DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
Atlanta, GA 30333

August 7, 2013

Cheryl H. Bullard
Deputy General Counsel, Public Health
South Carolina Department of Health and Environmental Control
2600 Bull Street
Columbia, South Carolina 29201

Dear Ms. Bullard,

Thank you for inviting the Centers for Disease Control and Prevention (CDC) to provide technical assistance to the South Carolina Department of Health and Environmental Control (DHEC) in the investigation an outbreak of tuberculosis (TB) in Greenwood County. As we discussed previously, my colleague, Dr. Tracie Gardner, and I were thoroughly impressed with the dedication and knowledge of the staff at DHEC.

The enclosed report contains CDC's findings and recommendations based on our investigation in South Carolina. We hope that these recommendations assist DHEC in its mission to interrupt *Mycobacterium tuberculosis*.

We appreciate the opportunity to work with you to achieve the goal of eliminating TB in the United States, and look forward to our ongoing collaborations.

Please feel free to contact me if you have any questions or concerns regarding the content of this report.

Best regards,

Krista Powell

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Date: August 7, 2013

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Centers for Disease Control and Prevention (CDC)

Subject: Technical assistance: Tuberculosis outbreak — Greenwood County, South Carolina, 2013

To: Cheryl H. Bullard, Deputy General Counsel, Public Health
South Carolina Department of Health and Environmental Control

Through: TN Thomas Navin, Chief, NCHHSTP/DTBE/SEOIB
Kenneth Castro, Director, NCHHSTP/DTBE

BACKGROUND

On March 8, 2013, the South Carolina Department of Health and Environmental Control (DHEC) received notification of a positive nucleic acid amplification test performed on broncheoalveolar lavage (BAL) specimen obtained from a patient in Greenwood County, South Carolina, suggesting pulmonary infection with *Mycobacterium tuberculosis* complex. The patient was a 71-year-old man working as a custodian at an elementary school. The DHEC tuberculosis (TB) program immediately instructed the patient not to return to work pending additional evaluation, and enrolled the patient in TB clinic to initiate treatment for TB disease. Upon enrollment in TB clinic, microscopic sputum examination revealed numerous acid fast bacilli (AFB), suggesting infectious pulmonary TB disease. Consequently, DHEC initiated a contact investigation on March 18, 2013. Evaluation of household contacts and close contacts suggested transmission, and during the week of May 27, the contact investigation was expanded to include students, faculty, and volunteers at the school. The investigation identified 13 additional TB cases, including 1 extrapulmonary case in a household contact, 1 infectious TB case in a person who worked at the same school, 1 infectious TB case in a person who was a close social contact, and 10 extrapulmonary TB cases in children who attended the school. As of June 26, 2013, of the approximately 2,000 persons in the community, nearly 1,500 persons had been tested for TB infection as

part of investigation-related activities. On June 26, 2013, the South Carolina DHEC requested on-site epidemiologic assistance from CDC for the investigation in Greenwood County.

On July 1, 2013, Drs. Krista Powell (Medical epidemiologist, Lead, NCHHSTP/DTBE/SEOIB/OIT) and Tracie Gardner (Epidemiologist, NCHHSTP/DTBE/SEOIB/MEA) arrived in Columbia, South Carolina, to assist DHEC with the investigation. The team returned to Atlanta, Georgia, on July 3, then traveled to Greenwood County on July 8. On July 11, the team presented preliminary findings and recommendations to DHEC in Columbia.

OBJECTIVES

1) Determine the chain of transmission of *Mycobacterium tuberculosis*
2) Review contact investigation data and assist with prioritization of contact investigation activities
3) Assist with data management systems
4) Make recommendations to interrupt *Mycobacterium tuberculosis* transmission

METHODS

Outbreak Case Definitions:

- **Confirmed case:** TB disease caused by an *M. tuberculosis* strain with the G00444 genotype[1] diagnosed in a South Carolina resident during 2013
- **Probable case:** TB disease without genotyping results (i.e., cases with pending genotype results or no *M. tuberculosis* complex isolate available for genotyping) diagnosed in a South Carolina resident during 2013 who had a linkage to an already included case

Case reviews. The CDC team used a standardized abstraction form (**Appendix A**) to review all G00444 TB cases in South Carolina. The team also reviewed TB cases without genotyping results if TB program staff from DHEC suspected those cases had a link to another G00444 case. Data sources for case reviews included TB clinic records, hospital records if the patient had been hospitalized, radiographic and bacteriologic reports, unstructured interviews of DHEC staff members who had been involved in the investigation, and interviews of patients or a proxy using a standardized interview form **(Appendix B).** Priorities of the case reviews included determination of patient characteristics, estimation of infectious periods, elucidation of chains of transmission, and identification of contacts (i.e., persons exposed to an infectious outbreak TB case) and sites of potential transmission. Although infectious periods cannot be measured precisely, CDC guidelines [1], which are based on expert opinion, recommend that for patients with TB symptoms, pulmonary cavities, or AFB detected by sputum-smear microscopy, the estimated infectious period begin 3 months before the onset of symptoms or the first diagnostic finding consistent with TB (e.g., AFB smear-positive sputum or abnormal chest radiograph), whichever was earlier. For asymptomatic patients without AFB smear-positive sputum or pulmonary cavities, the estimated infectious period began 1 month before the date of the first diagnostic

[1] The index patient was infected with an *M. tuberculosis* strain having the G00444 genotype; spoligotype: 000000000003771, 24-locus MIRU-VNTR: 222325173543 445544423328. Universal genotyping was introduced in the United States in 2004 using spoligotype and 12-locus MIRU-VNTR. Though the G00444 genotype appears to be rare in the United States based on available data, 24-locus MIRU-VNTR data are only routinely available for reported cases starting in 2009 (source: CDC, National TB Genotyping Service).

finding consistent with TB (e.g., an abnormal chest radiograph without evidence of cavitary disease or the collection of a specimen from which *M. tuberculosis* was isolated). The CDC team considered the end of the infectious period to be the time of effective isolation. Infectious periods were not estimated for patients with only extrapulmonary disease.

Review of contact investigations. Results of the contact investigations conducted by DHEC were reviewed by CDC using investigation notes recorded in TB clinic records. The team conducted unstructured interviews with DHEC staff members and reviewed aggregate data provided by DHEC. Because the CDC team was not provided access to electronic records, this review was limited to aggregate data, and more rigorous analyses using line-listed data were not possible.

Review of data management procedures for tracking outbreak investigation data. DHEC used two software applications to manage data related to the outbreak investigation. The CDC team interviewed DHEC staff members to identify the intended uses and objectives of each system, to describe the types of data available in each system, and to determine mechanisms through which the data systems exchange information.

RESULTS

Outbreak cases. The CDC team reviewed records for 14 patients, interviewed 2 of 3 patients (or their proxies) with infectious TB, and interviewed 9 DHEC staff members. Although one patient with infectious TB refused re-interview by CDC investigators, the team reviewed interview notes recorded by DHEC staff members and interviewed DHEC staff members familiar with the patient's case. Letters were assigned to designate patients; the index patient was designated as Patient A.

In total, the outbreak involved 14 cases, including 3 confirmed cases and 11 probable cases (**Table 1**). Reviews of confirmed cases are summarized in **Appendix C**. **Table 2** summarizes the characteristics of patients in the outbreak. Outbreak cases except for Patient A's case were detected through contact investigation activities conducted by DHEC.

Table 1. Summary table of patients with outbreak cases in Greenwood County, South Carolina, as of July 10, 2013

Patient designation	**Age (years) at diagnosis**	**Outbreak case classification**	**Site of TB disease**	**Relationship to Patient A**
A	71	Confirmed	Pulmonary	-----
B	43	Confirmed	Pulmonary	Worked at school
C	79	Confirmed	Pulmonary	In same singing group
D	37	Probable	Extrapulmonary	Household contact
E	7	Probable	Extrapulmonary	Student at school
F	5	Probable	Extrapulmonary	Student at school
G	6	Probable	Extrapulmonary	Student at school
H	6	Probable	Extrapulmonary	Student at school
I	8	Probable	Extrapulmonary	Student at school
J	7	Probable	Extrapulmonary	Student at school
K	6	Probable	Extrapulmonary	Student at school
L	5	Probable	Extrapulmonary	Student at school
M	8	Probable	Extrapulmonary	Student at school
N	8	Probable	Extrapulmonary	Student at school

Table 2. Characteristics of patients in the outbreak in Greenwood County, South Carolina, as of July 20, 2013

Characteristics	**Adult patients (i.e., aged >15 years) N=4**	**Pediatric patients (i.e., aged ≤15 years) N=10**
Demographic characteristics, n		
Born in the United States	4	9
Non-Hispanic black	3	5
Male	2	5
Clinical characteristics, n		
Diabetes	2	0
Immunocompromising condition other than HIV infection	2	0
Disease characteristics, n		
TB symptoms	3	2
Cavitary disease on chest radiograph	0[a]	0
Sputum smear-positive	2[b]	0[c]
Receiving treatment for TB disease under direct observation, n	3	10
Died, n	1[d]	0

[a] One patient had cavitary disease evident on computed tomography of the chest.

[b] A patient who died and a patient with extrapulmonary disease did not have sputum specimens submitted for examination.

[c] One patient had sputum submitted for examination. Culture was pending as of July 10, 2013.

[d] One patient received a diagnosis of TB after death. This patient had culture-confirmed disease (BAL fluid).

Based upon the onset of symptoms in August 2012, the CDC team estimated that Patient A's infectious period began in May 2012 (i.e., 3 months before the onset of symptoms) (see **Appendix C** for additional details). Patient A was employed as a custodian at a school at the time of TB diagnosis in March 2013. Patient A's last day of working at the school was March 8 (i.e., when DHEC staff members instructed Patient A not to return to work pending additional evaluation). Patients B and E–N had been at the school during Patient A's infectious period. Patient B was employed as a teacher at the school. Although Patient A did not clean Patient B's classroom, Patient A cleaned the rooms adjacent to Patient B's classroom. During testing performed at the school in early June as part of contact investigation activities for Patient A's case, Patient B and Patients E–N, who were students at the school, were found to have TB disease. Because Patients E–N had extrapulmonary disease, their cases were non-infectious. Patient B, however, had sputum smear-positive disease at the time of evaluation in June 2013, suggestive of infectious TB.[2]

Patients C and D had no exposure to Patient A at the school, and only had recognized contact with Patient A, not with any other outbreak patients. Patient C and Patient A had been in a singing group together for many years; they were last known to sing together during December 2012. Patient C's family reported that his health had been steadily deteriorating since a cerebrovascular accident about 3 years before TB diagnosis, and that his health had markedly declined beginning in December 2012. Symptoms of weight loss, extreme fatigue, anorexia, and fevers worsened between December and early March 2013, when Patient C was hospitalized in Georgia. On the basis of these symptoms, the CDC team estimated the start of Patient C's infectious period in September 2012 (i.e., 3 months before the onset of symptoms) (see **Appendix C** for additional details). Patient C's family reported that Patient A visited Patient C during the hospitalization the first week of March (i.e., before Patient A initiated TB treatment). Following a brief period of discharge at home, Patient C subsequently returned to the hospital, where he eventually died from complications of acute respiratory distress syndrome.[3]

Patient D was Patient A's household contact and had non-infectious extrapulmonary disease.[4]

Contact investigation results. Because the CDC team had access to aggregate but not line-listed data, analyses looking for associations between certain factors (e.g., age) among persons tested during contact investigation activities and positive tests were not possible. In addition, the CDC team was unable to discern whether contacts with negative tests for infection were tested 8–10 weeks after last exposure.

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[2] Patient B underwent bronchoscopy on June 4, 2013. Kinyoun stain performed on a specimen obtained from a left upper lobe endobronchial biopsy during the bronchoscopy showed rare AFB and necrotizing inflammation. (Note: The specimen culture later yielded *Mycobacterium tuberculosis*.) Sputum examination performed on a specimen collected on June 9 showed numerous AFB; the culture later yielded *Mycobacterium tuberculosis*. No AFB were seen on smear examination of sputum collected on June 10. Few AFB were seen on smear examination of sputum collected on June 11.

[3] After Patient C's death, *Mycobacterium tuberculosis* was isolated from BAL fluid. Even before genotyping results became available, DHEC staff members had already identified Patient C as a contact to Patient A, and considered his case as part of the outbreak.

[4] Both Patients A and D had been exposed to a household member with TB in 2003 (i.e., before the introduction of universal genotyping) but genotyping results were not available for that case. Because no *Mycobacterium tuberculosis* isolate was available for Patient D's case, the source case could not be confirmed for Patient D based on genotyping data.

DHEC staff members had identified 11 locations other than the school that Patient A had visited during his infectious period. **Table 3** summarizes the results for Patient A's contact investigation outside the school.

Table 3. Results of evaluations of contacts to Patient A outside of the school, as of July 3, 2013 (Source: DHEC, Greenwood Master Data Report)

Location of exposure	**Number of contacts (i.e., persons exposed)**	**Number of contacts with a prior positive test for TB infection**	**Number of contacts with testing results during Patient A's contact investigation**	**Number of persons with a positive test for infection[a] (% of contacts with testing results)**
Patient A's household	30	5	7	5 (71%)
Health facility A	3	0	1	0
Community site A	6	1	5	0
Community site B	6	0	4	0
Community site C	6	0	0	--
Community site D	2	0	2	0
Radio station	12	0	10	2 (20%)
Transport to facility in Columbia	2	0	2	0
Church A	70	2	18	0
Church B	38	0	1	1 (100%)

[a] Tests for infection included tuberculin skin test (TST) or an interferon-gamma release assay (IGRA).

During the entrance meeting with the CDC team on July 1, 2013, DHEC officials explained that DHEC had initiated discussions with the "interim principal/superintendent" at the school during the week of May 27. On May 31, DHEC initiated testing of students, faculty, and volunteers at the school. **Table 4** summarizes the results of the evaluations conducted at the school as part of Patient A's contact investigation.

Table 4. Results of evaluations of students, faculty, and volunteers at the school, as of July 3, 2013 (Source: DHEC, Greenwood Master Data Report)

Classification	Number of persons tested	Number of persons with a prior positive test for TB infection	Number of persons with testing results	Number of persons with a positive test for infection[a] (% of persons with testing results)
Students	493	0	463	53 (11%)[b]
Staff/volunteers	114	1	106	19 (18%)
District staff members[c]	16	0	14	3 (21%)

[a] Tests for infection included tuberculin skin test (TST) or an interferon-gamma release assay (IGRA).

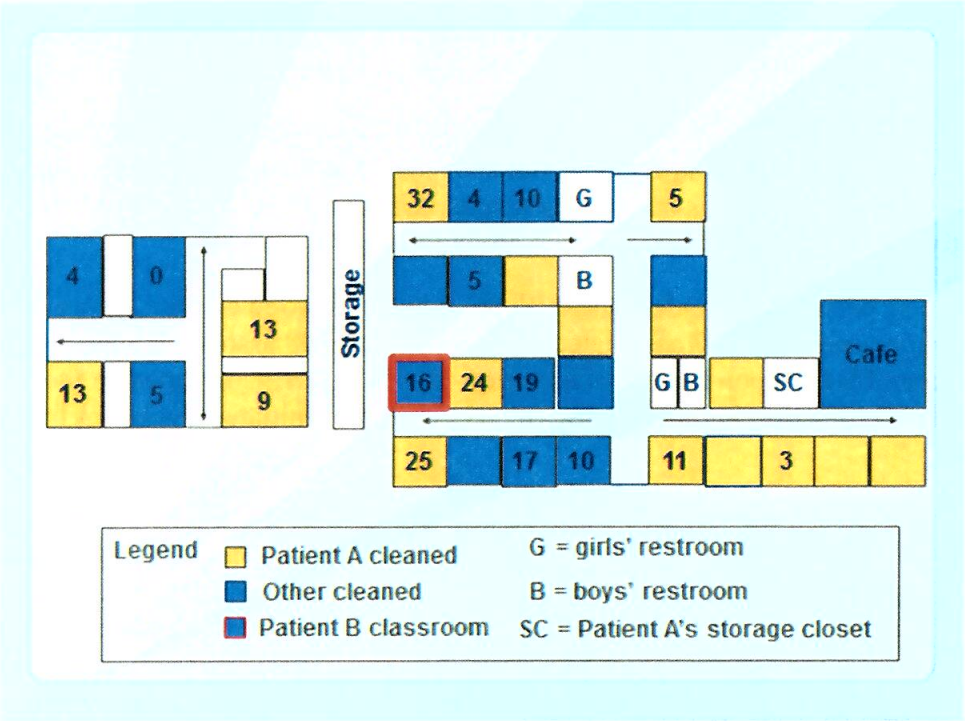
[b] Includes 10 students with extrapulmonary TB who had positive skin tests.

[c] Although not necessarily exposed at the school, district staff members were included in testing because Patient A visited with district staff members during his infectious period.

As part of the contact investigation activities for Patient A, DHEC staff members visited the school to assess the physical environment, understand the layout of the school, obtain Patient A's work schedule, and discuss with school officials Patient A's usual routine at the school. Notes from these discussions and assessments were documented in Patient A's clinic record. The CDC team obtained additional details from DHEC staff members during unstructured interviews.

The school was grouped into sections by grade (**Figure**). The kindergarten area was located in a separate building. Heating and ventilation units generally serviced two or three classrooms. Patient A's storage closet (indicated by "SC" in the **Figure**) shared an open grill vent with a classroom utilized by classes from all grades for language classes or for recess during inclement weather. Patient A casually socialized while at the school with at least one faculty member (a coach) and cafeteria staff members. Using the fire drill evacuation map for the school, DHEC staff members plotted where students with positive tests for infection were located and which rooms were cleaned routinely by Patient A (**Figure**).

Figure. Tuberculin skin test percent positivity among students at the school according to location, as of July 10, 2013



Of 236 students in classrooms cleaned by Patient A, 32 (14%) had positive tests. Of 228 students in rooms not cleaned by Patient A, 20 (9%) had positive tests.

Table 5 summarizes the results of the contact investigation for Patient B.

Table 5. Results of evaluations of contacts to Patient B, as of July 3, 2013 (Source: DHEC, Greenwood Master Data Report)

Location of exposure	**Number of contacts (i.e., persons exposed)**	**Number of contacts with a prior positive test for TB infection**	**Number of contacts with testing results during Patient B's contact investigation**	**Number of persons with a positive test for infection[a] (% of contacts with testing results)**
Patient B's household	15	0	8	0
Church C	150	3	37	0
Super Bowl party	10	1	8	0
Outpatient health facility A	10	0	9	0
Bus during field trip chaperoned by Patient B	15	1	14	0

[a] Tests for infection included tuberculin skin test (TST) or an interferon-gamma release assay (IGRA).

Because some of Patient C's close contacts were undergoing evaluations in states other than South Carolina, collection of data for Patient C's contact investigation by DHEC was ongoing. However, of three close household contacts for Patient C, two had been evaluated ≥10 weeks after last exposure, and both had negative tests for infection. The third contact had a negative initial test for infection, but had not yet undergone testing ≥10 weeks after last exposure.

In response to media attention and public concern, 654 persons in Greenwood County sought testing and evaluation for TB, but had no identifiable exposure to an outbreak case. Excluding 5 persons with prior positive tests, 573 persons had testing results. Of the 573 persons with testing results, 16 (3%) had a positive test; no TB cases were found among these 573 persons.

In total, 1,531 persons had undergone evaluation in Greenwood County, either as part of DHEC-directed investigation activities (617 associated with the school, 108 associated with Patient A, 152 associated with Patient B) or upon their own initiation (n=654). DHEC reported to the CDC team that of 85 persons with TB infection but no TB disease, 65 (77%) had initiated treatment for TB infection as of July 9, 2013.[5]

Data management systems. Two software applications were used by DHEC to manage outbreak investigation data. The Tuberculosis Contact Investigation System (TBCIS) existed before the outbreak investigation, but a second system using Lotus Approach was developed for the purposes of tracking data for this outbreak investigation. The systems, developed for different purposes, were not set up in a manner to share data easily between systems.

TBCIS is a HIPAA-compliant, web-based computer program used to collect information for TB cases and contacts to those cases [2]. The system automates processes for routine tracking of contact investigation progress, data analysis, and performance evaluation. Users generate aggregate reports related to evaluation and treatment of contacts, contact investigation summary reports, and repeat tuberculin skin test schedules. Users at the state, regional, and local levels have access to TBCIS. For each TB case, TBCIS contains variable fields for entry of TB case status, location of disease, smear and culture status, and infectious period. For contacts, demographic data, exposure information, treatment, and disposition are recorded in TBCIS (adapted from [2]). TBCIS is a relational database that can link multiple contacts to a single TB case. Users search for or create a record for a new TB case; each contact record is entered and associated with a specific TB case in the program. Users may enter data for multiple cases and contacts; however, the system does not allow for simultaneous entry of data for multiple contacts associated with the same case. Data may be exported from TBCIS into line lists for further analyses. Approximately 100 contacts for Patient A had already been entered into TBCIS at the time of on-site CDC technical assistance. Sources for TBCIS included the TB Contact Evaluation Records (DHEC Form # 1436) and Chest Clinic Record and X-Ray Reports (DHEC Form # 1400), which were stored at the DHEC office in Greenwood. During the on-site investigation, CDC investigators had access to hard copies of these forms and entered data into TBCIS for 160 records while onsite. When duplicate forms were identified, only the form containing the most up-to-date information was entered into TBCIS. As of July 10, 2013, approximately 1,200–1,400 records still needed entry into TBCIS.

A standalone database in Lotus Approach was developed to manage and report data associated with clinic encounters for each person either identified as a contact to an outbreak case or who presented for evaluation but had no identifiable outbreak exposure. Access to the system was limited to regional

[5] Because data were provided in aggregate, the CDC team was unable to determine whether persons who had initiated treatment for TB infection had been exposed during the outbreak.

staff members; staff members at the state level did not have access to Approach but received weekly aggregate reports. Approach is a relational database designed to manage, analyze, and report information, and allows users to connect to data stored in most formats (e.g., dBASE, DB2, Oracle, Lotus Notes) [3]. Versions compatible with Windows 95/98/ME/NT/2000 can be downloaded from the internet for free. Users enter data via a data entry screen, and data can be exported in multiple formats, including Microsoft Excel. Variables in the Approach database included name, date of birth, dates and results of testing for TB infection (e.g., TST or an IGRA), chest radiography results, reason for evaluation, job description, teacher and grade for students of the school, and last date of directly observed treatment. However, the database did not include variables related to medical history or TB risk factors. As of July 3, 2013, 1,531 records had been entered into Approach. Since the system was designed to collect data on each encounter, and not by individual person, some persons could have been tested multiple times, so it is possible the denominator value overestimates the number of persons tested. Furthermore, limited information on type or amount of exposure limits the user's ability to determine "true" contacts among persons who underwent TB evaluation.

DISCUSSION

Most transmission in the G00444 TB outbreak in Greenwood County, South Carolina, appears to have occurred in the school setting and in Patient A's household. However, Patient C, who had a confirmed outbreak case (i.e., with same genotype), had not been present at the school during the infectious periods of Patients A or B, so transmission was not limited to these settings. Patient A's case could have been the source for all other cases in the outbreak, but Patient C's case could not be excluded as the source for Patient A. Patient C had multiple chronic conditions that could have accounted for symptoms that acutely worsened in December, complicating the estimation of the start of his infectious period.

The distribution of positive tests for infection among students at the school could be explained by several hypotheses. First, Patient A could have been the source for all transmission at the school. Based on CDC guidelines for the estimation of infectious periods [1], Patient B was also at the school during the infectious period, but the lack of infections identified among close household contacts of Patient B is reassuring and suggests limited transmission associated with Patient B. However, TB infection and disease were detected among students in classrooms not cleaned by Patient A, indicating either the influence of shared air resulting in widespread transmission associated with Patient A, or an alternative source case, such as Patient B. Unfortunately, these hypotheses remain untestable without more rigorous analyses, so transmission associated with Patient B, although unlikely, cannot be excluded definitively.

These conclusions are made with acknowledgment of several limitations of the CDC team's investigation. CDC investigators did not have access to line-listed data for contacts, limiting the ability to determine likelihood of transmission associated with patients and to prioritize contacts. In addition, Patient B declined re-interview by CDC investigators; however, Patient B had already been interviewed by DHEC staff members, and the CDC team had access to their investigation notes and interviewed DHEC staff members involved in the investigation.

RECOMMENDATIONS

1) Conduct second-round testing at the school based on Patient B's estimated infectious period. This recommendation is made out of an abundance of caution based on CDC guidelines [1] in the absence of data that more conclusively excludes transmission associated with Patient B.
    a. Consider pre-testing messaging to the community through the media and letters to parents and students.
    b. Staff members aiding in the testing should receive introductory TB training if they lack TB experience to facilitate consistent messaging during testing.
2) Modify systems to track outbreak investigation data. Ideally, the two data tracking systems utilized for this outbreak investigation would be integrated to integrate data from multiple overlapping contact investigations, to identify the most infectious cases to target outbreak response activities, to assess the completeness of contact investigations, and to assist with the prioritization of contacts. This integrated system should be used for this outbreak investigation and future outbreak investigations.
    a. Suggested data elements for this integrated system include medical risk factors, exposure information, and evaluation and treatment status — information that is already included in TBCIS, but not all of which is included in the Approach system.
    b. Data should be available to investigators in an electronic line-listed format and allow for repeat data analyses at frequent intervals (e.g., weekly). DHEC staff members at all levels (local, regional, and state) should be able to access line-listed data for analyses.
    c. Multiple persons should be able to enter data simultaneously and in real time.
    d. Consider consultation with jurisdictions in similar settings to identify practical and feasible options in light of data management resources.
3) Prioritize persons for LTBI treatment based on conditions associated with increased risk of progression to TB disease (e.g., age <5 years, recent exposure, presence of immunocompromising conditions) [4].

REFERENCES

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2. Tuberculosis Contact Investigation System (TBCIS). User Guide. December 2009. South Carolina Department of Health and Environmental Control, TB Control Division, Columbia, South Carolina.

3. Lotus Approach - CNET Download.com http://download.cnet.com/Lotus-Approach/3000-2065_4-18834.html#ixzz2ZKQaiAYA

4. American Thoracic Society, Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med 2000; 161(4):S221–S247.

APPENDICES

Appendix A. Standardized case abstraction form

Appendix B. Standardized interview form for patients with confirmed outbreak cases

Appendix C. Clinical summaries for patients with confirmed outbreak cases

APPENDIX A

CHART ABSTRACTION FORM v1

Demographics

Question	Code	Variable
RVCT number		RVCT
Last Name		Lname
First Name		Fname
Contact Information, if available: Addresses: Phones:		
Alternate Names/Nicknames/Aliases:		Alias
Date of Birth (MM/DD/YY)		DOB
Age (years)		Age
Gender (1=Male, 2=Female, 3=Other, 99=missing)		Sex
Race/Ethnicity (1=Black, 2=White, 3=Hispanic/Latino, 4= American Indian/Alaskan Native, 5=Native Hawaiian/Pacific Islander, 6=Asian, 7=Other, 99=Missing)		Race
Country of Birth (1=United States, 2=Other [foreign-born], 99=missing) If foreign-born, then specify country:		Birth Country
Date of arrival (MM/DD/YY) For patients born outside the United States, enter the date of arrival in the United States.		Arrival

Risk Factors

Question	Code	Variable
HIV infection (0=No, 1=Yes, 99=Unknown)		HIV
Diabetes (0=No, 1=Yes, 99=Unknown)		DM
Chronic Renal Failure (0=No, 1=Yes, 99=Unknown)		ESRD
Immunosuppression other than HIV (e.g. organ transplant, chemotherapy, medications such as steroids, TNF blockers. 0=No, 1=Yes, 99=Unknown)		Immune
Mental illness (0=No, 1=Yes, 99=Unknown) (Axis I diagnosis not related to substance abuse, e.g. mood disorders, schizophrenia, anxiety disorders)		Mental
Injection drug use (Within 1 year of TB diagnosis. 0=No, 1=Yes, 99=Unknown)		IDU
Non-injection drug use (Within 1 year of TB diagnosis. 0=No, 1=Yes, 99=Unknown)		NIDU
Excess alcohol use ($\geq$5 drinks $\geq$ 5 times/month within 1 year of TB diagnosis). 0=No, 1=Yes, 99=Unknown)		EtOH
Smoking commercial tobacco regularly (i.e., most days) for at least 1 year at time of diagnosis (0=No, 1=Yes, 99=Unknown)		Smokes
Homeless/unstable housing within 1 year of diagnosis? 0=No, 1=Yes 99=Unknown.		Home1
Homeless/unstable housing >1 year before diagnosis? 0=No, 1=Yes 99=Unknown.		Home2
Use of homeless shelter within 1 year of diagnosis? 0=No, 1=Yes 99=Unknown		Shelter1
Use of homeless shelter >1 year before diagnosis? 0=No, 1=Yes 99=Unknown		Shelter2
At least 1 night in correctional/detention facility within 1 year of diagnosis? 0=No, 1=Yes 99=Unknown.		Jail1
At least 1 night in correctional/detention facility >1 year before diagnosis? 0=No, 1=Yes 99=Unknown.		Jail2

APPENDIX A

Residence in long term care facility within 1 year of diagnosis? 0=No, 1=Yes 99=Unknown.		LTCF1
Residence in long term care facility>1 year before diagnosis? 0=No, 1=Yes 99=Unknown.		LTCF2
If known exposure to TB case, exposure type: 1=own household, 2=homeless shelter, 3=jail, 4=other household, 5=bar, 6= hotel, 7=Other: _____ List name of site if known:_____ List name of patient if known: _____		TBexp ExpOth ExpSite ExpPat

TB Case Characteristics

Question	Code	Variable
How was case recognized or detected? (1=symptoms, 2=contact investigation, 3=routine screening by healthcare provider, 4=shelter screening, 5=jail screening, 6=other, 99=unknown)		Caserec
Cough (0=not present 1= present, 99=unknown)		Cough
Fever (0=not present 1= present, 99=unknown)		Fever
Night Sweats (0=not present 1= present, 99=unknown)		Sweats
Weight Loss (0=not present 1= present, 99=unknown)		Weight
Date of first symptom onset (Enter the first date the patient began experiencing symptoms in the format MM/DD/YY)		Datesx
Site of disease (1=pulmonary, 2=extrapulmonary, 3=both pulmonary and extrapulmonary)		TBSite
Diagnostic CXR result (1=Negative, 2=Abnormal, possibly TB, 3=Abnormal, not consistent with TB, 4=Unknown [not completed or not available])		CXRrslt
Diagnostic chest radiograph (CXR) result date (Enter the date of the patient's most recent CXR completed as part of current diagnostic workup leading to patient's current diagnosis of TB. MM/DD/YY)		CXRdate
Cavitary disease on CXR? (0=No, 1=Yes, 99=Unknown)		CavCXR
Cavitary disease on CT? (0=No, 1=Yes, 99=Unknown)		CavCT
Sputum AFB smear positive disease? (0=No, 1=Yes, 2=Sputum never submitted)		Sputum
Sputum smear converted to negative 0=No, 1=Yes ≤2 months of treatment, 2=Yes >2 months of treatment, 3=Unknown/NA		Smearconv
Other site AFB smear positive? (0=No, 1=Yes, 99=Unknown) Specify Site:_____		OthSmear OthSite
Culture-confirmed disease? (0=No, 1=sputum only, 2=non-sputum specimen, 3=both sputum and non-sputum specimens, 4=specimens never submitted, 99=Unknown)		Culture
Culture converted to negative 0=No, 1=Yes ≤2 months of treatment, 2=Yes >2 months of treatment, 3=Unknown/NA		Cxconv
Diagnosis date (MM/DD/YY) (the earliest date of the following: positive smear, positive culture, positive PCR test, or abnormal chest x-ray/CT scan)		Dxdate
Drug susceptibility (1=Pan-susceptible, 2=INH resistance, 3=rifampin resistance, 4=multiple resistance, including MDR TB, 88=pending, 99=unknown)		Suscept
Diagnostic TST result (Enter the patient's TST result, if completed as part of the diagnostic workup leading to the patient's current diagnosis of TB. 1=negative, 2=positive, 3=positive with conversion [≥10mm increase in last 2 years], 4=not done due to prior positive TST, 5=not done for other reason, 99=result unknown)		TST
Diagnostic TST reading (mm reading)		TSTmm

APPENDIX A

Diagnostic TST date (MM/DD/YY)		TSTdate
Diagnostic QFT result (Enter the patient's QFT result, if completed as part of the diagnostic workup leading to the patient's current diagnosis of TB. 1=negative, 2=positive, 3=indeterminate, 4=not done, 99=unknown)		QFT
Diagnostic QFT value (result-nil). (Enter the quantitative result of the patient's current QFT result, 99=Unknown. Leave blank if not performed.)		QFTvalue
Diagnostic QFT date (MM/DD/YY)		QFTdate
Treatment (1=On treatment, 2=Completed full treatment, 3=Completed partial treatment, 4=Died during treatment, 5= Died before treatment, 6=died after treatment, 7=awaiting treatment initiation, 8=refused treatment, 99=Unknown)		TBrx
Date of treatment initiation (Enter the date of antituberculosis medication in the format MM/DD/YY.)		Rxdate
Date of treatment completion if done (Enter the date of antituberculosis medication in the format MM/DD/YY.)		Rxcomp
History of loss to follow-up or non-compliance during this TB treatment course (0= No, 1= Yes, 99=Unknown)		TBfu
If died, then enter date of death (MM/DD/YY)		Deathdate

Previous TB episodes and LTBI history

Question	**Code**	**Variable**
Prior TB disease? (0=No, 1=Yes, 99=Unknown)		PrevTB
Year of previous diagnosis (YYYY)		Prevyr
If prior TB, exposure type (1=own household, 2=homeless shelter, 3=jail, 4=other household, 5=bar, 6= hotel, 7=Other: _____)		PrevTBexp PrevTBexpoth
If prior TB, drug susceptibility (1=Pan-susceptible, 2=INH resistance, 3=rifampin resistance, 4=multiple resistance, incl. MDR TB, 88=pending, 99=unknown)		Prevresist
If prior TB, Genotype (PCR type)		PrevPCRtype
TB treatment completed (0= No, 1= Yes, 2=In progress, 99=Unknown)		PrevTBRx
History of loss to follow-up or non-compliance during TB treatment (0= No, 1= Yes, 99=Unknown)		PrevTBfu
Previous positive test for LTBI 0= No, 1= Pos TST, 2=Pos QFT, 99=Unknown)		HxLTBI
Previous TST result date (Enter the date of the patient's most recent TST *before* any test conducted as part of current diagnostic workup leading to patient's current diagnosis of TB. MM/DD/YY)		PrevTSTdate
Previous TST result (MM) (Enter the mm reading of the patient's previous TST result. 99=Unknown)		PrevTSTmm
Previous TST interpretation (1=Negative, 2=Positive, 3=Unknown)		PrevTSTrslt
Previous QFT result date (Enter the date of the patient's most recent QFT *before* any a test conducted as part of current diagnostic workup leading to patient's current diagnosis of TB. MM/DD/YY)		PrevQFTdate
Previous QFT result (Enter value [result-nil] Enter 99 if unknown)		PrevQFTnum
Previous QFT interpretation (1=Negative, 2=Convertor, 3=Unknown)		PrevQFTrslt
Previous chest radiograph (CXR) result date (Enter the date of the patient's most recent CXR *before* any a CXR conducted as part of current diagnostic workup leading to patient's current diagnosis of TB. MM/DD/YY)		DateprevCXR
Previous CXR result (1=Negative, 2=Abnormal, possibly TB, 3=Abnormal, not consistent with TB, 99=Unknown [not completed or not available])		PrevCXRrslt
Initiated treatment for LTBI? 0=offered but refused, 1=never offered by provider, 2=yes, initiated, 99=unknown		LTBIRxStart
Prior LTBI treatment completed 0= No, 1= Yes, 99=Unknown		HxLTBIRx

APPENDIX A

Infectious Period Determination

Question	Code	Variable
Date of infectious period beginning (format MM/DD/YY) -For symptomatic patients, start the infectious period 3 months before "Date of symptom onset" recorded on page 2. -For asymptomatic patients who have sputum smear-positive or cavitary disease, start the infectious period 3 months before the "Diagnosis date" recorded on page 2. -For asymptomatic patients without sputum smear-positive or cavitary disease, start the infectious period 1 month before the "Diagnosis date" recorded on page 2		IPopen
Date of infectious period end (format MM/DD/YY) For patients who are not isolated, the infectious period can be closed when the following three conditions are met: 1) Treatment with an adequate regimen (based on drug susceptibility results) for ≥2 weeks, AND 2) The patient shows clinical improvement, AND 3) Three consecutive sputum smears are negative (which have been obtained at least 8 hours apart) For patients who are isolated (e.g. in a hospital) until these three conditions are met, then use date of isolation as the end of the infectious period.		IPend

HPI for most recent case:

APPENDIX A

Social Network Information: Draw/describe links between this case and other TB cases if known, including location of contact, dates of contact, activities done together, etc:

Case Worker:
Questions for case worker re: information not in charts:

APPENDIX A

Sites visited up to 3 years before infectious period (potential exposures)

Site	Dates at site	Comments (e.g. any contacts at site)

Sites visited during infectious period

Site	Dates at site	Comments (e.g. any contacts at site)

APPENDIX B

PATIENT INTERVIEW FORM v1

Participant Information

Question	Response	Variable Name
Case Last Name		Lname
Case First Name		Fname
Alternate Names/Nicknames/Aliases:		Alias
Age		Age
Date of Birth		DOB
If proxy interviewed, name and relationship to case patient:		

Check the database for the patient's estimated infectious period.

Start of infectious period: _____

End of infectious period: _____

Explain to the patient that you have been asked by the health department to help determine why there have been more cases of tuberculosis, or TB. Explain that you will be asking a series of questions to try to identify where the health department might be able to find other people who have TB, as well as to figure out where the patient might have gotten sick. Acknowledge that the patient has already participated in many interviews with health care providers. Reassure the patient that all answers will be kept confidential, and that the purpose of the interview is to learn information that can help stop the spread of TB and prevent other people from getting sick (emphasize protection of families). Thank the patient for his or her time and for speaking with us.

Note that throughout the interview, the period of interest is 2 years before the start of the infectious period to the end of the infectious period.

Ask patient whether they are from Ninety Six. If not, ask where patient came from and when he/she came to Ninety Six.

Discuss symptom onset date. *Confirm based on chart data.*

"We are interested in learning where you could have been exposed to TB in the 2 years before you got sick with TB. People sick with TB often have a bad cough, or might lose a lot of weight. TB is spread through the air when a person who is sick coughs or speaks and does anything that brings up air from the lungs. How do you think that you got TB?" *Mention household exposure (i.e. people you visited or people who visited you). Attempt to elicit names of sick contacts who might have been source patients. Note when and where the exposure occurred. Emphasize that these people are not in trouble, and we are not trying to blame anyone. We are trying to make sure we can find all sick people and treat them.*

"TB is commonly spread among people staying in the same household. We're worried about people who may have been staying with you or people you may have stayed with when you were coughing a lot or started feeling sick. I know it might be hard to remember, but please try your best. During [infectious period]**, where did you live, and who was staying with you?"** *Emphasize protecting family.*

Time period(s)	Last time visited	Location	People in household

Time period(s)	Last time visited	Location	People in household

"TB can also be spread to people you spend a lot of time around, even if you don't stay in the same household. During [infectious period]**, could you tell us where you worked, where you hung out, and who else was usually there?"** *Emphasize protecting friends and family. Mention work sites, bars, friends' homes, churches, community centers.*

Location	Dates of first attendance	Dates of most recent attendance	Frequency of attendance	Contacts present

If the patient has not already brought up the following locations, ask about them specifically.

Location	Dates of first attendance	Dates of most recent attendance	Frequency of attendance	Activities/Contacts/ Comments

Ask patient how else he/she passes time. *Mention cards, bingo, singing if not mentioned. Record locations and contacts present.*

Activity	Location	Dates of first attendance	Dates of most recent attendance	Contacts present

Ask the patient whether he/she visits friends or family or attends social events in the area, or whether friends/family from the areas visited the patient. *Ask for location and dates of visit. Record exposed contacts.*

Explain to patient that certain activities make the body less able to fight off a TB infection, and make a person more likely to become sick. Ask about the following TB risk factors. *Circle response.*

Smoking commercial tobacco during the year before diagnosis?
0=None
1=Less than Daily
2=Daily
3=Does not recall or refuses

Smoking traditional tobacco during the year before diagnosis?
0=None
1=Less than Daily
2=Daily
3=Does not recall or refuses

If so:

What substance:_____

Participates in "sweats" (traditional sweat lodge purification ceremony): Y N

Location: _____

Excess alcohol use ("drinking") within 1 year before diagnosis (≥ 5 drinks on one occasion, ≥5 times a month)
0=Never
1=Rarely (1-2 times ever)
2=Occasionally (more than 1 or 2 times, but less than most days or nights)
3=Frequently (most days or nights of the week)
4=Does not recall or refuses

Note the locations where patient drank alcohol? Smoked?

With whom would the patient usually drink? Smoke?

Among the group that the patient drank with/smoked with, did anyone possibly have TB?

Non-injection drug ("taking anything for recreation, e.g. marijuana") use within 1 year before diagnosis
0=Never
1=Rarely (1-2 times ever)
2=Occasionally (more than 1 or 2 times, but less than most days or nights)
3=Frequently (most days or nights of the week)
4=Does not recall or refuses

What kinds of drugs were used before diagnosis? *Circle all that apply.*
Refused to specify Marijuana Crack or cocaine Prescription drugs
Other street drugs: _____
Note the locations where non-injection drugs were used:

Drug use with anyone with possible TB?

Injection drug use ("shooting up") within 1 year before diagnosis
0=Never
1=Rarely (1-2 times ever)
2=Occasionally (more than 1 or 2 times, but less than most days or nights)
3=Frequently (most days or nights of the week)
4=Does not recall or refuses

Note the locations where injection drugs were used or obtained:

Drug use with anyone with possible TB?

Does the patient have any other ideas about places where TB might have spread (i.e. where people were coughing a lot) or people we should contact?

Any other contacts not yet discussed:

Name of Contact (and contact info if available)	Where and when had contact	How often had contact? (1=daily, 2=few times/week, 3=weekly or less, 99=unk)	Activities Together	Smoked together? (0=no, 1=yes, 99=unk)	Drank together? (0=no, 1=yes, 99=unk)	Drugs together? (0=no, 1=yes, 99=unk)	Comments

APPENDIX C

Patient A

Patient A was a 71-year-old U.S.-born, non-Hispanic, black man with diabetes, hyperlipidemia, hypertension, and glaucoma who was employed at a school as a janitor at the time of TB diagnosis in March 2013. Medications at the time of diagnosis included metformin, valsartan-hydrochlorothiazide, pravastatin, and ophthalmic drops (for glaucoma).

Patient A reported no history of drug, alcohol, or tobacco use. In the distant past, Patient A had worked at a foundry. He later worked at a local hospital as an orderly. A tuberculin skin test (TST), performed as part of occupational testing at the hospital, was interpreted as positive in May 1999. The chest radiograph from 1999 had been destroyed, so was not available for review around the time of TB diagnosis in 2013. Patient A completed 6 months of isoniazid for LTBI. (Note: Documentation was obtained at the time of TB diagnosis to confirm treatment history, but treatment had been self-administered.) Subsequently in 2003, Patient A's daughter (who lived in the same household) was diagnosed with infectious TB. (Note: The genotype of the *Mycobacterium tuberculosis* isolate for the daughter's case is unknown as the case was identified before universal genotyping implementation.)

Patient A began working at the school in September 2003 on a part-time basis. In May 2005, he began full-time employment as a janitor at the school.

According to records obtained from Patient A's primary care provider (PCP) by the Greenwood County Health Department, Patient A presented to his PCP on September 27, 2012, complaining of "a cold for about 3 weeks" with a "loose cough." (Note: The PCP listed "obesity" as one of Patient A's medical conditions.) The PCP prescribed a 1-week course of azithromycin for "bronchitis." Patient A presented to his PCP again on December 12, 2012, complaining of "cold symptoms" for 16 weeks. He weighed 190 pounds. (Note: Patient A had weighed 205 pounds during a visit to the PCP on December 27, 2011.) The PCP prescribed a 10-day course of levofloxacin for "bronchitis" and "pneumonia." The PCP noted that a chest radiograph showed "consolidation R side with pneumonia." On January 8, 2013, Patient A presented to his PCP complaining of shortness of breath, but reported an improved cough. A chest radiograph showed a "persistent right pleural effusion (may be loculated)" and "no significant interval improvement," so he was referred to a pulmonologist. On February 11, 2013, Patient was seen in clinic for a "lipid order" and referral for a diabetic eye examination; Patient A weighed 188 pounds at that visit, but no other history or physical examination information was found in the records for this visit. On February 20, 2013, computed tomography (CT) examination of the chest showed a right upper lobe cavitation. On March 6, 2013, Patient A underwent bronchoscopy with broncheoalveolar lavage (BAL). A 2-view chest radiograph performed after bronchoscopy showed persistent large emphysematous bleb or cavity in the right lung apex, airspace opacifications throughout the right middle lobe, and mild pulmonary congestion; the left lung remained "essentially clear."

On March 8, 2013, public health officials learned that the acid fast bacilli (AFB) stain performed on the BAL fluid was positive, consistent with TB disease, and instructed Patient A not to return to work pending additional evaluation. Standard four-drug treatment was initiated on March 8. Sputum specimens collected on March 8, March 9, and March 10 had numerous AFB (≥100 AFB per high powered field), suggesting infectiousness. At the time of TB clinic evaluation on March 14, Patient A reported cough productive of brownish phlegm and night sweats. Patient A's contact investigation was initiated on March 14.

Review of TB clinic records revealed that numerous interviews with Patient A reported inconsistent details regarding his social and work activities. In addition, some information conflicted with that provided by proxy sources. Although adherent with treatment under direct observation, Patient A did not comply with health department instructions to remain isolated during the infectious period, so on June 6, an isolation order was issued, and Patient A was transferred to Carolina Care in Columbia, South Carolina, to complete treatment during the infectious period. At the time of CDC technical assistance, Patient A remained in isolation at the facility, and was receiving treatment under direct observation.

Case characteristics

Sputum smear-positive, cavitary disease (by computed tomography)
Confirmed outbreak case (based on sputum culture)

Infectious period estimation:

	DHEC's estimation	CDC team's estimation	Basis for CDC team's estimation
Infectious period start	July 7, 2012	May 18, 2012	Patient's report of onset of symptoms in August or September was consistent with PCP notes
Infectious period end		June 6, 2012	Date of confinement

Patient B

Patient B was a 43-year-old U.S.-born, white, non-Hispanic woman with a history of inflammatory bowel disease who worked as a second-grade teacher at the school at the time of TB diagnosis in June 2013. Patient B had been receiving infliximab since August 2012. A TST in July 2012 had been interpreted as negative before Patient B began infliximab. Patient B reported no history of drug, alcohol, or tobacco abuse.

Patient B was treated for "pneumonia" in April 2013 with "several rounds of antibiotics" and prednisone after presenting with complaints of a cough. A TST was placed on April 17 by her rheumatologist, and was interpreted as negative on April 23. Her cough persisted, and on May 7, 2013, a chest radiograph was interpreted as showing "interval progression of bilateral ill-defined lung opacities. On May 10, she presented to an outpatient clinic complained of fevers, weakness, fatigue, and cough. Computed tomography of the chest showed a mass or consolidation "in the right lower lobe with numerous nodularity throughout both lungs." A right adrenal mass was "indeterminate." On June 4, Patient B underwent bronchoscopy with a left upper lobe endobronchial biopsy that showed "necrotizing inflammation with Kinyoun stain positive for rare AFB; *M. tuberculosis* was later isolated from this specimen. Sputum examination on June 9 showed numerous AFB; *M. tuberculosis* was later isolated from this specimen. Smear microscopy showed no AFB on a sputum specimen collected on June 10 showed no AFB. Few AFB were found on smear microscopy performed on a sputum specimen collected on June 11. Standard four-drug treatment for TB was initiated on June 5.

Patient B's contact investigation was initiated on June 5.

Case characteristics

Sputum smear-positive, cavitary disease
Confirmed outbreak case (based on sputum and endobornchial biopsy specimen culture)

Infectious period estimation:

	DHEC's estimation	CDC team's estimation	Basis for CDC team's estimation
Infectious period start	January 1, 2013	January 1, 2013	Onset of symptoms
Infectious period end		June 5, 2012	Date of home isolation

Patient C

Patient C was a 79-year-old U.S.-born, non-Hispanic, black man with a history of coronary artery disease status post coronary artery bypass surgery, diabetes, end-stage renal disease status-post renal transplant in 1999 (likely etiology diabetic nephropathy, medications included cyclosporine and mycophenolate), history of cerebrovascular accident, hypothyroidism, and multiple toe amputations for chronic wound infections at the time of his death from acute respiratory distress syndrome on April 12, 2013. On March 26, Patient C arrived at the emergency department via EMS after a fall complaining of low back pain. Initial testing and evaluation results suggested a volume overloaded state, but he was unresponsive to attempted diuresis with furosemide, and required transfer to the intensive care unit shortly after presentation for worsening hypoxic respiratory failure. On April 1, he underwent amputation of the right third metatarsal for onsteomyelitis and gangrene. While intubated for worsening respiratory failure, Patient C underwent bronchoscopy with BAL of the right middle lobe. Cytology revealed alveolar macrophages, neutrophils, and lymphocytes; no viral inclusions were noted; GMS stain was negative for *Pneumocystis*. (Note: *M. tuberculosis* complex was later isolated from the BAL fluid, as reported on April 26, after Patient C's death.) Testing for HIV infection was negative. Patient C experienced multiple organ failure. Based on wishes previously expressed by Patient C, Patient C's family declined dialysis, and on April 8, the goals of care were transitioned to palliative care. On April 12, a "terminal intubation" was planned. The final diagnosis listed on the discharge summary was "fatal ARDS [acute respiratory distress syndrome] secondary to TB."

Patient C had been in a singing group with Patient A. DHEC had identified Patient C as a contact to Patient A, and on April 9, DHEC located the patient in the hospital because Patient C had been identified as a contact. Patient C and Patient A were last known to sing together during December 2012. Patient C's family reported that his health had been steadily deteriorating since a cerebrovascular accident about 3 years before TB diagnosis, and that his health had markedly declined beginning in December 2012. Symptoms of weight loss, extreme fatigue, anorexia, and fevers worsened between December and early March 2013, when Patient C was hospitalized in Georgia. On the basis of these symptoms, the CDC team estimated the start of Patient C's infectious period in September 2012 (i.e., 3 months before the onset of symptoms). Patient C's family reported that Patient A visited Patient C during the hospitalization the first week of March (i.e., before Patient A initiated TB treatment). Following a brief period of discharge at home, Patient C subsequently returned to the hospital, where he eventually died from complications of acute respiratory distress syndrome (hospital course described above).

Case characteristics

Unknown sputum smear status, non-cavitary disease
Confirmed outbreak case (based on BAL fluid culture)

Infectious period estimation:

	DHEC's estimation	CDC team's estimation	Basis for CDC team's estimation
Infectious period start		September 1, 2013	Onset of symptoms
Infectious period end		April 12, 2013	Date of death