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ORIGINAL ARTICLE

A social network approach for the study of leprosy transmission beyond the household

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Background: *Mycobacterium leprae* was the first microorganism directly associated with a disease, however, there are still important gaps in our understanding of transmission. Although household contacts are prioritized, there is evidence of the importance of extrahousehold contacts. The goal of this article is to contribute to our understanding of the transmission of leprosy ex-household.

Methods: We compare co-location data of 397 leprosy cases and 211 controls drawn from the Centro de Dermatologia Sanitária D. Libânia in Fortaleza, Brazil. We collected lifetime geolocation data related to residence, school attendance and workplace and developed novel methods to establish a critical distance (R_c) for exposure and evaluated the potential for transmission for residence, school and workplace.

Results: Our methods provide different threshold values of distance for residence, school and workplace. Residence networks demonstrate an R_c of about 500 m. Cases cluster in workplaces as well. Schools do not cluster cases.

Conclusions: Our novel network approach offers a promising opportunity to explore leprosy transmission. Our networks confirm the importance of coresidence, provide a boundary and suggest a role for transmission in workplaces. Schools, on the other hand, do not demonstrate a clustering of cases. Our findings may have programmatic relevance.

Keywords: Brazil, *Mycobacterium leprae*, schools, social networking, workplace

Introduction

Mycobacterium leprae was the first microorganism associated with a disease, however, there are important gaps in our understanding of fundamental epidemiologic, pathologic and immunologic features of leprosy.[1] Several studies have shown that even in endemic areas there is often no history of contact with known cases, suggesting possible involvement of other factors in transmission.[2]

Although household contacts are the currently emphasized mode of transmission,[3] a substantial proportion of cases cannot be attributed to household contacts.[2] Another argument suggesting the possible importance of extrahousehold contact is the higher prevalence of leprosy in men in many settings.[2,4] The inference here is that—in general—men spend more time outside their households and hence are potentially exposed to more sources of transmission. This reinforces the importance of considering possible extrahousehold contact in attempting to better understand the transmission of *M. leprae*.[5] In other words, as a consequence of their different social roles, it seems likely—especially in urbanizing, developing societies—that susceptible and sick individuals become embedded in complex social networks involving repeated close contact in (non-household) shared locations potentially relevant to transmission.

In epidemiology, network approaches have been used in the analysis of sexually transmitted diseases, including human immunodeficiency virus (HIV). For HIV, with relatively good knowledge of the modes of transmission, exposure can be estimated through tracing sexual or needle-sharing links and attributing a probability of transmission.[6–10] With leprosy, where there are no good markers of infection, only of disease,[11] transmission is much less well understood and, as a number of genetic, environmental and behavioural factors interact to produce disease, such network analyses have not yet proven fruitful.

A network is a graph defined as a set of vertices (nodes) and edges (connections among the nodes). In network science literature, graphs with large numbers of nodes are referred to as complex networks.[12] Research has shown that the global properties of many natural and social systems can be analysed by complex networks from the perspective of graph theory.[13] Methods originating in statistical physics are also being utilized in this approach.[14] Complex networks can be generated by simple mathematical algorithms, as, for instance, in small-world networks and scale-invariant networks.[15] Other examples of complex networks are biological networks (such as metabolic or genetic/epigenetic protein networks) and communication networks (such as the internet).[16,17] Our goal here is to present a framework that might contribute to the understanding of possible extrahousehold leprosy transmission by analysing complex, colocation networks based on data from both healthy and sick individuals.

Methods

Setting

We constructed and characterized the networks of geolocated leprosy cases and a group of controls in each demographic area (census district) in the city of Fortaleza, Ceará State, Brazil. Social networks most often describe relationships between different individuals and sometimes between individuals and groups.

Study population

A case–control study was conducted among patients attending the national dermatological centre (Centro de Dermatologia Sanitária D. Libânia [CDERM]) from 9 September 2008 to 12 November 2010. Leprosy cases were diagnosed based on the presence of one or more of the following criteria: typical skin lesion with loss of sensitivity, enlargement of one of the major nerves with loss of sensitivity, positive skin smear for *M. leprae* and histopathological results of skin biopsies. Cases were grouped according to the Ridley and Jopling classification.[18–20]

Controls were individuals living in Fortaleza who presented to the CDERM with other skin problems (skin cancer, infections, aesthetic skin issues and other skin diseases). No other matching criteria were applied. Trained health professionals in the CDERM examined all cases and controls.

Recruitment proceeded as follows. The team, consisting of two permanent clinical staff for exams and three trained interviewers, conducted the research in the clinic 2 d each week. Days of the week were selected on a rotating schedule. On recruitment days, all new patients in the waiting room were approached and asked if they wished to participate in the study. If they agreed, the study was explained, they were consented and the interview guide was applied. All consenting eligible participants were interviewed each day by the study team. Months with reduced recruitment included December, January and July, holiday periods for all staff. No incentive was provided to participate in the study. The number of patients interviewed each day varied greatly, with some days recruiting no patients or controls. An average of three cases were enrolled each day.

Sample size was calculated based on two cases for each control, since finding cases in a specialized referral clinic is easier than finding controls. We estimated an odds ratio of 1.625 (40% of exposure in controls vs 52% among cases), power of 80% and a two-sided confidence level of 95%. The final sample size was estimated at 202 controls and 403 cases.

Ethics statement

All eligible recruits were informed of the study goals and procedures and signed informed consent forms. The research project was approved by the Research Ethics Committee of the CDERM.

Data collection

Socio-economic and demographic information about residences, schools and worksites was collected covering the last 10 y for cases and controls. The participant addresses, as well as addresses of schools and worksites were geolocated by a trained technician using physical maps and Google Maps data.

Network analysis

We applied a method based on network concepts using colocation data of leprosy cases and controls. Person-to-person

Table 1. Sociodemographic characteristics of recruited leprosy cases and controls

Variable	Cases	Controls	p-Value
Sex, n (%)			
Male	206 (80.2)	51 (19.8)	<0.001
Female	205 (53.4)	179 (46.6)	
Age (years)			
Age (years), P_{50} (P_{25}–P_{75})	41 (28–52)	28 (19–41)	
Mean	40	30	
SD	16	14	
Range	4–81	4–75	
Age group (years), n (%)			
≤15	38 (52.1)	35 (48.0)	0.027
>15	373 (65.7)	195 (34.3)	
Marital status, n (%)			
Single	134 (51.7)	125 (48.3)	<0.001
Married/in union	218 (69.4)	96 (30.6)	
Divorced/separated	38 (88.6)	8 (17.4)	
Widowed	15 (96.8)	1 (6.3)	
Race, n (%)			
White	105 (59.7)	71 (40.3)	0.223
Parda (mixed)	249 (64.8)	135 (35.2)	
Black	49 (73.1)	18 (26.9)	
Indigenous	8 (57.1)	6 (42.9)	
Education, n (%)			
None/primary incomplete	232 (71.4)	93 (28.6)	<0.001
Primary complete/high school incomplete	100 (68.0)	47 (38.0)	
High School complete/college	79 (46.8)	90 (53.3)	

P_{50} (P_{25}–P_{75}): 50th percentile (25th percentile–75th percentile).

networks are based on participant reports of their contacts while geolocation or colocation networks are based on geographic proximity. We worked with the hypothesis that the closer cases are to other cases (compared with controls) in physical space, the greater the likelihood of transmission among cases. More details about the techniques involved in the developed network methodology, as well as its application to tuberculosis (TB) data, are presented in Pinho et al.[21]

Colocation relationships were said to occur if two individuals reported residing, attending school or working in the same location (within a proximity radius R). R could be varied in the analysis (e.g. 'neighbourhood' R, 'school' R and so on). A minimum period of 1 y of overlap was used to classify respondents as colocated. Epidemiological evidence provides some support for this classification.[22,23] In the two cohort studies cited, 23% and 75% of secondary cases, respectively, were identified in a 1-y follow-up. A 1-y overlap period was also justified in reducing the burden of recall for participants and assisting in data collection.

Proximity was considered for three different contexts: residence, school and workplace. Topological network analysis of colocation of cases provides information about the social dynamics of cases that may share a location (allowing possible transmission); colocation of controls indicates the likelihood of contacts not related to transmission. For both cases and controls, network topology was characterized using statistical indices defined in complex network theory.

While there are a number of public and commercial social network analysis tools and libraries available to conduct our analysis (e.g. Gephi, NetworkX, R and many others), we took advantage of tools developed by the team at the Federal University of Bahia for the study of TB transmission[21] that were adapted for our project. The data used in the analysis are available upon request for academic use. The software is included as a supplemental file.

To reconstruct networks of contacts among persons and places we used the following steps: (1) the primary data in the questionnaires were transferred to a spreadsheet; (2) the team applied GRAPHTUBE, a novel computational system to generate activity and geographic networks as described in Pinho et al.[21]; (3) attributes, such as being a case or control, male or female or any other attribute selected from primary data, were added to the database; and (4) using suitable filters, the software builds bimodal person-to-person (PP) networks that can be based on a combination of social activities, geographic location (measured by the proximity radius R) and time. Because we collected fewer controls than cases, for a comparative analysis we draw 10 000 samples of networks of equivalent size from cases and controls based on a simulation procedure described in Pinho et al.[21]

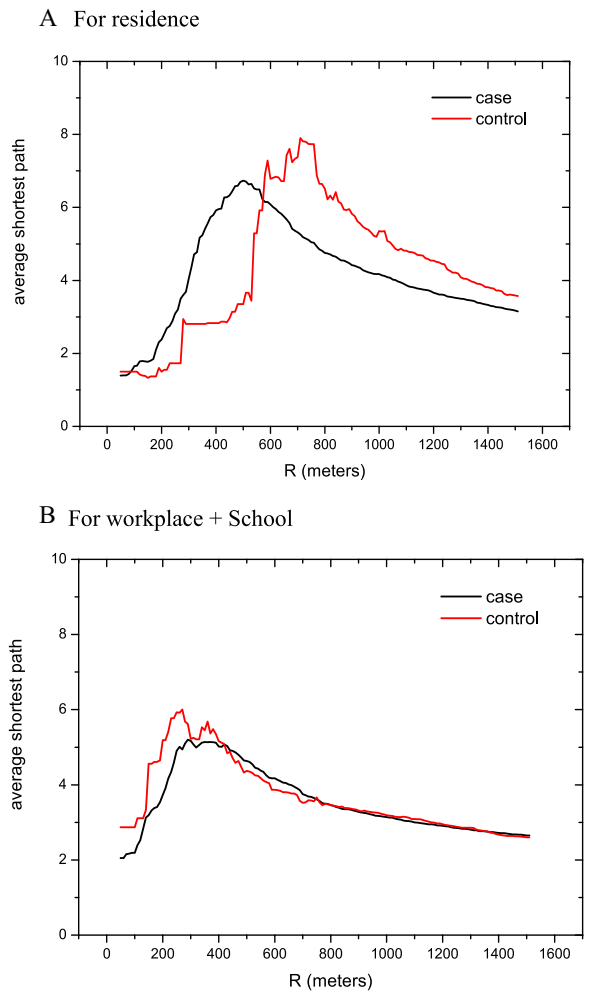

Figure 1. Critical distance for cases and controls.

The data were filtered with attributes set either to case or to control. Then we calculated the average degree (number of contacts), diameter, average minimum path, clustering coefficient[24] and betweenness centrality for each node.[25] The nodes were then rescaled according to their betweenness centrality measures.

By entering different values for the proximity radius R and time we were able to explore appropriate settings for analyses. The PP networks depend primarily on the geographical distance in locales frequented by cases and controls, which were assessed by using both individual geolocation and neighbourhood. As mentioned previously, using geolocation, the choice of the minimum value of R for the distance between places visited by two individuals—overlapping for a period of time—determines whether they are potentially connected by an edge (link) in the network or not.

By definition, the geographical distance between any two persons who occupied the same school or workplace for the same interval of time is zero. Thus such persons would always be connected by a link, irrespective of the value of R. In this context, these individuals (same schools, same workplace) were considered analogous to individuals in the same household.

By comparing reconstructed networks using slightly different values of R, it becomes possible to identify one or a small set of critical values (R_c, critical distance) for sets of individuals close enough to interact with each other and possibly transmit infection. This strategy has been used with success in phylogenetic studies.[26]

To generate these networks, a threshold (cut-off) value of R (R_c) must be chosen. This value represented the minimum distance between the locations occupied by two different individuals used to define a direct node–node connection in the generated networks, e.g. for place of residence, two nodes were considered to be connected in the network if the geographical distance between their residences was smaller than R_c. It followed that the value of R_c directly affects the value of the average shortest path to connect all nodes (X_{avg}).

If the cut-off value was large, the network had many connections (everyone can be connected to everyone else), whereas if the cut-off was small, the network could have few connections (and be divided into small isolated subnetworks). By varying the value of R between these two extremes, there would be one (or a few) values R_c for which X_{avg} attained a maximum value. At this value of R_c, which we label the critical distance, a network was generated with the minimum number of connections to connect all nodes.

Once critical values of R_c had been obtained, we proceeded with analysis of the networks generated with the cut-off R_c. We began with estimation of the topological distance, or minimal dissimilarity, between cases and controls in order to compare the case network (CA-network) with the control network (CO-network). This value was obtained by calculating the average minimum distance (in network steps) between the pair of nodes for critical CA- and CO-networks.

We also estimated the contact probabilities between cases and controls using the contact neighbour ratio T, assuming the network was formed by all individuals (cases and controls); as a consequence, there are three types of node pairs: case–case, case–control and control–control. The variable T is a measure of network density and proximity that can be expressed as the degree ratio of connections of a certain type to total degree.[27] For example, one might calculate the number of contacts with fellow workers relative to a person's total number of contacts. Here, the contact neighbour ratio of cases and controls was estimated by dividing the number of cases connected with controls by the total number of edges in the case–control network (which is the same as if one did this for each individual and summed the total).

To assess whether the finite (non-zero) estimate of T obtained from node pairs was merely due to stochastic fluctuations of a stationary linear process, a null distribution of T was generated and compared for each class of nodal connection. Using the same numbers of cases and controls (as required by analysis), for each kind of network constructed (residence, workplace or school) and for the relevant values of R and time interval, 10 000 random networks were generated and a p-value was obtained for all random Ts greater than the measured T.[27]

Results

We recruited a total of 411 newly diagnosed cases, a mean of 3 cases interviewed per day. The majority of cases were

Table 2. Distance between cases and controls

	Matrix of p-value of *T* index		Matrix of distance (m)	
Location	Case	Control	Case	Control
Residence: clusters of cases closer than controls				
Case	<0.001**	1.000	6479	7040
Control	0.957	0.096		7429
Workplace: cases are proximate to each other and surrounded by individual controls				
Case	0.016*	0.995	5018	5494
Control	0.551	0.702		5818
School: controls are proximate to each other and surrounded by individual cases				
Case	0.650	0.475	6876	6862
Control	0.999	0.009**		6645

*p<0.05, **p<0.01.

borderline (219 [57%]), with the remaining as lepromatous (85 [22.1%]), tuberculoid (63 [16.4%]) and indeterminate (17 [4.4%]). A total of 384 of the 411 cases enrolled were classified, 27 were missing. Controls were more difficult to involve in the study, as recruitment was conducted in a referral centre for leprosy and potential control patients were less enthusiastic about participating in a study about leprosy. We recruited a total of 230 controls, a mean of 1.5 controls interviewed per day. Only 397 cases and 211 controls could be adequately geolocated and were used in the network analysis.

The social demographic characteristics of the collected data of leprosy cases and controls are presented in Table 1. As shown, cases were more likely to be male (p<0.001), older (p=0.027), married (p<0.001) and less educated (p=0.001).

Regarding the results obtained from the network analysis, there were differences in the residence and extrahousehold networks. In Figure 1a we show the average shortest path X_{avg} versus the geographical cut-off R for the residence network. The figure shows that R_c is equal to 750 m for controls and 550 m for cases. In Figure 1b we show a similar graph for the school+workplace network (extrahousehold networks), indicating that R_c is equal to 400 m for both cases and controls.

Using those values of R_c for each one of four networks—case and control networks for residence and extrahousehold (school+workplace) filters—we obtained the topological distance between CA-network and CO-network for residence and extrahousehold contact filters. Although there were differences between the CA-network and CO-network for residence (Δ_{min}=0.35) and extrahousehold (Δ_{min}=0.30) filters, these were not significant. Moreover, both of these are very different from the corresponding random versions of the respective CA-network ($\Delta_{r,\ min}$=0.75) and CO-network ($\Delta_{r,\ min}$=0.70).

In terms of the whole network, using all individuals to evaluate the contact probability between cases and controls, we analysed the effects of workplace and school filters individually, showing in Table 2 the p-value of the T index for the three filters. Three values achieved p-values on the T statistic of <0.05: cases in the residence networks, cases in the workplace network and controls in the school network. In terms of maximum network distance (along shortest paths between connected nodes), networks of cases were shorter than controls in the residence and workplace networks, while they were almost identical in the school networks, as represented in Figure 2.

Discussion

Our results, as presented in a schematic representation in Figure 2, confirmed the central position of households in transmission. In general, this analysis allowed us to connect people to people at different times in diverse venues, such as extrahousehold or workplace venues, as well as within bounded outdoor spaces.

For residence networks, we observed a pattern of linked cases indicating the potential for transmission from one or more cases. Our modelling of the area around the residence of a case in which year-long (or more) contact may occur generated an R_c of approximately 500 m. With a different methodology, another study identified a radius of 150 m of a seropositive patient in which a contact would be at higher risk of being seropositive.[28] Interestingly, the value we found for R_c roughly coincides with the findings of van Beers et al.[3] Thus a complex network approach not only supports their biological findings, but may also provide a systematic approach to identify parameters for the most cost-effective case-finding strategy.

Other studies have shown that proximity to leprosy patients is an important determinant of transmission.[3,29] Although the target area we found was larger, social network behaviour and geographic characteristics of each location undoubtedly play a

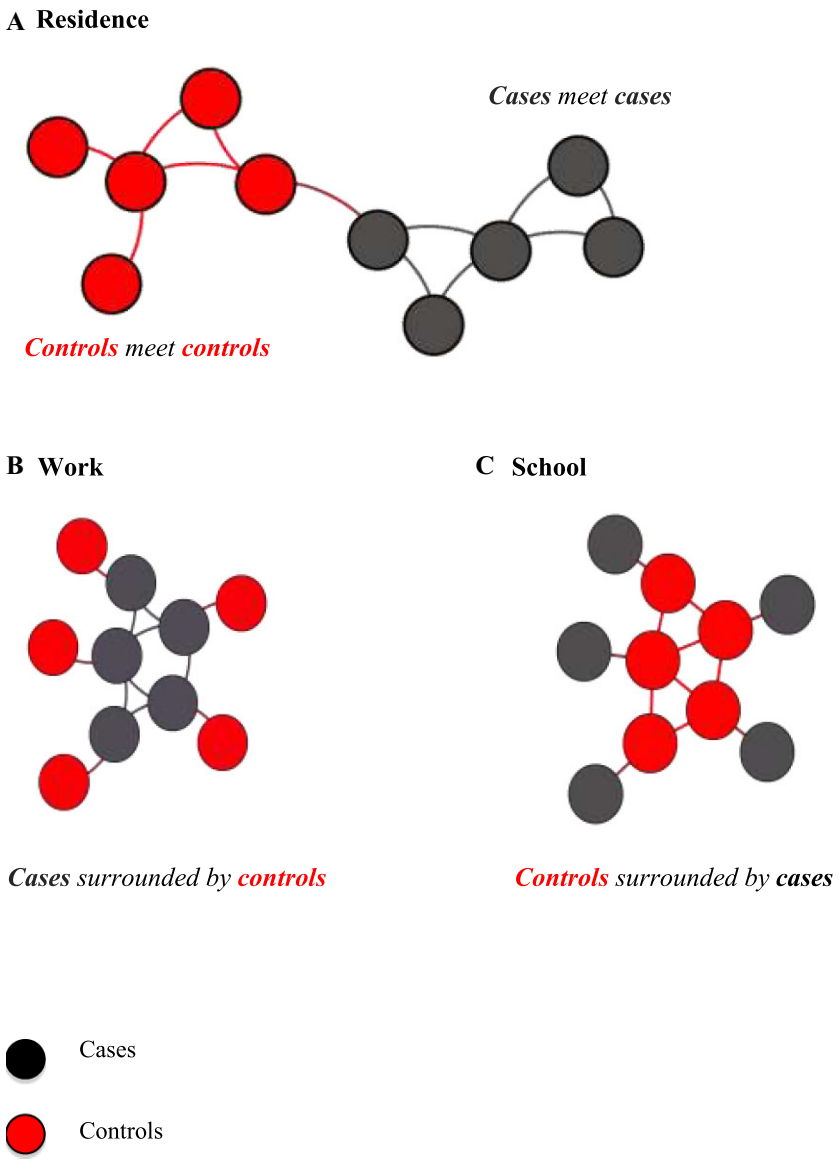

Figure 2. Diagram of cases and controls according to their (a) residence, (b) work and (c) school network.

role in determining a 'contact zone'. Van Beers et al.[3] also used social and work contacts in their analysis, independent of the distance from the cases identified. A number of recent studies have discussed contact tracing as part of leprosy post-exposure prophylaxis[30–32] and the success of that network approach. Our approach complements contact tracing, potentially identifying inadvertent and unreported contacts or potential exposure from other sources.

In our results, we used R_c to construct our networks, becoming the focal or target area within which we looked for possible transmission. The analysis could be performed for any R value but, taking into account the previous discussion, the networks evaluated within R_c provided a more objective starting point for exploring contacts associated with possible transmission. In other words, it defined the most parsimonious number of links required for potential spread through the network.

If R_c is too large, everyone is connected to everyone else in our reconstructed network and the area we would need to examine for possible transmission is the entire geographic area of Fortaleza. In contrast, if R_c is too small, many members of our sample would not be connected and hence many potential contacts/transmissions would be missed. This is the reason the proposed strategy to find a useful value—in statistical physics terms—leads to a network that is close to (but inside) the transition point between a multicluster and a percolated structure, the former being a set of isolated nodes (or small clusters) and the latter a structure in which all nodes are connected to all others by a path of some length.

To summarize, our modelling of the area around the residence of a case in which 1 y was allowed for possible contact to occur generated an R_c of approximately 500 m (Figure 1). With reference to workplaces and schools, our results suggest potential for workplace transmission: cases clustered topologically in work networks. This does not prove transmission among these cases but it does suggest workplaces should be a high priority for further study, especially when genotyping of *M. leprae* strains (or substrains) becomes affordable. While schools have been targeted as a location to base active surveillance and contact tracing, especially for cases <15 y of age,[33] we believe this choice is as much a target of opportunity (and opportunity for health education) as it is an efficient tool for identifying new cases. Pedrosa et al.[33] reviewed >34 000 schoolchildren to identify 40 new cases (0.12%). Ten of those children lived in households with either a history of treatment for leprosy or were currently being treated. It is possible that the role of proximity in clustering cases is minimized in our analysis of schools because they may draw students from different areas farther from the school. This is hardly likely in Fortaleza, where each neighbourhood has several schools meant to be within safe walking distance of students' homes.

The use of a case–control design, while uncommon in network research, constitutes a major difference from classical network analysis applied in epidemiology. The finding of the household as the primary locus of transmission provides support for the methodological approach we have used and suggests the potential fruitfulness of future studies along these lines.

Before closing, we would like to stress that the approach in the current study cannot be reduced to a conventional geographic cluster analysis. We are not looking at clusters per se in a traditional sense, but in a contact network over time. The peak of each curve in Figure 1 corresponds to the geographic distance R_c for maximizing the size of the principal component of each network while minimizing the number of links. We re-emphasize that this provided an optimal, parsimonious contact network from which to draw our conclusions.

As with any novel methods, there are limitations in our study in terms of design, implementation and interpretation. The differences in terms of cases and controls, both in number and attributes, and our solution, require a number of assumptions. The sampling of networks in general, as opposed to the sampling of populations, is not as well understood. At the same time, the complex network methods we used have proved valuable for the analysis of TB transmission and have a proven track record in other fields. Additionally, our findings are substantiated in the literature.

In view of the current analyses, we conclude that there are differences in the topologies of case and control networks for residence and workplace demonstrating the potential for systematic differences in contact and resulting transmission of *M. leprae* from cases to contacts. While the application of approaches derived from the analysis of complex networks to leprosy is new, it is a potentially powerful tool in the understanding of extrahousehold transmission of leprosy.

Authors' contributions: LRFSK was the principal investigator of the project, supported by GOP. LRFSK and CK designed the project and the research instrument. LRFSK and MAAP supervised the fieldwork. MAAP and HC conducted the clinical exams. CCF conducted all laboratory tests. STRP and RFSA developed the analysis plan. NAA developed the software (Graphtube) for analysis. JGVM organized the network analysis. JGVM, FBM, RBCG, LGSF and SBS analysed the network data. JGVM, RMSM and RLFA analysed the data. LRFSK and CK shared equal effort to write the paper, with input in the first version from LCR, AK and MLB. All authors made contributions to the final version.

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Competing interests: None declared.

Ethical approval: All participants were informed of the study and signed consent forms. All forms are stored in a locked file cabinet at the Federal University of Ceara in Fortaleza and are available for review. The Institutional Review Board of the National Reference Dermatology Hospital D. Libânia (CDERM) reviewed and approved the study (approval 011-2007).

Data availability: De-identified data are available to qualified researchers upon written request to the corresponding author. Researchers should describe the purpose of the review and acknowledge the source of the data in any subsequent use.

References

1 Visschedijk J, van de BJ, Eggens H, et al. Review: *Mycobacterium leprae*—millennium resistant! Leprosy control on the threshold of a new era. Trop Med Int Health. 2000;5(6):388–99.

2 Fine PE, Sterne JA, Ponnighaus JM, et al. Household and dwelling contact as risk factors for leprosy in northern Malawi. Am J Epidemiol. 1997;146(1):91–102.

3 van Beers SM, Hatta M, Klatser PR. Patient contact is the major determinant in incident leprosy: implications for future control. Int J Lepr Other Mycobact Dis. 1999;67(2):119–28.

4 Bakker MI, Hatta M, Kwenang A, et al. Risk factors for developing leprosy—a population-based cohort study in Indonesia. Lepr Rev Mar. 2006;77(1):48–61.

5 Klovdahl AS, Graviss EA, Yaganehdoost A, et al. Networks and tuberculosis: an undetected community outbreak involving public places. Soc Sci Med. 2001;52(5):681–94.

6 Hethcote HW, Van Ark JW. Modeling HIV transmission and AIDS in the United States. New York: Springer-Verlag; 1992.

7 Jacquez JA, Simon CP, Koopman J, et al. Modeling and analyzing HIV transmission: the effect of contact patterns. Math Biosci. 1988;92(2):119–99.

8 Kaplan EH. Modeling HIV infectivity: must sex acts be counted? J Acquir Immune Defic Syndr. 1990;3(1):55–61.

9 Wagner B, Blower S. Voluntary universal testing and treatment is unlikely to lead to HIV elimination: a modeling analysis. Nat Preced. 2009; https://doi.org/10.1038/npre.2009.3917.1.

10 Weusten JJ, Van Drimmelen HA, Lelie PN. Mathematic modeling of the risk of HBV, HCV, and HIV transmission by window-phase donations not detected by NAT. Transfusion. 2002;42(5):537–48.

11 Klovdahl AS. Networks and pathogens. J Sex Transm Dis. 2001;28(1):25–8.

12 Barabási A-L. Network science. Cambridge: Cambridge University Press; 2016.

13 Newman ME, Watts DJ, Strogatz SH. Random graph models of social networks. Proc Natl Acad Sci USA. 2002;99(Suppl 1):2566–72.

14 Albert R, Barabási A-L. Statistical mechanics of complex networks. Rev Mod Phys. 2002;74(1):47–97.

15 Newman MEJ, Barabaśi A-LS, Watts DJ. The structure and dynamics of networks. Princeton: Princeton University Press; 2011.

16 Newman MEJ. Networks: an introduction. Oxford: Oxford University Press; 2010.

17 Newman MEJ. Networks. Oxford: Oxford University Press; 2018.

18 Ridley DS. Histological classification and the immunological spectrum of leprosy. Bull World Health Org. 1974;51(5):451–65.

19 Ridley DS. Indeterminate leprosy. Lepr Rev. 1974;45(2):95–7.

20 Ridley DS, Jopling WH. Classification of leprosy according to immunity. a five-group system. Int J Lepr Other Mycobact Dis. 1966;34(3):255–73.

21 Pinho STR, Pereira SM, Miranda JGV, et al. Investigating extradomiciliary transmission of tuberculosis: an exploratory approach using social network patterns of TB cases and controls and the genotyping of *Mycobacterium tuberculosis*. Tuberculosis. 2020;125:102010.

22 Duppre NC, Camacho LA, da Cunha SS, et al. Effectiveness of BCG vaccination among leprosy contacts: a cohort study. Trans R Soc Trop Med Hyg. 2008;102(7):631–8.

23 Goulart IM, Bernardes Souza DO, et al. Risk and protective factors for leprosy development determined by epidemiological surveillance of household contacts. Clin Vaccine Immunol. 2008;15(1):101–5.

24 Latapy M, Magnien C, Del Vecchio N. Basic notions for the analysis of large two-mode networks. Soc Networks. 2008;30(1):31–48.

25 Brandes U. On variants of shortest-path betweenness centrality and their generic computation. Soc Networks. 2008;30(2):136–45.

26 Andrade RF, Rocha-Neto IC, Santos LB, et al. Detecting network communities: an application to phylogenetic analysis. PLoS Comput Biol. 2011;7(5):e1001131.

27 Manly BF. Randomization, bootstrap and Monte Carlo methods in biology. Boca Raton, FL: CRC Press; 2006.

28 Bakker MI, Hatta M, Kwenang A, et al. Population survey to determine risk factors for *Mycobacterium leprae* transmission and infection. Int J Epidemiol. 2004;33(6):1329–36.

29 Moet FJ, Meima A, Oskam L, et al. Risk factors for the development of clinical leprosy among contacts, and their relevance for targeted interventions. Lepr Rev. 2004;75(4):310–26.

30 Smith WC, Aerts A. Role of contact tracing and prevention strategies in the interruption of leprosy transmission. Lepr Rev. 2014;85(1):2–17.

31 Lockwood DN, Krishnamurthy P, Pannikar V, et al. Reply to the role of contact tracing and prevention strategies in the interruption of leprosy transmission. Lepr Rev. 2015;86(1):124–5.

32 Barth-Jaeggi T, Steinmann P, Mieras L, et al. Leprosy Post-Exposure Prophylaxis (LPEP) programme: study protocol for evaluating the feasibility and impact on case detection rates of contact tracing and single dose rifampicin. BMJ Open. 2016;6(11):e013633.

33 Pedrosa VL, Dias LC, Galban E, et al. Leprosy among schoolchildren in the Amazon region: a cross-sectional study of active search and possible source of infection by contact tracing. PLoS Negl Trop Dis. 2018;12(2):e0006261.