



**UNIVERSITY
OF ALBERTA**

The Limitations of the Chest Radiograph In Diagnosing Subclinical Pulmonary Tuberculosis in Canada

Angela Lau MD, MSc, FRCPC, DTMH
Assistant Professor, Division of Pulmonary Medicine
Department of Medicine, University of Alberta

Adult, Culture-positive Pulmonary Tuberculosis Patients in the Province Of Alberta, Canada, 2005-2020

The Radiographic and Mycobacteriologic Correlates of Subclinical Pulmonary TB in Canada



A Retrospective Cohort Study

Angela Lau, MD; Christopher Lin, MD; James Barrie, MD; Christopher Winter, MD; Gavin Armstrong, MD; Mary Lou Egedahl, BScN; Alexander Doroshenko, MD, MPH; Courtney Heffernan, PhD; Leyla Asadi, MD, MPH; Dina Fisher, MD; Catherine Paulsen, MSc; Jalal Moolji, MD; and Richard Long, MD

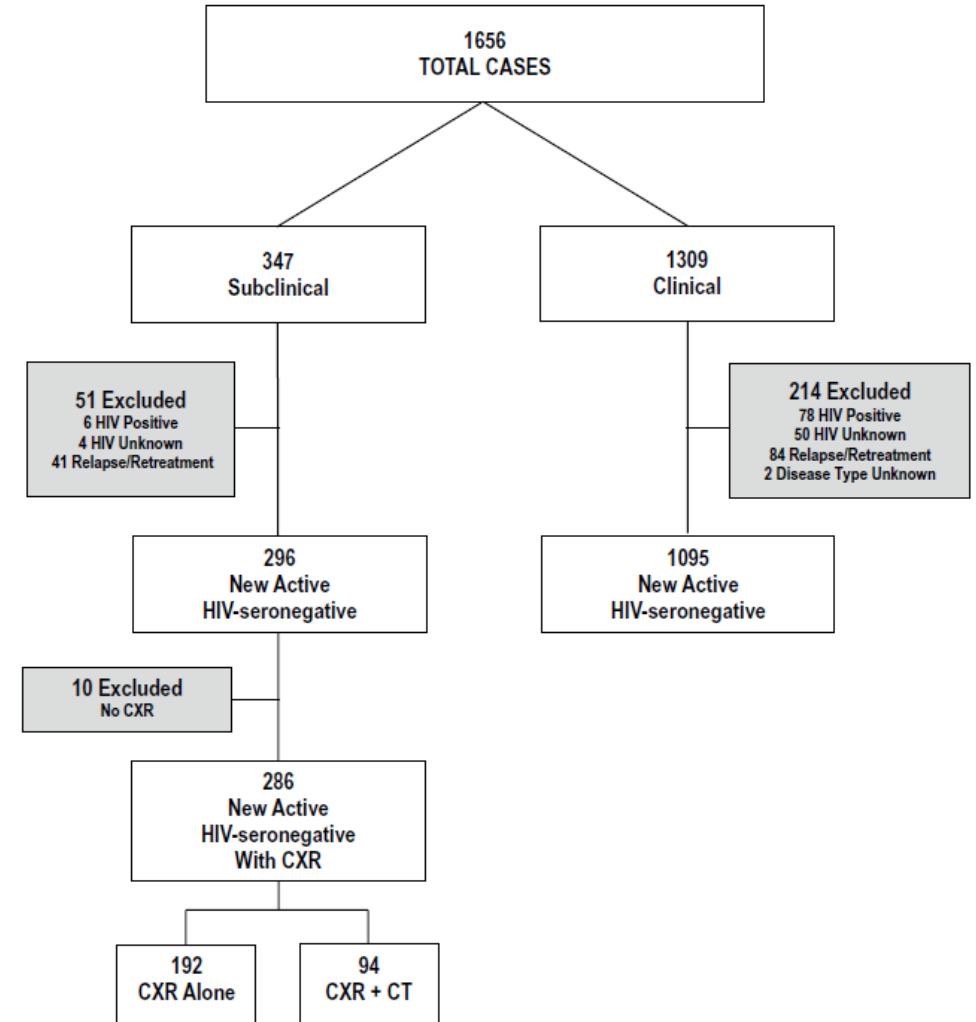
Patient symptom status was determined to be **symptomatic** or **asymptomatic**

Clinical features included their reason for assessment, given that they were asymptomatic

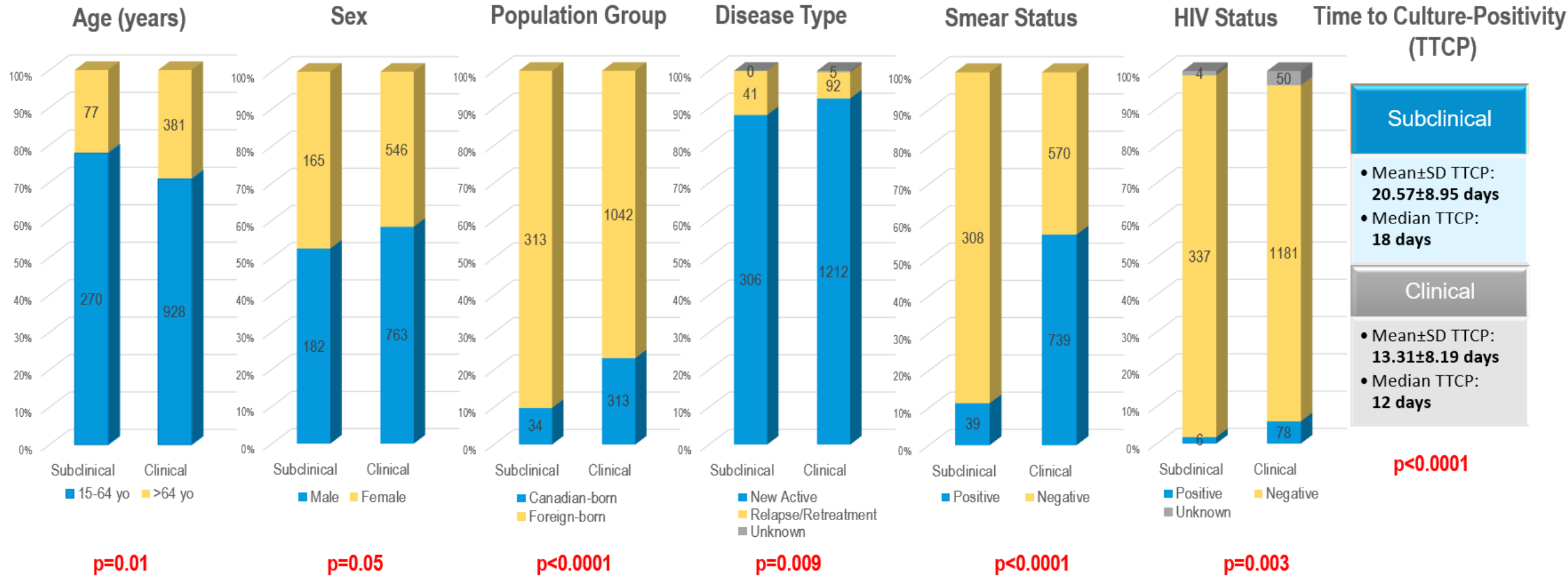
Mycobacteriologic data included smear-status, time to culture-positivity and DNA fingerprints of initial isolates

Radiographic features were independently read by two experienced chest radiologists

Field reader radiograph reports were retrieved and information systematically abstracted



Demographic Features, Disease Type, and Mycobacteriologic Features of Pulmonary Tuberculosis Patients by Symptom Status

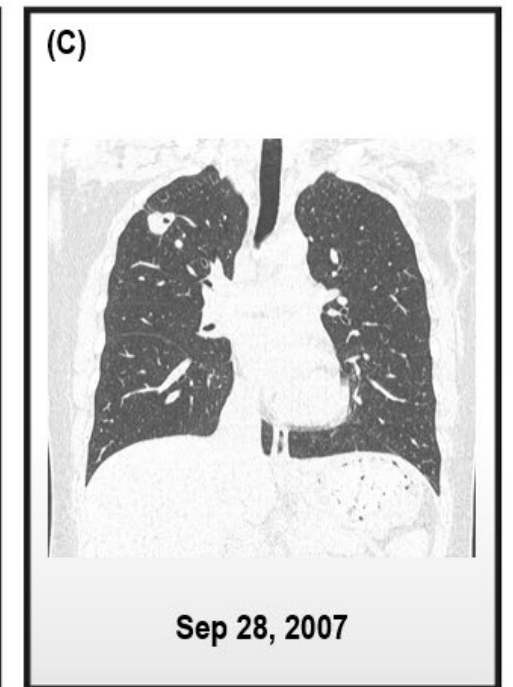
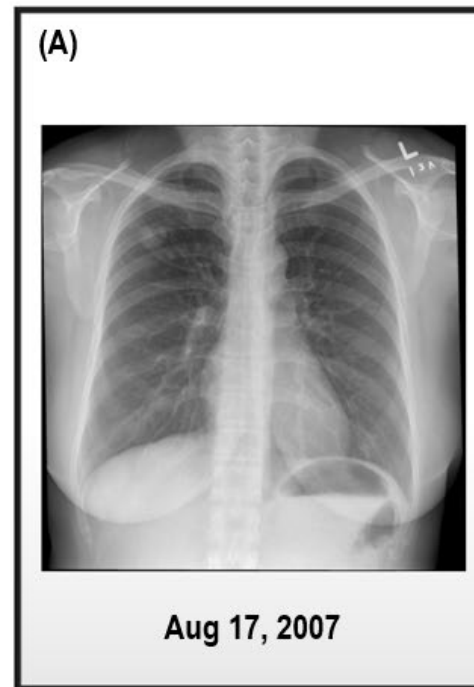


Chest Radiographic Features in Patients with Subclinical Pulmonary TB

Feature	Total
No. assessed	286
Category	
Typical	195 (68.2)
Atypical	41 (14.3)
Normal	50 (17.5)
Laterality	
Unilateral disease	162 (56.6)
Bilateral disease	70 (24.5)
Normal	54 (18.9)
Cavitation	
Yes	19 (6.6)
No	267 (93.3)
Acinar shadows ^a	
Yes	19 (6.7)
No	264 (93.3)
Lymph node enlargement	
Yes	9 (3.1)
No	277 (96.9)
Extent of parenchymal disease	
Normal	54 (18.9)
Minimal	193 (67.5)
Moderately advanced	37 (12.9)
Far advanced	0 (0.0)
Miliary	2 (0.7)

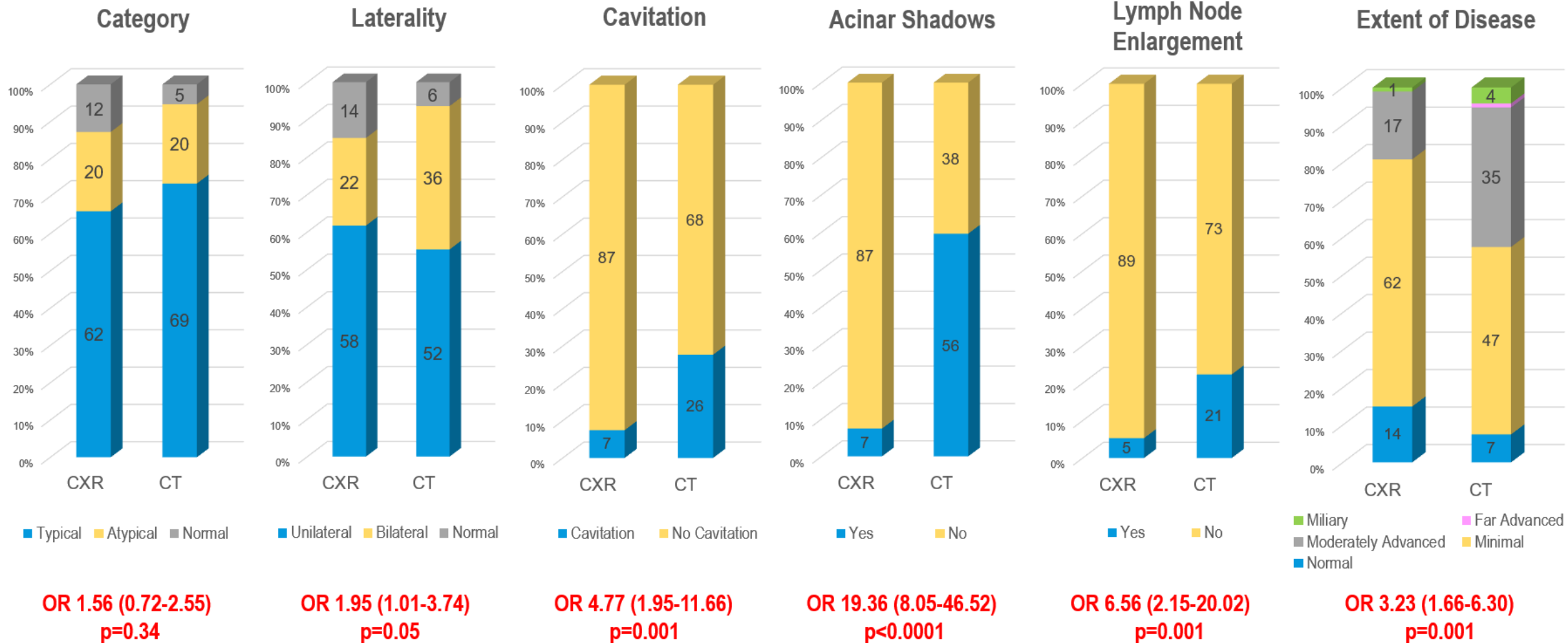
Data are presented as No. (%), unless otherwise indicated.

^aInformation on acinar shadows on the chest radiograph was unavailable in three patients.



Frontal chest radiograph (A) and thin section (1.0 mm) coronal reformat computed tomographic (CT) images (B and C) in a patient diagnosed with smear-negative, culture-positive subclinical pulmonary tuberculosis on August 28, 2007. A small cavity is visible on CT scan but not on chest radiograph; the abnormality in the right upper lobe is stable over several months

Age and Sex Adjusted Odds of Having the Radiologic Features (Dependent Variable) if One Goes From One Diagnostic Method to Another (CXR to CT)



Inter-reader variability of subclinical PTB chest radiograph interpretations

EXPERT A VS EXPERT B			
FEATURE	AGREEMENT	K STATISTIC	95% CI
Parenchymal abnormality	Substantial agreement	0.747	0.649-0.842
Typical Pattern	Substantial agreement	0.754	0.677-0.832
Laterality (EOD)	Substantial agreement	0.724	0.656-0.791
Cavitation	Moderate agreement	0.490	0.327-0.661
Enlarged IT nodes	Moderate agreement	0.580	0.295-0.860
Pleural effusion	Almost perfect agreement	0.818	0.632-0.992
FIELD READERS VS EXPERT A			
Parenchymal abnormality	Substantial agreement	0.629	0.527-0.729
Typical Pattern	Substantial agreement	0.671	0.588-0.755
Laterality (EOD)	Substantial agreement	0.623	0.550-0.697
Cavitation	Fair agreement	0.240	0.062-0.406
Enlarged IT nodes	Substantial agreement	0.760	0.555-0.988
Pleural effusion	Substantial agreement	0.783	0.584-0.966
FIELD READERS VS EXPERT B			
Parenchymal abnormality	Moderate agreement	0.591	0.487-0.698
Typical Pattern	Substantial agreement	0.663	0.579-0.748
Laterality (EOD)	Moderate agreement	0.572	0.495-0.650
Cavitation	Fair agreement	0.390	0.172-0.596
Enlarged IT nodes	Moderate agreement	0.556	0.298-0.816
Pleural effusion	Substantial agreement	0.800	0.615-0.969

Reporting of radiographic features in subclinical PTB - field readers compared to the consensus of expert readers

Radiographic feature	Radiograph Reader		p-value
	Field No (%)	Expert No (%)	
Parenchymal Abnormality			
Yes	245 (74.9)	266 (81.3)	0.047
No	82 (25.1)	61 (18.7)	
Pattern			
Typical	204 (62.4)	229 (70.0)	0.039
Atypical or Normal	123 (37.6)	98 (30.0)	
Laterality (Extent of Disease)			
Unilateral	157 (48.0)	177 (54.1)	0.117
Bilateral	88 (26.9)	89 (27.2)	
Normal	82 (25.1)	61 (18.7)	
Cavitation			
Yes	11 (3.4)	24 (7.3)	0.024
No	316 (95.6)	303 (92.7)	
Enlarged Intrathoracic Nodes			
Yes	11 (3.4)	9 (2.8)	0.650
No	316 (95.6)	318 (97.2)	
Pleural Effusion			
Yes	13 (4.0%)	9 (2.8%)	0.386
No	314 (96.0%)	318 (97.2%)	

Over-reading and under-reading of chest radiographs in subclinical PTB patients

Feature	Reading	Field vs Expert A No (%)	Field vs Expert B No (%)	Range
Parenchymal Abnormality	Over	10/62 (16.1)	7/52 (13.5)	13.5 -16.1
	Under	31/265 (11.7)	38/275 (13.8)	11.7-13.8
Laterality (Extent of Disease)	Over	26/327 (8.0)	26/327 (8.0)	8.0 - 8.0
	Under	52/327 (15.9)	57 (327) 17.4	15.9 - 17.4
Typical Pattern	Over	17/106 (16.0)	11/92 (12.0)	12.0 - 16.0
	Under	31/221 (14.0)	39/235 (16.6)	14.0 - 16.6
Cavitation	Over	4/244 (1.4)	4/304 (1.3)	1.3 - 1.4
	Under	27/33 (81.8)	16/23 (69.6)	69.6 – 81.8
Enlarged IT Nodes	Over	4/319 (1.3)	5/317 (1.6)	1.3 – 1.6
	Under	0/7 (0.0)	4/10 (40.0)	0.0 – 40.0
Pleural Effusion	Over	4/317 (1.2)	2/315 (0.6)	0.6 – 1.2
	Under	1/10 (10.0)	1/12 (8.3)	8.3 – 10.0

Summary of Study

- Subclinical patients accounted for 21.0% of incident culture-positive PTB patients
- Subclinical patients were generally young/middle-aged foreign-born persons; they were usually AFB smear-negative (88.2%) and had longer times to culture-positivity
- When strictly defined, most subclinical PTB patients have minimal or no lung parenchymal disease apparent on CXR
- CXRs may be shown to significantly under-detect the presence of key features
- Field interpretation of CXRs increases the likelihood that these features will be missed
- Under-reading by field readers was more common than over-reading for most features
- Ideally, in the context of active case finding, CXRs should be read by experienced readers and induced sputum should be submitted regardless of the radiographic findings

References

- Drain PK, Bajema KL, Dowdy D, et al. Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection. *Clin Microbiol Rev* 2018;**31**(4):e00021-18. doi:10.1128/CMR.00021-18.
- Kendall EA, Shrestha S, Dowdy DW. The epidemiological importance of subclinical tuberculosis. A critical reappraisal. *Am J Respir Crit Care Med* 2021;**203**(2):168-74. doi:10.1164/rccm.202006-2394PP.
- Onozaki I, Law I, Sismanidis C, Zignol M, Glaziou P, Floyd K. National tuberculosis prevalence surveys in Asia, 1990-2012: an overview of results and lessons learned. *Trop Med Int Health*. 2015 Sep;**20**(9):1128-1145.
- Frascella B, Richards AS, Sossen B, et al. Subclinical Tuberculosis Disease-A Review and Analysis of Prevalence Surveys to Inform Definitions, Burden, Associations, and Screening Methodology. *Clin Infect Dis*. 2021;**73**(3):e830-e841.
- The Canadian Tuberculosis Standards, 8th Edition. Available at Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, Volume 6, Issue sup1.
- Long R. Making a timely diagnosis of pulmonary tuberculosis. *Can Respir J*. 2015;**22**(6):317-21.
- Lau A, Lin C, Barrie J, et al. The Radiographic and Mycobacteriologic Correlates of Subclinical Pulmonary TB in Canada: A Retrospective Cohort Study. *Chest*. 2022;**162**(2):309-320.
- Lau A, Lin C, Barrie J, et al. A comparison of the chest radiographic and computed tomographic features of subclinical pulmonary tuberculosis. *Sci Rep*. 2022;**12**(1):16567. Published 2022 Oct 4.

Thank you!

Special thanks to:

Dr. Richard Long

Dr. Courtney Heffernan

Dr. Leyla Asadi

Cathy Paulsen

Mary-Lou Egedahl

Dr. Alexander Doroshenko

and all the staff and students at the Tuberculosis Program Evaluation and Research Unit, University of Alberta, staff of the Edmonton TB Clinic, Calgary TB Clinic and the Provincial TB Clinic, Alberta Health Services, the Provincial Laboratory for Public Health, and the Radiology and Diagnostic Imaging Department, University of Alberta Hospital, Edmonton, Alberta

Funding Acknowledgements: Alberta Innovates, CIHR, Respiratory Health SCN, University Hospital Foundation, Department of Medicine (Alberta Respiratory Centre)



**UNIVERSITY
OF ALBERTA**