Original Article

Determinants of sputum smear non-conversion after intensive phase treatment among pulmonary TB patients in southern Thailand

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Abstract

Background: Tuberculosis remains a global health challenge, with sputum conversion serving as a critical indicator of treatment success during the intensive phase. This study aimed to identify factors associated with sputum smear non-conversion at the end of intensive phase treatment among patients with pulmonary tuberculosis.

Methodology: This case-control study utilized data from the National Tuberculosis Information Program (NTIP) Registry database between 2014 and 2019. Newly diagnosed pulmonary tuberculosis patients were included. The study comprised 322 cases of sputum smear non-conversion and 644 controls who achieved sputum smear conversion. Descriptive statistics and multiple logistic regression were used to analyze the data.

Results: Factors significantly associated with sputum smear non-conversion included male sex (Adjusted Odds Ratio [AOR] = 1.57, 95% CI: 1.10-2.25), age 35-59 years (AOR = 1.75, 95% CI: 1.19-2.59), age ≥ 60 years (AOR = 1.72, 95% CI: 1.09-2.71), sputum AFB smear grading of 2+ (AOR = 2.74, 95% CI: 1.20-6.28) and 3+ (AOR = 4.72, 95% CI: 2.14-10.43), and receiving treatment at a private hospital (AOR = 4.94, 95% CI: 2.34-10.44). In contrast, patients weighing ≥ 50 kg at baseline treatment were less likely to experience non-conversion (AOR = 0.72, 95% CI: 0.54-0.96).

Conclusions: Patients' sex, age, sputum acid-fast bacilli [AFB] smear grading, and private hospital access were significant risk factors for sputum smear non-conversion, while higher baseline weight appeared protective. Enhanced monitoring of high-risk groups could improve treatment outcomes.

Key words: Sputum conversion; pulmonary tuberculosis; intensive phase treatment; Southern Thailand.

Introduction

Tuberculosis (TB) remains a major global public health concern and a leading cause of illness and death worldwide [1]. Caused by the airborne pathogen *Mycobacterium tuberculosis*, TB primarily affects the lungs, accounting for approximately 80% of cases [2]. It leads to significant healthcare costs, social stigma, and disruption to daily life. Globally, around 10 million people contract TB annually, with an incidence of 132 per 100,000 population. The burden is highest in Southeast Asia and Africa, reaching 220 per 100,000 [3]. TB results in about 1.3 million deaths each year, mostly in Asia and the Pacific [4]. Thailand remains a high-burden country, with a prevalence of 171 per 100,000 and persistent challenges in meeting the World Health Organization (WHO) treatment success targets [5].

The first-line anti-tuberculosis regimen – comprising isoniazid, rifampicin, pyrazinamide, and ethambutol (2HRZE/4HR) – is considered highly effective [6]. The intensive phase, which spans the initial two months of treatment, plays a crucial role in

reducing transmission. Sputum acid-fast bacilli (AFB) smear conversion during this period is a key indicator of treatment effectiveness. In upper southern Thailand, although conversion rates have shown some improvement, they continue to fall short of the WHO's targets [5].

Over the past decade, multiple studies have explored factors influencing sputum smear non-conversion in pulmonary TB patients. However, findings remain inconclusive, with varying reports on risk and protective factors [7]. Much of the existing literature originates from African countries, with limited research from other regions. In Thailand, only three small-scale studies – conducted in the northern and northeastern provinces – have been published, each constrained by small sample sizes and low statistical power [8-10]. To date, no large-scale investigation has focused on southern Thailand. This study aims to address that gap by identifying factors associated with sputum smear non-conversion during the intensive treatment phase in this region.

Methodology

Study design

This case-control study was conducted between January and February 2021 using secondary data from the National Tuberculosis Information Program (NTIP) Registry, managed by the Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health (MOPH). The data were monitored by the Office of Disease Prevention and Control 11 (ODPC 11), located in Nakhon Si Thammarat. The study was conducted in healthcare facilities providing TB services across seven provinces in upper southern Thailand: Chumphon, Ranong, Surat Thani, Phang-nga, Nakhon Si Thammarat, Phuket, and Krabi.

Study samples

The study included newly diagnosed pulmonary TB patients with a positive sputum smear for AFB at the baseline treatment. Pulmonary TB was classified under code A150 according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

Cases were defined as new pulmonary TB patients with a positive sputum smear AFB at both baseline and the end of the intensive phase of treatment. Controls were similarly defined, but with a negative sputum smear AFB at the end of the intensive phase. A 1:2 ratio of cases to controls was used, and controls were systematically and randomly selected based on identification numbers from the NTIP Registry database. The sample size was calculated using a continuity correction to fit the case-control study design with a dichotomous outcome [11-13]. We set the significance level (α) at 0.01 and the power (1-β) at 0.90. The area under the normal curve ($Z_{1-α/2} = 1.96$) and ($Z_{1-β} = 0.84$) was used for calculations. The case-to-control ratio (r) was set at 1:2. Based on a previous study [8], sputum smear conversion rates were 0.235 for cases and 0.381 for controls. This yielded a minimum required sample size of 119 cases and 258 controls.

Initially, 10,818 subjects were enrolled in the study. The inclusion criteria were: 1) being a new case of pulmonary TB, 2) having a laboratory-confirmed AFB test result, and 3) receiving a susceptible drug regimen (2HRZE/4HR). The exclusion criteria included: 1) transfer out of the study settings, 2) a positive drug susceptibility testing (DST), 3) loss to follow-up, 4) death during the intensive phase of treatment, and 5) incomplete sputum smear AFB results at the end of the intensive phase. Of the initial sample, 8,832 patients (81.64%) did not meet the inclusion criteria for the following reasons: 1) transfer out (155 cases, 1.42%),

2) loss to follow-up (346 cases, 3.20%), 3) death during treatment (987 cases, 9.12%), and 4) incomplete sputum smear AFB results at both baseline and the end of the intensive phase (6,438 cases, 59.51%). Additionally, 828 patients (7.65%) were still undergoing treatment, and 78 cases (0.72%) lacked sputum smear AFB evaluations. After exclusions, 1,986 subjects remained. Of these, 322 subjects met the criteria for cases, and 1,644 were eligible as controls. For this study, we included all 322 eligible cases and randomly selected 644 controls for analysis.

Data collection

The variables of interest were obtained from the NTIP Registry database and included demographic characteristics, clinical factors, and sputum smear AFB results at baseline and at the end of the intensive phase of treatment.

The primary outcome of this study was sputum conversion at the end of the intensive phase. Sputum conversion was verified through the NTIP Registry database. Sputum samples were collected and tested using the AFB method, with results categorized as negative, scanty, 1+, 2+, or 3+. The outcome was treated as a dichotomous variable: sputum smear non-conversion (positive AFB = 1) and sputum smear conversion (negative AFB = 0). The outcome data were electronically recorded and reported in the NTIP Registry database by health professionals trained in TB care. Additionally, the NTIP Registry database is routinely monitored and supervised by ODPC 11 in Nakhon Si Thammarat, Thailand, ensuring the accuracy of all data before analysis. Sputum smears were also routinely processed following the guidelines of the National Tuberculosis Control Program (NTP). All participating laboratories operated under the Ministry of Public Health (MOPH) regulations and received regular supervision and training to ensure standardization of procedures.

Statistical analysis

Descriptive statistics were used to summarize demographic characteristics and variables of interest. Bivariate analysis using simple logistic regression was conducted to explore factors associated with sputum smear non-conversion among subjects with pulmonary TB. Multiple logistic regression analysis was then performed to determine the relationship between these factors and sputum smear non-conversion, adjusting for potential confounding variables.

Initially, a simple logistic regression analysis was utilized to evaluate potential factors influencing

mortality. A separate model was constructed for each variable of interest. Continuous variables, such as patient age, were categorized, and polytomous variables – including patient age and occupation, as well as the grading of sputum smear AFB at baseline treatment – were converted into dummy variables before being included in the model. Factors with a Wald test $p \leq 0.25$ were entered into the initial model. Backward elimination was applied to remove factors with a Wald test $p \geq 0.05$. The p-value of the partial likelihood ratio

test was used to assess the model fit, resulting in the final model that included all relevant factors. Although this model selection approach aimed to adjust for potential confounding, residual confounding due to unmeasured or unknown variables cannot be entirely excluded.

The results are presented as odds ratios (OR) and adjusted odds ratios (AOR), with 95% confidence intervals (95% CI). Risk factors for sputum smear non-conversion were defined as OR > 1, protective factors

Table 1. Bivariate analysis of factors associated with sputum smear non-conversion at the end of intensive phase treatment among patients with pulmonary tuberculosis in Upper Southern, Thailand.

Factors	n (%) of sputum smear non-conversion		Crude OR	95%CI	*p*
	n	%			
Sex					0.003
Female	57	25.22	Ref.		
Male	265	35.81	1.65	1.18-2.31	
Age (years)					0.011
< 35	48	24.62	Ref.		
35-59	202	36.14	1.73	1.20-2.51	
≥ 60	72	33.96	1.58	1.02-2.43	
Weight at baseline treatment (kg)					0.027
< 50	152	37.25	Ref.		
≥ 50	170	30.47	0.74	0.56-0.97	
Occupations					0.616
Agricultures	126	33.07	Ref.		
Employees and sales	112	31.91	0.95	0.70-1.30	
Government and Entrepreneur officers	16	30.77	0.90	0.48-1.68	
Unemployees or others	68	37.36	1.21	0.84-1.74	
Grading of sputum smear AFB at baseline treatment					< 0.001
Scanty	8	14.55	Ref.		
1+	59	20.34	1.50	0.67-3.35	
2+	59	31.89	2.75	1.22-6.19	
3+	196	44.95	4.80	2.21-10.40	
Comorbidity					0.395
No	253	32.69	Ref.		
Yes	69	35.94	1.15	0.83-1.61	
Health services accessibility					0.002
Community hospitals	204	30.77	Ref.		
Secondary hospitals	81	34.91	1.21	0.88-1.66	
Tertiary hospitals	16	43.24	1.71	0.88-3.35	
Private hospitals	21	61.76	3.63	1.79-7.40	
Direct observation therapy (DOT)					0.710
Health staff	198	33.79	Ref.		
Non-health staff	124	32.63	0.95	0.72-1.25	
Timeliness of following up (with 70 days)					0.228
Yes	284	34.05	Ref.		
No	38	28.79	0.78	0.52-1.17	
Risk group					0.408
No	270	32.81	Ref.		
Yes	52	36.36	1.17	0.81-1.70	
History of contacts to TB patients					0.237
No	173	35.09	Ref.		
Yes	149	31.50	0.85	0.65-1.11	
History of contacts to MDR-TB patients					0.083
No	301	34.13	Ref.		
Yes	21	25.00	0.64	0.39-1.07	

ve+: Positive; OR: Odds ratio; 95%CI: 95 Percent confidence interval; Ref.: Reference group; *p was calculated by using a partial likelihood ratio test.

as OR < 1, and no association as an OR that includes 1.

Results

The demographic characteristics of the cases and controls showed that most subjects were male, comprising 82.30% of cases and 73.76% of controls. Approximately one-third of both groups were aged 60 or older (22.36% of cases and 21.74% of controls), with the mean age being 49.01 years (SD = 14.64) for cases and 47.04 years (SD = 15.80) for controls. Both groups had similar rates of employment in agriculture (39.13% and 39.60%, respectively).

More than half of both groups had an initial treatment weight of 50 kg or more (52.80% of cases and 60.25% of controls). A high proportion of cases (60.87%) and one-third of controls had a baseline sputum smear AFB grading of 3+. Comorbidities were present in approximately one-third of both groups. Among cases, the most common comorbidities were diabetes, asbestosis, and HIV whereas among controls, they were diabetes, silicosis, and HIV.

Directly observed therapy (DOT) by non-health staff was reported by 38.51% of cases and 39.75% of controls. Both groups had high follow-up rates during the first two months (88.20% of cases and 85.40% of controls), with no notable tuberculosis risk factors identified in most participants (83.85% of cases and 85.87% of controls). Around half had a history of TB contact, including close contacts (44.41% of cases and 47.36% of controls) and household contacts (1.86% of cases and 2.95% of controls), while 6.52% of cases and 9.78% of controls had contact with MDR-TB patients. Most participants accessed community healthcare services (63.35% of cases and 71.27% of controls).

Logistic regression revealed that male subjects were more likely to experience sputum smear non-conversion than females. Subjects aged 35-59 and those aged 60 or older had a higher likelihood of non-conversion compared to those under 35. Subjects with a body weight of 50 kg or more were 26% less likely to experience non-conversion. Higher sputum smear AFB gradings (2+ and 3+) at baseline were significantly associated with non-conversion. Additionally, receiving treatment at a private hospital was significantly associated with increased odds of sputum smear non-conversion (Table 1).

Multivariate logistic regression confirmed significant associations between sputum smear non-conversion and several factors, including male gender, older age, lower body weight, higher AFB grading at baseline, and receiving private care at a private hospital. Male subjects and those aged 35 or older had an approximately a twofold increased risk of non-conversion. Higher baseline AFB gradings were also significantly associated with increased odds of non-conversion. Notably, receiving treatment at a private hospital was linked to nearly a fivefold increase in the risk of sputum smear non-conversion (Table 2).

Table 2. Multivariate analysis of factors associated with sputum smear non-conversion at the end of intensive phase treatment among patients with pulmonary tuberculosis in Upper Southern, Thailand.

Factors	Crude OR (95%CI)	Adjust OR (95%CI)	*p**
Sex			0.012
Female	Ref.	Ref.	
Male	1.65 (1.18-2.31)	1.57 (1.10-2.25)	
Age (years)			0.013
< 35	Ref.	Ref.	
35-59	1.73 (1.20-2.51)	1.75 (1.19-2.59)	
≥ 60	1.58 (1.02-2.43)	1.72 (1.09-2.71)	
Weight at baseline treatment (kg)			0.027
< 50	Ref.	Ref.	
≥ 50	0.74 (0.56-0.97)	0.72 (0.54-0.96)	
Grading of AFB Smart at baseline treatment			< 0.001
Scanty	Ref.	Ref.	
1+	1.50 (0.67-3.35)	1.45 (0.64-3.29)	
2+	2.75 (1.22-6.19)	2.74 (1.20-6.28)	
3+	4.80 (2.21-10.40)	4.72 (2.14-10.43)	
Health services accessibility			< 0.001
Community hospitals	Ref.	Ref.	
Secondary hospitals	1.21 (0.88-1.66)	1.33 (0.95-1.87)	
Tertiary hospitals	1.71 (0.88-3.35)	1.69 (0.83-3.41)	
Private hospitals	3.63 (1.79-7.40)	4.94 (2.34-10.44)	

ve+: Positive; OR: Odds ratio; 95%CI: 95 Percent confidence interval; Ref.: Reference group; *p was calculated by using a partial likelihood ratio test.

Discussion

In summary, our study identified several factors significantly associated with sputum smear non-conversion among pulmonary tuberculosis patients at the end of the intensive treatment phase. These include sex, age, baseline weight, baseline sputum smear grading, and access to healthcare services.

Males were found to be twice as likely as females to experience sputum smear non-conversion. Physiological differences between sexes – such as variations in chromosomes, hormones, and immune response – contribute to this disparity [14]. Females generally exhibit higher levels of white blood cells and stronger immune responses, which aid in combating *Mycobacterium tuberculosis* infections [15]. In contrast, males tend to have lower white blood cell counts and may develop more severe cavitary disease due to higher pathogen loads [16]. Additionally, behavioral factors – such as lower treatment adherence and reduced self-care practices among males, particularly over the long course of TB treatment – further exacerbate their elevated risk [17,18].

These findings align with previous studies. A cohort study conducted in Portugal found that males were ten times more likely to experience non-conversion (OR = 10.80) [19], while a study in South African demonstrated a smaller increased risk (OR = 1.44) [20]. Conversely, studies from The Gambia and Tanzania reported a reduced association between male sex and non-conversion, with odds ratios of 0.58 and 0.49, respectively [21,22]. In Thailand, one study also observed a reduced, though non-significant, association (OR = 0.88) [10].

Our findings indicate that older age is significantly associated with sputum smear non-conversion. Aging weakens the immune system, making it more difficult for older patients to eliminate infections effectively [23]. Additionally, older adults are more likely to experience adverse reactions to TB treatment, which can further complicate recovery [24]. Studies conducted in Suriname (AOR = 6.10), Tanzania (OR = 6.70), and Portugal (OR = 4.40) support this association between older age and an increased risk of non-conversion [19,25,26], A study from Thailand also reported a smaller but significant risk in individuals over 40 years of age (AOR = 2.88) [9]. However, studies in Rwanda [27], Tanzania [28], and Iran [29] found no statistically significant association between age and sputum smear non-conversion.

Patients with a baseline weight of ≥ 50 kg were 28% more likely to achieve sputum smear conversion, possibly due to better health status, greater nutritional reserves, and improved tolerance to anti-tuberculosis treatment. A higher body weight may help mitigates the adverse effects of anti-TB drugs, thereby supporting treatment adherence and efficacy [30,31]. However, this association should be interpreted with caution, as previous studies have reported inconsistent findings across different settings, including Thailand [9,10], Malaysia [33], Pakistan [34], Rwanda [27], Tanzania [28, 35], and Uganda [36], where found no significant link was observed between baseline weight and sputum smear non-conversion. Nevertheless, a study from Lithuanian similarly found that a lower body mass index (BMI) was associated with a reduced conversion rate (OR = 0.81) [32].

A higher baseline sputum smear AFB grading (2+ and 3+) was associated with a significantly increased risk of non-conversion. AFB testing quantifies the bacterial load of *Mycobacterium tuberculosis*, with higher grades indicating more severe infections that typically require longer periods to resolve [37]. Studies from Cameroon [38], Tanzania [26], and Lithuania [32] similarly reported that patients with 2+ and 3+ grades had higher odds of non-conversion. However, studies from South Africa [20,39], Suriname [25], and Thailand [10] reported only moderate or non-significant association. Our findings also indicate that patients receiving treatment at private hospitals had a nearly fivefold higher risk of sputum smear non-conversion compared to those treated at community hospitals. This disparity may stem from several factors. Private hospitals may not implement DOT as rigorously, may have less standardized laboratory quality control procedures, and may lack the comprehensive TB control programs typically found in public health facilities. These systemic differences likely contribute to reduced treatment adherence and inadequate follow-up, ultimately compromising patient outcomes. This highlights the urgent need to strengthen TB control strategies in the private healthcare sector. Key action should include enhanced staff training, strict implementation of DOT, and the standardization of treatment protocols to align with national TB guidelines. Such improvements are essential to ensure consistent and effective tuberculosis management across all healthcare settings.

Our findings show a significant association between health service accessibility and sputum smear non-conversion at the end of intensive TB treatment. Patients treated in private hospitals had a fivefold higher risk of non-conversion compared to those treated in community hospitals. This study, conducted in upper southern Thailand, covered seven provinces where

most healthcare facilities are affiliated with the MOPH. Approximately 80.81% of these facilities are public, comprising three tertiary hospitals (3.03%), nine secondary hospitals (9.09%), and 68 community hospitals (68.69%). In contrast, private hospitals constitute 19.19% of the total. TB clinics in these public facilities are subject to annual monitoring by the Division of Tuberculosis, ensuring compliance with high standards of care, including adherence to the International Standards for Tuberculosis Care (ISTC). Moreover, the provision of DOT by trained health personnel in these settings is associated with lower, and often non-significant sputum, rates of sputum smear non-conversion – particularly in secondary and tertiary hospitals – ultimately improving treatment outcomes.

This study's strengths include the use of secondary data from the NTIP Registry, managed by ODPC 11 in Nakhon Sri Thammarat, where treatment outcomes were recorded by trained professionals, ensuring data accuracy. The large sample size allowed for precise detection of associations with sputum smear non-conversion, as evidenced by the narrow confidence intervals. A power analysis, using continuity correction for the case-control design with sputum grading proportions of 0.41 and 0.59 for cases and controls, respectively, demonstrated a power of 99.70% (1-β) at an alpha level of 0.05 [11-13]. Despite the large initial sample size, approximately 82% of eligible cases were excluded due to transfer out, death, incomplete sputum smear results, or ongoing treatment. This high exclusion rate may introduce selection bias and limit the generalizability of the findings to all pulmonary tuberculosis patients in the region. Patients with more severe disease or poor treatment adherence may have been underrepresented, potentially influencing the observed associations. Additionally, the study did not account for certain clinical and behavioral factors – such as cavitary lesions [32], smoking [40], alcohol use, substance abuse [32,41], nutritional status, or treatment side effects - due to limitations in the NTIP Registry. These unmeasured variables may affect sputum smear conversion, particularly among patients treated in private hospitals or those in high-risk groups, and should be considered when interpreting the results.

The identified factors—sex, age, weight, sputum grading, and healthcare accessibility—highlight the need for targeted interventions to improve TB treatment outcomes. In particular, the markedly higher risk of non-conversion in private hospitals calls for urgent policy action. Standardizing the implementation of DOT, enhancing patients' follow-up, and providing tailored education for high-risk groups – such as older males and those with higher AFB sputum grades – are essential strategies. Policymakers should strengthen TB control efforts through improved resource allocation, inter-sectoral collaboration, and public-private partnerships to ensure equitable and high-quality care.

Conclusions

The study concludes that sex, age, baseline weight, sputum grading, and healthcare accessibility significantly affect sputum smear non-conversion among pulmonary tuberculosis patients. Tailored interventions are essential, especially for high-risk groups such as older males and those treated in private hospitals. Concrete strategies – such as implementing standardized DOT protocols, enhancing follow-up systems, and providing targeted TB education and counselling in private healthcare settings – are recommended to improve treatment adherence and outcomes. Strengthening the capacity of healthcare providers, allocating appropriate resources, and fostering public-private collaboration are also critical. Continued monitoring and future research into behavioral and lifestyle factors will further inform clinical practice and public health policy.

Ethics statement

The tuberculosis database was authorized for use and obtained from the Office of Disease Prevention and Control, 11, Nakhon Si Thammarat. This study received approval from the Ethics Committee on Human Rights Related to Human Experimentation at Thaksin University, Thailand, under COA No. TSU 2021-007 and REC No. 0247 on January 22, 2020.

Authors' contributions

W.B., B.C., and S.W. conceptualized and designed the study. W.B. and S.W. participated in the study's data collection and literature review. W.B. and B.C. analyzed and interpreted the data. W.B. and B.C. drafted the initial manuscript. S.W. and B.C. supervised the project. All authors approved the manuscript, and the final version of the manuscript was submitted.

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Conflict of interest

No conflict of interest is declared.

References

1. Koenig SP, Furin J (2016) Update in tuberculosis/pulmonary infections 2015. Am J Respir Crit Care Med 194: 142-6. doi: 10.1164/rccm.201601-0129UP.
2. Furin J, Cox H, Pai M (2019) Tuberculosis. Lancet 393: 1642-56. doi: 10.1016/S0140-6736(19)30308-3.
3. MacNeil A, Glaziou P, Sismanidis C, Date A, Maloney S, Floyd K (2020) Global epidemiology of tuberculosis and progress toward meeting global targets - worldwide, 2018. MMWR Morb Mortal Wkly Rep 69: 281-285. doi: 10.15585/mmwr.mm6911a2.
4. Sulis G, Roggi A, Matteelli A, Raviglione MC (2014) Tuberculosis: epidemiology and control. Mediterr J Hematol Infect Dis 6: e2014070. doi: 10.4084/MJHID.2014.070.
5. Bhuket JR, Pungrassami P, Chongsuvivatwong V (2013) Hospital tuberculosis control activities and treatment success in Thailand during the implementation year of the admission policy for new smear positive pulmonary tuberculosis patients. J Med Assoc Thai 96: 782-785.
6. World Health Organization (2024) Treatment of tuberculosis: guidelines, 4th edition 2010. Available: https://apps.who.int/iris/handle/10665/44165. Accessed: 11 October 2024.
7. Buatong W, Chaimay B, Woradet S (2021) Factors associated with sputum not conversion after intensive treatment among new cases of pulmonary tuberculosis: academic article. KKU J for Public Health Res 14: 60-77. [Article in Thai]
8. Pramual P, Khiewyoo J, Tesana N (2014) Factor related to a sputum conversion after 2-3 months among new smear positive pulmonary tuberculosis patients in Sisaket. KKU Res J GS 14: 93-105. [Article in Thai]
9. Yodkalw E (2017) Factors associated with sputum smear positive after intensive phase of treatment in pulmonary tuberculosis, Satuek Hospital, Burirum Province. Dis Control J 43: 111-119. [Article in Thai]
10. Mahatthanaphak S, Tiraratchakul S, Thattiampong N, Doncommul P, Saengsawang K. (2022) Sputum conversion among patients with pulmonary tuberculosis: Are two weeks enough for respiratory isolation?. Lampang Medical Journal 32: 60-73. [Article in Thai]
11. Bernard R (2000) Fundamentals of biostatistics, 5th edition. California: Duxbury Press. 792 p.
12. Fleiss JL, Levin B, Paik MC (2003) Statistical methods for rates and proportions. 3rd edition. New Jersey: John Wiley & Sons. 760 p.
13. Ngamjarus C (2016) n4Studies: Sample size calculations for an epidemiology study on a smart device. Siriraj Med J 68: 160-170.
14. vom Steeg LG, Klein SL (2016) SeXX matters in infectious disease pathogenesis. PLoS Pathog 12: e1005374. doi: 10.1371/journal.ppat.1005374.
15. Silveyra P, Fuentes N, Rodriguez Bauza DE (2021) Sex and gender differences in lung disease. Adv Exp Med Biol 1304: 227-258. doi: 10.1007/978-3-030-68748-9_14.
16. Tan W, Soodeen-Lalloo AK, Chu Y, Xu W, Chen F, Zhang J, Sha W, Huang J, Yang G, Qin L, Wang J, Huang X, Shi J, Feng Y (2018) Sex influences the association between haemostasis and the extent of lung lesions in tuberculosis. Biol Sex Differ 9: 44. doi: 10.1186/s13293-018-0203-9.
17. Horton KC, MacPherson P, Houben RM, White RG, Corbett EL (2016) Sex differences in tuberculosis burden and notifications in low- and middle-income Countries: a systematic review and meta-analysis. PLoS Med 13: e1002119. doi: 10.1371/journal.pmed.1002119.
18. Jankowska-Polanska BK, Kamińska M, Uchmanowicz I, Rycombel A (2015) Quality of life and health behaviours of patients with tuberculosis - sex differences. Pneumonol Alergol Pol 83: 256-265. doi: 10.5603/PiAP.2015.0046.
19. Caetano Mota P, Carvalho A, Valente I, Braga R, Duarte R (2012) Predictors of delayed sputum smear and culture conversion among a Portuguese population with pulmonary tuberculosis. Rev Port Pneumol 18: 72-79. doi: 10.1016/j.rppneu.2011.12.005.
20. Mlotshwa M, Abraham N, Beery M, Williams S, Smit S, Uys M, Reddy C, Medina-Marino A (2016) Risk factors for tuberculosis smear non-conversion in Eden district, Western Cape, South Africa, 2007-2013: a retrospective cohort study. BMC Infect Dis 16: 365. doi: 10.1186/s12879-016-1712-y.
21. Lienhardt C, Manneh K, Bouchier V, Lahai G, Milligan PJ, McAdam KP (1998) Factors determining the outcome of treatment of adult smear-positive tuberculosis cases in The Gambia. Int J Tuberc Lung Dis 2: 712-718.
22. Senkoro M, Mfinanga SG, Mørkve O (2010) Smear microscopy and culture conversion rates among smear positive pulmonary tuberculosis patients by HIV status in Dar es Salaam, Tanzania. BMC Infect Dis 10: 210. doi: 10.1186/1471-2334-10-210.
23. Lowery EM, Brubaker AL, Kuhlmann E, Kovacs EJ (2013) The aging lung. Clin Interv Aging 8: 1489-1496. doi: 10.2147/CIA.S51152.
24. Yen YF, Feng JY, Pan SW, Chuang PH, Su VY, Su WJ (2017) Determinants of mortality in elderly patients with tuberculosis: a population-based follow-up study. Epidemiol Infect 145: 1374-1381. doi: 10.1017/S0950268817000152.
25. Commiesie E, Stijnberg D, Marín D, Perez F, Sanchez M (2019) Determinants of sputum smear nonconversion in smear-positive pulmonary tuberculosis patients in Suriname, 2010-2015. Rev Panam Salud Publica 43: e86. doi: 10.26633/RPSP.2019.86.
26. Gunda DW, Nkandala I, Kavishe GA, Kilonzo SB, Kabangila R, Mpondo BC (2017) Prevalence and risk factors of delayed sputum conversion among patients treated for smear positive PTB in Northwestern Rural Tanzania: A retrospective cohort study. J Trop Med 2017: 5352906. doi: 10.1155/2017/5352906.
27. Kayigamba FR, Bakker MI, Mugisha V, De Naeyer L, Gasana M, Cobelens F, Schim van der Loeff M (2013) Adherence to tuberculosis treatment, sputum smear conversion and mortality: a retrospective cohort study in 48 Rwandan clinics. PLoS One 8: e73501. doi: 10.1371/journal.pone.0073501.
28. Jeremiah K, PrayGod G, Faurholt-Jepsen D, Range N, Andersen AB, Grewal HMS, Friis H (2010) BCG vaccination status may predict sputum conversion in patients with pulmonary tuberculosis: a new consideration for an old vaccine? Thorax 65: 1072-6. doi: 10.1136/thx.2010.134767.
29. Behnaz F, Mohammadzadeh M, Mohammadzade G (2015) Five-year assessment of time of sputum smears conversion and outcome and risk factors of tuberculosis patients in central iran. Tuberc Res Treat 2015: 609083. doi: 10.1155/2015/609083.
30. Zhang HQ, Xi XE, Wang YL, Han W, Zhang CX, Jiao JH (2015) Side effects of tuberculosis treatment with fixed-dose combinations. J Biol Regul Homeost Agents 29: 379-388.

31. Warmelink I, ten Hacken NH, van der Werf TS, van Altena R (2011) Weight loss during tuberculosis treatment is an important risk factor for drug-induced hepatotoxicity. Br J Nutr 105: 400-408. doi: 10.1017/S0007114510003636.

32. Diktanas S, Vasiliauskiene E, Polubenko K, Danila E, Celedinaite I, Boreikaite E, Misiunas K (2018) Factors associated with persistent sputum positivity at the end of the second month of tuberculosis treatment in Lithuania. Tuberc Respir Dis (Seoul) 81: 233-240. doi: 10.4046/trd.2017.0096.

33. Shariff NM, Safian N (2015) Diabetes mellitus and its influence on sputum smear positivity at the 2nd month of treatment among pulmonary tuberculosis patients in Kuala Lumpur, Malaysia: a case control study. Int J Mycobacteriol 4 :323-329. doi: 10.1016/j.ijmyco.2015.09.003

34. D'Souza KA, Zaidi SMA, Jaswal M, Butt S, Khowaja S, Habib SS, Malik AA (2018) Factors associated with month 2 smear non-conversion among Category 1 tuberculosis patients in Karachi, Pakistan. J Infect Public Health 11: 283-285. doi: 10.1016/j.jiph.2017.06.009.

35. Nagu TJ, Spiegelman D, Hertzmark E, Aboud S, Makani J, Matee MI, Fawzi WW, Mugusi F (2014) Anemia at the initiation of tuberculosis therapy is associated with delayed sputum conversion among pulmonary tuberculosis patients in Dar-es-Salaam, Tanzania. PLoS One 9: e91229. doi: 10.1371/journal.pone.0091229.

36. Atwine D, Orikiriza P, Taremwa I, Ayebare A, Logoose S, Mwanga-Amumpaire J, Jindani A, Bonnet M (2017) Predictors of delayed culture conversion among Ugandan patients. BMC Infect Dis 17: 299. doi: 10.1186/s12879-017-2335-7.

37. Bayot ML, Mirza TM, Sharma S (2024) Acid fast bacteria. [Updated 2023 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Available: https://www.ncbi.nlm.nih.gov/books/NBK537121/. Accessed: 11 January 2025.

38. Djouma FN, Noubom M, Ateudjieu J, Donfack H (2015) Delay in sputum smear conversion and outcomes of smear-positive tuberculosis patients: a retrospective cohort study in Bafoussam, Cameroon. BMC Infect Dis 15: 139. doi: 10.1186/s12879-015-0876-1.

39. Kigozi NG, Chikobvu P, Heunis JC, van der Merwe S (2014) A retrospective analysis of two-month sputum smear non-conversion in new sputum smear positive tuberculosis patients in the Free State Province, South Africa. J Public Health Afr 5: 324. doi: 10.4081/jphia.2014.324.

40. Pefura-Yone EW, Kengne AP, Kuaban C (2014) Non-conversion of sputum culture among patients with smear positive pulmonary tuberculosis in Cameroon: a prospective cohort study. BMC Infect Dis 14: 138. doi: 10.1186/1471-2334-14-138.

41. Hermosilla S, You P, Aifah A, Abildayev T, Akilzhanova A, Kozhamkulov U, Muminov T, Darisheva M, Zhussupov B, Terlikbayeva A, El-Bassel N, Schluger N (2017) Identifying risk factors associated with smear positivity of pulmonary tuberculosis in Kazakhstan. PLoS One 12: e0172942. doi: 10.1371/journal.pone.0172942.