# REVIEW A Systematic Review on Pulmonary TB Burden and Associated Factors Among Immigrants in the UK

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Background: The rapid growth of international human migration has positioned the UK in the top five countries in the world with 9.4 million immigrants in 2022. These immigrants originate from low- and middle-income countries and remain particularly at risk of developing TB. In the UK, the number of TB cases has been increasing, and the influx of immigrants could be a contributing factor. Objective: This review aims to map the burden of pulmonary TB among immigrants in the UK and investigate associated factors. It also reviews the TB management approaches among immigrants in the UK.

Design: The study utilized PRISMA guidelines to search electronic databases (PubMed and EMBASE) for articles published from 2000 to 2022 on TB prevalence and factors in immigrants and explored government websites for TB management strategies.

Results: Nineteen out of 530 initially identified articles were included. The included studies reported a prevalence rate of TB among immigrants ranging from 0.04 to 52.1%, showing a decrease in the burden over time. Additionally, a higher number of TB cases were observed among immigrants from the Asian region, particularly immigrants from South Asia, followed by those from sub-Saharan Africa. Stigma, misconception about the disease, language barrier, lack of confidentiality, and unfriendly healthcare system for immigrants were the main drivers of the TB burden among immigrants. The TB management approaches in the UK include preentry screening for active TB, LTBI testing for a specific population group, and antibacterial therapy for 3-6 months for TB patients. **Conclusion:** The UK's control and prevention efforts in reducing tuberculosis prevalence among immigrants show optimism, but challenges persist. Key improvements include healthcare delivery, TB improvement programs, and policies addressing stigma and patient confidentiality.

Keywords: TB, UK, immigrants, pulmonary infection, tuberculosis

### Study Background

From the time Dr. Robert Koch discovered Mycobacterium (M.) Tuberculosis in 1882 until now, tuberculosis (TB) has remained a "global health emergency", particularly in Asia and Africa, which account for 58% and 28% of all the cases globally, respectively.<sup>1</sup> M. Tuberculosis infection was the leading cause of mortality caused by a single infectious disease in 2019, with an estimated 10 million people contracting the disease.<sup>2</sup> Low- and middle-income countries accounted for more than 95% of all deaths.<sup>1</sup> Although advancements in science and medical technology have partially succeeded in controlling the disease by reducing its incidence and mortality rates, the progress is slow. WHO's designed End TB strategy 2016–2035, a global plan for eradication of TB, has envisioned TB elimination by 2035, but it seems unlikely. The Global TB 2020 reports which provide up-to-date assessment of the TB epidemic and the progress about the disease prevention, diagnosis and treatment, at global, regional and country levels, showed only a 9% reduction in TB incidence between 2015 and 2020, while the goal was to reduce it by 20%. Similarly, the mortality reduction objectives of 35% were not met either, with a 14% drop in death rates occurring between 2015 and  $2020.^2$ 

There are two types of TB presentations: latent TB infection and active TB disease.<sup>3</sup> A latent type of infection is when people are exposed to M. tuberculosis, their bodies fight the bacteria, preventing it from growing, yet they do not eliminate it. These people do not feel sick, nor do they have any symptoms, and they cannot spread the bacteria to others.<sup>3</sup> However, if the

cc 0 (1) (2023 Saleem et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms by and incorporate the Creative Commons Attribution — Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php). bacteria become active and multiply in the body, the person becomes sick with active TB disease, which is the virulent form of TB. Screening for the active form of TB is feasible, and detection is easier; however, it is the latent form that cannot be controlled and requires special testing in order to diagnose.<sup>3</sup>

Transmission of TB disease happens when a sick person coughs, sneezes or speaks; the bacterium that causes TB spreads through the air, and people in the vicinity may inhale these germs and become ill.<sup>3</sup> The development of TB in an exposed person occurs in two stages. While the majority of infected individuals' immune systems prevent rapid growth of the bacteria by walling it off, 5% of the infected individuals may rapidly develop TB disease within the first two years.<sup>4</sup> Similarly, about 10% of those with latent infection may reactivate half during the first year, whereas the remainder over their lifetime through reactivation dormant bacteria acquired from the original infection or sometimes from reinfection.<sup>4</sup>

In recent decades, increased movement of people between countries has led to a change in the epidemiological profile of TB in many low-incidence countries. Globalization, conflicts, and financial reasons have been the main driving factors for the migration flow from high-incidence countries. According to the International Organization for Migration (IOM), there were around 281 million immigrants in the world in 2020, which made up about 3.6% of the global population.<sup>5</sup> According to Bolter (2019), "An immigrant is a person living in a country other than that of his or her birth". Regardless of whether that individual has obtained citizenship in the destination country, served in its military, married a resident, or has another status, he or she is an international immigrant.<sup>5</sup>

The migration of immigrants to high-income countries has differed based on historical, linguistic, and cultural ties as well as physical closeness. For example, in the United Kingdom, a considerable number of immigrants come from former colonies in sub-Saharan Africa (SSA) and the Indian subcontinent, while a significant proportion of immigrants in the United States are from Central and South America.<sup>6</sup> Studies showed that in the country of origin of most immigrants TB is widespread and far less controlled in comparison to the host countries, resulting in an addition to the TB burden in the host country and an impediment to the decline in TB incidence.<sup>7</sup> Various general factors that influence TB prevalence among immigrants are their place of origin, age, sociodemographic characteristics, exposure and travel to the country of origin, access to care, medication resistance, and weak immune competence are all variables that pose the risk of TB prevalence of TB among immigrants after settling in low-incidence countries. 1) Post-arrival reactivation of a remotely acquired latent tuberculosis infection (LTBI); 2) Infection or reinfection after travel to home country; 3) acquired TB following arrival, through local transmission and social mixing.<sup>7</sup>

In European Union and European Economic Area (EU/EEA) countries, the estimated number of TB cases among the foreign-born population in individuals in 2020 was 35%, but looking at the country level, TB patients of foreign origin represent a large majority in several countries: Iceland, Liechtenstein (100% each), Malta (96.4%), Cyprus (94.2%), Norway (86.4%), Sweden (86.2%), Israel (83.9%), Luxembourg (81.0%), and the Netherlands (76.8%) (ECDC Europe, 2020). Additionally, a descriptive study of data from 1996 to 2005 from 21 European countries reports a rise in the TB rates in the United Kingdom, Norway, and Sweden, where almost three-quarters of the cases were among foreign-born people.<sup>8</sup> Similarly, looking at the United States, a recent report published in 2020 by the Centers for Disease Control and Prevention shows the total number of TB cases has been declining; however, notifications in foreign-born persons were 71.5%.<sup>3</sup> Furthermore, McCarthy et al studied the scale of illness among immigrants from 41 GeoSentinel clinics in 19 countries from 1997 to 2009. GeoSentinel clinics are a worldwide communication and data collection network that is based on the concepts that it effectively detects trends in travel-related morbidity among travelers, immigrants and refugees. The study highlighted that one-third of the immigrants were diagnosed with either latent or active infections. The majority of the cases (67%) were confirmed more than a year after migration, whereas 29% of the cases were discovered after more than 5 years.<sup>9</sup>

Screening for TB is a common intervention used to reduce TB among new immigrants in low-incidence nations. Screening foreign-born individuals from countries with a high prevalence of TB may assist in ensuring that onward transmission is minimized and that they receive early treatment. Thus, the requirement of performing TB screening for visa application for immigration is the only dependable point of contact for screening with the new entrants.<sup>7</sup> Taking that into consideration, most high-income countries perform screening of immigrants, although the specifics of how it is done

vary across countries. Chest radiography examination, alone or with clinical evaluation, is the most commonly used method to screen for active TB upon entry, which is helpful only to detect the prevalence of active TB, whereas, for the detection of latent types of TB, a skin test called Tuberculin Skin test (TST) is used. It is a method of determining if a person has been infected by M. Tuberculosis by injecting a fluid (called tuberculin) into the skin. After 48–72 hours, the reaction on the arm is examined. The result depends on the size of the reaction of skin to the fluid. However, recently, an advanced whole-blood-based test called the interferon-gamma release assay (IGRA) is being used for screening latent tuberculosis infection (LTBI). This blood test is more specific and reliable in diagnosing M. Tuberculosis.<sup>10</sup>

In Norway, TB screening is mandatory upon entry for all immigrants coming from countries with a high TB prevalence. It includes countries that have more than 40 cases per 100,000 inhabitants per year. TB screening includes taking a chest X-ray for detection of active TB, while LTBI screening is done for the subset of immigrants who are >35 years old and want to stay in Norway for more than two years.<sup>11</sup> Likewise, in the Netherlands, all foreign-born people, specifically from low- and middle-income countries, who intend to stay for more than three months are required to undergo obligatory TB screening by performing an x-ray in the first week of arrival and later every six months for the first two years of residence.<sup>12</sup> However, there are countries in Europe that do not have a national screening policy for immigrants, like Italy and Denmark.<sup>12</sup> In these countries, TB control among immigrants is entirely dependent on the passive finding of cases, which indicates a difference in screening policies in different low-prevalence countries.

Just like in every other high-income country, migration to the UK continues to happen. It is stated that in March 2020, 715,000 people migrated into the UK, while in 2019, immigrants made up an estimated 14.2% of the total the UK population, making it the top five countries in the world with the most immigrant population.<sup>13</sup> Among them, 71% migrated to the UK to work or study, whereas 13% came to accompany or join a family member, and 6% sought asylum or resettlement.<sup>14</sup>

The flow of immigrants to the UK has affected the health status of the UK-born population as well as changed the pattern of certain diseases like TB.<sup>14</sup> Immigrants from countries with a high rate of TB burden are more likely to develop TB in the first few years after arriving in the UK.<sup>15</sup> Most of these immigrants develop TB from reactivation of LTBI. Berrocal-Almanza et al concluded in his study that the progression from LTBI to active TB is a short time among immigrants in the UK since infection; however, daily stressors such as migration and adaption processes, the presence of existing medical conditions and their living and working environments play an additional important factor. Furthermore, immigrants in the UK experience challenges accessing healthcare services, which is especially important given that LTBI screening is delivered through primary care services.<sup>15</sup> A study in the UK following up on immigrants between 16 and 34 years of age, mostly from the Indian subcontinent, reported that 16.3% individuals who presented with a normal chest x-ray but a positive tuberculin skin test initially progressed to have active TB disease after 10 to 15 years.<sup>16</sup>

According to the UK health agency report (2021), there were 4125 people diagnosed with TB in 2020, at a rate of 7.3 per 100,000 population, and foreign-born people living in the UK made up 2948 of these cases that is almost 71% compared to 35% in the EU. Although the number has decreased compared to the previous year by 13.8% for non-UK born individuals, TB remains 15 times higher among them compared to those born in the UK. The TB incidence was highest among people aged 20 to 24 years, at a rate of 49.8 per 100,000 people compared to the UK-born people, where the rate was 3.0 per 100,000 people.<sup>17</sup>

Studies show that the high prevalence of TB among immigrants is largely acquired abroad rather than due to recent transmission.<sup>18</sup> Currently, to limit the number of people with active TB in the UK, pre-entry screening is performed as part of the visa application. It applies to anybody who is travelling from a country with a TB incidence of more than 40 cases per 100,000 people and plans to stay for six months or longer.<sup>18</sup> It is believed that screening this way prevents the risk of forward transmission of the disease in the community; however, the risk of TB from reactivation of LTBI still remains high.

Currently, TB control and treatment programs in the UK face challenges from the changing pattern of TB due to a large immigrant influx. Previously, a systematic review about the burden and screening effectiveness of TB among immigrants in Europe has been conducted that included the UK,<sup>15,19</sup> however, no previous systematic overview on the burden and management of TB specifically for the UK was found. The present study specifically examines the trend of TB burden among the immigrant population in the UK and investigates the factors associated with the high burden of TB in this population as well as the screening as treatment approaches. The result of this study will inform public health response in the UK to the health needs of immigrants and help in designing interventions around screening and management policies for

immigrants. Such efforts will in turn contribute to the decreasing prevalence of TB among immigrants in the UK. And, on the global level, they will help in accomplishing WHO's END TB strategy global plan.

# **Research Objectives**

The goal of the proposed study is to systematically review to study the burden and management of TB among immigrants in the UK. The study will address the following objectives;

- 1. To map the burden of TB among immigrants in the UK
- 2. To investigate factors associated with the TB burden among immigrants in the UK
- 3. To review the management approaches of TB among immigrants in the UK.

# Methods

A review was conducted in 29/08/2022 following Preferred Reporting Items for Systematic Review and Meta-Analysis Statement (PRISMA) guidelines.

# Eligibility Criteria

Inclusion Criteria

- Qualitative and quantitative studies, descriptive and analytic observational studies, and experimental studies that looked into the progression of LTBI to active disease and government official reports
- Published in English
- Studies that included information about the UK
- Studies that covered non-forced economic immigrants, migrants, refugees, and asylum seekers
- Studies were published after the year 2000 because increase movement of people as a result of globalization, migration, war and conflict happened from year 2000 onwards.
- Studies with subjects aged 16 years and older.
- Studies that discussed either burden, screening, diagnosis or treatment.
- Relevant studies from the reference list of included studies.

#### **Exclusion** Criteria

- Systematic review and meta-analysis studies (Appendix Item 1).
- Studies about TB in children due to decreased notification rate (Appendix Item 1).
- Multi-drug-resistant TB (MDRTB) as treatment approaches are different compared to active and latent TB, and its prevalence is higher among homeless, drug addicts, and prisoners.
- Studies that discussed non-pulmonary TB.
- Studies that included high-risk groups such as HIV- positive or neoplastic patients.

### **Outcome Measurements**

For the review, the outcome measurements were the number of TB cases among immigrants, including the incidence and prevalence of the disease. Additionally, factors mentioned that were associated with the disease burden among them and management approaches guidelines by the primary care organization regarding TB.

### Search Strategy

A systematic literature search was carried out by consulting PubMed and EMBASE databases. Medical Subject Headings (MeSH) and Embase subject heading (Emtree) terms and free-text terms combined with Boolean (AND, OR) terms were used. The developed search strategy used for each database is presented in Table 1. Relevant keywords were: "Tuberculosis", "Pulmonary Tuberculosis", "Lung Tuberculosis", "Tb", "United Kingdom", "England", "Britain", "UK", "Northern Ireland", "Scotland", "Wales", "London", "Birmingham", "Migrant", "Immigrant", "Refugee", "Foreign-born", "Non-UK". Since many migrations occurred after 2000, the literature search was limited to published articles between 2000 and July 27, 2022.

Databases	Search Terms	
PubMed	#I Tuberculosis[Text Word]	#22 United Kingdom[MeSH Terms]
	#2 Tuberculosis[MeSH Terms]	#23 United Kingdom[Text Word]
	# <b>3</b> I OR 2	# <b>24</b> 22 OR 23
	#4 Pulmonary Tuberculosis[Text Word]	<pre>#25 England[MeSH Terms] #26 England[Text Word]</pre>
	#5 Pulmonary Tuberculosis[MeSH Terms]	# <b>27</b> 25 OR 26
	#6 4 OR 5	#28 Britain[Text Word]
	# <b>7</b> TB[Text Word]	# <b>29</b> UK[Text Word]
	#8 3 OR 6 OR 7	# <b>30</b> London[Text Word]
	# <b>9</b> Immigrant[Text Word]	#31 Birmingham[Text Word] #32 Wales[Text Word]
	#10 Immigrant[MeSH Terms]	# <b>33</b> Scotland[Text Word]
	#11 9 OR 10	#34 Northern Ireland[Text Word] #35 24 OR 27 OR 28 OR 29 OR 30 OR
	#12 Migrant[MeSH Terms]	31 OR 32 OR 33 OR 34 # <b>36</b> 8 AND 21 AND 35
	# <b>I3</b> Migrant[Text Word]	#37 8 AND 21 AND 35 (english[Filter] AND 2000:2022[pdat])
	# <b>14</b> 12 OR 13	
	# <b>15</b> Refugee[MeSH Terms]	
	#16 Refugee [Text Word]	
	# <b>17</b> I5 OR I6	
	#18 (Migration[Text Word] #19 Foreign born	
	[Text Word] #20 non UK[Text Word]	
	#21 11 OR 14 OR 17 OR 18 OR 19 OR 20	
EMBASE	#I exp Tuberculosis/	#20 exp United Kingdom/
	#2 Tuberculosis.tw.	#21 United Kingdom.tw.
	# <b>3</b> I OR 2	# <b>22</b> 20 OR 21
	#4 exp lung tuberculosis/	#23 exp England/
	#5 Pulmonary Tuberculosis.ab,ti.	# <b>24</b> England.tw.
	# <b>6</b> 4 OR 5	# <b>25</b> 23 OR 24
	# <b>7</b> TB.tw.	# <b>26</b> Britain.tw.
	#8 3 OR 6 OR 7	# <b>27</b> UK.tw.
	# <b>9</b> exp immigrant/	# <b>28</b> London.tw.
	#10 Immigrant.tw.	# <b>29</b> Birmingham.tw.
	#11 9 OR 10	#30 Wales.tw.
	# <b>I2</b> Migrant.tw.	# <b>31</b> Scotland.tw.
	# <b>I3</b> exp migration/	# <b>32</b> Northern Ireland.tw.
	# <b>I4</b> Migration.ab,ti.	#33 22 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 #34 8
	# <b>15</b> I3 OR 14	AND 19 AND 33
	#16 Refugee.tw.	#35 limit 34 to (english language and yr="2000 -Current")
	# <b>17</b> Foreign born.tw.	
	# <b>18</b> non UK.tw.	
	#19    OR  2 OR  5 OR  6 OR  7 OR 8	

 Table I Search Strategies Used for Searching Electronic Databases

Moreover, only articles published in the English language were searched. Additionally, to ensure that no studies were missed, the reference list of the studies was searched through the snowballing technique for additional potential studies. It also included a reference list of studies that were not included in the study but were particularly interesting.

Furthermore, government websites and organizations working on the subject were searched to search for management approaches to TB in the United Kingdom. The list of websites that were browsed for the guidelines and policies regarding TB management is provided in Table 2.

# Selection of Articles

The result of search strategies from the PubMed and EMBASE databases was exported to Rayyan. This online web-tool application helps facilitate the screening of articles during the review process. After exportation, the de-duplication of the

I	Public Health England (PHE)
2	National Health Service UK (NHS UK)
3	Health Protection Agency (HPA)
4	National Institute for Health and Care Excellence UK (NICE)
5	Health Care Improvement Scotland (HCIS)
6	National Health Service England (NHS England)
7	National Resource for Infection Control (NRIC)
8	Royal College of Nursing (RCN)
9	Office for Health Improvement and Disparities (OHID)

 Table 2 List of Organization Contacted During Grey Literature Search

articles was carried out. Rayyan has better accuracy in the de-duplication of articles than other reference managers.<sup>20</sup> After eliminating duplicate articles, a two-stage process was adopted to examine the available resources from the mentioned databases. In the first stage, titles and abstracts were screened against the inclusion and exclusion criteria. Similarly, in the second stage, full-text articles were retrieved for the studies that had met the inclusion criteria. Screening the full text of articles also led to the exclusion of more articles from the review (Appendix Item 1). In addition, during screening, studies that did not mention the site of the disease but provided diagnostic methods utilized and indicated pulmonary TB were also included in the review.

A grey literature search for reports and guidelines was conducted in a pre-defined list of government websites or organizations that deal with TB management in the UK. Documents were included if the reported information was relevant and provided guidelines on screening, diagnosis, and treatment of TB for immigrants and new entrants. If no information about immigrants could be found, general guidelines were reviewed (ie, those without a section for immigrants).

# Data Extraction Process

All the relevant information from included articles was summarized using an Excel sheet. The extracted data from articles that reported the burden of TB and factors associated with the burden of TB contain the following information presented in the Excel sheet:

- Bibliographic Reference: Title, author, year
- Study characteristics: study objective, study design, study period, location, and setting
- Study population: Number of participants and origin of the participants.
- Outcome Results: The prevalence rate was calculated in percentage measurement from the reported data by dividing the number of cases by the total number of participants and multiplying it by 100.
- Factors associated with burden of TB.
- Additional information that was relevant to interpreting the results.

For documents that provided information about management approaches to TB among immigrants in the UK, the Excel sheet contained the following information.

- Source: The organization that prepared the document.
- Type of document, eg, guidelines.
- The specific group of immigrants, if any.
- Management guidelines, eg, screening, diagnosis, and treatment protocol.

# Risk of Bias in Individual Studies

The methodological quality of the included papers that seemed to offer data relevant to the review was extensively evaluated during the selection process using standardized, evidence-based medicine criteria to find quality issues. For the

review, Joanna Briggs Institute (JBI) critical appraisal tool was used based on the type of the study to determine the possibility of bias in the design, conduction, and analysis of a study. JBI offers a checklist for the following study designs: Analytical cross-sectional studies, case–control studies, case reports, case series, cohort studies, diagnostic test accuracy studies, economic evaluations, prevalence studies, qualitative research, quasi-experimental studies, randomized control trials, systematic reviews, and text and opinion. Depending on the type of study, the checklist contains questions with answers of 'yes', 'no, "unclear", and "not applicable". The answer to the question was awarded a point based on the answer yes (1), no (0), unclear (0.5), and not applicable (0). The total points a study scored were then converted into a percentage of  $\geq$ 70% represented high quality or low risk of bias; a percentage of 50–69% was considered a moderate-quality or moderate bias risk; and a percentage of <50% indicated a very low-quality study or high risk of bias.

### Results

#### Study Selection

In the peer-reviewed article search, the PubMed search yielded 178 hits, and the Embase search yielded 347 hits, a total of 525 records. After the removal of 138 duplicates, 387 unique hits remained. A total of 89 articles were identified after the titles and abstracts were scrutinized. The main reason for the exclusion of articles during the title and abstract screening is given in <u>Appendix (Item 2)</u>.

After reading the entire text of the chosen articles, 75 articles were excluded. Articles excluded and reason for exclusion during the full-text selection step are given in <u>Appendix (Item 3</u>). Among the 14 publications included, six of which were pertinent to the TB burden among immigrants, three addressed the reasons related to the burden among immigrants, and five dealt with both objectives. The PRISMA flow diagram describing the steps of study selection is shown in Figure 1.

The grey literature search was limited to pre-defined websites of government health sectors that actively manage TB in the UK. A total of 5 documents were retrieved that provided information about TB diagnosis, screening, and treatment.

#### Population and Study Characteristics

The studies included were published between 2007 and 2022 (Table 3), while the sampling of those studies was conducted between 1999 and 2017. The included studies used different types of TB diagnostic strategies and sampling methods. The main study design was cross-sectional – six studies – followed by five cohort studies and three qualitative studies. Three studies provided pre-entry screening data from International Organization for Migration clinics, one provided national surveillance data, one used enhanced TB surveillance data from England and Wales, one screening data from Heathrow and Gatwick airports, and the rest local electronic databases.

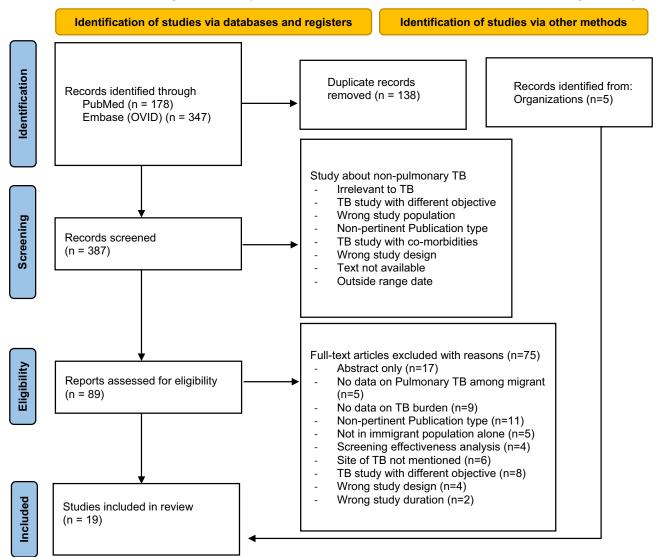
The sample size ranged from 10 to 519, 955 subjects reflecting the varying study designs (Table 3). The age of participants varied in each study, with an age range of 16–35 dominating the sample population pool. However, few studies had subjects aged 0–14 years in their sample study. In addition, the subjects varied between studies: some included screening of applicants staying for more than six months in the UK or belonging to a country with a TB prevalence rate of more than 150 per 100000 population. Others followed up on immigrants living more than six months in the UK based on their visa status. Only one study screened a specific group of immigrants; asylum seekers.

Considering the region of the origin of the immigrants, Asia was predominant, with a higher percentage of immigrants born in South Asia in five retrieved studies, followed by sub-Saharan Africa and South East Asia.

Due to the heterogeneity of the included studies, a single prevalence figure for TB could not be estimated. In addition, the study population, the measurement used, the research methodology, and the study quality differed among studies. Therefore, studies are summarized narratively with descriptive reports of prevalence estimates.

#### **Risk of Bias Within Studies**

Among the included resources for the review, 11 studies had a low risk of bias, whereas three had moderate risks of bias. Among the six cross-sectional studies, Crofts et al and Cegolon et al had unclear inclusion criteria, and study subjects and



#### PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

Figure I PRISMA based Flow diagram displaying the study selection.

Notes: PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.<sup>21</sup>.

settings were not described. It also failed to provide a clear strategy to deal with confounding factors. Similarly, Crawshaw et al and French et al did not identify the confounding factor in their study or mention strategies to deal with it. On the other hand, out of five cohort studies included in the review, only Severi (2016) did not address the confounding factors and strategy to overcome it. The detailed scoring of each study can be found in <u>Appendices (Item 1</u>).

It was not possible to perform quality assessment for the five governmental documents covering the management approaches.

### TB Burden

Prevalence measures of Pulmonary TB disease were reported in 11 of the 14 studies selected in this review (Table 4).

Of the 11 studies, three studies provided prevalence data of more than five years. Of it, two studies conducted by Aldridge et al<sup>29</sup> were based on data collected by International Organization for Migration clinics. The first study with participants of 476455 reported 439 (0.01%) confirmed TB diagnoses between 2005 and 2013, whereas the second study estimating TB prevalence among 519,955 subjects between 2006 and 2012 reported a prevalence of 49 per 100000 population. Similarly, a ten-year cohort study from 2000 to 2010 by Panchal et al<sup>26</sup> collected data via a local networked

First Author	Year	Study Duration	Location	Participants	Origin	Type of Study
(Aldridge et al, 2016a) <sup>1</sup>	2016	Oct I, 2005, and Dec 31, 2013	Various	476 455	South Asia 81.1%; South East Asia 9.6%; Africa 9.32%	Cross- Sectional Study
(Aldridge et al, 2016b) <sup>1</sup>	2016	Jan I, 2006, and Dec 31, 2012	Various	519,955		Cohort Study
(Berrocal- Almanza et al, 2022) <sup>5</sup>	2022	Jan I, 2014, and Jan 20, 2015	55 high-burden Clinical Commissioning Group areas of England	37,268	South Asia 76.9%; Africa 19.1%; The Americas or Europe 0.8%; East and southeast Asia 2.7%	Cohort Study
(Cegolon et al, 2010) <sup>11</sup>	2010	2003–2006	London	11,044	Asia/South Asia/ SouthEast Asia: 35%; Sub- Saharan Africa: 37%; Rest of the world: 28%	Cross- Sectional Study
(Chinouya & Adeyanju, 2017) <sup>14</sup>	2017	2015	London	10	African	Qualitative Study
(Crawshaw et al, 2018) <sup>17</sup>	2018	March 2013 and August 2017	Various	9759	Middle East 73.73%; sub-Saharan Africa 19.56%; South and West Asia 6.62%	Cross- Sectional Study
(Crofts et al, 2008) <sup>18</sup>	2008	1999 to 2003	Inside London	1858		Cross- Sectional Study
(French et al, 2008) <sup>22</sup>	2009	2000–2005	England and Wales	11,934	South Asia 48.3%; Sub Saharan Africa 35.2; South-East Asia 3.3%; Western Europe 3.2%; others: 20%	Cross- Sectional Study
(Harling et al, 2007) <sup>23</sup>	2007	June 2002 to June 2003	Kent Port	8258	East Mediterranean 61.3%; Europe 15.6%; Africa 11.9%; Unknown 10.1%; others 1.2%	Cross- Sectional Study
(Humphreys et al, 2017) <sup>24</sup>	2017	26th November to 23rd December 2013.	Kirklees, an urban district in the north of England	221	South East Asia	Qualitative Study
(Loutet et al, 2018) <sup>25</sup>	2018	August 2014 and August 2015	Newham, London	2269	Southern Asia 78.5%; Sub-Saharan Africa 18.7%; East and South-East Asia 2.5%; Eastern Europe 0.1%; Northern Africa 0.2%	Cohort Study
(Panchal et al, 2013) <sup>26</sup>	2014	I January 2000 and 31 December 2010	Leicestershire	59,007	SE Asia 57%; African 21%; Eastern Mediterranean 17%; European 2%; West Pacific 3%	Cohort Study
(Seedat et al, 2014) <sup>27</sup>	2014		West London (Hammersmith and Fulham)	20	Africa, Asia, Europe, Americas	Qualitative Study
(Severi, 2016) <sup>28</sup>	2016	10 June 2009 to 30 September 2010	Heathrow and Gatwick airports	200 199	South Asia 53.3%; Sub-Saharan Africa 13.6%; South America 28.7	Cohort Study

Table 3 Main Characteristics of the Studies Included in the Review

electronic database on 59,007 subjects and reported 0.17% TB among the recent immigrant population. However, the study French et al<sup>22</sup> noted an increase in TB prevalence between 2001 and 2003. It reported a 52.1% prevalence among non-UK-born subjects.

Concerning the prevalence of TB in different regions of the UK, six studies provide information about the geographical location where the studies were conducted (Table 4). Among these studies, the highest prevalence (31%) was reported in Newham in a cohort study by Loutet et al.<sup>30</sup> Similarly, two studies conducted in London reported

Table 4	Prevalence	Rate	of TB	Among	Immigrants
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Author	Prevalence Rate	Region	Origin	Diagnostic Method
(Aldridge et al, 2016a) <sup>1</sup>	0.09%			Chest X-ray, in case of doubt,
				Sputum Smear Test
(Aldridge et al, 2016b) <sup>1</sup>	0.04%			Chest X-ray, in case of doubt,
				Sputum Smear Test
(Berrocal-Almanza et al, 2022) <sup>5</sup>	17.80%			IGRA testing
(Cegolon et al, 2010) <sup>11</sup>	24%	London	Sub- Saharan Africa 37%; Asia/South Asia/	Sputum smear test
			South East Asia 35%; Rest of the world 28%	
(Crawshaw et al, 2018) <sup>17</sup>	0.09%			Chest X-ray
(Crofts et al, 2008) <sup>18</sup>	21%	London		Sputum smear test
(French et al, 2008) <sup>22</sup>	52.10%		South Asia 48.3%; Sub Saharan Africa 35.2;	Sputum smear test
			South-East Asia 3.3%; Western Europe 3.2%;	
			others: 20%	
(Harling et al, 2007) <sup>23</sup>	2.20%	Kent Port		Chest X-ray
(Loutet et al, 2018) <sup>25</sup>	31.70%	Newham,	Southern Asia 77.5%; Sub-Saharan Africa	IGRA testing
		London	20.55%; Others 2%	
(Panchal et al, 2013) <sup>26</sup>	0.17%	Leicestershire	South East Asia 57%; African 21%; Eastern	Sputum smear test
			Mediterranean 17%; European 2%	
(Severi, 2016) <sup>28</sup>	0.03%	Heathrow		Chest X-ray
		and Gatwick		
		airports		

a prevalence rate of  $24\%^{31}$  and  $21\%^{32}$  (<u>Appendix Item 4</u>). However, contradictory results were observed in Kent port (2.2%), Leicestershire (0.17%), and Heathrow and Gatwick airports (0.03%).<sup>24,33,34</sup>

Four studies (Table 4) reported the prevalence of pulmonary TB per immigrants' region of origin, namely African, Asian regions, European, and the rest of the world. The highest TB percentages were observed in immigrants from the Asian region (range 1.5–77.5%), particularly immigrants from South Asia (range 35%–77.5%), followed by sub-Saharan Africa (range 20.5–37%), from Europe (range 0.41–3.2%).<sup>23,30,31,33</sup>

Nine authors mentioned the diagnostic method used in each study (Table 4). Four studies used a sputum smear test to diagnose pulmonary TB among the subjects.<sup>23,31–33</sup> In contrast, three studies used chest x-ray for screening for active TB.<sup>28,34,35</sup> If the radiograph suspects TB, it was confirmed via a sputum smear test. IGRA test was utilized only in two cohort studies conducted in Newham and 55 high-burden clinical commission group areas of England<sup>30,36</sup> (Appendix Item 4).

### Factors Associated with the Burden of TB

Eight research reported aspects linked with the burden of TB in the immigrant community. The following is a general thematic explanation of the linked factors reported in the included studies.

#### Attitude Towards TB Factor

Two studies reported that immigrants believed that they are personally protected against TB and that BCG vaccination protects them against TB. Further, a lack of preventive measures among the families of the immigrants was reported by Seedat et al. The study by Chinouya & Adeyanju (2017) stated that immigrants had no awareness of the symptoms of TB, while the qualitative study by Seedat et al indicated that immigrants were not confident in using the new systems of health care.

#### Socio-Economic Status Factor

Poor living conditions and poverty were highlighted in two studies by Chinouya & Adeyanju (2017) and Humphreys et al as disengaging immigrants from health intervention. Additionally, a study aiming to explore views around barriers, accessibility, and acceptability of screening among immigrants by Seedat et al indicated that immigrants had a fear of

cost and being eligible for TB service. Furthermore, the lack of entitlement to free health and confidentiality issues prevented them from seeking health care. Crofts et al research on immigrants inside and outside London reported that the residence of immigrants in the least deprived area exposed immigrants to TB disease.

#### Seeking Healthcare Factors

Three studies<sup>33,37,38</sup> reported that most immigrants lacked primary care service registration or registration with a general practitioner (GP). Similarly, Cegolon et al and Seedat et al also report a lack of awareness about healthcare services and misunderstanding of how the health system in the UK functions vs their country of origin. Furthermore, in hospitality and unfriendly behavior of healthcare providers in the hospitals is reported by Seedat et al, which explains delayed referral for medical advice as observed by Humphreys et al. Concurrently, the study by Chinouya & Adeyanju (2017) reports that immigrants have no education about self-refer to TB clinics and self-medicate when they suffer from TB symptoms. Also, immigrants fear that the fact after diagnosis, they have to isolate themselves from their family and community and thus report late to TB clinics.

#### The Social Repercussion of TB Factor

Three studies cited stigma as the most social repercussion.<sup>25,37,39</sup> For example, 19 out of 20 participants in the study by Seedat et al expressed that stigma is the reason why new migrants fail to share about their illness.<sup>37</sup> Adding on, lack of understanding of the language was the second cited factor for the burden of TB reported in three qualitative studies by Seedat et al, Humphreys et al and Cegolon et al. Keeping the disease quiet in the family, fear of rejection and isolation from the family community was another reported factor in two studies conducted by Humphreys et al and Chinouya & Adeyanju (2017). Furthermore, the fact presented by Seedat et al in the research reported that the perception of new immigrant communities holds about key diseases prevented immigrants from seeking healthcare services adding up to the factor resulting in the burden of the disease among them.

### Management Guidelines

Five practice-based guidelines from health authorities in the UK that reported on screening, diagnosis and treatment of TB. These guidelines formulate the following relevant recommendations (Tables 5–7).

### Discussion

This review found that numerous approaches to detection of TB among migrants were adapted across the UK with respect to pre- and post-arrival of settings and immigrant subpopulations. The screening methods were focused on new entrants, migrants, asylum seekers, and migrants living for longer time in the UK. The main focus was on pulmonary TB detection, either active or latent, or both.

Across the 11 included studies, TB prevalence among migrants ranged from 0.09% to 52.1%. The striking element among the prevalence study was the time period of the different studies. It was surprising that studies that had a longer time period of more than five years reported a lesser percentage of TB prevalence among the immigrant population,<sup>29,33,35</sup> whereas studies that had time duration of  $\leq 3$  years reported a higher prevalence rate<sup>30–32</sup> (<u>Appendix</u> <u>Item 4</u>). Since the UK government rolled out pre-entry TB screening in 2012 and fully transitioned to the new policy in 2014, the possible explanation can be that the sample population of studies with a lower prevalence rate had undergone pre-screening procedures required to enter the UK.<sup>35</sup> Additionally, another possible explanation can be the selection of the target population for the study. The study by Aldridge et al included a target population who intended to stay longer than six months and did not include undocumented migrants, asylum seekers, or people who stay for shorter periods. As a result, a lesser burden has been observed. However, among the included studies, French et al reported a higher prevalence of immigrants, while the study was conducted in 2004 when a pre-screening policy was not implemented.

When considering the country of origin, the highest prevalences were observed in immigrants originating from Asian regions. It has been documented that the TB burden among the communities of South Asian immigrants in the UK partially resembles the magnitude of TB burden in their home countries. A recent systematic review found various factors, including poverty, deprivation, return to visit the Indian subcontinent, and possible dietary factors, such as Vit D deficiency, resulting

## Table 5 Guidelines Based on Screening of Pulmonary TB

Screening of Pulmonary TB	
Guidelines	
Public Health England (2015)	If a person is 16 to 35 years old, arrived in the UK within the last five years from a country with a high incidence (150/100,000 or SSA), and has previously resided in that high incidence country for at least six months, they should be tested for LTBI. Primary care is the ideal location for new entrant LTBI testing. However, to choose the most appropriate and efficient location for local implementation of LTBI case finding, local services, situations, and choices should be taken into account. Data and information must be recorded exactly as in primary care if LTBI testing is conducted in a non-primary care setting, such as an educational or congregational environment or secondary care. The LTBI testing and treatment findings are sent to the patient's general practitioner. Either intradermal Mantoux (skin) test or interferon-gamma release assay (IGRA) blood test is used to perform screening.
Public Health England (2014)	<b>Employee:</b> Employees may be exposed to tuberculosis (TB) through interaction with service users/customers who have active TB, or the employee was born or spent a significant amount of time in a region where TB is prevalent. The danger of contracting TB is greatest within the first five years after arriving in the UK. If an individual contracts TB of the lungs, he or she is infectious in the workplace. The person should be kept off work until he or she is no longer contagious, which occurs two weeks after completing the referral pathway's TB treatment. Employers and organizations are required by the public health law to provide information about the employee with TB that may help identify close connections to the individuals who may need screening.
National Health Service UK (2019)	A person who has recently been to a country with a high TB prevalence or who has lately been in close contact with someone known to have active TB affecting the lungs needs to get tested. Information and guidance on the necessity of testing should be acquired if an individual has recently relocated to the UK from a country where TB is widespread. Mantoux test, also known as tuberculin skin test (TST), is the standard test that should be used for latent TB screening. It entails injecting purified protein derivative (PPD) tuberculin into the skin of the forearm in a bit quality. However, in case of severe skin reaction to the TST, a chest x-ray should be performed to determine if it is an active TB disease. IGRA should be used to help diagnose latent TB, if the Mantoux test is positive, or if individuals had previous BCG vaccination, or as part of a health check while registering with a GP. Also, individuals who have moved to the UK from a country with a TB prevalence of more than 40 per 100,000 population or are applying for a UK visa for longer than six months must undergo pre-entry screening. A chest x-ray, symptom evaluation, and a sputum examination are part of the screening. Children under II are not screened for chest X-rays unless a clinician finds it essential. However, a history of recent contact with a case of pulmonary TB will be taken together with a symptom screen and a physical examination if the physician believes it appropriate where TB is common.
Office for Health Improvement and Disparities (2021)	LTBI testing should be conducted on those aged 16 to 35 who have moved to England in the past five years and who were born or resided in Sub-Saharan Africa or countries with a TB prevalence of more than 150 per 100,000 people.
NICE (2019)	<ul> <li>The following details should be used to identify new arrivals to the UK for TB screening:</li> <li>Reports from the port of arrival.</li> <li>Registration with primary care</li> <li>Entry to education, including universities</li> <li>Links with governmental and nonprofit organizations that assist with incoming immigrants.</li> <li>All vulnerable immigrants who have not already been screened should be tested by healthcare experts, especially primary care providers, who are in charge of screening new arrivals. Regardless of when they came to England, this is the case. It should be a top priority to screen for latent TB in those born in nations with an incidence of more than 150 per 100,000 people per year when they come to the UK.</li> </ul>

#### Table 6 Guides Based on Diagnosis of Pulmonary TB

Diagnosis of Pulmonary TB				
Guidelines				
Public Health England (2015)	If the new entrant fits the local approved LTBI testing requirement, blood samples should be collected and sent to the IGRA test-processing laboratory using the agreed-upon local procedure. If the new entrant exhibits indications of active TB, an emergency referral to TB service should be arranged. And new patients who are children from high-risk countries, the BCG vaccine should be provided if they have not previously received it. The LTBI testing information should be entered into the GP system or online template.			
Public Health England (2014)	IGRA tests should not be used as a regular diagnostic tool for active TB and only be taken into consideration to support the primary diagnosis of active TB or when it has been impossible to confirm the diagnosis by culture or when there is insufficient radiological and histopathological evidence to support the diagnosis. The use of the IGRA test is recommended if the diagnosis is still uncertain, and the outcome will impact the choice of whether to treat or not. Clinical judgment should be used to make the ultimate choice.			
National Health Service UK (2019)	A chest X-ray is performed to check for TB-related changes in the appearance of the lungs. Adding up, Phlegm samples are also often obtained and examined for the presence of TB germs.			
Office for Health Improvement and Disparities (2021)				
NICE (2019)	In the case of Active TB, perform a chest X-ray and subsequent diagnostic tests if the chest X-ray appearances imply TB. In addition, send three deep cough sputum samples, ideally one in the morning, for TB microscopy and culture. If feasible, this should be done before commencing therapy or within seven days of starting treatment in persons with a life-threatening illness.			

#### Table 7 Guidelines Based on Treatment of Pulmonary TB

Treatment of Pulmonary TB	
Guidelines	
Public Health England (2015)	Patients who have been diagnosed with active TB illness should be sent to their local TB service and treated according to their area's active TB treatment regimen. Persons with LTBI but no HIV should be given either three months of rifampicin and isoniazid combination treatment or six months of isoniazid monotherapy. Chemoprophylaxis treatment is restricted to patients younger than 35 years of age unless a person older than 35 is a healthcare professional or has an underlying condition with a high risk of reactivation (eg, HIV).
Public Health England (2014)	TB treatment to be provided and monitored by TB service for at least six months. Employees should return to work when they are no more infectious, usually two weeks after the treatment starts.
National Health Service UK (2019)	Combination of antibiotics course for at least six months if diagnosed with active pulmonary TB. The standard therapy is; Six months of isoniazid and rifampicin and two additional antibiotics (pyrazinamide and ethambutol) during the first two months of six-month therapy.
Office for Health Improvement and Disparities (2021)	Individuals with active TB of the lungs must finish treatment before their visa is approved. Treatment consists of a mixture of antibiotics for at least six months, with treatment progress monitored by an expert team. For latent illness, treatment may last 3 to 6 months, depending on the antibiotics regimen.
NICE (2019)	Latent TB should be treated with isoniazid (with pyridoxine) and rifampicin for three months in patients under the age of 35 years. In patients with HIV or who have undergone a transplant, six months of isoniazid (with pyridoxine).

in more TB among the mentioned population.<sup>40</sup> The described reasons underlying the burden among South Asian immigrants are the interaction of migration from high TB burden countries and the reactivation in host countries. Thus, these prevalences might be related to origin from high TB prevalence countries in Asia, especially those from South Asian region. Nevertheless, since in this review, only a few studies provided information about the TB cases based on the immigrant's origin, more data regarding regions of origin could provide a clear view.

Furthermore, at the geographical level, the prevalence of TB was more pronounced in London compared to other cities. It can be because the majority of the included studies were conducted in England. Albeit, this result coincides with the TB annual report, reporting increased TB prevalence in London compared to the other cities of England, where TB cases are 20 times more among immigrants than the national population.<sup>41</sup> London, the capital city of England, has attracted more migration movement compared to other cities of England as people presume more benefits while residing there. However, the poor living conditions and the housing issue, compelling immigrants to live in homeless shelter environments, can be the reason behind the increased TB incidence.<sup>41</sup> Additionally, a substantial proportion of non-UK-born immigrants located in urban areas outside London could be driving the observed temporal trends. According to a survey by the London Assembly (2015), many Londoners have little to no knowledge about TB and its transmission. Nearly one in five Londoners polled were unable to name even one contagious TB symptom.<sup>42</sup> It explains the reason why there is more prevalence of TB in London compared to other cities.

Moreover, misconceptions about the disease, its causation, and prognosis are identified while assessing factors associated with the TB burden. In many cases, the first contact with the source of knowledge about the disease was the previous TB-related experiences of family members and in the place of origin—where the frequency and severity of TB are higher than the UK. As a result, some immigrants owned the belief of being protected against TB in the UK, while others believed that BCG vaccination in their country of origin was enough to protect them and that further interventions were not required.<sup>39</sup> BCG vaccine is administered to newborns and early children to protect them against TB meningitis, but its effectiveness against TB of the lungs is questionable.<sup>43</sup> This finding concurs with the systematic review conducted by Abarca Tomás et al on misconception and lack of knowledge about TB disease among immigrants. Therefore, TB intervention programs commencing in the UK should be directed toward the awareness of immigrants during the primary registration process to ensure that they understand how vulnerable they are to the disease.

What is more, the lack of proper housing and poverty among the immigrants has been a factor in the spread of disease in the community of immigrants. As immigrants prefer living in the same neighborhood, a lack of preventive measures and awareness about the symptoms of the TB disease has resulted in unrestricted spread among them. This factor seems more applicable to immigrants living in the least deprived areas of London.<sup>32,39</sup> Likewise, if immigrants are ill with the disease, they try to self-medicate themselves instead of visiting GP.<sup>25,44</sup> The reasons corresponding for this attitude have been attributed to the fear of being charged while visiting primary care service or discriminatory behavior by a health professional.<sup>37</sup> Hence, they continue self-medication until their condition worsens. This attitude of immigrants has been cited in the study by Abarca Tomás et al, stating that immigrants frequently neglect the significance of symptoms at first, only to later self-diagnose and self-medicate using pharmacies, private clinics, and finally, public healthcare centers.<sup>43</sup> It can be assumed that previous experience with the healthcare system or lack of understanding of healthcare providers resulted in containing the disease between themselves.

Interestingly, the lack of motivation to visit primary care services was suggested to be relevant to how immigrants were treated in the hospital. Most of the immigrants confronted unfriendly behavior from professionals and being judged about their immigration status affected their health-seeking behavior in the UK.<sup>37</sup> Despite negative experiences, some immigrants are willing to visit GP but are not familiar with the UK's health system. Further, having no knowledge of what services are entitled to them without being charged, they hesitate to reach out for medical help. All these factors sum up to make immigrants less confident in seeking assistance. Adding up, language difficulties among the refugee and asylum-seeking subpopulation of immigrants are barriers that create miscommunication.<sup>39</sup> Without proper presentation of illness to the professional, proper care cannot be obtained. Hence, the miscommunication creates misunderstanding and discourages the subject from visiting professionals in the future.<sup>45</sup> However, this issue has now been, at least in part, addressed by the UK government by employing available online translators in different primary healthcare departments so that proper communication can occur between patients and the doctor.<sup>46</sup>

The most undesirable factor associated with the TB burden among immigrants in the included studies was the stigma.<sup>47,48</sup> Stigma develops due to societal and institutional standards on undesirable or devalued behaviors or features. When diseases are stigmatized, individuals may be hesitant to seek and undergo medical care due to fear of the social and economic ramifications of a diagnosis. Therefore, the structure of a community's beliefs, particularly in specific groups like immigrants, and norms regarding TB can significantly influence poor health outcomes and continued TB transmission. In the systematic review by Nofalia et al, the role of stigma and its undesirable effects on the health of TB patients have been observed. However, among the included studies, participants in the study by Humphreys et al were convinced that the stigma is a thing of the past and individuals have a different mindset about TB and its treatment. This can be true in case immigrants are more knowledgeable about the disease and understand the pathways of transmission and treatment of TB.<sup>49,50</sup> Nevertheless, stigma is high among the immigrant population,<sup>27</sup> and stigma reduction should be prioritized at the patient and healthcare professional levels.

Immigrant TB screening is becoming more widely recognized as a strategy that may assist in lessening the burden of imported TB in low-incidence nations. In order to reduce TB prevalence among immigrants, primary care organizations (PCOs) in the UK have formulated guidelines that are followed before they enter the UK and after living in the UK for a certain period of time or when the disease infects them. The current functioning PCOs in the UK are National Health Service (NHS), Public Health England (PHE), and National Institute for Health and Care Excellence (NICE). Thus, various concerns are being actively researched by PCOs, such as whether to screen for active or latent TB (or both), which immigrant groups to screen, when to screen, and how to screen. As per guidelines, all new entrants should undergo a pre-entry screening program to detect active TB. This pre-entry program takes place in 101 world countries where 152 clinics are set up.<sup>26</sup> All applicants who want to stay longer than 6 months in the UK or belong to one of those countries where the prevalence of TB is more than 40 per 100,000 population or have origin of SSA must be tested.<sup>51</sup> The pre-entry screening includes performing a chest x-ray for the detection of active TB. In case of abnormal findings, a sputum test is advised. In such circumstances, three samples are taken during a different time period to confirm the presence of bacteria.<sup>52</sup> However, if an applicant is diagnosed with TB, he/she must undergo an active TB treatment regimen for at least six months before applying for a visa again. Likewise, if an employee has contracted TB, he/she should be left off work until he/she is no more contiguous.<sup>46</sup> However, an employee can rejoin the work after two weeks as the infectivity of the bacteria is gone following starting treatment. The UK pre-entry TB screening program is similar to screening programs in Australia, Canada, New Zealand, and the USA, except that in the UK, the focus is only on TB screening, whereas in the other countries, many other infectious and non-infectious diseases are screened in immigrants (Pareek et al, 2012). The effectiveness of the pre-entry TB screening is reported by Aldridge et al in a systematic review. The author indicates that preentry screening is probably successful in preventing the entrance of new immigrants who have infectious active pulmonary TB.<sup>29</sup> However, critics understand that it is unlikely to have a significant influence on TB control on its own.<sup>2,53</sup> Screening new immigrants for LTBI infection should be the priority, as a majority of active TB in foreign-born people in low-incidence countries occurs from reactivation of LTBI, acquired years earlier in their country of origin.<sup>2</sup>

The primary care organization recommendations for dealing with the issue of latent tuberculosis include systematic latent tuberculosis testing for immigrants. The requirements of inclusion for systematic latent tuberculosis testing are that an individual must be between ages of 16 to 35 and belong to a country where the TB incidence is  $\geq$ 150 per 100, 000 or SSA. Similarly, if a person visits a nation with a high TB incidence and stays there for at least six months, they are also eligible for screening.<sup>51</sup> It is anticipated that persons with reactivated TB would be identified and future transmission will be prevented by this comprehensive LTBI testing. The diagnostic test used is the Mantoux test also known as TST. However, diagnosis with TST becomes challenging if a person is vaccinated against TB. Hence, IGRA test is recommended to diagnose latent TB in those subjects.<sup>51</sup> The same screening protocol for LTBI is followed in the Netherlands except that both tests are recommended at the same time, ie, an initial TST followed by an IGRA if TST reaction is more than 5mm.<sup>54</sup> Taking into account the cost-effectiveness of systematic latent TB testing, Pareek et al study concluded that the majority of immigrants with LTBI could be identified, which will prevent future active TB cases and restrict forward infection transmission in the UK (Pareek et al, 2011).

The treatment policy for active TB includes a combination course of antibiotics. As per standard therapy, six months of isoniazid and rifampicin are advised along with two additional antibiotics (pyrazinamide and ethambutol) for two months during the six-month therapy.<sup>51</sup> On the other hand, latent TB as per NICE guidelines is treated with isoniazid and

rifampicin for three months.<sup>52</sup> This treatment guideline matches other countries' treatment protocols, like the Netherlands. The advised treatment in the Netherlands includes isoniazid/rifampicin for three months' or isoniazid only for six months' or four months' rifampicin.<sup>54,55</sup> Although the treatment protocol is important for the eradication of the bacteria, it is more important that patients should be followed up ensure that they follow the prescribed treatment plan. It is understood that most TB patients feel better after two weeks of taking the drugs and hence stop taking them.<sup>51</sup> In case of failing to complete the course of the TB treatment regime, a serious problem of drug resistance results which is such more challenging to treat.<sup>56</sup> A review conducted to explore the treatment policies of high-income countries reveals that successful treatment completion in the UK was 82.1% compared to 90.7% in the Netherlands.<sup>57,58</sup> It indicates that TB treatment monitoring programs need to play an active role in the UK in order to achieve the goal of eliminating TB from the country.

# Limitations

In this review, methodological heterogeneity was noted among the included studies, particularly with regard to study design, sample size, sampling technique, and epidemiological results. These differences make it difficult to compare and interpret different studies. Although there have been a number of rigorous studies conducted specifically on immigrants, this review discovered that research is frequently based on data from pre-entry screening, registered immigrants, and TB surveillance, which may omit a significant portion of the immigrant population and may not be representative of the immigrant sub-population. For instance, undocumented immigrants were not represented in the included studies, and these people may be at high risk of TB and face significant barriers to care.

Furthermore, the absence of clear stratification between pulmonary and non-pulmonary TB resulted in difficulty in understanding the site of disease among the immigrants, as studies report TB disease as a whole. It was observed that most of the studies that reported the sites of the diseases failed to report their prevalence based on the origin of the immigrants. Thus, it was not possible to establish a population that is at greater risk. Finally, the review was conducted based on the PubMed and EMBASE databases. It is possible that a different result would have been yielded if more than two databases were included.

# Conclusions

This review concludes that the reported prevalence of TB among immigrants over the data collection period shows promising findings and can be interpreted as a success of control and prevention in the UK. However, the UK still faces many obstacles that must be overcome in order to provide better care for immigrants, including a lack of professional confidentiality concerns, fears of social stigma and rejection due to illness, fears of immigration consequences due to disease diagnosis, a lack of knowledge about the screening and treatment process, and communication issues caused by language barriers, among others.

What is obvious is that targeted strategies are required among underserved or marginalized groups to increase the uptake of TB screening, including removing obstacles to receiving free statutory health services upon arrival in the UK and fostering full and meaningful access. To combat the high rates of TB in London and other major cities, Public Health England recently launched the Collaborative Tuberculosis Strategy, which targets high-risk immigrant groups in England for latent TB testing.

# **Recommendations**

A comprehensive strategy that includes TB infection screening and treatment is required to address the disease burden in this population. However, because of a higher chance of exposure to infectious cases in the UK or when returning to their country of origin, immigrants will continue to be at a higher risk than those who were born in the UK. This risk would not be entirely eliminated by including latent TB screening at some point, so a more thorough strategy should be investigated. Instead of concentrating only on TB, this strategy could include better integration between pre-entry screening and health services provided after arrival, as well as appropriate delivery of health care and TB improvement programs. Additionally, the prevention of TB depends heavily on policies that promote the inclusion of these populations. These policies should not only render awareness about TB and reduce stigma among the immigrants, instead include the

protection of immigrant data policy, so that immigrants could be diagnosed and treated without revealing their names and not fear of being reported to police or migration officials. Therefore, given the well-documented difficulties immigrants face in accessing health services once they arrive in the UK, such an approach would be appreciated.

# Abbreviations

BCG, Bacillus Calmette-Guérin vaccine; GP, General Practitioner; IGRA, Interferon-gamma Release Assay; IOM, International Organization for Migration; JBI, Joanna Briggs Institute; LTBI, Latent Tuberculosis Infection; MDRTB, Multi-Drug-resistant TB; NHS', National Health Service; NICE, National Institute for Health and Care Excellence; PCO, Primary care organization; PPD, Purified protein derivative; PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analysis Statement; SSA, sub-Saharan Africa; TB, Tuberculosis; TST, Tuberculin Skin Test.

# **Data Sharing Statement**

The data that support the findings of this study are available from research ethics committee of Maastricht University with the registered code of i6245882, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors and the mentioned committee upon reasonable request and with permission of Uzair Ahmad Saleem and Hedaytullah Ehsan.

# **Ethical Approval and Guidelines**

Prior to the start of this study, the research protocol was submitted for review to research ethics board of Maastricht University. This committee usually consists of qualified experts who transparently provide comment, guidance, and approval of research. This study was supervised and confirmed based on the ethical principles (10 specific principles of Helsinki; scientific requirements and research protocols, informed consent, privacy and confidentiality, research registration and publications, and so on) of this committee.

The supervision and registration of this study within the research ethics committee of Maastricht University was done (code: i6245882) by Professor Dr. Elena Ambrosino. Therefore, we would like to thank our study advisor Dr. Elena Ambrosino for always being there and providing guidance throughout the study period. She allowed this study to be our own work but steered us in the right direction with her valuable feedbacks.

# **Consent for Publication**

There are no limits or ethical concerns for publication because this is a systematic review and not original research. Additionally, the research committee of Maastricht University evaluated this manuscript and after evaluating and making changes, the committee approved its publishing. So, all of them gave their consent for publication.

# Acknowledgment

First and foremost, I am thankful to Almighty ALLAH for giving us the strength, knowledge, ability and opportunity to undertake this study and complete it.

Secondly, we would like to thank my thesis advisor Dr. Elena Ambrosino for always being there and providing guidance throughout the study period. She allowed this study to be our own work but steered us in the right direction with her valuable feedbacks.

# Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

# Disclosure

We have read and understood the journal policy on declaration of interests and declare that we have no competing interests.

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