High Risk for transmission inside prison and to the community

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The WHO Europe good practices in the prevention and care of tuberculosis in correctional facilities[1] published earlier this year highlights some promising practices for prevention, diagnosis and treatment of tuberculosis (TB). The case studies of promising practices range from low to high incidence settings (Denmark to India and Russian Federation) and in wide range of economic contexts from low to high- income countries. According to the report an estimated one in 16 of the new TB cases notified in the WHO European Region occur in the penitentiary system. Overall, the TB notification rate in correctional facilities in 2016 was 958 per 100,000 population (based on data from 27 Member States in the Region), over 30 times higher than in the general population. The ratio of 20-30 is consistent with studies from other countries[2–4].

In addition, it is estimated that TB in inmates contributes 6-9% of active TB in the community[2]. Lower treatment success rate of new and relapsed TB cases treatment in prisons in 2015 was only 59.7% versus 77.2% in general population and these lower completion rates may impact transmission in prison and to the community at large[1].

The many interventions presented in the examples within the document highlight the need for minimal requirements and a standardized approach to TB screening and management in prisons. The two key points we would like to highlight are the systematic screening for latent tuberculosis infection (LTBI), and early diagnosis of all forms of TB and universal access to drug-susceptibility testing (DST), including with rapid tests and diagnostic testing for documentation of treatment success and molecular epidemiology.

Systematic screening for active and LTBI: Most of the case studies in the report provide no details regarding the symptoms (duration and definition) that prompt diagnostic testing for active TB[1]. The duration of respiratory symptoms, specifically a cough lasting 15 days or more is frequently used as the trigger for further investigations.

We have been working in prisons to study active and latent tuberculosis since 2010[5–8] and found:

1. TB incidence in prisons is 8 to 20 times greater than in general population (Our study: 500 cases/100,000 prisoners compared to general population: 72 cases/100,000 inhabitants), **therefore TB should be considered in people with lower respiratory symptoms of any duration** (25% of people with active TB had less than 15 days of respiratory symptoms)[5] and **it is crucial to culture for TB diagnosis to all people with lower respiratory symptoms**, ideally with rapid culture for TB diagnosis and follow-up[6]. We defined lower respiratory

symptoms as a person who presents a cough of any duration and/or expectoration, and abnormal breath sounds on lung auscultation. The fact that we found that 25% of TB cases had less than 15 days of respiratory symptoms (despite the absence of immunosuppression), of whom 66.7% were sputum-smear positive and presumably highly infectious, questions the validity of using the two-week criterion for screening individuals for TB in such a high-risk setting like prisons[5].

2. A **higher prevalence of latent TB infection in prisoners** (77.6%) compared to general population[7]. The prevalence of TST positivity among household contacts of pulmonary TB patients in a study conducted in Medellin, Colombia between 2005 and 2006 was 65.9%; in the source population, this was 42.7%[9].
3. **High incidence of LTBI in prisoners**: we found higher conversion of latent tuberculosis infection within 2 years (Incidence: 29.5%) compared to other high risk like we show in table 1. Among 129 prisoners with an initial negative TST by two-step administration, 10 individuals developed active TB during two years of follow-up, of these nine were new TST converters (TB incidence rate in those TST negative: 6976/100,000 prisoners). The numbers needed to screen to detect a new LTBI case for 2 years was 3.4, and the number needed to screen to detect an active TB case among TST converters was 14.3[8].

Table 1. Prevalence of LTBI and active TB incidence among selected medium to high risk predisposing conditions.

Risk group	Prevalence of LTBI	TB incidence /100,000
Diabetes mellitus[1]	28.2% a 42.4%	7.4 a 32 cases
Children <15 years[2]	3.5% a 47.5%	388 a 721 cases
Healthcare workers[3]	33% a 79%	67 a 5780 cases
HIV[4]	16.8% a 76%	121 a 151 cases
Prisoners[5]	53.3% a 87.6%	61 a 6799 cases

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Early diagnosis of all forms of TB and universal access to drug-susceptibility testing (DST), including with rapid tests, diagnostic testing for documentation of treatment success and molecular epidemiology. The WHO Europe good practices in prisons included the report of three strategies in Azerbaijan, Brazil and United Kingdom. In Azerbaijan mass screening with mandatory questionnaire surveys were implemented, chest-x rays, sputum examinations with liquid cultures like the BACTEC mycobacteria growth indicator tube 960 system for first and second line drug, GenXpert and line probe assays detection for drug susceptibility for first and second line drugs, resulting in increased rates of bacteriological confirmation from 55% to 98%

of among new pulmonary TB cases in the penal system in Azerbaijan between 2011 and 2015, and from 68% to 85% for retreated cases. United Kingdom implemented multiple activities including evaluation of the TB services, training all people incarcerated and those working inside prison to identify early symptoms of TB, TB control and infection prevention, early contact screening approach, mobile digital chest x-rays to be used for case-finding during outbreaks, and whole genome sequencing to investigate clusters and transmission patterns. The strategy led to 'far higher proportion of LTBI' identified, and the mobile x-ray helped to identify early TB cases[1]. Those experiences highlight the importance of the implementation of multiple strategies to control and prevent TB transmission.

In addition to those strategies, in our studies we found:

4. **Induced sputum is safe and easy to obtain** when prisoners do not spontaneously produce sputum, without transfer prisoners to hospitals or other high complexity institutions[6].

5. Our data demonstrate that patients receiving adequate anti-TB treatment remain infectious for prolonged periods, **suggesting that the duration of isolation should be guided by liquid cultures to decrease or minimize the exposure of prisoners to positive TB cases**: Long interval between TB treatment initiation and conversion to negative sputum by culture and smear. Culture conversion by sputum smear: Negative sputum smear: 33 days (IQR: 29.9 – 36.2), 1+ sputum smear: 62 days (IQR: 47.4 – 76.6), 2+ or 3+ sputum smear: 63 days (IQR: 60.3 – 63.7)[5].

6. In a study of all TB cases diagnosed between 2010 and 2012, and during follow-up for two years, genotyping (using mycobacterial interspersed repetitive units) of strains demonstrated that 19% of pulmonary TB cases were acquired inside prisons, 3.1% reinfection, 9.4% mixed infection, and 3.1% relapse (Article submitted). The remaining individuals arrived to prisons from places where the TB incidence is high, many represent *M. tuberculosis* acquired outside prison and developed active TB while incarcerated. This suggests that events leading to and during incarceration may be associated with risk of developing active disease, and therefore it is mandatory to implement infection prevention measures to control TB transmission.

7. Well-established TB program, with assessment at the end of TB treatment is associated with successful treatment completion and good treatment outcomes (88.9% of patients were successfully cured, 6.94% were released and lost to follow-up, 2.78% discontinued the treatment, 1.39% patient died (HIV and disseminated TB)[5]. Collaborative activities within prison and healthcare authorities and transfer of care to guarantee the completion of TB treatment is required.

8. Contact tracing among visitors coming in contact with individuals diagnosed with active TB yielded 3 secondary TB cases outside the prison[5]. This mechanism of spread to the community is of paramount importance and needs resources allocated in order to track.

Suggestions based on our results:

The management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries[10] divided the systematic testing and treatment of LTBI to three groups: Highest risk- where LTBI should be performed. This group includes, but is not limited to the following: people living with HIV, adult and child contacts of pulmonary TB cases, persons initiating anti-TNF-alpha treatment. The second group- where LTBI testing should be considered includes: prisoners, healthcare workers, immigrants from high TB burden countries, homeless persons and illicit drug users. Unfortunately, the 2018 Latent TB Infection: Updated and consolidated guidelines for programmatic management guidelines[11] retained the recommendation for LTBI stating "In countries with a low TB incidence, systematic testing for and treatment of LTBI may be considered for prisoners, health workers, immigrants from countries with a high TB burden, homeless people and people who use illicit drugs".

Based on the very high rates of LTBI and the risk of active TB along with the high risk for spread within the confines of prison- we recommend adding incarceration to the group of conditions that should prompt LTBI screening.

Individuals who test negative on LTBI screening at the time of entry to prison represent a group of susceptible individuals. We have demonstrated very high rates of *M. tuberculosis* acquisition during a 2 year follow up (29.5%)[8]. The number needed to screen in order to find a transmission event was 3.4 and in order to identify active TB it was 14.3. The findings suggest that repeated screening of individuals with negative initial TB screening may represent an intervention with a potential to limit the spread of TB in prisons.

Symptomatic screening should include an entry questionnaire assessing the presence of risk factors for TB including prior incarceration, prevalence of TB at the home community, contact with TB in conjunction to body mass index (BMI) measurement. Screening for respiratory symptoms of any duration is suggested as we have documented one out of four individuals with active TB to have symptoms present for less than 2 weeks. Our proposal is summarized in the Figure 1.

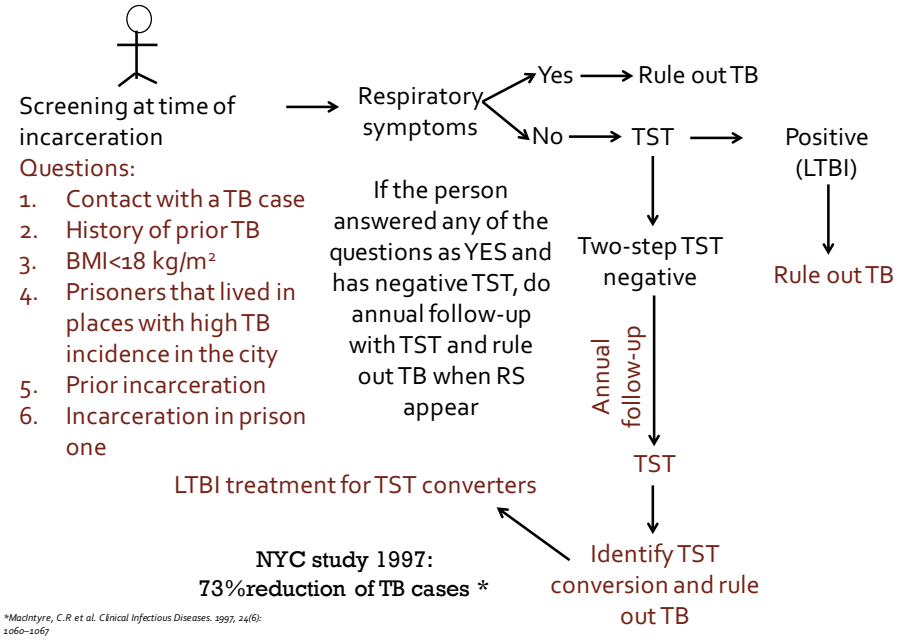

Figure 1. Summarizes our recommendations for screening. A questionnaire at the time of entry to prison along with screening for respiratory symptoms should be used to trigger testing. Repeated annual testing for those with initial negative LTBI screen should be offered and convertors prioritized for therapy.

Finally, we found long duration of smear and culture positivity among treated active TB. The findings suggest that the duration of respiratory isolation should be extended until culture negativity is confirmed in order to decrease transmission within the prisons.

In Conclusions:
Prisons have high prevalence of LTBI and incidence of active TB. The conditions in prisons are conducive to transmission and serve as amplifiers of TB transmission within and outside of the prison. The risk is frequently higher than the WHO high risk conditions and therefore we suggest that screening should be mandatory. Prisons also present an opportunity to treat LTBI in individuals that will be difficult to reach upon return to the community at the end of sentence. Individuals that have negative results of initial screening at the time of incarceration represent high risk for *M. tuberculosis* acquisition and should therefore be screened annually. Improving risk assessment and respiratory symptom screening are important in order to achieve control of TB transmission. Long duration of infectivity suggests that discontinuation of respiratory isolation after on TB treatment should be dictated by the results of culture.

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