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The Intersection Between TB & Mental Health

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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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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

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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

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

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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). *BJPsych* . 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

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

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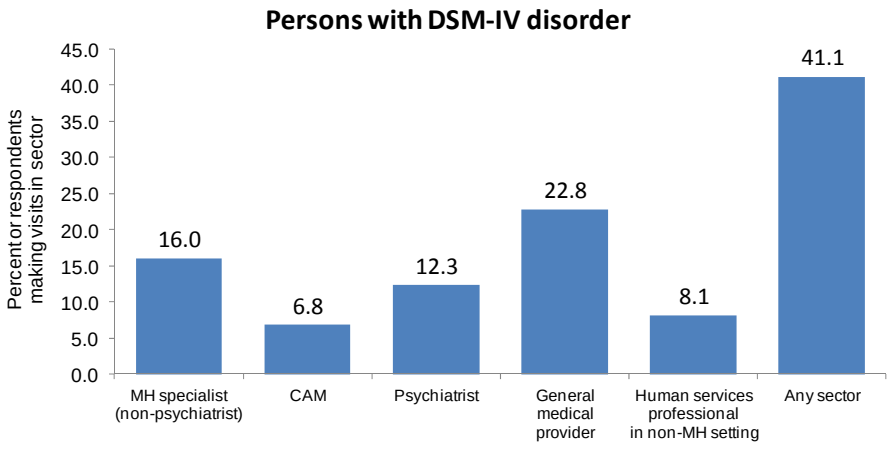
II. Introduction to mental health

Twelve-month use of mental health services
(National Comorbidity Survey Replication, 2001-2003)



Source: Wang P, et al (2005) *Arch Gen Psychiatry.* 62:629-640.

III. TB and Mental Health

Comorbid mental and medical illness

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

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III. TB and Mental Health

Associated with poor medical outcomes

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

Source: CDC (2014). *MMRW Weekly* 63(11);229-233; Gfroerer & Tan (2003) *Am J Public Healt*h. 93(11):1892-95; Ohta et al (1988) *J Psychiatry Neurol* 42(1)41-47. Fullilove et al (1993) *J Law Med Ethics.* 21(3-4):324-31.

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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)

Source: Adapted from Pachi et al (2013). *Tuberc Res Treat* 2013:1-37

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%

Source: Acha, Sweetland et al (2007) *Global Pub Health* 2(4):404-17; Deribew et al (2009) *BMC Infect Dis* 10:201

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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)

Source: Pachi et al (2013) Tuberc Res Treat 1-37; Sweetland (unpublished literature search, 2015)

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%

Source: Hwang et al 2013, *Int J Tuberc Lung Dis 17(10):* 1257-66; Doherty et al (2013) *Gen Hosp Psychiatr* 35:398–406; Vega, Sweetland, et al (2004) *IJTLD 8(6):*749-59; Pachi et al (2013). *Tuberc Res Treat* 2013:1-37

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

Source: Pachi et al (2013) *Tuberc Res Treat* 1-37; Doherty et al (2013) *Gen Hosp Psychiatr* 35:398–406

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

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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

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IV. Challenges & responses

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

Over the last two weeks, how often have you been bothered by the following symptoms:	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)

Source: Arroll et al (2010) *Ann Fam Med* 8(4):348-53

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)

Source: Bush et al (1998) *Arch Internal Med* 3:1789-1795; Bradley et al (2003) *Arch Internal Med* 163:821-829.

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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

SAMHSA: http://www.samhsa.gov/sbirt/resources;
USPSTF: http://www.uspreventiveservicestaskforce.org/Page/Topic/recommendation-summary/alcohol-misuse-screening-and-behavioral-counseling-interventions-in-primary-care?ds=1&s=

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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

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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 & Trifluperazine (anti-psychotics)

- have been shown to have anti-tuberculous agency in vitro and in vivo

Source: Doherty et al (2013) *Gen Hosp Psychiatr* 35:398–406; Amaral et al 2001 J Antimicrob Chemother 47(5):505-11; Kristiansen et al (1997) J Antimicrob Chemother 40(3):319-27; Amaral et al (2010) In Vivo 24(4):409-424; Pai et al (2012) Psychiatry Clin Neurosci 66(6):538; Dutta et al (2013) J Antimicrob Chemother 68(6):1327-30

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IV. Challenges & responses

Primary care – Mental health care integration

"Collaborative Care Model"

- Mental health care integrated in 1º 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

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

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Resources: Collaborative Care

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

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

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

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Case studies

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Case 1

Patient Background

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

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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

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Case 1

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

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Case 2

Patient Background

- 23 y.o. woman from Peru, emigrated as a child
- Recently visited family in Peru
- 2 children: Age 3 years and 3 months
- Currently in divorce proceedings

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Case 2

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

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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

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Thank you for your participation!