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Outcomes from a national screening program for Ukrainian refugees at risk of drug resistant tuberculosis in Wales

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ABSTRACT

High rates of drug-resistant tuberculosis in Ukraine suggest screening is necessary to mitigate public health hazards for host populations. A pathway was implemented in Wales and data prospectively collected Between 8 April and 21 December 2022. Of 5425 Ukrainian arrivals, notifications were received by TB teams on 2395 (44%) of whom 1955 (82%) were screened. The refugees were young (median age 30, IQR 14–41), and predominantly female (66.1%). Interferon-gamma release assay (IGRA) tests were positive in 112 (6.5%). One Case of active tuberculosis was identified (0.05%). Our data supports European guidelines that routine screening of this population is not recommended, but we remain uncertain as to the risks of this population going forwards.

METHODS

Prospective observational study of Ukrainian refugees arriving in Wales from April until 21 December 2022.

Data collection

Data on Ukrainian arrivals to Wales were provided from the Home Office/Welsh Government Ukraine sponsorship Scheme. However, this did not include Ukrainians arriving through more informal routes such as the family settlement scheme.

Data collected on arrivals between 8 April and 21 December 2022 included; age, sex, date of arrival, the presence of symptoms suggestive of TB and the results of tests (chest radiograph, interferon-gamma release assays (IGRA) and mycobacterial culture sensitivities). All tests were labelled with a specific Ukrainian signifier to aid data collection. Chest radiographs were reported by radiology departments in each Health Board (HB). Data was inputted by TB screening teams in each HB onto an online data dashboard.

Guideline development and implementation

A TB screening guideline was developed by senior clinicians using a standard format (figure 1) and launched on April 8 2022. Briefly, the expectation was that screening would be undertaken by TB teams and/or welcome centres in each HB. All TB teams attended a webinar on the pathway which was also disseminated to primary care through a digital framework as previously described.⁹ The guideline was changed on 5 August to only screen children under 11 who were symptomatic or close contacts of active TB cases.

Outcomes

The primary outcome was identification of cases of active or latent tuberculosis.

Statistical analysis

Continuous variables are presented as median and inter-quartile range. Differences between ages were assessed using the Wilcoxon rank sum test. Differences between sexes were assessed using Fishers exact test. The confidence intervals for the age and sex specific rates used the Wilson method. All analyses were conducted in Stata 17.0.

INTRODUCTION

As of 10 January 2023, the war in Ukraine has resulted in 4.9 million Ukrainian refugees in Europe, including 1.5 million in Poland, 1 million in Germany and 155 000 in the UK.¹ This upheaval has produced significant traumas for the Ukrainians involved, but also presents public health issues for the host nations. TB incidence rates in the Ukraine are moderately high at 71 (CI 47 to 100)/100,000,² but of more concern is the fact that Ukraine has rifampicin-resistant TB (RR-TB) rates of 25 (CI 16 to 35)/100,000 with 24% of all new cases and 58% of those previously treated being multi-drug resistant (MDR-TB).³ Evidence suggests that the burden of drug resistant TB is higher in the east of the country⁴ and associated with HIV co-infection.^{3 5} In view of these facts, concerns were raised about the risk of housing refugees in host families without an adequate TB screening programme.

In England, routine screening including chest radiographs was recommended for those more than eleven years old,⁶ to identify those with pulmonary TB who could pose an infection risk to host families. By contrast, European Centre for Disease Control (ECDC) guidelines recommended screening only those in high risk groups.⁷ Wales implemented a more comprehensive screening programme utilising a digital implementation framework,⁸ which has been used successfully to implement a national COVID-19 guideline.⁹



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All Wales Management of Refugees at risk of Drug-Resistant Tuberculosis



Current version: 1.2

CORE PRINCIPLES

Asylum seekers and refugees are at high-risk of reactivation of Tuberculosis. Early screening, particularly to detect active TB, is vital to exclude ongoing transmission and ensure treatment success.

Assessment and management should be delivered by designated TB teams within each health board.

DID YOU KNOW?

Ukraine has one of the highest rates of Multi Drug-Resistant Tuberculosis in the world.

The humanitarian crisis in Ukraine has prompted the arrival of refugees into the UK, resulting in an impending public health situation.

Find out more from the TB clinical lead for Wales



STEP 1: ASSESSMENT

Symptom checklist

- ☒ Cough
- ☒ Fever
- ☒ Weight loss
- ☒ Night sweats

History checklist

- ☒ Past history of TB (especially recent treatment interruption due to conflict)?
- ☒ BCG vaccination status?
- ☒ Risk of drug-resistant TB? ¹
- ☒ Nutritional status?
- ☒ Immunosuppression?

STEP 1 INFORMATION ASSESSMENT

1 Risk of drug-resistant TB

- Known household contact of drug-resistant TB
- HIV+, IVDU or Hep C+
- History of prison
- Failure to complete previous TB treatment

STEP 2 INFORMATION INVESTIGATE

1 BBV Test

- HIV test
- HCV antibody
- Hep B sAg

STEP 2: INVESTIGATE (all patients)

Age <11 years

If asymptomatic, no investigations

Only screen if symptomatic or if positive parent/ close contact

Age ≥11 years, or <11 years with symptoms

Bloods (IGRA, BBV ¹, LFT, FBC, Vit D) and Chest x-ray (in pregnancy, avoid CXR unless symptomatic)

STEP 3: MANAGE

IGRA or TST (-ve) and Normal CXR and asymptomatic

INFORM AND ADVISE DISCHARGE

IGRA or TST (+ve) and Normal CXR and asymptomatic

CONSIDER LATENT TB INFECTION ¹

Initiate 3-months Rifampicin and Isoniazid unless contact of drug resistant TB

IGRA or TST (+ve) and Normal CXR and symptomatic

CONSIDER NON-PULMONARY ACTIVE TB

Urgent clinical review by TB service and further investigations (samples for TB culture)

Abnormal CXR with/without symptoms

INVESTIGATE FOR ACTIVE TB

Send 2x Sputa for TB smear, PCR (using code UKR2022) and culture to determine sensitivity to Rifampicin

STEP 3 INFORMATION MANAGE

1 LATENT TB INFECTION

Inform and advise patient

Collect sputum if productive

Initiate 3-months Rifampicin and Isoniazid unless contact of drug resistant TB

Follow-up every 6 months for 2 years

1 TB IN CHILDREN

Make every effort to get a microbiological specimen in children

Babies need to be seen by a specialist as a matter of urgency

Please discuss any patients <16yrs who are being investigated for Active TB with paediatric ID in UHW, or the tertiary ID services in Alder Hey (in BCUHB)

Find out more about TB in children here



Determine drug sensitivity

RIFAMPICIN SENSITIVE

Start standard WHO Quadruple therapy
Wait for full sensitivities
Admit to local hospital as appropriate
Discuss in MDT if concerns

RIFAMPICIN RESISTANT

Assume MDR/XDR-TB
Refer to hospital with negative pressure rooms
Inform Public Health
Follow WHO Guidelines

BBV: Blood borne virus screen
CXR: Chest x-ray
ID: Infectious diseases
IGRA: Interferon Gamma Release Assay
LTBI: Latent TB infection
MDR: Multi-drug resistant
TST: Tuberculin Skin Test
XDR: Extensively-drug resistant

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Designed by The Institute of Clinical Science & Technology

Figure 1 All Wales pathway for screening refugees at risk of drug resistant tuberculosis.

Table 1 Health Board, demographic and IGRA positive rates

Health Board	Number	Age (M, IQR)	Age<18 years (%)	Female (%)	IGRA+ (%)
1	572	31 (14–41)	174 (30.4)	350 (61.2)	25 (4.4)
2	360	32 (18–41)	89 (24.7)	221 (61.4)	24 (7.3)
3	340	26 (11–40)	133 (39.1)	242 (71.2)	24 (9.2)
4	112	29.5 (16–41)	33 (29.5)	78 (69.6)	5 (4.5)
5	46	36 (28–41)	3 (6.5)	41 (89.1)	1 (2.2)
6	519	29 (10–41)	203 (39.1)	356 (68.6)	31 (8.0)
Not recorded	6	33 (23–56)	1 (16.7)	4 (66.7)	2 (33.3)
All Wales	1955	30 (14–41)	636 (32.5)	1292 (66.1)	112 (6.5)

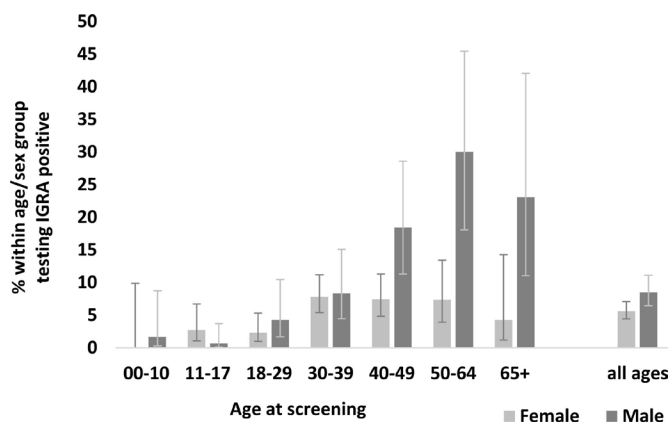
RESULTS

2395 cases were screened by the TB teams and data inputted into the online tool. 118 cases were excluded due to missing data on sex or age, leaving 2277. A further 322 cases were excluded as they did not record chest radiograph and IGRA data on those 11 or older, leaving 1955 cases for analysis (online supplemental figure). The majority of arrivals were women (1292, 66.1%), and most arrivals of both sexes were young (median age 30 IQR 14–41), [table 1](#).

There were 112 positive IGRA tests giving a latent TB rate of 6.5%. 96 IGRA tests were done in children under 11 before the guideline changed and only one of these was positive. Those with positive IGRA results were older (median age 40.5, IQR: 35–50) than those with a negative test (median age 33, IQR: 18–42), ($p<0.001$), and more likely to be male, 42% vs 31.7%, ($p=0.03$). There were quite different patterns of IGRA positive rates between the sexes with over a quarter of all males 50+ testing positive, compared with just one in 20 females aged 50+ ([figure 2](#)). Overall, 93% (104/112) of IGRA positive cases were aged less than 65 and thus would potentially qualify for Latent TB treatment. One asymptomatic case had an abnormal chest radiograph and underwent bronchoscopy. Washings confirmed smear negative, fully sensitive mycobacterium tuberculosis. No other chest radiographs were reported as suggestive of tuberculosis.

DISCUSSION

We present the results of screening 1955 Ukrainian refugees for tuberculosis in Wales. The lack of data on precise arrival time or location, together with the fact that many arrived through informal routes highlights the difficulties of the screening

**Figure 2** Latent TB cases (IGRA+) by age and sex.

process. It is of interest that the ECDC guidelines did not recommend routine screening of this population, although a number of European countries did in fact implement screening programmes.

The strengths of this study are; first, that we implemented a national screening pathway which all screening teams were familiar with. Second, to our knowledge, this is the first analysis of the outcomes of screening this population. The low rate of positive results with a single case of pulmonary TB who was of low infectivity supports the ECDC guidelines that routine screening is not recommended. It is of interest that those with Latent TB infection (LTBI) were significantly older and more often male, so our findings are likely to underestimate LTBI rates in the country as a whole as our population was predominantly female and young. Recent UK screening of refugees from Afghanistan found LTBI rates of 15% among adults.¹⁰

The major limitations of this study relate to the lack of precise data on arrivals. TB teams received notifications on 44% and screened 36% of all arrivals, highlighting significant missing data. However, comparison of the study population to the total arrivals data indicated no substantive demographic differences.¹¹ Second, data on where in the Ukraine arrivals came from was not collected, so we cannot compare latent TB infection rates between the east and west of the country. Third, a large number of individuals aged over 11 (322) were excluded from the analysis due to failure to undergo an IGRA or chest radiograph. Lastly, the guideline was changed to no longer recommend screening asymptomatic children under 11 years, partly as a result of frequent refusals from parents to screen their children whom they believed were healthy. The low rates of positive IGRA tests in those under 11 who were screened (1/96) suggests that they were right.

While our results support the European guidelines that routine screening is not recommended, we remain uncertain of the risks for this population going forwards. The majority of TB cases have always been from the east of the country, and the trauma of war creates the perfect conditions for the spread of this disease. Moreover, the WHO goal of TB eradication will only be achieved by identifying and treating latent TB, ultimately necessitating screening of populations such as this.

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Contributors SMB conceived the screening guideline and data collection tool and wrote the first draft of the paper with contributions from TDB. GD performed all of the statistical analysis and had substantial input into the key arguments. CD created the guideline and data tool and HS coordinated implementation of the guideline and data collection. GH and JS provided overall denominator data. All other co-authors were involved directly with both the screening process and with data acquisition

across Wales and contributed to intellectual content. All authors critically revised and approved the final version.

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