

## Added value of bleach sedimentation microscopy for diagnosis of tuberculosis: a cost-effectiveness study

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### SUMMARY

**SETTING:** Bleach sedimentation is a method used to increase the diagnostic yield of sputum microscopy for countries with a high prevalence of human immunodeficiency virus (HIV) infection and limited resources.

**OBJECTIVES:** To compare the relative cost-effectiveness of different microscopy approaches in diagnosing tuberculosis (TB) in Kenya.

**METHODS:** An analytical decision tree model including cost and effectiveness measures of 10 combinations of direct (D) and overnight bleach (B) sedimentation microscopy was constructed. Data were drawn from the evaluation of the bleach sedimentation method on two specimens (first on the spot [1] and second morning [2]) from 644 TB suspects in a peripheral health clinic. Incremental cost per smear-positive detected case was measured. Costs included human resources and materials using a micro-costing evaluation.

**RESULTS:** All bleach-based microscopy approaches detected significantly more cases (between 23.3% for B1 and 25.9% for B1+B2) than the conventional D1+D2 approach (21.0%). Cost per tested case ranged between respectively €2.7 and €4.5 for B1 and B1+D2+B2. B1 and B1+B2 were the most cost-effective approaches. D1+B2 and D1+B1 were good alternatives to avoid using approaches exclusively based on bleach sedimentation microscopy.

**CONCLUSIONS:** Among several effective microscopy approaches used, including sodium hypochlorite sedimentation, only some resulted in a limited increase in the laboratory workload and would be most suitable for programmatic implementation.

**KEY WORDS:** tuberculosis; microscopy; diagnosis; cost-effectiveness

DESPITE its low sensitivity, direct sputum smear microscopy remains the cornerstone of tuberculosis (TB) diagnosis in limited-resource countries.<sup>1</sup> More sensitive methods, such as *Mycobacterium tuberculosis* culture, are only available in referral TB laboratories. Although several promising diagnostic tests are in the development pipeline, very few are likely to be suitable replacements for smear microscopy and none in the short term. Alternatively, smear microscopy can be optimised using light-emitting diode (LED) based fluorescence microscopy to increase sensitivity and reduce laboratory workload, and specimen processing methods prior to smear microscopy.<sup>2-8</sup> Proposed specimen processing methods include bleach digestion of sputum, followed by a specimen concentration step, such as centrifugation or sedimentation.<sup>2,9</sup> The latter has the advantage of being suitable for any laboratory setting.

In a previous study, we compared smear-positive case detection after overnight sedimentation of sputum specimens treated with sodium hypochlorite (NaOCl)

with conventional direct smear microscopy among pulmonary TB (PTB) suspects in a peripheral health clinic in Kenya. We reported a significant increase of 23%.<sup>10</sup> The study concluded that overnight NaOCl sedimentation could be an affordable method for improving TB diagnosis in microscopy laboratories. Nevertheless, this method has several limitations, such as the one-day delay in obtaining microscopy results due to overnight sedimentation, variations in quality of NaOCl across countries (including stability, depending on storage conditions) and the increase in laboratory workload. The increased workload might be a serious limitation in countries with a high human immunodeficiency virus (HIV) burden already facing a human resources crisis in their health services.<sup>2,10</sup>

Using the data from this prospective field evaluation conducted in Kenya, we measured the cost-effectiveness of different diagnostic approaches combining direct smear and smear after overnight NaOCl sedimentation based on their smear-positive detection yield and their health service costs. Data from a

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recent unpublished study conducted in the Mindouli, Republic of Congo, were used to test the robustness of the model.

## METHODS

We constructed four analytical decision tree models including the cost and effectiveness measures of different smear microscopy combinations of direct Ziehl-Neelsen (ZN) smear microscopy (D) and ZN smear microscopy after overnight NaOCl sedimentation (B) to diagnose PTB. The first specimen was collected on the spot at the clinic at the time of the first consultation (1), while the second was an early morning specimen collected the next day at home and taken to the clinic on the same day (2). The first model evaluated all potential combinations and included only health service costs. In the second model, the approaches exclusively based on smear microscopy after NaOCl sedimentation were excluded (B1 and B1+B2). The third and fourth models were identical to the two previous models, with the addition of patient transport costs to reflect patient access to the diagnostic centre.

The models used source data from the prospective field evaluation of smear microscopy after overnight NaOCl sedimentation among 644 consecutive PTB suspects in an urban health clinic in Nairobi, Kenya.<sup>10</sup> Suspicion of TB was defined by the presence of cough of at least 2 weeks.<sup>11</sup> Table 1 summarises the study method. The different smear microscopy combinations are presented in Table 2.

### Measurement of effectiveness

Effectiveness was measured by the smear-positive detection rate, calculated as the proportion of smear-

**Table 1** Summary of the field evaluation of smear microscopy after overnight NaOCl sedimentation in Mathare, Kenya, and Mindouli, Republic of Congo<sup>6</sup>

|                                   | Mathare  | Mindouli   |
|-----------------------------------|--|--|
| Sites and population              | Urban health clinic<br>644 consecutive TB<br>suspects presenting<br>with cough of<br>>2 weeks<br>50% HIV co-infection  | Referral district<br>hospital<br>280 consecutive TB<br>suspects presenting<br>with cough of<br>≥3 weeks  |
| NaOCl sedimentation method        | Same quantity of 3.5% local NaOCl added to the specimen in 15 ml conical tube<br>Mixture homogenised using a vortex<br>Overnight sedimentation on the bench at room temperature          | Same quantity of 2.6% local NaOCl added to the specimen in 15 ml conical tube<br>Mixture homogenised by hand shaking<br>Overnight sedimentation on the bench at room temperature |
| Definition of smear-positive case | Examination of two sputum specimens<br>First on the spot on the first day of consultation<br>Second at home in morning of the second day<br>One smear-positive result with >1 AFB/100HPF |  |

NaOCl = sodium hypochlorite; TB = tuberculosis; HIV = human immunodeficiency virus; AFB = acid-fast bacilli; HPF = high-power fields.

**Table 2** Smear microscopy approaches

| Approach | Description  |
|----------|--|
| D1+D2    | Standard: direct smear on first specimen and direct on second specimen if the first smear is negative.                                     |
| B1       | Bleach smear on first specimen.  |
| B1+B2    | Bleach smear on first specimen and bleach on second if the first smear is negative.  |
| D1+B1    | Direct smear on first specimen and bleach on first if the first smear is negative.   |
| B1+D2    | Bleach smear on first specimen and direct smear on second specimen.  |
| D1+B2    | Direct smear on first specimen and bleach smear on second if the first smear is negative.  |
| D1+B1+D2 | Direct smear on first specimen, bleach on first and direct on second if the first smear is negative.                                       |
| D1+D2+B2 | Direct smear on first specimen, direct on second if first is negative and bleach on second specimen if second smear also negative.         |
| D1+B1+B2 | Direct smear on first specimen, bleach on first if first smear is negative and bleach on second specimen if second smear is also negative. |
| B1+D2+B2 | Bleach smear on first specimen and direct on second specimen. Bleach smear on second specimen if 2 previous smears are negative.           |

B = bleach smear; D = direct smear.

positive patients detected among the total number of PTB suspects. It was assumed that all smear-positive cases would be treated, which was the case in the clinic where the study was conducted.<sup>12</sup> The inter-reader agreement for microscopy was very high, with kappa values of 0.83 for direct smear and 0.86 for smear after NaOCl sedimentation. External quality control of smear reading showed 99% agreement between the site and the reference laboratory of the Kenyan Research Medical Institute (KEMRI), Kenya.<sup>10</sup> We used the McNemar test for matched data to compare smear-positive detection rates.

### Cost estimates

We adopted a health service provider perspective. The costs were limited to smear microscopy costs in any PTB suspect and did not include the cost of diagnosing smear-negative TB cases or non-TB cases. These costs included the cost of human resources (laboratory technicians), consumables and reagents. A micro-costing approach was used.<sup>13</sup> All the costs were based on the Kenyan market in 2006 and converted from Kenyan shillings to euros (€) using the exchange rate €1 = 90.4 Kenyan shillings.\* The analysis used undiscounted costs.

The cost of human resources was calculated by multiplying the time needed by laboratory technicians to perform analyses (coaching in collecting sputum specimens; preparation and addition of the bleach solution to specimens; smearing, staining and reading the slides) by the cost of 1 min of the working time of a laboratory technician. The cost per min of a laboratory technician working time was based on a monthly

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salary of €600. All data used for this analysis were collected during the feasibility assessment of smear microscopy after overnight NaOCl sedimentation.<sup>10</sup> The consumption of bleach, ZN reagents, small material (slides, tubes and pipettes) and specimen containers were measured during the feasibility assessment.

The number of smears per approach was corrected based on the proportion of cases detected on the first smear (among the 644 PTB suspects) and which did not require a second smear, and on the number of extra smears performed to replace unreadable smears. During the study, respectively 0.2% and 1.9% of direct and bleach smears were unreadable.<sup>10</sup>

Patient transport costs to the clinic were estimated for each approach. A micro-costing approach could not be used because patients' provenance and use of transport were not prospectively assessed. The number of health clinic visits per approach was calculated and multiplied by €1 per visit (return trip), i.e., the mean return transport cost for the population covered by the clinic at the time of the study, based on interview with clinic personnel. The number of visits was corrected based on the proportion of patients already detected as smear-positive on the first specimen.

#### *Cost-effectiveness analysis*

An average cost-effectiveness ratio was calculated for each approach by dividing the total cost of one approach by its measure of effectiveness. Approaches were ranked in order of increasing cost. The model used the least costly as the reference approach. Any approach that was more costly and detected fewer smear-positive TB cases than another approach was considered dominated. The incremental cost-effectiveness ratio (ICER) for each remaining approach was calculated by dividing the additional cost compared to the next most costly approach by the additional benefit (newly detected smear-positive case).<sup>14</sup> The cost-effectiveness analysis was performed using Tree Age Pro® 2004 (Tree Age Software Inc, Williamstown, MA, USA).

#### *Sensitivity analysis*

One-way sensitivity analyses were performed to determine the robustness of the model and the influence of interest variables on its results. Because human resource costs represent an important part of the health service costs of the different smear microscopy approaches, a first sensitivity analysis was performed using variations of the monthly salary of a laboratory technician of between €200 and €1000 per month. To reflect the impact of the increased costs of accessing a TB diagnostic centre, the second analysis doubled the patient transport costs per return trip (€2).

As effectiveness and cost criteria will vary between programmes, a third sensitivity analysis was performed using different effectiveness and cost criteria estimated from another data set. We used recently completed data for a project performed at the referral district hospital of Mindouli in the Pool Region of the Repub-

lic of Congo (unpublished data). This study evaluated a very similar NaOCl sedimentation method among PTB suspects and enrolled 280 patients between October 2006 and March 2008. The smear-positive case definition and the study methodology were similar to those of the Mathare study (Table 1). The cost estimates were based on the same method as that used for the Mathare study, and the monthly salary of a laboratory technician in Mindouli was €200. This analysis did not include patient transport costs.

The National Ethical Review Committee, KEMRI and the Comité de Protection des Personnes, Saint Germain en Laye, France, approved the study. Written informed consent was obtained from the participants.

## RESULTS

#### *Effectiveness measures*

The smear-positive TB case detection rate of each smear microscopy approach for the base-case (Mathare) and the sensitivity analysis (Mindouli) is presented in Table 3. All approaches using the NaOCl sedimentation method significantly detected more cases than the conventional D1+D2 approach. Approaches based on the examination of two bleach smears were found to be most sensitive.

#### *Cost estimates*

The costs of each approach for the base-case and sensitivity analysis are presented per tested case in Tables 4 and 5, respectively. The total health service costs ranged between €1.20 for the approach based on the examination of one bleach smear (B1) at a monthly salary of €200 for a laboratory technician, and €5.65 for the approach combining direct smear of the first specimen and bleach smear of the first and second specimens at a monthly salary of €1000. Between one

**Table 3** Effectiveness criteria (smear-positive case detection rate) per approach for the base-case and sensitivity analyses

| Approach <sup>†</sup> | Base-case analysis<br>(n = 644) |      |                      | Sensitivity analysis*<br>(n = 280) |      |                      |
|-----------------------|---------------------------------|------|----------------------|------------------------------------|------|----------------------|
|                       | n                               | %    | P value <sup>‡</sup> | n                                  | %    | P value <sup>‡</sup> |
|                       | Smear-<br>positive<br>cases     |      |                      | Smear-<br>positive<br>cases        |      |                      |
| D1+D2                 | 135                             | 21.0 | —                    | 120                                | 42.9 | —                    |
| B1                    | 150                             | 23.3 | 0.001                | 125                                | 44.6 | 0.23                 |
| B1+B2                 | 167                             | 25.9 | <0.001               | 131                                | 46.8 | <0.01                |
| D1+B1                 | 152                             | 23.6 | <0.001               | 128                                | 45.7 | 0.01                 |
| B1+D2                 | 153                             | 23.8 | <0.001               | 127                                | 45.4 | 0.04                 |
| D1+B2                 | 159                             | 24.7 | <0.001               | 127                                | 45.4 | 0.02                 |
| D1+B1+D2              | 153                             | 23.8 | <0.001               | 128                                | 45.7 | 0.01                 |
| D1+D2+B2              | 159                             | 24.7 | <0.001               | 127                                | 45.4 | 0.02                 |
| D1+B1+B2              | 167                             | 25.9 | <0.001               | 132                                | 47.1 | <0.01                |
| B1+D2+B2              | 159                             | 24.7 | <0.001               | 127                                | 45.4 | 0.02                 |

\*Data set from Mindouli.

<sup>†</sup>See Table 2 for definitions.

<sup>‡</sup>All approaches were evaluated in the same patient population. McNemar's test for matched data was used to compare different approaches with the conventional approach (D1+D2).

**Table 4** Costs data (in euros) per approach for the base-case analyses

| Approach* | Excluding transport cost |                          |       | Including transport cost |       |
|-----------|--------------------------|--------------------------|-------|--------------------------|-------|
|           | Labour†                  | Reagents and consumables | Total | Transport cost‡          | Total |
| D1+D2     | 1.76                     | 0.95                     | 2.70  | 2.79                     | 5.49  |
| B1        | 1.22                     | 0.79                     | 2.01  | 2                        | 4.01  |
| B1+B2     | 1.92                     | 1.41                     | 3.33  | 2.77                     | 6.10  |
| D1+B1     | 1.84                     | 1.10                     | 2.94  | 2                        | 4.94  |
| D1+B2     | 1.84                     | 1.17                     | 3.01  | 2.79                     | 5.8   |
| B1+D2§    | 1.83                     | 1.21                     | 3.03  | 2.77                     | 5.80  |
| D1+B1+D2  | 2.45                     | 1.51                     | 2.93  | 2.76                     | 6.73  |
| D1+D2+B2  | 2.48                     | 1.51                     | 3.96  | 2.79                     | 6.79  |
| D1+B1+B2  | 2.54                     | 1.72                     | 4.00  | 2.76                     | 7.02  |
| B1+D2+B2  | 2.52                     | 1.75                     | 4.25  | 2.77                     | 7.03  |

\*See Table 2 for definitions.

† In the Médecins Sans Frontières project in Mathare the monthly salary of a laboratory technician was €600.

‡ €1 per return multiplied by the estimated number of patient visits.

§ D2 was prepared only if B1 was found to be negative.

third and two thirds of the health service costs were for human resources.

#### Base-case analysis

A graphic representation of the results of the cost-effectiveness analysis is shown in the Figure. In the model including all approaches (Figure, A), B1 was the least costly approach and was used as the reference. The approach with the lowest ICER compared to B1 was the most cost-effective approach (B1+B2). Therefore, all approaches above the line linking B1 and B1+B2 (less effective or more costly) were dominated. The results were not modified after including patient transport costs.

In the model excluding B1 and B1+B2 (Figure, B), D1+D2 (the least costly approach) was used as the reference. D1+B2 had the lowest ICER and was the most cost-effective approach. Therefore, all approaches above the line linking D1+D2 and D1+B2 were dominated. Although it was the most effective approach, D1+B1+B2 was very costly and had

a higher ICER than D1+B2. After inclusion of patient transport costs, both D1+B2 and D1+B1 were more cost-effective than D1+D2. There was no significant difference in smear-positive TB case detection between D1+B1 and D1+B2 (23.6% vs. 24.7%,  $P = 0.21$ ).

#### Sensitivity analysis

Varying the monthly salary of the laboratory technician between €200 and €1000 did not modify the base-case findings with the inclusion of all potential smear combinations and after exclusion of B1 and B1+B2, respectively (data not shown). The results did not change after doubling the transport costs in the model to include all potential approaches. On the other hand, D1+B2 was dominated by a blend of D1+B1 and D1+B1+B2 after the transport cost was increased in the model without B1 and B1+B2.

A sensitivity analysis using a different data set from Mindouli, Republic of Congo, did not affect the base-case findings. Indeed, B1 and B1+B2 were the two dominant approaches when the model that included all potential smear combinations was used. After the exclusion of B1 and B1+B2, D1+B1 dominated.

## DISCUSSION

Considering all potential combinations of direct smear and smear after overnight NaOCl sedimentation, the approaches based on the single examination of the first concentrated specimen or based on the examination of two concentrated specimens were the most cost-effective: B1 due to its low cost, and B1+B2 due to its effectiveness and low ICER compared to B1. The results were not affected by variations in human resource costs and the addition of patient transport costs. Nevertheless, the introduction of diagnostic approaches exclusively based on smear after NaOCl sedimentation in routine programme conditions would face two major operational constraints discussed in greater detail in a previous paper: the variability of the

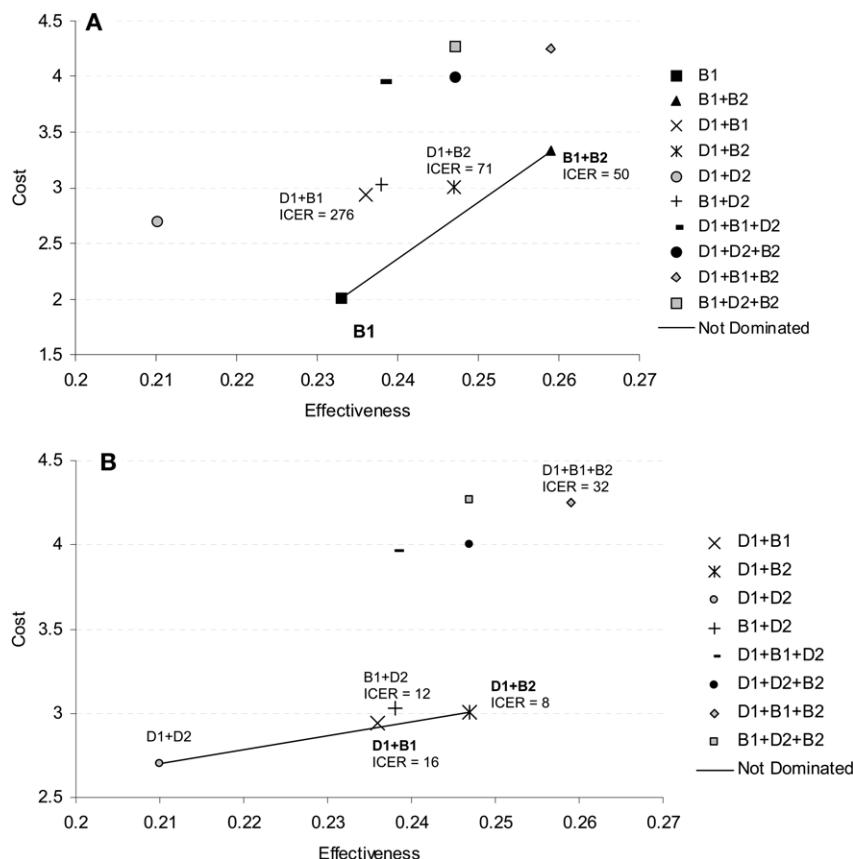
**Table 5** Costs data (in euros) per approach for the sensitivity analyses

| Approach* | Variation of labour cost |       |             |       | Increase of transport cost, €2/return |        | Dataset from Mindouli, €200/month |       |
|-----------|--------------------------|-------|-------------|-------|---------------------------------------|--------|-----------------------------------|-------|
|           | €200/month               |       | €1000/month |       | Transport costs                       | Total† | Labour                            | Total |
|           | Labour                   | Total | Labour      | Total |                                       |        |                                   |       |
| D1+D2     | 0.84                     | 2.56  | 4.20        | 5.94  | 5.58                                  | 8.28   | 0.72                              | 2.46  |
| B1        | 0.59                     | 1.53  | 2.93        | 3.88  | 4                                     | 6.01   | 0.52                              | 1.47  |
| D1+B1     | 0.41                     | 1.20  | 2.03        | 2.82  | 5.53                                  | 8.87   | 0.40                              | 1.19  |
| D1+B2     | 0.61                     | 1.71  | 3.07        | 4.17  | 4                                     | 6.94   | 0.57                              | 1.99  |
| B1+D2‡    | 0.61                     | 1.78  | 3.07        | 4.24  | 5.53                                  | 8.57   | 0.55                              | 1.64  |
| D1+B1+D2  | 0.61                     | 1.81  | 3.05        | 4.25  | 5.58                                  | 8.59   | 0.55                              | 1.75  |
| B1+B2     | 0.82                     | 1.70  | 4.09        | 4.15  | 5.53                                  | 9.49   | 0.55                              | 1.72  |
| D1+D2+B2  | 0.64                     | 2.05  | 3.19        | 4.61  | 5.58                                  | 9.58   | 0.69                              | 2.20  |
| D1+B1+B2  | 0.83                     | 2.33  | 4.14        | 5.60  | 5.53                                  | 9.78   | 0.70                              | 2.22  |
| B1+D2+B2  | 0.85                     | 2.35  | 4.23        | 5.65  | 5.53                                  | 9.80   | 0.72                              | 2.43  |

\*See Table 2 for definitions.

†Using €600 monthly salary of laboratory technician in the Médecins Sans Frontières project in Mathare.

‡D2 was prepared only if B1 was found to be negative.



**Figure** Graphic representation of the results of the base-case analysis. **A.** All approaches. In this analysis, B1 was the least costly approach and represented the reference approach. B1 was more effective and less costly than the conventional D1+D2 approach. All other approaches were more effective than B1. Of these, B1+B2 was the approach with the lowest ICER, as compared to B1. The slope of the line between B1 and B1+B2 is the graphic representation of the ICER. The higher the slope, the higher the ICER. **B.** After excluding approaches B1 and B1+B2. The ICER of the different approaches was calculated using D1+D2 as the reference approach. D1 = first on-the-spot direct smear; B1 = first on-the-spot bleach smear; D2 = second morning direct smear; B2 = second morning bleach smear; ICER = incremental cost-effectiveness ratio.

quality of NaOCl across countries and the absence of a smear microscopy quality assurance system that takes into consideration the fragility of bleach smears.<sup>10</sup> Furthermore, B1, which is relatively cheap in comparison to standard D1+D2 smear microscopy, relies on a single sputum specimen and would therefore require a very good specimen collection procedure before implementation, which is often difficult to obtain in programme conditions.

For these reasons, it might be unwise to rely only on smear microscopy approaches exclusively based on NaOCl sedimentation. Therefore, after removing B1 and B1+B2 from the model, D1+B2 and D1+B1 were the most cost-effective approaches. Although D1+B2 detected more cases than D1+B1, the difference was not significant and their costs were very similar. Both are based on the use of a first on-the-spot direct smear examination followed by a bleach smear for patients with a first smear-negative result. In our study, two thirds of smear-positive cases were identified on the first on-the-spot direct smear.<sup>10</sup> Ideally, these patients should be placed on treatment at their first health care visit, which would reduce the risk of dropout during smear examination. In our

setting, however, as is the case in most programmes, slides are stained and read once or twice a day, and patients are asked to come back the next day to pick up their results. More frequent smear preparation and reading would limit the risk of patient dropout, but would also increase human resource costs.

There are minor differences between D1+B2 and D1+B1. D1+B2 includes the examination of a morning specimen, which has the potential of a better detection yield due to its usual better quality.<sup>15,16</sup> D1+B1 relies on the collection of a single specimen and is likely to be more affected by a poor specimen collection procedure. On the other hand, with the D1+B2 approach, patients with a first smear-negative result must visit the clinic once more in comparison with the use of the D1+B1 approach (to bring in the second specimen and collect the smear result the next day). This can explain why D1+B2 was dominated in the sensitivity analysis using double patient transport costs.

This cost-effectiveness study is based on the use of a simple analytical decision model limited to measuring direct health service costs. NaOCl sedimentation uses cheap consumables and reagents and does not require any additional laboratory equipment other

than that used for conventional smear microscopy. In addition, the level of expertise is similar to that required for performing direct smear microscopy. As human resource costs represent an important part of the total costs, this model provides a good assessment of the human resource impact of the different smear microscopy approaches. This is crucial for high HIV burden countries, which face a serious human resources crisis.<sup>17</sup> Furthermore, the choice of a micro-costing approach to measure health service costs reflects the true variation of cost between the different microscopy approaches evaluated.<sup>12</sup> The use of a single health criterion (smear-positive detected case) in this analysis was justified by the immediate goal of the introduction of NaOCl sedimentation method, which was to increase the detection of smear-positive TB cases.<sup>18</sup> The source data were obtained from prospective evaluation of the overnight NaOCl sedimentation method in a peripheral clinic of a high HIV prevalence, resource-limited setting, which is exactly the type of setting for which this method is suitable. Finally, the low variability of the base-case results after sensitivity analysis, specifically when using a different data set, shows the robustness of the model.<sup>12</sup>

The cost-effectiveness study has further limitations in addition to those of the NaOCl sedimentation method itself, previously discussed.<sup>10</sup> Despite the high inter-observer agreement and good external quality control of smear microscopy, the absence of an independent gold standard (*M. tuberculosis* culture) to measure the effectiveness criterion does not exclude the possibility of an increase in smear positivity owing to reduced specificity. The analysis did not include the cost of missed TB cases who could infect other people, and this would require further investigation. This can explain the major difference in costs with a previous study in Kenya that reported a cost of US\$55 using the standard D1+D2 approach.<sup>19</sup> Patient costs were not prospectively assessed in this study, and we could only include an estimation of transport costs. Accommodation and food costs and loss of daily income for patients living at a distance from the diagnostic centre were not considered. Methods requiring a greater number of visits would certainly increase the costs for these patients.

Economic analysis is an important tool for the introduction of a new diagnostic approach. Nevertheless, the choice of the best approach among those identified as cost-effective will depend on the quality of the specimen collection, patient access to smear microscopy services, patient dropout rate during microscopy investigation, laboratory workload and the laboratory's ability to ensure good bleach quality. The B1 approach could be a good alternative for programmes with high laboratory workload and poor access to TB diagnostic health facilities, but would require good specimen collection and reliable bleach source and storage conditions. B1+B2 would be a better alternative, as it has a higher rate of smear-

positive case detection, but is more costly and requires more health care visits. The NaOCl sedimentation method is currently being assessed in a multicentre trial sponsored by the World Health Organization/TDR (Research & Training for Tropical Diseases), which will aid in standardising the method. Meanwhile, D1+B1 and D1+B2 could be acceptable alternatives. Cost-effectiveness analysis using data collected under programme conditions and comparison with the cost-effectiveness of LED fluorescence-based microscopy for peripheral laboratories is needed. Evaluation of strategies combining different methods to optimise smear microscopy, such as NaOCl sedimentation, the front-loaded specimen collection approach and LED fluorescence microscopy, are required.<sup>20,21</sup> Nevertheless, the benefits of optimisation of smear microscopy should not obviate the need for an affordable, rapid diagnostic test with better sensitivity than microscopy to diagnose PTB in peripheral health clinics.<sup>22</sup>

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## RÉSUMÉ

**CONTEXTE :** La sémentation à l'eau de Javel est une méthode qui vise à augmenter le rendement diagnostique de l'examen microscopique des crachats dans les pays à prévalence élevée de virus de l'immunodéficience humaine et à ressources limitées.

**OBJECTIFS :** Comparer le rapport coût-efficacité relatif de différentes approches microscopiques sur le diagnostic de la tuberculose (TB) au Kenya.

**MÉTHODES :** On a élaboré un arbre de décision analytique incluant les mesures de coût et d'efficacité de 10 combinaisons d'examen microscopique direct (D) et de sémentation à l'eau de Javel (B) pendant une nuit pour l'examen microscopique. Pour la méthode de sémentation à l'eau de Javel, les données ont été obtenues sur deux échantillons (le premier sur place [1] et le deuxième du petit matin [2]) provenant de 644 sujets suspects de TB dans une polyclinique de santé périphérique. Le coût supplémentaire par cas détecté à bacilloscopie positive des frottis a été mesuré. Les coûts incluaient les ressources

humaines et les produits en utilisant une évaluation de micro-coût.

**RÉSULTATS :** Toutes les approches d'examen microscopique basées sur l'eau de Javel ont détecté un nombre significativement plus élevé de cas (respectivement entre 23,3% et 25,9% pour B1 et pour B1+B2) que les approches conventionnelles D1+D2 (21,0%). Le coût par cas testé s'étalait entre 2,7 et 4,5 euros respectivement pour B1 et B1+D2+B2. B1 et B1+B2 se sont avérés les meilleures approches dont le rapport coût-efficacité était le meilleur. D1+B2 et D1+B1 ont été de bonnes alternatives pour éviter d'utiliser les approches basées exclusivement sur l'examen microscopique après sémentation par l'eau de Javel.

**CONCLUSIONS :** Parmi différentes approches efficaces d'examen microscopique utilisant la sémentation avec l'hypochlorite de sodium, un petit nombre seulement ont entraîné une augmentation limitée de la charge du travail du laboratoire et pourraient être plus adaptés à la mise en œuvre dans le cadre des programmes.

## RESUMEN

**MARCO DE REFERENCIA:** La sedimentación con hipoclorito de sodio ( $\text{NaOCl}$ ) es una técnica que mejora el rendimiento diagnóstico de la baciloscopía del esputo en entornos con alta prevalencia de infección por el virus de la inmunodeficiencia humana de países con recursos limitados.

**OBJETIVOS:** Comparar el rendimiento de diferentes métodos en el diagnóstico de la tuberculosis (TB) en Kenya.

**MÉTODOS:** Construyó un árbol modelo de análisis de decisiones que comprendía mediciones de rendimiento de diez combinaciones de técnicas baciloscopía con sedimentación directa (D) y sedimentación de una noche con  $\text{NaOCl}$  (B). Los datos se extrajeron del examen de dos muestras de esputo (la primera tomada de inmediato [1] y la segunda una muestra de la mañana [2]) de 644 personas con presunción de TB en un consultorio periférico. Se midió el incremento del costo por cada baciloscopía positiva detectada. En los costos se tuvieron en

cuenta los recursos humanos y los materiales y se calcularon mediante una evaluación detallada de los costos de todos los artículos y los servicios.

**RESULTADOS:** Todas las estrategias de sedimentación con  $\text{NaOCl}$  detectaron significativamente más casos (entre 23,3% con B1 y 25,9% con B1+B2) que la técnica convencional D1+D2 (21,0%). El costo por caso examinado osciló entre 2,7€ con B1 y 4,5€ con B1+D2+B2. Las estrategias más rentables fueron B1 y B1+B2. Las opciones D1+B2 y D1+B1 fueron buenas alternativas a fin de evitar la aplicación exclusiva de técnicas de baciloscopía basadas en la sedimentación con  $\text{NaOCl}$ .

**CONCLUSIÓN:** Entre las estrategias eficaces de baciloscopía estudiadas, que incluían sedimentación con  $\text{NaOCl}$ , unas pocas dieron lugar a un aumento limitado de la carga de trabajo del laboratorio y serían las más adecuadas en la ejecución programática.