Title: Tuberculosis in healthcare workers in the UK: A cohort analysis 2009 to 2013

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What is the key question? Are healthcare workers (HCWs) at increased risk of TB due to occupational exposure in the UK?
What is the bottom line? Although HCW in the UK have an overall higher incidence of TB than non-HCW, they do not have a higher incidence after stratifying by country of birth; this, combined with the evidence of very few transmission events in the healthcare setting, suggests that TB in HCW in the UK is not generally acquired through UK occupational exposure.
Why read on? This is the first national study of TB in HCW in the UK which is able to investigate the incidence of TB in HCW in the UK after adjusting for country of birth, and incorporating genotyping data on recent transmission events; the findings have important implications for occupational health guidance on the prevention of TB in HCW.

Abstract

Objectives: To describe the burden of TB in healthcare-workers (HCWs) in the UK and determine whether HCWs are at increased risk of tuberculosis (TB) due to occupational exposure.

Methods: Retrospective cohort analysis of national UK TB surveillance and genotyping data between 2009 and 2013. The rate of TB in HCWs compared to non-HCWs, to calculate incidence rate ratios stratified by country of birth.

Results: 2,320 cases of TB in HCWs were notified in the study period, 85% were born abroad. The TB rate in HCWs was 23.4 (95% confidence interval (CI) 22.5-24.4) per 100,000 compared with 16.2 (95% CI 16.0-16.3) per 100,000 in non-HCWs. After stratifying by country of birth, there was not an increased TB incidence in HCWs for the majority of countries of birth, including in the UK born.. Using combined genotyping and epidemiological data, only ten confirmed nosocomial transmission events involving HCWs were identified between 2010 and 2012. Of these only two involved transmission to patients.

Conclusions: The lack of an increased incidence of TB after stratifying by country of birth, and the very few transmission events involving nosocomial transmission in the UK suggests that TB in HCWs in the UK is not generally acquired through UK occupational exposure. The majority of cases in foreign-born HCWs are likely to result from reactivation of latent TB infection (LTBI) acquired abroad, and is not likely to be prevented by BCG vaccination in the UK. Testing and treatment of LTBI in HCWs with exposure to high TB burden countries should be the focus of occupational health prevention activities.

INTRODUCTION

Tuberculosis (TB) in healthcare-workers (HCWs) has implications for public health and occupational health. HCWs are at potential risk of infection from occupational exposure,(1) and active pulmonary disease in HCWs presents a risk of nosocomial transmission to colleagues and patients. In the UK, a study in the 1990s identified an increased risk of TB in HCWs compared to the general population,(2) although this study did not adjust for country of birth, the most important risk factor for TB in the UK. A previous small local study of 26 HCW cases in the West Midlands reported that most of this increased risk may be associated with reactivation of disease acquired overseas.(3) Since these studies were carried out the epidemiology of TB in the UK has changed, with a substantial increase in case numbers, mostly among the foreign-born population from high TB incidence countries.(4) HCW recruitment trends have also changed during this time, with a large number of HCWs recruited from abroad.(5)

In the UK, guidelines recommend that all new employees working in a healthcare setting who will be in contact with patients should be given pre-employment screening using a Mantoux test and/or an interferon gamma release assay test.(6, 7) In all those who screen negative and are previously unvaccinated, the guidelines recommend that Bacillus Calmette-Guerin (BCG) should be given.

To inform the continued relevance of existing occupational health guidance, an understanding of the current burden of TB in HCW in the UK and assessment of the extent to which this is acquired due to occupational exposure in the UK is required. In this study, we use national TB surveillance data to describe the epidemiology of TB in HCW in the UK, and compare the incidence of TB in HCWs and non-HCWs after stratifying by country of birth. In addition, we use a combination of genotyping data and data on epidemiological links between cases to assess the extent to which HCWs have been involved in recent transmission events in healthcare settings.

METHODS

Study population

TB cases aged between 16 and 64 years, fulfilling the definition outlined for national surveillance,(8) with known occupation notified in the UK between 2009 and 2013 were included in the analysis. Patients were classified as HCWs or non-HCWs following the World Health Organization definition of a health service provider working in the health industry engaged in the promotion, protection or improvement of the health of the population excluding health management and support workers.(9)

Notified TB cases were identified through the Enhanced TB Surveillance System in England, Wales and Northern Ireland and Enhanced Surveillance of Mycobacterial Infections in Scotland. The occupation recorded for notified cases was used to identify HCWs. HCWs were also classified into further occupational subcategories where possible, which were: doctor, nurse, healthcare assistant, or other. The following additional data were used: patient demographic characteristics (age, sex, ethnicity, country of birth, and time since entry to the UK grouped as five or less years before diagnosis (≤5) or more than five years before diagnosis (>5)) and clinical characteristics (site of disease, previous TB, time from symptom onset to treatment start for pulmonary cases, and BCG vaccination). TB outcomes were also collected at 12 months and reported for cases notified between 2009 and 2012.

Rates of TB in HCWs by country of birth were calculated using 2011 Office for National Statistics Census population estimates by occupational breakdown as the denominator (10). Rates of TB in non-HCWs by country of birth were calculated by subtracting the HCW population estimates from overall National Statistics Census population estimates in those aged 16 to 64 years (11). The rates of TB over the five years study period were calculated by dividing the total number of TB cases by the Census population estimates multiplied by five. Denominator data by occupational group was not available for Northern Ireland and Scotland, therefore all rates presented are for England and Wales only (which accounted for 94.5% of TB cases in the study population).

TB case notifications were matched to *Mycobacterium tuberculosis* complex (MTBC) culture positive laboratory isolates received from the Mycobacterium Reference Laboratories for the relevant time period to collect drug susceptibility and 24 loci mycobacterial interspersed repetitive unit-variable number tandem (MIRU-VNTR) strain typing results. Matching was conducted using the Enhanced Matching System.(12)

Statistical Analysis

Demographic and clinical differences between HCWs and non-HCWs were compared using the Chi squared test, p-value of less than 0.05 was considered to be statistically significant. Incidence rate ratios were calculated comparing the incidence of TB in HCWs with non-HCWs; 95% confidence intervals were derived based on a Poisson distribution. All analysis was conducted using Stata 13.1.

Assessment of recent transmission in England, Wales and Northern Ireland

For HCWs with culture confirmed TB notified in England, Wales and Northern Ireland between 2010 and 2012, 24 loci MIRU-VNTR strain type clustering was used to identify any possible nosocomial transmission events. Since 2010, all culture confirmed TB cases have been strain typed using MIRU-VNTR.(13) A cluster of two or more cases with the same strain type may represent recent

transmission, or could be due to common endemic strain types in circulation in the UK or abroad. To establish whether a strain type cluster was likely to represent recent transmission, epidemiological investigation of all strain typing clusters containing a HCW was recommended between 2010 and 2012.(13)

Using a combination of strain typing and epidemiological data on links between cases, cases were classified as having been involved in a confirmed, probable, possible or refuted transmission event. Two cases with an epidemiological link and an indistinguishable 24 loci MIRU-VNTR profile (or with an indistinguishable profile, but with one case only typed to 23 loci) were defined as having been involved in a confirmed transmission event. Two cases with an epidemiological link and an indistinguishable MIRU-VNTR profile, but where one or both cases were not typed to 23 loci were defined as probable transmission. Two cases with an epidemiological link where one or both did not have a MIRU-VNTR profile were defined as possible transmission, and two cases with an epidemiological link but with distinguishable MIRU-VNTR profiles (one or more loci different) were defined as refuted transmission.

RESULTS

Between 2009 and 2013, 34,573 TB cases aged 16 to 64 were notified in the UK. Occupation was recorded for 86.8% (30,001/34,573) of these cases. Where occupation was recorded, 7.7% (2,320) were HCWs. The proportion of TB cases recorded as HCWs each year remained stable (between 7% and 8%) over the five year period.

Demographic Characteristics

Compared to non-HCWs a higher proportion of HCWs were female (68.9%; 1,581/2,295 vs 40.4%; 11,155/16,488), aged 25 to 44 years (70.2%; 1,628/2,320 vs 55.1%; 15,249/27,680) and foreign-born (85.0%; 1,893/2,227 vs 77.3%; 20,937/27,075) (Table 1). HCWs were born in 86 different countries, with 81.9% (1,788/2,182) originating from only ten countries (Table 2).

Table 1. Basic demographics of TB cases in HCWs and non-HCWs

	HCW TB cases (n=2,320)		Non HCW TB cases (n=27,681)		Chi squared p-value
	n	%	n	%	
Sex	n=2,295		n=27,643		
Male	714	31.1	16,488	59.6	p<0.001
Age group (years)	n=2,320		n=27,681		
16-24	126	5.5	5,213	18.8	p<0.001
25-34	785	33.8	9,273	33.5	
35-44	843	36.4	5,976	21.6	
45-54	400	17.2	4,161	15.0	
55-64	166	7.1	3,057	11.0	
Country of birth	n=2,182		n=26,658		
UK	334	15.3	6,138	23.0	p<0.001
India	559	25.6	5,913	22.2	
Pakistan	128	5.9	3,860	14.5	
Somalia	31	1.4	1,535	5.8	
Nigeria	106	4.9	660	2.5	
Nepal	74	3.4	654	2.4	
Zimbabwe	200	9.2	459	1.7	
Philippines	249	11.4	322	1.2	
Kenya	44	2.0	331	1.2	
South Africa	63	3.0	159	0.6	
All other countries	394	18.1	6,627	24.9	
Ethnicity	n=2,252		n=27,201		
White	270	12.0	4,824	17.7	p<0.001
Black African	644	28.6	4,936	18.0	
Black Caribbean	45	2.0	555	2.0	
Black Other	18	0.8	247	0.9	
Indian	670	26.6	7,201	26.5	
Pakistani	171	7.6	4,810	17.7	
Bangladeshi	24	1.1	1,169	4.3	
Chinese	23	1.0	378	1.4	
Mixed / Other	387	17.2	3,081	11.3	
Years since entry to the UK	n=1,633		n=18,906		
<2	161	9.8	4,188	22.2	p<0.001
2-5	473	29.0	5,825	30.8	
6-10	624	38.4	3,840	20.3	
>10	375	22.9	5,053	26.7	
Site of disease	n=2,312		n=27,611		
Pulmonary	1,005	43.5	14,423	52.2	p<0.001
Extrapulmonary only	1,307	56.5	13,188	47.8	
Social risk factor	n=1,852		n=22,221		

Yes	43	2.3	2,754	12.4	p<0.001
Previous diagnosis	n=2,219		n=26,502		
Yes	97	4.4	1,687	6.4	p<0.001
BCG vaccination*	n=1,665		n=19,356		
Yes	1,456	87.5	14,282	73.8	p<0.001
Time to treatment start (pulmonary cases)	n=765		n=10,631		
<2 months after symptom onset	337	44.0	4,885	45.9	p=0.162
2-4 months after symptom onset	214	28.0	3,101	29.2	
>4 months after symptom onset	214	28.0	2,645	24.9	
Clustered (≥2 indistinguishable 24 loci MIRU-VNTR)	n=883		n=11,554		
Yes	423	48.0	6,402	55.4	p<0.001
MDR-TB	n=1,425		n=17,226		
Yes	20	1.4	285	1.7	p=0.473

* At any time

Table 2. Risk of TB in HCWs by most frequent country of birth

Country of Birth	n HCW TB cases (population denominator*)	n Non-HCW TB cases (population denominator*)	% HCW TB cases**	Rate of TB in HCW per 100,000 (95% CI)	Rate of TB in non-HCW per 100,00 (95% CI)	Incidence rate ratio (95% CI)
All~	2,320 (1,983,571)	27,681 (34,290,136)	7.7	23.4 (22.5-24.4)	16.1 (16.0-16.3)	1.5 (1.4-1.5)
India	559 (55,466)	5,913 (470,349)	8.6	201.6 (185.2-219.0)	251.4 (245.1-257.9)	0.8 (0.7-0.9)
UK	334 (1,550,756)	6,138 (28,689,940)	5.2	4.3 (3.9-4.8)	4.3 (4.2-4.4)	1.0 (0.9-1.1)
Philippines	249 (40,187)	322 (64,071)	43.6	123.9 (109.0-140.3)	100.5 (89.8-112.1)	1.2 (1.0-1.5)
Zimbabwe	200 (24,503)	459 (77,207)	30.3	163.2 (141.4-187.5)	118.9 (108.3-130.3)	1.4 (1.2-1.6)
Pakistan	128 (13,923)	3,860 (395,444)	3.2	183.9 (153.4-218.6)	195.2 (189.1-201.5)	0.9 (0.8-1.1)
Nigeria	106 (27,289)	660 (139,454)	13.8	77.7 (63.6-94.0)	94.7 (87.6-102.2)	0.8 (0.7-1.0)
Nepal#	74	654	10.2	-	-	-
South Africa	63 (13,900)	159 (146,808)	28.4	90.6 (70.0-116.0)	21.7 (18.4-25.3)	4.2 (3.2-5.5)
Kenya	44 (10,703)	331 (106,091)	11.7	82.2 (59.7-110.4)	62.4 (55.9-69.5)	1.3 (1.0-1.8)
Somalia	31 (2,937)	1,535 (79,288)	2.0	211.1 (143.4-299.6)	387.2 (368.1-407.1)	0.5 (0.4-0.8)
All other countries	394 (243,907)	6,627 (4,121,484)	5.6	32.3 (29.2-35.7)	32.2 (49.3-51.7)	1.0 (0.9-1.1)

* For a single year
** Proportion of TB cases from each country which are HCWs
# Population estimates not available for Nepal so rates and incidence rate ratio could not be calculated
~ Includes those with unknown country of birth

Of the UK-born HCWs, the majority (61.1%; 203/332) were of White ethnicity, comparable to the proportion (58.8%; 3,556/6,052) in non-HCWs. The age distribution of UK-born HCWs differed to non-UK-born HCWs; only 54.2% (181/334) of UK-born HCWs were aged 25 to 44 years of age compared to 72.7% (1,376/1,893) in non-UK-born HCWs.

Further occupational information was available for 56.3% (1,307/2,320) of HCWs. The majority of these were nurses (41.9%; 547), doctors (31.7%; 414) or healthcare assistants (19.8%; 259); other

occupational sub-groups contributed a low proportion (6.7%; 87) of cases. Place of birth (UK/non-UK) did not vary by occupation.

Clinical Characteristics

87.4% (1,456/1,665) of HCWs had been BCG vaccinated compared to 73.8% (14,282/19,356) of non-HCWs (Table 1). There was no difference in the time between symptom onset and treatment initiation for HCWs with pulmonary disease compared to non-HCWs; however it is noteworthy that a high proportion of HCWs (28.0%; 214) were symptomatic for longer than four months. Treatment completion was higher in HCWs compared to non-HCWs (83.8% vs 79.6% p<0.001) with a lower proportion of deaths (1.0% vs 1.9% p=0.001) and cases lost to follow-up (2.3% vs 4.6% p<0.001).

Twenty HCWs had multidrug resistant TB (MDR-TB), the majority of which (75%; 15) had extra-pulmonary disease only and none were UK-born.

Incidence of TB

The overall incidence of TB in HCWs during this time period was 23.4 (95% CI: 22.5-24.4) per 100,000, compared to 16.2 (95% CI: 16.0-16.3) per 100,000 in non-HCWs (incidence rate ratio 1.5 (95% CI: 1.4-1.5)). On stratification by country of birth, the incidence of TB was not higher in HCWs for the majority of countries of birth (Table 2). Importantly, UK-born HCWs did not have a higher incidence than UK-born non-HCWs, and for the other countries of birth contributing significant numbers of HCW TB cases (>100 cases over the study period), only those born in the Philippines or Zimbabwe had an incidence in HCWs that was higher than in non-HCWs (Table 2).

The incidence of TB was found to differ between specific HCW occupational groups with the highest rate observed in doctors (41.2 (95% CI: 37.2-45.5) per 100,000), followed by nurses (19.5 (95% CI: 17.8-21.3) per 100,000). In non-UK-born doctors the rate was 86.0 (95% CI: 76.9-96.0) per 100,000 and in nurses 68.5 (95% CI: 62.1-75.4) per 100,000.

Recent transmission in the UK

Between 2010 and 2012, 45.8% (306/667) of HCWs with a culture confirmed strain typed MTBC isolate had the same strain type as at least one other TB case within the three year period. These HCWs were in 238 different molecular clusters which ranged in size from 2-131 cases. 53.8% of the clusters contained less than 5 cases. Following cluster investigation, only 24 of these HCWs were identified as having been involved in a confirmed transmission event in the UK, with a total of 28 epidemiological links identified between a HCW and another TB case, or between two HCWs. The majority of the epidemiological links were between a HCW and a household contact (17), followed by 10 epidemiological links in a healthcare setting. One case had an epidemiological link in an unknown setting.

The ten epidemiological links in healthcare settings represented eight confirmed transmission events (Figure 1). Six were between a HCW and a patient; in four of these instances the patient was identified as the HCW's source of infection. In the other two instances the same HCW was identified as the source of infection for two patients. The remaining four links in a healthcare setting were two separate instances of two HCWs who were contacts at work. Of the links identified in healthcare settings, the majority (75.0%; 6/8) involved UK-born HCWs.

A further four HCWs were found to have been involved in probable transmission, three of these involved probable transmission with household contacts and one between work contacts. 53 possible transmissions were identified involving 49 HCWs. The majority (48) of these were between household cases, four were between two sets of work contacts and one was with a social contact. Five epidemiological links had transmission refuted following strain typing; none of these involved epidemiological links in healthcare settings.

Ten out of 13 MDR-TB cases in HCWs which occurred between 2010 and 2012 had a unique strain type. Of the three which did cluster with another case, all were Indian-born and were each in different clusters; within these clusters no epidemiological links between the clustered cases were identified.

DISCUSSION

This large retrospective cohort study shows there is a significant burden of TB in HCWs in the UK, with more than 400 cases per year over the five year study period, accounting for nearly 8% of working-age TB cases. The demographic characteristics of HCWs with TB compared with non-HCW reflect the characteristics of the HCW population, with a disproportionate number of HCWs being female, foreign-born, and aged between 25 and 44 years.

Our study is the first to estimate the risk of TB in HCWs across the UK by country of birth, and to investigate the molecular epidemiology of TB in HCWs in the UK to assess whether cases were likely to have been involved in a recent transmission event. Consistent with a previous national study,(2) we found that the overall incidence of TB in HCW was significantly higher than in non-HCWs. However, our study found that this increased incidence was no longer observed once country of origin, the most important risk factor for TB in the UK, was accounted for, a factor which was not adjusted for in the previous national study. Importantly, the incidence of TB in UK-born HCWs was not raised compared to the general working-age UK-born population, nor was it raised for HCWs born in most of the other countries of origin with significant numbers of HCW TB cases (India, Pakistan and Nigeria).. This suggests that occupational exposure is not a significant risk factor for TB in HCWs in the UK, and is consistent with a previous local study conducted in the West Midlands of England in 1992 to 1995 which also identified no increased risk of TB in doctors from the Indian Subcontinent ethnic group compared to the working-age population from the same ethnic group and corresponding socio-economic status.(3) The incidence of TB was only raised in HCWs compared to the general working-age population for those born in a small number of countries (the Philippines, South Africa, Zimbabwe and Kenya); the type of migration from these countries (South Africa and Zimbabwe) over the past decades means that HCWs from these countries do not necessarily have a higher TB incidence than those of a similar socio-demographic background. Both South Africa and Zimbabwe have a high rate of TB-HIV co-infection,(14) with a particularly high HIV burden in females in the reproductive age group.(15,16) Recruitment of HCWs from South Africa and Zimbabwe to the UK has predominantly been of nurses, likely to be young females. This may in part explain the higher risk identified for South African and Zimbabwean HCWs compared to other migrants from these countries.

The results of MIRU-VNTR strain typing showed that 46% of cases were part of a strain typing cluster, lower than the overall proportion of TB cases that are in a cluster nationally (54%).(4) A large proportion of clustered TB cases in the UK are thought not to represent recent transmission, especially in the foreign-born population, where much of the observed clustering is likely to reflect common endemic strains in patients' countries of origin. Additional information on epidemiological links identified through cluster investigation is required to demonstrate recent transmission in the UK. Cluster investigation between 2010 and 2012 identified very few epidemiological links for HCWs cases that were part of a strain typing cluster. Of the 667 culture confirmed cases with a strain type, only eight were identified as having been involved in a confirmed nosocomial transmission event, of which four involved patient to HCW transmission, two involved HCW to HCW transmission, and two events involved transmission from one HCW to two separate patients. The finding of low transmission within health settings is supported by previous UK findings of a very low yield of

additional TB cases during extensive contact tracing exercises.(17) Of the four HCWs who are likely to have acquired their infection through occupational exposure in the UK, with a molecular and confirmed epidemiological link to a symptomatic patient, all were UK-born. Similarly, a study from the Netherlands (another low TB incidence country), found that all HCWs likely to have acquired TB due to nosocomial transmission within the country were native-born.(1) This suggests foreign-born cases predominantly acquired infection abroad or, in a more limited number of cases, due to household transmission in the community.

The finding of no increased risk of TB in HCW compared to non-HCW after stratifying by country of birth for all but two countries of birth, combined with the very small number of cases with a molecular and epidemiological link consistent with nosocomial transmission, suggests that TB diagnosed in HCWs in the UK is generally not acquired as a result of UK occupational exposure. Given that the vast majority of TB in HCWs (more than 82%) occurs in those born abroad in high TB burden countries, it is likely that the majority occur due to reactivation of latent TB infection (LTBI) contracted in their country of origin. This has clear implications for occupational health policies. For HCWs from high TB burden countries, exposure and infection is likely to have already occurred prior to UK entry and occupational health assessment, so BCG vaccination in those without evidence of prior infection, as recommended in current guidance,(6,7) is likely to be of little benefit to the general HCW population.(18,19) As speciality and location of HCWs place of work was not known, our study does not provide information on whether those at high risk of occupational exposure to TB patients (e.g. those working in TB clinics) have a higher incidence of TB, and for whom BCG vaccination may still be warranted.

Following existing guidance, all HCWs should be screened for LTBI as part of pre-employment health checks.(6,7) This action, and the provision of treatment of LTBI for those found to be latently infected, is likely to be most effective at preventing active cases of TB in HCWs, and any subsequent transmission. It is particularly important to ensure that HCWs from high TB burden countries are appropriately screened.

There was no difference found between the length of time between symptom onset and treatment start for HCWs with pulmonary TB compared to non-HCWs, despite presumed access to occupational health departments and better knowledge about TB symptoms. As nearly a third (28%) of HCWs with pulmonary disease were symptomatic for more than four months before starting treatment, additional awareness raising of the signs and symptoms of TB, including in those who have been treated for LTBI, is important to ensure that any HCW who develops active disease presents to healthcare quickly.

Our study has a number of strengths. We used the full cohort of TB cases notified to national surveillance systems in the UK over the study period, so will have captured the vast majority of TB cases that occurred in this time period. Data completion for the occupation field was high (86%), and we were able to use national population data on occupational breakdown as our denominator. Unlike the previous national study of TB in HCW conducted in the UK,(2) we were able to stratify our incidence rate ratios by country of birth, which is the strongest risk factor for TB in the UK. In

addition, we were able to use MIRU-VNTR strain typing and data on epidemiological links between cases obtained through cluster investigations to investigate recent transmission events.

Our study also has some limitations. Although we stratified our incidence ratios by country of birth, which is by far the most important risk factor for TB in the UK, we were not able to adjust for all the factors identified to differ between HCWs and non-HCWs such as age, sex and social risk factors, as these breakdowns were not available along with country of birth and occupation in the denominator data. HIV status was not known for the TB cases in our study, and is likely to be a contributing factor in many of the cases from sub-Saharan Africa, with a previous UK study showing 14% of HCWs with TB from these countries were co-infected with HIV.(8) In addition, the speciality and location of HCWs place of work was not known, so we were not able to assess whether there is an increased risk of TB in those working in settings where they are more likely to be exposed to TB. Although cluster investigations were conducted to search for epidemiological links in strain type clusters containing HCWs, some links may not have been identified. In addition, non-culture confirmed cases without an otherwise apparent epidemiological link in a healthcare setting would not have been routinely investigated, so nosocomial transmission involving HCWs may have been underestimated. However, the fact that so few epidemiological links in healthcare settings were discovered during active cluster investigation supports the conclusion that nosocomial transmission involving HCWs in the UK is very rare.

In conclusion, the occurrence of large numbers of cases of TB in HCWs in the UK highlights the need to strengthen occupational health practices for the prevention and early identification of TB in the UK. The lack of evidence of an increased risk of TB among HCWs in the UK, the evidence of only very rare occurrences of nosocomial transmission in the UK, and the majority of HCW TB cases originating from high TB burden countries likely reactivating from latent infection, suggests guidelines on the prevention of TB in HCWs should focus less on preventing infection through BCG vaccination, and more on identifying and treating LTBI, especially in HCWs from high TB burden countries.

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Ethics statement: Public Health England has authority under the Health and Social Care Act 2012 to hold and analyse national surveillance data for public health and research purposes.

References

1. Vries G de, Šebek MMGG, Weezenbeek CSBL. Healthcare workers with tuberculosis infected during work. Eur Respir J. 2006 Dec 1;28(6):1216–21.

2. Meredith S, Watson JM, Citron KM, Cockcroft A, Darbyshire JH. Are healthcare workers in England and Wales at increased risk of tuberculosis? BMJ. 1996 Aug 31;313(7056):522–5.

3. Hill A, Burge A, Skinner C. Tuberculosis in National Health Service hospital staff in the west Midlands region of England, 1992-5. Thorax. 1997 Nov 1;52(11):994–7.

4. Public Health England. Tuberculosis in the UK: Annual report on tuberculosis surveillance in the UK, 2013. 2014.Available from: https://www.gov.uk/government/publications/tuberculosis-tb-in-the-uk

5. Buchan J, Jobanputra R, Gough P, Hutt R. Internationally recruited nurses in London: a survey of career paths and plans. Hum Resour Health. 2006 Jun 26;4:14.

6. National Institute for Health and Clinical Excellence. Tuberculosis: Clinical diagnosis and management of tuberculosis, and measures for its prevention and control [Internet]. Available from: https://www.nice.org.uk/guidance/cg117

7. Department of Health. Health clearance for tuberculosis, hepatitis B, hepatitis C and HIV: New healthcare workers [Internet]. 2007. Available from: http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_073132

8. Crofts JP, Kruijshaar ME, Delpech V, Ncube F, Abubakar I. Tuberculosis and HIV co-infection in healthcare workers in England and Wales, 1999-2005. Epidemiol Infect. 2012 Oct;140(10):1873–9.

9. Dal Poz MR, Kinfu Y, Dräger S, Kunjumen T. Counting health workers: definitions, data, methods and global results. World Health Organization; 2007.

10. Office for National Statistics. 2011 census country of Birth by occupation [Internet]. Available from: http://www.ons.gov.uk/ons/about-ons/business-transparency/freedom-of-information/what-can-i-request/published-ad-hoc-data/census/labour-market/ct0281-2011-census---country-of-birth-by-occupation.xls

11. Office for National Statistics. Country of birth by sex by age [Internet]. Available from: https://www.nomisweb.co.uk/census/2011/dc2109ewr

12. Aldridge RW, Shaji K, Hayward AC, Abubakar I. Accuracy of Probabilistic Linkage Using the Enhanced Matching System for Public Health and Epidemiological Studies. PLoS ONE. 2015 Aug 24;10(8):e0136179.

13. Public Health England. TB Strain Typing and Cluster Investigation Handbook 3rd Edition, February 2014. 2014. Available from: https://www.gov.uk/government/publications/tb-strain-typing-and-cluster-investigation-handbook

14. World Health Organization. Global tuberculosis report 2014. 2014. Available from: http://www.who.int/tb/publications/global_report/en/

15. Gilbert L, Walker L. Treading the path of least resistance: HIV/AIDS and social inequalities—a South African case study. Soc Sci Med. 2002 Apr;54(7):1093–110.

16. World Health Organization. Global health sector strategy on HIV/AIDS 2011-2015. 2011. Available from: http://www.who.int/hiv/pub/hiv_strategy/en/

17. Anderson C, Abubakar I, Maguire H, Sonnenberg P. Survey of tuberculosis incidents in hospital healthcare workers, England and Wales, 2005. J Public Health Oxf Engl. 2007 Sep;29(3):292–7.

18. Abubakar I, Pimpin L, Ariti C, Beynon R, Mangtani P, Sterne J, et al. Systematic review and meta-analysis of the current evidence on the duration of protection by bacillus Calmette–Guérin vaccination against tuberculosis. Health Technol Assess [Internet]. 2013 Sep [cited 2015 May 19];17(37). Available from: http://www.journalslibrary.nihr.ac.uk/hta/volume-17/issue-37

19. Mangtani P, Abubakar I, Ariti C, Beynon R, Pimpin L, Fine PEM, et al. Protection by BCG vaccine against tuberculosis: a systematic review of randomized controlled trials. Clin Infect Dis Off Publ Infect Dis Soc Am. 58(4):470–80.