

RUTGERS

Global Tuberculosis
Institute

NEW JERSEY MEDICAL SCHOOL

Tuberculosis & Mental Health

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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

II. Introduction to mental health

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

II. Introduction to mental health

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

COMORBIDITY	PREVALENCE	Source
HIV	0-48%	Rabkin (2008) <i>Curr HIV/AIDS Rep</i> 5(4):163-71.
Cancer	4-49%	Walker et al (2013) <i>Ann Oncol</i> 24(4):895-900
COPD	7-42%	van Ede et al (1999) <i>Thorax</i> 54(8):688-92
Diabetes	6-43%	Roy & Lloyd (2012) <i>J Affect Disord.</i> 142 Suppl:S8-21

I. Introduction to mental health

Associated with poor medical outcomes

Outcomes	Mental	Medical	Source
Non-adherence (3x higher risk)	Depression, anxiety	Medical conditions (multiple)	DiMatteo
Lower quality of medical care*	Mental disorder (any)	Medical conditions (multiple)	Mitchell et al (2009). <i>BJPsych</i> . 194(6):491-499
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

II. Introduction to mental health

U.S. Mental Health System

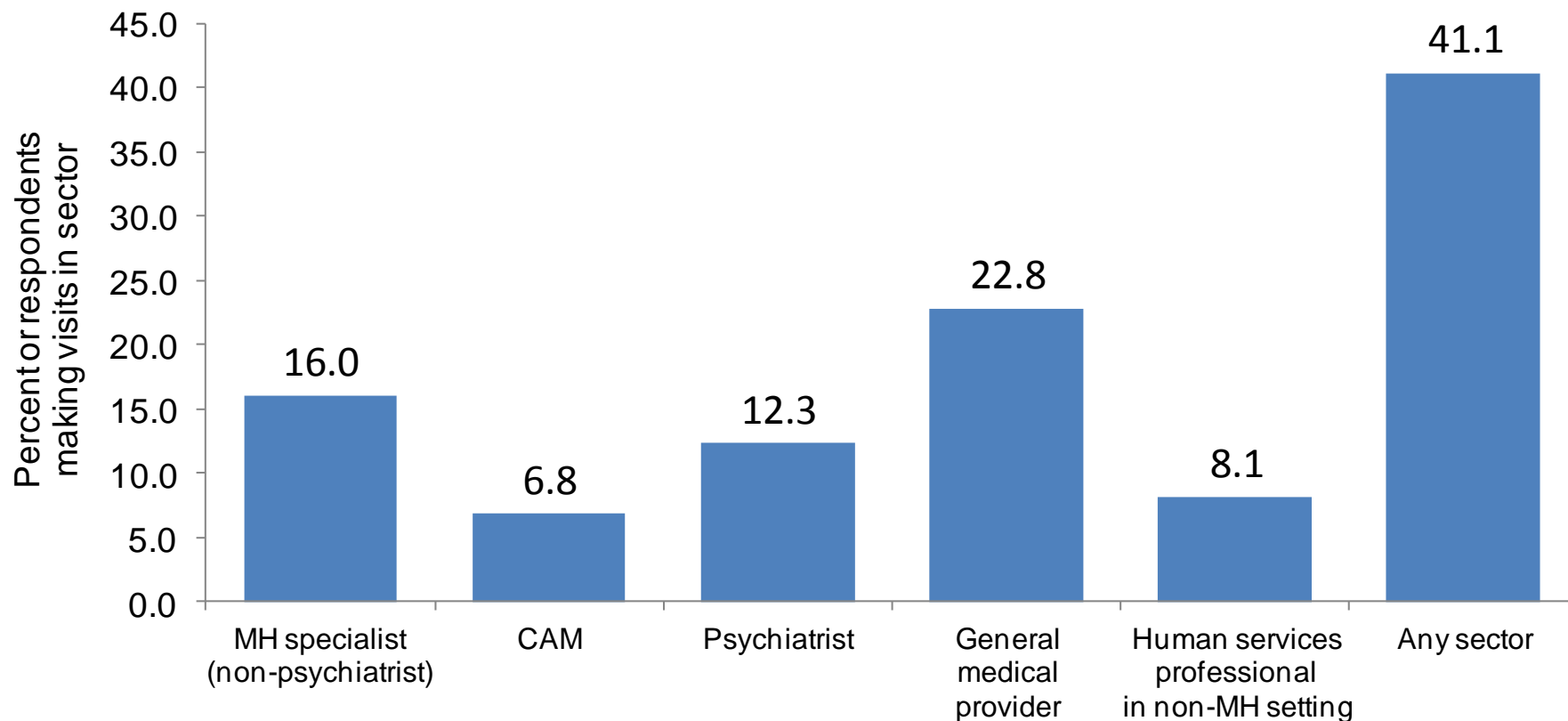
- Typically regulated and reimbursed separately from “medical” system
- Managed care models
- Distinct federal oversight (SAMHSA)
- Influence of Medicaid
- Variety of clinical practitioners – Physicians, Psychologists, Social Workers, Nurse Practitioners
- Recovery perspective / Community-based health,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

II. Introduction to mental health

Twelve-month use of mental health services

(National Comorbidity Survey Replication, 2001-2003)

Persons with DSM-IV disorder



III. TB and Mental Health

Comorbid mental and medical illness

COMORBIDITY	MENTAL DISORDER	PREVALENCE	Source
Tuberculosis	Depression	11-80%	Sweetland et al (2014) <i>World Psychiatry</i> 13(3):325-326
Tuberculosis	Depression/ Anxiety	46-72%	Pachi et al (2013) <i>Tuberc Res Treat</i> 2013:1-37
Tuberculosis	Any Mental Disorder	Up to 70%	Doherty et al (2013) <i>Gen Hosp Psychiatr</i> 35(4):398-406
TB/HIV co-infection	Depression	1.7x higher risk	Deribew et al (2010) <i>BMC Infect Dis</i> , 10:201

III. TB and Mental Health

Associated with poor medical outcomes

Outcomes	Mental	Medical	Source
Treatment delays	Alcoholism	TB	Storla, DG, et al (2008) <i>BMC Public Health</i> 8:15
Drug resistance	Mental disorder	TB	Johnson et al (2003) <i>Indian J Chest Dis Allied Sci.</i> 45:105-9
Treatment default	Substance abuse	MDR-TB	Franke et al 2008 <i>Clin Infect Dis</i> 46(12):1844-51
Death (1.6x and 1.8x higher risk)	Alcoholism/ mental disorder	TB	Duarte EC et al (2009) <i>J Epidemiol Community Health.</i> 63(3):233-8
Death	Mental disorder	MDR-TB	Franke et al 2008 <i>Clin Infect Dis</i> 46(12):1844-51

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)
- Levofloxacin (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

IV. Challenges & responses

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

IV. Challenges & responses

Screening for depression with the PHQ-2 and PHQ-9

<i>Over the last <u>two weeks</u>, how often have you been bothered by the following symptoms:</i>	Not at all	Several days	> half the days	nearly every day
1.Little interest or pleasure in doing things	0	1	2	3
2.Feeling down, depressed, or hopeless	0	1	2	3
3.Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4.Feeling tired or having little energy	0	1	2	3
5.Poor appetite or overeating	0	1	2	3
6.Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7.Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
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	0	1	2	3
9.Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

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

PHQ-9: Sensitivity=74%, Specificity=91% (cut off 10 or higher)

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

IV. Challenges & responses

TB/psychotropic drug interactions

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 activity in vitro and in vivo

IV. Challenges & responses

Primary care – Mental health care integration

“Collaborative Care Model”

- Mental health care integrated in 1^o 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

QUESTIONS?

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TB & MH Resources

Doherty, A., Kelly, J., McDonald, C., O'Dywer, A. M., Keane, J., Cooney, J. (2013) A review of the interplay between tuberculosis and mental health. *Gen Hosp Psychiatr* 35:398–406.

Pachi, A., Bratis, D., Moussas, G., Tselevis, A. (2013) Psychiatric morbidity and other factors affecting treatment adherence in pulmonary tuberculosis patients. *Tuberc Res Treat* 2013:1-37

Sweetland, A., Oquendo, M.A., Wickramaratne, P., Weissman, M., Wainberg, M. (2014) *World Psychiatry* 13(3):325-326

Acha-Albuja, J., Sweetland, A., Guerra, D., Chalco, K., Castillo, H., Palacios, E. (2007) Psychosocial support groups for patients with multidrug-resistant tuberculosis: Five years of experience. *Global Public Health* 2(4):404-17

Resources: Collaborative Care

http://www.cochrane.org/CD006525/DEPRESSN_collaborative-care-for-people-with-depression-and-anxiety

<http://www.thecommunityguide.org/mentalhealth/collaborative-care.html>

<http://aims.uw.edu/collaborative-care>