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Effects of distance to treatment centre and case load upon tuberculosis treatment completion

To the Editors:

The prompt identification and adequate treatment of tuberculosis (TB) cases are key components of the global control effort [1]. In many high-income countries, TB is relatively uncommon, implying that many clinicians do not have regular and continuing experience of managing TB. To address this, a policy response is a trend towards small numbers of centralised treatment facilities where individuals may receive better and more complete treatment [2, 3]. This centralising trend is the opposite to many low-income countries, where there is a move towards larger numbers of more decentralised TB services to facilitate patient access [4]. The difference is that such countries have sufficient cases to allow clinical staff to maintain their expertise, even in rural areas.

If TB services become more centralised, then patients may experience greater difficulty in accessing TB services due to increasing the distance between the home and treatment centre. There is little research on how distance affects TB completion, but rural residence is a known risk factor associated with a delay in the diagnosis and treatment of TB

[5] and may therefore affect treatment completion. However, most of this evidence comes from low-income countries. In contrast, in high-income countries, good transport links and reasonable social security systems imply that such barriers may not exist.

This epidemiological study examined whether treatment centre case load (annual number of TB patients seen) and healthcare accessibility (proximity of patient residence to TB treatment centre) have an influence upon the completion of TB treatment in England and Wales, UK.

The study was based upon a sample of 21,954 patients reported to the national enhanced TB surveillance system (ETS) from 2001 to 2006 in England and Wales. These TB patients all had their diagnosis confirmed by bacteriological culture or had clinical/radiological/histopathological features suggestive of TB, and their clinician had taken the decision to treat the patient with a full course of anti-TB therapy. This sample was 50.3% of the total cases reported to the ETS during this period. Cases had to be excluded from the study mainly due to missing information on where the patient was actually treated

for TB. This may have been different to the original clinic where TB was diagnosed. A comparison of all patients on the ETS within our study sample indicated close demographic similarities.

Treatment outcome was categorised as either completion or noncompletion based on clinical information 12 months after the date of notification or start of TB treatment (further details of ETS is provided in [6]). Patients with multidrug-resistant TB were excluded because current treatment regimens recommend a course of therapy of ≥ 18 months.

For each patient, the experience of the TB centre where they were treated was obtained by calculating the number of cases seen by that centre for the year in which their case was notified. The median centre case load for patients was 71 cases·yr⁻¹ (interquartile range (IQR) 26–130 cases·yr⁻¹). For each patient, a measure of healthcare accessibility was calculated by obtaining the road distance from their home (based on postcode) to the TB treatment centre using a geographical information system. The majority of patients lived in close proximity to their treatment centre and the median road distance was 4.4 km (IQR 2.9–7.3 km).

For each patient, the potentially confounding variables age, sex, place of birth (country), number of years living in the UK, ethnicity, previous history of TB, site of the disease and isoniazid susceptibility were obtained from the ETS. At the ecological level, confounding variables were also collected, specifically the 2004 index of multiple deprivation [7] and an urban rural classification [8]. The region of residence was obtained from the ETS.

The analysis proceeded in stages. The first stage produced a univariable model to examine the impact of all the potential explanatory variables upon completion of treatment. This was investigated using logistic regression to determine odds ratios for each of the explanatory variables. In these analyses, the TB centre load variable was dichotomised to >26 or ≤ 26 cases *per annum*. The road distance to the TB treatment centre variable was also dichotomised to >7.3 or <7.3 km. These categories

were decided upon by examining plots of treatment outcome against the individual variables. A multivariable model was then fitted including all of the individual confounding variables as well as the centre load and healthcare accessibility measures.

The results of the univariable and multivariable results indicated that attending a TB centre with a low case load was associated with poorer treatment outcomes ($p<0.01$) and travelling a greater distance to the TB treatment centre was associated with poorer treatment outcomes ($p<0.001$).

During these analyses, significant interactions were observed between both the centre load and healthcare accessibility variables with the variables measuring whether or not the patient was born in the UK. Significant interactions were also observed between the healthcare accessibility variables and the patient age variable. Therefore, in the final analysis, multivariable models were produced for UK- and non-UK-born patients separately, who were additionally subdivided into individuals <45 and >44 yrs of age. All the models were tested with and without the potentially confounding ecological variables (urban rural classification, index of multiple deprivation and region). The results presented were unaffected by the inclusion of these variables. Analysis was undertaken in STATA SE 8.0 (StataCorp, College Station, TX, USA).

The final results are presented in table 1, and it is important to emphasise that these are based upon a multivariable model that included a number of other variables listed in the table. These indicated that for both young and older individuals born in the UK, TB centre load was insignificant (OR 0.79 ($p=0.05$) and OR 1.13 ($p=0.15$), respectively). For individuals born outside the UK, TB centre load was significant for young individuals, indicating poorer completion of treatment at centres with low case loads (OR 0.75; $p<0.001$). There was no effect on older individuals (OR 0.91; $p=0.358$). Turning our attention to road distance to the TB treatment centre, for individuals born in the UK, this was insignificant for young and older individuals (OR 1.05 ($p=0.68$) and OR 0.94 ($p=0.446$)). For those born outside the UK, road distance to

TABLE 1 Odds ratio (multivariable) analyses of factors affecting completion of tuberculosis (TB) cases in England and Wales, UK in 2001–2006 for young and older individuals born in and outside the UK

	Born in the UK				Born outside the UK			
	Age <45 yrs		Age >44 yrs		Age <45 yrs		Age >44 yrs	
	Cases [#] n	OR [‡] (95% CI)	Cases [#] n	OR [‡] (95% CI)	Cases [#] n	OR [‡] (95% CI)	Cases [#] n	OR [‡] (95% CI)
TB centre load cases·yr⁻¹								
>26	2282	Reference	1307	Reference	8325	Reference	3236	Reference
≤ 26	863	0.79 (0.63–1.00)	1426	1.13 (0.96–1.34)	1976	0.75 (0.65–0.85)***	785	0.91 (0.75–1.11)
Road distance to TB treatment centre km								
<7.3	2347	Reference	1574	Reference	8143	Reference	3201	Reference
>7.3	798	1.05 (0.83–1.33)	1159	0.94 (0.79–1.11)	2158	0.81 (0.72–0.92)**	820	0.71 (0.59–0.86)***

[#]: numbers do not always add up to total because of missing data; [‡]: adjusted for sex, age, ethnic group, place of birth, previous TB history, disease site, isoniazid susceptibility, road distance to TB treatment centre and TB centre load. **: $p<0.01$; ***: $p<0.001$.

the TB treatment centre was significant for young and older individuals (OR 0.81 ($p < 0.01$) and OR 0.71 ($p < 0.001$), respectively), indicating lower completion of treatment if the patient lived >7.3 km from the treatment centre.

TB is a rare disease in many high-income countries, which leads to pressures for the pooling of expertise to larger centres [2]. This results in patients being treated in TB centres with higher case loads but greater distances for patients to travel. This study demonstrates that such merging has positive health benefits, as larger centres (load >26 cases·yr⁻¹) had significantly higher completion rates for TB treatment for young individuals born outside the UK (~50% of TB patients). However, if centralisation leads to patients having to travel greater distances to receive treatment, then this has negative consequences, as this study shows that all patients born outside the UK (~65% of TB patients) were less likely to complete treatment if they had to travel >7.3 km to the TB treatment centre. Other studies have indicated the importance of provider experience to treatment outcome [3] but the present study is the first to demonstrate that such experience has a differing impact on subgroups of the population. Previous studies investigating delay in the diagnosis and treatment of TB have identified the importance of health-care accessibility [5], but this is the first to be conducted in a high-income country. Additionally, it focuses upon treatment outcome as opposed to diagnosis delay, and examines differential effects amongst population subgroups.

Further research is needed to understand why young individuals born outside the UK are less likely to complete treatment at small TB centres. Migrants may face difficulties in accessing healthcare due to language problems or poor understanding of the health system [3]. They may also require culturally appropriate services [9]. Young migrants may face further difficulties as they require tailored health information. Small TB centres may be unable to address such issues. Many migrants are materially deprived, which, alongside language difficulties [10], may explain why travelling short distances to TB treatment centres appears difficult. This result was unexpected due to the high-income country setting and the fact that most patients lived close to their TB treatment centre.

This research indicates that moves towards centralisation of TB services, such as implementation of the UK recommendations that clinicians see ≥ 10 TB patients per year [2], should be implemented alongside measures to ensure accessibility of

services, targeted to individuals born outside the UK who live far from the treatment centres.

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Tuberculosis-specific T-cell response after recent treatment and remote cure

To the Editors:

Tuberculosis (TB) remains a major global health problem. A major factor contributing to the current TB epidemic is the resistance of *Mycobacterium tuberculosis* to first-line anti-TB

treatment. Therefore, there is a need for an appropriate and reliable tool to evaluate treatment efficacy.

Several studies using the T-SPOT®.TB assay (Oxford Immunotec Ltd, Oxford, UK) reported a decline in the number of