

Evaluation of prediagnosis emergency department presentations in patients with active tuberculosis: the role of chest radiography, risk factors and symptoms

S C Appleton,¹ D W Connell,¹ A Singanayagam,¹ P Bradley,² D Pan,² F Sanderson,¹ B Cleaver,² A Rahman,² O M Kon¹

To cite: Appleton SC, Connell DW, Singanayagam A, *et al*. Evaluation of prediagnosis emergency department presentations in patients with active tuberculosis: the role of chest radiography, risk factors and symptoms. *BMJ Open Resp Res* 2017;**4**:e000154. doi:10.1136/bmjresp-2016-000154

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjresp-2016-000154>)

Received 2 August 2016
Revised 24 October 2016
Accepted 26 October 2016



CrossMark

¹Tuberculosis Service, Imperial College Healthcare NHS Trust, London, UK
²Department of Emergency Medicine, Imperial College Healthcare NHS Trust, London, UK

Correspondence to Professor O M Kon; onn.kon@imperial.nhs.uk

ABSTRACT

Introduction: London has a high rate of tuberculosis (TB) with 2572 cases reported in 2014. Cases are more common in non-UK born, alcohol-dependent or homeless patients. The emergency department (ED) presents an opportunity for the diagnosis of TB in these patient groups. This is the first study describing the clinico-radiological characteristics of such attendances in two urban UK hospitals for pulmonary TB (PTB) and extrapulmonary TB (EPTB).

Methods: We conducted a retrospective cohort study using the London TB Register (LTBR) and hospital records to identify patients who presented to two London ED's in the 6 months prior to their ultimate TB diagnosis 2011–2012.

Results: 397 TB cases were identified. 39% (154/397) had presented to the ED in the 6 months prior to diagnosis. In the study population, the presence of cough, weight loss, fever and night sweats only had prevalence rates of 40%, 34%, 34% and 21%, respectively. Chest radiography was performed in 76% (117/154) of patients. For cases where a new diagnosis of TB was suspected, 73% (41/56) had an abnormal radiograph, compared with 36% (35/98) of patients where it was not. There was an abnormality on a chest radiograph in 73% (55/75) of PTB cases and also in 40% (21/52) of EPTB cases where a film was requested.

Conclusions: A large proportion of patients with TB present to ED. A diagnosis was more likely in the presence of an abnormal radiograph, suggesting opportunities for earlier diagnosis if risk factors, symptoms and chest radiograph findings are combined.

INTRODUCTION

The WHO estimated that 9.6 million people developed tuberculosis (TB) in 2014.¹ In England, the incidence of TB is persistently high. In 2014, 6520 cases of TB were

KEY MESSAGES

- 39% of tuberculosis cases present to A+E in the preceding 6 months.
- Symptoms alone are insufficiently sensitive to rule out TB in an acute setting.
- Plain chest radiography in combination with risk factors and symptoms offers the best diagnostic yield.

reported.² For the same year in the USA, which has a population nearly five times that of the UK's, 9421 cases of TB were reported.³ Countries similar to the UK have made steady but intensive efforts to control TB and have seen a reduction in the number of new cases.⁴

Mycobacterium tuberculosis infection may have a prolonged subclinical phase during which the diagnosis and isolation of infectious cases can be difficult. In addition, current diagnostic methods have either a low specificity (eg, chest radiographs/Interferon Gamma Release Assays (IGRA)) or there is a long delay until results are available, especially when sputum smear results are negative and microbiological culture can take several weeks. These factors all contribute to making screening programmes for active TB more challenging to implement.⁵ Therefore, identification of factors that will lead to the consideration of a diagnosis of TB may prompt a more rapid initiation of investigations and sampling to allow for TB control measures.

In the UK, the majority of new cases are concentrated in densely populated, urban areas. In 2014, London saw 2572 new cases of TB, nearly 40% of the national total, a rate of



30.1 per 100 000 which is nearly three times that of the UK average (12.0 per 100 000). The majority of these cases were in patients who were born outside the UK; the incidence was also higher in patients who were homeless, drug and alcohol misusers or immunosuppressed.² The UK health authorities already recognise the difficulty in identifying and treating these patient groups and have released specific guidance to achieve early identification and successful treatment.⁶ The emergency department (ED) is an important facet of healthcare usage for these patient groups who do not regularly attend other healthcare services such as general practitioners (GPs) or may not be registered.^{7 8 9}

There have been a small number of US-based studies looking at ED presentations of pulmonary TB (PTB), finding a high frequency of these patients born outside the USA, and with pulmonary symptoms and an abnormal chest radiograph increasing the likelihood of a TB diagnosis.^{10 11} In the UK, although one study has investigated TB symptoms and blood results in inpatients,¹² and two short reports have examined cases at ED presentation,^{13 14} we have made a specific analysis of the usefulness of risk factors, symptoms and chest radiographs in the diagnosis of PTB and extrapulmonary TB (EPTB) in the ED.

The aim of this study was to evaluate prediagnosis ED attendances in patients with a final diagnosis of confirmed active TB infection, to identify factors that are associated with delayed diagnosis, and investigate strategies to help identify such cases.

METHODS

Study population

We performed a retrospective cohort analysis of patients that were diagnosed with active TB at two large central London hospitals between 1 January 2011 and 31 December 2012. ED discharge records were then used to identify patients with TB who had visited the ED in the previous 6 months. No age restriction was applied. Patients were only discounted from the study if there were no records available; this occurred in two cases. The study was approved as a service evaluation and ethics committee approval was not required.

Data collection

The London TB Register (LTBR) is a database recording new TB cases and demographic, comorbidities, disease and outcome data; this along with ED notes, blood results and imaging databases were used in our data collection. We recorded the presence of a number of factors of interest, including demographic factors such as age, gender, country of birth, ethnicity, English speaking and number of years since entry into the UK. We also included known TB risk factors (eg, previous TB, TB contacts, alcohol misuse, homelessness and so on) as well as baseline physiological observations taken on presentation to ED and the presence of TB-related

symptoms (cough, subjective fevers, night sweats, weight loss, sputum production, dyspnoea, haemoptysis and chest pain) and other symptoms. Any abnormal clinical findings related to TB on chest examination (crepitations, reduced air entry, dull percussion note or reduced expansion), lymphadenopathy or tenderness during an abdominal examination, were noted. We recorded whether the ED notes commented on the chest radiograph, the findings of the chest radiograph and any other imaging performed and the outcome of the encounter.

Radiological evaluation

The chest radiograph reports were reviewed. Any reports that referenced possible TB-related changes, for example, cavitation, infiltrates, effusion, lymphadenopathy or pleural thickening or if the report raised the possibility of TB as the cause were recorded as 'abnormal'. If no reference to TB-related changes was made or the report found no abnormalities, it was recorded as 'normal'.

Statistical methods

All data are presented as n (%) unless otherwise stated. The χ^2 test or Fisher's exact test was used to compare categorical variables. The Mann-Whitney U test was used to compare continuous variables. Multivariable analysis was used to evaluate the association of variables recorded on presentation with suspicion of TB diagnosis in ED. The variables were included in the regression model are shown in online supplementary table S1. The threshold for statistical significance was $p < 0.05$.

RESULTS

Study cohort

There were 397 patients included in the study, out of these 397 cases, 156 (39%) presented to the ED in the 6 months prior to their diagnosis. Two cases were excluded due to inadequate records being available. Baseline demographics of the study population are shown in [table 1](#).

Comparison of patients with TB who presented to ED prior to diagnosis with those who did not

There were 154 (39%) of the study population who presented to ED in the 6-month period prior to their diagnosis of TB. [Table 2](#) shows comparison of demographic and comorbid variables between patients who attended ED versus those who did not.

Symptomatic presentation and baseline observations in patients who attended ED

We next conducted an evaluation of the symptoms reported by patients who attended ED prior to TB diagnosis. [Table 3](#) shows the most common symptoms reported and also the proportion of patients with

Table 1 Baseline demographics of study cohort

| Demographics/patient factors | Frequency (%) |
|------------------------------|---------------|
| Population size | 397 |
| Male | 231 (58%) |
| Median age (IQR) | 35 (25) |
| Pulmonary TB | 166 (42%) |
| Non-pulmonary TB | 231 (58%) |
| Indian subcontinent | 117 (29%) |
| Black African | 111 (28%) |
| White | 74 (19%) |
| Black Caribbean | 22 (6%) |
| Arabic | 26 (7%) |
| Other ethnicity | 47 (12%) |
| Born outside UK | 309 (78%) |
| Previous BCG vaccination | 223 (56%) |
| Previous TB infection | 16 (4%) |
| Unemployed | 67 (17%) |
| Homelessness | 29 (7%) |
| Drug misuse | 22 (6%) |
| History of imprisonment | 17 (4%) |
| Not registered with GP | 79 (20%) |

GP, general practitioner; TB, tuberculosis.

Table 2 Baseline demographics and patients factors in subgroup who attended ED versus group who did not

| | Attended ED (%) | Did not attend ED (%) | χ^2 test (p value) |
|------------------------------|-----------------|-----------------------|-------------------------|
| Demographics | | | |
| Population size | 154 | 243 | – |
| Male | 100 (65%) | 131 (54%) | 0.030 |
| Age (IQR) | 34 (23) | 35 (22) | 0.408 |
| Pulmonary TB | 75 (49%) | 91 (37%) | 0.045 |
| Non-pulmonary TB | 79 (51%) | 152 (63%) | |
| Ethnicity | | | |
| Indian subcontinent | 40 (26%) | 77 (32%) | 0.224 |
| Black African | 44 (29%) | 67 (28%) | 0.829 |
| White | 31 (20%) | 43 (18%) | 0.544 |
| Black Caribbean | 12 (8%) | 10 (4%) | 0.119 |
| Arabic | 13 (8%) | 13 (5%) | 0.225 |
| Other ethnicity | 14 (9%) | 33 (14%) | 0.177 |
| Comorbidities | | | |
| Born outside UK | 120 (78%) | 189 (78%) | 0.973 |
| Previous BCG vaccination | 89 (58%) | 134 (55%) | 0.604 |
| Previous TB infection | | | |
| Unemployed | 9 (6%) | 7 (3%) | 0.143 |
| Homelessness | 27 (18%) | 40 (16%) | 0.781 |
| Drug misuse | 12 (8%) | 17 (7%) | 0.766 |
| Prison history | 11 (7%) | 11 (5%) | 0.267 |
| Not registered with GP | 8 (5%) | 9 (4%) | 0.475 |
| Not registered with GP | 38 (25%) | 41 (17%) | 0.058 |

ED, emergency department; GP, general practitioners; TB, tuberculosis.

baseline abnormalities in routine observations. Thirty-one per cent of cases presenting to the ED had no abnormal observations (48/154).

Of the PTB cases, the three most prevalent symptoms recorded in the ED clerking were cough (64%), weight loss (49%) and subjective fevers (41%). EPTB cases were far less likely to have classical TB symptoms with the three most prevalent of these being subjective fevers (28%), weight loss (20%) and cough (18%). Fifty-eight per cent (90/154) had any of the three most prevalent symptoms (cough, weight loss and fevers). In patients with PTB the incidence was 72% (54/75), compared with the lower rate for EPTB 46% (36/79).

Seventy-five per cent of the EPTB cases had other symptoms recorded, 38% (30/79) had gastrointestinal symptoms, 20% (16/79) had central nervous system (CNS)/headache symptoms and 16% (13/79) had back or joint pain symptoms.

Comparison of patients who had TB suspected in ED versus those who did not

TB was included in the differential diagnosis in the ED in 56 of 154 cases (36%). Table 4 shows a comparison between patients who had TB suspected in ED versus those who did not.

This rate of clinical suspicion of TB was significantly higher in patients with PTB than those with EPTB (55% vs 19%; $p < 0.01$).

There was also a significant difference between the median time from ED attendance to starting treatment. In patients where TB was suspected, median was 9.75 days (3–12.75), compared with 71.25 days (13–84.25) in those where it was not listed as a differential diagnosis (Mann-Whitney U test, $p < 0.001$).

Multivariable analysis

On multivariable analysis, the following factors were independently associated with suspicion of TB in ED: cough (OR 6.30 (1.71–23.21)), birth outside UK (OR 5.48 (1.29–23.30)), known contact with TB infected person (OR 18.63 (2.49–139.27)), history of night sweats (16.09 (3.39–76.42)) and abnormal chest radiograph (OR 5.90 (1.70–20.53)) (see online supplementary table S1).

Chest radiograph

Of the 154 patients visiting the ED in the 6 months prior to their diagnosis, 24% (37/154) did not have a chest radiograph or other imaging performed on presentation to ED. For PTB cases, 86% (55/64) patients who had a chest radiograph had an abnormality. As would be expected, EPTB had a lower rate of abnormal radiographs, 40% (21/53), but it is notable that there is still a significant proportion with plain chest radiology abnormalities. Of all patients with an abnormal radiograph, many had multiple abnormal findings; the three most common abnormalities seen on radiograph were consolidation in 55% (42/76), effusions in 26% (20/76) and decreased volume or collapse in 22% (17/76). In the patients where TB was not suspected but who had an abnormal chest X-ray (CXR), the most common

Table 3 Symptoms and baseline observations of patients who attended ED prior to diagnosis of TB

| Risk factors | Frequency (% of study population) | Pulmonary TB symptoms | Frequency (% of study population) |
|-----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Current smoker | 27 (18%) | Cough | 62 (40%) |
| Recent travel | 19 (12%) | Fever | 53 (34%) |
| Known TB contacts | 13 (8%) | Weight loss | 53 (34%) |
| Airways disease | 12 (8%) | Night sweats | 33 (21%) |
| Diabetes (type 1 or 2) | 12 (8%) | Chest pain | 31 (20%) |
| HIV positivity | 6 (4%) | Sputum production | 28 (18%) |
| Hepatitis B or C positivity | 3 (2%) | Dyspnoea | 28 (18%) |
| Alcohol misuse | 13 (8%) | Haemoptysis | 11 (7%) |
| Immunosuppressive treatment | 3 (2%) | Other symptoms | |
| Observations | | Gastrointestinal | 30 (19%) |
| Tachycardia (<100/min) | 53 (34%) | CNS/headache | 16 (10%) |
| Fever (>38°C) | 30 (19%) | Back/joint pain | 13 (8%) |
| Tachypnoea (>20/min) | 20 (13%) | Neck lump | 8 (5%) |
| Pulse oximetry <95% | 8 (5%) | Generalised weakness and malaise | 8 (5%) |
| Hypotension (workup SBP<90 mm Hg) | 3 (2%) | Other | 9 (6%) |

CNS, central nervous system; ED, emergency department; SBP, systolic blood pressure; TB, tuberculosis.

features were consolidation 46% (16/35), reduced volume 31% (11/35) and effusion 23% (8/35).

Of those 35 patients where the chest radiograph was abnormal and TB was not suspected, 63% (22/35) were men, the average age was 45 years and 71% (25/35) were born outside the UK. Thirty-seven per cent (13/35) of patients had other symptoms present. Fewer patients had any of the three most prevalent symptoms: cough (40%), weight loss (31%) and subjective fevers (29%). Thirty-one per cent (11/35) of these patients reattended the same ED compared with 26% (40/154) overall.

Of patients attending the ED, 69% (107/154) had an abnormal chest radiograph report, presence of cough, subjective fevers or weight loss.

There is no validated probability score in acute TB and we therefore used the features of night sweats and cavitation on chest radiograph as a proxy for cases where TB should have reasonably been suspected. Five per cent (7/154) patients had night sweats and cavitation and all of these patients had TB suspected in the ED. Of the 7% (11/154) patients who had cavitation but no night sweats on chest radiograph, all 11 patients had TB suspected. Eight out of 33 patients who had night sweats but not cavitation did not have TB suspected in the ED.

Forty per cent (21/53) of patients with EPTB who had a radiography performed had an abnormality recorded in the report. Thirty-three per cent (26/79) had no radiography performed.

Treatment and outcomes

Fifty-four per cent (83/154) of patients were admitted following their accident and emergency (A&E) department attendance and 26% (40/154) of patients

reattended A&E following their first presentation. Of those patients who were admitted, 35% (29/83) had TB suspected in the ED and 51% (42/83) had an abnormal CXR compared with 38% (27/71) and 48% (34/71), respectively, for those who were not admitted. The mean interval between presentation to the ED and the initiation of TB treatment was 39 days (range 0–185 days, median 17 days). Thirty-one per cent (48/154) patients were started on TB treatment within a week of their A&E visit. For those patients where TB was considered as part of the differential, the time to starting treatment was dramatically lower, average of 14.4 days compared with 53.6 days.

DISCUSSION

In our study population, a high proportion of patients, 39%, presented to the ED in the 6 months prior to their diagnosis, demonstrating the importance of this particular location as an opportunity for the detection of patients suffering from this disease. In those suspected to have TB during their attendance, the ED has allowed a timely diagnosis and it is possible that had the individual not accessed healthcare through the ED the case would have remained undiagnosed. In addition, 7% (11/154) had sputum smear performed within 24 hours of attending A&E and these patients may not have had sputum sent in other healthcare settings.

It has also been established that large Western European cities have significantly higher rates of TB infection compared with national rates; London has experienced a continued rise in TB notification rates from 24 per 100 000 in 1990 to 45 per 100 000 in 2011.^{15 16} This high incidence of TB coupled with the high use of emergency care in this urban population

Table 4 Comparison of patients where TB was suspected in the ED and those where it was not

| | TB suspected in ED Frequency (%) | TB not suspected in ED Frequency (%) | χ^2 test (p value) |
|--|-------------------------------------|---|-------------------------|
| Demographics | | | |
| Population size | 56 | 98 | – |
| Male | 37 (66%) | 63 (64%) | 0.823 |
| Age (IQR) | 30.5 (16.75) | 36.5 (30.5) | 0.276 (Mann-Whitney) |
| Pulmonary TB | 41 (73%) | 34 (35%) | <0.001 |
| Non-pulmonary TB | 15 (27%) | 64 (65%) | |
| Indian subcontinent | 14 (25%) | 26 (27%) | 0.835 |
| Black African | 19 (34%) | 25 (26%) | 0.266 |
| White | 10 (18%) | 21 (21%) | 0.595 |
| Black Caribbean | 6 (11%) | 6 (6%) | 0.306 |
| Arabic | 5 (9%) | 8 (8%) | 0.870 |
| Other ethnicity | 2 (4%) | 12 (12%) | 0.086 |
| Born outside UK | 47 (84%) | 73 (74%) | 0.174 |
| Previous BCG vaccination | 37 (66%) | 52 (53%) | 0.116 |
| Unemployed | 13 (23%) | 14 (14%) | 0.161 |
| Homelessness | 5 (9%) | 7 (7%) | 0.691 |
| Prison history | 2 (4%) | 6 (6%) | 0.711 |
| Comorbidities | | | |
| Current smoker | 12 (21%) | 15 (15%) | 0.336 |
| Recent travel | 14 (25%) | 5 (5%) | <0.001 |
| Previous TB infection | 6 (11%) | 3 (3%) | 0.0734 |
| Known TB contacts | 11 (20%) | 2 (2%) | <0.001 |
| Airways disease | 6 (11%) | 6 (6%) | 0.306 |
| Diabetes (type 1 or 2) | 4 (7%) | 8 (8%) | 1.000 |
| HIV positivity | 3 (5%) | 3 (3%) | 0.6686 |
| Hepatitis B or C positivity | 1 (0%) | 2 (2%) | 1.000 |
| Drug misuse | 5 (9%) | 6 (6%) | 0.515 |
| Alcohol misuse | 5 (9%) | 8 (8%) | 0.870 |
| Immunosuppressive treatment | 0 (0%) | 3 (3%) | 0.5541 |
| Observations | | | |
| Tachycardia (<100/min) | 22 (39%) | 31 (32%) | 0.336 |
| Fever (<38°C) | 13 (23%) | 17 (17%) | 0.376 |
| Tachypnoea (>20/min) | 9 (16%) | 11 (11%) | 0.389 |
| Pulse oximetry <95% | 3 (5%) | 5 (5%) | 1.000 |
| Hypotension (SBP<90 mm Hg) | 1 (2%) | 2 (2%) | 1.000 |
| Symptoms | | | |
| Cough | 41 (73%) | 21 (21%) | <0.001 |
| Fever | 30 (54%) | 23 (23%) | <0.001 |
| Weight loss | 33 (59%) | 20 (20%) | <0.001 |
| Night sweats | 25 (45%) | 8 (8%) | <0.001 |
| Chest pain | 14 (25%) | 17 (17%) | 0.255 |
| Sputum production | 18 (32%) | 10 (10%) | <0.001 |
| Dyspnoea | 14 (25%) | 14 (14%) | 0.097 |
| Haemoptysis | 7 (13%) | 4 (4%) | 0.0991 |
| Chest radiograph | | | |
| Chest radiography performed | 52 (93%) | 65 (66%) | <0.001 |
| Normal radiograph (% of those who had radiography performed) | 11 (21%) | 30 (46%) | 0.138 |
| Abnormal radiograph (% of those who had radiography performed) | 41 (79%) | 35 (54%) | <0.001 |

Bold indicates significant statistics.

ED, emergency department; SBP, systolic blood pressure; TB, tuberculosis.

emphasises the importance of case detection being initiated promptly by clinicians in the ED.

Our cohort reflected the national picture of TB being more prevalent in patients born outside the UK, homeless,

drug and alcohol misusers or immunosuppressed.² This again emphasises the importance of considering TB in any cases presenting with these epidemiological risk factors. A quarter of patients who presented to the ED

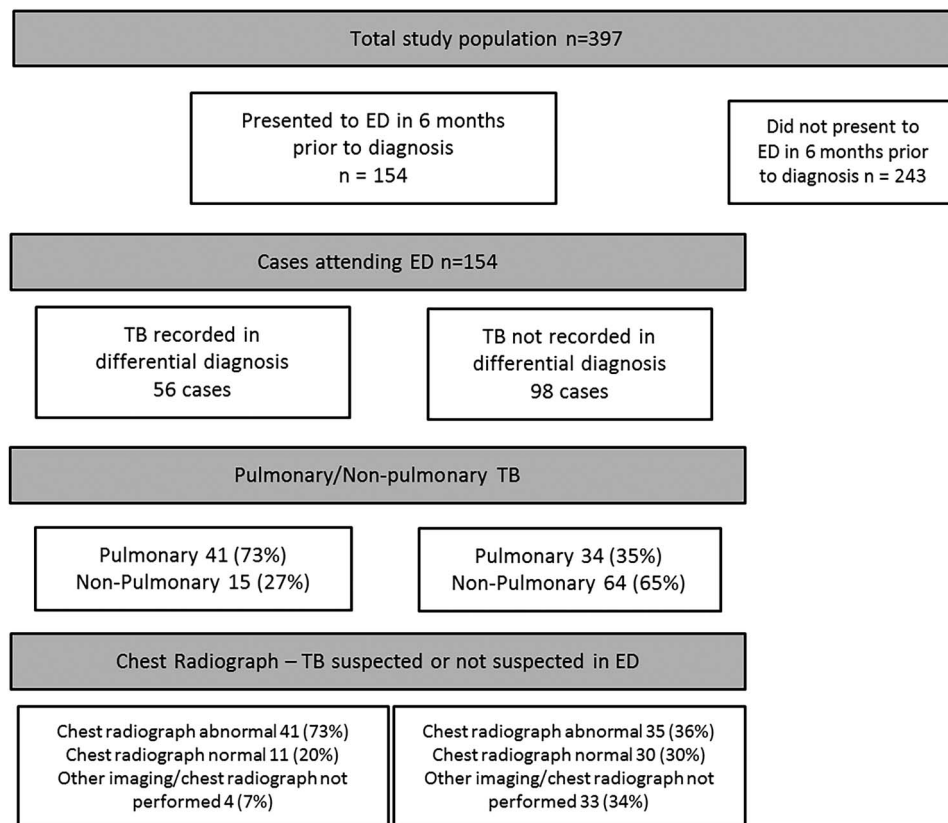


Figure 1 Chest radiograph findings and type of TB in patients presenting to ED. ED, emergency department; TB, tuberculosis.

were not registered with a GP, a higher rate than those not attending the ED. Although the difference was not statistically significant, it highlights that many patients with TB underuse primary care services and are therefore more likely to present to emergency care services.

Apart from male gender, there were no statistically significant differences between the demographics and comorbidities of those who presented to the ED compared with those who did not. Nationally, 50% of ED attenders are men, whereas 65% of the study patients with TB who attended ED were men.¹⁷ However, the study relied on the accuracy of documentation for these risk factors and comorbidities which will have varied between clinicians.

Pulmonary TB cases represented approximately half of the study population; in this group tachycardia and fever were the most commonly abnormal observations and cough, weight loss and fevers were the most common classical TB symptoms that were present. Almost half of the EPTB patients had no classical TB symptoms and three-quarters presented with other symptoms of which gastrointestinal were the most common. The low incidence rate of classical symptoms, particularly in the EPTB group, makes diagnosis on symptoms alone unfeasible. As would be expected, cases of PTB more frequently displayed chest radiograph abnormalities than EPTB. In keeping with these findings, PTB was more often suspected as a diagnosis in the ED than EPTB (55% vs 19% of cases).

Overall, patients where TB was suspected in the ED had a much greater frequency of chest radiograph, 93% compared with 66%. However, patients where TB was suspected had a greater frequency of all pulmonary symptoms and were therefore more likely to have had a chest radiograph requested. On multivariable analysis, cough, country of birth outside the UK, a TB contact history, a history of night sweats and an abnormal chest radiograph were independently associated with suspicion of TB in ED. The significant proportion of patients where TB was not suspected in the ED but had abnormal radiograph findings (35 patients, 54%) highlights the importance of carefully reviewing all imaging undertaken in the ED and ensuring that any abnormal reports are acted on. Contemporary reporting of imaging while the patient is still in the ED could mean that clinical review can be correlated with radiograph findings. It is important to note that the plain chest radiograph had the best sensitivity when comparing this to symptoms. Importantly, our results indicate that even in cases of EPTB, there is an important role for performing a plain chest radiograph and that this has a broadly similar sensitivity compared with the incidence of classical symptoms. However, the most common chest radiograph abnormalities were consolidation, reduced volume and effusion; these radiographic characteristics can be present for a wide differential of respiratory infections.

This study has a number of strengths and is, to the best of our knowledge, the first study of its kind in the

UK to look systematically at radiographs in combination with risk factors and symptoms. We collected and analysed data on a large study population across two sites and it was conducted in a moderately high-incidence urban area. This study also links the initial ED presentation to TB clinic visit events. Previous similar studies have been in lower prevalence areas and in insurance-led healthcare rather than free at the point of use health systems.^{10 11}

Other studies in the USA have previously investigated the use of chest radiographs to help TB diagnosis in the ED.^{10 11} These studies found that frequently there is a wide range of symptoms and the chest radiograph helps in assisting the clinician's diagnosis. Our study supports these findings and this is in keeping with recently published national guidelines that encourage a chest radiograph to be performed in all patients with suspected TB (even in cases of EPTB) and to ensure that those with relevant radiographic changes are referred directly to local TB services.¹⁸ Mobile chest radiographs have previously been shown to have a high sensitivity but in the context of imaging in select high-risk groups.¹⁹ Our study lends support to interventions such as the 'Find and Treat' initiative in London that uses such units to actively find PTB cases.^{20 21}

As the study was retrospective, collection of data relied on availability of scanned or electronic records. Importantly, we cannot assume that all patients had active infection with TB 6 months before their diagnosis, or that a diagnosis could have been made on their ED visit. The study only included two EDs and patients may have attended other EDs within the study period and the figure of 39% may underestimate the actual number of visits. The point of contact this group makes with healthcare will increasingly be urgent care centres which were not part of the UK healthcare infrastructure at the time of the study. Also, our study did not have a control group to allow comparisons with the wider population. Ideally, this would be a control group of patients with another respiratory condition, for example, pneumonia which may allow us to look more closely at symptoms and patient factors predicting TB.

The high proportion of patients subsequently diagnosed with TB, that present to the ED prior to their diagnosis, lends support to rapid molecular-based TB diagnostics such as GeneXpert as an adjunct to conventional microscopy, culture and drug sensitivity testing. This would allow timelier testing as part of the workup for patients with suspected TB. It also highlights that patients that are potentially infective are attending a clinical environment where there is a high density of patients and there should be a lower threshold for consideration of isolation especially in higher prevalence, urban areas.

Our study also shows that in cases of EPTB, there was an even greater range of presenting symptoms potentially making the diagnosis even more challenging. Approximately, half of TB patients presenting to the ED have EPTB and although these patients were less likely

to have an abnormal chest radiograph (46% vs 86% in PTB), this yield is still important and a chest radiograph should be recommended in any case of potential EPTB. In addition, this study supports the development of a defined diagnostic pathway between ED and TB services when an individual has epidemiological risk factors for TB. These data also support the need for there to be a rapid and direct referral pathway from radiology to TB services should there be any abnormalities indicating potential TB when formally reported.

CONCLUSIONS

This study highlights the importance of the ED as a common key healthcare point of access for TB patients and demonstrates the value of TB departments working across healthcare services as the patient population may access healthcare in a less traditional way. To improve detection and control rates for TB, the diagnosis should be suspected in any patient with a demographic profile or symptoms associated with TB risk and the ED physician should have a low threshold for further investigations for TB. The results of this study suggest that the classical symptoms of TB alone are insufficient in assessment of patients with suspected disease as it frequently presents in a non-specific manner. Our results support the use of chest radiographs in helping alert a potential diagnosis in PTB and EPTB. Importantly, it also raises the difficulties of diagnosing EPTB given its wide varying presentations and highlights that a plain chest radiograph has the highest sensitivity of all the factors normally reviewed in an ED and should be requested in any possible case even when there are no respiratory symptoms.

Acknowledgements Kevin Kow, Imperial College London, contributed data on patient demographics.

Contributors OMK, SCA and DWC devised the study and SCA, PB and DP performed the data collection. SCA and PB performed the data analysis. SCA, DWC, AS, PB, DP, BC and OMK contributed to data interpretation. SA wrote the manuscript with assistance from DC, OMK and AS. All authors contributed to the review and editing of the manuscript.

Funding The research was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Imperial College Healthcare NHS Trust and Imperial College London.

Disclaimer The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests AS has received honoraria for speaking from GlaxoSmithKline.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

Open Access This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: <http://creativecommons.org/licenses/by/4.0/>

REFERENCES

1. Global tuberculosis report 2015, World Health Organisation.
2. Public Health England. *Tuberculosis in England: 2015 report*. London: Public Health England.



3. Reported tuberculosis in the United States, 2014. CDC, October 2015.
4. Zenner D, Zulma A, Gill P, *et al*. Reversing the tide of the UK tuberculosis epidemic. *Lancet* 2013;382:1311–12.
5. Golub JE, Dowdy DW. Screening for active tuberculosis: methodological challenges in implementation and evaluation. *Int J Tuberc Lung Dis* 2013;17:856–65.
6. National Institute for Health and Care Excellence. *Identifying and managing tuberculosis among hard-to-reach groups*. NICE Public Health guidance, PH37, 2012.
7. The unhealthy state of homelessness, Health audit results 2014. Homeless Link 2014. <http://www.homeless.org.uk/sites/default/files/site-attachments/The%20unhealthy%20state%20of%20homelessness%20FINAL.pdf>.
8. Stagg HR, Jones J, Bickler G, *et al*. Poor uptake of primary healthcare registration among recent entrants to the UK: a retrospective cohort study. *BMJ Open* 2012;2:pii: e001453.
9. Hargreaves S, Friedland JS, Gothard P, *et al*. Impact on and use of health services by international migrants: questionnaire survey of inner city London A&E attenders. *BMC Health Serv Res* 2006;6:153.
10. Geyer BC, Godwin P, Powell TJ, *et al*. Patient factors associated with failure to diagnose tuberculosis in the emergency department. *J Emerg Med* 2013;45:658–65.
11. Sokolove PE, Rossman L, Cohen SH. The emergency department presentation of patients with active pulmonary tuberculosis. *Acad Emerg Med* 2000;7:1056–60.
12. Breen RA, Leonard O, Perrin FM, *et al*. How good are systemic symptoms and blood inflammatory markers at detecting individuals with tuberculosis? *Int J Tuberc Lung Dis* 2008;12:44–9.
13. Smith A, Miller RF, Story A, *et al*. A&E department: a missed opportunity for diagnosis of TB? *Thorax* 2006;61:364–5.
14. Lad TS, Packe GE. Tuberculosis: a missed opportunity for early diagnosis at the front line? *Emerg Med J* 2014;31:942–3.
15. de Vries G Aldridge RW, Caylà JA, *et al*. The Tuberculosis in European Union Big Cities Working Group. Epidemiology of tuberculosis in big cities of the European Union and European economic area countries. *Euro Surveill* 2014;19:pii: 20726.
16. Hayward AC, Darton T, Van-Tam JN, *et al*. Epidemiology and control of tuberculosis in Western European cities. *Int J Tuberc Lung Dis* 2003;7:751–7.
17. Hospital Episode Statistics. *Accident and emergency attendances in England—2012–13*. Health and Social Care Information Centre, 2014.
18. Public Health England: collaborative tuberculosis strategy for England 2015 to 2020. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020_.pdf.
19. Story A, Aldridge AW, Abubakar I, *et al*. Active case finding for pulmonary tuberculosis using mobile digital chest radiography: an observational study. *Int J Tuberc Lung Dis* 2012;16:1461–7.
20. De Vries G, van Hest RAH, Richardus JH. Impact of mobile radiographic screening on tuberculosis among drug users and homeless persons. *Am J Respir Crit Care Med* 2007;176:201–7.
21. Jit M, Stagg HR, Aldridge RW, *et al*. Find and Treat Evaluation Team. Dedicated outreach service for hard to reach patients with tuberculosis in London: observational study and economic evaluation. *BMJ* 2011;343:d5376.

Evaluation of prediagnosis emergency department presentations in patients with active tuberculosis: the role of chest radiography, risk factors and symptoms

S C Appleton, D W Connell, A Singanayagam, P Bradley, D Pan, F Sanderson, B Cleaver, A Rahman and O M Kon

BMJ Open Resp Res 2017 4:
doi: 10.1136/bmjresp-2016-000154

Updated information and services can be found at:
<http://bmjopenrespres.bmj.com/content/4/1/e000154>

These include:

References

This article cites 14 articles, 3 of which you can access for free at:
<http://bmjopenrespres.bmj.com/content/4/1/e000154#BIBL>

Open Access

This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See:
<http://creativecommons.org/licenses/by/4.0/>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

[Tuberculosis](#) (3)

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>