Assessing Risk Factors for Tuberculosis Treatment Failure Among Pulmonary Tuberculosis Patients in Four Health Regions of Burkina Faso, 2009

Participant Guide

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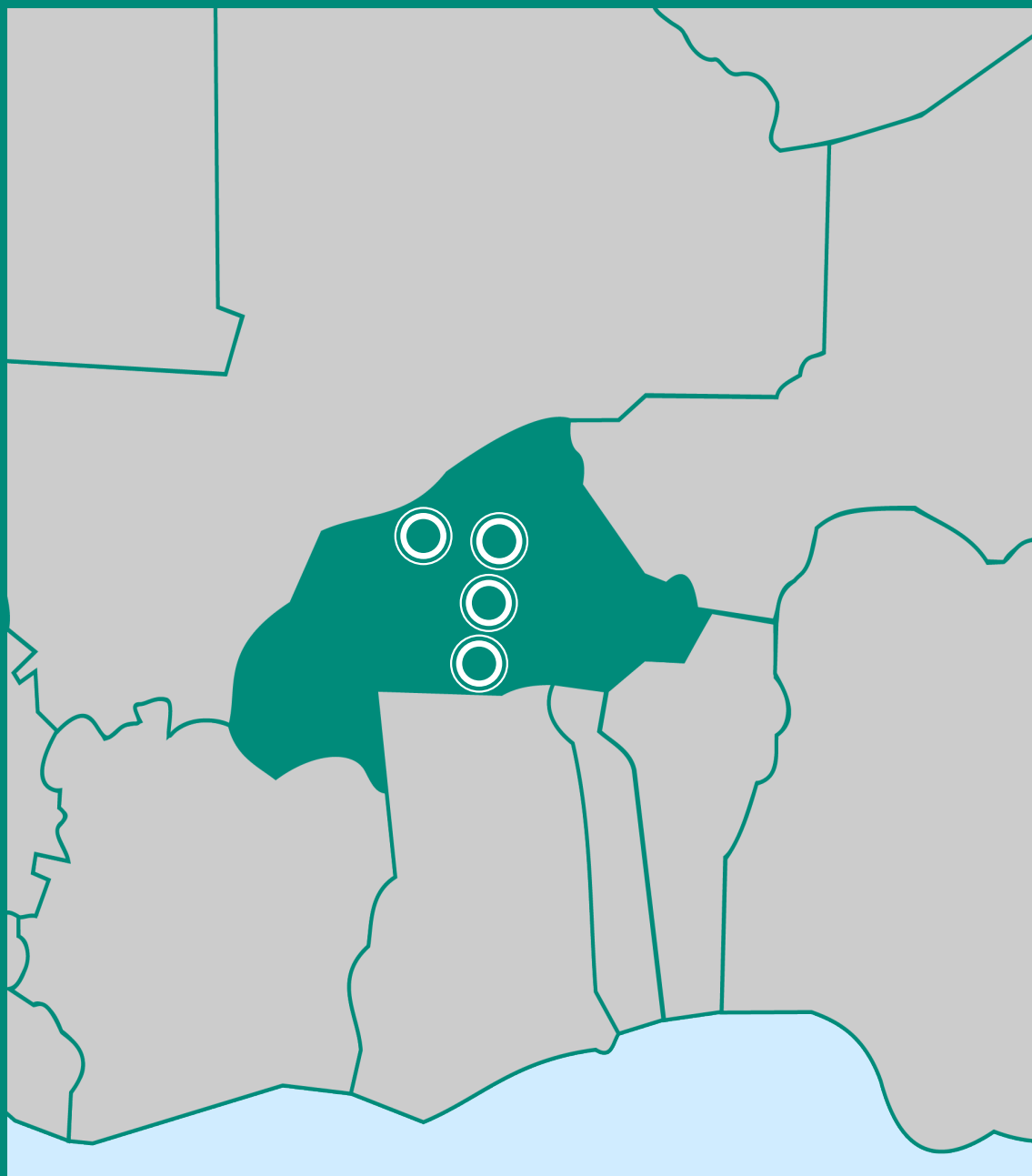AFENET
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Assessing Risk Factors for Tuberculosis Treatment Failure Among Pulmonary Tuberculosis Patients in Four Health Regions of Burkina Faso, 2009

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Abstract

Conducting research studies is one of the competencies that epidemiology students should have after two years training as a crucial component to identifying and resolving public health problems. This case study is developed from a research study on assessing risks factors on tuberculosis treatment failure in Burkina Faso in 2009 to help student to cover these competences. This case study is ideal for reinforcing principles of conducting case-control studies for risk-factor assessment. The case study will help epidemiology learners outline a study proposal, reinforce knowledge about research design, data collection and data analysis issues, recognize the importance of ethics in research, and interpret results and use them to make conclusions and recommendations.

How to Use the Case Study

General instructions: Ideally 1 to 2 instructors facilitate the case study for 15 to 20 trainees in a classroom. The instructor should direct participants to read the paragraphs out loud, going around the room to give each participant a chance to read. When the participant reads a question, the instructor directs all participants to perform calculations, construct graphs, or engage in discussions. The instructor may direct the class to play different roles or take different sides in answering a question. As a result, participants learn from each other, not just from instructors. Specific instructor's notes are included with each question in the instructor's version of this case study.

Audience: Learners in epidemiology and other public health practitioners who are interested in this topic

Prerequisites: Before using this case study, participants should have received lectures on study design, data management, and protocol writing.

Materials needed: Laptop with Microsoft Word with Excel, Power Point and Epi Info, graph paper, flipchart or white board with markers

Level of training and associated public health activity: FETP Resident 2nd years – conducting research study

Time required: 2-3 hours

Language: English

Participant Guide

Goal of Case Study: To review and simulate the process of planning, analysis and interpretation of research study using assessment of risk factors for tuberculosis treatment failure to improve tuberculosis cases management in TB diagnosis and treatment centers in Burkina Faso.

Learning Objectives - After completion of this case study, the participants should be able to:

1. Outline a study proposal
2. Demonstrate an understanding of study protocol submission to the National Ethics Committee for Health
3. Identify appropriate study design
4. Select study population
5. Discuss data collection process
6. Outline data analysis plan to address research question
7. Interpret study results in a logical sequence
8. Draw conclusions based on results

Introduction

Pulmonary tuberculosis (TB) is a contagious bacterial infection that involves the lung. It is caused by the bacterium *Mycobacterium tuberculosis*. It's a re-emerging severe disease in developing countries. A case of pulmonary tuberculosis (PTB) refers to a patient with two or more initial sputum smear examinations positive for Acid-Fast Bacilli (AFB) [1], or one sputum smear examination positive for AFB plus radiographic abnormalities consistent with active PTB as determined by a clinician, or one sputum smear positive for AFB plus sputum culture positive for *M. tuberculosis*.

The treatment involves many medications. The World Health Organization recommends that a patients (those who have no history of prior TB treatment or who received less than one month of anti-TB drug) should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR [1]. After failing to the first line regimen, patients should take retreatment regimen: 2HRZES/1HRZE/5HRE [1]. For smear-positive pulmonary TB patients treated with first-line drugs, sputum smear microscopy should be performed at completion of the intensive phase of treatment (after 2 months) and after 5 months of the treatment. In a new patient, if the specimen obtained at the end of the intensive phase (after 2 months) is smear-positive, sputum smear microscopy should be performed at the end of the third month. If the specimen obtained at the end of month 3 is smear-positive, sputum culture and drug susceptibility testing should be performed. At the end of the treatment course for each individual patient, the treatment outcomes must be recorded.

In Burkina Faso 2,614 pulmonary tuberculosis cases have been reported in 2007, of which 73% were successfully treated while the WHO target is an 85% treatment success rate. The low treatment success rate may be explained by treatment failure which increased from 4.1% in 2003 to 7% in 2007 [3]. Burkina Faso National Tuberculosis Programme began the DOTS strategy in 1995, which currently covers 100% of the country with 81 TB diagnostic and treatment centres. The country has 106 laboratories where routine sputum-smear examination is done and two national referral laboratories. The drug susceptibility testing (DST) and microbiological culture tests are not yet available at the national referral laboratories.

Part 1

Four of the 13 regions of Burkina Faso (North, North-Centre, South-Centre and Central-Plateau) reported a 50% treatment failure rate (Figure 1) [3]. Treatment failure is a health and economic burden as the patient remains a source of infection in the community and it may lead to the development of multidrug resistance, apart from the indirect economic burden attributed to absence from work and inability to work. There is limited information on factors leading to TB treatment failure in Burkina Faso. Knowledge of factors associated with TB treatment failure could assist healthcare workers in identifying the particular personal stressors that inhibit compliance with TB treatment, as well as provider-level impediments to achieving treatment completion. It's necessary to conduct studies in order to investigate possible causes of TB treatment failure.

In Burkina Faso the TB treatment outcomes are defined as follows:

- Cured: A patient who was initially culture or sputum smear microscopy positive at the beginning of the treatment but who was smear-negative in the last month of treatment and on at least one previous occasion;

- Treatment completed: A patient who completed treatment but who did not meet the criteria to be classified as a cure or a treatment failure;

- Treatment failure: A new patient who is culture or sputum smear microscopy positive after five months or later during treatment;

- Died: A patient who died from any cause during the course of treatment;

- Defaulted: A patient whose treatment was interrupted for two consecutive months;

- Transferred out: A patient who was transferred to a health facility in another basic management unit and for whom the treatment outcome is not known;

- Successfully treated: A patient who was cured or who completed treatment.

Figures 1 & 2. Maps of Burkina Faso showing area with high Tuberculosis treatment failure rate in red
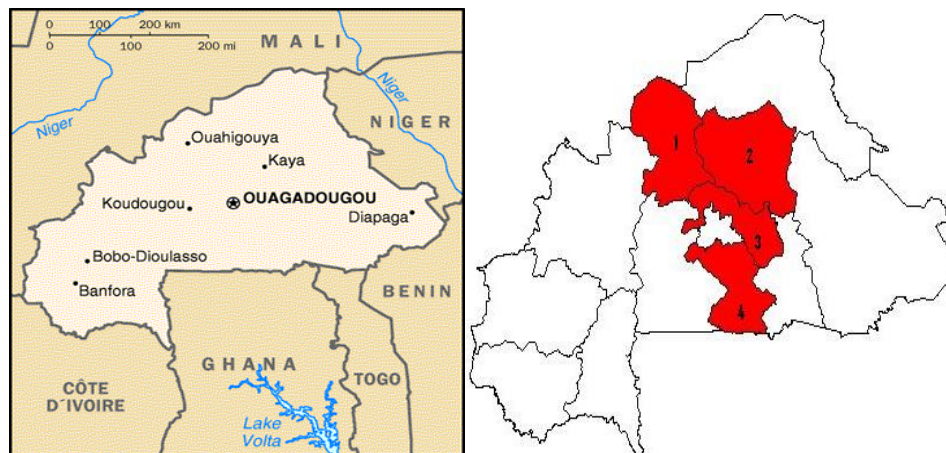
In January 2010, investigators from academic institutions in the country wrote a research proposal to study risk factors for TB treatment failure. The proposal was submitted to the Burkina Faso National Ethics Committee for Health in April 2010 and approval was obtained in May 2010.

Question 1. What is an appropriate research question for this study?

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Question 2. What are the standard sections of a research proposal? Discuss each section.

Question 3. What are the requirements of study protocol submission to the National Ethics Committee (or Institutional Review Board)?
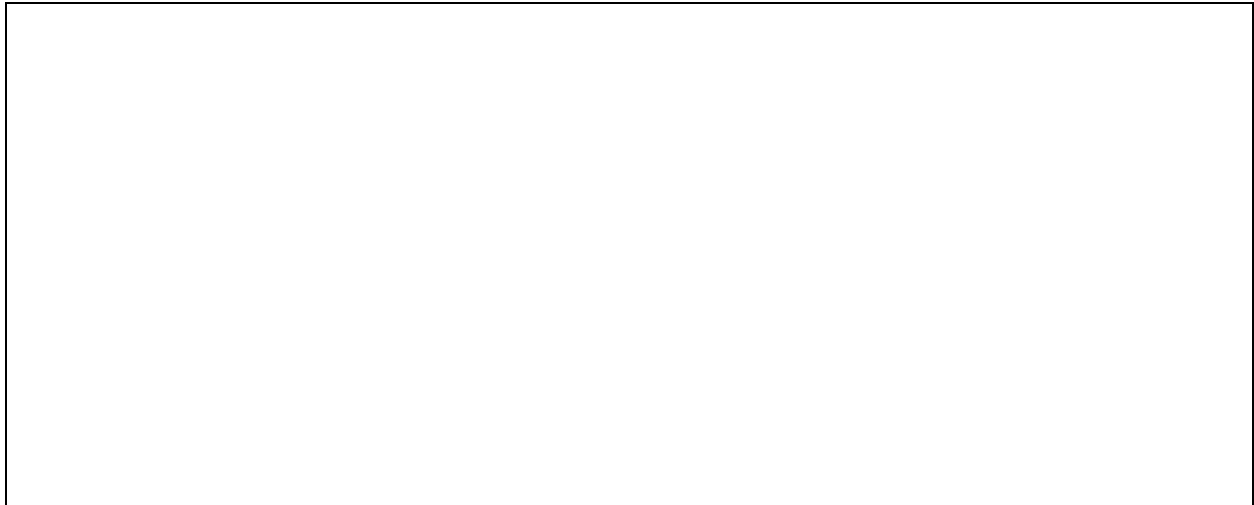
Part 2

The investigators proposed a study that is feasible to implement within their financial and time constraints, leveraging existing records to the extent possible. Burkina Faso has 81 tuberculosis diagnostic and treatment centers including laboratories for sputum smear examination. All TB patients diagnosed are registered and managed by TB diagnosis and treatment center staff. TB registers are not always complete because some patients are lost to follow up and some leave health facilities for traditional healers. Some patients, while taking TB drugs, use traditional medicines [4,5,6].

Question 4. What possible study designs could be used to address the research question?
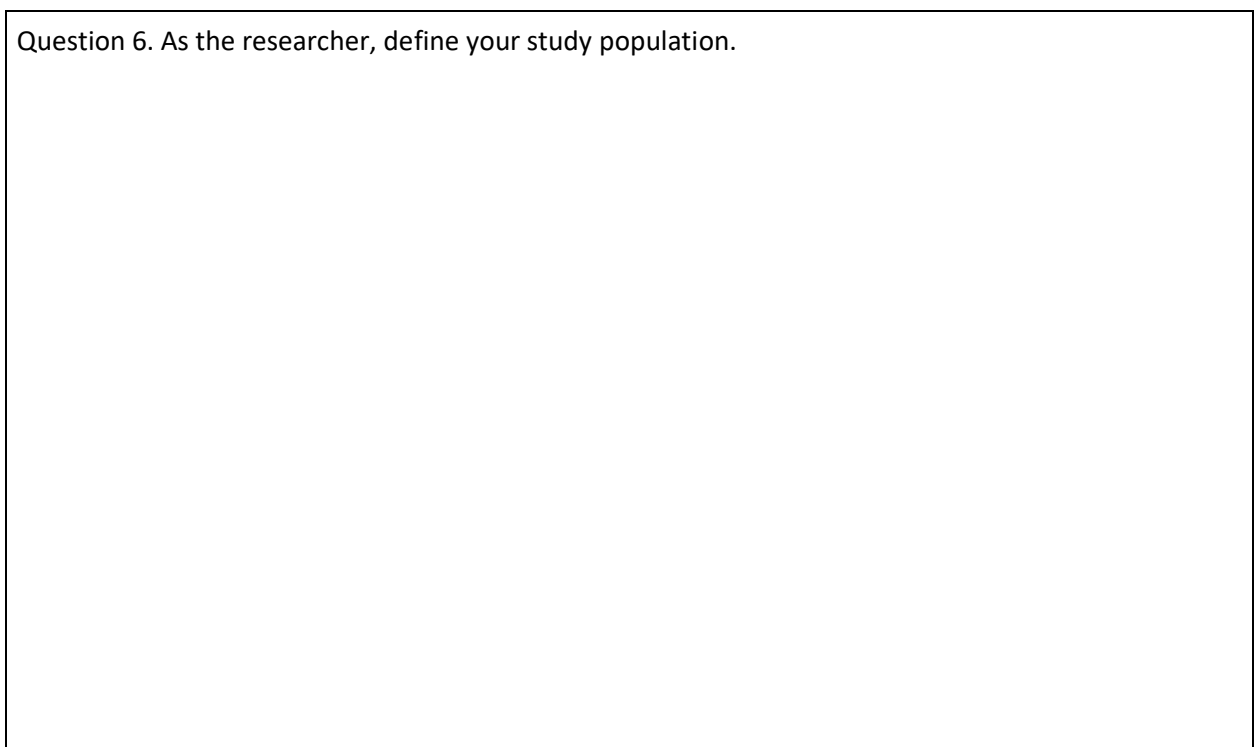
Question 5. Which design would you pick and why?

After developing the research questions and selecting the study design, the investigators began to define the population for study.

Question 6. As the researcher, define your study population.

Question 7. What records can you review to identify study participants?

Question 8. What variables would you consider for data collection?

Part 3

In July 2010, Investigator recruited 10 health workers in Tuberculosis Treatment Centers for data collection. Interviewers were trained in interviewing techniques. Interviewers collected data by face-to-face interviews using a structured interviewer-administered questionnaire, and by review of laboratory record registers. The team piloted the questionnaires to determine the feasibility of the sampling and whether the questions measure the desired variables based on study objectives. Patient interviews were carried out by health workers at the patient's residence in a relaxed and conducive atmosphere.

A data manager entered the data in Epi Info version 3.5.1 and cleaned the data by double entry to detect and correct errors and inconsistencies in the database not detected during the first quality check. Missing information was added by going back to the paper-based questionnaire. Data analysis was done using Epi Info version 3.5.1.

Question 9. What steps should be taken to conduct a data analysis?

Demographic characteristics have been collected for study participants and the results were tabulated in Table 1.

Table 1: Demographics characteristics of study participants, Burkina Faso, 2009

Characteristics	Cases n (%)	Non-cases n (%)
Age group		
< 25 years	2 (2%)	12 (12%)
25-44 years	59 (59%)	54 (54%)
45-54 years	21 (21%)	17 (17%)
> 55 years	18 (18%)	17 (17%)
Sex		
Female	27 (27%)	44 (44%)
Male	73 (73%)	56 (56%)

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:152

Question 10. Interpret Table 1.

The investigators then conducted a bivariate analysis to evaluate characteristics of the TB patients versus non-cases. The results from this analysis are shown in Tables 2 – 4.

Table 2: Demographic characteristics of study participants, Burkina Faso, 2009

Factors	Cases n (col%)	Non-cases n (col%)	Measure of Association	95% CI	p-value
Age					
< 45 years	61 (61%)	66 (66%)	0.80	0.45 – 1.43	0.23
45+ years	39 (39%)	34 (34%)			
Sex					
Female	27 (27%)	44 (44%)	2.12	1.17 – 3.84	0.006
Male	73 (73%)	56 (56%)			

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:15

Table 3: Clinical and family support factors of study participants, Burkina Faso, 2009

Factors	Cases n (col%)	Non-cases n (col%)	Measure of Association	95%CI	p-value
Sputum smear positive at 2nd month					
Yes	80 (80%)	31 (31%)	8.90	4.65–17.01	<0.001
No	20 (20%)	69 (69%)			
Underlying condition					
Yes	23 (23%)	6 (6%)	4.67	1.82-12.07	<0.001
No	77 (77%)	94 (94%)			
Failed to collect tuberculosis treatment drug					
Yes	12(12%)	3 (3%)	4.40	1.2–16.14	0.014
No	88 (88%)	97 (97%)			
Family member available to take care of patient					
Yes	82 (82%)	89 (89%)	0.56	0.25–1.26	0.08
No	18 (18%)	11 (11%)			
Patient receives support from family					
Yes	80 (80%)	86 (86%)	0.65	0.30–1.37	0.13
No	20 (20%)	14 (14%)			

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:152

Table 4: History of tuberculosis treatment of study participants, Burkina Faso, 2009

Factors	Cases n (col%)	Non-cases n (col%)	Measure of Association	95%CI	P-value
History of previous Tuberculosis treatment					
Yes	16 (16%)	3 (3%)	6.15	1.73 – 21.87	<0.001
No	84 (84%)	97 (97%)			
Failed to take TB drug					
Yes	35 (35%)	3 (3%)	17.41	5.13 – 58.98	< 0.001
No	65 (65%)	97 (97%)			
Use of traditional medicines/herbs					
Yes	36 (36%)	11 (11%)	4.55	2.15 – 9.61	< 0.001
No	64 (64%)	89 (89%)			
History of TB drug side effect					
Yes	77 (77%)	57 (57%)	2.52	1.37 – 4.65	0.001
No	23 (23%)	43 (43%)			
Treatment delay					
< 14 days	98 (98%)	99 (99%)	0.49	0.04 – 5.54	0.5
14+ days	02 (2%)	01 (01%)			

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:152

Question 11. What could be potential risk factors for treatment failure based on the Tables 2–4?

In the subsequent statistical analysis step following bivariate analysis, the data analyst stratified the analysis by age group and by sex to assess for possible confounding and effect modification. Results are shown in Tables 5 and 6.

Table 5. Factors associated with TB treatment failure stratified by age group in four health regions of Burkina Faso, 2009.

Risk Factor by Age Group	Cases	Non-cases	Stratum-specific measure of association (95% CI)	Crude measure of association (95%CI)	Mantel Haenszel adjusted measure of association
History of previous tuberculosis treatment					
< 45 years					
Yes	10	1	12.74		
No	51	65	(1.57-102.84)	6.15 (1.73-21.87)	Not applicable (NA)
45+ years					
Yes	6	2	2.90		
No	33	32	(0.54-15.49)		
Failed to collect tuberculosis drug from TB centre					
< 45 years Yes					
No	7	1	8.42		
	54	65	(1.00-70.63)	4.40 (1.20-16.14)	NA
45+ years					
Yes	5	2	2.35		
No	34	32	(0.42-13.00)		
Sputum-smear positive at 2nd month of treatment					
< 45 years Yes					
No	51	19	12.61		
	10	47	(5.32 – 29.87)	8.90 (4.65 – 17.01)	NA
45+ years					
Yes	29	12	5.31		
No	10	22	(1.94 – 14.53)		
Underlying condition					
< 45 years Yes					
No	12	4	3.79		
	49	62	(1.15-12.50)	4.67 (1.81-12.07)	NA
45+ years					
Yes	11	2	6.28		
No	28	32	(1.28-30.81)		

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Risk Factor by Age Group	Cases	Non-cases	Stratum-specific measure of association (95% CI)	Crude measure of association (95%CI)	Mantel Haenszel adjusted measure of association
Failed to take tuberculosis drug					
< 45 years					
Yes	20	2	15.60		
No	41	64	(3.46 – 70.34)		
				17.41 (5.13 – 58.98)	NA
45+ years					
Yes	15	1	20.62		
No	24	33	(2.54– 166.99)		
Use of traditional medicine or herbs					
< 45 years					
Yes	20	6	4.87		
No	41	60	(1.80-13.19)		
				4.55 (2.15-9.61)	4.49 (2.12-9.52)
45+ years					
Yes	16	5	4.03		
No	23	29	(1.28-12.66)		
History of tuberculosis drug side effects					
< 45 years					
Yes	45	36	2.34		
No	16	30	(1.10-4.95)		
				2.52 (1.37-4.65)	2.49 (1.35-4.60
45+ years					
Yes	32	21	2.82		
No	7	13	(0.96-8.25)		
Receives support from family					
< 45 years					
Yes	47	55	0.67		
No	14	11	(0.27-1.61)		
				0.65 (0.30-1.37)	0.63 (0.29-1.33)
45+ years					
Yes	33	31	0.53		
No	6	3	(0.12-2.31)		

Table 6: Factors associated with tuberculosis treatment failure stratified by sex in four health regions of Burkina Faso, Jan-Dec 2009.

Risk Factors by Sex	Cases	Non-cases	Stratum specific measure of association	Crude measure of association (95%CI)	Mantel Haenszel adjusted measure of association
Sputum-smear positive after 2nd month					
Male					
Yes	58	23	5.54		
No	15	33	(2.54-12.08)		
				8.90	NA
Female				(4.65-17.01)	
Yes	22	8	19.80		
No	5	36	(5.74-68.20)		
Failure to take tuberculosis drugs					
Male					
Yes	30	1	38.37		
No	43	55	(5.02-292.74)		
				17.41	NA
Female				(5.13-58.98)	
Yes	5	2	4.77		
No	22	42	(0.85-26.62)		
History of tuberculosis drugs side effects					
Male					
Yes	54	30	2.46		
No	19	26	(1.17-5.16)		
Female				2.52	2.75
				(1.37-4.65)	(1.46-5.18)
Yes	23	27	3.62		
No	4	17	(1.06-12.29)		
Use of traditional medicines or herbs					
Male					
Yes	27	6	4.89		
No	46	50	(1.85-12.91)		
				4.55	4.52
				(2.15-9.61)	(2.11-9.68)
Female					
Yes	9	5	3.90		
No	18	39	(1.14-13.31)		

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Risk Factors by Sex	Cases	Non-cases	Stratum specific measure of association	Crude measure of association (95%CI)	Mantel Haenszel adjusted measure of association
Underlying condition					
Male					
Yes	17	3	5.36		
No	56	53	(1.48-19.35)		
Female				4.67 (1.81-12.07)	4.77 (1.80-12.58)
Yes	6	3	3.90		
No	21	41	(0.88-17.19)		
History of previous tuberculosis treatment					
Male					
Yes	11	3	3.13		
No	62	53	(0.83-11.83)		
				6.15 (1.73-21.87)	5.28 (1.54-18.03)
Female					
Yes	5	0	NA		
No	22	44			
Failure to visit tuberculosis centre to get Tuberculosis drugs					
Male					
Yes	9	0	NA		
No	64	56			
Female				4.40 (1.20-16.14)	5.56 (1.35-22.77)
Yes	3	3	1.70 (0.31-9.14)		
No	24	41			

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:152

Question 12: Define confounding and effect modification.

Question 13: According to Tables 5 and 6, which factors appear to be confounders or effect modifiers?

The data analyst subsequently performed a multivariable regression analysis as shown in Table 7.

Table 7: Multivariable analysis of factors associated with tuberculosis treatment failure in four health regions of Burkina Faso, Jan-Dec 2009

Risk factors	Measure of Association	95%CI	P-value
Failure to take TB drug	18.53	4.56 - 75.22	<0.001
Sputum smear positive after 2 months of treatment	11.52	5.18 - 25.60	<0.001
Existence of Underlying condition	5.74	1.69 - 19.44	0.004
Use of traditional medicine/herbs	2.97	1.12 - 7.85	0.02
Sex of patient	1.19	0.54 - 2.65	0.65
Failure to collect TB drug	2.67	0.27 - 25.97	0.39
Family member take care	1.44	0.20 - 10.02	0.71
Received support from family	1.32	0.21 - 8.32	0.76
History of previous TB treatment	3.90	0.72 - 21.05	0.11
History of TB drug side effects	1.33	0.57 - 3.10	0.49

Source: Risk factors for tuberculosis treatment failure among pulmonary tuberculosis patients in four health regions of Burkina Faso, 2009. Pan African Medical Journal. 2015; 21:152

Questions 14: What conclusion can you draw from Table 7?

Question 15. Based on risk factors identified, what clinical recommendations would you make?

Question 16: What further research question can you raise from the findings?

Question 17: Based on these findings, to whom would you disseminate your results to decrease TB treatment failure? And how would you conduct this dissemination?

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Conclusion

[The conclusion will be distributed separately.]

Background Readings

1. https://www.iarc.fr/en/publications/pdfs-online/epi/cancerepi/CancerEpi-9.pdf

2. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1706071/

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4. https://nciph.sph.unc.edu/focus/vol4/issue1/4-1AdvancedData_slides.ppt

5. https://wwwn.cdc.gov/epiinfo/user-guide/StatCalc/How-to-Analysis-of-Single-and-Stratified-Tables.html

6. Michael B. Gregg. Field Epidemiology. Third Edition, 2008, p138

Competing Interests

The authors declare no competing interests.

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