ADDED VALUE OF BLEACH SEDIMENTATION MICROSCOPY FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS: A COST EFFECTIVENESS STUDY

Maryline Bonnet[1], Ayden Tajahmady[2], Willie Githui[3], Andrew Ramsay[4], Laramie Gagnidze[1], Francis Varaine[5], Philippe J Guerin[1]

[1] Epicentre, Paris, France, [2] Mission nationale d'expertise et d'audit hospitaliers, Paris, France, [3] Centre for Respiratory Diseases Research, Kenya Medical Research Institute, [4] Liverpool School of Tropical Medicine (Present address: WHO/TDR, Geneva, Switzerland), [5] Médecins Sans Frontières, Paris, France

BACKGROUND

- Poor tuberculosis (TB) diagnostic in peripheral health clinics of high HIV prevalence countries
  - Smear microscopy too insensitive and no access to *M tuberculosis* culture
  - No sensitive test expected to replace smear microscopy in a short time
- Overnight bleach sedimentation: simple and affordable method to optimise smear microscopy
  - Meta-analysis: average of 23% increase of smear positive detection[1]
  - 20-23% increase in a peripheral health clinic in Mathare (Kenya)[2]
- How to introduce the bleach sedimentation in current practices?
  - Replacement / combination with direct smear microscopy?
  - Impact on laboratory workload for setting with human resource crisis?
  - Limitations of the method: fragility of smears, poor stability of bleach, delay of results by 1 day

[1] *Steingart KR, et al . Lancet Infect Dis 2006;6:664–74*

[2] *Bonnet M, et al. Clin Infect Dis. 2008 Jun 1;46(11):1710-6*

OBJECTIVES

To measure and compare the incremental cost per smear positive (SP) detected case of different approaches combining direct (D) and/or bleach (B) smear to diagnose TB among suspects in a peripheral health clinic of a high HIV prevalence country

METHODS

- Cost effectiveness analysis (CEA): Decision analytical model
  - Health service provider perspective
    - Including all potential smear microscopy approaches combining direct and/or bleach sedimentation on 2 sputum specimens examination
    - After exclusion of approaches exclusively based on use of bleach sedimentation
  - Addition of patients' transport cost to reflect the difference of health clinic visits per approach
- Sensitivity analysis
  - Variation of labour cost
  - Variation of patients' transport cost

DATA SOURCE

- Field evaluation (diagnostic yield and feasibility) of smear microscopy after overnight sodium hypochlorite (NaOCl) sedimentation in Mathare, Nairobi (Kenya)[1]
- Sites and population
  - Urban health clinic of Mathare, Nairobi (Kenya)
  - 644 consecutive TB suspects presenting cough for more than 2 weeks
  - 50% HIV co-infection
- **Standardised NaOCl sedimentation method**
  - Same quantity of 3.5% local NaOCl to the specimen in 15ml conical tube
  - Mixture homogenized using a vortex
  - Overnight sedimentation on the bench at room temperature
- SP case definition
  - 2 sputum specimens examination
    - 1st on spot on the 1st day of consultation
    - 2nd morning at home on 2nd day
  - ≥ 1 smear positive result with ≥ 1AFB/100HPF

[1] *Bonnet M, et al. Clin Infect Dis. 2008 Jun 1;46(11):1710-6*

SMEAR MICROSCOPY APPROACHES

Approach	Description
D1+D2	Standard: direct smear on 1st specimen and direct on 2nd specimen if the 1st smear is negative
B1	Bleach smear on 1st specimen
B1+B2	Bleach smear on 1st specimen and bleach on 2nd if the 1st smear is negative
D1+B1	Direct smear on 1 st specimen and bleach on 1 st if the 1st smear is negative
B1+D2	Bleach smear on 1st specimen and direct smear on 2nd specimen
D1+B2	Direct smear on 1st specimen and bleach smear on 2nd if the 1st smear is negative
D1+B1+D2	Direct smear on 1st specimen, bleach on first and direct on 2nd if the 1st smear is negative
D1+D2+B2	Direct smear on 1st specimen, direct on 2nd if 1st is negative and bleach on 2nd spécimen if 2nd smear also negative
D1+B1+B2	Direct smear on 1st specimen, bleach on first if 1st smear negative and bleach on 2nd specimen if 2nd smear also negative
B1+D2+B2	Bleach smear on 1st specimen and direct on 2nd specimen. Bleach smear on 2nd spécimen if 2 previous smears are negative

Approaches based on the examination of only the 2nd specimen were not included

EFFECTIVENESS AND COSTS PARAMETERS

- Effectiveness: smear positive case detection rate
- Costs
  - Direct health service costs
    - Labour cost
      - Measure of time spent by laboratory technicians for specimen collection coaching, bleach specimen preparation and smear microscopy
      - Base-case analysis: 600€ monthly salary
      - Sensitivity cases analysis: 200€ and 1000€ per month
    - Consumables and reagents based on the Kenyan market cost (2007)
    - Increase by 0.2% and 1.9% to take into account unreadable D and B smear, respectively
    - Micro costing approach
  - Patients' transport cost estimates
    - Base-case analysis: 1€/return
    - Sensitivity analysis: 2€/return

RESULTS

Smear positive detection rate per approach

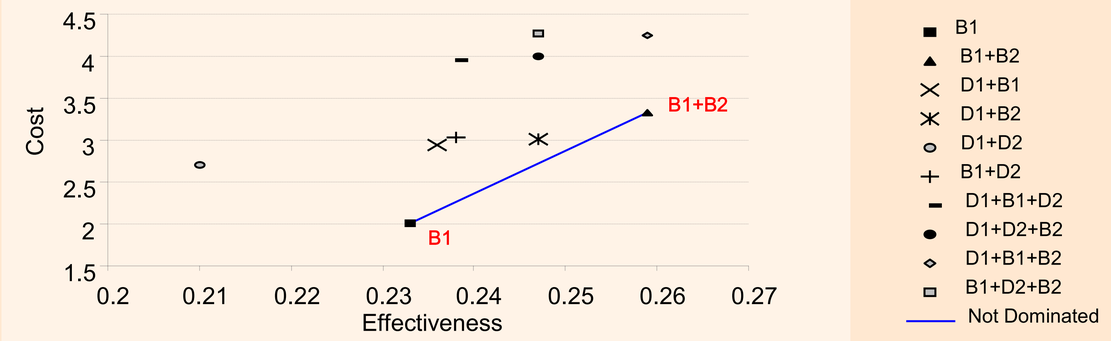
Approach	Smear positive detection rate n	%	95%CI	Comparison with D1+D2 *P**	Visits n
D1+D2	135	**21.0**	17.9 - 24.3	-	2.79
B1	150	**23.3**	20.1 - 26.7	0.001	2
B1+B2	167	**25.9**	22.6 - 29.5	<0.001	2.767
D1+B1	152	**23.6**	20.4 - 27.1	<0.001	2
B1+D2	153	**23.8**	20.5 - 27.2	<0.001	2.767
D1+B2	159	**24.7**	21.4 - 28.2	<0.001	2.79
D1+B1+D2	153	**23.8**	20.5 - 27.2	<0.001	2.764
D1+D2+B2	159	**24.7**	21.4 - 28.2	<0.001	2.79
D1+B1+B2	167	**25.9**	22.6 - 29.5	<0.001	2.764
B1+D2+B2	159	**24.7**	21.4 - 28.2	<0.001	2.767

* McNemar test for matched data

Costs (€ 2007)

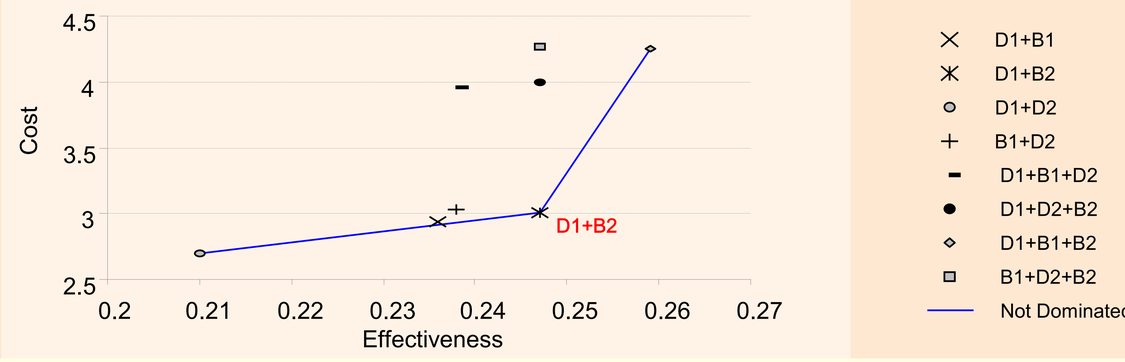
	Base- case analysis				Sensitivity analysis				
	Labour	Reagents & consumables	Total	Total + transport	200 €		1000€		Total + transport
					Labour	Total	Labour	Total	
D1+D2	1.76	0.95	2.70	2.79	0.59	1.53	2.93	3.88	5.58
B1	1.22	0.79	2.01	2	0.41	1.20	2.03	2.82	4
D1+B1	1.84	1.10	2.94	2	0.61	1.71	3.07	4.17	4
D1+B2	1.84	1.17	3.01	2.79	0.61	1.78	3.07	4.24	5.58
B1+D2	1.83	1.21	3.03	2.77	0.61	1.81	3.05	4.25	5.53
D1+B1+D2	2.45	1.51	2.93	2.77	0.82	1.70	4.09	4.15	5.53
B1+B2	1.92	1.41	3.33	2.77	0.64	2.05	3.19	4.61	5.53
D1+D2+B2	2.48	1.51	3.96	2.79	0.83	2.33	4.14	5.60	5.58
D1+B1+B2	2.54	1.72	4.00	2.77	0.85	2.35	4.23	5.65	5.53
B1+D2+B2	2.52	1.75	4.25	2.77	0.84	2.56	4.20	5.94	5.53

1. CEA: ALL APPROACHES WITHOUT TRANSPORT COST



Sensitivity analysis: no variation when using lower (200€/month) or higher (1000€/month) labour cost

2. CEA: EXCLUSION OF B1 AND B1+B2 WITHOUT TRANSPORT COST

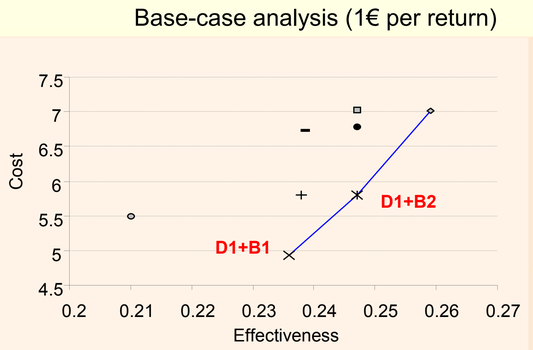


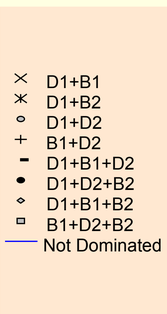
Sensitivity analysis: no variation when using lower (200€/month) or higher (1000€/month) labour cost

3. CEA: ADDITION OF PATIENTS' TRANSPORT COST

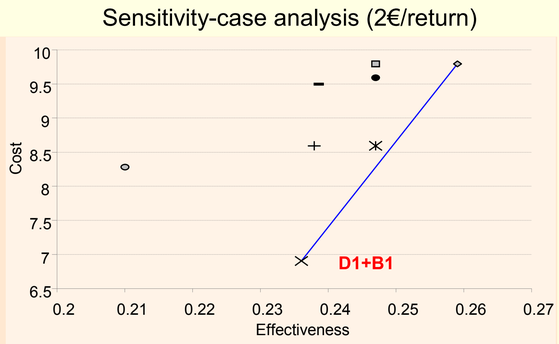
- All approaches: B1 and B1+B2 most cost-effective approaches
- Exclusion of B1 and B1+B2: variation of results according to transport costs

Base-case analysis (1€ per return)





Sensitivity-case analysis (2€/return)



DISCUSSION

- A simple decision analytical model can give informative programmatic information
- Robust model
  - Using observed and published data collected in a peripheral health clinic in a high HIV prevalence country
  - Use of micro costing approach
  - Not sensitive to variation of labour cost
- B1 and B1+B2 best approaches based on our model
- Variability of bleach quality and fragility of smears: CEA after exclusion of B1 and B1+B2
  - D1+B2 best option - But most patients will only get results on 3rd day
  - D1+B1 good alternative - Would require a good specimen collection (1 specimen)

LIMITATIONS

- Absence of patient's cost perspective despite the estimates of transport costs
- Doesn't reflect the risk of patients' drop out during smear microscopy
  - 4.5% in the study conditions of Mathare

CONCLUSIONS

- Choice of approach based on different criteria
  - Laboratory experiences in using bleach microscopy
  - TB program priority between detection and cost
  - Patients' access to smear microscopy services
- 4 possible scenarios (see table next)
- Improvement of the model using routine program data

Scenarios	Possibility to use only B approach	Program priority	Access to health care services	Best approach
1	Yes	Cost	Indifferent	B1
2	Yes	Detection	Indifferent	B1+B2
3	No	Indifferent	Bad	D1+B1
4	No	Indifferent	Good	D1+B2

Maryline Bonnet (Epicentre)
Rue de Lausanne 78, CH-1211 Genève 21
maryline.bonnet@geneva.msf.org