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Oral swab testing by Xpert® MTB/RIF Ultra for mass tuberculosis screening in prisons

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ABSTRACT

Diagnosis of pulmonary tuberculosis is usually achieved by testing sputum for presence of *Mycobacterium tuberculosis* by microscopy, culture or nucleic acid amplification tests. However, many individuals are unable to produce sputum, particularly early in the course of illness. Studies have reported that oral swabs, assayed by nucleic acid amplification tests, may be a suitable substitute or complement to sputum testing. To determine whether this method could be useful of case finding, in which bacillary load is often lower, we evaluated it in the setting of a mass tuberculosis screening study in prison inmates in Brazil. For this sub-study, we enrolled 128 individuals with pulmonary tuberculosis confirmed by sputum Xpert testing, and 128 controls who tested negative by sputum culture and Xpert. We collected two oral swabs by participant, prior to starting treatment. Swabs were collected from the tongue by brushing along the surface for 10 times. The sensitivity of a single oral swab was 43% (N = 55/128; 95% CI: 34–52%). Using two consecutive oral swabs the sensitivity increased to 51% (N = 66/128; 95% CI: 43–60%). The specificity was 100% (128/128). In participants with high mycobaterial load in the sputum, the combined sensitivity was 90% (N = 9/10). In the participants with medium mycobaterial load in the sputum, the combined sensitivity was 79% (N = 23/29). In the participants with low or very low mycobaterial load in the sputum, the combined sensitivity was 38% (N = 34/89). Our data suggest that oral swab sampling, assayed by Xpert, has comparable sensitivity to sputum in participants with high and medium mycobacterial load in the sputum. However, 70% (89/128) of individuals identified through our mass screening study (Carbone et al.) had detection number low or very low in their sputum. In this population, oral swab testing may not have sufficient sensitivity as currently performed. Further studies are needed to identify alternative non-sputum sampling strategies in this population.

Diagnosis of pulmonary tuberculosis is usually achieved by testing sputum for presence of *Mycobacterium tuberculosis* by microscopy, culture or nucleic acid amplification tests.

However, many individuals are unable to produce sputum, particularly early in the course of illness. In our studies[1] of mass screening among inmates in Brazil, we have high prevalence of undiagnosed active tuberculosis; however, two-thirds of individuals are unable to produce sputum for testing.

The World Health Organization has identified non-sputum based diagnostic tests as a key priority for diagnostic development. Studies have reported that oral swabs, assayed by nucleic acid amplification tests, may be a suitable substitute or complement to sputum testing [2,3,4]. One recent study found that two orals swabs had equivalent sensitivity as a sputum sample [5]. To determine whether this method could be useful in case finding, in which bacillary load is often lower, we evaluated it in the setting of a mass tuberculosis screening study in prison inmates in Brazil.

This study was approved by Federal University of Grande Dourados

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Table 1
Sensitivity of oral swab testing with Xpert® MTB/RIF Ultra compared with sputum Xpert® MTB/RIF copy number classification.

Sputum Xpert MTB/RIF copy number classification	Detected by one oral swab (%)	Detected by two oral swabs (%)	Mean number of symptoms[a] (± SD)
High	9/10 (90)	9/10 (90)	4.1 (± 2.7)
Medium	22/29 (76)	23/29 (79)	3.0 (± 2.6)
Low	16/60 (27)	23/60 (38)	2.4 (± 2.4)
Very Low	8/29 (28)	11/29 (38)	2.6 (± 1.9)
All	55/128 (43)	66/128 (51)	2.7 (± 2.3)

[a] Tuberculosis symptoms according to World Health Organization guidelines: cough, expectoration, fever, night sweats, weight loss, recent loss of appetite, chest pain, and dyspnea.

of Institutional Review Board. Between 2017 and 2018, inmates from the three prisons in Brazil were screened for tuberculosis by symptom assessment, chest radiography, sputum testing by Xpert® MTB/RIF 4th generation and culture. This sub-study was performed between April and September of 2018 we enrolled 128 individuals with pulmonary tuberculosis confirmed by sputum Xpert testing, and 128 controls who tested negative by sputum culture and Xpert. Two oral swabs were collected by participants. The first swab was collected prior to starting treatment and the second was collected the next day. Swabs were collected from the tongue by brushing along the surface for 10 times. Swabs were stored in ependorf with 700 uL sterile lysis buffer for 24 h at room temperature, and analyzed on Xpert Ultra assay. The second specimen was stored in a −80°C freezer for up to 12 weeks and then retested. Threshold-cycle (Ct) of multiple probes targeting the *rpoB* gene was used to estimate mycobaterial load. From that, the Xpert MTB/RIF Ultra quantifies the mycobacterial load as high, medium, low, and very low.

The sensitivity of a single oral swab was 43% (N = 55/128; 95% CI: 34–52%). Using two consecutive oral swabs the sensitivity increased to 51% (N = 66/128; 95% CI: 43–60%). The specificity was 100% (128/128). In participants with high mycobaterial load in the sputum, the combined sensitivity was 90% (N = 9/10). In the participants with medium mycobaterial load in the sputum, the combined sensitivity was 79% (N = 23/29). In the participants with low or very low mycobaterial load in the sputum, the combined sensitivity was 38% (N = 34/89) (Table 1).

Studies suggest that oral swabs have comparable sensitivity to sputum testing by Xpert in individuals diagnosed with tuberculosis [5]. Oral swabs enable sampling in individuals who cannot provide sputum and potentially reduce bioaerosol hazards during collection. However, these studies did not report results stratified by mycobaterial load.

Our data suggest that oral swab sampling, assayed by Xpert, as comparable sensitivity to sputum in participants with high and medium mycobacterial load in the sputum. However, 70% (89/128) of individuals identified through our mass screening study [6] had detection number low or very low in their sputum. In this population, oral swab testing may not have sufficient sensitivity as currently performed. Further studies are needed to identify alternative non-sputum sampling strategies in this population.

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