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Presentation and healthcare delays among people with tuberculosis in London, and the impact on treatment outcome

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ABSTRACT

Background A quarter of London's pulmonary tuberculosis (TB) patients have over 4 months of delay. Late diagnosis increases disease severity and the risk of transmission. We aim to classify delays, identify associated risk factors and assess treatment outcome.

Methods We conducted a retrospective cohort study using London surveillance data, 2012–2018 on adults aged ≥18 years with pulmonary TB. We defined presentation delay (days from symptom onset to first healthcare visit) and healthcare delay (first healthcare visit to treatment commencement) as dichotomous variables; positive delay being days equal or greater than the third quartile. We applied logistic regression models to identify risk factors associated with delays and treatment outcome at 12 months.

Results Of 7216 people, 4539 reported presentation and 5193 healthcare delays. The third quartiles for presentation and healthcare delay were 84 and 61 days, respectively. Presentation delay was associated with female sex (adjusted OR (aOR)=1.21; 95% CI 1.04 to 1.39), increasing age (aOR=1.004; 95% CI 1.001 to 1.008), white compared to Asian ethnicity (aOR=1.35; 95% CI 1.12 to 1.62), previous imprisonment (aOR=1.66; 95% CI 1.22 to 2.26) and alcohol misuse (aOR=1.44; 95% CI 1.04 to 1.89). Healthcare delay was associated with female sex (aOR=1.39; 95% CI 1.21 to 1.59), increasing age (aOR=1.014; 95% CI 1.009 to 1.018) and white ethnicity (aOR=1.41; 95% CI 1.19 to 1.68). 16% of 5678 people with known outcome did not complete treatment. Neither delay was associated with non-completion (p value <0.05).

Conclusions Female, white and older people with TB were more likely to experience both presentation and healthcare delays. Social risk factors were also associated with delay in presentation. Early diagnosis and treatment remain critical to reduce transmission, regardless of whether delay affected completion.

Key messages

What is the key question?

- What are the risk factors associated with presentation and healthcare delay and is delay (presentation or healthcare delay) associated with treatment non-completion at 12 months?

What is the bottom line?

- Social risk factors such as imprisonment and alcohol misuse are the two most important risk factors for presentation delay, for healthcare delay female sex, increasing age and white ethnicity were associated and finally neither presentation delay nor healthcare delay were associated with treatment non-completion.

Why read on?

- Reducing delays in diagnosis is an opportunity to reduce transmission of tuberculosis (TB): by identifying characteristics and groups at risk of long delays, our findings will support local improvement strategies for TB programmes to try and reduce extreme delays further.

BACKGROUND

Tuberculosis (TB) is caused by the gram-positive aerobic bacteria of the *Mycobacterium tuberculosis* complex. TB is one of the top 10 causes of death worldwide.[1] Although England is a low incidence country, TB is still a major public health concern in London, with a notification rate of 21.7 per 100 000 and accounting for 37% of all cases in England in 2017.[1–3] Studies in London have identified groups at increased risk of TB such as homeless people, prisoners, drug users, HIV positivity and people with comorbidities such as diabetes, asthma and immune-suppression.[4–6]

To reduce the TB burden, early diagnosis is crucial. Late diagnosis induces a more advanced and complex disease, higher rates of transmission and greater costs to the health service.[7–9] Studies have shown delay in starting treatment to be an issue in both high and low TB incidence countries.[10–19] Delay can be defined in various ways. Total delay is the time from symptom onset to treatment start. This can be subdivided into diagnostic delay (time from symptom onset to diagnosis) and treatment delay (from diagnosis to treatment start), or into presentation delay (time from symptom

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onset to first visit to a place of healthcare) and healthcare delay (from first visit to a place of healthcare to treatment start). In London, 27% of people with pulmonary TB had over 4 months of delay from symptom onset to treatment commencement, lower than the national proportion of 31%.[2] The relative contribution of presentation delay or delay within the health service, and which groups are most at risk is unknown.[3] Though there is no universally accepted period for total delay, the WHO recommend a delay of less than 3 weeks from symptom onset to seeking healthcare.[20]

Total delay is associated with poorer treatment outcomes in high TB incidence countries.[16 17] In London, treatment completion at 12 months for people notified with pulmonary drug sensitive TB in 2016 was 87%, but the outcome among people who had delayed diagnosis has not been described.[3] The aim of this study was to describe presentation and healthcare delay among people with TB in London, in order to identify associated risk factors and the effect on treatment outcome to help inform TB strategies in London.

METHODS

Study design

A retrospective cohort study was performed to identify factors associated with delay and treatment outcome of TB in London from 2012 to 2018. Presentation delay was defined as the time from symptom onset to the first visit to a place of healthcare. Healthcare delay was defined as the time from the first visit to a place of healthcare to the start of TB treatment. Due to the non-normal distribution of delay as a continuous variable, we dichotomised it into two groups, delayed and not delayed. The right skew observed in the distribution showed extreme lengths of delay, possibly due to mis-recording or forgetting exact dates, but this would still imply a significant delay while the exact length of delay at extremes had little clinical relevance. To avoid excluding people with extreme delays a dichotomous variable was preferred. We chose the third quartile as our binary cut-off point as it allowed us to focus on the risk factors associated with people who had the longest delays. Also, the third quartile corresponded to time intervals that were reasonable and achievable for health services to aim to reduce. A person would be considered as being delayed if their delay was equal or superior to the third quartile of the study population. For the secondary objective analysing the impact of delay on treatment outcome, outcome was defined as completed or not completed (all other remaining outcomes at 12 months from starting treatment).

Study population

People were selected from the Public Health England London TB register, a routine surveillance system used throughout London. Patient information is entered in the database by TB clinic staff. People diagnosed with pulmonary TB (with or without extrapulmonary sites), notified from 2012 to 2018 and 18 years of age or over at the start of treatment were included in this study. People with TB identified through contact tracing or TB screening programme were excluded. We analysed presentation delay and healthcare delay separately. All people with a negative or missing delay were excluded from the analysis of the respective delay.

To analyse treatment outcome, we excluded cases with central nervous system, miliary or spinal extrapulmonary TB sites, multidrug-resistant TB and rifampicin-resistant TB and people who started their treatment after the 31 December 2017.

To reduce the number of categories of ethnicity, Indian, Pakistani, Bangladeshi and Chinese were grouped into 'Asian/Asian-British' and black-African, black-Caribbean and black-other categories grouped into 'Black-African/Black-Caribbean/Black-British'.[21]

Statistical analysis

The study population was described by median and range for age (due to the non-normal distribution), median and IQR for delay and categorical variables were described by proportion (per cent).

Explanatory variables were selected, and missing data were quantified. In the subsets of data, there were less than 5% of missing data for each variable of interest therefore complete case analysis was performed.

We used logistic regression to analyse factors associated with presentation delay, healthcare delay and treatment outcome. After univariable analysis, all variables of interest associated with delay with a p value <0.25 or clinically appropriate for the analysis were included in a first multivariable model. A backward selection was performed following the recommendations by Hosmer and Lemeshow to obtain the final model.[22] Sensitivity analyses were performed by changing the point of positive delay, for

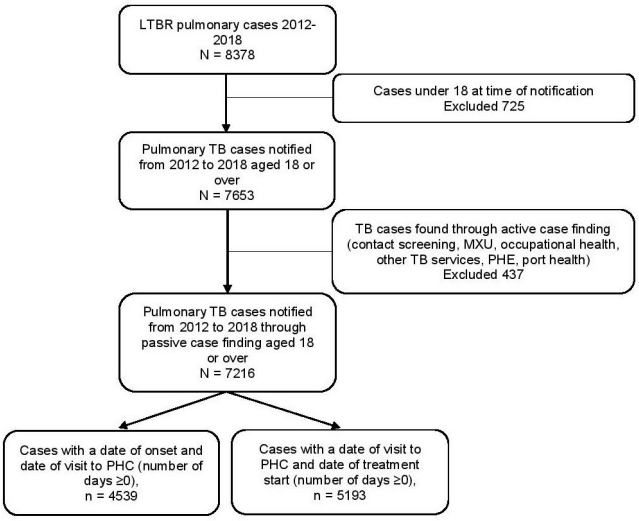


Figure 1 Flow chart of case selection for delay. LTBR, London TB register; MXU, mobile X-ray unit; PHC, place of healthcare; PHE, public health England; TB, tuberculosis.

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Table 1 Summary of characteristics of the study populations

Variable	Total cohort,n=7216 (%)	Presentation delay cohort,n=4539 (%)	Healthcare delay cohort,n=5193 (%)	Outcome cohort,n=5678 (%)
Male	4580 (63)	2918 (64)	3300 (64)	3588 (63)
Age, median (range)	38 (18–105)	38 (18–105)	39 (18–105)	37 (18–105)
UK born	1487 (21)	942 (21)	1083 (21)	1221 (22)
Ethnicity				
Asian/Asian-British	2624 (36)	1538 (34)	1751 (34)	2037 (36)
Black-African/black-Caribbean/black-British	1720 (24)	1139 (25)	1281 (25)	1335 (24)
White	1585 (22)	1022 (23)	1205 (23)	1277 (22)
Other	1253 (17)	827 (18)	938 (18)	1007 (18)
History of drug use	479 (6.6)	310 (6.8)	357 (6.9)	381 (6.7)
History of homelessness	458 (6.3)	310 (6.8)	353 (6.8)	354 (6.2)
History of imprisonment	332 (4.6)	215 (4.7)	253 (4.9)	265 (4.7)
Alcohol misuse	438 (6.1)	282 (6.2)	331 (6.4)	340 (6.0)
Mental health concerns	485 (6.7)	315 (6.9)	365 (7.0)	375 (6.6)
Employed	5052 (70)	3274 (72)	3739 (72)	3984 (70)
Place of healthcare				
Accident & emergency (A&E)	1783 (25)	1576 (35)	1717 (33)	1354 (24)
General practitioner	2431 (34)	2054 (45)	2338 (45)	1982 (35)
Private sector	71 (1.0)	56 (1.2)	68 (1.3)	57 (1.0)
Other	1121 (16)	834 (18)	1048 (20)	891 (16)

presentation delay we used the 21-day WHO recommendation, and for both presentation and healthcare delay we used the median. Another sensitivity analysis was to change the missing data for social risk factors to the 'No' group. Statistical significance of the variables was set for two-sided p values <0.05.

All analysis and data cleaning were performed in R V.3.5.2.

Patient and public involvement

People included in this study were not involved in the analysis or the writing of this manuscript.

RESULTS

Of the 7216 people with pulmonary TB included in the study population, 37% were excluded from the presentation delay analysis and 28% were excluded from the healthcare delay analysis (figure 1).

The characteristics of our complete study population and in the two subsets for study of presentation and healthcare delay as well as the subset for treatment outcome, are shown in table 1.

Presentation delay

Of the 4539 people with a recorded presentation delay, the median age was 38 years, 64% were male and 21% born in the UK (table 1). The median presentation delay was 35 days (IQR 13–84). Using the third quartile (84 days) as the cut-off, 1149 cases were classed as delayed for presentation delay.

Univariable analysis (table 2) showed that social risk factors, such as a history of imprisonment (OR=1.90), a history of drug use (OR=1.58), alcohol misuse (OR=1.56), mental health concerns (OR=1.34) and history of homelessness (OR=1.30) were associated with being delayed 84 days or more. Other risk factors for delay included white ethnicity (OR=1.40) compared with Asian/Asian-British ethnicities, unemployment (OR=1.30) and increasing age (OR=1.004).

In the multivariable analysis, history of imprisonment (adjusted OR (aOR)=1.66), alcohol misuse (aOR=1.44), white ethnicity (aOR=1.35) compared with Asian/Asian-British ethnicities, female sex (aOR=1.21) and increasing age (aOR=1.004) were significantly associated with being delayed (table 3).

Sensitivity analyses (table 4) showed that if presentation delay was dichotomised at 21 days, which is the recommended limit for presentation delay by the WHO, only the social risk factors (history of imprisonment and alcohol misuse) remained associated with being delayed. Similarly, when using the median as a cut-off point, only imprisonment and alcohol misuse were associated with being delayed.

Healthcare delay

Of the 5193 people with reported healthcare delay, the median age was 39 years, 64% were male and 21% were

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Table 2 Description and ORs for univariable analysis for presentation delay, complete case analysis per individual variable

Variable	Total, n (%)	Delayed, n (% delayed)	OR	95% CI	P value
Sex					
Male	2918 (64)	716 (25)	Ref		
Female	1621 (36)	433 (27)	1.12	0.98 to 1.29	0.11
Age, median (range)	38 (18–105)	40 (18–105)	1.004	1.001 to 1.008	**0.02**
Born in the UK or time of residency					
UK born	942 (21)	274 (29)	Ref		
Recent resident (<5 years in the UK)	1016 (22)	246 (24)	0.78	0.64 to 0.95	**0.01**
Longer resident (≥5 years in the UK)	2423 (54)	587 (24)	0.78	0.66 to 0.92	**0.004**
Years since arrival unknown	145 (3.2)	41 (28)	0.96	0.65 to 1.41	0.84
Ethnicity					
Asian/Asian-British	1538 (34)	354 (23)	Ref		
Black-African/black-Caribbean/black-British	1139 (25)	293 (26)	1.16	0.97 to 1.38	0.11
White	1022 (23)	301 (29)	1.40	1.17 to 1.67	**<0.001**
Other	827 (18)	199 (24)	1.06	0.87 to 1.29	0.57
Sputum smear result (at diagnosis)					
Positive	1971 (44)	507 (26)	Ref		
Negative	1799 (40)	452 (25)	0.97	0.84 to 1.12	0.67
Other (awaiting results, not done, unknown …)	768 (17)	190 (25)	0.95	0.78 to 1.15	0.58
Chest X-ray or CT (at diagnosis)					
Cavities reported	1368 (30)	359 (26)	1.09	0.94 to 1.26	0.26
Abnormalities reported	3035 (67)	748 (25)	Ref		
Other (awaiting results, not done, unknown …)	136 (3.0)	42 (31)	1.37	0.93 to 1.97	0.10
History of drug use					
Yes	310 (7.0)	106 (34)	1.58	1.23 to 2.01	**<0.001**
No	4139 (93)	1024 (25)	Ref		
History of homelessness					
Yes	310 (6.9)	94 (30)	1.30	1.01 to 1.67	**0.04**
No	4162 (93)	1041 (25)	Ref		
History of imprisonment					
Yes	215 (4.8)	83 (39)	1.90	1.43 to 2.52	**<0.001**
No	4234 (95)	1053 (25)	Ref		
Alcohol misuse					
Yes	282 (6.4)	96 (34)	1.56	1.21 to 2.02	**<0.001**
No	4131 (94)	1025 (25)	Ref		
Mental health concerns					
Yes	315 (7.1)	97 (31)	1.34	1.04 to 1.71	**0.02**
No	4105 (93)	1025 (25)	Ref		
Occupation					
Employed*	3274 (76)	807 (25)	Ref		
Unemployed†	1019 (24)	304 (30)	1.30	1.11 to 1.52	**<0.001**

Significant p values (<0.05) are highlighted in bold.
*Employed included all employment types, Plus housewives/husbands, students and retired people.
†Unemployed includes reported unemployed, prisoners, asylum seekers and immigration detainees.
Ref, reference group.

born in the UK (table 1). Using the third quartile of delay (61 days), 1320 cases were found to have a healthcare delay.

Univariable analysis showed that a negative sputum smear result at diagnosis (OR=2.51) was associated with being delayed, as was female sex (OR=1.43), white ethnicity

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Table 3 Final model for multivariable analysis for presentation delay

Variable	aOR	95% CI	P value
Sex			
Male	Ref		
Female	1.21	1.04 to 1.39	**0.01**
Age	1.004	1.000 to 1.008	**0.03**
Ethnicity			
Asian/Asian-British	Ref		
Black-African/black-Caribbean/black-British	1.15	0.95 to 1.38	0.14
White	1.35	1.12 to 1.62	**0.002**
Other	1.06	0.86 to 1.29	0.59
History of imprisonment			
Yes	1.66	1.22 to 2.26	**0.001**
No	Ref		
Alcohol misuse			
Yes	1.44	1.08 to 1.89	**0.01**
No	Ref		

Significant p values (<0.05) are highlighted in bold.
aOR, adjusted OR; Ref, reference group.

(OR=1.34) compared with Asian/Asian-British ethnicities and increasing age (OR=1.015). However, being born abroad (resident less than 5 years: OR=0.70, resident 5 years or more: OR=0.84, time since arrival unknown: OR=0.64) compared with UK born, having cavities reported from a chest X-ray (OR=0.61) compared with other abnormalities reported on the X-ray, a history of drug use (OR=0.75), homelessness (OR=0.60) and alcohol misuse (OR=0.60), and attending any place of healthcare other than a general practitioner (accident and emergency service (A&E): OR=0.22, private sector: OR=0.51, other place for healthcare: OR=0.68) were significantly associated with not being delayed (table 5).

For the multivariable analysis, white ethnicity (aOR=1.41) compared with Asian/Asian-British ethnicities, female sex (aOR=1.39) and increasing age (aOR=1.014) remained associated with being delayed. Attending any place of healthcare than a general practitioner was associated with not being delayed over 60 days (A&E: aOR=0.22, private sector: aOR=0.48 and any other place of healthcare: aOR=0.60) (table 6).

In sensitivity analysis using the median (21 days) for the cut-off, we found the same associations except for white ethnicity which was no longer associated with delay. Also, we found people with a history of homelessness and who were resident in the UK less than 5 years were less likely to be delayed 21 days or more (table 7).

Treatment outcome

We included 5678 (79%) cases according to our criteria. The median age was 37 years, 63% were male and 78% were born abroad. A total of 4793 cases (84%) had completed treatment at 12 months.

Univariable analysis (table 8) showed that neither a presentation delay of 84 days or more nor healthcare delay of 61 days or more was associated with non-completion of treatment at 12 months. Factors that were associated with not completing included alcohol misuse (OR=2.56), homelessness (OR=2.08), attending A&E (OR=2.00) compared with a general practitioner, drug use (OR=1.90), mental health concerns (OR=1.69), unemployment (OR=1.48) and increasing age (OR=1.016). Female sex (OR=0.73), black-African/black-Caribbean/black-British ethnicities (OR=0.75) compared with Asian/Asian-British ethnicities and a negative sputum smear result at diagnosis (OR=0.76) compared with a positive result were variables associated with treatment completion at 12 months.

In multivariable analysis (table 9), presentation delay (aOR=0.98) and healthcare delay (aOR=1.00) were not associated with treatment non-completion at 12 months. Alcohol misuse (aOR=1.97), history of drug use (aOR=1.71), attending A&E (aOR=1.66) compared with a general practitioner, resident <5 years in the UK (aOR=1.44) compared with UK born and increasing age (aOR=1.018) were all associated with not completing. People of black-African/black-Caribbean/black-British (aOR=0.72) and white ethnicity (aOR=0.64) compared

Table 4 Significant variables in sensitivity analyses for presentation delay

	Cut-off=21 days (WHO recommendation)		Cut-off=35 days (median)		Cut-off=84 days (third quartile)	
Variable	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Female sex	*	*	*	*	**1.21**	**1.04 to 1.39**
Age	*	*	*	*	**1.004**	**1.00 to 1.008**
White ethnicity	*	*	*	*	**1.35**	**1.12 to 1.62**
History of imprisonment	1.30	0.92 to 1.86	**1.48**	**1.08 to 2.04**	**1.66**	**1.22 to 2.26**
Alcohol misuse	**1.43**	**1.04 to 1.98**	1.32	0.99 to 1.75	**1.44**	**1.08 to 1.89**

In bold the significant results in analyses.
*Variables not selected in final model.
aOR, adjusted OR.

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Table 5 Description and ORs for univariable analysis for healthcare delay, complete case analysis per individual variable

Variable	Total, n (%)	Delayed, n (% delayed)	OR	95% CI	P value
Sex					
Male	3300 (64)	755 (23)	Ref		
Female	1893 (36)	565 (30)	1.43	1.26 to 1.63	**<0.001**
Age, median (range)	39 (18–105)	43 (18–95)	1.015	1.011 to 1.018	**<0.001**
Born in the UK or time of residency					
UK born	1083 (21)	314 (29)	Ref		
Recent resident (<5 years in the UK)	1143 (22)	253 (22)	0.70	0.57 to 0.84	**<0.001**
Longer resident (≥5 years in the UK)	2765 (53)	707 (26)	0.84	0.72 to 0.98	**0.03**
Years since arrival unknown	188 (3.6)	39 (21)	0.64	0.44 to 0.92	**0.02**
Ethnicity					
Asian/Asian-British	1538 (34)	432 (28)	Ref		
Black-African/black-Caribbean/black-British	1139 (25)	274 (24)	0.83	0.70 to 0.98	**0.03**
White	1022 (23)	367 (36)	1.34	1.13 to 1.58	**<0.001**
Other	827 (18)	242 (29)	1.06	0.88 to 1.27	0.52
Sputum smear result (at diagnosis)					
Positive	2151 (42)	321 (15)	Ref		
Negative	2151 (42)	657 (31)	2.51	2.16 to 2.92	**<0.001**
Other (awaiting results, not done. Unknown …)	891 (17)	342 (38)	3.55	2.97 to 4.25	**<0.001**
Chest X-ray or CT (at diagnosis)					
Cavities reported	1530 (30)	292 (19)	0.61	0.53 to 0.71	**<0.001**
Abnormalities reported	3506 (68)	972 (28)	Ref		
Other (awaiting results, not done, unknown …)	157 (3.0)	56 (36)	1.45	1.03 to 2.01	**0.03**
History of drug use					
Yes	357 (7.0)	74 (21)	0.75	0.57 to 0.97	**0.03**
No	4747 (93)	1230 (26)	Ref		
History of homelessness					
Yes	353 (6.9)	62 (18)	0.60	0.45 to 0.79	**<0.001**
No	4773 (93)	1246 (26)	Ref		
History of imprisonment					
Yes	253 (5.0)	57 (23)	0.84	0.62 to 1.13	0.26
No	4847 (95)	1245 (26)	Ref		
Alcohol misuse					
Yes	331 (6.6)	58 (18)	0.60	0.44 to 0.80	**<0.001**
No	4720 (93)	1234 (26)	Ref		
Mental health concerns					
Yes	365 (7.2)	97 (27)	1.06	0.83 to 1.34	0.64
No	4695 (93)	1196 (25)	Ref		
Place of healthcare					
A&E	1717 (33)	184 (11)	0.22	0.18 to 0.26	**<0.001**
General practitioner	2338 (45)	832 (36)	Ref		
Private sector	68 (1.3)	15 (22)	0.51	0.28 to 0.89	**0.02**
Other (inpatient, outpatient, laboratory, prison)	1048 (20)	285 (27)	0.68	0.58 to 0.79	**<0.001**
Unknown	22 (0.42)	4 (18)	0.40	0.12 to 1.08	0.10
Occupation					
Employed*	3739 (76)	1011 (27)	Ref		
Unemployed†	1150 (24)	266 (23)	0.81	0.69 to 0.95	**0.008**

Significant p values (<0.05) are highlighted in bold.
*Employed included all employment types, plus housewives/husbands, students and retired people.
†Unemployed includes reported unemployed, prisoners, asylum seekers and immigration detainees.
A&E, accident and emergency; Ref, reference group.

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Table 6 Final model for multivariable analysis for healthcare delay

Variable	aOR	95% CI	P value
Sex			
Male	Ref		
Female	1.39	1.21 to 1.59	**<0.001**
Age	1.014	1.009 to 1.018	**<0.001**
Ethnicity			
Asian/Asian-British	Ref		
Black-African/black-Caribbean/black-British	0.97	0.81 to 1.16	0.75
White	1.41	1.19 to 1.68	**<0.001**
Other	1.22	1.00 to 1.47	0.05
Place of healthcare			
A&E	0.22	0.18 to 0.26	**<0.001**
General practitioner	Ref		
Private sector	0.48	0.26 to 0.85	**0.01**
Other (inpatient, outpatient, laboratory, prison)	0.60	0.51 to 0.71	**<0.001**
Unknown	0.40	0.11 to 1.09	0.10

Significant p values (<0.05) are highlighted in bold.
A&E, accident and emergency; aOR, adjusted OR; Ref, reference group.

with Asian/Asian-British ethnicities were more likely to complete treatment. Though when both delays were taken out of the model, unemployment was associated with non-completion, whereas females were significantly associated with treatment completion.

When changing the cut-off point of healthcare delay to the median (21 days) for the sensitivity analyses, people who were delayed were less likely to complete treatment (aOR=1.32, 95% CI 1.09 to 1.59). There remained no association between presentation delay and outcome even after changing the threshold (21 or 35 days) (data not shown).

DISCUSSION

In our study, people with pulmonary TB took longer from first onset of symptoms to first presenting at healthcare, than the delay between presenting and starting treatment for TB. This was similar to previous studies in London,[23 24] and around the world.[10 12 13 19 25] However, in some places healthcare delay was longer than presentation delay, notably studies in the south east of England,[18] France[15] and Norway.[26] This may be due to differences in service provision and low clinical suspicion for TB since these areas have low TB incidence.

The increased risk of both presentation and healthcare delay experienced by females is a common finding around the world and in the UK.[8 14 18 23 27–29] In our study, this association was no longer found if we lowered the threshold for presentation delay. Reasons for this finding are not clear. Nevertheless, the association with healthcare delay persisted, suggesting an inherent bias in suspicion of TB or even other health issues by health providers. White ethnicity as compared with Asian ethnicity has also been associated with longer overall delay in other studies in the UK.[27 28] White ethnicity in our study could be associated with vulnerable and marginalised groups which are likely to have a delay in presentation. The longer healthcare delay for people of white ethnicity could be explained by a heightened clinical suspicion and investigation in Asian ethnicities. The association of increasing age with overall delay was found in many studies.[17 18 24 28] While underlying medical conditions or more common alternative diagnoses could result in a healthcare delay among older people, it is not clear why they should present later.

Concerning presentation delay alone, previous imprisonment and alcohol misuse were associated with presentation delay. These indicate the individual may have a chaotic lifestyle leading to a lack of attention to their health, as well as poor past experience with health professionals resulting in delaying visits to healthcare. Multiple studies have found alcohol misuse to be associated with longer total delay.[8]

Table 7 Significant variables in sensitivity analysis for healthcare delay

	Cut-off=21 days (median)		Cut-off=61 days (third quartile)	
Variable	**aOR**	**95% CI**	**aOR**	**95% CI**
Female sex	**1.29**	**1.14 to 1.47**	**1.39**	**1.21 to 1.59**
Age	**1.013**	**1.009 to 1.017**	**1.014**	**1.009 to 1.018**
White ethnicity	1.13	0.94 to 1.34	**1.41**	**1.19 to 1.68**
Less than 5 years in the UK	**0.77**	**0.64 to 0.94**	*	*
History of homelessness	**0.69**	**0.53 to 0.89**	*	*
A&E	**0.19**	**0.17 to 0.22**	**0.22**	**0.18 to 0.26**
Private sector	**0.35**	**0.21 to 0.57**	**0.48**	**0.26 to 0.85**
Other PHC	**0.48**	**0.41 to 0.56**	**0.60**	**0.51 to 0.71**

In bold the significant results in analyses.
*Variables not selected in final model.
A&E, accident and emergency; PHC, place of healthcare.

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Table 8 Description and ORs for univariable analysis for non-completion of treatment at 12 months, complete case analysis per individual variable

Variable	Total, n (% of population)	Not completed, n (% not completed)	OR	95% CI	P value
Sex					
Male	3588 (63)	612 (17)	Ref		
Female	2090 (37)	273 (13)	0.73	0.63 to 0.85	**<0.001**
Age, median (range)	37 (18–105)	43 (18–95)	1.016	1.011 to 1.021	**<0.001**
Born in the UK or resident					
Born in the UK	1221 (22)	192 (16)	Ref		
Recent resident (<5 years in the UK)	1347 (24)	240 (18)	1.16	0.94 to 1.43	0.16
Longer resident (≥5 years in the UK)	2784 (49)	385 (14)	0.86	0.71 to 1.04	0.11
Time since entry unknown	303 (5.4)	64 (21)	1.44	1.04 to 1.96	**0.03**
Ethnicity					
Asian/Asian-British	2037 (36)	323 (16)	Ref		
Black-African/black-Caribbean/black-British	1335 (24)	166 (12)	0.75	0.62 to 0.92	**0.006**
White	1277 (23)	226 (18)	1.14	0.95 to 1.37	0.17
Other	1007 (18)	164 (16)	1.03	0.84 to 1.27	0.76
Sputum smear result (at diagnosis)					
Positive	1895 (33)	347 (18)	Ref		
Negative	1818 (32)	266 (15)	0.76	0.64 to 0.91	**0.003**
Other (awaiting results, not done, unknown …)	1965 (35)	272 (14)	0.72	0.60 to 0.85	**<0.001**
Chest X-ray or CT (at diagnosis)					
Cavities reported	1337 (24)	228 (17)	1.07	0.90 to 1.27	0.46
Abnormalities reported	2915 (51)	471 (16)	Ref		
Other (awaiting results, not done, unknown …)	1426 (25)	186 (13)	0.78	0.65 to 0.93	**0.007**
History of drug use					
Yes	381 (6.9)	93 (24)	1.90	1.48 to 2.43	**<0.001**
No	5184 (93)	752 (15)	Ref		
History of homelessness					
Yes	354 (6.3)	93 (26)	2.08	1.62 to 2.66	**<0.001**
No	5245 (94)	767 (15)	Ref		
History of imprisonment					
Yes	265 (4.8)	64 (24)	1.85	1.37 to 2.46	**<0.001**
No	5314 (95)	782 (15)	Ref		
Alcohol misuse					
Yes	340 (6.3)	101 (30)	2.56	1.99 to 3.26	**<0.001**
No	5104 (94)	724 (14)	Ref		
Mental health concerns					
Yes	375 (6.8)	84 (22)	1.69	1.30 to 2.17	**<0.001**
No	5139 (93)	751 (15)	Ref		
First healthcare practitioner to visit					
A&E	1354 (24)	286 (21)	2.00	1.66 to 2.42	**<0.001**
General practitioner	1982 (35)	234 (12)	Ref		
Private sector	57 (1.00)	4 (7.0)	0.56	0.17 to 1.39	0.27
Other (inpatient, outpatient, laboratory, prison)	891 (16)	172 (19)	1.79	1.44 to 2.21	**<0.001**
Unknown	1394 (25)	189 (14)	1.17	0.95 to 1.44	0.13
Occupation					
Employed*	3984 (76)	559 (14)	Ref		
Unemployed†	1248 (24)	243 (19)	1.48	1.25 to 1.75	**<0.001**

Continued

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Table 8 Continued

Variable	Total, n (% of population)	Not completed, n (% not completed)	OR	95% CI	P value
Presentation delay					
Not delayed (<84 days)	2653 (74)	426 (16)	Ref		
Delayed (≥84 days)	933 (26)	145 (16)	0.97	0.78 to 1.19	0.76
Healthcare delay					
Not delayed (<61 days)	3105 (75)	525 (17)	Ref		
Delayed (≥61 days)	1060 (25)	152 (14)	0.82	0.67 to 1.00	0.05

Significant p values (<0.05) are highlighted in bold.
*Employed included all employment types, plus housewives/husbands, students and retired people.
†Unemployed includes reported unemployed, prisoners, asylum seekers and immigration detainees.
A&E, accident and emergency; Ref, reference group.

Concerning healthcare delay alone, people who attended a general practitioner were more likely to be delayed than those attending A&E or other services which is consistent with many studies.[10–14 24 25] General practitioners are in a primary healthcare setting and have to refer to specialised services for TB diagnosis and treatment, which will incur some delay. However, additional delays in referral may occur due to low suspicion of TB. People who attend A&E may have more severe symptoms or have difficulty accessing primary care services due to misunderstanding the healthcare service or immigration status. This would induce a shorter healthcare delay due to faster investigation, and easier access to diagnostic tools and specialists within a hospital setting.

In our cohort, 84% of people completed treatment, higher than other European countries,[30 31] yet below the WHO target of 90%.[1] We found no evidence that delay was associated with not completing treatment. Delay is known to negatively affect treatment outcome in high-TB-incidence countries like Ethiopia or China in terms of death, loss to follow-up and treatment failure but we did not identify any studies from low-TB incidence countries.[17 32] No association was found between either delay and not completing treatment when using the third quartile for dichotomisation though an association was found with healthcare delay when using the median. This finding could be attributed to chance or that a longer presentation or healthcare delay relate to less severe symptoms or disease, since we are controlling for other social risk factors and sociodemographic variables. Conversely, some patients at risk of poor treatment outcome due to symptom severity may be fast-tracked through the health service. Therefore, it is more difficult to judge the relationship of healthcare delay to treatment outcome. Moreover, our outcome simply characterises treatment completion at 12 months, and cannot cover more subtle consequences of delay such as worsening patient health or necessity for extended treatment.

Strengths and limitations

This study is subject to recall bias due to the dates of symptom onset and visit to a place of healthcare being reported retrospectively by the people included in the study only after diagnosis. This bias could be differential if recall differed between subgroups. We chose to make delay a binary variable, meaning we lost information from the continuous variable, however, the extreme right skew of delay would have otherwise implied associations with long delay that may not have been directly related to the length of delay. The choice of dichotomisation also allowed us to focus on the most delayed group. When we reduced the cut-off for delay, this made the outcome variable broader, in this situation we found similar results, but finer associations were not captured. Data for presentation delay and healthcare delay were missing in 37% and 28% of cases, respectively. We believe that the subsets of the population were representative of the whole study population but due to complete case analysis, our findings may be under or over-estimated. Also, when considering the missing values for social risk factors as 'no', our results were the same as those found in our initial analysis. When analysing outcome, we included isoniazid-resistant TB as their treatment should be completed within 12 months. We used treatment completion which is a broad outcome since this does not assess the actual health outcomes of people after they have completed their treatment regimen. Finally, extrapolation of these results must be done with caution, as the London population of people with TB is likely to differ from other parts of the UK or abroad, as will access to local healthcare services.

Recommendations

Though there is no recommendation on an acceptable length of delay, overall delay in London was shorter than for England as a whole.[2] In London, presentation delay was longer than healthcare delay, so a focus on reducing this will lead to more overall reduction in delays. In London, increasing TB knowledge among people who work with vulnerable groups could help ensure that these groups are registered with a general practitioner and early healthcare assessment could be arranged for those who have symptoms. TB awareness in healthcare practitioners must be maintained, especially in the context of

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Table 9 Final model for multivariable analysis for treatment non-completion at 12 months

Variable	aOR	95% CI	P value
Sex			
Male	Ref		
Female	0.82	0.66 to 1.01	0.07
Age	1.018	1.012 to 1.024	**<0.001**
Born in the UK or resident			
Born in the UK	Ref		
Recent resident (<5 years in the UK)	1.44	1.05 to 1.98	**0.02**
Longer resident (≥5 years in the UK)	0.78	0.58 to 1.03	0.08
Time since entry unknown	1.22	0.65 to 2.18	0.51
Ethnicity			
Asian/Asian-British	Ref		
Black-African/black-Caribbean/black-British	0.72	0.54 to 0.95	**0.02**
White	0.64	0.48 to 0.86	**0.003**
Other	1.01	0.77 to 1.32	0.95
History of drug use			
Yes	1.71	1.17 to 2.46	**0.005**
No	Ref		
Alcohol misuse			
Yes	1.97	1.36 to 2.81	**<0.001**
No	Ref		
First healthcare practitioner to visit			
A&E	1.66	1.32 to 2.09	**<0.001**
General practitioner	Ref		
Private sector	0.60	0.14 to 1.71	0.41
Other (inpatient, outpatient, laboratory, prison)	1.37	1.03 to 1.80	**0.03**
Unknown	1.25	0.19 to 4.87	0.77
Occupation			
Employed*	Ref		
Unemployed†	1.16	0.91 to 1.47	0.22
Presentation delay			
Not delayed (<84 days)	Ref		
Delayed (≥84 days)	0.98	0.78 to 1.22	0.86
Healthcare delay			
Not delayed (<61 days)	Ref		
Delayed (≥61 days)	1.00	0.77 to 1.28	0.98

Significant p values (<0.05) are highlighted in bold.
*Employed included all employment types, plus housewives/husbands, students and retired people.
†Unemployed includes reported unemployed, prisoners, asylum seekers and immigration detainees.
A&E, accident and emergency; aOR, adjusted OR; Ref, reference group.

reducing TB rates. Our study found that social risk factors are associated with delays, supporting the UK guidance on heightened awareness and where appropriate active case finding in these groups.[33]

Unnecessary delays along the patient pathway should be assessed locally to identify any systematic issues that can be addressed. Cohort review provides an opportunity to improve quality of data collection on delays and identify local issues for action.

Additional studies are needed to better understand why females in particular are at increased risk of delays.

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