The Intersection Between TB & Mental Health

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Global Tuberculosis Institute

Objectives

• Understand the complex relationship between TB and mental health
• Assess the mental health status of TB patients in order to determine appropriate interventions
• Develop strategies to manage psychiatric complications in TB patients in order to improve overall treatment outcomes
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Outline

I. Introduction
II. Mental Health overview
III. Tuberculosis and Mental Health
   ▪ Impact
   ▪ Types and causes
   ▪ Epidemiology
IV. Challenges and Responses
V. Conclusions

I. Introduction

*People with mental illnesses and substance use disorders are more likely to...*

- Be exposed to TB
- Develop active TB
- Delay seeking care
- Miss doses
- Default from treatment
I. Introduction

*And therefore, have greater risk for...*
- Advanced disease
- Drug resistance
- Treatment failure
- Death
- Community transmission (prolonged infectiousness)

I. Introduction

*Treating mental illnesses can improve...*
- Medication adherence
- Treatment completion/Cure rates

*While reducing...*
- Emergence of further drug-resistance
- Community transmission
- Reduce mortality
II. Introduction to mental health

• What is mental “illness”?  
  – A full range of normative emotions and behaviors are part of the human experience  
    • sadness/fear reactions to adverse events or circumstances, context specific/situational  
  – What qualifies as a “disorder”?  
    • Significant functional impairment (social or occupational)  
    • Duration  
    • Severity

The most common types of mental disorders include:

  – Mood disorders (e.g. depression, bipolar disorder)
  – Anxiety disorders (e.g. generalized anxiety, phobias)
  – Non-affective/psychotic disorders (e.g. schizophrenia)
  – Trauma-related disorders (PTSD)
  – Substance-use disorders (e.g. alcohol, opioids)

*Psychosis may be present in a variety of disorders*
II. Introduction to mental health

Terminology

– Mental health, mental illness
– Substance use, substance abuse, substance dependence, addiction, substance use disorders
– Serious mental illness (SMI), severe and persistent mental illness (SPMI)
– Patients, consumers, persons living with mental illness
– Behavioral health, mental hygiene, mental disorders

Some causes of mental illness

• Genetic predisposition
• Exposure to trauma (domestic violence, child neglect and abuse, interpersonal/community violence, severe family disruption, etc.)
• Psychosocial triggers (immigration status, divorce, urbanicity, job loss)
• Medical comorbidities
I. Introduction to mental health

Comorbid depression and medical illness

<table>
<thead>
<tr>
<th>COMORBIDITY</th>
<th>PREVALENCE</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>6-43%</td>
<td>Roy &amp; Lloyd (2012) <em>J Affect Disord.</em> 142 Suppl:S8-21</td>
</tr>
</tbody>
</table>

Outcomes Mental Medical Source  

Non-adherence (3x higher risk) Depression, anxiety Medical conditions (multiple) DiMatteo  
Premature death Multiple Multiple WHO, 2015  

People with serious mental disorders die an average of 10-25 years earlier than healthy individuals  
- Chronic physical conditions  
- Infectious disease  
- Suicide  
- Lifestyle and health risk behaviors  

WHO (http://www.who.int/mental_health/management/info_sheet.pdf)
II. Introduction to mental health

U.S. Mental Health System

- Typically regulated and reimbursed separately from “medical” system
- Managed care models
- Distinct federal oversight (SAMHSA)
- Influence of Medicaid
- Variety of clinical practitioners – Physicians, Psychologists, Social Workers, Nurse Practitioners
- Recovery perspective / Community-based health, rehab, and social services for SMI

Twelve-month use of mental health services

Persons with DSM-IV disorder

<table>
<thead>
<tr>
<th>Service</th>
<th>Percent of Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>MH specialist (non-psychiatrist)</td>
<td>16.0</td>
</tr>
<tr>
<td>CAM</td>
<td>6.8</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>12.3</td>
</tr>
<tr>
<td>General medical provider</td>
<td>22.8</td>
</tr>
<tr>
<td>Human services professional in non-MH setting</td>
<td>8.1</td>
</tr>
<tr>
<td>Any sector</td>
<td>41.1</td>
</tr>
</tbody>
</table>

### III. TB and Mental Health

#### Comorbid mental and medical illness

<table>
<thead>
<tr>
<th>COMORBIDITY</th>
<th>MENTAL DISORDER</th>
<th>PREVALENCE</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB/HIV co-infection</td>
<td>Depression</td>
<td>1.7x higher risk</td>
<td>Deribew et al (2010) <em>BMC Infect Dis</em>, 10:201</td>
</tr>
</tbody>
</table>

#### Associated with poor medical outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Mental</th>
<th>Medical</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment default</td>
<td>Substance abuse</td>
<td>MDR-TB</td>
<td>Franke et al 2008 <em>Clin Infect Dis</em> 46(12):1844-51</td>
</tr>
<tr>
<td>Death (1.6x and 1.8x higher risk)</td>
<td>Alcoholism/mental disorder</td>
<td>TB</td>
<td>Duarte EC et al (2009) <em>J Epidemiol Community Health.</em> 63(3):233-8</td>
</tr>
<tr>
<td>Death</td>
<td>Mental disorder</td>
<td>MDR-TB</td>
<td>Franke et al 2008 <em>Clin Infect Dis</em> 46(12):1844-51</td>
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</tbody>
</table>
III. TB and Mental Health

TB in the United States

- 65% foreign born, but rates vary regionally, lower substance abuse
- 5.8% homeless
- 3.9% incarcerated
- 6.8% HIV positive
- Severe mental illness (higher rates than the general population)


III. TB and Mental Health

Five types of mental health problems associated with TB

1) Psychological reaction to the diagnosis or treatment
2) Psychiatric side effects from TB medications
3) Physiological consequence of the disease
4) Exacerbation or emergence of mental health issues
5) Comorbidity as a result of shared risk factors (substance abuse, low socioeconomic status)

III. TB and Mental Health

1) Psychological reaction to the diagnosis or treatment
   - Social stigma
     • External: rejection, blame & discrimination
     • Internal: shame, social withdrawal / isolation, depression
   - Social/occupational/functional impairment
   - Infectiousness/household exposure
   - Vulnerable populations
     • Poverty
     • Seriously mentally ill
     • Homeless
     • Incarcerated
     • 65% foreign born from endemic settings (LMIC)
   - Co-infection with HIV may significantly increase the risk of depression by up to 70%


III. TB and Mental Health

2) Psychiatric side effects from anti-TB meds
Psychiatric side-effects have been associated with the following anti-TB medications:
   - Isoniazid (27)
   - Rifampin (1)
   - Ethambutol (4)
   - Ethionamide (5)
   - Streptomycin (3)
   - Para-Aminosalicylate Sodium (3)
   - Cycloserine (14)
   - Ofloxacin (5)
   - Levofoxacin (5)
   - Moxifloxacin (1)

III. TB and Mental Health

2) Psychiatric side effects from anti-TB meds
   Isoniazid
     • Case studies
     • Psychosis
     • Liver toxicity
   Cycloserine
     • Systematic review and meta-analysis found 5.7% psychiatric side effects
     • MDR-TB study in Peru (n=75) found new onset of depression, anxiety, and psychosis during treatment to be 13%, 12%, 12%, respectively.
     • Previous reviews of case studies estimate frequency of 10-50%


III. TB and Mental Health

3) Physiological reaction to the disease
   – inflammation

4) Exacerbation of mental health issues
   – Relapse
   – New onset

5) Comorbidity as a result of shared risk factors
   – substance abuse
   – low socioeconomic status

IV. Challenges & responses

1) Under- and misdiagnosis
   – Some symptoms are overlapping (anhedonia, appetite, etc)
   – Misconceptions about situational distress vs. clinical illness
   – Conflating poverty/illness with depression
2) Not integrated into standard protocols
3) Low priority/limited services available
4) Limited evidence-base for best practices

1. Assessment and screening
   – Situational vs. clinical distress?

2. Intervention
   a. Supportive
      • Problem solving
      • Motivational interviewing/harm reduction
   b. Clinical
      • Psychotherapeutic interventions
        – Group
        – Individual
      • Psychopharmacology & TB drug interactions

3. Health/mental health systems integration
IV. Challenges & responses

Screening for mental disorders

- Self-assessment tools to identify “probable cases”
  - 2 – 20 questions
  - Likert scale (often but not always)
  - Cut-off scores (may vary by culture)
  - NOT diagnostic – formal diagnosis must be determined by a trained clinician

### PHQ-2

- Sensitivity=86%, Specificity=78% (cut off 2 or higher)

### PHQ-9

- Sensitivity=74%, Specificity=91% (cut off 10 or higher)


<table>
<thead>
<tr>
<th>Over the last two weeks, how often have you been bothered by the following symptoms:</th>
<th>Not at all</th>
<th>Several days</th>
<th>&gt; half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
IV. Challenges & responses

Screening for *alcohol abuse or dependence* with the AUDIT-C

1. How often do you have a drink containing alcohol?
   - Never; Monthly or less; 2 to 4 times a month; 2-3x/wk; 4 or more/wk

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   - 1-2; 3-4; 5-6; 7-9; 10+

3. How often do you have six or more drinks on one occasion?
   - Never; <monthly; monthly; weekly; daily or almost daily

AUDIT-C (Men): Sensitivity=86%, Specificity=78% (cut off 4 or higher)
AUDIT-C (Women): Sensitivity=90%, Specificity=45% (cut off 4 or higher)


II. Introduction to mental health

*Treatments for mental illness:*

- Psychopharmacological
- Psychotherapeutic
  - Talk therapy/Insight-oriented
  - Cognitive-Behavioral
  - Interpersonal therapy
- Supportive (psychosocial)
  - Problem-solving
  - Harm reduction (motivational interviewing)
IV. Challenges & responses

Addressing excessive drinking

• Screening, Brief Intervention, Referral to Treatment (SBIRT)
  – Screen (AUDIT-C, AUDIT); Brief education, support, and/or referral based on level of risk
  – USPSTF B recommendation
  – Delivered by primary care providers
  – Leverages influence of the primary care provider
  – Applies elements of motivational interviewing
  – Evidence for decreasing binge drinking frequency; average consumption; hospital admissions


IV. Challenges & responses

Psychopharmacological treatments

Types of psychiatric medications
  – Anti-psychotics
  – Anti-depressants
  – Mood-stabilizers
  – Stimulants
  – Anxiolytics (anti-anxiety)

Most medications have shown maximum effectiveness when used in combination with other types of non-pharmacological therapies
IV. Challenges & responses

Drug interactions (TB/psychotropic)

Isoniazid
- Weak MAO inhibitor, anti-depressant properties
- Interactions with psychotropic medications:
  - **Anti-depressants**: theoretically contraindicated for use with SSRIs & tricyclic anti-depressants due to increased risk for serotonin syndrome but no cases reported
  - **Anti-anxiety medications** (benzodiazepines)
  - **anti-psychotic medications** (haloperidol) inhibits metabolism, therefore may be necessary to lower doses of haloperidol during isoniazid treatment

Rifampicin
- May lower the serum levels of several psychotropic medications through enhanced metabolism, often leading to symptoms of withdrawal:
  - Antidepressants (nortryptiline)
  - Anti-anxiety medications (diazepam, tiazolam, alprazolam, busiprone)
  - Anti-psychotic medications (haldol, quetiapine)
  - Mood-stabilizers/anti-seizure medications (lamotragine, phenytoin, valproic acid)
  - Sleep disorders (zopiclone, zolpidem)
  - Substance addiction (methadone)
- Patients may need to take higher doses of these psychotropic medications for the duration of drug therapy with rifampicin
IV. Challenges & responses

**TB/psychotropic drug interactions**

**Linezolid (TB drug)**
- Weak MAOI and therefore contra-indicated with SSRIs due to risk of serotonin syndrome

**Phenothiazines (anti-psychotic, esp. thioridazine)**
- may increase bacterial activity of anti-TB drugs, allowing them to be used at smaller doses; mixed evidence from animal models

**Chlorpromazine & Trifluoperazine (anti-psychotics)**
- have been shown to have anti-tuberculous agency in vitro and in vivo


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**IV. Challenges & responses**

Primary care – Mental health care integration

“**Collaborative Care Model**”
- Mental health care integrated in 1° care practice
- Cochrane and Community Guide to Preventive Services reviews found benefits for depression and anxiety disorders
  - Symptom reduction; adherence to medication; remission/recovery; quality of life; treatment satisfaction
- Principles include: team-based approach, use of registry, quantitative monitoring of treatment progress
- Key staff
  - Primary care provider
  - Care manager (screening, coordinating treatment, follow-up, facilitating communication with the psychiatric consultant, brief counseling)
  - Psychiatric consultant
IV. Challenges & responses

Research gaps

• Increase awareness between situational/reactive mental distress (requiring psychosocial support) and mental comorbidity (requiring clinical intervention)
• Understand prevalence of psychiatric issues and association with TB outcomes
• Identify evidence-based practices for dissemination
  - Supportive (psychosocial)
  - Psychotherapeutic
  - Pharmacological
• Using existing data, tacking MH onto existing trials
• Prospective studies (to date most evidence is cross-sectional)

V. Conclusions

International Union Against Tuberculosis and Lung Disease

TB & Mental Health Working Group

• Link researchers with clinicians
• Build an evidence base for best practices
• Develop guidelines
TB & MH Resources


Resources: Collaborative Care


http://www.thecommunityguide.org/mentalhealth/collab-care.html

http://aims.uw.edu/collaborative-care
Case studies

Case 1

Patient Background
- 28 y.o. male migrant worker from Mexico
- Emigrated to US 4 years prior
- Family in Mexico
- Speaks minimal English

Inpatient Course
- Nurse/Field worker visit home
- Patient and roommates inebriated
- Upon clinic follow-up pt again appears intoxicated
- Pt denied alcohol problem and reported consuming 2 beers/day
- Pt had difficulty remaining employed
- Unstable housing
- Intermittently adherent due to above
Case 1

Follow-up

- Patient lost to follow-up after 2 months of treatment
- 4 months later presented to a different clinic due to continued symptoms TB clinic was notified, pt found to be smear positive
- Admitted to hospital for 1 month
- Upon discharge, case management team had similar difficulties as before due to unstable employment

Outcome

- Ultimately social issues and liver dysfunction stabilized
- Housing was provided by American Lung Association and Dept of Health
- Pt completed treated almost 18 months after initiation due to multiple interruptions and liver dysfunction
## Case 2

<table>
<thead>
<tr>
<th>Patient Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 23 y.o. woman from Peru, emigrated as a child</td>
</tr>
<tr>
<td>- Recently visited family in Peru</td>
</tr>
<tr>
<td>- 2 children: Age 3 years and 3 months</td>
</tr>
<tr>
<td>- Currently in divorce proceedings</td>
</tr>
</tbody>
</table>

### Follow-up

- Currently in treatment
- Somewhat more accepting
- Has gone back to work; irregular schedule
- Multiple financial and social stressors
- Adherent to DOT, but requires significant effort from field worker
- Has not brought children in for follow-up with pediatrician
- Missed last appointment
Case 3

Patient Background

- 50 y.o. AA woman diagnosed with HIV in 1998, during last pregnancy
- 4 male children, 2 incarcerated
- Remote history of cocaine and alcohol abuse
- History of depression and suicide attempt in 2007
- Domestic abuse – former partner
- Intermittent follow-up with mental health services

Medical Information

- Missed many appointments with both ID and TB clinics
- Referred to mental health services but patient did not go
- Currently employed, making most appointments with TB clinic and states she is doing well

Case management & Follow-up

Thank you for your participation!