



# Active Case Detection of Rifampicin Sensitive and Resistant Tuberculosis by Systematic Screening Among Household Contacts of Rifampicin-Resistant Tuberculosis Patients in Dhaka, Bangladesh

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## Abstract

**Background/Aim:** Patients with rifampicin resistant-tuberculosis (RR-TB) may remain a source of infection longer than patients with rifampicin sensitive-tuberculosis (RS-TB). This study aimed to detect active cases of RS-TB and RR-TB through systematic screening among household contacts of RR-TB patients in Dhaka, Bangladesh.

**Methods:** This cross-sectional study was conducted among the 355 household contacts (HHCs) of 93 RR-TB primary cases identified from various centres in Dhaka, diagnosed between November 2020 and October 2021. For the identification of active cases of tuberculosis (TB), systematic screening among HHCs was done, where verbal screening was performed to check the presence of symptoms of TB. Those who had at least one symptoms of TB were considered as symptomatic contacts. Later GeneXpert analysis of sputum was done among the screened symptomatic contacts. Data was collected using a pretested, semi-structured, interviewer-administered questionnaire.

**Results:** An estimated 30.4 % of respondents were  $\leq 15$  years of age. TB-like symptoms were prevalent among 9.9 % of respondents. Loss of appetite (45.7 %), unexplained weight loss (40.0 %) and cough (37.1 %) were the most common symptoms. Among the contacts with TB-like symptoms, 6.7 % were diagnosed as a case of TB (3.35 % were RR-TB and 3.35 % were RS-TB). The number needed to be screened to find an active case of TB was established at 178 among the HHCs of RR-TB.

**Conclusions:** About one in ten RR-TB HHCs showed TB-like symptoms. One in fifteen HHCs with TB-like symptoms was an active case of TB. Regular, effective screening of RR-TB contacts is needed to stop the transmission.

**Key words:** Tuberculosis; Drug-resistant tuberculosis; Rifampicin; Close-contact transmission; Bangladesh.

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## Introduction

Among 10.6 million tuberculosis (TB) cases in the world, 450,000 cases developed rifampicin-re-

sistant tuberculosis (RR-TB) in the year 2021.<sup>1</sup> Patients with RR-TB/multi-drug resistance tu-

berculosis (MDR-TB) may remain a source of infection for longer duration than those with drug-susceptible TB (DS-TB), which may increase the risk of infection, especially among household contacts (HHCs).<sup>2</sup> This risk needs to be addressed so that the diagnosis and treatment of HHCs TB patients can be initiated early to decrease transmission and counsel the at-risk persons to take necessary precautions to minimise the chances of infection and to reduce the likelihood of any TB related morbidity and mortality.<sup>3</sup>

According to the Global Tuberculosis report 2022, Bangladesh ranks seventh among the 30 high-TB burden countries with 375,000 cases and the number of MDR/RR-TB burden was 4500 cases.<sup>1</sup> An estimated 70,000 TB patients remain undiagnosed annually and only 40 % of drug-resistant TB (DR-TB) cases are enrolled for proper treatment regimens.<sup>4</sup> Hence, to combat TB, the National TB Control Program (NTP) of Bangladesh emphasised on the early diagnosis and prevention of TB among the HHCs of DR-TB.<sup>5</sup> It is suggested that if one or more TB related signs or symptoms is present, *GeneXpert* test should be performed for the confirmation of active TB cases among the HHCs of MDR-TB, before commencing TB preventive therapy.<sup>6</sup>

Though NTP has specific guideline for TB screening among HHCs of TB patients, any research describing the screening outcomes of TB among HHCs with RR-TB by tracing the primary cases in the context of Bangladesh was not explored previously. On that account, this study was conducted to investigate and analyse the distribution of TB cases among the HHCs of RR-TB patients in Dhaka, Bangladesh.

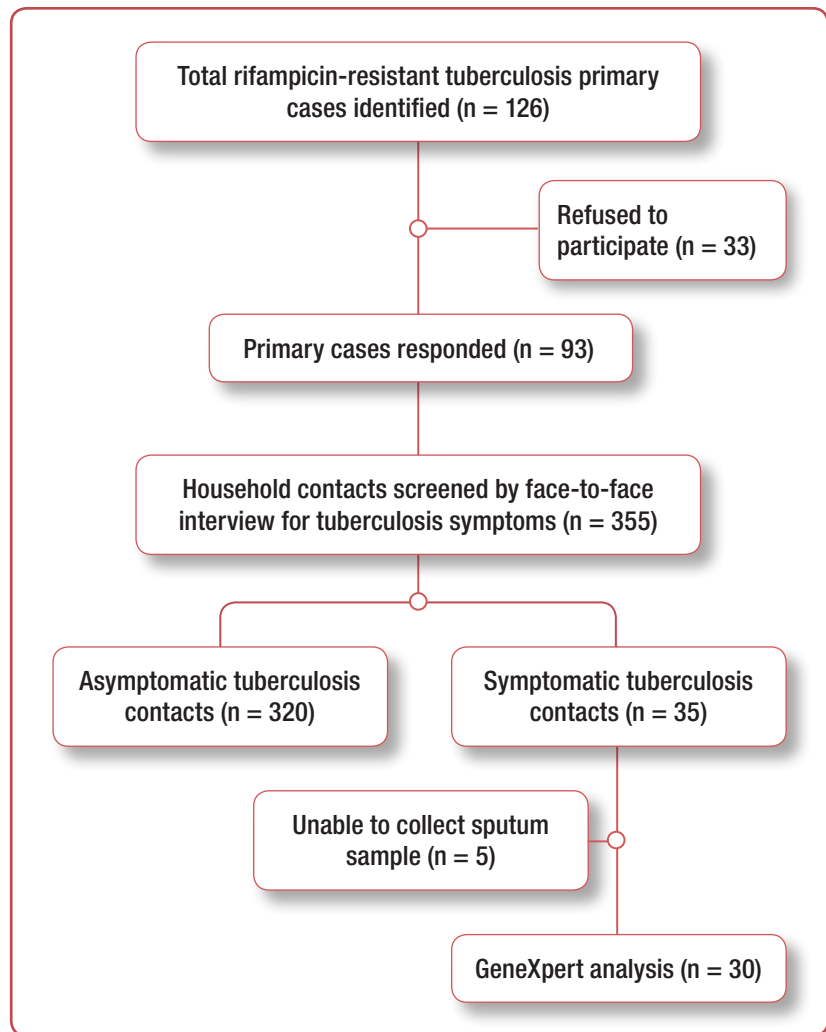
## Methods

A cross-sectional study was conducted among the HHCs of RR-TB, where data collection was done from November 2021 to January 2022. The study population was all HHCs of RR-TB patients diagnosed between November 2020 to October 2021, identified from multiple TB centres located in Dhaka, Bangladesh. The HHCs of RR-TB patients were also residing in Dhaka, Bangladesh. HHC was considered as individuals living under the

same roof and sharing air space with the RR-TB patient in an indoor setting for > 15 hours/week,<sup>7, 8</sup> at least for the last three months from the date of the interview.

The identified primary cases (n = 93) were initially contacted over the phone and motivated to provide necessary information about their HHCs. The list/sampling frame for HHCs (n = 355) was created and their geographical location was plotted on a map for visualising the participant concentration and movement for data collection. Systematic screening, verbal screening followed by *GeneXpert* analysis of sputum sample of the symptomatic contacts was done among the HHCs to detect the active cases of RR-TB and RS-TB. Verbal screening was done through a face-to-face interview of the HCCs using a semi-structured, interviewer-administered questionnaire to identify the symptomatic contacts. The symptoms of TB included were cough, haemoptysis, loss of appetite, unexplained weight loss, frequent fever with chills, night sweats, frequent shortness of breath, chest pain, swelling of lymph nodes in the neck or other parts of the body.<sup>6</sup> Contacts were considered symptomatic of TB if they reported any of the mentioned symptoms.

A sputum sample was collected in a sealed container from symptomatic contacts on the same day of the interview. The participant was asked to gargle and rinse their mouth with water, then was instructed to stand upright and take deep breaths followed by forceful expiration and then cough up the sputum to the marked value of 10 mL. The sample was transported to the nearest TB screening centre for *GeneXpert* analysis, maintaining a 2-8 °C temperature. At the screening centre, the sample was mixed with a sample reagent in a 2:1 ratio to decontaminate and liquefy the sputum. After manual shaking and a ten-minute incubation at room temperature, followed by a second vortexing, the processed sample was transferred into the *GeneXpert* MTB/RIF cartridge. This cartridge was then inserted into the *GeneXpert* instrument, which performed automated lysis, DNA extraction and real-time PCR amplification. Fluorescent probes detected specific DNA sequences, confirming the presence of *Mycobacterium tuberculosis* and identifying mutations in the *rpoB* gene indicative of rifampicin resistance. Results were available within two hours and automatically interpreted by the *GeneXpert* software, facilitating rapid and accurate diagnosis (Figure 1).



**Figure 1:** Detection of tuberculosis among household contacts of rifampicin-resistant tuberculosis

Physical activity of the participants were measured using, Saltin-Grimby Physical Activity Level Scale.<sup>9</sup> After the interview, physical measurements were taken. To measure the weight a digital bathroom scale was used. The respondents were requested to stand up on the scale straight and the reading was taken in kilograms. The respondent was asked to stand up straight against a wall to measure the height. The highest point of their stature was marked with a pencil and the height of the mark from the floor was taken in meters.

Variables were descriptively expressed by frequency and percentage and cross-tabulation was used to assess the number of people screened in the household. For the variable of age in years, the closest integer value was used. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and then categorised into four groups for an adult of  $\geq 20$  years of age: underweight ( $< 18.5$  kg/m<sup>2</sup>), normal (18.5-24.9 kg/m<sup>2</sup>), overweight

(25-29.9 kg/m<sup>2</sup>), obese ( $\geq 30$  kg/m<sup>2</sup>) and for a children and people of  $< 20$  years of age, the same categorisation was done using corresponding BMI-for-age percentile.<sup>10</sup>

The number needed to screen (NNS) to detect one active case of TB was obtained by dividing the total number of respondents by the number of diagnosed cases of TB. A p-value of  $< 0.05$  was considered statistically significant. Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 23 for Windows.

## Results

Symptomatic screening was conducted among 355 HHCs of 93 RR-TB primary cases diagnosed from various TB centres in Dhaka and found that among the HHCs of RR-TB patients 9.9 % had at least one symptom suggestive of TB (Figure 2).

Table 1 reveals that among the HHCs of RR-TB patients, the most common symptom was the loss of appetite (45.7 %), followed by unexplained weight loss (40.0 %) and cough (37.1 %).

Table 2 shows that among the HHCs of RR-TB, highest proportion (30.4 %) were in ≤ 15 years age group. Majority of the respondents were female (55.5 %). Among the smokers 15.6 % and

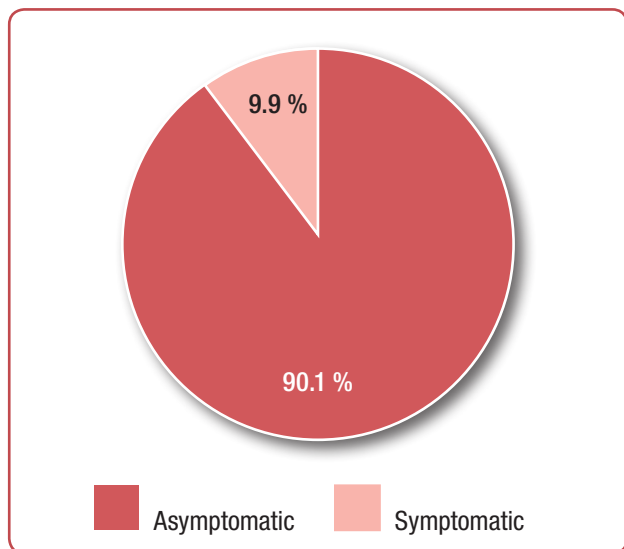


Figure 2: Distribution of respondents according to tuberculosis symptoms (N = 355)

Table 1: Distribution of symptoms among respondents symptomatic of tuberculosis\*

Distribution of symptoms (n = 35)	n	%	% of cases
Loss of appetite	16	19.8	45.7
Unexplained weight loss	14	17.3	40.0
Cough	13	16.0	37.1
Chest pain	11	13.6	31.4
Frequent fever with chills and rigor	10	12.3	28.6
Shortness of breath	6	7.4	17.1
Excessive night sweat	5	6.2	14.3
Swelling of lymph nodes in the neck or other parts of the body	5	6.2	14.3
Haemoptysis	1	1.2	2.9

\*Multiple responses;

Table 2: Socio-demographic and behavioural characteristics of the respondents

Variable – n (%)	Total (n = 355)	Asymptomatic (n = 320)	Symptomatic (n = 35)	p-value
<b>Age category</b>				
≤ 15 years	108 (30.4)	104 (96.3)	4 (3.7)	0.070 <sup>b</sup>
16-30 years	105 (29.6)	92 (87.6)	13 (12.4)	
31-45 years	81 (22.8)	70 (86.4)	11 (13.6)	
46-60 years	45 (12.7)	39 (86.7)	6 (13.3)	
> 60 years	16 (4.5)	15 (93.8)	1 (6.3)	
<b>Gender</b>				
Male	158 (44.5)	143 (90.5)	15 (9.5)	0.860 <sup>a</sup>
Female	197 (55.5)	177 (89.8)	20 (10.2)	
<b>Education</b>				
No formal education	78 (22.0)	73 (93.6)	5 (6.4)	0.522 <sup>a</sup>
Below secondary	193 (54.4)	172 (89.1)	21 (10.9)	
Secondary and above	84 (23.6)	75 (89.3)	9 (10.7)	
<b>Occupation</b>				
Employed	105 (29.6)	93 (88.6)	12 (11.4)	0.066 <sup>a</sup>
Unemployed	153 (43.1)	144 (94.1)	9 (5.9)	
Homemaker	97 (27.3)	83 (85.6)	14 (14.4)	
<b>Smoking history</b>				
Smoker	64 (18.0)	54 (84.4)	10 (15.6)	0.104 <sup>a</sup>
Non-smoker	291 (82.0)	266 (91.4)	25 (8.6)	
<b>Alcohol consumption history</b>				
Consumer	33 (9.3)	28 (84.8)	5 (15.2)	0.351 <sup>a</sup>
Non-consumer	322 (90.7)	292 (90.7)	30 (9.3)	
<b>Physical activity</b>				
Physically inactive	246 (69.3)	219 (89.0)	27 (11.0)	0.461 <sup>b</sup>
Some light physical activity	20 (5.6)	20 (100.0)	0 (0.0)	
Regular physical activity	17 (4.8)	15 (88.2)	2 (11.8)	
Regular hard physical activity	72 (20.3)	66 (91.7)	6 (8.3)	

\*Variable are expressed as row % in Asymptomatic and symptomatic groups; a: Chi square test; b: Fisher's exact test;

**Table 3:** Distribution of health-related issues among respondents

Variable – n (%)	Total (n = 355)	Asymptomatic (n = 320)	Symptomatic (n = 35)	p-value <sup>b</sup>
History of diabetes	29 (8.2)	24 (82.8)	5 (17.2)	0.186
History of kidney disease	7 (2.0)	4 (57.1)	3 (42.9)	0.023
History of cancer	2 (0.6)	1 (50.0)	1 (50.0)	0.188
History of using steroids	21 (5.9)	16 (76.2)	5 (23.8)	0.044
History of BCG vaccination	343 (96.6)	309 (90.1)	34 (9.9)	1.000
<b>BMI</b>				
Underweight	65 (18.3)	57 (87.7)	8 (12.3)	0.591
Normal	169 (47.6)	154 (91.1)	15 (8.9)	
Overweight	83 (23.4)	73 (88.0)	10 (12.0)	
Obese	38 (10.7)	36 (94.7)	2 (5.3)	

*b:* Fisher's exact test; BMI: body mass index; BCG: Bacillus Calmette–Guérin vaccine;

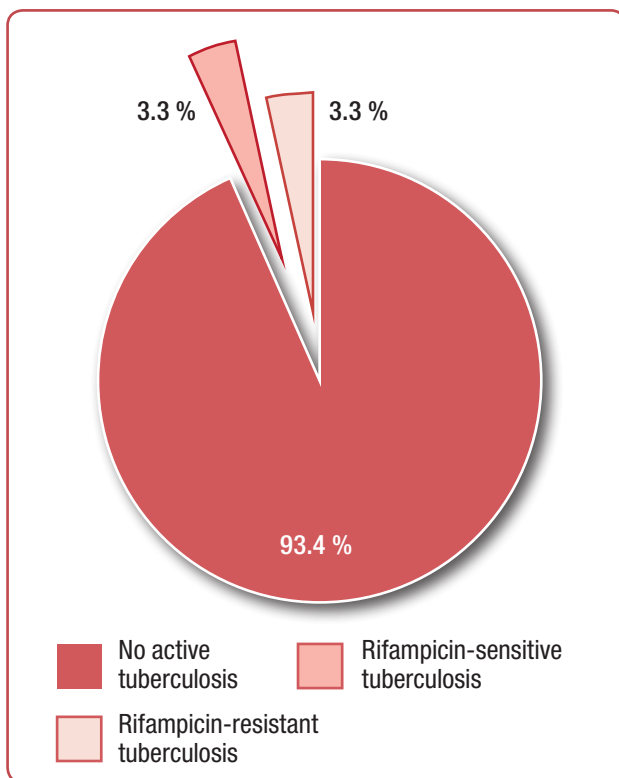
among the alcohol consumers 15.2 % revealed to have TB-like symptoms. More than two-thirds (69.3 %) of the respondents were physically inactive.

Table 3 shows that there was a significant (p = 0.023) relation between symptoms of TB and history of kidney disease. Significant (p = 0.044) relation was also observed among the contacts using steroids and had symptoms of TB.

This study found that there were 6.7 % active cases of TB among the symptomatic HHCs of RR-TB, among which, respondents diagnosed as RR-TB, and rifampicin-sensitive TB (RS-TB) were in equal proportion (Figure 3). The NNS to detect 1 case of TB among the HHCs of RR-TB patients was identified as 178 (data not shown).

## Discussion

This current study revealed that 9.9 % of the HHCs of RR-TB had one or more TB-like symptoms. Much higher rates of TB like symptoms among the HHCs of MDR-TB patients were observed in Andhra Pradesh and Telangana states of India (16.6 %),<sup>11</sup> in Myanmar (39.0 %),<sup>12</sup> in three cities (Karachi, Lahore, Murree) of Pakistan (12.0 %)<sup>13</sup> and in a study of eight countries (Botswana, Brazil, Haiti, India, Kenya, Peru, South Africa and Thailand) 23.0 % was found.<sup>14</sup> The lower occurrence of symptoms in the current study might be explained by the difference in study population, as this study considered HHCs of RR-TB patients where other studies included HHCs of MDR-TB patients. Also, the list of symptoms of TB explored in the current study and the others were different. This study used the guideline of National TB Control Program, Bangladesh<sup>6</sup> while other studies used guidelines according to their regions, which are different from the guideline used in the current study. Another fact might be that all the studies, other than the current one, were conducted between the years 2011–2017, which was pre-COVID. The current study was conducted during the COVID-19 pandemic period. It is evident that infection control with



**Figure 3:** Proportion of diagnosed active cases of tuberculosis among symptomatic household contacts of rifampicin-resistant tuberculosis (n = 30)

personal safety precautions can reduce the risk of developing tuberculosis<sup>15</sup> and due to the improvement in personal hygiene, use of masks and social distancing during COVID-19 pandemic period might have reduced the chance of transmission of TB bacilli. This statement is supported by the global TB report 2022, where it mentioned that in comparison to 2019, there was a significant decrease (18 %) in the number of new cases of TB recorded in 2020.<sup>1</sup>

Among the TB like symptoms reported by the respondents in this study, most common were loss of appetite (45.7 %), unexplained weight loss (40 %) and cough (37.1 %). Similarly, a study in Andhra Pradesh and Telangana states of India, found that among the symptomatic contacts the most common symptoms were cough (75 %), fever (35 %), weight loss (8 %).<sup>11</sup> Another study in Pakistan found that among HHCs screened the most common symptoms were cough (91 %) and fever (62 %).<sup>13</sup>

The present study observed 6.7 % cases of active TB among screened symptomatic HHCs of RR-TB. An almost similar finding was observed in an active case finding study of RS-TB and RR-TB among HHC's of drug resistant TB patients in Andhra Pradesh and Telangana states of India, where they revealed that 4.4 % of the participants were confirmed with TB by *GeneXpert* analysis.<sup>11</sup> In contrast with this study finding, a much higher rate of TB among screened symptomatic HHCs of MDR-TB was observed in three high-burden TB sites (Karachi, Lahore and Murree) in Pakistan (49.0 %),<sup>13</sup> in Agra, India (35.8 %)<sup>16</sup> and in the Amhara and Oromia regions of Ethiopia (45.0 %).<sup>17</sup>

This current study found that the NNS to find a case of TB among the HHCs of RR-TB patients was 178. But similar data among the HHCs of RR-TB patients in other literature was not available. Therefore, the NNS was compared among HHCs of MDR-TB patients. In countries like Myanmar the NNS was 26 in the year 2016,<sup>12</sup> in Pakistan it was 27 in the year 2014<sup>13</sup> and 37 in the Amhara and Oromia regions of Ethiopia in the year 2015.<sup>17</sup> The disparity in study periods between the current study and other studies could be one explanation for the discrepancy. As this study was carried out during the COVID-19 pandemic, it was likely to lessen the spread of TB bacilli. The method of TB diagnosis

investigation may also be a contributing factor. The mentioned studies<sup>11-13,16,17</sup> combined different ways of diagnostic tests, ie microbiological tests (sputum for Acid-fast bacillus by Ziehl-Neelsen stain, sputum for Cartridge-Based Nucleic Acid Amplification Test, *GeneXpert*, Line Probe Assay, sputum for TB liquid culture and sensitivity and Drug Susceptibility Testing), radiological tests, clinical evaluation and others. In comparison, this current study only used *GeneXpert* analysis to confirm the presence of TB, which might have limited the opportunity to detect more TB cases.

The epidemiological significance of this study's findings cannot be overstated. Regular screening of HHCs of RR-TB patients, who are particularly vulnerable, is essential for the early detection and treatment of TB. The study findings suggest that an estimated 97 new TB cases among the HHCs of RR-TB patients could be identified annually, based on the diagnosed RR-TB cases in Bangladesh as reported in the 2022 Global TB report. Without consistent screening and monitoring, these cases will likely be missed, underscoring the critical need for systematic and routine surveillance to protect this high-risk population.

The study had some limitations. As TB and COVID-19 share common symptoms and the study was conducted during the COVID-19 pandemic, there was a possibility for the symptoms to be misclassified. The study only tested symptomatic contacts. Any TB among the asymptomatic contacts of RR-TB patients were not determined which might have impacted the detection of active cases of TB. Only one investigative procedure for diagnosing active TB cases was used and since other means of detection were not used, some TB cases might have been missed. Due to the small number of participants who tested positive for tuberculosis, it was not feasible to perform advanced statistical analysis, which typically require larger datasets to ensure robustness and validity of the results. Consequently, the analysis was constrained to basic statistical techniques to accommodate the available data.

Despite the limitations, this study found active cases of TB among the HHC's of RR-TB patients which presents the effectiveness and importance of regular screening of TB among HHCs of RR-TB patients.

## Conclusion

This study identified that approximately 10 % of the RR-TB HHCs showed TB-like symptoms. Nearly one in fifteen individuals having TB-like symptoms was found to be an active case of TB. Higher NNS for TB case detection among the HHCs of RR-TB patients suggest extensive systematic screening programs. Multiple diagnostic tests along with *GeneXpert* to identify the active cases should be introduced in regular screening of the HHCs of RR-TB for early and accurate detection.

## Ethics

This study was conducted after obtaining ethical clearance from the Institutional Review Board (decision No BSMMU/2021/8055 (C), dated: 5 September 2021). Written informed consent was taken from the adult participants above 18 years of age. From participants of 10-18 years of age, assent was taken from the participants, as well as consent from their legal guardians. For participants below 10 years of age, data was collected from their legal guardians with informed consent. Proper explanation was given to all participant regarding study objectives, methodology, procedure, importance of their voluntary participation and right to withdraw from the study at any point as well as right to refuse to give any information prior to giving consent.

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## Conflicts of interest

The authors declare that there is no conflict of interest.

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## Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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