Estimates of the impact of diabetes on the incidence of pulmonary tuberculosis in different ethnic groups in England

Caron Walker,¹ Nigel Unwin²

ABSTRACT
Background There is good evidence that diabetes is a risk factor for pulmonary tuberculosis. In England, the rates of both diabetes and tuberculosis vary markedly by ethnic group.

Objective To estimate the proportion of incident cases of pulmonary tuberculosis attributable to diabetes (population attributable fraction, PAF) for Asian, black and white men and women aged ≥15 years in England.

Methods An epidemiological model was constructed using data on the incidence of tuberculosis, the prevalence of diabetes, the population structure for 2005 and the age-specific relative risk of tuberculosis associated with diabetes from a large cohort study.

Results The estimated PAF of diabetes for pulmonary tuberculosis is highest for Asian men (19.6%, 95% CI 10.9% to 33.1%) and women (14.2%, 95% CI 7.1% to 26.5%). The PAF for all ages is similar in white and black men (6.9%, 95% CI 3.1% to 12.4% and 7.4%, 95% CI 4.6% to 12.9%, respectively) and women (8.2%, 95% CI 3.0% to 15.6% and 8.9%, 95% CI 5.3% to 15.6%, respectively). The similarity of these overall figures, despite a higher prevalence of diabetes in the black population, reflects a much younger mean age of pulmonary tuberculosis in the black population. Overall, of 3461 new cases of pulmonary tuberculosis in England in 2005, 384 (202–780) were estimated to be attributable to diabetes.

Conclusion Given the nature of the data available, considerable uncertainty surrounds these estimates. Nonetheless, they highlight the potential importance of diabetes as a risk factor for pulmonary tuberculosis, particularly in groups at high risk of both diseases. Further research to examine the implications of these findings for tuberculosis control is urgently needed.

INTRODUCTION
It is acknowledged that both tuberculosis (TB) and diabetes mellitus (DM) are major global health problems. However, there is little recognition that the rapid escalation of DM in some places may conceivably have as great an impact on TB control as the spread of HIV.¹ TB is a major cause of illness and death worldwide; in 2006 there were an estimated 9.2 million new cases of TB with 1.6 million deaths attributable to tuberculosis.² For DM there were an estimated 246 million people with the condition worldwide in 2007.³

In the 1950s joint treatment clinics for TB and DM were held in the UK,⁴ ⁵ and the idea that there is an association between TB and DM is not new. Descriptions of this association have been traced back to Roman times⁶ and, in the 5th century, ‘phthisis’ (TB) was portrayed as a ‘complication’ of diabetes⁷—echoing the description by Root in 1934 that DM precedes TB.⁸

The association between TB and DM is now becoming an area of increasing interest and significance because of their global impact,⁹ ¹⁰ although this link is rarely highlighted in current research or control priorities. For example, the action plan ‘Stopping Tuberculosis in England’¹¹ published by the Department of Health makes no mention of the increased risks associated with diabetes.

A previous literature review, co-authored by one of the authors of this paper, of analytical studies assessing the possible association between pulmonary TB and DM found nine studies, all of which showed a positive association.¹ It was concluded that the risk of TB is 2–3 times higher in people with DM than in those without DM, but it can be up to 8 times higher.¹ More recently a systematic review of 13 observational studies also found a consistent positive relationship and, in a meta-analysis of three cohort studies (one an occupational-based cohort, the other two in patients with renal disease), the overall relative risk (RR) was 3.11 (95% CI 2.27 to 4.26).¹² In three studies that provided age-specific relative risks, these were highest in the younger age groups. The mechanisms by which DM increases the risk of TB are not fully understood. Hypothesised mechanisms include changes in immune function associated with DM, including reduced macrophage activation and less efficient immune signalling and deficiencies in micronutrients such as vitamin D which may increase the risk of both diseases.¹

The prevalence of DM tends to vary markedly by ethnic group with, for example, black and South Asian populations in the UK having an age-specific prevalence of DM several times higher than the white population.¹³ TB also varies greatly by ethnic group. In 2008, for example, there were four cases per 100 000 in the UK-born population compared with 86 per 100 000 in the non-UK-born population. Among the latter, those belonging to the Indian, Pakistani and Bangladeshi ethnic groups accounted for the largest number of cases (n=2858), while the highest rates occurred in the black African ethnic group (314 per 100 000).Among populations born in the UK, the lowest rates occur in the white population (3 per 100 000), with much higher rates in those of Indian/Pakistani/Bangladeshi origin (41/46/17 respectively per 100 000) and black African origin (53 per 100 000).¹⁴
It is within this context that we wished to define better the impact that increasing levels of DM may have on the incidence of TB and, subsequently, the control of TB in the community. The aim of the work presented here was to model the potential impact of DM on pulmonary TB for different ethnic groups in England. Pulmonary TB was chosen as the evidence is strongest for this type of TB, with some evidence that the association between DM and extrapulmonary TB is less strong.\textsuperscript{1} Pulmonary TB is responsible for the majority of the TB incidence in England, accounting for 55% of all reported TB cases in 2008.\textsuperscript{14}

**METHODS**

**Sources of data**

Data were obtained from the Health Protection Agency (HPA) for pulmonary TB. Incidence was stratified by gender, age and ethnic group. Analyses were based on the adult population aged \( \geq 15\) years split into five age categories (table 1). In addition, data from the Yorkshire and Humber Public Health Observatory (YHPHO) were obtained (table 2).\textsuperscript{15} Note that the DM prevalence estimates are based on total (diagnosed and undiagnosed) DM. Denominator populations were the same as those used by the YHPHO and were based on the Office of National Statistics 2005 mid-year population estimates.

Age-specific relative risks for the association between DM and incident TB (for total pulmonary TB) were taken from a study of 814,713 South Korean civil servants.\textsuperscript{16} This is the best quality study available that provides age-specific estimates of the population attributable fraction (PAF).

The upper and lower 95% confidence limits on the age-specific RR estimates from the Korean study (table 3) were used to calculate upper and lower levels (effectively 95% CIs)\textsuperscript{17} of the population attributable fraction (PAF).

**Ethnic group categories**

The data from the YHPHO are available for only four ethnic group categories: white, black, Asian (which includes South Asian but not Chinese) and other (which includes Chinese). The data from the HPA are available in the following categories: white, black, Asian (which includes South Asian but not Chinese) and other (which includes Chinese). The data from the HPA are therefore combined into the same four categories as the YHPHO and in the analyses the ‘other/unknown’ category was not included.

**Estimation of population attributable fraction**

The data were used to construct an epidemiological model, as previously described,\textsuperscript{18} to calculate for each ethnic group, men and women, the estimated PAF for pulmonary TB associated with DM. The following formula was used:

\[
AF(P) = \frac{P_d (RR - 1)}{1 + P_d (RR - 1)}
\]

where \( P_d \) is the prevalence of diabetes and \( RR \) is the RR for TB in people with DM compared with people without.

As both the prevalence of DM and the RR associated with TB varies by age, the PAF was calculated separately for each for each age group. The PAF can be defined as the proportion by which the incidence rate of the outcome of interest (incident TB) in the entire population would theoretically be reduced if the exposure of interest (DM) was eliminated. Assumptions in this interpretation include that the exposure is causal and that other causative factors are equally distributed between those with and without the exposure.\textsuperscript{19} It clearly therefore provides an idealised estimate of the potential impact of the exposure (DM) on the outcome (pulmonary TB) and needs to be interpreted in this light.

This study did not require ethical approval, being based on routinely collected and fully anonymised data. No external funding was required for the study.

**RESULTS**

The highest estimated PAF for TB attributable to DM in people aged \( \geq 15\) years was in Asian men (19.6%, 95% CI 10.9% to 33.1%) and women (14.2%, 95% CI 7.1% to 26.5%) (table 4). The figures for black and white subjects were similar, being 7.4% (95% CI 4.6% to 12.9%) and 6.9% (95% CI 5.1% to 12.4%), respectively, in men and 8.9% (95% CI 5.5% to 15.6%) and 8.2% (95% CI 5.0% to 15.5%) in women. However, the age structure of incident TB cases is markedly younger in black people than in white people (table 1), and the similarity in PAF for all ages between white and black people hides marked differences in age-specific PAF estimates (table 4). For example, in the age group 45–64 years, the estimated PAF in black and white men is 11.6% and 7.0%, respectively, and in women it is 23.0% and 7.4%, respectively. These age-specific differences in PAF reflect age-specific differences in the prevalence of DM, being higher in black people than in white people.

Out of 5461 new cases of pulmonary TB in the three ethnic groups (table 4) in England in 2005, it is estimated that 384

---

**Table 1** Cases of pulmonary tuberculosis by age, sex, and ethnic group in England, 2005

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
<td>Asian</td>
<td>White</td>
</tr>
<tr>
<td>15–24</td>
<td>45</td>
<td>126</td>
<td>153</td>
<td>31</td>
</tr>
<tr>
<td>25–34</td>
<td>79</td>
<td>205</td>
<td>219</td>
<td>65</td>
</tr>
<tr>
<td>35–44</td>
<td>134</td>
<td>166</td>
<td>83</td>
<td>60</td>
</tr>
<tr>
<td>45–64</td>
<td>244</td>
<td>65</td>
<td>127</td>
<td>90</td>
</tr>
<tr>
<td>65+</td>
<td>267</td>
<td>17</td>
<td>115</td>
<td>150</td>
</tr>
</tbody>
</table>

Source: Health Protection Agency.

**Table 2** Estimated prevalence (%) of diabetes by age, sex and ethnic group in England, 2005

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
<td>Asian</td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>15–24</td>
<td>0.3</td>
<td>0.3</td>
<td>0.9</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>25–34</td>
<td>0.6</td>
<td>0.6</td>
<td>3.5</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>35–44</td>
<td>2.2</td>
<td>3.7</td>
<td>9.3</td>
<td>1.9</td>
<td>5.9</td>
</tr>
<tr>
<td>45–64</td>
<td>5.8</td>
<td>10.1</td>
<td>21.0</td>
<td>6.1</td>
<td>23.0</td>
</tr>
<tr>
<td>65+</td>
<td>10.8</td>
<td>22.8</td>
<td>37.2</td>
<td>16.3</td>
<td>32.8</td>
</tr>
</tbody>
</table>

Source: Yorkshire and Humber Public Health Observatory.

**Table 3** Relative risks (RR) for diabetes and tuberculosis

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–24</td>
<td>7.8</td>
<td>1.2 to 51.3</td>
</tr>
<tr>
<td>25–34</td>
<td>10.0</td>
<td>6.8 to 14.5</td>
</tr>
<tr>
<td>35–44</td>
<td>4.7</td>
<td>3.6 to 6.2</td>
</tr>
<tr>
<td>45–64</td>
<td>2.3</td>
<td>1.8 to 2.9</td>
</tr>
<tr>
<td>65+</td>
<td>1.8</td>
<td>1.1 to 2.9</td>
</tr>
</tbody>
</table>

Source: Kim et al.\textsuperscript{14}
(11.1%, 95% CI 5.8% to 19.6%) were attributable to DM. Of these, 212 (55%) were in people in the Asian group and the rest were evenly divided between white and black people (22% and 23%, respectively).

DISCUSSION
The objective of this study was to estimate the proportion of incident cases of pulmonary TB in adults in England that may be attributable to DM. Part of the motivation for doing this is that, despite the evidence recently summarised in two reviews,1 12 DM is a strong risk factor for TB but currently receives very limited attention in guidance on TB control. The results of this study suggest that around 11% of cases may be attributable to DM, over half of which will be in people of Asian origin (who are at high risk of DM and a comparatively high risk of TB). In black and white subjects roughly 8% of cases were attributable to DM.

Before considering the potential implications of these findings, it is essential to acknowledge the limitations and uncertainties inherent in this study. The most robust data that were used are those from the HPA on the number of cases of pulmonary TB in England in 2005 by age, sex and ethnic group. The prevalence estimates for DM by ethnic group are taken from the data source used nationally for public health planning and include those with diagnosed and undiagnosed DM (around 40% of the total). Despite being the best available source of data on total prevalence of DM in England, these estimates are based on extrapolations from old and relatively small population-based studies and hence must contain a large degree of (unacknowledged) uncertainty. The denominator populations are based on the Office of National Statistics mid-year estimates.

Finally, age-specific RRs for TB in people with DM from a large cohort study in Korea were applied. There are only three studies available at the time of writing that present age-specific RRs.13 As age is related to the risk of both TB and DM and the age structures of the populations in this paper are quite different, particularly the older white population compared with the younger Asian and black populations, it is essential to use age-specific RRs. As described in the Methods section, the Korean study is by far the best quality study of the three to provide age-specific RRs. The study by Ponce-de-Leon et al from Mexico found a very similar relationship between age and the RR of TB in people with DM (eg, RR of 10.8 in those aged 20–44 years and 2.6 in those age ≥65 years). It is impossible to know, given the currently available published data, to what extent the same age-specific RRs from the Korean study will apply in the three ethnic groups considered in this paper. For example, there is evidence from a cohort study in Hong Kong in patients aged ≥65 years that the risk of pulmonary TB associated with DM is directly related to blood glucose control.21 It may seem reasonable to assume, in the absence of comparable data, that this finding will also apply to younger age groups and that control of DM in England in 2005 may be better than it was in Korea in 1988–90. This could suggest that the RRs from the Korean study are too high. However, a comparison with the only available study from the UK suggests that, overall, the strength of the association is similar. The UK study was a case–control study from the General Practice Research Database based on data collected between 1990 and 2001.22 It found an overall OR for TB in people with DM, adjusted for age, glucocorticoid use and several other potential confounders, of 3.8 (95% CI 2.3 to 6.1), not dissimilar to the overall age-adjusted RR of 5.57 (95% CI 3.07 to 5.16) from the Korean study. Nonetheless, for all the reasons discussed here, the results should be interpreted as providing an illustration, based on the best available data, of the potential contribution DM makes to the incidence of TB in England and how this contribution may differ between different ethnic groups.

Assuming that the estimates presented of the impact of DM on the incidence of TB are about right, what are their implications? They fall into three broad categories. One category

Table 4 Estimated number of cases of pulmonary tuberculosis attributable to diabetes and population attributable fraction (PAF) for white, black and Asian ethnic groups in England, 2005

<table>
<thead>
<tr>
<th>Age</th>
<th>Diabetes attributable cases</th>
<th>N</th>
<th>Estimate</th>
<th>Range*</th>
<th>PAF %</th>
<th>N</th>
<th>Estimate</th>
<th>Range*</th>
<th>PAF %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>45</td>
<td>1.0</td>
<td>0.0–6.2</td>
<td>2.1</td>
<td></td>
<td>31</td>
<td>1.1</td>
<td>0.0–6.5</td>
<td>3.5</td>
</tr>
<tr>
<td>25–34</td>
<td>79</td>
<td>4.0</td>
<td>2.7–5.9</td>
<td>5.1</td>
<td></td>
<td>65</td>
<td>3.3</td>
<td>2.2–4.9</td>
<td>5.1</td>
</tr>
<tr>
<td>35–44</td>
<td>134</td>
<td>10.0</td>
<td>7.2–13.7</td>
<td>7.5</td>
<td></td>
<td>60</td>
<td>4.0</td>
<td>2.9–5.5</td>
<td>6.7</td>
</tr>
<tr>
<td>45–64</td>
<td>244</td>
<td>17.2</td>
<td>10.9–24.3</td>
<td>7.0</td>
<td></td>
<td>90</td>
<td>6.6</td>
<td>4.2–9.4</td>
<td>7.4</td>
</tr>
<tr>
<td>65+</td>
<td>267</td>
<td>21.2</td>
<td>2.8–45.4</td>
<td>7.9</td>
<td></td>
<td>150</td>
<td>17.3</td>
<td>2.4–35.4</td>
<td>11.5</td>
</tr>
<tr>
<td>Total</td>
<td>769</td>
<td>53.4</td>
<td>23.6–95.6</td>
<td>6.9</td>
<td>3.1 to 12.4*</td>
<td>396</td>
<td>32.3</td>
<td>11.7–61.7</td>
<td>8.2 (3.0 to 15.6)*</td>
</tr>
<tr>
<td>Black</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>126</td>
<td>2.7</td>
<td>0.1–17.5</td>
<td>2.1</td>
<td></td>
<td>127</td>
<td>3.2</td>
<td>0.1–20.4</td>
<td>2.5</td>
</tr>
<tr>
<td>25–34</td>
<td>205</td>
<td>10.3</td>
<td>6.8–15.1</td>
<td>5.0</td>
<td></td>
<td>198</td>
<td>7.7</td>
<td>5.0–11.3</td>
<td>3.9</td>
</tr>
<tr>
<td>35–44</td>
<td>166</td>
<td>19.9</td>
<td>14.5–26.7</td>
<td>12.0</td>
<td></td>
<td>104</td>
<td>18.6</td>
<td>13.8–24.4</td>
<td>17.9</td>
</tr>
<tr>
<td>45–64</td>
<td>65</td>
<td>7.5</td>
<td>4.9–10.5</td>
<td>11.6</td>
<td></td>
<td>42</td>
<td>9.7</td>
<td>6.5–12.8</td>
<td>23.0</td>
</tr>
<tr>
<td>65+</td>
<td>17</td>
<td>2.6</td>
<td>0.4–5.1</td>
<td>15.4</td>
<td></td>
<td>21</td>
<td>4.4</td>
<td>0.7–8.1</td>
<td>20.8</td>
</tr>
<tr>
<td>Total</td>
<td>579</td>
<td>43.1</td>
<td>26.6–74.9</td>
<td>7.4</td>
<td>4.6 to 12.9*</td>
<td>492</td>
<td>43.6</td>
<td>26.2–77.0</td>
<td>8.9 (5.3 to 15.6)*</td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>153</td>
<td>9.1</td>
<td>0.3–48.8</td>
<td>5.9</td>
<td></td>
<td>130</td>
<td>6.5</td>
<td>0.2–36.6</td>
<td>5.0</td>
</tr>
<tr>
<td>25–34</td>
<td>219</td>
<td>52.9</td>
<td>37.3–70.8</td>
<td>24.2</td>
<td></td>
<td>155</td>
<td>26.0</td>
<td>17.8–36.0</td>
<td>16.8</td>
</tr>
<tr>
<td>35–44</td>
<td>83</td>
<td>21.3</td>
<td>16.2–27.1</td>
<td>25.7</td>
<td></td>
<td>52</td>
<td>8.6</td>
<td>6.3–11.3</td>
<td>16.4</td>
</tr>
<tr>
<td>45–64</td>
<td>127</td>
<td>27.2</td>
<td>18.3–36.2</td>
<td>21.4</td>
<td></td>
<td>87</td>
<td>15.6</td>
<td>10.3–21.0</td>
<td>17.9</td>
</tr>
<tr>
<td>65+</td>
<td>115</td>
<td>26.4</td>
<td>4.1–47.6</td>
<td>22.9</td>
<td></td>
<td>104</td>
<td>18.3</td>
<td>2.7–35.0</td>
<td>17.6</td>
</tr>
<tr>
<td>Total</td>
<td>697</td>
<td>136.9</td>
<td>76.2–230.5</td>
<td>19.6</td>
<td>10.9 to 33.1*</td>
<td>528</td>
<td>75.0</td>
<td>37.3–139.9</td>
<td>14.2 (7.1 to 26.5)*</td>
</tr>
</tbody>
</table>

*Based on the age-specific 95% CIs shown in table 3.
concerns the management and treatment of people with newly diagnosed TB. Given that DM is a strong risk factor for TB, one would expect a high proportion of incident cases of TB to have DM. For example, based on the attributable risk calculations and the Tuberculosis Section at the Respiratory Diseases Department at the Health Protection Agency, especially Drs Ibrahim Abubakar and Clare French for the tuberculosis incidence data. They would also like to thank Dr Meng Khaw and Dr Chris Stenton, Professor Julia Critchley and Ms Fiona Young for helpful advice in planning this work.

Funding No specific funding was needed for the work contained in this article. NU is funded by Newcastle University and CW by the North East Strategic Health Authority.

Competing interests None.

Contributors NU had the original idea for the study. CW with NU developed the study plan and organised the collection and collation of the data. Both CW and NU contributed to the analysis and interpretation of the data. CW undertook the first drafting of the paper, with final input from NU. Both have approved the submitted version.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

Estimates of the impact of diabetes on the incidence of pulmonary tuberculosis in different ethnic groups in England
Caron Walker and Nigel Unwin

Thorax 2010 65: 578-581 originally published online April 26, 2010
doi: 10.1136/thx.2009.128223

Updated information and services can be found at:
http://thorax.bmj.com/content/65/7/578

These include:

References
This article cites 15 articles, 4 of which you can access for free at:
http://thorax.bmj.com/content/65/7/578#BIBL

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
TB and other respiratory infections (1273)
Tuberculosis (51)
Epidemiologic studies (1829)

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/