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Chest radiography for active tuberculosis case finding in the homeless: a systematic review and meta-analysis

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SUMMARY

SETTING: In low-incidence regions, tuberculosis (TB) often affects vulnerable populations. Guidelines recommend active case finding (ACF) in homeless populations, but there is no consensus on a preferred screening method.

OBJECTIVE: We performed a systematic review and meta-analysis to evaluate the use of chest X-ray (CXR) screening in ACF for TB in homeless populations.

DESIGN: Articles were identified through EMBASE, Medline and the Cochrane Library. Studies using symptom screens, CXRs, sputum sweeps, tuberculin skin tests and/or interferon-gamma release assays to detect active TB in homeless populations were sought. Data were extracted using a standardised method by two reviewers and validated with an objective tool.

RESULTS: Sixteen studies addressing CXR screening of homeless populations for active TB in low-incidence regions were analysed. The pooled prevalence of active TB in the 16 study cohorts was 931 per 100 000 population screened (95%CI 565–1534) and 782/100 000 CXR performed (95%CI 566–1079). Six of seven longitudinal screening programs reported a reduction in regional TB incidence after implementation of the CXR-based ACF programme.

CONCLUSION: Our data suggest that CXR screening is a good tool for ACF in homeless populations in low-incidence regions.

KEY WORDS: chest X-ray; screening; under-housed

IN LOW TUBERCULOSIS (TB) incidence regions, the burden of active TB is concentrated in vulnerable populations, including the homeless and under-housed.[1,2] Although prevalence estimates vary depending on region, the estimated TB prevalence in the homeless is 46 times higher than that among the general population of the United States.[3] The high incidence of TB in homeless populations has been attributed to poverty, overcrowded conditions, poor nutrition, limited access to health care, poor mental health, substance use and high rates of co-infection with the human immunodeficiency virus (HIV).[4,5] The same conditions predispose homeless populations to TB outbreaks, which are often difficult to distinguish from endemic burden of disease due to challenges with contact tracing, poor access to health care and lack of longitudinal follow-up.[6] Because of these many factors, homeless populations are particularly recalcitrant to traditional TB control activities. Evidence-based screening and treatment strategies should be developed to improve health outcomes in this population.[3,6,7]

North American and European guidelines strongly advocate for active case finding (ACF) in homeless populations.[8,9] ACF has been effective in reducing TB incidence, prevalence and mortality.[9] Numerous screening methods have been employed and evaluated in homeless populations, including chest X-rays (CXRs), symptom questionnaires, sputum sweeps, tuberculin skin tests (TST) and interferon-gamma release assays (IGRAs).[10,11]

With the emergence of digital radiography, CXR screening has once again gained popularity for ACF in homeless and under-housed populations after enthusiasm for this modality waned in the 1980s.[11,12] Digital CXR is accessible, portable, inexpensive, non-invasive and does not require routine return visits. Furthermore, recent data suggest that screening CXR carries a sensitivity of >80% for active TB in high-risk populations.[13]

In the present article, we performed a systematic review to evaluate the utility of CXR screening in ACF for TB in homeless and under-housed populations. We aimed to measure the prevalence of TB

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disease in CXR-based ACF programmes and the sensitivity of CXR-based ACF programmes in detecting TB among the homeless. We also considered symptom screening, sputum sweeps, TSTs and IGRAs as additional screening methods in CXR-based TB screening programmes.

METHODS

Articles were identified from EMBASE, Medline (including In-Process & Other Non-Indexed Citations) and the Cochrane Library up to 10 November 2012 (see Tables 1 and 2 for search strategy details). After examining the reference lists of identified studies for additional studies and removing all duplicates, the combined searches yielded 346 articles, all of which were reviewed for inclusion by one reviewer (KP). Articles were assessed to identify those that used CXR and/or symptom screens, sputum sweeps, TST or IGRA testing to detect active TB in a homeless or under-housed population. Articles were excluded if screening data specific to the homeless could not be extracted, if the method for diagnosing TB was not stated or was not an accepted standard, if primary data were included in another study from our data set or if data were derived from a high TB incidence country (incidence >30 per 100 000 population). Authors were contacted for additional information when appropriate.

The articles that met initial the inclusion criteria were independently reviewed and extracted by two reviewers (MPC and MJK); the studies were evaluated objectively using the quality items derived from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool.[14] Data were collected using a standard method, whereby each study's definitions of TB and test positivity, population, potential biases, test characteristics and treatment compliance were extracted and compiled for review. When articles did not provide the incidence of TB in their study's region, reviewers searched online databases to estimate regional TB incidence at the time the study was performed.[15] The data underwent a final independent review by two authors (KP and JCJ) before analysis to assess and correct for discrepancies.

Table 1 Medline search strategy

	Ovid search term	Results
1	exp Tuberculosis/	338 148
2	(tubercul* or tb*).ti,ab.	490 367
3	#1 OR #2	571 884
4	exp Mass Screening/or exp screening/or exp screening test/	506 573
5	screen*.ti,ab.	948 836
6	#4 OR #5	1 181 999
7	exp Tuberculosis/di [Diagnosis]	71 097
8	Contact tracing [MeSH]	13 149
9	(homeless* or indigent* or street* or shelter* or destitute* or vagabond*).ti,ab.	47 331
10	#8 or #9	50 291
11	#3 AND #6 AND #10	331
12	#3 AND #7 AND #10	361
13	#11 or #12	589
14	limit 13 to (destitu or destit)	500
15	remove duplicates from 14	327

Table 2 Cochrane Library search strategy

	Cochrane Library search term	Results
1	MeSH descriptor: [Tuberculosis] explode all trees	1423
2	(Tuberculo*):ti,ab,kw	2547
3	(homeless* or indigent* or street* or shelter* or destitute* or vagabond* or underhous*)	6279
4	#1 or #2	2549
5	#3 and #4	45

For the purposes of this review, a homeless person was defined as a person without a permanent residence, including those living on the streets or in shelters, frequenting hostels or single room occupancy (SRO) hotels, but not including migrant workers or nomadic peoples. Active TB was defined as per the Hopewell definition: smear-positive and/or culture-positive for *Mycobacterium tuberculosis* complex or a clinical diagnosis with specific clinical and radiologic features. Latent tuberculous infection was defined as a positive TST, which was defined as $\geqslant 5$ mm or $\geqslant 10$ mm in accordance with individual study criteria, or a positive IGRA in patients in whom active TB was excluded.

Quantitative analysis

Our first outcome of interest was the pooled prevalence of active TB per person screened and per CXR performed. Related to this, we calculated the number of people and the number of CXRs needed to screen (NNS) to detect one active TB case in CXR-based ACF programmes. Meta-regression was performed to examine whether additional screening tests increased the prevalence of active TB per CXR or person screened compared to CXR screening alone. A second analysis was then performed on studies that reported both screening and registry data. In this subset of studies, we calculated the pooled sensitivity of CXR-based ACF programmes by comparing the number of homeless people diagnosed with active TB in a CXR-based ACF programme to the number of homeless people identified in a regional active TB registry over the same period.

As significant heterogeneity was found in TB prevalence and programmatic sensitivity, the pooled estimates from inverse variance-weighted fixed effects model and random effects model were calculated. TB prevalence and programmatic sensitivity were logit-transformed for meta-analysis and back-transformed for ease of interpreting results. To avoid generating

missing data during logit transformation, a correction term of 0.01 was applied to the denominator, with a programmatic sensitivity of 0 or 1. Funnel plots and the Egger test were used to assess for publication bias. The study statistics were entered into Microsoft Excel version (Microsoft, Redmond, WA, USA). Pooled analysis was performed in Stata/IC 12.1 (Stata Corp, College Station, TX, USA).

Ethics approval was not required for this project.

RESULTS

Screening programs

A description of the study identification and selection process is given in Figure 1. Of the 62 studies that met the inclusion criteria, 46 were excluded: 33 studies did not include CXR data, 7 used targeted CXR screening, 3 used registry data alone (i.e., we could not differentiate a screening vs. diagnostic CXR), 2 were performed in a high TB incidence region, and 1 used a contact tracing strategy for ACF. Of the final 16 studies selected for analysis (Table 3), six had registry data that allowed us to estimate the sensitivity of the programme (Table 4).

All 16 studies used for analysis were conducted in large urban centres, including 11 from Western Europe, 2 from the United States, 2 from Japan and 1 from Australia. Three studies presented retrospective or cross-sectional data,[16–18] and 13 studies were prospective.[13,19–30] Regarding screening strategy, 13 studies used a location-based approach to screen in shelters and/or social services centres, while three studies screened homeless persons presenting to health care providers (Table 3). In addition to CXR screening, other tools were frequently used: 7/16 studies examined sputum smear and/or culture, 4 performed symptom screening, 4 reported TST results and 1 study assessed IGRAs (Table 3).

Quality assessment

Assigned quality rating using the QUADAS tool revealed two excellent studies (scores of 8–11),[13,22] 13 good studies (scores 4–7),[16–21,23–25,27–30] and one study with poor methodology (score 1–3).[26]

Prevalence and number needed to screen

The pooled prevalence of active TB was 931/100 000 persons screened (95% confidence interval [CI] 565–1534) or 782/100 000 CXRs performed (95%CI 566–1079) (Table 3). Using the inverse of these values, we calculated the NNS to detect one case of active TB at 107 people (95%CI 65–177) or 127 CXRs (95%CI 93–177). Using meta-regression, we compared programmes that used CXR alone with programmes that used additional screening modalities, and found a statistically non-significant increase in active TB prevalence per CXR (odds ratio [OR] 0.91, 95%CI 0.35–2.34) or per person screened (OR 0.39, 95%CI 0.13–1.20).

Analysis of registry-based programmes

The sensitivity of CXR screening programmes for identifying TB cases in homeless populations was established by comparing screening results in six studies with homeless registry data. Of the 48 398 screening CXRs performed in six cohorts that tracked screened individuals, 387 new cases of TB were diagnosed, giving a weighted prevalence of 523/

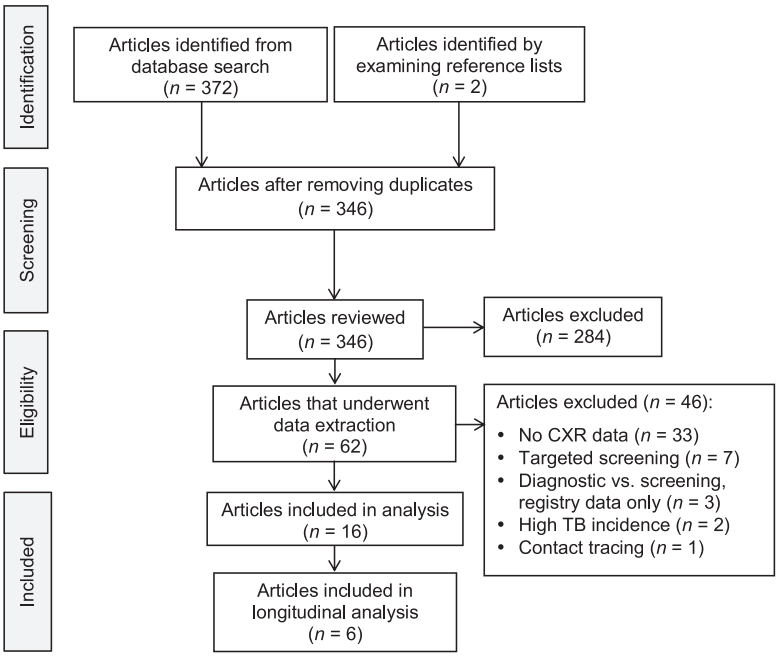

Figure Flow diagram describing study selection process. CXR = chest X-ray; TB = tuberculosis.

Table 3 Screening results from 16 active case-finding programmes

Author, year, reference	Location-based screening	CXR	Symptom screen	TST	Sputum	IGRA	Persons screened CXR *n*	Prevalence per 100 000 persons (95%CI)	Prevalence per 100 000 CXRs (95%CI)
Badiaga, 2009[19]	•	•	—	—	•	—	219	913	905
Barry, 1986[20]	•	•	•	•	•	—	465	645	645
Bernard, 2012[c]	•	•	—	—	—	—	22 000	—	814
Capewell, 1986[22]	•	•	—	—	—	—	4 687	—	896
de Vries, 2007[23]	•	•	—	—	—	—	8 559	862	327
Goetsch, 2012[24]	—	•	—	—	—	—	4 529	1 122	861
Kimerling, 1999[16]	•	•	•	•	•	—	127	—	—
Kumar, 1995[25]	•	•	—	—	•	—	595	1 513	1 512
Lau, 1997[26]	•	•	—	—	•	—	3 555	56	56
Patel, 1985[27]	•	•	—	—	•	—	9 132	—	1 456
Solsona, 2001[28]	•	•	—	•	—	—	447	1 119	1 119
Southern, 1999[29]	•	•	•	•	—	—	1 905	525	524
Story, 2012[13]	•	•	—	—	•	—	19 801	434	434
Tabuchi, 2011[17]	—	•	•	—	—	•	263	1 520	1 520
Valin, 2005[30]	•	•	—	—	—	—	1 360	2 647	1 721
Yamanaka, 1994[18]	—	•	—	—	—	—	398	3 015	—
Weighted prevalence							78 042	931 (565–1 534)	782 (566–1 079)

CXR = chest X-ray; TST = tuberculin skin testing; IGRA = interferon-gamma release assay; CI = confidence interval.

100 000 CXRs (95%CI 245–1113). Overall, programmatic sensitivity ranged from 12% to 100%, with a weighted sensitivity of 42% (95%CI 28–58). All six ACF programmes used location-based screening. We did not identify publication bias using funnel plot and statistical testing.

Longitudinal data

Six of seven programmes that assessed longitudinal data noted a significant reduction in TB.[17,18,20–23] Paradoxically, Yamanaka et al. noted a reduction in TB incidence among the non-homeless from 83 to 64/100 000 persons, but unchanged incidence in the homeless over the same period. Patel et al. reported on two screening periods; the second period screened 47% more individuals and diagnosed 800% more people with TB (Table 5).[22,31,32]

DISCUSSION

Over the past 30 years, numerous publications have described ACF among homeless and under-housed populations in low TB incidence countries. Not surprisingly, the effectiveness of ACF appears to vary according to screening modality, location and programme structure. Overall, the data suggest that CXR-based ACF programmes detect a substantial proportion of people with active TB in this vulnerable population. In the six studies comparing the number of active TB cases to regional registry data, the pooled proportion of homeless TB cases detected using CXR-based ACF screening programmes was 42%. Programmes that include symptom screens, sputum sweeps, TST and IGRA testing may further improve detection of active TB; however, there are insufficient data to draw conclusions about the superiority of one screening combination over another.

In addition to our quantitative analysis, we note that six of seven longitudinal cohorts reported a significant decline in TB incidence. The significance of this finding is unclear, as CXR screening programmes do not work in isolation and are often part of a multidisciplinary response to high TB rates in a target population. Health care provider education

Table 4 Data for programme sensitivity of CXR screening

Author, year, reference	Type of screening	Frequency of screening	CXRs performed *n*	Cases detected using CXR *n*	Total cases among the homeless (sensitivity)
Barry, 1986[20]	Symptoms, TST, CXR, sputum smears and cultures	4 nights in 1 month	465	3	26 (12%)
Bernard, 2012[21]	CXR	514 days in 14 years	22 000	179	313 (57.2%)
Capewell, 1986[22]	CXR	1 day every 6 months in 7 years = 14 days	4 687	42	68 (62%)
de Vries, 2007[23]	CXR	12 days every 6 months in 4 years = 96 days	8 559	28	71 (39%)
Lau, 1997[26]	CXR	23 visits over 5 years	3 555	2	9 (22%)
Patel, 1985[27]	CXR	22 sites every 6 months over 5 years	9 132	133	133 (100%)

TST = tuberculin skin testing; CXR = chest X-ray.

Table 5 Longitudinal data: tuberculosis trends in the homeless and the general population

Author, year, reference	Incidence/ prevalence	Trend homeless (per 100 000 persons)	Trend general population (per 100 000 persons)
Barry, 1986[20]	Incidence	Boston: 10.1 (1984); 8.4 (1985)	USA:[31] 9.4 (1984); 9.3 (1985)
Bernard, 2012[21]	Incidence	Paris: 223 (2007)	Paris: 53.1 (1994); 27.6 (2007)
Capewell, 1986[22]	Prevalence	Edinburgh: 1265 (1968–1975); 896 (1976–1982)	Scotland: 5% annual decline[22]
de Vries, 2007[23]	Incidence	Rotterdam: 511 (2001); 244 (2005)	Netherlands: 9.0 (2001); 3.5 (2003)[32]
Patel, 1985[27]	Incidence	Glasgow: 1313 (1975–1978); 1460 (1978–1982)	Scotland: 5% annual decline[22]
Tabuchi, 2011[17]	Prevalence	Airin District: 1400 (2000); 653 (2007)	Osaka: 50% decline (2000–2008)
Yamanaka, 1994[18]	Incidence	Nakamura Ward: 1800 (1982); 800 (1991)	Nakamura Ward: 83 (1982); 64 (1991)

and intensified contact tracing, along with community engagement and health promotion initiatives, are often part of a package of interventions used to target high TB rates in marginalised populations. These interventions would presumably also influence TB incidence in the target and general populations. In addition, the background epidemiology of a population may change with shifting socio-economic indices in urban environments. Decline in TB incidence in longitudinal studies may simply reflect a constellation of interventions and/or shifting TB epidemiology due to demographic change, rather than the success of CXR screening programmes alone. We attempted to remove studies that were clearly reports from outbreak settings to address this source of bias, but we cannot remove the effect of multidisciplinary interventions that may be initiated alongside CXR screening.

The results of this study are comparable to those published by Shapiro et al. in a recent WHO-sponsored systematic review of TB ACF in low-incidence settings from 1980 to 2010.[11] Shapiro et al. reported a mean NNS of 70 persons (range 33–1778) to detect one case of active TB in homeless ACF programmes using different screening strategies, and a mean NNS of 67 in programmes that used CXR among other screening tools. We report a pooled NNS of 107 persons (95%CI 65–177) and 127 CXRs (95%CI 93–177) in programmes that use CXR for all screened individuals. The discrepancy in pooled NNS between studies likely reflects the differing inclusion and exclusion criteria. We specifically evaluated programmes that used CXR-based ACF strategies, while Shapiro et al. evaluated all ACF programmes, regardless of CXR usage. Our analysis does share eight studies with Shapiro et al., but also includes an additional two studies from 1980 to 2010[18–25] and four studies published since 2010.[14,17,21,24] We also calculated an NNS based on the number of CXRs performed. We believe that the NNS per CXR may be a more useful metric for screening programmes, as, in our experience, homeless individuals are often repeatedly screened by overlapping efforts and programmes.

Study strengths and limitations

There are two major strengths to our analysis: we identified longitudinal studies for evaluation and used stringent inclusion and exclusion criteria to eliminate reports from outbreak settings. This should limit bias and allow for cautious interpretation of the longitudinal effects of CXR-based ACF programmes. However, there are limitations to these data. First, we cannot completely rule out publication bias. Programmes that are successful in detecting active TB cases through CXR screening may be more likely to report their results than unsuccessful screening programmes. We could not appreciate any publication bias using funnel plots and statistical testing; however, this cannot be completely ruled out.

A second limitation is that we evaluated not one type of CXR screening programme, but rather an assortment of screening programmes involving CXR as part of the screening algorithm. There was variability in the frequency and location of CXR screening, additional screening tests used and the epidemiological context of the screening programme used, not to mention the structure of the surrounding TB control programme itself. Nonetheless, the pooled results from our analysis of registry-backed screening programmes do demonstrate that CXR screening programmes are able to detect nearly half of the TB cases diagnosed in homeless people recorded in a regional database. Thus, regardless of implementation practices, CXR seems to be an important component of an effective screening strategy in this population.

We recognise that the pooled detection rate of 42% in registry-based screening programmes may overestimate the programme sensitivity of CXR-based ACF for detecting regional TB cases. A CXR-based ACF programme may detect transient individuals who do not normally reside in the region of interest, but happen to be present in the region on the day of screening. These additional individuals may inflate the sensitivity of a regional ACF programme. Despite this limitation, we feel that our estimate of programme sensitivity highlights the value of CXR-based ACF programmes.

CONCLUSIONS

The results of our study are encouraging and point towards CXR screening as a viable ACF strategy for homeless populations in low-incidence regions. Our data also suggest a decreasing trend in TB prevalence in areas with ACF programmes. To improve ACF in this population, new evidence should be developed with a focus on the utility of various combinations of screening modalities such as symptom screening, sputum sweeps and TST. In addition, new technologies should be assessed in this population, including IGRAs and polymerase chain reaction-based rapid testing technologies. Programmes might also consider harnessing the infrastructure from CXR screening programmes for other public health efforts, including HIV, diabetes, lung cancer and hepatitis screening.

Conflicts of interest: none declared.

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RESUME

CONTEXTE : Dans les régions à faible incidence, la tuberculose (TB) affecte souvent les populations vulnérables. Les directives recommandent une recherche active des cas (ACF) dans les populations sans domicile fixe, mais il n'y a pas de consensus sur une méthode de dépistage préférée.

OBJECTIF : Réaliser une revue systématique et une méta-analyse afin d'évaluer l'utilisation du dépistage par radiographie pulmonaire (CXR) en ACF de TB chez les personnes sans domicile fixe.

SCHÉMA : Les articles ont été identifiés grâce à EMBASE, Medline et à la bibliothèque Cochrane. Nous avons recherché des études utilisant le dépistage par symptômes, la CXR, les recueils de crachats, le test cutané à la tuberculine et/ou le test de libération de l'interféron gamma pour détecter une TB active chez des populations sans domicile fixe. Les données ont été extraites grâce à une méthode standardisée, par deux réviseurs, et validées grâce à un outil objectif.

RÉSULTATS : Seize études utilisant le dépistage par CXR chez des personnes sans domicile fixe d'une TB active dans des régions à faible incidence ont été analysées. La prévalence accumulée de TB active dans les cohortes de ces 16 études était de 931 par 100 000 personnes dépistées (IC95% 565–1534) et 782/100 000 CXR (IC95% 566–1079). Six programmes sur sept de dépistage longitudinal ont rapporté une diminution de l'incidence régionale de la TB après la mise en œuvre de ce programme ACF basé sur la CXR.

CONCLUSION : Nos données suggèrent que le dépistage par CXR est un bon outil d'ACF dans les populations sans domicile fixe dans des régions à faible incidence.

RESUMEN

MARCO DE REFERENCIA: En las regiones con baja incidencia de tuberculosis (TB), la enfermedad suele afectar a las poblaciones vulnerables. Las directrices recomiendan la búsqueda activa de casos (ACF) en las poblaciones sin hogar, pero no existe unanimidad con respecto al método preferido de detección sistemática.

OBJETIVO: Llevar a cabo un examen sistemático y un metanálisis de las publicaciones científicas, con el objeto de evaluar la aplicación de la ACF mediante la radiografía de tórax (CXR) en las poblaciones sin techo.

MÉTODO: Se examinaron las siguientes bases de datos: EMBASE, Medline y la Biblioteca Cochrane y se buscaron artículos en los cuales se hubiese practicado la detección de síntomas, la CXR, el frotis de esputo, la prueba de la tuberculina o las pruebas de liberación de interferón gama con el propósito de detectar la TB activa en las poblaciones sin techo. Dos examinadores extrajeron los datos con métodos normalizados que se validaron luego mediante un método objetivo.

RESULTADOS: Se analizaron 16 estudios que examinaban la detección de la TB activa mediante la CXR en las poblaciones sin techo de regiones con baja incidencia. La prevalencia acumulada de TB activa en las 16 cohortes de estudio fue 931 por 100 000 personas examinadas (IC95% 565–1534) y 782/100 000 CXR practicadas (IC95% 566–1079). En seis de siete programas longitudinales de detección se informó una disminución de la incidencia regional de TB después de la introducción del programa de ACF con base en la CXR.

CONCLUSIÓN: Los resultados del presente análisis indican que la CXR representa un instrumento eficaz de ACF en las poblaciones sin techo de las regiones con baja incidencia de TB.