## **Emotional Impacts of TB amongst Adolescents Patients**

Andrea Cruz, MD, MPH March 20, 2024

> World TB Day March 20, 2024 Webcast

Andrea Cruz, MD, MPH has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

# Emotional Impact of TB Among Adolescent Patients

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## Disclosures & Acknowledgments

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- Author, UpToDate (not on TB)

- I would like to acknowledge:
  - Dr. Silvia Chiang, whose work on mental health for adolescents with TB in Peru has been inspirational
  - My patients, who have taught me so much

## Objectives

- Identify common mental health considerations in adolescent TB
- Recognize validated tools to screen patients if concerns arise
- Identify strategies to make TB care easier for adolescents

## Adolescent TB: Epidemiology

## "ADOLESCENTS" AND "YOUNG ADULTS" (AYA)

## WHO definitions:

Adolescent 10-19 years

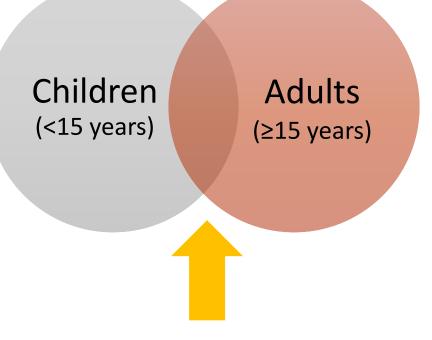
### Young adult 20-24 years

Adolescence begins with the onset of puberty and ends with transitions to adult life

Earlier onset of puberty has led to an earlier beginning of adolescence Later achievement of self-sufficiency has delayed the transition to adult life

Alternative definition of adolescence: 10-24 years

## ADOLESCENT TB HAS BEEN INVISIBLE



## Survey of 28 European NTPs about TB in Adolescence

Policy	High-burden (n=9)	Low-burden (n=19)
Specific TB care policy for adolescents	44%	11%
Expect adolescents to have increased risk of getting TB	44%	16%

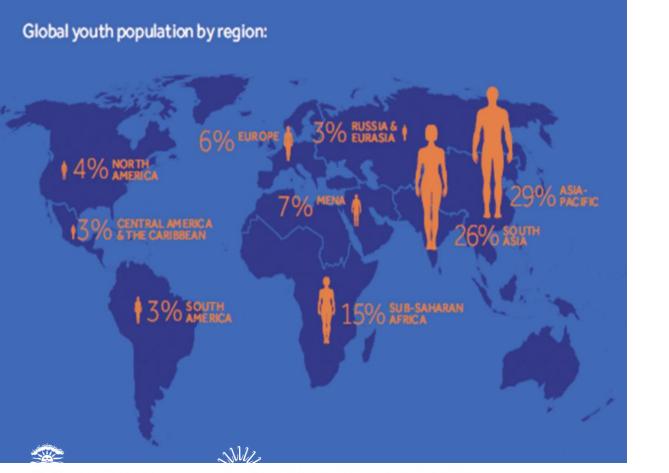
### AYA (10-24 years)

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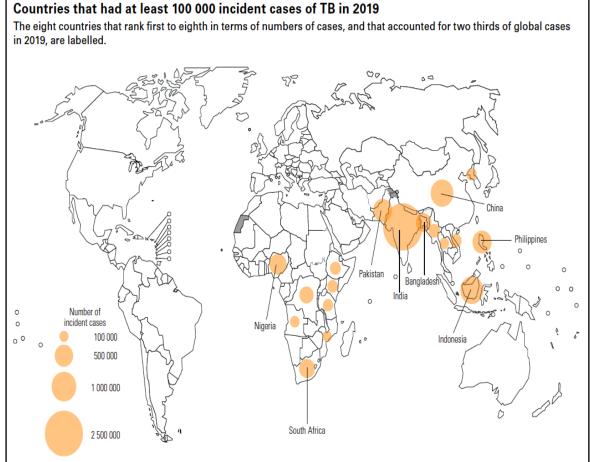
Blok N, et al. Eur Respir J 2016.

## EPIDEMIOLOGICAL SIGNIFICANCE

#### ESTIMATED 1,800,000 INCIDENT TB CASES/YEAR IN 10-24 YEAR-OLDS



Kakar R and Sen A. Financing for Youth Development. doi: 10.14217/23102322.



World Health Organization. Global Tuberculosis Report 2019. Geneva, Switzerland: WHO, 2020.

## Why do we care about mental health in TB?

- Humanistic:
  - Depression is common, but uncommonly addressed
  - Their encounter with us may be one of the few opportunities to establish care for our patients
- Practical:
  - Adherence improves with addressing mental health conditions
  - Clinical outcomes almost uniformly better, across conditions, if patients are not depressed

Are trajectories of depressive symptoms during the first half of drug-sensitive pulmonary tuberculosis treatment associated with loss to follow-up? A secondary analysis of longitudinal data

> **Results** Three trajectories were identified: 'declining', 'growth' and 'high'. These trajectories were observed in 182 (68.7%), 53 (20%) and 30 (11.3%) of the 265 individuals, respectively, during the first half of PTB treatment. Compared with those with a 'declining' trajectory, individuals with a 'growth' trajectory had a higher likelihood of experiencing LTFU during the second half of PTB treatment, after controlling for sociodemographic factors and at least weekly alcohol use (OR 3.9; 95% CI 1.09 to 13.97, p=0.036).

# Stigma & Guilt

## Stigma: What happens when you Google TB?

PHOTOGRAPHS BY NATALLIA GORMALOVA FOR THE NEW Y Weighing a patient with tuberculosis at the Kaneshie Polyclinic in Accra, Ghana. TB has passed Covid as the deadliest infectious disease, despite new medicines and diagnostic too

## Curable but still so deadly

#### ACCRA, GHANA

BY STEPHANIE NOLEN

At Kaneshie Polyclinic, a health center in a hardscrabble neighborhood of Accra, the capital of Ghana, there is a rule. Every patient who walks through the door - a woman in labor, a construction worker with an injury, a child with malaria - is screened for tuberculosis.

This policy, a national one, is meant to address a tragic problem: Two-thirds of the people in this country with tuberculosis don't know they have it.

Tuberculosis, which is preventable and curable, has reclaimed the title of the world's leading infectious disease killer, after being supplanted from its long reign by Covid-19. But worldwide, 40 percent of people who are living with TB are untreated and undiagnosed, according to the World Health Organization. The disease killed 1.6 million people

The numbers are all the more trouin 2021. bling because this is a moment of great hope in the fight against TB: Significant innovations in diagnosing and treating it have started to reach developing countries, and clinical trial results show promise for a new vaccine. Infectious disease experts who have battled TB for decades express a new conviction that, with enough money and a commitment

An end to tuberculosis could be within reach. So why are millions dying from it?



Examining scans at the Kaneshie clinic. Worldwide, 40 percent of people who are living with TB are untreated and undiagnosed, according to the World Health Organization.

to bring those tools to neglected communities, TB could be nearly vanquished. "This is the best news we've seen in Dewan, an epidemiologist with the TB

Cup's most unlikely hero: Afghanistan

program at the Bill & Melinda Gates Foundation. "But there's a gap between having an exciting pipeline and actually tuberculosis in decades," said Puneet reaching people with those tools." A recent visit to the Kaneshie clinic re-

maining barriers. Despite the clinic's policy of screening everyone for TB. which most often attacks the lungs, by asking a few questions about coughs and other symptoms, patients streaming into the single-story building were sent for care without any such queries. A / in, member of the TB team, it turned out, Tru was on holiday, another was on maview ternity leave and a third was out sick. / back In b That left just two, who were busy processing tests and doling out drugs. overh So no one was screened, not that day seems or any other day in the previous week. pected. "It is a good policy, it works well when plier of a we can do it, but personnel is a problem," cause the said Haphsheitu Yahaya, the tuberculostruggles and Ukrai sis coordinator at the clinic. When the screening policy is working, free and in new medications - the first to come to dent's lega market since the 1970s - can be taken tries act, an "There is as just a couple of pills each day, rather than as handfuls of tablets and painful dents realiz injections, the way TB treatments have leverage ov said Repre been delivered in the past. Those diagnosed with drug-resistant Massachuse TB receive medication to take for six Marine who And he said t months - a far shorter time than previously required. For decades, the stand-"where this ard treatment for drug-resistant TB was fight, even i to take drugs daily for a year and a half, outcome." sometimes two years. Inevitably, many History, g patients stopped taking the medicines tional interes cally differen before they were cured and ended up RIDEN, PAGE TUBERCULOSIS, PAGE 2

**RICHARD MII** 

vealed both the progress and the re-



## STIGMA

"My neighbors knew I had TB, so they used to tell everyone that they should stay away from me else I will spread the disease to them. I was asked not to sit outside home; they used to scold me that don't come outside."

— 15-year-old female, Mumbai, India

"Wealthy people were there [at a tennis court in front of the hospital] . . . they disliked our company because we were poor. They humiliated us . . . said unpleasant things . . . " — 19-year-old female, Kyiv City, Ukraine

"[The children in the neighborhood] call me names and they hit me and stuff like that. [They say] 'TB thing, just go away.' They think I'm going to infect them." — 12-year-old adolescent, Cape Town, South Africa

"When I had tuberculosis, I felt that, as if no one wanted to get close to me, because they found out that I had the disease and they thought I was going to infect them ... I felt like, as if I was something from another world no one wants to get close to me." — 11-year-old female, Lima, Peru Adaptation and validation of a TB stigma scale for adolescents in Lima, Peru

- >15 years (*n* = 181)\*
  - 1 Scared to tell my family members that I have TB
  - 2 Scared to go to the health center to get my pills for fear that others will see me
  - 3 Scared to tell other people I have TB because they may think I have AIDS
  - 4 Guilty that I got TB because I didn't eat well
  - 5 Guilty because I have TB and therefore am a burden for my family
  - 6 Careful about whom I tell I have TB
  - 7 Scared that I will lose my friends if I tell them I have TB
  - 8 Scared to tell people outside my family that I have TB
  - 9 Alone because I have TB
  - 10 Hurt because of the way others have reacted when they find out I have TB

## Adaptation and validation of a TB stigma scale for adolescents in Lima, Peru

**Table 3** Correlations between adolescent TB stigma scale scores and other key psychosocial indicators among adolescents undergoing TB treatment in Lima, Peru, stratified by age\*

	γ	P value
Overall ( $n = 231$ )		
Adverse childhood events	0.13	< 0.05
Depression	0.39	< 0.001
Suicidal ideation	0.27 <sup>+</sup>	< 0.001
Self-efficacy	0.01	
Social support	-0.19	< 0.01
Age $\leq$ 15 years ( $n = 65$ )		
Adverse childhood events	0.17	
Depression	0.36	< 0.01
Suicidal ideation	0.25 <sup>+</sup>	<0.05
Self-efficacy	-0.07	
Social support	-0.06	
Age >15 years ( $n = 166$ )		
Adverse childhood events	0.11	
Depression	0.39	< 0.001
Suicidal ideation	0.28 <sup>+</sup>	< 0.001
Self-efficacy	0.05	
Social support	-0.26	< 0.01

## Feelings of Guilt

- Risk to family, friends
- Understanding of causation
- Cannot contribute economically
- Increased costs to families (transport to clinics, CXRs)

Isolation: respiratory isolation → social isolation, school disruption

- Meaningful interpersonal relationships
- Being valued, respected, and accepted as part of the community

Interpersonal relationships Prolonged home (family isolation or members, peers, hospitalization romantic (physical partners) exclusion) Stigma (emotional, social exclusion)

 Image: State of the state o

... He was sad because he doesn't like to miss school, he doesn't like it ... He felt sad, a little depressed because he wanted to go to school, but they forbade him to go to school. (Participant #82, mother of a 14 years old male)

At the beginning [I felt] a little, a little down, like sad ... because all of your progress in your studies stops. You were moving forward, and from one moment to another everything ends. You have to stay away from people because you are infectious to others. (Participant #6, 19 years old male) Impact of prolonged isolation on adolescents with drug-susceptible tuberculosis in Lima, Peru: a qualitative study

For the first few months I did feel a bit, like, forgotten, closed off ... from my friends ... I was separated [from them]. (Participant #52, 18 years old male)

The most difficult thing for me is to leave my family and feel alone ... and live alone for a while until I recover ... during those days I felt alone, without even a single family member. (Participant #32, 18 years old male)

[She was] different, depressed. My daughter is [usually] very happy ... She was sad, down ... [for] three months she was like this here at home. (Participant #8, mother of a 12 years old female)

## IMPACT OF ISOLATION IN LIMA, PERU

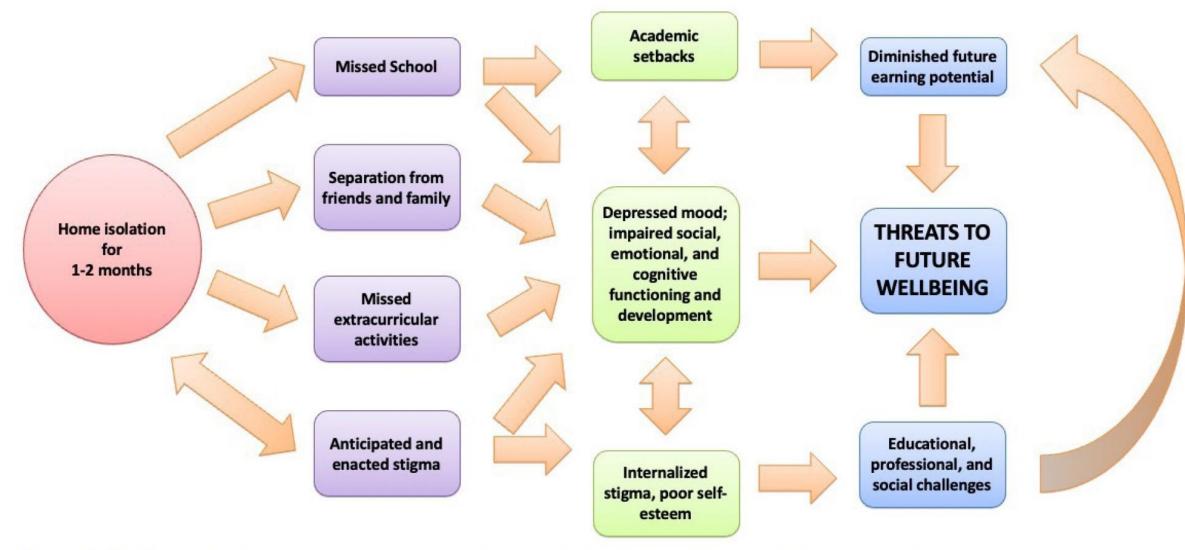


Figure 2 Pathways between prolonged home isolation and threats to adolescents' future well-being.

Oliva Rapoport VE, et al. BMJ Open 2022.

## EDUCATIONAL DISRUPTIONS

"I couldn't read Afrikaans [anymore]." — 12-year-old female, Cape Town, South Africa

"It's not easy when you have a child with MDR, because those tablets were making him very, very dizzy. I was worried in the morning when he must go to school, you can see he is dizzy."

- Caregiver of a 14-year-old male, Mumbai, India

"I felt bad because I was doing fine in everything, grades [and] all that, and to leave all that . . . Yes, I lost the year . . . I had to leave my vocational [school] and then dedicate myself to the health center." |

— 17-year-old male, Lima, Peru

"I spent 4 years with TB. I wanted to study more, become a teacher. This disease has taken important years of my life."

— 15-year-old female, Mumbai, India

Exclusion from classes, schedule conflicts Treatment side effects

Missed classes Learning difficulties

Desertion of school or professional training Change in career trajectory Regression of skills, knowledge Need to repeat semester or year Loss of scholarships and other opportunities

Negative repercussions on present and future earnings

Social Determinants of Adherence to Treatment for Tuberculosis Infection and Disease Among Children Adolescents, and Young Adults: A Narrative Review

Tuberculosis Infection and Disease Among Children, Adolescents, and Young Adults: A Narrative Review	Late childhood (0-4 years)Late childhood 
Structural/Community Factors	TB stigma and discrimination; poverty; violence; inequitable gender norms Community and peer support networks, social protection programs
Health System Factors	Negative provider attitudes and gaps in knowledge of TB infection/disease; treatment stock outs, pill burden, longer regimens, injectable agents for MDR-TB, lack of pediatric formulations; centralized diagnosis and initial management Youth-friendly TB services, provider education on TB, adherence support services
Household/Caregiver Factors	Material-need insecurity (food, finances, housing); distance to health facility/travel costs Caregiver perception that TB is low risk, caregiver schedule conflicts Caregiver knowledge and attitudes about TB and treatment Caregiver/family support
Individual Factors	Schedule conflicts with work         Schedule conflicts with schooling; comorbidities (HIV co- infection, substance use, mental health problems); social isolation; perception that TB is low risk; treatment side effects
	Treatment self-efficacy; higher educational attainment; accurate knowledge about TB and treatment

Health system  The most substantial barrier was in-person DOT, which was adminimum person DOT.	
<ul> <li>This barrier was mitigated by allost treatment after-hours. However, always reliable.</li> <li>Adolescents could receive DOT nearest their home. Therefore, ad accessing treatment when they to those with divorced/separated p parent's house.</li> <li>A few adolescents and caregiver treatment by health providers.</li> <li>Very few adolescents complaine health centre.</li> </ul>	to access as not Unlike adolescents and caregivers, healthcare providers did not report any problems with after-hours DOT. entre ficulty l, and for he other ectful

#### Potential solution:

- vDOT
- Texting reminders

- Socioeconomic related
- One adolescent needed to work to support his family, and the best job opportunity for him was located in a rural part of Peru where TB treatment was difficult to access.
- Two adolescents with divorced/separated parents missed doses when they went to stay with their fathers and lacked bus fare back to the health centre, which was near their mothers' homes.
- TB diagnosis and treatment were free, but sometimes CXR machines at health centres did not work, and families had to pay for CXRs at private facilities. One adolescent did not have enough money for the CXR that is required to transition to the continuation phase of treatment.

- Occasionally, adolescents did not have enough money for transportation to the health centre.
- Like adolescents and caregivers, providers also reported that TB diagnosis and treatment were free of charge, but sometimes CXR machines at health centres did not work, and adolescents had to pay for CXRs at private facilities.

#### Potential solution(s):

- Food baskets
- Assistance with transport
- Flexibility to see adolescents without parent physically present or telemedicine visits

Patient related

- Adolescents often felt ashamed to be seen in the TB treatment area of their neighbourhood health centre.
- Some adolescents felt invulnerable to TB and believed that they would be fine regardless of TB treatment adherence.
- Adolescents occasionally forgot to go to the health centre for DOT, but forgetfulness was not a major treatment barrier.
- Three adolescents missed doses due to fears about TB treatment. One adolescent missed a dose because she skipped breakfast one morning and thought the pills would harm her if she did not eat first. Another adolescent was nearly lost to follow-up because she was pregnant, and family members told her that TB treatment would harm her fetus. The third adolescent missed doses because he feared TB medications were addicting.

- Adolescents who were not supervised and supported by their parents or other family members during treatment tended to have worse adherence.
- Providers also observed that many adolescents felt ashamed to be seen in the TB treatment area of their neighbourhood health centre.
- Some adolescents were described as too 'lazy' or 'unmotivated' to adhere to treatment. A few healthcare providers complained that some adolescents could not manage to show up at the health centre during the designated hours.
- Most adolescents and their families were able to be educated about the importance of treatment, though occasionally, adolescents' family members believed that alternative therapies (such as herbs or moving to the mountains) were sufficient to cure TB.

Potential solution(s):

- vDOT
- Addressing food insecurity
  - <u>https://www.feedingamerica.org/find-your-local-foodbank</u>
- Family-based care

- Therapy related
- Adolescents had difficulty staying motivated throughout the long treatment.
- Adolescents did not like to take so many pills at once.
- Adolescents experienced frequent adverse treatment events. For some adolescents, these adverse treatment events were barriers to adherence.
- Two of the youngest adolescents were unable to swallow the pills, which had to be crushed by their caregivers.
- Providers agreed that adolescents had difficulty staying motivated throughout the long treatment and did not like to take so many pills at once.
- According to healthcare providers, adverse treatment events occurred infrequently in adolescents, especially in comparison with older patients.

#### Condition related, including comorbidities

- Once adolescents began feeling better, they became less motivated to adhere strictly to TB treatment.
- Comorbidities, specifically depression and substance use disorders, were treatment obstacles for several adolescents.
- Multiple factors that occur at the transition from intensive to continuation phase—symptom resolution, treatment fatigue, three times a week (instead of daily) dosing and resumption of normal activities—impeded treatment adherence.
- Substance use disorders were mentioned much more frequently by healthcare providers than by adolescents or caregivers.

#### Potential solution(s):

- Communicating directly with adolescent (vs parent)
- Educational materials targeting adolescents, addressing perceptions of invulnerability
- Fixed-dose pills
- Dissolving tablets and other child-friendly formulations
- Incorporate medicines into daily routine
- 'Treasure chest' or cell phone minutes

## Tying adherence to positive outcomes

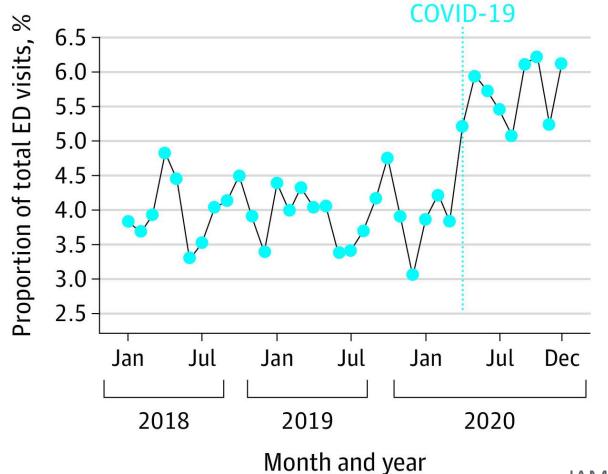
- Pilot in South Africa using urine dipsticks
- If have therapeutic concentrations of TB medication metabolites in urine, a code appears
- Code could be redeemed for cell phone minutes

## Depression & Suicidality

\*Depression seen in 30-65% of adults with TB

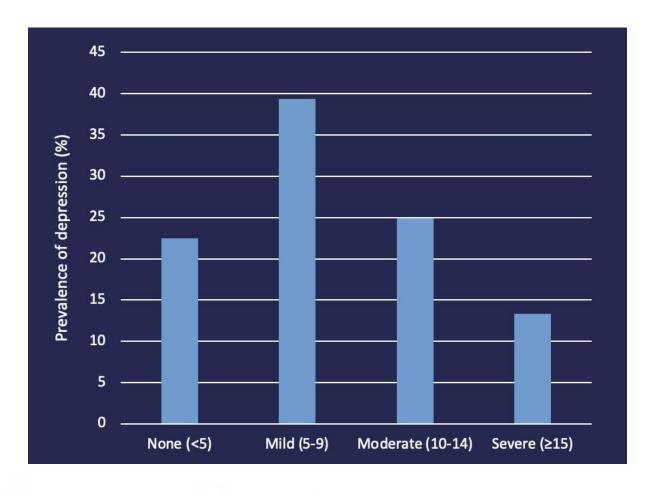
## COVID and Mental Health

**B** Proportion of ED visits for MH conditions



JAMA Netw Open. 2021 1;4(4):e218533

## MENTAL HEALTH



#### Preliminary data from Lima cohort (n = 249) using PHQ-9

#### <u>Variables associated with depression ( $\chi^2$ ):</u>

- Gender (female > male)
- Age group (highest in 13-16 year-olds)
- ACEs
- Hunger

# Suicide Screening Tools: ASQ [Ask Suicide (screening) Questions]

- In the past few weeks, have you wished you were dead?
- In the past few weeks, have you felt that you or your family would be better off if you were dead?
- In the past week, have you had thoughts about killing yourself?
- Have you ever tried to kill yourself?

## Interaction with psychotropic medications: RIF and INH

Drug Class	Drug	Interaction
Mood stabilizers	Valproate	↓ valproate
Antipsychotics	Olanzapine	↓ olanzapine
Antidepressants	SSRIs	↓ SSRI (INH can increase levels)
	SNRIs	(INH can increase levels)
	Tricyclics	↓ TCAs
Anxiety	Benzodiazepines	↓ benzodiazepine (INH can increase levels)

# Don't you forget about me: TB infection

## Latent TB and depressive symptoms in household contacts of persons with active TB

 Table 1
 Association between baseline LTBI and depressive symptoms at 12 months of follow-up among HHCs of patients receiving TB treatment

	Depressive symptom status at 12 months of follow-up*		Univariato	Multivorioto
Baseline LTBI status	PHQ-9 scores 0–4 n (%)	PHQ-9 scores 5–27 n (%)	Univariate         Multivariate $(n = 557)$ $(n = 514)^{\dagger}$ cOR (95% CI)         aOR (95% CI)	
Negative Positive	375 (89.5) 113 (81.9)	44 (10.5) 25 (18.1)	Reference 1.89 (1.09–3.19)	Reference 1.93 (1.08–3.39)

After adjusting for potential confounders, HHCs with LTBI at baseline had almost two times the odds of exhibiting depressive symptoms at follow-up compared with those without LTBI at baseline

Int J Tuberc Lung Dis 2023;27(9):682

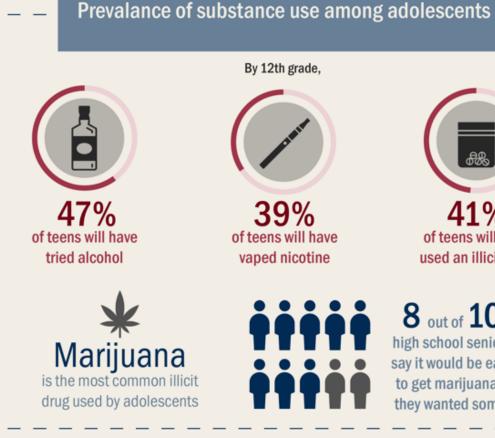
## **TB** Infection

- Emphasize isolation not needed
  - Privacy and vDOT
  - Can avoid giving medication at school
  - Chest 'clearance' letter
  - Social media considerations
- Discuss substance use/abuse
- Rifamycin urine and the adolescent boy

What leads to youth drug use?

- the desire for new experiences
- · wanting to deal with problems
- · lack of positive peer or parental support
- · availability of substances, lack of adult supervision
- · family drug use
- genetic predisposition

drugabuse.gov | monitoringthefuture.org



By 12th grade,

SUBSTANCE USE

39% of teens will have vaped nicotine



8 out of 10 high school seniors say it would be easy to get marijuana if they wanted some.

41%

of teens will have

used an illicit drug

$\mathbf{F} = \mathbf{F}$ Risks and out	comes
Substance use disorder or prolor	and use can lead to:
	igeu use can leau to.
mental health problems	2 out of 3
<ul> <li>school failure</li> </ul>	juveniles with a substance
<ul> <li>impaired memory</li> </ul>	use disorder also have a
<ul> <li>loss of interest in activities</li> </ul>	least one menta health disorde
<ul> <li>problems with family and</li> </ul>	
other relationships	
increased risk of contracting	
an infectious disease	
<ul> <li>overdose and/or death</li> </ul>	
Multisystemic Therapy (MST) is an eviden	ce-based program endors DA) and the Substance A
	DA) and the Substance

among adolescents

treats troubled youth and their families by utilizing a built-in suite of services within the home, school, and community settings. Services include but are not limited to: drug and alcohol intervention, social skills training, mental health services, and peer management.

For more information, visit www.mstservices.com



## Substance use screening questions

NIAAA single screening question for alcohol (data suggest it also is correlated with use of other substances:

- How many times in the past year have you had...
  - 4 or more drinks in a day? (for women)
  - 5 or more drinks in a day? (for men)

#### Figure 3.7 Current Alcohol Use among Persons Aged 12 to 20, by Age: 2002-2013

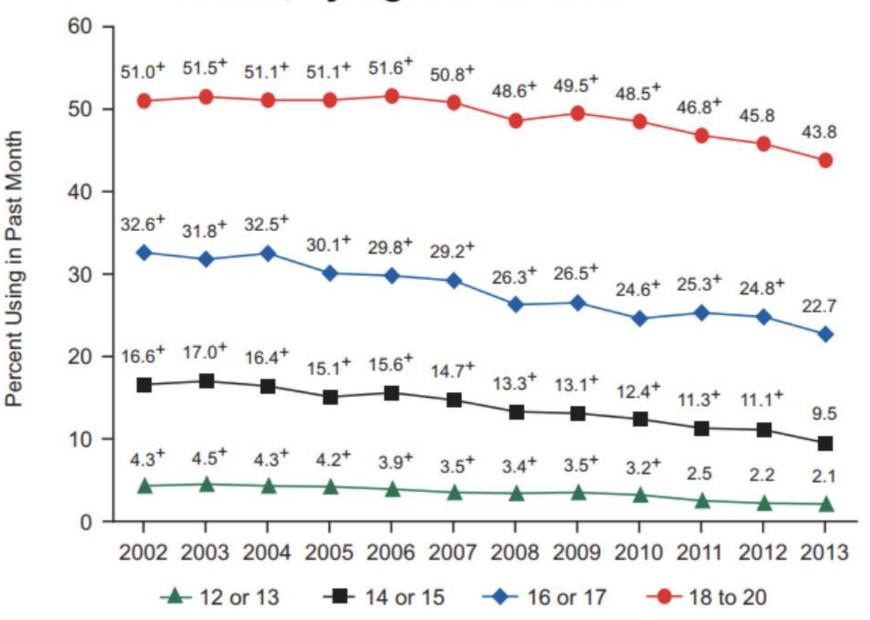
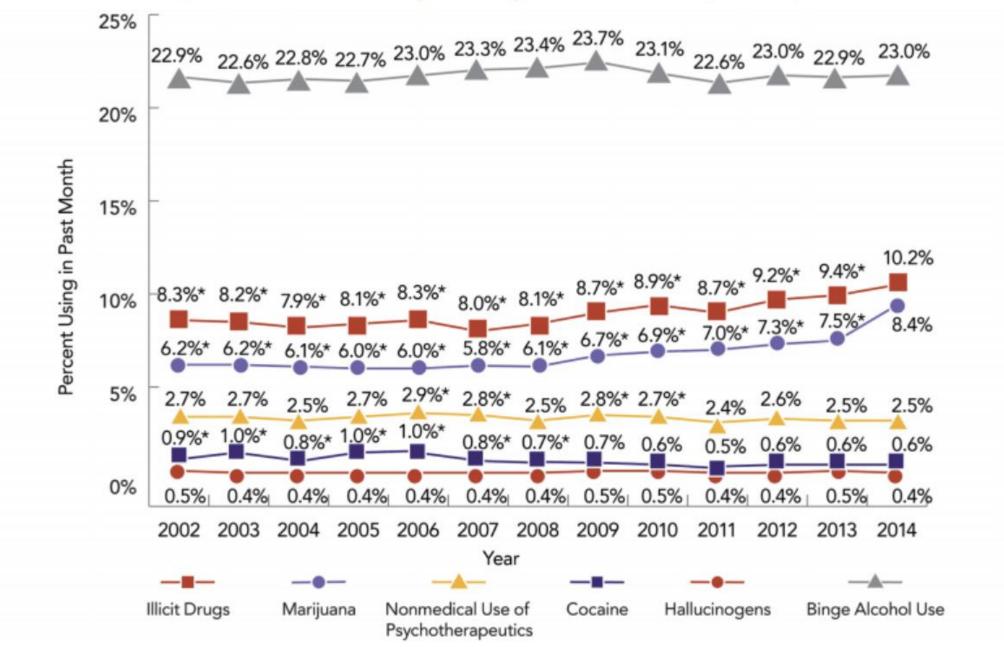


Figure 1.2: Trends in Binge Drinking and Past 30-Day Use of Illicit Drugs among Persons Aged 12 Years or Older, 2014 National Survey on Drug Use and Health (NSDUH)



## Rifamycin urine





## Take-home message: we can help!

- Obtain frequent sputum smears to clear to return to school
- Use validated depression/suicidality screening tools
- If concern, do NOT leave TB medications in the home
  - INH and seizures in overdose