with 5 from urban areas and 2 from rural areas. Two patients

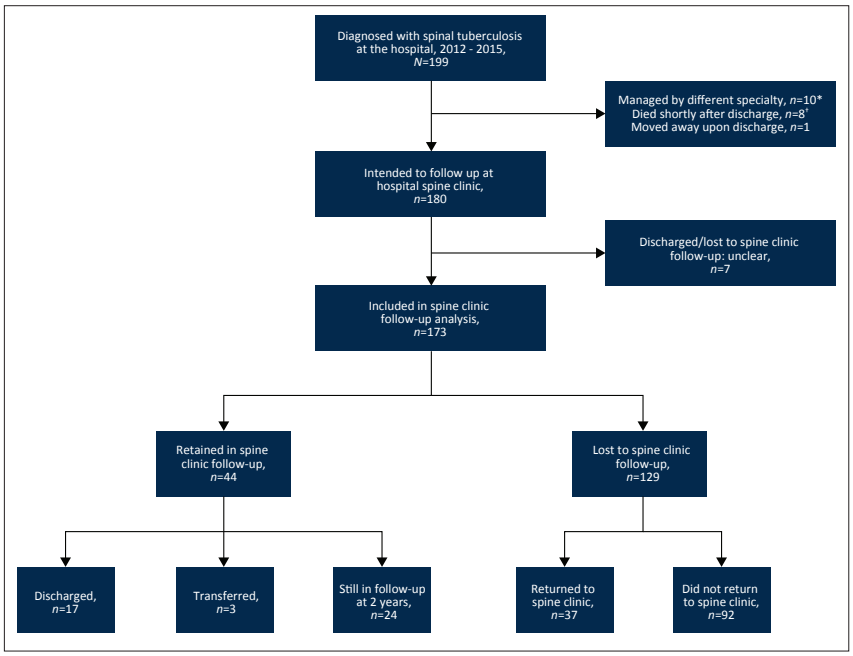

*Fig. 1. Overview of patients included in spine clinic follow-up analysis and follow-up outcomes. (*Nine patients were managed by neurosurgery and one by abdominal surgery; †Median time from discharge to death 5 weeks, range 0 - 20 weeks.)*

Table 1. Demographic and clinical characteristics of patients followed up at the spine clinic, in total and by follow-up outcome

	Total (*N*=173)	LTFU (*N*=129)	Retained (*N*=44)	LTFU v. retained, *p*-value
Age (years), median (IQR)	36 (29 - 48)	38 (32 - 50)	36 (28 - 47)	0.11
Sex, *n* (%)				
Male	75 (43)	58 (45)	17 (39)	0.46
Female	98 (57)	71 (55)	27 (61)	
Residence, *n* (%)				
Urban	139 (80)	101 (78)	38 (86)	0.25
Rural	34 (20)	28 (22)	6 (14)	
Travel distance (km), *n* (%)				
<50	151 (87)	110 (85)	41 (93)	0.17
≥50	22 (13)	19 (15)	3 (7)	
HIV status, *n* (%)				
Positive	73 (42)	57 (44)	16 (36)	0.59
Negative	84 (49)	61 (47)	23 (52)	
Unknown	16 (9)	11 (9)	5 (11)	
Previous TB episode, *n* (%)				
≥1	15 (9)	12 (9)	3 (7)	1.00
None	156 (90)	117 (91)	39 (89)	
Unknown	2 (1)	0	2 (5)	
Spinal TB diagnosis, *n* (%)				
Bacteriologically confirmed	130 (75)	97 (75)	33 (75)	0.98
Clinically diagnosed	43 (25)	32 (25)	11 (25)	
Drug susceptibility, *n* (%)				
Sensitive	115 (66)	85 (66)	30 (68)	0.98
Mono- or multidrug resistant	13 (8)	10 (8)	3 (7)	
Unknown	45 (26)	34 (26)	11 (25)	
Vertebrae affected, *n* (%)				
1 - 2	97 (56)	74 (57)	23 (52)	0.56
≥3	76 (44)	55 (43)	21 (48)	
Spine deformity, *n* (%)				
Kyphosis	133 (77)	97 (75)	36 (82)	0.37
No kyphosis	40 (23)	32 (25)	8 (18)	
Surgery, *n* (%)				
Minor procedure/none	143 (82)	106 (82)	37 (80)	0.77
Corrective surgery	30 (18)	23 (18)	9 (20)	
Discharge pathway, *n* (%)				
Discharged home	121 (70)	92 (71)	29 (66)	0.62
Admitted to secondary health facility	52 (30)	37 (29)	15 (34)	

LTFU = lost to follow-up from the spine clinic; Retained = retained in follow-up at the spine clinic; IQR= interquartile range; TB = tuberculosis.

received corrective surgery and 5 minor procedures, with 1 patient HIV-infected, 3 HIV-negative and 3 with HIV status unknown. The small number of patients with a missing spine clinic outcome precluded valid statistical comparison with those included in the LTFU analysis. However, no obvious differences were observed in these or other characteristics.

Spine clinic loss to follow-up

Of the 173 patients included in the analysis, 129 (75%) were LTFU within 2 years of diagnosis (Fig. 1). Although 37 patients (29%) who met the criteria for LTFU returned to the spine clinic for at least one further appointment within 2 years of diagnosis (median (IQR) absence 8 (7 - 11) months), 92 (71%) had no further spine clinic contact (Fig. 1). When examining how the percentage of patients in spine clinic follow-up decreased over time, the pattern showed a relatively steady attrition, with a median duration of 11 months in spine clinic follow-up (Fig. 2A) and a median (IQR) of 3 (1 - 5) spine clinic appointments over the 2 years. Incidental findings included 5 patients who were, erroneously, not booked for spine clinic follow-up at inpatient discharge. Furthermore, of the 129 patients LTFU, 42 (33%) had a follow-up appointment indicated in the clinical records but no appointment booked on the patient administration system.

TB treatment

There were 150 patients for whom treatment start and end could be established, with the distribution of treatment duration shown in Fig. 3. Overall, there were 45 patients (30%) who completed <9 months of treatment (Table 2). Of 54 patients who had treatment stopped by an orthopaedic specialist, 28 went on to complete one or more post-treatment spine clinic visits prescribed by the specialist, whereas 26 were LTFU after stopping treatment and did not return for the post-treatment visit (Table 2). In the ETR.net, 121 patients (70%)

Table 2. TB treatment outcomes, in total and by follow-up outcome

	Total (*N*=150)	LTFU (*N*=110)	Retained (*N*=40)	LTFU v. retained, *p*-value
TB medication duration (months), *n* (%)				
<9	45 (30)	45 (41)	0	<0.0001
≥9	105 (70)	65 (59)	40 (100)	
Who stopped TB treatment, *n* (%)				
Orthopaedic specialist	54 (36)	26 (24)	28 (70)	<0.0001
Other/unclear	96 (64)	84 (76)	12 (30)	

LTFU = lost to follow-up from the spine clinic; Retained = retained in follow-up at the spine clinic; TB = tuberculosis.

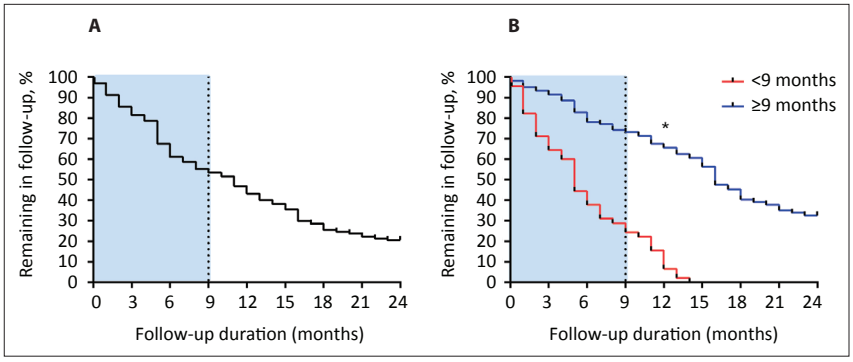

*Fig. 2. Loss to spine clinic follow-up among all patients (A) and patients grouped by TB treatment duration (B). Blue shading indicates the minimum recommended treatment duration. (TB = tuberculosis; *Significant difference in the pattern of LTFU between patients completing <9 and ≥9 months of TB treatment (*p<*0.0001.)*

were recorded as extrapulmonary TB and 9 (5%) as pulmonary TB, with this information missing for the remaining 43 patients (25%). No ETR.net treatment outcome was recorded for 104 patients (60%), with 63 others (36%) recorded as 'treatment completed', 4 (2%) as 'cured', 1 (<1%) as 'died' and 1 (<1%) as 'still on treatment'. There was no difference in age (p=0.91), sex (p=0.64), HIV status (p=0.78), surgery (p=0.56) or LTFU (p=0.32) between the patients for whom treatment duration could be established and the 23 patients with missing treatment duration data. However, there was a significant association between missing treatment duration data and residing in a rural district (n=25, 17% v. n=9, 39%; p=0.02).

Spine clinic follow-up v. TB treatment duration

LTFU was associated with an increased risk of premature treatment cessation compared with retention in spine clinic follow-up (RR 1.62; 95% CI 1.39 - 1.88). Furthermore, all 45 patients who completed <9 months of treatment were patients who had been LTFU (Table 2). There was also a significant difference in the pattern of LTFU between those completing <9 and ≥9 months of TB treatment, with a median time in spine clinic follow-up of 5 months and 16 months, respectively (p<0.0001) (Fig. 2B).

Univariate and multivariate associations with LTFU

There were no significant univariate associations between LTFU and the clinical or demographic variables in Table 1 at p<0.05, or an association between LTFU and kilometres of travel to the hospital (p=0.21) or year of admission (p=0.86). Age and travel distance ≥50 km were entered into a logistic regression model based on p≤0.20, but the model was not statistically significant (p=0.10) and prediction of LTFU from the available variables was not investigated further.

Discussion

The first finding of the study was that 75% of patients with spinal TB were LTFU within 2 years of diagnosis. This result suggests that the majority of patients did not receive the current standard of care in terms of specialist monitoring, including assessment of treatment response and management of secondary complications. Although some patients returned for at least one further appointment, the potential impact of LTFU remained in that patients were typically without spine specialist care for 7 - 11 months and may have experienced worsening pathology over this period. Furthermore, most patients had no further contact with the spine clinic once LTFU and therefore discontinued all spine specialist care before being deemed clinically ready to do so.

The second finding of the study was that 30% of patients with spinal TB received less than the 9 months minimum recommended treatment duration. In practice, the necessary duration of TB treatment is likely to vary between individuals.[12,14] However, it is challenging to confirm clinical cure in spinal TB, and treatment is frequently extended to 12 months or even more for patients remaining in orthopaedic follow-up.[3,14] This prolonged treatment is supported by advanced imaging studies[12-14] and is intended to allow for adequate antibiotic penetration of dead bone tissue, abscesses and granulomas as well as effective treatment in patients who are malnourished or HIV-infected – a common concern in the SA public health setting.[3] Premature cessation of TB treatment may place individuals at increased risk of disease recurrence, which in turn risks additional spine pathology and further hospital admissions, scans, surgery and treatment. Given these implications for both the patient and the health system, the finding that almost one in three patients received relatively short courses of TB treatment presents a considerable concern.

Another pertinent finding from the current study was that LTFU was associated with a 62% increased risk of stopping treatment early. Patients collected their TB medication monthly from the local primary healthcare clinic rather than from the spine clinic, so spine clinic LTFU did not automatically imply treatment termination. However, primary healthcare clinics may have stopped TB treatment after the conventional period of 6 months if there had not been additional communication from the hospital – a scenario that may help to explain the association between rapid LTFU from the spine clinic and <9 months of treatment. With the risk of premature treatment cessation in mind, it had become common practice for the spine specialist to use spine clinic follow-up visits to send

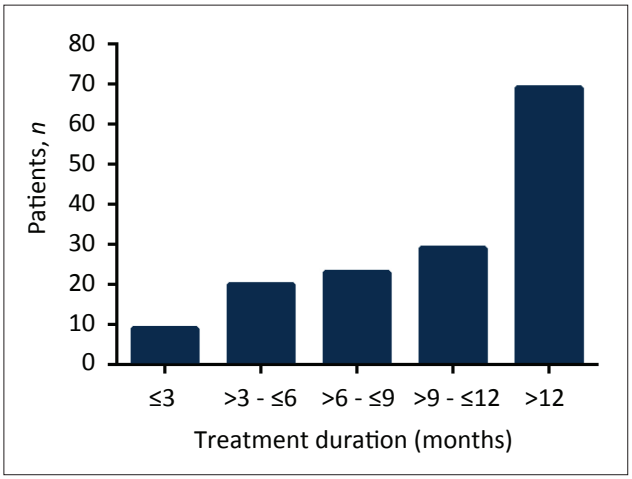

Fig. 3. Duration of TB treatment completed by patients with spinal TB. (TB = tuberculosis.)

a letter with the patient to the primary healthcare clinic. This letter would confirm the longer treatment duration and request continuation with the four-drug regimen throughout treatment. In addition, at every spine clinic visit, patients were routinely counselled about their TB treatment and received feedback on an ESR test and spine radiograph conducted on the day. In this way, spine clinic follow-up may have helped to consolidate patient awareness of the longer treatment duration, encouraged adherence, and increased the likelihood of patient objection should the primary healthcare clinic initiate treatment termination. The finding that 60% of patients had no treatment outcome reported in the ETR.net may suggest some uncertainty in the treatment of spinal TB at primary healthcare level and further supports the benefit of spine clinic follow-up.

Although spine clinic LTFU may be linked with premature treatment cessation, the study was not able to identify any baseline variables predicting LTFU that could hence inform retention-in-care strategies. While the lengthy study period and systematic inclusion of patients was intended to mitigate the low incidence of spinal TB, the study may yet have lacked statistical power to detect certain baseline associations. For example, previous studies have on some occasions shown that younger age,[21,23,29] male sex,[21,23,29,30] increased distance from the hospital[32,34] and less severe clinical presentation[29,31] were associated with poor follow-up outcomes. However, it is even more likely that baseline characteristics included in the current analysis explain less variation in LTFU than other, unmeasured variables – variables not reliably available through retrospective record review. For example, smoking,[28-30,32,33] substance abuse,[28,29,33,40] feeling well[24,40,41] and a low level of education[17,31,33,40] have all been linked with loss to follow-up in TB- and trauma-related studies. Furthermore, the previously identified role of low income or poverty[28,31] may be particularly important in the current population, most of whom come from a low socioeconomic background, are unable to work for extended periods of time, and may have to weigh the expense of travel to the hospital against competing costs such as food.[24] With this in mind, anecdotal evidence suggests that some patients may also be LTFU after choosing to return to family in other provinces while they recuperate. Finally, this study did not account for the role of health system factors in LTFU.[24,40] For example, the fact that 5 patients were not booked for a follow-up appointment at discharge and 33% of those LTFU had an appointment indicated in the follow-up plan but not booked on the patient administration system suggests that administrative factors may be associated with LTFU and warrant further investigation.

Study limitations

Notable limitations of the current study include its retrospective nature and variation in the quality and completeness of the routine health data on which it was based. Related to this was the fact that TB treatment start and end dates had to be determined using a hierarchy of evidence, as this information was not always available in the medical record. Differences in the source of treatment dates for each patient may have introduced some information bias into the study, as patients LTFU were more likely to have end of treatment determined by ETR.net or pharmacy records than those who were retained in spine clinic follow-up. Other limitations include the aforementioned constraints in statistical power and unmeasured explanatory variables. These limitations may explain why the study was not able to identify causes of LTFU. Furthermore, the study did not assess other primary, secondary and tertiary health system contacts over and above spine clinic follow-up, or relate the primary outcomes to clinical outcomes such as repeated hospital admissions or spinal TB recurrence in subsequent years. While this additional information fell beyond the scope of the study objectives, it may well have been valuable for interpretation of the findings. Strengths of the current study included collation of different sources for determining the primary outcomes – a strategy that allowed for less missing data and more patients included in the analysis. Furthermore, patients who were excluded on the basis of missing data showed similar characteristics to those who were included, suggesting a low risk of selection bias in the findings.

Conclusions

The present study demonstrated that 75% of patients with spinal TB did not complete follow-up at the tertiary hospital spine clinic and that almost one in three patients received less than the minimum 9 months of TB treatment. The long-term outcome of these patients fell beyond the scope of the study, and the clinical significance of being LTFU and/or completing shorter treatment is unclear. It is likely that the required duration of TB treatment varies between individuals. However, in the absence of a feasible measure of clinical cure, extended treatment serves to err on the side of caution. The present study found that remaining in spine clinic follow-up was significantly associated with completing at least 9 months of TB treatment, and arguably supports the role of this monitoring under the present circumstances.

In the future, qualitative interviews of patients attending follow-up and LTFU could improve understanding of follow-up determinants and inform strategies for retaining patients in care. However, novel measures of clinical cure in spinal TB, suitable for use in the SA public health setting, should also be considered a research priority. Such measures may allow for more individualised, evidence-based treatment duration and decrease the overall burden of follow-up required. In time, these research findings could form an evidence base for new policy, improving both the treatment of spinal TB and use of health system resources.

Declaration. The research for this study was done in partial fulfilment of the requirements for TNM's MPhil in Health Systems and Services Research degree at Stellenbosch University.

Acknowledgements. The authors thank Ms F Phelanyane and the Western Cape Department of Health for their invaluable assistance in providing the health dataset and responding to subsequent queries. They also thank Dr B Ayele of the Stellenbosch University Biostatistics Unit for his advice on certain aspects of the analysis.

Author contributions. TNM conceptualised and designed the study, collected the data, analysed the data and wrote the manuscript. JHD provided clinical consultation during data collection and reviewed drafts of the manuscript. RD provided input during the study design, data collection and data analysis and reviewed drafts of the manuscript.

Funding. TNM was supported by a postdoctoral fellowship from the Vice-Dean of Research in the Faculty of Medicine and Health Sciences, Stellenbosch University.

Conflicts of interest. None.

1. Talbot JC, Bismil Q, Saralaya D, Newton DAG, Frizzel RM, Shaw DL. Musculoskeletal tuberculosis in Bradford – a 6-year review. Ann R Coll Surg Engl 2007;89(4):405-409. https://doi.org/10.1308/003588407x183328
2. De la Garza Ramos R, Goodwin CR, Abu-Bonsrah N, et al. The epidemiology of spinal tuberculosis in the United States: An analysis of 2002 - 2011 data. J Neurosurg Spine 2017;26(4):507-512. https://doi.org/10.3171/2016.9.spine16174
3. Dunn RN, Ben Husien M. Spinal tuberculosis. Bone Joint J 2018;100-B(4):425-431. https://doi.org/10.1302/0301-620x.100b4.bjj-2017-1040.r1
4. Shi T, Zhang Z, Dai F, et al. Retrospective study of 967 patients with spinal tuberculosis. Orthopedics 2016;39(5):e838-e843. https://doi.org/10.3928/01477447-20160509-03
5. Batirel A, Erdem H, Sengoz G, et al. The course of spinal tuberculosis (Pott disease): Results of the multinational, multicentre Backbone-2 study. Clin Microbiol Infect 2015;21(11):1008e9-1008e18. https://doi.org/10.1016/j.cmi.2015.07.013
6. Mwachaka PM, Ranketi SS, Nchafatso OG, Kasyoka BM, Kiboi JG. Spinal tuberculosis among human immunodeficiency virus-negative patients in a Kenyan tertiary hospital: A 5-year synopsis. Spine J 2011;11(4):265-269. https://doi.org/10.1016/j.spinee.2011.01.033
7. Mann TN, Schaaf HS, Dunn RN, et al. Child and adult spinal tuberculosis at tertiary hospitals in the Western Cape, South Africa: 4-year burden and trend. Epidemiol Infect 2018;146(16):2107-2115. https://doi.org/10.1017/s0950268818002649
8. Massyn N, Peer N, Padarath A, Barron P, Day C, eds. District Health Barometer 2015/16. Durban: Health Systems Trust, 2016. http://www.hst.org.za/publications/Pages/-District-Health-Barometer-201516.aspx (accessed 12 January 2018).
9. Donald PR. The chemotherapy of osteo-articular tuberculosis with recommendations for treatment of children. J Infect 2011;62(6):411-439. https://doi.org/10.1016/j.jinf.2011.04.239
10. Dunn R. The medical management of spinal tuberculosis. S Afr Orthop J 2010;9(1):37-41.
11. Van Loenhout-Rooyackers JH, Verbeek AL, Jutte PC. Chemotherapeutic treatment for spinal tuberculosis. Int J Tuberc Lung Dis 2002;6(3):259-265.
12. Mittal S, Jain AK, Chakraborti KL, Aggarwal AN, Upreti L, Bhayana H. Evaluation of healed status in tuberculosis of spine by fluorodeoxyglucose-positron emission tomography/computed tomography and contrast magnetic resonance imaging. Indian J Orthop 2019;53(1):160-168. https://doi.org/10.4103/ortho.ijortho_224_18
13. Dureja S, Sen IB, Acharya S. Potential role of F18 FDG PET-CT as an imaging biomarker for the noninvasive evaluation in uncomplicated skeletal tuberculosis: A prospective clinical observational study. Eur Spine J 2014;23(11):2449-2454. https://doi.org/10.1007/s00586-014-3483-8
14. Jain AK, Srivastava A, Saini NS, Dhammi IK, Sreenivasan R, Kumar S. Efficacy of extended DOTS category I chemotherapy in spinal tuberculosis based on MRI-based healed status. Indian J Orthop 2012;46(6):633-639. https://doi.org/10.4103/0019-5413.104191
15. Dunn R, van der Horst A, Lippross S. Tuberculosis of the spine – prospective neurological and patient reported outcome study. Clin Neurol Neurosurg 2015;133:96-101. https://doi.org/10.1016/j.clineuro.2015.03.015
16. Dudley L, Mukinda F, Dyers R, Marais F, Sissolak D. Mind the gap! Risk factors for poor continuity of care of TB patients discharged from a hospital in the Western Cape, South Africa. PLoS One 2018;13(1):e0190258. https://doi.org/10.1371/journal.pone.0190258
17. Voss de Lima Y, Evans D, Page-Shipp L, et al. Linkage to care and treatment for TB and HIV among people newly diagnosed with TB or HIV-associated TB at a large, inner city South African hospital. PLoS One 2013;8(1):e49140. https://doi.org/10.1371/journal.pone.0049140
18. Edginton ME, Wong ML, Phofa R, Mahlaba D, Hodkinson HJ. Tuberculosis at Chris Hani Baragwanath Hospital: Numbers of patients diagnosed and outcomes of referrals to district clinics. Int J Tuberc Lung Dis 2005;9(4):398-402.
19. Jacobson KB, Moll AP, Friedland GH, Shenoi SV. Successful tuberculosis treatment outcomes among HIV/TB coinfected patients down-referred from a district hospital to primary health clinics in rural South Africa. PLoS One 2015;10(5):e0127024 https://doi.org/10.1371/journal.pone.0127024
20. Budgell EP, Evans D, Schnippel K, Ive P, Long L, Rosen S. Outcomes of treatment of drug-susceptible tuberculosis at public sector primary healthcare clinics in Johannesburg, South Africa: A retrospective cohort study. S Afr Med J 2016;106(10):1002-1009. https://doi.org/10.7196/SAMJ.2016.v106i10.10745
21. Kigozi G, Heunis C, Chikobvu P, Botha S, van Rensburg D. Factors influencing treatment default among tuberculosis patients in a high burden province of South Africa. Int J Infect Dis 2017;54:95-102. https://doi.org/10.1016/j.ijid.2016.11.407
22. Mohr E, Cox V, Wilkinson L, et al. Programmatic treatment outcomes in HIV-infected and uninfected drug-resistant TB patients in Khayelitsha, South Africa. Trans R Soc Trop Med Hyg 2015;109(7):425-432. https://doi.org/10.1093/trstmh/trv037
23. Moyo S, Cox HS, Hughes J, et al. Loss from treatment for drug resistant tuberculosis: Risk factors and patient outcomes in a community-based program in Khayelitsha, South Africa. PLoS One 2015;10(3):e0118919. https://doi.org/10.1371/journal.pone.0118919
24. Skinner D, Claassens M. It's complicated: Why do tuberculosis patients not initiate or stay adherent to treatment? A qualitative study from South Africa. BMC Infect Dis 2016;16:712. https://doi.org/10.1186/s12879-016-2054-5
25. Theron G, Peter J, Zijenah L, et al. Psychological distress and its relationship with non-adherence to TB treatment: A multicentre study. BMC Infect Dis 2015;15:253. https://doi.org/10.1186/s12879-015-0964-2
26. Webb Mazinyo E, Kim L, Masuku S, et al. Adherence to concurrent tuberculosis treatment and antiretroviral treatment among co-infected persons in South Africa, 2008 - 2010. PLoS One 2016;11(7):e0159317. https://doi.org/10.1371/journal.pone.0159317
27. Birch S, Govender V, Fried J, et al. Does treatment collection and observation each day keep the patient away? An analysis of the determinants of adherence among patients with tuberculosis in South Africa. Health Policy Plan 2016;31(4):454-461. https://doi.org/10.1093/heapol/czv084
28. Naidoo P, Peltzer K, Louw J, Matseke G, McHunu G, Tutshana B. Predictors of tuberculosis (TB) and antiretroviral (ARV) medication non-adherence in public primary care patients in South Africa: A cross sectional study. BMC Public Health 2013;13(1):396. https://doi.org/10.1186/1471-2458-13-396
29. Madden K, Scott T, McKay P, et al. Predicting and preventing loss to follow-up of adult trauma patients in randomized controlled trials: An example from the FLOW trial. J Bone Joint Surg Am 2017;99(13):1086-1092. https://doi.org/10.2106/jbjs.16.00900
30. Zelle BA, Buttacavoli FA, Shroff JB, Stirton JB. Loss of follow-up in orthopaedic trauma. J Orthop Trauma 2015;29(11):510-515. https://doi.org/10.1097/bot.0000000000000346
31. Tejwani NC, Takemoto RC, Nayak G, Pahk B, Egol KA. Who is lost to followup? A study of patients with distal radius fractures. Clin Orthop Relat Res 2010;468(2):599-604. https://doi.org/10.1007/s11999-009-0968-6
32. Whiting PS, Greenberg SE, Thakore RV, et al. What factors influence follow-up in orthopedic trauma surgery? Arch Orthop Trauma Surg 2015;135(3):321-327. https://doi.org/10.1007/s00402-015-2151-8
33. Neuner B, Fleming M, Born R, et al. Predictors of loss to follow-up in young patients with minor trauma after screening and written intervention for alcohol in an urban emergency department. J Stud Alcohol Drugs 2007;68(1):133-140. https://doi.org/10.15288/jsad.2007.68.133
34. Badenhorst DHS, van der Westhuizen CA, Britz E, Burger MC, Ferreira N. Lost to follow-up: Challenges to conducting orthopaedic research in South Africa. S Afr Med J 2018;108(11):917-921. https://doi.org/10.7196/SAMJ.2018.v108i11.13252
35. Western Cape Department of Health. Tygerberg Hospital Facts and Figures. Cape Town: Western Cape Department of Health, 2016. https://www.westerncape.gov.za/your_gov/153 (accessed 16 November 2016).
36. Shepherd BE, Blevins M, Vaz LME, et al. Impact of definitions of loss to follow-up on estimates of retention, disease progression, and mortality: Application to an HIV program in Mozambique. Am J Epidemiol 2013;178(5):819-828. https://doi.org/10.1093/aje/kwt030
37. Chi BH, Yiannoutsos CT, Westfall AO, et al. Universal definition of loss to follow-up in HIV treatment programs: A statistical analysis of 111 facilities in Africa, Asia, and Latin America. PLoS Med 2011;8(10):e1001111. https://doi.org/10.1371/journal.pmed.1001111
38. World Health Organization. Definitions and Reporting Framework for Tuberculosis – 2013 Revision. Geneva: WHO, 2013. http://www.who.int/tb/publications/definitions/en/ (accessed 12 January 2018).
39. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and elaboration. PLoS Med 2007;4(10):e297. https://doi.org/10.1371/journal.pmed.0040297
40. Finlay A, Lancaster J, Holtz TH, Weyer K, Miranda A, van der Walt M. Patient- and provider-level risk factors associated with default from tuberculosis treatment, South Africa, 2002: A case-control study. BMC Public Health 2012;12(1):56. https://doi.org/10.1186/1471-2458-12-56
41. Casp AJ, Wells J, Holzgrefe R, Weiss D, Kahler D, Yarboro SR. Evaluation of orthopedic trauma surgery follow-up and impact of a routine callback program. Orthopedics 2017;40(2):e312-e316. https://doi.org/10.3928/01477447-20161229-01

Accepted 16 September 2019.