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Impact of a 14-year screening programme on tuberculosis transmission among the homeless in Paris

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SUMMARY

OBJECTIVE: To evaluate the impact of an active case-finding programme on tuberculosis (TB) transmission in homeless shelters in Paris, France.

DESIGN: Between 1994 and 1997, an active case-finding programme was implemented in homeless shelters using a mobile radiological screening unit, and continued from 1997 to 2007. During these periods, the strains isolated from TB cases diagnosed in the homeless were genotyped by restriction fragment length polymorphism analysis using the insertion sequence IS*6110* as a probe.

RESULTS: Between 1994 and 2007, 313 new TB cases were diagnosed among the homeless population: 179 through the programme among shelter users, and 134 among homeless people not using shelters. Half of the strains were clustered in 35 distinct patterns (2–48 cases/cluster). The clustering of TB cases steadily decreased in shelters during the 13 years of the survey, from 14.3 to 2.7 related cases per year ($P < 0.01$) and from 75% to 30% of related cases among all TB cases ($P < 0.01$). In contrast, there was only a slight trend towards a decrease in homeless people not using shelters.

CONCLUSION: Active case finding in homeless shelters resulted in a decrease in case clustering, mainly in shelter users. Genotyping contributed to confirming the positive impact of the intervention.

KEY WORDS: tuberculosis; homeless; active case-finding programme; DNA fingerprinting

BETWEEN 1991 AND 2007, the incidence of tuberculosis (TB) in France declined from 17 to 8.9 cases per 100 000 population.[1] In Paris, TB incidence decreased sharply, from 54 to 28/100 000 between 2002 and 2007.[1] As individual TB risk factors often overlap with risk factors for homelessness, the homeless constitute a high-risk population, contributing to a large number of TB cases in industrialised countries.[2,3] In 2007, in Paris, a city with 2.2 million inhabitants intra muros and 20 000–30 000 homeless people, the incidence of TB cases among the homeless population was estimated at 223/100 000.[1] In the USA, the incidence of TB among the homeless population is around 20 times higher than that in the general population, and the majority of cases in the homeless are most likely due to ongoing transmission of *Mycobacterium tuberculosis* complex.[4] Several studies have suggested that active case finding may reduce TB transmission and the overall rate of TB in the homeless population.[5–7]

Due to the high TB rates prevailing in Paris, particularly among the homeless, and a previous genotyping study strongly suggesting transmission in this population,[8] the city level TB health authorities implemented an active case-finding programme in Parisian homeless shelters. This report measures the impact of the programme on the transmission of TB among the homeless in Paris.

MATERIALS AND METHODS

Shelters

The 28 shelter facilities with the highest number of beds or in which TB cases had already been identified were included in the study. These shelters operate daily and provide several services, such as meals served in large dining halls, washing, bathing, etc., mainly from late evening to early morning. Most shelters also provide sleeping facilities, mainly in large dormitories. The aim of the shelters is to offer beds and meals for emergency accommodation; there is no medical or paramedical staff present. In the shelters, which are run by various non-profit organisations, medical or paramedical monitoring based on clinical examination

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is impossible, and there is no systematic organisation of screening of individuals for TB before their entry into the shelter system.

Screening programme

An active TB case-finding programme was progressively implemented in 28 shelters between the end of 1994 and 1997 by the Direction de l'Action sociale, de l'Enfance et de la Santé (DASES), a health institution supervised by the Paris city council. The programme was triggered by the principal results of a previous study that strongly suggested TB transmission in shelters,[9] and the DASES continued the programme after the study period. The programme was based on 1-day sessions of active chest X-ray (CXR) screening. Several sessions were organised each year in each shelter using mobile X-ray equipment, with the number and frequency of the sessions based on the yield in new TB cases identified during previous sessions and on the population turnover in the shelter. Active CXR screening was free of charge, and the shelter users were clearly informed that the medical team would not undertake any investigation of their administrative situation.

After the agreement of each shelter community had been obtained, all people present in the shelter on the day of screening were invited to participate, irrespective of whether they were regular or occasional users of the facility. Patients with an abnormal CXR were referred for complete diagnosis to nearby hospitals, mainly Pitié-Salpêtrière (PSL) hospital, the largest hospital in Paris (2000 beds), located in the south-east of the city. All homeless individuals with infectious TB were hospitalised for treatment. At least 2 weeks of TB treatment and/or negative sputum results are required by some shelters before agreeing to host a TB patient, but others do not have any requirements. We did not collect data on treatment completion.

Laboratory investigation

Culture, species identification and drug susceptibility testing were performed in the laboratories of the hospitals to which patients were referred. These laboratories were asked to send the *M. tuberculosis* isolates to the National Reference Centre for Mycobacteria and Resistance to Antimycobacterial Agents (CNR-MyRMA), located at PSL hospital. Genotyping was performed at the CNR-MyRMA around the same time that the cases were being diagnosed, using restriction fragment length polymorphism (RFLP), as described previously by Van Embden et al.[8] This method has been used for a previous study on TB in the homeless,[9] using IS*6110* as a probe and *Pvu*II as restriction endonuclease. RFLP patterns were compared and analysed using Gel Compare software (Applied Maths, Kortrijk, Belgium). Each RFLP pattern was compared with the other patterns of the strains isolated in the homeless population. Spoligotyping was performed for the strains that exhibited <6 bands by RFLP.

Case definition

A case was defined as a homeless person with active TB confirmed by positive culture of *M. tuberculosis* complex who was or was not using shelter facilities. The distinction between sheltered and non-sheltered was based on the situation of the patient at the time of diagnosis. Patients were asked if they used the shelters on a regular basis (referred to as 'shelter users'), or if they did not use the shelters or only rarely (referred as to 'shelter non-users').

Bacteriologically related cases were defined as culture-positive TB cases whose strains shared an identical DST pattern and an identical RFLP fingerprint.[10] Other cases whose strain exhibited a unique RFLP fingerprint were considered non-related cases.

Whereas the sheltered population was diagnosed through both active and passive case finding, the non-sheltered population was diagnosed almost exclusively through passive case finding.

Statistical analysis

Time trends in count data were analysed using Poisson regression analysis before and after 1997, the first year of full implementation of the active case-finding programme. To smooth trend data over time, we computed 3-year moving averages in proportion of related cases from 1997 to 2007. Time trends in these 3-year moving average proportions were analysed using χ^2 for trend analysis.

RESULTS

Between 1994 and 2007, 514 1-day active screening sessions were organised in the 28 shelters, with around 22 000 CXRs performed. The number of CXRs performed each year increased progressively over the implementation period (i.e., between 1994 and 1997), and remained stable at around 2000/year from 1998 to 2007 (Figure 1A). During the study period, the number of beds in the shelters remained stable, at around 4000–5000, and the shelter facilities always remained full.

A total of 313 TB cases were diagnosed in the homeless population during the study: 179 through the active case-finding programme, in homeless people regularly using the shelter facilities (Figure 1A), and 134 in homeless people not or rarely using them (Figure 1B). Among shelter users (Figure 1A), the number of cases detected increased sharply during the implementation period between 1994 and 1997 ($P < 0.01$), and then decreased progressively from 1997 onwards after the programme plateaued ($P < 0.01$). Among those who did not use the shelters, the

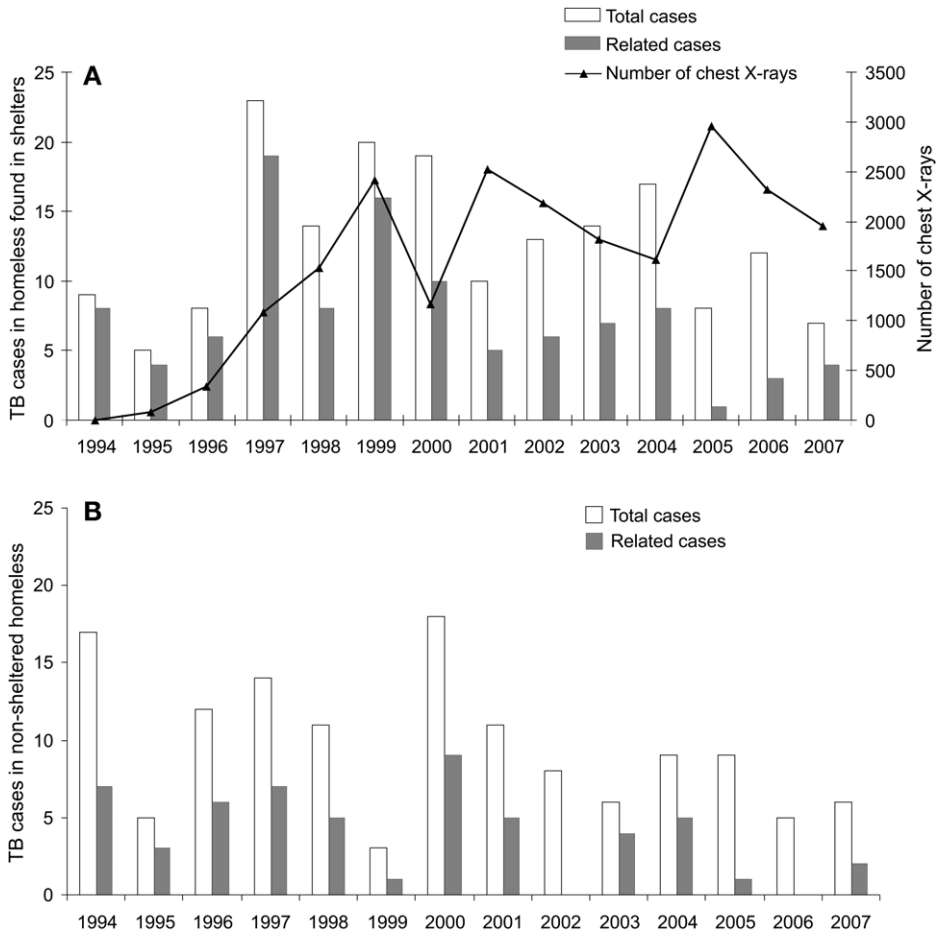

Figure 1 **A.** Global epidemic curve of tuberculosis cases among homeless people using shelter facilities in Paris, and number of chest X-rays performed through the active case-finding programme in shelters, 1994–2007. **B.** Global epidemic curve of tuberculosis cases among homeless people not using shelter facilities in Paris, 1994–2007.

number of cases fluctuated between 1994 and 2000, and then decreased (Fig 1B).

Overall, 160/313 TB cases (51%) were related to at least one other case, i.e., they shared an identical RFLP pattern and DST. Related cases decreased steadily among homeless people using the shelters between 1997 and 2007, both in terms of crude numbers ($P < 0.01$), from an average of 14.3/year in 1997–1999 to 2.7/year in 2005–2007 (Figure 2), and as a proportion of related cases among all TB cases ($P < 0.01$), from an average of 75% in 1997–1999 to 30% in 2005–2007 (Figure 3). In contrast, the number of related cases among all cases decreased significantly ($P < 0.01$), but less markedly, among homeless people not using shelters, from an average of 4.3/year in 1997 to 2.7/year in 2007 (Figure 2), and the proportion of related cases among all TB cases remained relatively stable, at around 40% between 1997 and 2004, and declined only in 2005–2006 (Figure 3); the global trend was non-significant. Interestingly, the number of non-related cases remained stable both among homeless people who used shelters and among those who did not (Figure 2).

None of the TB cases was multiresistant (i.e., resistant to isoniazid and rifampicin) among either related or non-related cases. Based on RFLP analysis, the related cases were scattered over 35 clusters containing 2–48 patients each; 30 contained <4 patients, and five contained respectively 7, 13, 14, 15 and 48 patients. The two largest clusters are described below.

The first cases of Cluster 11 (a strain susceptible to all anti-tuberculosis drugs) were found in Shelter A. Of the 48 cases in this cluster, 41 were diagnosed between 1994 and 2000, of which 16 were identified in Shelter A, 2 in Shelter B, 3 in Shelter C, 3 in Shelter D and 4 in other shelters; 13 cases were diagnosed among homeless people not using shelters. In contrast, only 7 cases in Cluster 11 were diagnosed between 2001 and 2007 (2 in Shelter A, 2 in other shelters, and 3 in homeless people not using shelters), and no new cases were diagnosed after 2004 (Figure 4A).

The cases belonging to Cluster 64 ($n = 15$ cases, a strain susceptible to all anti-tuberculosis drugs) were scattered over seven distinct shelters from 2000 to 2006 (Figure 4B). This cluster also included three cases diagnosed in homeless people not using shelters.

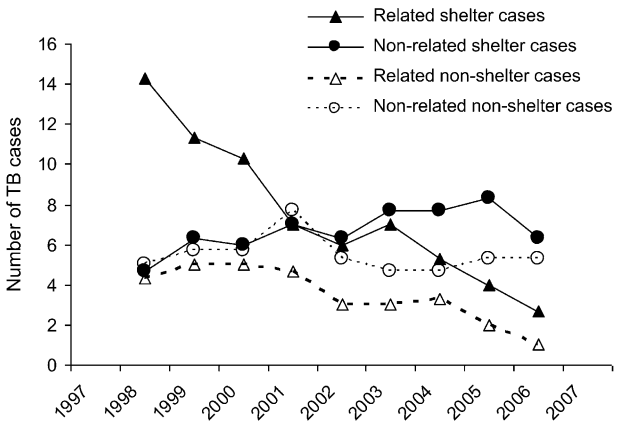

Figure 2 Number of related and non-related tuberculosis cases among homeless people using shelters and those not using shelters, computed as a 3-year moving average from 1997, first year of full implementation of the active case-finding programme, to 2007.

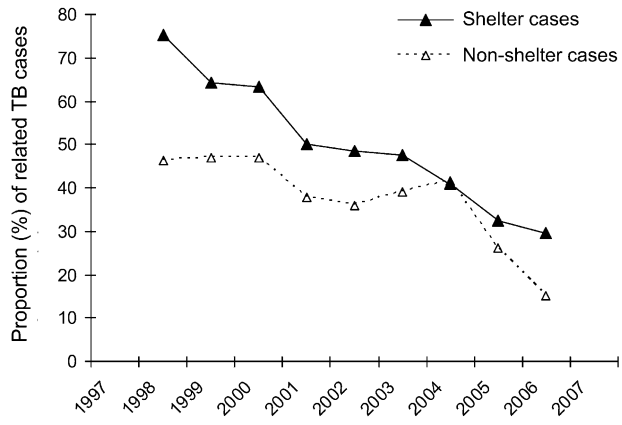

Figure 3 Proportion of related cases among all tuberculosis cases in homeless people using shelters and those not using shelters, computed as a 3-year moving average from 1997, the first year of full implementation of the active case-finding programme, to 2007.

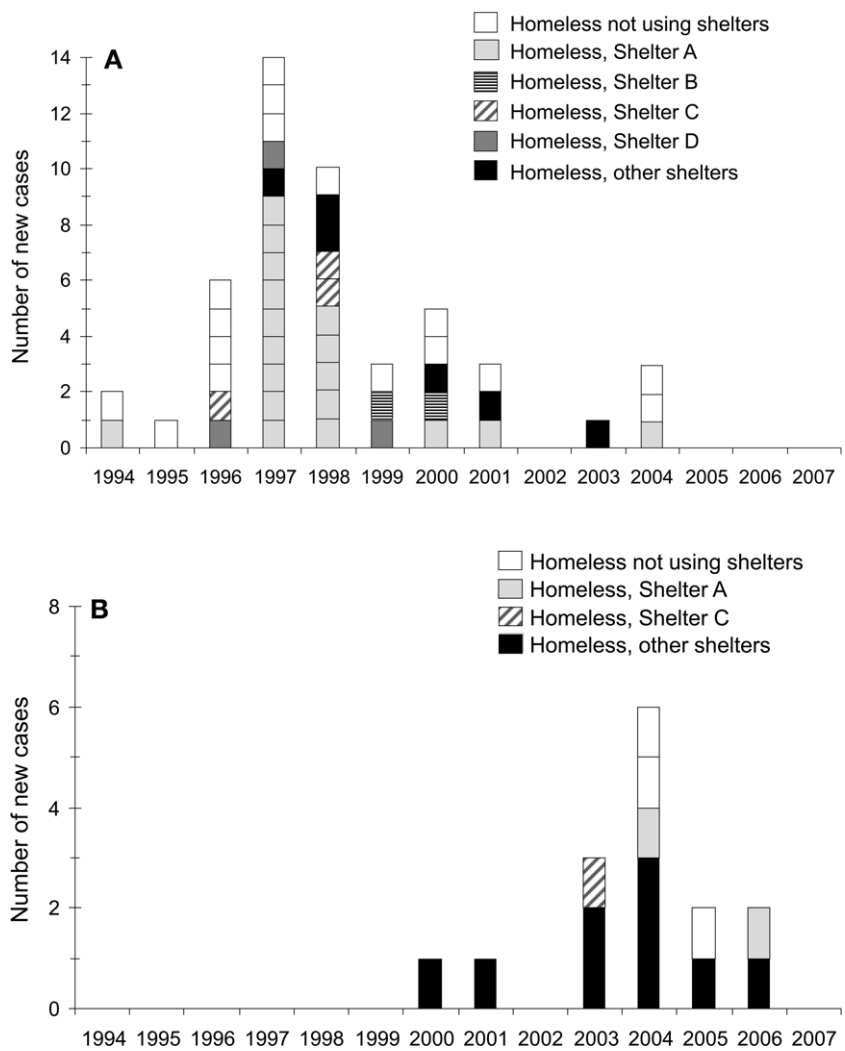

Figure 4 **A.** Epidemic curve of TB cases belonging to RFLP Cluster 11 among homeless people in Paris (n = 48 cases), 1994–2007. **B.** Epidemic curve by year of TB cases belonging to RFLP Cluster 64 among homeless people in Paris (n = 15 cases), 1994–2007. TB = tuberculosis; RFLP = restriction fragment length polymorphism.

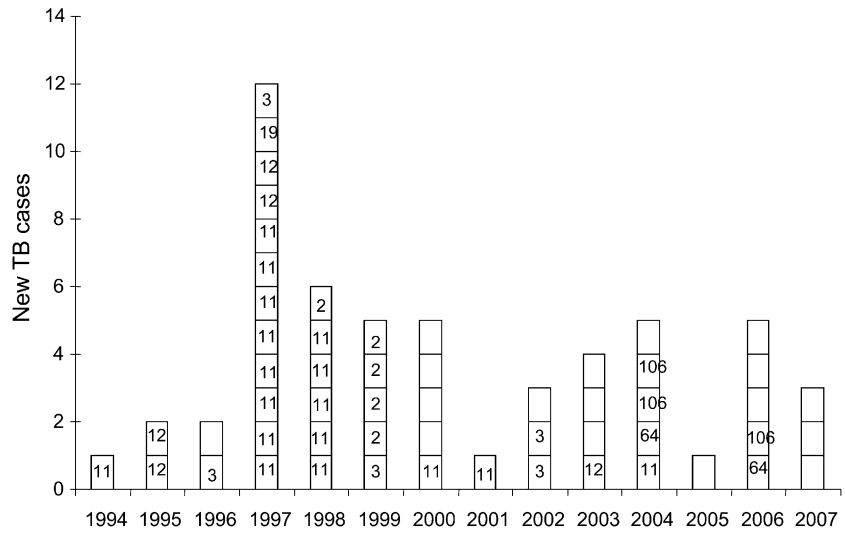

Figure 5 Epidemic curve of tuberculosis cases in homeless people using Shelter A, 1994–2007. The numbers indicate the RFLP code of the clusters.

During the study period, 55 cases were diagnosed at the most affected shelter (Shelter A; Figure 5), including 38 related cases (24% of all related cases in the study) and 17 non-related cases (11% of all non-related cases in the study, $P < 0.01$). The proportion of related cases in this shelter was globally very high, but decreased over time from 85% during the period 1994–2000 to 45% during the period 2001–2007 ($P < 0.01$). The 38 related cases from this shelter were scattered over seven distinct clusters, mainly Cluster 11 ($n = 17$), with the other clusters containing 2–5 cases each.

DISCUSSION

The main result of this study is the demonstration by fingerprinting that at the beginning of the 1990s, i.e., before the implementation of active case finding in homeless shelters in Paris, a large proportion of TB cases among the homeless (58% in 1994) were related to at least one other case and involved a few distinct strains. This result is in agreement with the conclusion by Vries et al. that the absence of local TB control strategies can lead to an increase in related cases.[11] In our study, the clustering of cases was particularly striking among homeless people using shelters (88% in 1994), and to a lesser extent in those not using shelters (41% in 1994). As the number of patients included and the length of the study period greatly influence clustering,[12] the proportion of clustering in various studies should be compared with caution. However, the proportion of clustering in this study is dramatically different from that observed in whole population-based large-scale studies in France, which found proportions of related cases of less than 20%,[13,14] and indicates intense ongoing transmission among the homeless, particularly those who use shelters. Homeless people are known to be vulnerable to transmissible diseases such as TB when crowded into small, poorly ventilated living spaces.[2]

A dramatic, steady decrease in clustering (i.e., the number and proportion of related cases) occurred among homeless people using shelters following the implementation of a sustained active case-finding programme in the shelters supervised by the Paris city council. In contrast to the shelter population, among homeless people not using shelters the number of related cases and the proportion of related cases among all TB cases decreased less markedly, and mainly at the end of the survey. This result strongly suggests that the screening programme has had a very positive impact on TB transmission in the shelters. The contrasting evolution in the two homeless populations is not surprising, as the active case-finding programme specifically targeted homeless people using shelters. However, as it is likely that the shelter-using population have many opportunities during the day to meet other homeless people in the street who do not use the shelters, it is possible that the programme implemented among the former also had a slight, indirect impact on the latter. Movement of the homeless between shelters, and connections between those using shelters and those not using them, is strongly suggested by the fact that, in each cluster, the cases were mainly concentrated in one shelter, whereas some cases occurred in other shelters and among homeless people not using shelters (Figure 4A and B).

Various screening programmes have been proposed to reduce TB transmission among the homeless.[15] Symptom review is effective for identifying suspected cases and ensuring that they are quickly evaluated.[15] Systematic sputum smear examination is difficult to implement for large numbers of people, and does not detect smear-negative cases.[16] Tuberculin skin testing

(TST) does not provide an immediate assessment of active TB, but rather of latent TB, and yields negative results for up to 25% of people with active pulmonary TB.[17] Preventive treatment of latent TB is not effective among the homeless population, due to lack of treatment adherence and frequent comorbidities that limit the use of most effective drugs. CXR screening was used in our programme, as it is the most pragmatic and effective approach for investigating large homeless populations who are often of foreign origin and for whom clinical investigations are particularly difficult. This method of active case finding has already been used to diagnose TB among the homeless,[18–20] and a previous study showed the impact of a 4-year mobile radiographic screening programme on TB.[21] That study, conducted in 14 facilities among homeless people and illicit drug users in Rotterdam (a city of about 600 000 inhabitants), covered 206 TB cases, among which only 28 were found via mobile screening. That study was started due to the doubling of TB cases over an 8-year period; the number of related TB cases found in 2002 was as high as 82% (compared to 58% in our study), reflecting intense transmission of TB from multiple sources among drug addicts and the homeless in Rotterdam.[11] To the best of our knowledge, the present study is the first to demonstrate the long-term effect on TB transmission in shelter users and non-shelter users among the homeless of a long lasting (14-year) active case-finding programme based on systematic CXR screening implemented in the shelters of a large European city. This approach seems efficient when properly organised.

Among the three most commonly used techniques for *M. tuberculosis* genotyping (RFLP, spoligotyping and mycobacterial interspersed repetitive unit variable-number tandem-repeat), RFLP is considered particularly effective in demonstrating recent transmission of *M. tuberculosis* strains.[8] DNA fingerprinting of *M. tuberculosis* isolates proved a useful tool for investigating TB transmission among the homeless. This tool has largely been used to study the molecular epidemiology of TB in whole populations of several cities and countries.[13,14,22–25] RFLP genotyping has also been used in a number of studies to describe outbreaks of TB in homeless shelter populations and to evaluate transmission.[6,9,15,26–29] However, few studies have used genotyping for long-term evaluation of active case-finding programmes. Kong et al. showed that a mandatory TB screening programme by RFLP coupled with TST for the homeless using shelters led to a decrease in the transmission of TB among this population in the United States.[17]

There are several limitations to the present study. First, it was observational, and despite sustained efforts to identify all cases and to concentrate the strains in a single laboratory, it is possible that some of the TB cases diagnosed in Paris were not notified as occurring in homeless people, and subsequently were not typed. Moreover, despite recommendations to send all strains from homeless people to NRC-MyRMA, we cannot be sure that we received a specimen from each person. Second, although it is generally assumed that the proportion of clustered isolates identified by fingerprinting in a population reflects recent transmission of *M. tuberculosis,* the results of studies based on such an approach should be interpreted with caution, as groups of strains may be identical for reasons other than recent transmission.[30] Finally, we should be cautious in concluding that the statistically significant association between the decline in the proportion of related cases and our control programme implies a causal association. Certain data, however, support such an association: the global incidence of TB in Paris remained stable, at around 50/100 000, from 1994 to 2002 (53.1/100 000 in 1994, 50.1 in 1998 and 53.2 in 2002), then decreased to 28.1/100 000 in 2005 and remained stable in 2006 (26.7/100 000) and 2007 (27.6/100 000). The decrease in TB cases among the homeless, especially those using shelters, therefore started before global TB incidence began to decrease in Paris. As the programme continued throughout the duration of the study, and the number of CXRs performed in shelters remained steady, we believe that the decrease in numbers of cases among homeless people in shelters is due to the programme. Finally, the decline in related TB cases was first seen in those shelter populations where the programme was directly implemented. Based on the characteristics of the population studied, the length of the study, and the size of the territory covered, we believe that there is a direct relation between the programme implemented in homeless shelters and the decrease in TB transmission among the homeless population in Paris. The active case-finding programme in homeless shelters has shown a long-term benefit in reducing case clustering, mainly in shelter users, and in reducing the total number of TB cases among homeless people in Paris.

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RÉSUMÉ

OBJECTIF : Nous avons évalué l'impact d'un programme de dépistage sur la transmission de la tuberculose (TB) dans les foyers accueillant des personnes sans domicile fixe (SDF) à Paris, France.

MATÉRIELS ET MÉTHODES : Un programme de dépistage radiologique réalisé par une équipe mobile a été mis en place entre 1994 et 1997 dans des foyers accueillant des SDF et poursuivi jusqu'en 2007. Durant cette période, les souches isolées de cas de TB diagnostiqués chez des patients SDF ont été génotypées par polymorphisme de longueur des fragments de restriction IS*6110*.

RESULTATS : Entre 1994 et 2007, 313 nouveaux cas de TB ont été diagnostiqués chez des patients SDF, 179 grâce au programme chez les SDF vivant en foyer et 134 chez les SDF ne vivant pas en foyer. La moitié des souches ont été regroupées dans 35 grappes (regroupant de 2 à 48 cas). Le nombre de cas liés par an chez les SDF vivant en foyer a diminué de 14,3 à 2,7 durant les 13 années du programme ($P < 0{,}01$), et est passé de 75% à 30% pour ce qui concerne la totalité des cas de TB ($P < 0{,}01$). Seule une légère tendance à la diminution a été notée chez les SDF ne vivant pas en foyer.

CONCLUSION : Le programme de dépistage dans les foyers accueillant des SDF est à l'origine de la diminution du nombre de cas liés. Le génotypage a permis de confirmer l'effet positif de l'intervention.

RESUMEN

OBJETIVO: Se examinó la repercusión de un programa activo de búsqueda de casos sobre la transmisión de la tuberculosis (TB) en los refugios destinados a las personas sin techo en París, Francia.

MÉTODO: Entre 1994 y 1997 se introdujo un programa de búsqueda activa de casos de TB en los refugios para personas sin domicilio, por conducto de una unidad móvil de detección radiográfica, la cual permaneció operativa entre 1997 y el 2007. Durante estos períodos, se practicó la genotipificación de los aislados clínicos provenientes de los casos de TB diagnosticados, mediante el análisis del polimorfismo de la longitud de los fragmentos de restricción, utilizando como sonda la secuencia de inserción IS*6110*.

RESULTADOS: Entre 1994 y el 2007 se diagnosticaron 313 casos nuevos de TB en las personas sin techo, 179 en el marco del programa en los usuarios de los refugios y 134 en personas sin domicilio que no acudían a los albergues. La mitad de las cepas formaban parte de 35 conglomerados diferentes (de dos a 48 casos por conglomerado). La agrupación en conglomerados de los casos de TB de los refugios disminuyó de manera constante durante los 13 años del estudio, de 14,3 al comienzo hasta 2,7 casos relacionados por año ($P < 0{,}01$), y de 75% a 30% de casos relacionados en todos los casos de TB ($P < 0{,}01$). Por el contrario, en las personas sin techo que no acudían a los refugios se observó solo una discreta tendencia a la disminución de los casos en conglomerados.

CONCLUSIÓN: El programa de búsqueda activa de casos de TB en los refugios destinados a las personas sin techo tuvo como resultado una disminución de la aparición de conglomerados, sobre todo en los usuarios de estos establecimientos. La genotipificación contribuyó a confirmar la repercusión favorable de esta intervención.