**Appendix 7: External adjustment for ethnicity in the association between diabetes and tuberculosis**

Following methods set out by McNamee et al (2003)[1], we used the following equation to estimate the potential degree of confounding that could be due to an unmeasured confounder (in this case ethnicity).

*Degree of confounding=*$\frac{confoundedRR}{trueRR}=\frac{\left(100-p1\right)+RRsp1}{\left(100-p0\right)+RRsp0}$

Note: p1—percentage of subjects with S in the exposed group; p0—percentage of subjects with S in the unexposed group.

1. TB🡪DM (i.e., does TB increase the risk of DM)

Here p1 represents the percentage of subjects who are south Asian/black in the TB group, while p0 represents the percentage of subjects who are south Asian/black in the non-TB group.

**Table A1: TB cases in the UK\***

|  |  |  |
| --- | --- | --- |
| **Ethnicity**  | **Number of cases**  | **Proportion (%)** |
| **Total white** | 1118 | 20.4 |
| **Total black** | 823 | 15.0 |
| **Total South Asian** | 2524 | 46.0 |
| **Other** | 1023 | 18.6 |
| **Total**  | 5488 | 100.0 |

\*data was derived from UK TB report 2016[2] and UK census 2011[3]

Therefore, the percentage of both south Asian and black TB cases among all TB cases in the UK is 61% (p1); the percentage of both south Asian and black non-TB cases among all non-TB cases in the UK is 11% (p0)

From the literature, the RR for DM among south Asian is 6.2, and 5.3 for black in the UK population[4]. In order to add weight RRs for UK population structure, some simple calculations were performed:

$$proportion of south Asian TB cases among both south asian and black african TB cases=\frac{south asian TB cases}{UK total TB cases}÷\frac{south asian TB cases+black african TB cases}{UK total TB cases}=46\%÷61\%=75\%$$

$$proportion of black African TB cases among both south asian and black african Tb cases=\frac{black African TB cases}{UK total TB cases}÷\frac{south asian TB cases+black african TB cases}{UK total TB cases}=15\%÷61\%=25\%$$

So: $combined RR (RRs in equation) for diabetes among both south Asian and black African=6.2×75\%+5.3×25\%=6.0 $

 Therefore $degree of confounding=\frac{\left(100-61\right)+6.0×61}{\left(100-11\right)+6.0×11}=2.43$= confounded RR/true RR

So the true RR after adjusting for ethnicity would be 5.65 (95% CI 5.19 to 6.16) /2.43=**2.33 (95%CI 2.14-2.53).**

As a sensitivity analysis, another source was used to obtain estimates of the RR of diabetes among ethnic minority groups. This source was a large systematic review based on migrants in European countries[5]. The same calculation was performed using the RRs from this review (3.7 (95%CI 2.7-5.1) for south Asian, 2.6 (95%CI 2.0-3.5) from black African) from a systematic review including studies from different regions, and the degree of confounding was 1.95, so the adjusted RR was **2.90 (95%CI 2.66-3.16)**.

1. DM🡪TB (i.e., does DM increase the risk of TB)

Here p1 represents the percentage of subjects who are south Asian/black in the DM group, while p0 represents the percentage of subjects who are south Asian/black in the non-DM group.

**Table A2: DM cases in England by ethnic groups\***

|  |  |  |
| --- | --- | --- |
| **Ethnicity**  | **Number of cases**  | **Proportion (%)** |
| **Total white** | 1048312 | 50.5 |
| **Total black** | 81567 | 3.9 |
| **Total South Asian** | 203587 | 9.8 |
| **Other** | 744098 | 35.8 |
| **Total**  | 2077565 | 100.0 |

\* data was derived from Health Survey for England 2003 & 2004[6, 7], ONS research report[8], ONS 2007 ethnicity specific data from census[9].

**Table A3: DM cases in Scotland\***

|  |  |  |
| --- | --- | --- |
| **Ethnicity**  | **Number of cases**  | **Proportion (%)** |
| **Total white** | 211246 | 93.1 |
| **Total black** | 6494 | 2.9 |
| **Total South Asian** | 1018 | 0.4 |
| **Other** | 8178 | 3.6 |
| **Total**  | 226936 | 100.0 |

\* data was derived from Scottish Diabetes Survey 2015[10], Scottish Health Survey (2008-2011)[11], Scottish census 2011[12].

**Table A3: DM cases in different ethnic groups (England and Scotland combined)\***

|  |  |  |
| --- | --- | --- |
| **Ethnicity**  | **Number of cases**  | **Proportion (%)** |
| **Total white** | 1259558 | 54.7 |
| **Total black** | 82585 | 3.6 |
| **Total South Asian** | 210081 | 9.1 |
| **Other** | 752276 | 32.6 |
| **Total**  | 2304500 | 100.0 |

\*Note: DM cases by ethnicity could not easily be obtained from Wales and Northern Ireland. However, UK Census 2011 showed that England and Wales represent over 92% of the UK population[3].

Therefore, the percentage of both south Asian and black DM cases among all DM cases in the UK is 12.7% (p1); the percentage of both south Asian and black non-TB cases among all non-DM cases in the UK is 6.9% (p0).

According to TB Annual Report 2016[2], the RR for TB among south Asian ranges from 6.5 to 12.4, and 2.2-19.1 for black in the UK population. In order weight RRs for UK population structure, some simple calculation was carried out below:

$$proportion of south Asian DM cases among both south asian and black african DM cases=\frac{south asian DM cases}{UK total DM cases}÷\frac{south asian DM cases+black african DM cases}{UK total DM cases}=9.1\%÷12.7\%=72\%$$

$$proportion of black African TB cases among both south asian and black african DM cases=\frac{black African DM cases}{UK total DM cases}÷\frac{south asian DM cases+black african DM cases}{UK total DM cases}=3.6\%÷12.7\%=28\%$$

So: $combined RR (RRs in equation) for diabetes among both south Asian and black African=6.5×72\%+2.2×28\%=5.3$

Therefore $degree of confounding=\frac{\left(100-12.7\right)+5.3×12.7}{\left(100-6.9\right)+5.3×6.9}=1.19$= confounded RR/true RR

So the true RR after adjusting for ethnicity would be 1.50 (95%CI 1.27 to 1.76)/1.19=**1.26 (95%CI 1.07 to 1.48)**

The same calculation was performed using the upper range of RRs for both ethnic groups (i.e. 12.4 for south Asian, and 19.1 for black). In this sensitivity analysis, the degree of confounding was 1.40, and the true RR=1.50 (95%CI 1.27 to 1.76)/1.40=**1.07 (95%CI 0.91 to 1.26)**

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