



Ending Isolation: Making Guidelines Work in the Real World

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I have no relevant financial relationships
to disclose.

EMERGING INFECTIOUS DISEASES®

Tuberculosis and Other Mycobacteria



March 2024



Paulina Siniatkina (1989–), *Don't Speak*, 2016, Tempera on canvas, 100 in × 105 in/254 cm × 266.7 cm. <http://www.paulinasiniatkina.com>

Artwork used in the remainder of this presentation is also by Paulina Siniatkina and is from the patient brochure [Tuberculosis and you](#). She initiated this project in 2017 and was supported by the WHO, IFRC, and the Russian Ministry of Health to help others understand and overcome TB. It is available in 11 languages at tbpeople.org/.

Paulina Siniatkina (1989–), *Don't speak!*

Tempera on canvas (2016), 37.4 in × 41.3 in/100 cm × 105 cm.

<http://www.paulinasiniatkina.com>

Isolation of Patients with TB Disease

- ▶ The main source of TB transmission is not due to un-isolated or improperly isolated cases of TB disease. It is the **unsuspected/undiagnosed TB disease cases** and **unsuspected/unknown drug resistances** (i.e., those on ineffective therapy)
- ▶ Despite this, most transmission control efforts focus on patients with *known* TB disease that are *already on* effective therapy and unlikely to be infectious
- ▶ Isolation is done to benefit the public, not the patient and most costs and negative impact fall on the patient
 - ▶ Studies describe adverse impacts of isolation on employment, education, food/housing security, mental health, stigma, social isolation
 - ▶ Hospitalized patients under isolation receive less nursing attention and experience higher rates of medication errors and adverse events than patients not in isolation.



Current CDC Guidelines for Determining Noninfectious Status

Criteria for TB Patients to Be Considered Noninfectious

TB patients can be considered noninfectious when they meet the following three criteria:

1. They have three consecutive negative sputum smears collected in 8- to 24-hour intervals (including an early morning specimen).
2. Their symptoms have improved clinically (e.g., decreased frequency of cough, decreased fever, weight gain, etc.).

Based on expert opinion, not clear scientific evidence

Current CDC Standard

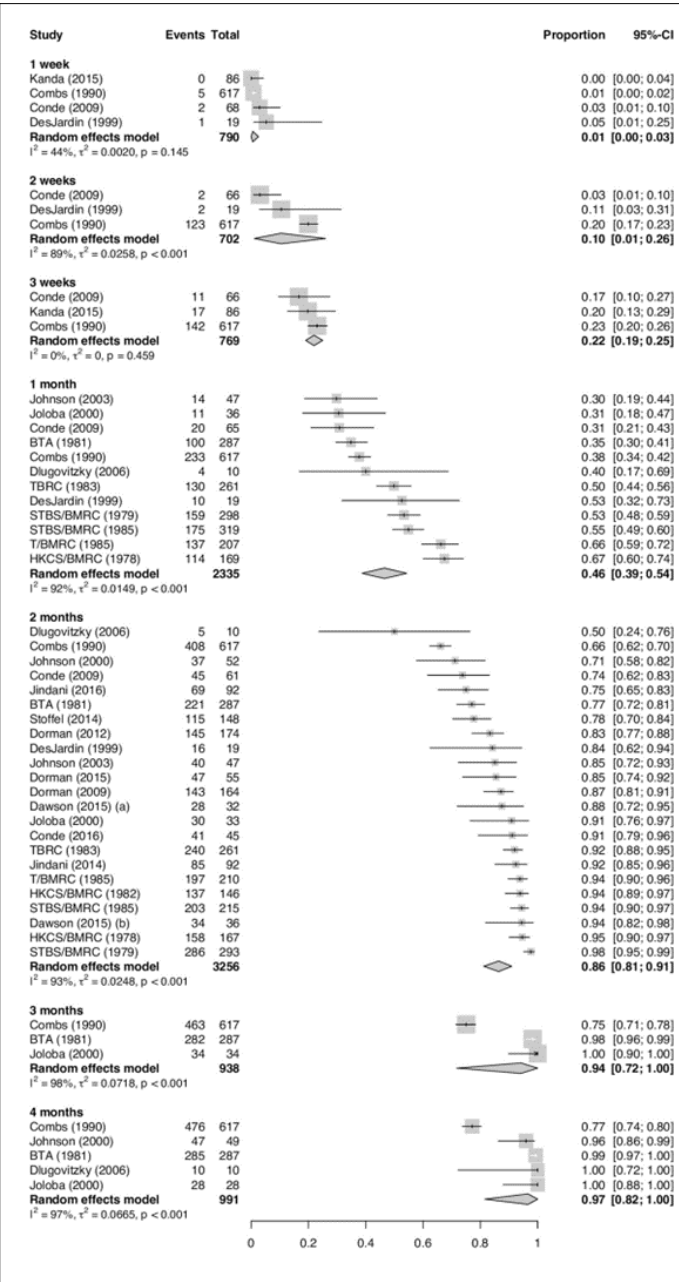
- ▶ Current US guidelines for infectiousness, and by extension need for isolation, are primarily based on “expert opinion”, *not* clear scientific evidence
- ▶ Until 1990, the CDC had “2-week” post-treatment start isolation guidance
 - ▶ This guidance was informed by human-to-guinea pig studies and observational clinical data.
- ▶ The requirement for three AFB negative sputum samples was added by the CDC in 1994 following high-profile health-care-associated MDR-TB outbreaks, fueled by the onset of the HIV epidemic
 - ▶ Sputum smear conversion can take weeks or months, even in drug-susceptible cases, and can prolong duration of isolation significantly



Systematic review and meta-analysis of 44 studies/thousands of patients with baseline smear-positive, DS-TB achieving smear conversion at specified time points during effective treatment

Key points of study:

- Up to 90% are still smear positive after two weeks of treatment
- Smear positivity of treated patients is not the only factor to consider in determining infectiousness
- Study also found:
 - Liquid cultures remained positive for longer than solid cultures
 - Smears assessed by fluorescence microscopy staining are positive for longer than those assessed by Ziehl-Neelsen staining



After 1 week:
1% convert to smear negative (99% positive)

After 2 weeks:
10% convert to smear negative (90% positive)

After 3 weeks:
22% convert to smear negative (78% positive)

After 1 month:
46% convert to smear negative (54% positive)

After 2 months:
86% convert to smear negative (14% positive)

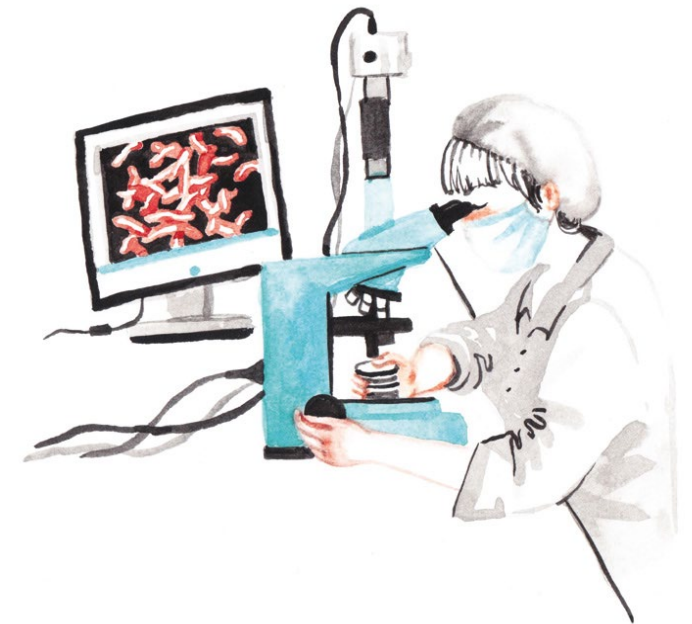
After 3 months:
94% convert to smear negative (6% positive)

After 4 months:
97% convert to smear negative (3% positive)

BMRC, British Medical Research Council; CI, confidence interval; ECA, East and Central African.

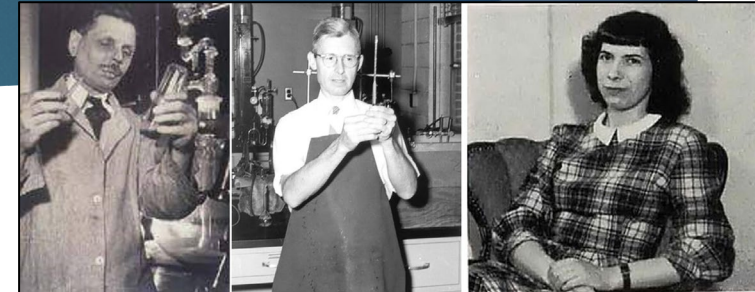
Sputum Smears and Treatment

- ▶ Sputum smear microscopy and culture have been the classic surrogate markers for monitoring treatment and assessing infectiousness in TB disease
- ▶ Prior to the start of treatment, smear status *can* be an indicator of transmission risk/infectiousness
- ▶ However, available evidence has shown that once **effective** treatment is started, sputum smear or culture status no longer predicts transmission
- ▶ The current research does not clearly define exactly how many days of treatment are needed to render *all* patients entirely non-infectious and what (if any) biomarkers best predict this



Sputum Smears and Treatment

- ▶ Guinea pigs are susceptible to TB infections
 - ▶ Much of our understanding of TB transmission was learned using human-to-guinea pig experimental transmission model
- ▶ Human-to-guinea pig studies have demonstrated that people with TB on effective treatment are much less infectious than people with TB not on effective treatment, even prior to sputum smear or culture conversion
 - ▶ Most transmission to guinea pigs appears to stop within a one to two days of treatment initiation
 - ▶ In the original studies, “effective treatment” was isoniazid combined with streptomycin and para-amino-salicylic acid (PAS) (no rifampin nor PZA).
- ▶ One study did show incidences where guinea pigs were infected after treatment was started; guinea pig infections were due to cases of unrecognized XDR-TB or medication noncompliance due to adverse effects



From left to right, William Firth Wells (1886–1963), Richard L. Riley (1911–2001), Cretyl Inez Mills (née Crumb) (1919–1990). These three scientists were key to proving that tuberculosis can be transmitted via aerosols and use of UVI for control. Used human-to-guinea pig studies.



Transmission. Air from a TB ward is vented into guinea-pig cages (above) at an experimental facility in Witbank.

South African human-to-guinea pig studies, 2008

Sputum Smears and Treatment

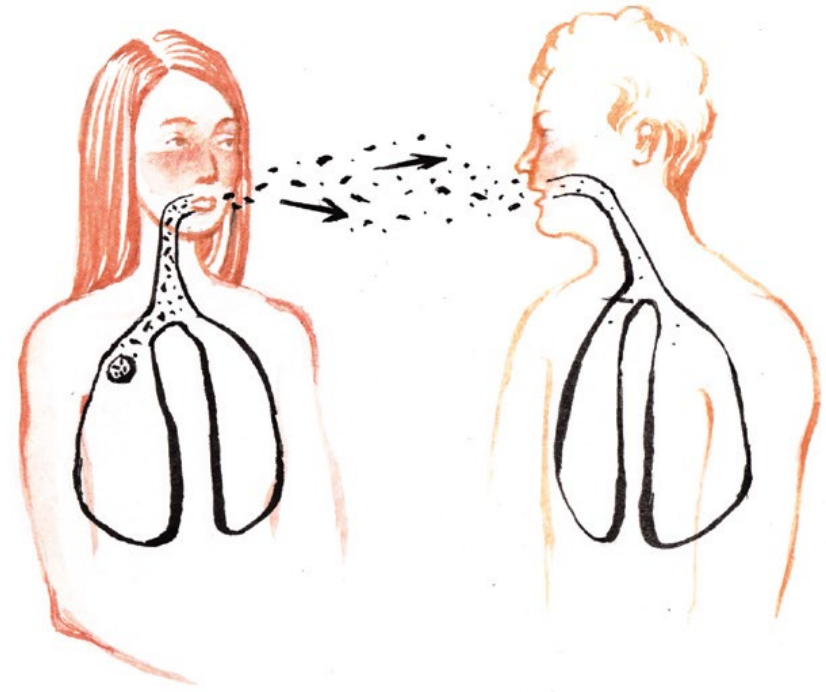
- ▶ No known controlled clinical trials in low-incidence settings address rates of transmission to susceptible contacts in the first weeks following TB treatment initiation.
 - ▶ Retrospective, observational studies suggest that once effective treatment is started, transmission risk quickly stops, and smear/culture status is no longer predictive of infectivity
- ▶ One large RCT in late 1950s in India that compared treatment while isolated in a sanatorium until cultures negative vs. treatment at home without isolation
 - ▶ Rate of TST conversion of contacts over one year was similar (25% at home vs 23% in sanatorium)
 - ▶ Incidence of active disease at 1 year and 5 years was also similar (occurred in 8.1%/10.5% in contacts of patients treated at home and 8.0%/11% in contacts of patients treated in sanatoria)
 - ▶ No relationship between duration of culture positivity following initiation of effective therapy and the rate of transmission to contacts.
 - ▶ “Effective treatment” did not include rifampin or pyrazinamide, so culture conversion took much longer than with current regimens

What Does
This All
Mean?



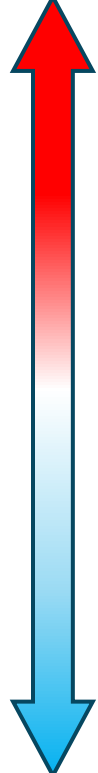
We need a more balanced and evidence-based approach to TB isolation

- ▶ New official US guidelines are coming...
- ▶ In the meantime:
 - ▶ First consider the patients infectiousness, which is estimated by many different factors



Factors Effecting Infectiousness Prior to Start of Treatment (not to scale):

HIGHER
INFECTIOUS
RISK



LOWER
INFECTIOUS
RISK

Sputum Factors

- High numbers of AFB in spontaneously produced sputum
- Low numbers of AFB in spontaneously produced sputum
- Low numbers of AFB in induced sputum smear
- Low numbers of AFB in bronchoscopy washing samples
- AFB smear negative, culture positive

Site Factors

- Larynx
- Pulmonary with cavities
- Widespread pulmonary or endobronchial lesions
- Pulmonary infiltrates on CXR
- Pulmonary infiltrates on chest CT but not CXR
- Pleural disease only
- Extrapulmonary disease with open lesions and no pulmonary disease
- Extrapulmonary with no open lesions and no pulmonary disease

Behavioral Factors

- Frequent vigorous coughing
- Rare cough
- Longer duration contact with others*
- No natural cough (only deliberate cough)
- Use of surgical mask and proper cough hygiene

*no absolute length of time has been determined as a risk for TB transmission

Environmental Factors

- Crowded area/small spaces
- Poor ventilation/recirculation of air
- Minimal UV light exposure
- HEPA filters
- Upper Room UVGI
- Fresh air

Clinical factors

- Delay in or missed diagnosis
- Delay in proper treatment
- Failure to isolate
- Increased contact/host susceptibility
- Index patient is a young child or has compromised immunity
- **INITIATION OF EFFECTIVE TREATMENT**

Then Use A More Evidence Based Approach

These are
my
thoughts...

- ▶ Taking the factors impacting infectiousness into consideration, a patient could be considered non-infectious when the following are met:
 - ▶ The patient is receiving standard multidrug anti-TB therapy that is anticipated to be effective (either based on drug-susceptibility test results OR local epidemiology OR known exposure history) AND
 - ▶ The patient is demonstrating acceptable adherence and tolerance to medication AND
 - ▶ The patient has demonstrated appropriate clinical response to treatment such as stabilization of clinical condition or reduction of cough or fever



Then Use A More Evidence Based Approach

These are
my
thoughts...

- ▶ The exact length of treatment required to consider the patient non-infectious is unknown.
 - ▶ A range of two days to two weeks could be considered based on the pre-treatment factors contributing to infectiousness
- ▶ It may reasonably to take a more conservative approach in situations including the following:
 - ▶ The person with TB may interact with immunocompromised individuals or young children
 - ▶ For example, consider delay in return to work in settings such as daycare, neonatal units, chemotherapy ward, etc.
 - ▶ The person is in a hospital or congregate setting
 - ▶ The TB is MDR or XDR

Where to
isolate?

Hospital

or

Home?



Difference Between Isolation/TB Care in Healthcare Setting and at Home

In Healthcare Setting

- ▶ Could come into contact with many unknown/unidentified people (either in person or by shared air)
- ▶ Vulnerable population could be exposed
- ▶ Healthcare workers could be exposed
- ▶ Isolation and PPE can make delivery of healthcare more difficult
- ▶ Increases cost for care
- ▶ Isolating/stigmatizing for patient
- ▶ May allow for better supervision

At Home

- ▶ Easier to identify those potentially being exposed (depending on living situation)
- ▶ Most contacts have already been exposed so no new or significantly increased risk (depending on living situation)
- ▶ Lower cost of care
- ▶ Improved mental health of patient
- ▶ May not allow for stability, depending on living situation

Consider limiting admission to hospital for:

- ▶ Main criteria: Patients ill enough to require hospital care
 - ▶ Complications of TB such as respiratory failure, pneumothorax, pleural effusion, etc.
 - ▶ Severe forms of TB such as TB meningitis, disseminated meningitis
 - ▶ Severe clinical manifestations of comorbidities
 - ▶ Life-threatening and serious medical events due to drug toxicity or side effects
- ▶ Additional criteria: Patients unable to safely comply with treatment as an outpatient
 - ▶ Patients for whom treatment cannot be ensured in an outpatient, community or home setting (i.e. homelessness, overcrowding, exposure of children aged <5 years and pregnant women in the household)
 - ▶ When there are accessibility problems (i.e. patient lives far from an outpatient facility)
 - ▶ Where there is nonadherence to treatment (this can be considered in some settings as a last resort once all other care options have been used/applied exhaustively, based on the legal framework in force)
- ▶ When in hospital: Patient in which pulmonary TB has been diagnosed or is suspected or if there are open wounds or drains involving extrapulmonary TB should be isolated in airborne infection isolation room (AIIR) (see [CDC. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. MMWR 2005; 54\(No. RR-17\)](#); [CDC. Availability of an Assay for Detecting Mycobacterium tuberculosis, Including Rifampin-Resistant Strains, and Considerations for Its Use — United States, 2013. MMWR 2013;62:\[821-827\].](#))

Isolation of cases at home while infectious

These are
my
thoughts...

- ▶ Goal: do not expose *new* individuals or those at higher risk for infection/disease
 - ▶ Most household members have already been exposed and will be tested/started on preventative treatment if indicated
- ▶ The patient should stay home and not visit places where there will be or could be any previously unexposed people or those at higher risk for infections/disease
- ▶ Limit visits to previously exposed individuals until noninfectious
 - ▶ If other visitors needed: meet outdoors, if possible. If not, patient should wear a mask, take efforts to increase ventilation
- ▶ When possible, patient with infectious TB disease should sleep in room alone. At a minimum should not sleep with any new contacts, young children, those at higher risk for infections/disease
- ▶ Train the patient in optimal cough etiquette (e.g., cover their mouth and nose when coughing or sneezing)



Isolation of cases at home while **infectious**

*These are
my
thoughts...*

- ▶ Try to increase ventilation and air exchange as much as possible
 - ▶ Keep windows and doors open if situation and weather permitting
- ▶ If a sputum sample needs to be collected at home, instruct the patient to do so in a well-ventilated area away from other residents (e.g., bathroom with an exhaust fan and windows open) or outside
- ▶ When in a car with others, open the windows (weather permitting) and turn off recirculating air controls

Isolation of cases at home while **infectious**

These are
my
thoughts...

- ▶ The patient does not need to wear mask at home when alone but should when in shared areas of the home
- ▶ The patient should wear a mask when attending medical appointments, in a car with others, or if they must use public transportation
- ▶ Healthcare workers should wear a fitted respirator when entering the home or other confined area when interacting with an infectious patient



Notes on Respirators and Surgical Masks

- ▶ Respirators are meant to protect wearer from what they are breathing in; surgical masks are designed to protect the area around them or others from the wearer
 - ▶ Masks will block some inhaled airborne particles but not the purpose in TB
- ▶ Respirator used by healthcare workers; must be properly fitted to work properly
- ▶ Surgical masks:
 - ▶ *Sometimes used temporarily on patients with known or suspected infectious TB as a form of cough hygiene*
 - ▶ In human-to-guinea pig transmission studies, 56% effective in preventing transmission when worn at all times other than for eating, brushing teeth, sleeping, etc.
 - ▶ *Masks can be stigmatizing, should be reserved for short term only when infectious*



Odds and Ends

These are
my
thoughts...

- ▶ First few weeks of treatment are the most important; stress need to comply with dosing
 - ▶ If being discharged from hospital, attempt to have 3-5 days of RIPE sent home at discharge
 - ▶ Consider stocking small supply of unexpired RIPE at your LHD for urgent needs
 - ▶ Have plans and preparations for side effects
 - ▶ Incentives or enablers seem to help certain patients be more compliant
- ▶ Unless otherwise indicated, routine re-evaluation of sputum after the initiation of effective anti-TB treatment should not be needed
 - ▶ Repeating cultures at two months in patients who are still coughing is useful to check that the organisms remain drug-susceptible
 - ▶ Repeat sputum/cultures (and CXR) at end of treatment is useful to set a new baseline



The best way to prevent TB is not isolation, it is finding and treating TB disease

But to do that we must all...



Recognize possible signs and symptoms of Tuberculosis. Early diagnosis and treatment reduces spread. Contact your Health Department or physician for more information.



Ultimately, Best Prevention is Finding and Treating TB Disease

- ▶ In lower TB incidence settings, the major proportion of TB disease is from remote transmission
 - ▶ Only about 14% of US cases of TB disease are attributed to recent transmission.
 - ▶ Markedly higher among US-born persons (27%), compared with non-US-born persons (8%)
 - ▶ Spread seen more often in homeless populations and shelters, institutional/congregational settings such as prisons, impoverished rural settings with minority and indigenous populations
- ▶ **Most useful strategy in lower TB incidence settings: appropriate screening and treating for LTBI and education to improve recognition and diagnosis of TB disease is**



Ultimately, Best Prevention is Finding and Treating TB Disease

- ▶ In *higher* TB incidence settings, a large proportion of tuberculosis disease cases are due to recent transmission. Most of the transmission in these areas occurs outside of households and may not necessarily be attributed to known close contacts.
 - ▶ In areas of *higher incidence*, **FAST** (find cases **a**ctively, **s**eparate temporarily, and **t**reat effectively) is a promising intervention model
 - ▶ Any patient with new or prolonged cough or other TB symptoms should be rapidly “ruled out” for TB

Thank You!

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