How many sputum samples should be examined during follow-up of tuberculosis patients in Myanmar: two or one?

E. E. Win,¹ A. M. V. Kumar,² N. T. T. Kyaw,³ N. N. Aye,⁴ K. M. Hteik,⁴ S. Saw,⁵ M. M. Oo,³ K. W. Y. Kyaw,³ S. T. Aung,⁶ T. L. Tun⁷

<http://dx.doi.org/10.5588/pha.18.0041>

Setting: Ten selected microscopy centres in Sagaing Region, Myanmar, functioning under an external quality assurance system with no reported major errors.

Objective: To assess the pattern of serial sputum results (NN, both smear-negative; NP, first smear-negative and second smear-positive; PN, first smear-positive and second smear-negative; and PP, both smear-positive) among follow-up sputum microscopy examinations of tuberculosis (TB) patients (end of intensive phase, mid-continuation phase and end of treatment) conducted from 1 November 2017 to 15 April 2018.

Design: Cross-sectional study using secondary data (laboratory registers).

Results: Of 2001 examinations, 94 (4.7%) were smear-positive: 66 PP (3.3%), 12 PN (0.6%) and 16 NP (0.8%); 75% of NP results were scanty. The proportion of NP results was 0.8% (95%CI 0.5–1.3), i.e., 125 smears (95%CI 77–200) were required to detect one additional smear-positive result in the second sample. Of the 16 NP results (15 patients), 14 were tested using Xpert® MTB/RIF and none had rifampicin resistance. During the continuation phase of treatment, 13 became smear-negative, one remained smear-positive and one had unknown follow-up smear status.

Conclusion: The benefit of the second sputum sample for monitoring anti-tuberculosis treatment was negligible. Given the favourable resource implications (reduced laboratory workload and costs), we recommend changing the policy from two sputum smears to one during follow-up sputum examinations of TB patients.

Previous operational research studies conducted in India and other countries in Africa have found that the proportion of patients with the first sample smear-negative and the second smear-positive (NP) was low, ranging from 0.3% to 4.1%, irrespective of the month of follow-up examination and category of TB patient.^{4–7} There is also evidence to suggest that most of these results, where only one of the two smears are positive, are culture-negative, meaning that there were no viable tubercle bacilli.⁸ Based on this evidence, India's Revised National Tuberculosis Control Programme made a national policy decision in 2016 to examine only one sputum specimen during follow-up examinations.⁹ This policy has several advantages: it reduces laboratory staff workload, cuts costs and is more patient-friendly, as it removes the additional visit required for the second sputum examination.

However, recommendations worldwide are conflicting. While the International Union Against Tuberculosis and Lung Disease (The Union) recommends examining a single specimen,¹⁰ the World Health Organization (WHO) continues to recommend testing two specimens at each follow-up examination.² A literature search showed that there were no previous studies from Myanmar on this issue. Generating local evidence on the subject can help inform national policy decisions in Myanmar.

We aimed to assess 1) the pattern of serial sputum examination results (NN, both smears negative; NP, first smear-negative and second smear-positive; PN, first smear-positive and second smear-negative and PP, both smears positive); and 2) the proportion of patients with NP results, disaggregated by month of follow-up, human immunodeficiency virus (HIV) status and previous history of anti-tuberculosis treatment among follow-up sputum microscopy examinations conducted in 10 selected microscopy centres in the Sagaing Region of Myanmar.

METHODS

Study design

This was a cross-sectional study involving the analysis of secondary data routinely collected by Myanmar's National Tuberculosis Programme (NTP).

General setting

The Republic of the Union of Myanmar, located in South-East Asia, has a population of ~51.5 million,¹¹ of which about 70% reside in rural areas. The per capita

AFFILIATIONS

- 1 Health Literacy Promotion Unit, Department of Public Health, Ministry of Health and Sports, Sagaing, Myanmar
- 2 International Union Against Tuberculosis and Lung Disease (The Union), Paris, France
- 3 The Union, Mandalay, Myanmar
- 4 National Tuberculosis Programme (NTP), Department of Public Health, Ministry of Health and Sports, Sagaing, Myanmar
- 5 Department of Medical Research, Yangon, Myanmar
- 6 NTP, Department of Public Health, Ministry of Health and Sports, Nay Pyi Taw, Myanmar
- 7 Department of Public Health, Ministry of Health and Sports, Sagaing, Myanmar

CORRESPONDENCE

Ei Ei Win
Health Literacy Promotion Unit
Department of Public Health
Ministry of Health and Sports
Sagaing, Myanmar
e-mail: eiwin86@gmail.com

KEY WORDS

number need to test; NNT; smear-positive culture-negative phenomenon; operational research; SORT IT

Tuberculosis (TB) remains a major global health problem and causes ill health in millions of people each year. In 2016, TB was the leading cause of death among infectious diseases worldwide.¹ Myanmar is one of the world's 30 high TB burden countries.¹ TB patients receiving treatment undergo periodic follow-up sputum smear microscopy for acid-fast bacilli (AFB) to monitor response to treatment.² In Myanmar, follow-up examinations are performed three times during the course of anti-tuberculosis treatment: at the end of the intensive phase of treatment, at the middle of the continuation phase 5 months after starting treatment and at the end of treatment. At each follow-up test, two sputum specimens ('spot' and 'early morning') are collected and examined. Patients with either of the two smears positive for AFB are considered to have poor response to treatment, thereby requiring changes in management.³

Received 23 June 2018
Accepted 6 September 2018

PHA 2018; 8(4): 169–174
© 2018 The Union

gross domestic product (GDP) is US\$1105, one of the lowest in the East Asia and Pacific region.¹¹ The country is divided administratively into one Council Territory (Nay Pyi Taw), seven states and seven regions.¹¹

Specific setting

Sagaing Region is situated in the north-western part of Myanmar (population 5.4 million).¹¹ The road and transport systems in Sagaing Region are weak and the mountainous terrain makes it difficult to access health facilities.¹¹ Health services are organised through primary and secondary health facilities. There are 10 district hospitals, 37 township and 89 station hospitals and 190 rural health centres (RHCs).

National Tuberculosis Programme

TB diagnostic services are decentralised and sputum microscopy is conducted in 83 health facilities (all district and township hospitals, 30 station hospitals and six microscopy centres run by non-governmental organisations). Sputum collection centres are situated at the RHCs, and basic health staff (public health supervisors, midwives, lady health visitors and health assistants) collect and send specimens to the township TB laboratory for testing.

Sputum microscopy is performed by trained laboratory technicians using either light microscopy with Ziehl-Neelsen (ZN) staining or light-emitting diode fluorescent microscopy (LED-FM) with auramine staining. Quality-assured laboratory consumables are procured and supplied by the NTP to all laboratories. There is a system of external quality assurance (EQA) under which a random sample of sputum smears are re-examined by senior laboratory supervisors once a month. The laboratories are under the supervision of the National TB Reference Laboratory in Yangon, and the regional reference laboratory in Mandalay. Anti-tuberculosis treatment is provided to all diagnosed TB patients free of charge at all townships according to national guidelines. During the course of treatment, sputum smear microscopy is performed periodically to monitor response to treatment. Patient management varies according to the results of the follow-up sputum examinations (Table 1).³

Study population

All follow-up sputum smear examinations performed in 10 selected township laboratories of Sagaing Region from 1 November 2017 to 15 April 2018 were included. The laboratories were purposively selected based on the following criteria: 1) no major errors as assessed in the EQA in 2016;¹² and 2) presence of a full-time trained laboratory technician. The rationale for this purposive selection was that we did not want poor quality of sputum microscopy to confound our assessment of the additional value of the second sputum specimen.

Data variables, sources of data and data collection

Data were collected during February–April 2018. We reviewed the laboratory register and extracted the following variables: laboratory serial number, age, sex, type of microscopy, HIV status, category of anti-tuberculosis

treatment (new/previously treated/not recorded), month of follow-up and microscopy results, including grading (negative/1+/2+/3+/scanty/not recorded).

Although it is recommended that ‘spot’ and ‘early morning’ specimen results are recorded as first and second in the laboratory register, this is not consistently practised. To ensure correct, uniform recording during the study period (first result as spot specimen and second result as early morning specimen), the following measures were taken. First, the regional director of public health and the regional TB officer sent an official memorandum to the laboratory technicians of the study laboratories. Second, the laboratory technicians were informed about the study protocol and the importance of accurate recording via telephone by senior laboratory supervisors and the principal investigator. Third, the laboratories were supervised periodically by senior laboratory supervisors, the regional TB officer and the principal investigator to ensure the implementation of study procedures.

We also collected data on the management of the TB patients with an NP pattern of follow-up sputum microscopy results. This included Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) assay results and the most updated clinical outcome.

Data entry and analysis

Data were double-entered, validated and analysed using EpiData v 3.1 for entry and v 2.2.2.186 for analysis (EpiData Association, Odense, Denmark). We calculated 1) the proportion of patterns of serial sputum examinations (NN, NP, PN, PP); and 2) the proportion of NP and 95% confidence intervals (CIs). The proportion of NP results was disaggregated by time of follow-up, HIV status and previous history of anti-tuberculosis treatment. The number of sputum smears required to find an additional positive on the second smear was calculated by taking a reciprocal of the proportion of NP (1/NP). The χ^2 test or Fisher's exact test was used to assess statistical significance. Logistic regression was used to assess factors associated with an NP sputum result; $P < 5\%$ was considered statistically significant.

Ethics

Ethics approval was obtained from the Ethical Review Committee, Department of Medical Research, Ministry of Health and Sports, Yangon, Myanmar and the Union Ethics Advisory Group, Paris, France. As this was a review of programme records, the need for individual informed consent was waived by the ethics committees.

RESULTS

There were a total of 2003 follow-up sputum examinations, including 2001 (99%) examinations with results of both sputum smears available. Of 2001 follow-up examinations, 69% were from males; the median age was 45 years (interquartile range 30–58). Of these, 76% were from new TB patients. LED-FM was used in 73% of the follow-up examinations. Forty-one per cent of examinations were performed at the end of the intensive phase, 22% in the middle of the continuation phase and the remainder at the end of treatment.

ACKNOWLEDGEMENTS

This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR). The model is based on a course developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins Sans Frontières (MSF/Doctors Without Borders). The specific SORT IT programme that resulted in this publication was jointly organised and implemented by The Centre for Operational Research, The Union, Paris, France; The Department of Medical Research, Ministry of Health and Sports, Yangon, Myanmar; The Department of Public Health, Ministry of Health and Sports, Yangon, Myanmar; The Union Country Office, Mandalay, Myanmar; The Union South-East Asia Office, New Delhi, India; and Burnet Institute, Melbourne, VIC, Australia. We also would like to thank the laboratory technicians working in the study health facilities and senior laboratory supervisors of Sagaing Region for their help in data collection and validation. We express our deep gratitude to the TB team leaders and focal persons working in the study area. The training programme within which this paper was developed was funded by the Department for International Development (London, UK), the United States Agency for International Development (Washington DC, USA) through Challenge TB and FHI 360. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Conflicts of interest: none declared.

TABLE 1 Management of TB patients based on the results of follow-up sputum microscopy in Myanmar*

Type of TB patient	Stage of treatment	Microscopy result	Management
New smear-positive TB patient	End of the intensive phase	Positive	Extend intensive phase by 1 month; perform Xpert testing. If Xpert-positive for RMP resistance, then move to second-line treatment. If negative, then continue with first-line treatment. Repeat microscopy after the end of the extended intensive phase
	Month 5	Positive	Declare as treatment failure and move to retreatment regimen; perform Xpert testing and decide in accordance with the result
	End of treatment	Positive	Declare as treatment failure and move to retreatment regimen; perform Xpert testing and decide in accordance with the result
Previously treated smear-positive TB patient	End of the intensive phase	Positive	Extend intensive phase by 1 month; perform Xpert testing. If Xpert-positive for RMP resistance, then move to second-line treatment. If negative, then continue with first-line treatment. Repeat microscopy after the end of extended intensive phase
	Month 5	Positive	Declare as treatment failure; perform Xpert testing and decide in accordance with the result. If negative, perform culture and DST
	End of treatment	Positive	Declare as treatment failure; perform Xpert testing and decide in accordance with the result. If negative, perform culture and DST
New smear-negative TB patient	End of the intensive phase or end of treatment	Positive	Declare as treatment failure and start retreatment regimen; perform Xpert testing and if positive for RMP resistance, start second-line treatment
	End of the intensive phase or end of treatment	Positive	Declare as treatment failure; perform Xpert testing and if positive for RMP resistance, start second-line treatment. If negative, perform culture and DST
Previously treated smear-negative TB patient	End of the intensive phase or end of treatment	Positive	Declare as treatment failure; perform Xpert testing and if positive for RMP resistance, start second-line treatment. If negative, perform culture and DST

*End of intensive phase = at the end of 2, 3 or 4 months; middle of the continuation phase = sputum examination at the end of month 5; end of treatment = at the end of 6, 7 or 8 months of treatment or later.

TB = tuberculosis; RMP = rifampicin; DST = drug susceptibility testing.

Overall, 94 (5%) examinations were smear-positive on at least one of the sputum specimens. Of these, 66 (3.3%) had a PP pattern, 12 (0.6%) had a PN pattern and 16 (0.8%, 95%CI 0.5–1.3%) had an NP pattern (Figure). The number of additional smear examinations required to detect one positive smear on the second sample was 125 (95%CI 77–200).

The proportion of NP was marginally higher among males, previously treated patients and among follow-up examinations conducted at the end of the intensive phase (Table 2). On adjusted analysis, only time of follow-up examination was independently associated with NP after adjusting for age, sex, type of microscopy, HIV status and previous history of TB, with higher yield among follow-up examinations performed at the end of the intensive phase.

Grading of sputum smears

The proportion of scanty smears was lowest among follow-up examinations with a PP pattern (29%) followed by those with PN (67%) and NP patterns (75%) (Table 3).

Management of and outcomes among patients with NP pattern

The 16 instances of NP pattern were among 15 patients (one patient had two instances of NP pattern—one at the middle of the continuation phase and another at the end of treatment). Of the 15 patients, 14 were tested using Xpert and none had rifampicin (RMP) resistance. Of the 11 patients who were positive at the end of the intensive phase, intensive phase treatment was extended by 1 month. Of these, 10 became smear-negative (NN) by the middle of the continuation phase; the status of one patient was

unknown. Of the five patients who were positive at middle of the continuation phase or at the end of treatment, all five patients were started on a retreatment regimen. Of these, four became smear-negative, while one remained smear-positive.

DISCUSSION

This is the first study to examine the value of a second sputum specimen in follow-up examinations of TB patients in Myanmar. We discuss the findings from two perspectives—from the perspective of individual patient management and from a public health perspective.

From the clinical perspective, does failing to perform a second sputum examination lead to patient mismanagement? We think the answer is no for the following reasons.

First, the proportion of NP results was very low; the value of the second smear in clinical management is limited to <1% of patients. This is similar to reports from other studies from India.^{4–6,8,13} Missing these would mean not extending the intensive phase of treatment or a delay in switching to the retreatment regimen for a very small number of patients. Both these measures are no longer recommended by the WHO.^{2,14} The current standard approach is to assess every instance of positive follow-up smear for treatment adherence and drug resistance, preferably using rapid molecular methods such as Xpert, a practice already being followed by the NTP in Myanmar.³

Second, three quarters of such instances (NP pattern) were graded 'scanty'. Previous studies indicate that nearly two thirds of

FIGURE Results of follow-up sputum examinations among tuberculosis patients in 10 selected township laboratories, Sagaing Region, Myanmar, 1 November 2017–15 April 2018. *Two sputum samples were collected, one ‘spot’ and the other ‘early morning’. NN = both sputum smears negative; PP = both sputum smears positive; PN = first sputum smear-positive and second smear-negative; NP = first sputum smear-negative and second smear-positive.

all follow-up smear-positives are culture-negative.^{15–23} This ‘smear-positive, culture-negative’ phenomenon is more pronounced in patients with an NP pattern (80–100% culture-negative), particularly those whose specimens receive a ‘scanty’ grad-

TABLE 3 Grading of positive smears among follow-up sputum examinations of TB patients, Sagaing Region, Myanmar, 1 November 2017–15 April 2018

Grade	PP n (%)	PN n (%)	NP n (%)
Total	66 (100)	12 (100)	16 (100)
Scanty	19 (29)	8 (67)	12 (75)
1+	38 (57)	4 (33)	4 (25)
2+	6 (9)	0 (0)	0 (0)
3+	3 (5)	0 (0)	0 (0)

TB = tuberculosis; PP = both sputum smears positive; PN = first sputum smear-positive and second smear-negative; NP = first sputum smear-negative and second smear-positive.

ing.⁸ This usually represents non-viable (dead) tubercle bacilli yet to be excreted by the body.⁸

Third, none of the patients with an NP pattern had RMP resistance when tested with Xpert, and all except one became smear-negative on continuing treatment. We believe therefore that the absence of a second sputum smear examination will have minimal effect on monitoring response to treatment.

From a public health and programme perspective, a policy change involving the reduction of the number of sputum smears from two to one has many advantages. First, this will save patient

TABLE 2 The proportion of NP results in follow-up sputum examinations of TB patients, disaggregated by demographic and clinical characteristics, Sagaing Region, Myanmar, 1 November 2017–15 April 2018

Characteristics	Total	NP n (%)	Number of additional smears required to detect a smear-positive case on second sample (1/NP)	P value
Total	2001	16 (0.8)	125	
Age, years				0.75
<15	111	0	NA	
15–44	859	7 (0.8)	125	
45–64	726	7 (1.0)	100	
≥65	305	2 (0.7)	143	
Sex				0.03
Female	630	1 (0.2)	500	
Male	1371	15 (1.1)	91	
Type of microscopy				0.19
ZN*	539	2 (0.4)	250	
FM†	1462	14 (1.0)	100	
Month of follow-up‡				0.05
End of intensive phase	812	11 (1.4)	71	
Mid continuation phase	436	3 (0.7)	143	
End of treatment	753	2 (0.3)	333	
HIV status				0.65
Positive	99	0	NA	
Negative	1562	13 (0.8)	125	
Unknown	227	3 (0.9)	111	
Previous history of TB				0.07
Yes	247	5 (2.0)	50	
No	1524	10 (0.7)	143	
Not recorded	230	1 (0.4)	250	

* ZN staining method under light microscopes.

† Auramine staining method under fluorescent microscopes.

‡ End of intensive phase = at the end of 2, 3 or 4 months; middle of the continuation phase = sputum examination at the end of month 5; end of treatment = at the end of 6, 7 or 8 months of treatment or later.

NP = first sputum smear-negative and second smear-positive; TB = tuberculosis; ZN = Ziehl-Neelsen; HIV = human immunodeficiency virus; NA = not applicable because it cannot be calculated.

costs and time by obviating the need for an additional visit required to submit the second sample. This is not trivial, given that TB disproportionately affects the poor in a low-income country such as Myanmar with difficult terrain.

Second, this will reduce the workload for laboratory technicians. About 125 sputum smears needed to be examined to find one instance of NP—this is equivalent to 5 working days for a laboratory technician, assuming an average of 25 smear examinations per day. Follow-up sputum examinations constitute about 35% of all sputum smear examinations performed in the microscopy centres in Myanmar.²⁴ In 2017, a total of 463 316 sputum examinations were performed for diagnosis, while 251 276 were performed for follow-up. Reducing the number of sputum smears examined from two to one will thus reduce overall laboratory workload by about 18%. The time thus saved may be reallocated for expanding the number of diagnostic specimens examined, improving quality and performing new tests such as Xpert—measures that will help Myanmar progress towards TB elimination. Third, the NTP will also benefit through savings in costs incurred on laboratory consumables. Assuming it costs US\$0.5 per sputum smear examined, this translates into a saving of ~US\$125 000 per year.

There were some other interesting findings. Although there were variations in the proportion of NP results in different subgroups of patients, this rate was nevertheless low overall, with a maximum of 2% in previously treated patients. This might be related to differences in drug susceptibility profiles of such patients, and needs further investigation.

The proportion of NP results was higher among follow-up examinations performed at the end of the intensive phase. This was expected, as it takes time for dead bacilli to be excreted and we are therefore likely to find more positive smears earlier during the course of treatment.

The proportion of NP results was higher among follow-up examinations performed using LED-FM than with ZN staining, and this may be ascribed to the higher sensitivity of LED-FM. While higher sensitivity may be beneficial in diagnostic sputum examinations, it is a disadvantage during follow-up. The emphasis during follow-up sputum microscopy should be to increase specificity and reduce false-positive (smear-positive, culture-negative) results. In this regard, the recommendation of The Union is relevant: every positive smear during follow-up should be confirmed by a repeat positive smear before declaring a patient to be a bacteriological failure.^{10,25}

Our study had several strengths. We included a large sample sourced from the routine programme records, and is therefore reflective of ground realities. We purposively selected laboratories with full-time, trained laboratory technicians and there were no major errors reported under EQA during the study period. Both sputum smears were examined and recorded in almost all of the study samples. Results of the sputum examination are therefore likely to be complete and accurate. Finally, we adhered to STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines for reporting the study results.²⁶ One limitation was that we did not perform culture on the positive follow-up sputum smears to confirm the viability of the bacilli. Another possible limitation relates to the generalisability of results. However, we feel this is not a major limitation, as the proportion of NP results remains small despite conducting the study at the best laboratories with highly trained personnel and a good EQA system. In other laboratories functioning in routine mode, the proportion of NP results is likely to be even lower.

CONCLUSION

The proportion of NP results (first sample negative, the second positive) in follow-up examinations of TB patients was low, and its use in monitoring anti-tuberculosis treatment was negligible. Given the favourable resource implications, we strongly recommend that the NTP in Myanmar consider reviewing the laboratory data in other regions of the country and then changing the policy from two sputum smears to one for follow-up sputum examinations of TB patients.

References

- 1 World Health Organization. Global tuberculosis report, 2017. WHO/HTM/TB/2017.23. Geneva, Switzerland: WHO, 2017.
- 2 World Health Organization. Treatment of tuberculosis: guidelines for national programmes. 3rd ed. WHO/CDS/TB/2003.313. Geneva, Switzerland: WHO, 2003; p 53.
- 3 Ministry of Health. Myanmar national tuberculosis treatment guidelines for basic health staff. Nay Pyi Taw, Myanmar: MoH, 2014.
- 4 Kundu D, Kumar A M V, Satyanarayana S, et al. Can follow-up examination of tuberculosis patients be simplified? A study in Chhattisgarh, India. *PLOS ONE* 2012; 7: e51038.
- 5 Nataraj G, Kanade S, Parikh R, et al. Incremental yield in sputum smear positivity by examining a second early morning sputum specimen in follow-up patients on DOTS: 7 year analysis of RNTCP laboratory register. *Indian J Tuberc* 2011; 58: 60–65.
- 6 Patel J, Dave P, Satyanarayana S, et al. Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India [Short communication]. *Public Health Action* 2013; 3: 308–310.
- 7 Rieder H L, Chiang C Y, Rusen I D. A method to determine the utility of the third diagnostic and the second follow-up sputum smear examinations to diagnose tuberculosis cases and failures. *Int J Tuberc Lung Dis* 2005; 9: 384–391.
- 8 Kumar R S, Kumar A M V, Claassens M, et al. Number of sputum specimens during treatment follow-up of tuberculosis patients: two or one? *Public Health Action* 2013; 3: 304–307.
- 9 Central TB Division Directorate General of Health Services, Ministry of Health with Family Welfare. National Strategic Plan For Tuberculosis Elimination 2017–2025. New Delhi, India: MOH, 2017. <http://tbcindia.gov.in/WriteReadData/NSP Draft 20.02.2017 1.pdf>
- 10 International Union Against Tuberculosis and Lung Disease. Management of tuberculosis: a guide to the essentials of good practice. 6th ed. Paris, France: The Union, 2010. <https://theunion.org/what-we-do/publications/technical/management-of-tuberculosis-a-guide-to-the-essentials-of-good-clinical-practice> Accessed September 2018.
- 11 Department of Population, Ministry of Labour Immigration and Population. The 2014 Myanmar population and housing census thematic report on population projections for the Union of Myanmar, states/regions, urban and rural areas, 2014–2050. Nay Pyi Taw, Myanmar: Department of Population, Ministry of Labour Immigration and Population, 2017. http://themimu.info/sites/themimu.info/files/documents/Report_Thematic_Report_On_Population_Projections_-_Census_Report_V4-F_DOP_Mar2017_ENG.pdf Accessed September 2018.
- 12 National Tuberculosis Programme. Annual report on external quality assessment for TB microscopy, 2015 Myanmar. Nay Pyi Taw, Myanmar: NTP, 2017.
- 13 Thapa B, Reza L W, Kumar A M, Pandey A, Satyanarayana S, Chadha S. Light-emitting diode fluorescence microscopy increased the detection of smear-positives during follow-up of tuberculosis patients in India: program implications. *BMC Res Notes* 2015; 8: 6–9.
- 14 World Health Organization. Guidelines for treatment of drug-susceptible tuberculosis and patient care. 2017 update. WHO/HTM/TB/2017.05. Geneva, Switzerland: WHO, 2017. <http://apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf> Accessed September 2018.
- 15 Kim T C, Blackman R S, Heatwole K M, Kim T, Rochester D F. Acid-fast bacilli in sputum smears of patients with pulmonary tuberculosis. Prevalence and significance of negative smears pretreatment and positive smears post-treatment. *Am Rev Respir Dis* 1984; 129: 264–268.
- 16 Newman R, Doster B E, Murray F J, Woolpert S F. Rifampin in initial treatment of pulmonary tuberculosis. A US Public Health Service tuberculosis therapy trial. *Am Rev Respir Dis* 1974; 109: 216–232.
- 17 Newman R, Doster B, Murray F J, Ferebee S. Rifampin in initial treatment of pulmonary tuberculosis. A US Public Health Service tuberculosis therapy trial. *Am Rev Respir Dis* 1971; 103: 461–476.
- 18 Al-Moamary M S, Black W, Bessuille E, Elwood R K, Vedral S. The significance of the persistent presence of acid-fast bacilli in sputum smears in pulmonary tuberculosis. *Chest* 1999; 116: 726–731.
- 19 Chamie G, Charlebois E D, Srikanthiah P, et al. *Mycobacterium tuberculosis* microbiologic and clinical treatment outcomes in a randomized trial of immediate versus CD4 (+)-initiated antiretroviral therapy in HIV-infected adults with a high CD4 (+) cell count. *Clin Infect Dis* 2010; 51: 359–362.

- 20 Domínguez J M, Vivas E S. Smear-positive and culture-negative results of routine sputum investigations for the detection and therapy control of pulmonary tuberculosis. *Tubercle* 1977; 58: 217–220.
- 21 Jae S L, Kim E C, Sei I J, et al. The incidence and clinical implication of sputum with positive acid-fast bacilli smear but negative in mycobacterial culture in a tertiary referral hospital in South Korea. *J Korean Med Sci* 2008; 23: 767–771.
- 22 Ogilvie C M. Bacteriological control during isoniazid therapy. *Lancet* 1953; 265: 451–452.
- 23 Van Der Kuyp F, Mahan C S. Prolonged positivity of sputum smears with negative cultures during treatment for pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2012; 16: 1663–1667.
- 24 National Tuberculosis Programme (NTP Myanmar), Ministry of Health and Sports. Myanmar National TB Programme annual report 2015. Yangon, Myanmar: NTP, 2017.
- 25 International Union Against Tuberculosis and Lung Disease. Guidelines for clinical and operational management of drug-resistant tuberculosis. Paris, France: The Union, 2013. <https://theunion.org/what-we-do/publications/technical/guidelines-for-the-clinical-and-operational-management-of-drug-resistant-tuberculosis> Accessed September 2018.
- 26 von Elm E, Altman D G, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.

Contexte : Dix centres de microscopie sélectionnés de la région de Sagaing, Myanmar, fonctionnant avec un système d'assurance de qualité externe sans erreurs majeures rapportées.

Objectif : Evaluer les profils de séries de résultats de crachats (NN, deux frottis négatifs ; NP, premier frottis négatif et deuxième frottis positif ; PN, premier frottis positif et deuxième frottis négatif ; et PP, deux frottis positifs) parmi les examens de suivi de microscopie de crachats de patients TB (à la fin de la phase intensive, au milieu de la phase de continuation et à la fin du traitement) réalisés du 1^{er} novembre 2017 au 15 avril 2018.

Schéma : Etude transversale grâce à des données secondaires (registres de laboratoire).

Résultats : Sur 2001 examens, 94 (4,7%) ont eu un frottis positif : 66 (3,3%) PP ; 12 (0,6%) PN ; 16 (0,8%) NP ; 75% des NP avaient

de rares bacilles. La proportion de NP a été de 0,8% (IC95% 0,5–1,3), impliquant qu'il a fallu 125 frottis (IC95% 77–200) pour détecter un frottis positif supplémentaire dans un deuxième échantillon. Sur les 16 NP (15 patients), 14 ont été testés par Xpert® MTB/RIF et aucun n'a eu de résistance à la rifampicine. Lors de la continuation du traitement, 13 sont devenus à frottis négatif, un patient est resté à frottis positif et un autre a eu un frottis de suivi « indéterminé ».

Conclusion : Le bénéfice du deuxième échantillon de crachats pour le suivi du traitement antituberculeux a été négligeable. Devant les implications favorables en termes de ressources (charge de travail et coûts réduits pour le laboratoire), nous recommandons de modifier la politique de deux frottis de crachats à un seul lors du suivi de patients TB par examens des crachats.

Marco de Referencia: Diez centros de microscopia escogidos en la región de Sagaing de Birmania, que funcionan con un sistema externo de garantía de la calidad y no notifican errores importantes.

Objetivos: Evaluar el perfil de los resultados seriados del esputo (NN, ambas baciloscopias negativas; NP, primera baciloscopia negativa y segunda positiva; PN, primera baciloscopia positiva y segunda negativa; y PP, ambas baciloscopias positivas) en las baciloscopias de esputo de seguimiento de los pacientes con tuberculosis (TB) (al final de la fase intensiva, en medio de la fase de continuación y al final del tratamiento), realizadas del 1^o de noviembre del 2017 al 15 de abril del 2018.

Métodom: Fue este un estudio transversal que utilizó datos secundarios (los registros de laboratorio).

Resultados: De las 2001 baciloscopias realizadas, 94 (4,7%) fueron positivas, a saber: 66 (3,3%) PP; 12 (0,6%) PN; 16 (0,8%) NP; 75% de los resultados NP se notificaron como 'escasos bacilos'. La

proporción de resultados NP fue 0,8% (IC95% 0,5–1,3), lo cual indica que se precisaron 125 baciloscopias a fin de detectar una baciloscopia positiva adicional en la segunda muestra (IC95% 77–200). De los 16 casos NP (15 pacientes), 14 se examinaron mediante la prueba Xpert® MTB/RIF y ninguno exhibió resistencia a rifampicina. Durante la fase de continuación del tratamiento, en 13 casos la baciloscopia se hizo negativa, uno permaneció positivo y en otro caso el resultado de la baciloscopia de seguimiento era 'desconocido'.

Conclusión: La utilidad de una segunda muestra de esputo en la supervisión del tratamiento antituberculoso fue insignificante. Teniendo en cuenta sus repercusiones económicas favorables (disminución de la carga de trabajo y los costos de laboratorio), se recomienda cambiar la norma de practicar dos muestras de esputo por una sola muestra, durante las baciloscopias de seguimiento de los pacientes con TB.