2021 Updates in C-L Psychiatry

Advances in Eating Disorder Care:
An Update for Consultation-Liaison Psychiatrists

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ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY
Advancing Integrated Psychiatric Care for the Medically Ill
## APM 2021

**Disclosure: Sanjeev Sockalingam, MD, FAPM**

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<th>Company</th>
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<th>Canadian Institute for Health Research (CIHR)</th>
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D – Relationship is considered directly relevant to the presentation
I – Relationship is NOT considered directly relevant to the presentation
AGENDA

- Overview of Anorexia and Bulimia Nervosa
  - Indications for Medical Inpatient Admission
  - Treatment Approaches
  - Compulsory / Involuntary Treatment for AN

- Eating Disorders in Obesity & Treatment
  - Binge Eating Disorder
  - Night Eating Syndrome
  - Eating Disorders After Bariatric Surgery
DSM 5 Eating Disorder Diagnostic Groups

- Anorexia nervosa
- Bulimia nervosa
- Binge eating disorder
- Avoidant/restrictive food intake disorder
- Other Specific Feeding or Eating Disorder (OSFED)
  - Atypical anorexia nervosa
  - Purging disorder
  - Night eating disorder
# Lifetime Prevalence of Eating Disorders: DSM5

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Lifetime Prevalence Rates (2018 Data)</th>
<th>Rates of Seeking Help for ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa</td>
<td>0.80%</td>
<td>34.5%</td>
</tr>
<tr>
<td>Bulimia nervosa</td>
<td>0.28%</td>
<td>62.6%</td>
</tr>
<tr>
<td>Binge eating disorder</td>
<td>0.85%</td>
<td>49%</td>
</tr>
</tbody>
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Sex Differences in Prevalence:
- Females > Males (especially in AN and BN)

Prognosis:
- AN - 40% make a good 5-year recovery & 40% have partial recovery
- BN – 50% or more have full recovery
- BED – higher rates of recovery than AN and BN

## Assessment of Eating Disorders: SCOFF Questions

<table>
<thead>
<tr>
<th>S</th>
<th>Do you make yourself SICK because you feel uncomfortably full?</th>
</tr>
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<tbody>
<tr>
<td>C</td>
<td>Do you worry that you have lost CONTROL over how much you eat?</td>
</tr>
<tr>
<td>O</td>
<td>Have you recently lost more than ONE stone (14 pounds) in a 3-month period?</td>
</tr>
<tr>
<td>F</td>
<td>Do you believe yourself to be FAT when others say you are thin?</td>
</tr>
<tr>
<td>F</td>
<td>Would you say that FOOD dominates your life?</td>
</tr>
</tbody>
</table>

One point for every “yes”; a score of 2 or more indicates a likely case of AN or BN.

# Medical Complications of Anorexia Nervosa

| Cardiac                  | Arrhythmia (bradycardia, tachycardia), ↑QTc, ↓BP  
|                         | Cardiomyopathy (ipecac), left ventricular atrophy |
| Endocrine               | Hypoglycemia  
|                         | Secondary hyperaldoseteronism, amenorrhea  
|                         | Poorly controlled DM1 |
| Electrolyte Abnormalities | Hypokalemia, hypophosphatemia, hypomagnesemia  
|                         | Hyponatremia, hypochloremia |
| Gastrointestinal        | Acute pancreatitis, Mallory-Weiss tears, esophagitis  
|                         | Parotid/salivary gland hypertrophy, ↑liver enzymes, ↓albumin  
|                         | Acute gastric dilatation, superior mesenteric artery syndrome |
| Other                   | Osteopenia, osteoporosis, non-alcoholic steatohepatitis  
|                         | Brittle hair, lanugo hair, dental erosions |

Triaging Eating Disorder Patients for Treatment

Models of Care (Adult and Youth)

- Outpatient
  - Medically Stable

- Day Treatment

- Inpatient
  - Medically Unstable

**Note:** PM consultation on medical wards for severe AN/BN should focus on most limited intervention to preserve life at that moment
<table>
<thead>
<tr>
<th>Anorexia Nervosa Indicator</th>
<th>Criteria for Medical Admission (Adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>BMI &lt; 12</td>
</tr>
<tr>
<td>Rapid Weight Loss</td>
<td>Severe weight loss over weeks (1 kg/week) or inadequate nutritional intake</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>&lt;80 mmHg</td>
</tr>
<tr>
<td>Postural BP</td>
<td>&gt;20 mmHg drop with standing</td>
</tr>
<tr>
<td>HR</td>
<td>≤ 40 bpm or &gt; 120 bpm or postural tachycardia &gt;20/min</td>
</tr>
<tr>
<td>Temperature</td>
<td>&lt; 97°F (&lt;35.0 °C)</td>
</tr>
<tr>
<td>12-lead ECG</td>
<td>Any arrhythmia (eg QTc prolongation)</td>
</tr>
<tr>
<td>Blood sugar</td>
<td>&lt;2.5 mmol/L (or poorly controlled diabetes)</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Na&lt;125, K&lt;3.0, Mg or Phosphate below normal</td>
</tr>
<tr>
<td>eGFR</td>
<td>&lt; 60 or rapid drop (25% drop in a week)</td>
</tr>
<tr>
<td>Albumin</td>
<td>&lt; 30 g/L</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>Markedly elevated</td>
</tr>
</tbody>
</table>

## MARSIPAN checklist

for Really Sick Patients with Anorexia Nervosa

<table>
<thead>
<tr>
<th>Assessing</th>
<th>Refeeding</th>
<th>Managing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Does the patient have anorexia nervosa?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Yes</td>
<td><strong>Is intensive medical care needed?</strong></td>
<td></td>
</tr>
<tr>
<td>□ Not sure and psychiatric review requested</td>
<td>□ Yes</td>
<td>□ Are medical and psychiatric staff collaborating in care?</td>
</tr>
<tr>
<td><strong>Are there significant risk factors?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ BMI &lt;13 (adults) or &lt;70% median BMI for age (under 18)?</td>
<td>□ No and regular risk monitoring in place</td>
<td>□ Yes</td>
</tr>
<tr>
<td>□ Recent loss of ≥1 kg for two consecutive weeks?</td>
<td><strong>Increased risk of refeeding syndrome?</strong></td>
<td>□ No and psychiatric consultation awaited</td>
</tr>
<tr>
<td>□ Little or no nutrition for &gt;5 days?</td>
<td>□ Low initial electrolytes</td>
<td><strong>Are nurses trained in managing medical and psychiatric problems?</strong></td>
</tr>
<tr>
<td>□ Acute food refusal or &lt;500 kcal/day for &gt;2 days in under 18s?</td>
<td>□ Low BMI (&lt;13 or mBMI &lt;70%)</td>
<td>□ Yes</td>
</tr>
<tr>
<td>□ Pulse &lt;40?</td>
<td>□ Significant comorbidities (e.g. infection, cardiac failure, alcoholism, uncontrolled diabetes)</td>
<td>□ No and appropriately skilled staff requested/training in place</td>
</tr>
<tr>
<td>□ BP low with postural dizziness?</td>
<td>□ Start at 5–10 kcal/kg/day</td>
<td><strong>Are there behaviours that increase risk?</strong></td>
</tr>
<tr>
<td>□ Core temperature &lt;35°C?</td>
<td>□ Monitor electrolytes twice daily and build up calories swiftly: avoid underfeeding</td>
<td>□ Purging behaviours</td>
</tr>
<tr>
<td>□ Na &lt;130 mmol/L?</td>
<td><strong>Lower risk of refeeding syndrome?</strong></td>
<td></td>
</tr>
<tr>
<td>□ K &lt;3.0 mmol/L?</td>
<td>□ Start at 15–20 kcal/kg/day and build up swiftly</td>
<td>□ Falsifying weight</td>
</tr>
<tr>
<td>□ Raised transaminase?</td>
<td>□ Avoid underfeeding syndrome</td>
<td>□ Disposing of feed</td>
</tr>
<tr>
<td>□ Glucose &lt;3 mmol/L?</td>
<td><strong>Give all adults oral thiamine and Pabrinex®</strong></td>
<td></td>
</tr>
<tr>
<td>□ Raised urea or creatinine?</td>
<td><strong>Monitor</strong></td>
<td>□ Exercising</td>
</tr>
<tr>
<td>□ ECG: e.g. bradycardia? QTc &gt;450 ms?</td>
<td>□ Electrolytes (especially P, K)</td>
<td>□ Self-harm, suicidality</td>
</tr>
<tr>
<td><strong>Is the patient consenting to treatment?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Yes</td>
<td>□ ECG</td>
<td>□ Family distress/anxiety</td>
</tr>
<tr>
<td>□ No and assessment for compulsory detention requested</td>
<td>□ Vital signs</td>
<td>□ Safeguarding concerns</td>
</tr>
<tr>
<td><strong>Managing</strong></td>
<td></td>
<td>□ Mobilise psychiatric team to advise on management</td>
</tr>
<tr>
<td><strong>Are medical and psychiatric staff collaborating in care?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Yes</td>
<td></td>
<td><strong>Are there behaviours that increase risk?</strong></td>
</tr>
<tr>
<td>□ No and psychiatric consultation awaited</td>
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<td>□ Purging behaviours</td>
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<td><strong>Are nurses trained in managing medical and psychiatric problems?</strong></td>
<td></td>
<td></td>
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<td>□ Yes</td>
<td></td>
<td>□ Falsifying weight</td>
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<tr>
<td>□ No and appropriately skilled staff requested/training in place</td>
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<td>□ Disposing of feed</td>
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<tr>
<td><strong>Are there behaviours that increase risk?</strong></td>
<td></td>
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<tr>
<td>□ Purging behaviours</td>
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<td>□ Self-harm, suicidality</td>
<td></td>
<td>□ Mobilise psychiatric team to advise on management</td>
</tr>
</tbody>
</table>
## Treatment of Anorexia Nervosa (AN)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Indication</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Therapy</td>
<td>Improved eating disorder symptoms &amp; weight</td>
<td>Level 1</td>
</tr>
<tr>
<td>Individual psychotherapy (CBT &amp; IPT)</td>
<td>Improved eating disorder symptoms &amp; weight</td>
<td>Level 1</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Improved weight gain</td>
<td>Level 1 – Inconsistent</td>
</tr>
<tr>
<td></td>
<td>Reduced ED symptoms</td>
<td>Level 2 – olanzapine</td>
</tr>
<tr>
<td></td>
<td>Improved mood</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reduced anxiety or ruminations</td>
<td></td>
</tr>
<tr>
<td>Antidepressants*</td>
<td>Improved weight gain or relapse prevention</td>
<td>No robust / conflicting evidence</td>
</tr>
</tbody>
</table>

*Ineffective in severely underweight patients

## Treatment of Bulimia Nervosa (BN)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Indication</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td>Reduction in binge eating &amp; reduced eating</td>
<td>Level 1 – CBT (CBT-E)</td>
</tr>
<tr>
<td>psychotherapy</td>
<td>disorder psychopathology</td>
<td>Level 1 – IPT (weaker evidence than CBT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level 2 - DBT</td>
</tr>
<tr>
<td>Family Therapy</td>
<td>Reduction in binge eating &amp; reduced eating</td>
<td>Level 2 – conflicting evidence (adults)</td>
</tr>
<tr>
<td></td>
<td>disorder psychopathology</td>
<td></td>
</tr>
<tr>
<td>Antidepressants*</td>
<td>Reduction in binge eating (especially in</td>
<td>Level 1 – SSRI (also TCA, MAOI)</td>
</tr>
<tr>
<td></td>
<td>combination with psychotherapy)</td>
<td>Level 3 – Other classes</td>
</tr>
<tr>
<td></td>
<td>Relapse Prevention</td>
<td>Level 2 – conflicting evidence</td>
</tr>
<tr>
<td>Mood Stabilizers</td>
<td>Reduced BE &amp; purging</td>
<td>Level 1 – topiramate</td>
</tr>
<tr>
<td></td>
<td>Improved QOL</td>
<td>Level 1 - topiramate</td>
</tr>
</tbody>
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*Avoid bupropion due to seizure risk

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Considerations with Involuntary Commitment and Eating Disorders:

1. Does the patient have capacity to refuse treatment?

2. Will hospitalization help the patient?

3. What is the impact of involuntary treatment on patients (i.e. autonomy)?
Diminished mental capacity identified in approximately 29%-34% of AN patients (mean BMI=15.5)
- Associated with lower mean BMI, more previous hospital admissions and more previous eating disorder treatments
- Occurs in 13%-44% of AN admissions

Poor mental capacity associated with higher admission rates, poor remission rates and deficiencies in capacity persisted despite weight restoration

Evidence suggests that AN leads to abnormalities in emotional regulation related to serotonin and dopamine dysfunction in mesolimbic system
- Complicates capacity in AN = cognition and emotion disturbances potentially affecting decision-making

Elzakkers IF et al. BrPsych Open 2016; Elzakkers IF et al. BJPsych Open 2017
Kaye W. Physiology and Behavior 2008; Clausen L. Front Psychiatry 2020
Effectiveness of Involuntary Commitment in Anorexia Nervosa

- Detained patients have more severe AN symptoms, higher comorbidity, and longer duration of inpatient stay.

- Beneficial in the short-term with respect to remission but long-term outcomes remain unclear.

- No conclusive data on long-term outcomes or reduction in mortality with involuntary commitment.
  - 5 year follow-up of 162 patients showed higher mortality in compulsory (12.5%) vs. voluntary (2.6%) treatment.

- Qualitative study of 29 patients with AN who underwent compulsory treatment identified that patients felt compulsory treatment was necessary when AN was life threatening.
  - Coercion also felt in voluntary treatment.
  - Compulsory treatment has not been associated with poorer therapeutic engagement.

Obesity and Eating Disorders
Severe Obesity & Eating Disorders:
Bariatric Surgery Candidate Studies

Psychological Interventions for Binge Eating Disorder (BED)

- **First-Line Treatments**: CBT (greatest evidence) and IPT
  - Effective for reducing disordered eating behaviours and cognition and improving mood
  - Limited effect alone on weight loss
  - Self-Help: Guided CBT - **Level 1 evidence** and reasonable alternative if CBT or IPT not available

- **Second Line Treatments**: DBT (weaker evidence – Level 2)

- **Weight Loss for Patients with BED**: Behavioral Weight Loss Therapy (1st line)
  - CBT has limited effect alone for weight loss

Pharmacotherapy for Binge Eating Disorder

**First Line Treatments:**
- Lisdexamfetamine (FDA approved)
- Antidepressants (off-label) - no clear difference between antidepressant types, may be preferred if comorbid depression
- Topiramate (off-label) – cognitive side effects a limitation but may help weight loss

**Other Treatment Options: Anti-Obesity Medications**
- Liraglutide – single RCT showing reduction in binge eating when combined with intense behavioral therapy
- Naltrexone/bupropion – single pilot RCT showing reduction in binge eating with combined behavioral therapy

Proposed Diagnostic Criteria for Night Eating Syndrome

A. Daily eating pattern (1 or both):
   1) At least 25% of food intake is consumed after evening meal
   2) At least 2 episodes of nocturnal eating per week

B. Awareness and recall

C. At least 3 of the following additional symptoms:
   1) Morning Anorexia (4 or more mornings per week)
   2) Strong urge to eat at night
   3) Insomnia (4 or more nights per week)
   4) Belief that there is a need to eat in order to sleep
   5) Depressed mood or mood worsens in the evening

D. Significant distress and/or impairment in functioning

E. Occurred for at least 3 months

F. Disorder is not secondary to another disorder

Stunkard AJ et al. Compr Psychiatry 2009
Prevalence of NES

- **General Population:** 1.5%-5.7%
  (Fischer et al, 2012; Nolan & Geliebter, 2012; Rand et al., 1997)

- **Overweight / obese weight-loss seeking populations:** 9%-14%
  (Gluck, Geliebter, & Satov, 2001; Allison et al, 2007)

- **Bariatric surgery candidates:** 9%-42% (higher rates in patients with comorbid BED)
  (Allison et al, 2007; Mitchell JE et al. 2015)

- **Co-Morbidity with binge eating disorder:** 7%-25%
  (Berner & Allison, 2013)
Differential Diagnosis for NES

Night Eating
(After Evening meal → Waking in the morning)

Evening Hyperphagia
→ Sleep Onset →

Night Eating
Binge-Eating Disorder
Bulimia Nervosa

Nocturnal Ingestions
→ Night Eating
Parasomnia (SRED)

Distress and impairment is key to diagnosis
Psychopharmacology & Other Treatments for Night Eating Syndrome

• Overall, very weak evidence for pharmacotherapy
• SSRIs (clinical trials)
  • Sertraline – positive open label and RCT
  • Escitalopram – mixed results, one negative RCT
• Topiramate (case reports)
• Melatonin (case reports)
• Light therapy (pilot study)

• CBT is the most promising treatment for NES

*Studies limited by heterogeneity in definition of NES and short duration

O’Reardon 2004; O’Reardon 2006; Vanderwal 2012; Kucukgoncu 2013
Bariatric Surgery And Eating Psychopathology

Roux-en-Y GB

Sleeve Gastrectomy
Eating Disorder vs. Bariatric Surgery

- Restricting food portions
- Avoiding high fat/high sugar foods
- Chewing food extensively
- Vigilance about calories
- Frequent weighing/measuring
- Rapid weight loss
- Vomiting after eating
- Food intolerances
Prevalence of Eating Disorders After Bariatric Surgery

Anorexia nervosa
• Anecdotal reports; unclear prevalence

Bulimia nervosa
• ~3% meet criteria in bariatric surgery candidates; unclear post-surgery

Binge Eating Disorder
• Rates range from 0%-10% post-surgery (influenced by inability for objective binges post-surgery)

Grazing Eating Behaviors
• Up to 46.6% in patients post-operatively

Note: Eating psychopathology after bariatric surgery is a predictor of weight regain after bariatric surgery

Conceicao EM et al. Eur Eat Disorders Rev 2015
Treating Eating Disorders After Bariatric Surgery: An Update

- Pre-surgery CBT interventions = inconclusive results
  - Responders ((downward arrow) binge eating) to CBT did better post-surgery

- Post-surgery interventions, including (tele-) CBT, have shown moderate to high effect sizes for improving emotional eating and binge eating

- Emerging literature for mindfulness-based and acceptance-based therapies:
  - Mindfulness-based therapies (e.g. Mindfulness-Based Eating Awareness Therapy (MB-EAT))
  - Acceptance and Commitment-based Therapies (ACT)

Additional Resources

Resource Document on Bariatric Surgery and Psychiatric Care

Prepared by the Council on Psychosomatic Medicine: Sarjvev Sockalingam, MD, Weronica Micula-Gondek, MD, Wynn Lundblad, MD, Alexis Fentey, MD, Raed Haws, MD

The purpose of this resource document is to highlight the role of psychiatrists in the care of patients undergoing bariatric surgery. The document identifies key psychiatric components to pre-bariatric surgery assessment and aftercare, which underscore the need for integrated psychiatric services throughout patients’ bariatric surgery care.


INTRODUCTION

Obesity is the fifth leading cause of global deaths and is associated with a myriad of serious health conditions, including coronary artery disease, type 2 diabetes and cancer (1). Moreover, global obesity rates have nearly doubled over the last 30 years giving rise to the “obesity epidemic” (2). Concerns about morbidity and mortality related to obesity are a significant concern in mental health populations, where obesity prevalence rates are as high as 60% in patients with severe mental illness (3).

Bariatric surgery is now recognized as an effective treatment for severe obesity for patients with a body mass index (BMI) > 40 or > 35 with one obesity-related co-morbidity (4). Types of bariatric surgery include restrictive procedures (e.g., laparoscopic gastric banding or sleeve gastrectomy), or combined restrictive and malabsorptive procedures (e.g., Roux-en-Y gastric bypass) (a more detailed description of bariatric surgery procedures can be reviewed in the bariatric surgery guidelines) (5). The benefits of bariatric surgery include sustained weight loss, resolution of obesity-related co-morbidities and improved quality of life (6-10). Despite the expansion of bariatric surgery procedures and their growing evidence, the role of psychiatric illness and interventions in bariatric surgery outcomes has been a less prominent focus in bariatric surgery programs and literature. Bariatric surgery guidelines recommend pre-surgery behavioral and psychosocial assessment; however, clear recommendations on post-operative psychosocial care are lacking (6). This is a concern given that up to 70% of bariatric surgery candidates have a history of a psychiatric illness according to structured psychiatric interview (9-11). Although the relationship between pre-existing psychiatric illness on weight loss outcomes is unclear, there is emerging literature on the range of mental health complications and challenges that can emerge following bariatric surgery.

This resource document aims to summarize key psychiatric issues related to bariatric surgery and advocates for psychiatric care throughout a patient’s bariatric surgery journey. The role for an integrated approach to bariatric surgery care involving psychiatric support will be highlighted based on the literature. Moreover, this resource document is aligned with the American Society for Metabolic and Bariatric Surgery Integrated Health Clinical Issues and Guidelines Committee “Recommendations for the Pre-Surgical Psychosocial Evaluation of Bariatric Surgery Patients” (12).

PRE-SURGERY PSYCHIATRIC ASSESSMENT

Successful bariatric outcomes are not only dependent on the surgical procedures but also require significant and lifelong changes in eating patterns and physical activity. At the same time, weight loss surgery has wide-ranging and profound psychosocial effects. Thorough and specialized pre-operative psychosocial assessment is an important part of a comprehensive bariatric treatment protocol (13) and it has become the standard of care for bariatric surgery centers (14). Pre-surgical mental health assessment is not diagnostic and should not be seen as a gatekeeper, but as an opportunity to prepare bariatric surgery candidates for surgery. It is essential to identify candidates’ vulnerability (e.g., presence of disordered eating behaviors such as emotional eating), and to provide support and education (e.g., patients should be warned about increased risk for alcohol use disorders after the surgery) (15). It is used to identify possible contraindications for
Summary

- Eating disorders remain a challenge to treat
- Multimodal approach with appropriate triaging to medical inpatient and outpatient services is needed
- Obesity is associated with several eating disorders including binge eating disorder and night eating syndrome
- Surgical treatments for obesity warrant long-term follow-up to monitor for emergence of eating disorders
- Further research on treatment, including role of pharmacotherapy, is needed in the management of eating disorders
Thank You...Questions

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Professor, Department of Psychiatry, University of Toronto

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Twitter: @SanjSockalingam
Updates and Trends in Substance use: Illicit Substances and Alcohol

Robert Weinrieb, MD - University of Pennsylvania
Sarah R. Andrews, MD - Johns Hopkins University
CLP 2021
Disclosure: Sarah R. Andrews, MD

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.
Objectives

▪ 1) Identify trends of **marijuana use**.
    ▪ Describe current state of legalization of marijuana.
    ▪ Evaluate the positive and negative effects of marijuana use.
▪ 2) Review the history and background of **psilocybin**.
    ▪ Describe the current research of psilocybin in treating psychiatric illness.
# What is marijuana?

## Hemp vs CBD vs THC in Food & Beverage

<table>
<thead>
<tr>
<th>HOW CONSUMED</th>
<th>HEMP</th>
<th>MARIJUANA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seeds (Hearts)</td>
<td>Whole or processed in variety of beverages and foods</td>
<td>Whole, ground, or turned into hash or concentrate, then smoked, vaped, or eaten</td>
</tr>
<tr>
<td>Cannabidiol (CBD)</td>
<td>Chemical compound extracted from lilies or flowers</td>
<td>Chemical compound consumed by smoking, extracted, or infused</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PHYSICAL EFFECTS</th>
<th>HEMP</th>
<th>MARIJUANA</th>
</tr>
</thead>
<tbody>
<tr>
<td>None, not psychoactive</td>
<td>None, not psychoactive</td>
<td>Contain THC, chemical compound that produces euphoria</td>
</tr>
<tr>
<td>CBD alone does not cause euphoria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LEGAL STATUS</th>
<th>HEMP</th>
<th>MARIJUANA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legal as long as there is &lt;0.3% THC</td>
<td>Legal to possess but not legal to add to food or topicals</td>
<td>Federally MJ is schedule I, but legal for medicinal and recreational use in many states</td>
</tr>
<tr>
<td>Depending on state laws</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Trends of marijuana use

- 12% of Americans identified as current users
- 22% of Americans between ages 18 and 25 years used marijuana in the last month

Legal updates on marijuana


Academy of Consultation-Liaison Psychiatry
American views on legalization

Academy of Consultation-Liaison Psychiatry
Cannabis sales

Despite the COVID-19 pandemic, year-over-year sales continued to grow steadily in established cannabis markets with three or more years of sales.

Retrieved:
Effects of marijuana

- **Psychiatric**
  - Increased risk of psychosis with repeated consumption
  - Anxiety and panic attacks, especially in naive users

- **Cognitive**
  - Increased risk of road accident

- **Respiratory**
  - Decreases airway resistance
  - Increased risk of airway disease
Medical benefits of marijuana

- Multiple sclerosis (MS)
  - Cannabis improves appetite and central pain
- Chronic pain
  - THC vs CBD
- CBD
  - Promising treatment for psychiatric illness


What is psilocybin?

WHAT IS PSILOCYBIN?
Psilocybin is a chemical obtained from certain types of fresh or dried mushrooms.

WHAT IS ITS ORIGIN?
Psilocybin mushrooms are found in Mexico, Central America, and the United States.

What are common street names?
Common street names include:
• Magic Mushrooms, Mushrooms, and Shrooms
History of psilocybin

- **6000-7000 years ago**: Religious use of magic mushroom
- **1922**: PCP synthesized
- **1938**: “First Psychedelic Renaissance” - LSD synthesized
- **1947**: LSD marketed as psychiatric drug for treated of alcoholism, halted in 1965
- **1958**: “Second Psychedelic Renaissance” - elucidated structure and synthesis of psilocybin
- **1960s**: Ketamine synthesized, Peyote as religious sacrament
- **1970**: Hallucinogens classified as schedule I
- **2004**: “Third Psychedelic Renaissance” - USLA researchers start trials on psilocybin
- **2006**: Johns Hopkins begins phenomenological studies on psilocybin use
- **2018**: FDA approves SPRAVATO (ketamine analog) for treatment-resistant depression
- **2019**: Usona Institute receives FDA “breakthrough therapy” for psilocybin treatment for depression
- **2020-present**: Johns Hopkins builds Center for Psychedelic & Consciousness Research

Psilocybin treating depression & substance abuse

Psilocybin (4-phosphorloxy-N,N-dimethyltryptamine)

Serotonin


Academy of Consultation-Liaison Psychiatry
Effects of psilocybin in humans & animals

- **Psychic Effects** (12-20 mg)
  - Stimulation of affect
  - Hypnagogic experience
  - Dreams
  - Enhanced ability for introspection
  - Mystical-type experience
    - Predicts success of therapy and likelihood of positive benefits
  - Illusions
  - Alterations of thoughts & time

- **Somatic Effects** (8-12 mg)
  - Accelerated /slowed heart rate
  - Hypo / hypertension
  - Nausea
  - Increased / decreased reflexes
  - Tremors
Psilocybin-assisted therapy

- **Substance abuse disorders**
  - Alcohol, stimulant, cocaine, tobacco, opioid, cannabis
- **Anxiety disorders**
  - PTSD, GAD, OCD, Existential crisis of terminal disease, adjustment disorder
- **Depressive disorders**
  - Major depression, treatment-resistant depression, suicidality
- **Pain disorders**
  - Chronic pain, cluster headaches, intractable phantom pain
- **Personality disorders**
  - Maladaptive narcissism, borderline personality disorder, narcissistic personality disorder
- **Inflammation**
Conclusions & next steps

- Marijuana and psilocybin schedule I drugs
  - Changing trends in drug use
- Marijuana
  - Movement toward legalization
- Psilocybin
  - Movement towards research
Substance Use Disorders Updates Course 2021

Robert M. Weinrieb, M.D. and Sarah Andrews, M.D
CLP 2021
Disclosure: Robert M. Weinrieb, MD

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.
TWO TOPICS:
1. Liver Transplantation for Alcohol Associated Hepatitis (AAH) and Short Sobriety
2. Stimulants (Amphetamines and Cocaine)

  - Landmark study legitimized transplantation for people with short sobriety, no fixed period abstinence, first liver decompensating event, failed medical management (pentoxifylline and steroids); highly selected population of n=26 AAH vs. 26 matched controls

- Justification for liver Transplant for AAH:
  - Worldwide increase in ALD related mortality is 3-fold in 25-34 y/o
  - Treatment for AUD available
  - If transplant offered for obese individuals (gastric bypass) and suicide attempts by APAP overdose, why not AAH?
Liver Transplantation for Alcohol Associated Hepatitis (AAH) and Short Sobriety
Dallas Consensus Conference by Asrani, et al. Liver Transplantation, Jan 2020

- **Mathurin, et al, 2011:**
  - AAH survival at 6 months without transplant (~23%) vs. with transplant (~77%)
  - Any drinking n= 3/26 or ~11% at 2 years

- **ACCELERATE-AH study: (Lee, et al, Gastroenterology 2018)**
  (12 sites, N= 141; retrospective, no control grp)
  - Any drinking: 25% at yr 1 and 34% at yr 3 (cumulative probability)
  - Sustained or binge drinking: 10% at yr 1 and 17% at yr 3 (cumulative probability)
  - Of N=40 with any drinking, N= 33 (82%) reported binge or frequent drinking
Selection of Patients for Liver Transplantation with Alcohol Associated Hepatitis with Short Sobriety

- Psychiatrists/Psychologist/Social Workers play key role in decision to transplant
- Most controversial and stressful era for liver transplant psychiatrists
- OPTIONS FOR PROCESS OF DECISION-MAKING
  
  **A. Use Mathurin criteria** (only 10% of patients were selected in trial)
  - First liver decompensating event, no psych/drug history, close (sober) family support, agree to lifetime abstinence, and all providers must agree

  **B. Use flexible, case-by-case approach**
  - Predictors of post-transplant drinking (Dew et al.); Multiple failed rehabs, less than 6 months abstinence, limited social support; family history of AUD
  - Predictors of post-transplant drinking with harm to liver (Deutch-Link, 2020); Prior relapse; failure to engage in treatment for AUD; ongoing alc consumption despite awareness of ALD
  - ACCELERATE-AH: Predictors of sustained post-transplant drinking: Younger age, more than 10 drinks/day
  - Any post-transplant drinking associated with 2X rate of graft rejection, and 3X rate of allograft cirrhosis
Psychiatric Evaluation of the Transplant Candidate with Alcohol Associated Hepatitis

What is our role?

For the multidisciplinary transplant team, to assist with decision to transplant

- Assess risk factors for alcohol, drug or nicotine use
- Estimate adherence to post-transplant medication and follow up visits
- Develop feasible behavioral health interventions to mitigate risk of post-transplant substance use

For the patient:

A. Explain the purpose of the evaluation to the patient/family
   ie. to develop a path to transplant wherever possible, not to be “the decider”
B. Clearly state that information from the evaluation is shared with the transplant team
Components of the Psychiatric Evaluation of the Transplant Candidate with Alcohol Associated Hepatitis

- Assess the physical condition of the patient
- Assess mental status of the patient
- Conduct standard psychiatric interview
- Use Motivational Interviewing strategies to address substances of abuse
  - Start by asking permission to discuss alcohol and drug use
  - “What did you like about alcohol?” “What didn’t you like about it?”
  - Social life and support systems
  - Are there healthy substitute activities once sober?
  - What motivates them to stay sober?
  - What triggers them?
  - Obtain history of quantity and frequency of alcohol use last
- Collateral information (GI doc, PCP, Counselor, P.O., etc.)
Post-Transplant Behavioral Health Interventions

- Not much evidence-based AUD treatments to guide the field
- **Setting:** Co-located within the transplant clinic and/or telepsychiatry
- **Talk Therapies:**
  - Motivational Enhancement Therapy (MET)
  - Symptom Triggered Intervention (STI)
  - CBT
  - Cell phone text messages for relapse prevention
  - 12-Step (start a specialized liver transplant recovery group?)
- **Pharmacotherapies:**
  - Appropriate treatment for co-existing psychiatric disorders
  - Naltrexone and Vivitrol
Methamphetamine (MA) and Cocaine Use Disorders (CUD)
PET Scans of MA vs. Cocaine Concentration

A. \([^{11}C]d\)-methamphetamine

B. \([^{11}C]c\)ocaine

Highest concentration of drug is red

Fig. 1

Diffuse binding

Binding only in striatum (reward ctr)
Treatment of Methamphetamine (MA) and Cocaine Use Disorders (CUD)

- **Scope of the problem:**
  - Cocaine: In the U.S. 2.2 million regular users with 1 million with CUD in past year
  - MA (more potent, longer acting vs. Amphet): In the U.S., 353,000 regular users

- **Focus of treatment is on CUDs** since metanalysis of 43 studies of pharmacotherapy for AMPH/MA found no “convincing results” due to low completion rates and underpowered studies

- **Psychosocial Treatments:** Similar for MA and CUDs
  1. Voucher Based Reinforcement Therapy (VBRT): Effective for promoting abstinence (most effective of all psychosocial therapies)
  2. Cognitive Behavioral Therapy (CBT): Beneficial for relapse prevention (avoiding craving)
  3. Intensive Outpatient Therapy (IOT); some reduction in use, but high dropout
Pharmacotherapy for Cocaine Use Disorders

- **Dopamine Agonists** (To exert similar effects but less abusable than cocaine)
  - ie. drugs that enter the brain more slowly, longer duration of action, partial agonists
    
    *For example*: long-acting dextroamphetamine or long-acting mixed amphetamine salts

- **GABAergic/Glutamatergic Medications**
  - Cocaine enhances dopaminergic reward system
  - Activation of GABA decreases activity of dopaminergic reward system (reduces euphoria and craving)
  - Blocking glutamatergic (NMDA) input reduces cocaine craving and prevents relapse
    
    *For example*: Topiramate
A Randomized Clinical Trial of Extended Release Mixed Amphetamine Salts (ER-MAS) and Topiramate for Cocaine Dependence in Frequent Users *

- N= 127
- Study duration was 12 weeks
- Pt received ER-MAS to a max of 60mg/day and Topiramate to a max of 100mg twice daily vs. placebo
- **Primary Outcome**: 3 consecutive weeks of sustained abstinence measured by urine toxicology and self-report
- **Results**: (3 weeks abstinence) Treatment (14.1%) vs. Placebo (0.0%) (P=.03)
- **Caveats**: ~ 20% of treatment group was discontinued from medication due to conservative cardiac safety parameters
- Not possible to assess which med drove the improvement w/o 4-arm design (placebo vs. Topiramate vs. ER-MAS vs. Topiramate plus ER-MAS

*(Levin, et al. Drug and Alcohol Dependence, in Press)*
Conclusions (1/2)

I. Liver Transplantation for Alcohol Associated Hepatitis and Short Sobriety

- Controversial process and complicated decision making required of psychiatrists
- Patients are younger and we are seeing more females, yet patient and graft survival seems as good as non-AAH liver recipients
- Role of psychiatrist and conduct of the psychiatric interview is to assist team with decision to list and assist patient with plan of care
- Recommendations: co-located treatment, anti-craving meds, psychosocial support and close follow-up
Conclusions (2/2)

- **II. Amphetamines/Cocaine Use Disorders**
  - Hard to treat population
  - Most effective psychotherapy is Voucher Based Reinforcement Therapy (VRBT)
  - Most effective (promising) medication is combination of Extended release mixed amphetamine salt and Topiramate
Updates of C-L Psychiatry: Neuropsychiatric Disorders

Durga Roy, MD
Department of Psychiatry and Behavioral Sciences
Johns Hopkins School of Medicine
## CLP 2021
**Disclosure: Durga Roy, MD**

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D – Relationship is considered directly relevant to the presentation
I – Relationship is NOT considered directly relevant to the presentation
Objectives

By the end of this course, participants will be able to:

• Recognize the prevalence, risk factors and correlates of neuropsychiatric complications after stroke
• Identify treatments used to manage depression, apathy and emotional lability after stroke
• Identify the most common neuropsychiatric symptoms after traumatic brain injury
• Identify treatments used to manage cognitive symptom, depression and post-concussive symptoms after traumatic brain injury
NEUROPSYCHIATRIC SYMPTOMS AFTER STROKE
Epidemiology of Stroke

- Fifth leading cause of death in the United States

- 85% of strokes are ischemic

- Prevalence of 2.6% in those over 20 years of age between 2009 and 2012

- 17.8% of those over 45 years of age have experienced stroke symptoms

- Stroke incidence and mortality have decreased over the past 30 years

https://radiologyassistant.nl/neuroradiology/brain-ischemia/imaging-in-acute-stroke
Disparities in Stroke

SEX
- More common in men than women when young and middle-aged
- Women have a higher lifetime risk of stroke than men (20% to 21% versus 14% to 17%)
- Women have poorer functional outcomes

RACE
- Higher in Black versus White patient populations
- Mexican Americans are also seen to have a higher stroke incidence in younger age groups and younger age at stroke death
Risk Factors for Stroke

MODIFIABLE
- Hypertension
- Hyperlipidemia
- Diabetes mellitus
- Tobacco use
- Antithrombotic therapy

NON-MODIFIABLE
- Age
- Sex
- Race
- Genetic (SERT polymorphism)
Types of Strokes

- Ischemic
- Hemorrhagic
- Transient ischemic attack
Neuropsychiatric Symptoms After Stroke

- Personality Change
- Depression
- Cognitive Decline
- Apathy
- Mania/Psychosis
- Fatigue
- Anosognosia
- Emotional Lability
Post-Stroke Depression

**Prevalence**
- 18-33%
- 25.4% with 2 years of stroke

**Risk Factors**
- Female sex
- History of psychiatric illness
- Large or multiple strokes
- Stroke occurrence within the past year
- Poor social support

**Correlates**
- Severity of impairment in activities of daily living.
- Strokes in frontal/anterior areas (L>R) or in the basal ganglia
- HTR3D and NEUROG3 genes

**Comorbidities**
- Anxiety
- Fatigue
- Sleep disturbance
- Apathy
Treatment of Post-Stroke Depression

**Pharmacologic**
- SSRIs (escitalopram, paroxetine)
- SNRI duloxetine
- TCAs, (nortriptyline imipramine), more effective than placebo (but more side-effects).

**Neuromodulation**
- rTMS most studies > placebo
- tDCS (3/4 studies > placebo)
- ECT limited studies

**Psychotherapy**
- CBT is effective alone or in combination with antidepressants
- Care management
- Psychoeducation
- Behavioral activation
- Family support

**Stroke-focused Interventions**
- Etiological investigation of the stroke
- Promotion of independence and quality of life
- Prevention of new strokes
- Rehabilitation (cognitive, PT, OT)
Post-Stroke Apathy

**Prevalence**
- 20-25%

**Risk Factors**
- Older age
- Higher pre-stroke functioning
- More severe cognitive impairment

**Correlates**
- Progressive functional decline
- Disruption of neural networks
  - anterior cingulate gyrus
  - dorsomedial frontal cortex
  - frontal pole
  - ventral caudate nucleus

**Comorbidities**
- Depression (21%)
- Fatigue
Treatment of Post-Stroke Apathy

**Pharmacologic**
- Dopamine agonists
- Stimulants
- Acetylcholinesterase inhibitors (donepezil > galantamine)
- Nefiracetam

**Psychotherapy**
- Care management
- Psychoeducation
- Family support

**Stroke-focused Interventions**
- Etiological investigation of the stroke
- Promotion of independence and quality of life
- Prevention of new strokes
- Rehabilitation
Post-Stroke Cognitive Decline

- **Prevalence:** 25-30% *(Stroke is the second most common cause of acquired cognitive decline)*
- **Comorbidities:**
  - Depression
  - Anxiety
  - Dementia
- **Correlates (Neuroimaging determinants of dementia after stroke):**
  - Silent brain infarcts
  - White matter changes
  - Lacunar infarcts
  - Medial temporal lobe atrophy
- **Treatment:**
  - Aerobic exercise, mental activity, and social engagement
  - Acesylcholinesterase Inhibitors (increase in MMSE score after 24 weeks Kim et al 2020)
Post-Stroke Fatigue

- Prevalence: 25% - 85% (affects about 50% of people after stroke)
- Comorbidities:
  - Depression
  - Anxiety
  - Poor quality of life
  - Pain
  - Apathy
  - Limb heaviness
  - Low TSH
- Correlates:
  - Stroke severity
  - Medication use and polypharmacy
  - Genetic polymorphism
- Treatment: Stimulants, Dopamine agonists
Post-Stroke Anosognosia

- Definition: lack of awareness or the underestimation of a specific deficit in sensory, perceptual, motor, affective, or cognitive function owing to a brain lesion
- Prevalence: 10%
- Associated with damage to:
  - right-hemisphere lesions involving cortical (insular, temporal, and parietal lobes) structures
  - subcortical structures (thalamus and basal ganglia)
- Clinical correlates: neglect, cognitive deficits, previous strokes, and older age.
Post-Stroke Emotional Lability

- Pathological crying or laughing: Provocation to non-emotive or incongruous stimuli (emotional display is socially abnormal and unstable)

- Emotional lability: socially familiar and provoked by typically emotive stimuli
  - Emotional incontinence
  - Involuntary emotional expression disorder
  - Pseudobulbar affect

- Prevalence: 17% of survivors in the first month, 20% between one and six months, and 12% more than six months after stroke

- Treatment: SSRI’s (citalopram, fluoxetine and sertaline most studied), TCAs, dextromethorphan/quinidine
Summary of Neuropsychiatric Symptoms after Stroke

- Ischemic strokes are the most common
- Depression and apathy are the most common neuropsychiatric complications
- Antidepressants (SSRIs and TCAs) have the most evidence for treatment of post-stroke depression and emotional lability
- Stimulants and dopamine agonists have the most evidence for post-stroke apathy
- Early physical rehabilitation portends better outcomes
NEUROPSYCHIATRIC SYMPTOMS AFTER TRAUMATIC BRAIN INJURY
TBI Definition

A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event:

• any period of **loss of consciousness**
• any **alteration in mental state** at the time of the accident (e.g. feeling dazed, disoriented, or confused)
• any **loss of memory** for events immediately before or after the accident
• neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient
• intracranial lesion
TBI as a Public Health Problem

- At least 3.6 million TBIs occur annually
- 2.8 million TBI-related ED visits, hospitalizations, and deaths in the United States annually
- 3.2 to 5.3 million people living with TBI-related disability
- Over $60 billion in annual direct and indirect medical costs
- 43% of those hospitalized for TBI subsequently develop functional or psychological sequelae
- **Leading cause of death and disability** in people younger than age 45 in the United States

Most Common Causes of TBI

Why Diagnose and Treat Psychiatric Problems After TBI?

TBI

Psychiatric problems

Disability

Occupational activities
Social integration
Workforce participation
Activities of daily living

Arciniega 2006, Gould et al., 2011; Whelan-Goodinson et al., 2009; Temkin et al., 2009; Selassie et al., 2008; Fleminger & Ponsford 2005; Rapoport et al., 2002; Levin et al 1990
Common Neuropsychiatric Problems after TBI

Neuropsychiatric Problems

- Emotional
- Cognitive
- Behavioral
- Physical

Pre-injury, Injury and Post-injury Factors

Silver and Arciniegas 2006
• difficulties in switching parameters and planning
• mental inflexibility
• irritability
• slowness in performance
• low frustration tolerance with potential social and performance repercussions

Bradbury et al 2011, Riggio et al. 2009
# Symptom-focused Approach to Pathology

<table>
<thead>
<tr>
<th>Emotional Dyscontrol</th>
<th>Behavioral Dyscontrol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affective lability</td>
<td>Aggression</td>
</tr>
<tr>
<td>Pathological laughter and crying</td>
<td>Disinhibition</td>
</tr>
<tr>
<td>Irritability</td>
<td></td>
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</tbody>
</table>

Arciniegas 2015
# Syndrome-Focused Approach

<table>
<thead>
<tr>
<th>Post-TBI Psychiatric Syndromes</th>
<th>Prevalence in Gen. Pop</th>
<th>Prevalence after TBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression</td>
<td>10%</td>
<td>35%</td>
</tr>
<tr>
<td>Mania</td>
<td>1-2%</td>
<td>1-9 %</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1%</td>
<td>1-7 %</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>18 %</td>
<td>25 %</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td>4%</td>
<td>25 %</td>
</tr>
<tr>
<td>New Behavior Problems</td>
<td></td>
<td>25 %</td>
</tr>
</tbody>
</table>

Deb et al. 1998; Kessler et al. 2004
# Syndrome-Focused Approach

<table>
<thead>
<tr>
<th>Syndromes</th>
<th>Prevalence</th>
<th>Core Features</th>
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</thead>
<tbody>
<tr>
<td>Cognitive deficits</td>
<td>5%–60%</td>
<td>• Poor Memory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Poor attention/processing speed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Executive dysfunction</td>
</tr>
<tr>
<td>Depression</td>
<td>13-53%</td>
<td>• Low mood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Irritability</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Suicidal ideation</td>
</tr>
<tr>
<td>Mania</td>
<td>1-9%</td>
<td>• Euphoric mood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Irritability</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Impulsivity</td>
</tr>
<tr>
<td>Anxiety</td>
<td>11-70%</td>
<td>• Persistent worry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Autonomic arousal</td>
</tr>
<tr>
<td>Apathy</td>
<td>10%</td>
<td>• Lack of motivation or drive, loss of initiative</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Euthymic mood</td>
</tr>
</tbody>
</table>
Neuropsychiatric Assessment of TBI: Stepwise Approach

1. Comprehensive psychiatric evaluation
2. Brief Neurological Exam
3. Problem-focused medical workup
4. Ancillary studies to help establish diagnosis
5. Multipronged formulation
6. Multidisciplinary treatment
7. Consultations and referrals
Management of Post-TBI Neuropsychiatric Symptoms is Multidisciplinary

- Psychiatry
- Neurology
- Audiology
- Sleep Medicine
- Pain Management
- Physical Medicine and Rehabilitation
- Neuropsychology
Pharmacologic Treatment: Basic Concepts

- General guidelines
  - choose a medication
  - start low, go slow
  - therapeutic trial of all medications
  - continuous reassessment of clinical condition
  - monitor drug–drug interactions
  - avoid polypharmacy
  - consider coexisting medical problems
  - avoid agents that can impair cognition and neuroplasticity: benzodiazepines, first generation antipsychotics, select antiepileptic drugs (phenytoin), anticholinergics and antihistaminics

Lee, Lyketsos, Rao 2003
<table>
<thead>
<tr>
<th>Psychiatric problems</th>
<th>First-line medications</th>
<th>Standard dosage</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Sertraline</td>
<td>50-150 mg/d</td>
<td>In bipolar disorder can cause switch to mania/hypomania</td>
</tr>
<tr>
<td></td>
<td>Citalopram</td>
<td>5-20 mg/d</td>
<td></td>
</tr>
<tr>
<td>Mania: acute</td>
<td>Quetiapine</td>
<td>25-300 mg/d</td>
<td>In elderly with cerebrovascular disease, dementia</td>
</tr>
<tr>
<td>Mania: maintenance</td>
<td>Valproate</td>
<td>250 to 1500 mg/d; in two divided doses</td>
<td>Can increase levels of other anticonvulsants</td>
</tr>
<tr>
<td>PTSD</td>
<td>Sertraline</td>
<td>50-150 mg/d</td>
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<tr>
<td>Psychosis</td>
<td>Risperidone</td>
<td>0.25 – 4 mg/d</td>
<td>Elderly, those with cerebrovascular disease, dementia</td>
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<td>Quetiapine</td>
<td>50-300 mg</td>
<td>Orthostasis, metabolic syndrome</td>
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<tr>
<td>Insomnia</td>
<td>Ramelteon</td>
<td>8 mg</td>
<td>Take within 30 minutes of going to bed</td>
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<tr>
<td></td>
<td>Trazodone</td>
<td>50-200mg</td>
<td>Orthostasis</td>
</tr>
<tr>
<td>Apathy</td>
<td>Methylphenidate</td>
<td>5-40 mg/d; divided doses</td>
<td>Second dose to be given early afternoon</td>
</tr>
<tr>
<td>Memory deficits</td>
<td>Donepezil</td>
<td>5-10 mg at night</td>
<td>Can cause bradycardia and syncope</td>
</tr>
<tr>
<td>Executive function deficits</td>
<td>Amantadine</td>
<td>100-400 mg; divided doses</td>
<td>Avoid in patients with history of seizures. Avoid or use lower doses in persons with kidney failure</td>
</tr>
<tr>
<td>Inattention</td>
<td>Methylphenidate</td>
<td>5-40 mg/d; divided doses</td>
<td>Second dose to be given early afternoon</td>
</tr>
</tbody>
</table>

Ozga et al 2018, Wortzel et al 2018
Psychiatric Rehabilitation after TBI

- Skills for Social Reintegration
- Vocational Rehabilitation
- Mindfulness-based Cognitive Therapy
- Occupational Therapy Groups
- Pharmacologic
- Anger Management
- Psychoeducation to Caregivers
- Emotional and Behavioral Dyscontrol
- Vocational Rehabilitation
- Mindfulness-based Cognitive Therapy
- Occupational Therapy Groups
- Pharmacologic
- Anger Management
- Psychoeducation to Caregivers
- Emotional and Behavioral Dyscontrol
Summary of Neuropsychiatric Symptoms after TBI

- Neuropsychiatric sequelae can develop within weeks to month after TBI
- Within the first-year patients suffer loss of quality of life, poor social function and risk of disability
- Can use both symptom and syndrome-based approach
- Pharmacologic interventions should involve medications at low doses, avoid polypharmacy and target acute symptom/syndrome
- Psychosocial rehabilitation is key


COVID-19 Updates

Understanding how we got where we are and where we are going from here
With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.

The presenter does not derive any material interest or benefit from the medications, devices, products, or publications discussed in the presentation.
COVID-19 Updates

- Objectives:
- To define the framework of historical, social, and medical context within which the current COVID-19 pandemic unfolded, to postulate its remaining course and identify possible consequences on global society and the practice of medicine and psychiatry.
- To provide overview of current knowledge on neuropsychiatric components and manifestations associated with COVID-19 and its treatment, including the indirect psychological toll associated with global mitigation measures.
- To identify and outline the areas with a prominent knowledge gap and areas with considerable situational opportunities as areas of interest for future research in psychiatry and public mental health.
Why are some of my patients/family members/friends/colleagues so adamantly refusing or questioning the vaccine?

How come there are still large swaths of population firmly believing that COVID-19 is a hoax or a mild disease with its features artificially inflated by the government agencies?

Is there a connection between the COVID-19 and social movements, such as BLM?

How does psychological and psychiatric toll of COVID-19 compare to the psychological toll of measures undertaken to mitigate the pandemic?

How will my practice and our profession change and evolve over the next several years?

How can I study the interplay between infectious diseases and mental health?
## Pandemics – Mental health burden

<table>
<thead>
<tr>
<th>Direct - mental health burdens caused by the disease itself</th>
<th>Indirect - mental health burdens caused by our response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical medicine (and psychiatry) domains</td>
<td>Public health and political domains</td>
</tr>
<tr>
<td>Understood and managed by studying medicine and psychiatry</td>
<td>Understood and managed by studying social sciences</td>
</tr>
<tr>
<td>Insufficient involvement and understanding by public health officials</td>
<td>Inadequate involvement by mental health professionals</td>
</tr>
</tbody>
</table>
Psychology of a Pandemic

- It is not possible to start practicing psychiatry of a pandemic without understanding the psychology of it.
- “Very few phenomena throughout human history have shaped our societies and cultures the way outbreaks of infectious diseases have; yet, remarkably little attention has been given to these phenomena in behavioral social science and in branches of medicine that are, at least in part, founded in social studies.”
- There is an inherent bias in studying rapid outbreaks:
  - They may be too intense to tolerate and too short in duration to sustain systemic attention.
  - They may be too rare and too unpredictable to attract resources in Western medicine.
  - There may be implicit institutional racism reflected in a lack of interest in Western medicine in studying diseases that affect primarily ‘societies and people of color’.
Psychology of a Pandemic

- “In a long succession throughout history, pandemic outbreaks have decimated societies, determined outcomes of wars, wiped out entire populations, but also, paradoxically, cleared the way for innovations and advances in sciences (including medicine and public health), economy, and political systems.”

- A pandemic of a considerable proportion is bound to change the course of history and we live in the midst of one

- Many staples of contemporary lifestyle will fall by wayside, giving rise to new forms of commerce, interaction, services, healthcare

- As mental health professionals, we are expected to provide support and reassurance through a scary and uncertain period of change to:
  - Ourselves and our loved ones
  - Our colleagues
  - Our patients
  - General public

- While doing so, we are dealing with a lot of unknowns
Rush to fill the knowledge gap – Retraction Watch


Structuring what we know about (Neuro)Psychiatric aspects of COVID-19

- What is our baseline? Are there emotional issues associated with impending outbreak without having been directly exposed to the microbial agent?
- What are the immediate, direct sequelae of acute COVID-19 for those who acquire it and survive it?
- What are the psychiatric aspects of losing a loved one to COVID-19?
- What are the Neuropsychiatric complications of protracted COVID-19?
- What are the indirect consequences - emotional and psychiatric toll of measures aimed at preventing the spread of the pandemics?
  - Social distancing
  - Delayed care/limited access to care
  - Economic hardship
## How big is this pandemic?

<table>
<thead>
<tr>
<th>Pandemic and Duration</th>
<th>“Spanish Flu” (1918 – 1920)</th>
<th>COVID-19 (2019 – 202?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waves</td>
<td>4 Waves</td>
<td>3 or 4 Waves</td>
</tr>
<tr>
<td>Global Cases</td>
<td>500 million (1/3 of population)</td>
<td>250 – 300 million (late 2021)</td>
</tr>
<tr>
<td>Global Deaths</td>
<td>25 – 50 million (as high as 100 million)</td>
<td>5 million (late 2021)</td>
</tr>
<tr>
<td>US Cases</td>
<td>30 million (28 percent)</td>
<td>50 million (late 2021)</td>
</tr>
<tr>
<td>US Deaths</td>
<td>Under 1 million</td>
<td>Approaching 1 million (late ’21)</td>
</tr>
<tr>
<td>Most Fatalities/Most Susceptible</td>
<td>&lt; 65 years of age</td>
<td>&gt; 65 years of age</td>
</tr>
</tbody>
</table>
How much does COVID-19 cost us?

- Estimated cost through October 2020 was $16 trillion
- Under $200,000 per 4-member family
- In addition to direct cost of the outbreak, one has to account for opportunity cost
- In economic terms, this money could not have been invested elsewhere (economic growth or warfare)
- In terms of healthcare, resources had to be diverted from different services to test, prevent, treat, and rehabilitate COVID-19 caseload
- Global healthcare was put on ‘pause’ to attend to COVID-19, missing the opportunity to treat and manage many conditions, including mental health issues
- How much does COVID-19 and its management interfere with our civil liberties?

Facing a Black Box full of Unknown Variables... that we knew we did not know

- A rare research from 2004 ("Redefining Readiness") suggests that the general population may not react to a public health crisis in the manner anticipated by emergency management professionals.
- Unanticipated behavior can complicate the management of a disaster situation and lead to higher rates of long-term mental health problems.
- Americans were twice more worried about smallpox vaccine than about contracting smallpox themselves (in an imagined scenario).
- **Contagion** exists as a psychological concept – emotional epidemiology (Ofri).
- Public reaction is guided by the **perception** that there is a limited opportunity for escape, a high-risk of being injured or killed, or that help will only be available to the very first people who seek it.

The Bad and the Ugly

- We knew that:
  - We could not anticipate and account for public behavior and attitudes in such situations
  - The concept of emotional epidemiology implies the ‘emotional outbreak’ that mirrors the actual outbreak
  - There will be a considerable vaccine hesitancy once there was one or more viable vaccines
  - The longer the outbreak, the bigger the chance for viral mutations
  - The longer the outbreak, the bigger the disproportionate burden of diseases on minorities and disenfranchised communities

- We did not know that:
  - There would be a significant proportion of ‘disease deniers’ interfering with public policies and measures to attenuate the outbreak
  - Segments of global and national public health systems responsible for combating the outbreak were not adequately prepared for it
  - How easily and skillfully political/partisan agents would use COVID-19 to advance their political agenda

COVID-19 Immunization Status

- Limited immunization process in the US
- 65.5 percent received at least one dose
- 56.6 percent fully vaccinated
- Globally: 47.5% of the world population has received at least one dose of a COVID-19 vaccine. 6.52 billion doses have been administered globally, and 24.53 million are administered each day.
- Only 2.5% of people in low-income countries have received at least one dose.
- The rate of immunization is slowing down globally

Age group breakdown
How much will COVID-19 continue to cost us?

- Because of stalled immunization process and the emergence of Delta variant (B.1.617.2) COVID-19 will remain a thorn in our side for the foreseeable short-term future (6-12 months)

- In healthcare, it will continue to present a considerable drain on our resources (including human resources) as we struggle to reestablish the pre-outbreak volume and level of care while keeping COVID-19 in check

- Between burnout and moral injury, we will continue to see healthcare professionals leave the profession and/or suffer the consequences, including relational problems, substance use, and other psychiatric disorders

- Telehealth will continue to gain ground as an effective modality of care

- Further fragmentation of societies and communities may lead to currently unforeseeable consequences
COVID-19 as a Unique Pandemic in History

- The first clinically relevant global outbreak in 100 years
- Epidemiologically, not a devastating pandemic
- As humans – individuals and cohorts, we have psychological resilience to sustain and survive much bigger pandemic outbreaks, as we have throughout history
- The question is – do we, as „advanced“ societies and as a sophisticated global civilization, possess the same resilience, even when hit by a less deadly outbreak?
- COVID-19 is difficult to curb because it is difficult to correctly approximate the risk it poses to cohorts and individuals
- There is no known study or method to understand the risk appraisal among individuals and populations
- There are instruments that capture perceived personal risk (e.g. CORAS), but do not explore how individuals and groups arrive at that decision

Risk Appraisal in COVID-19

- H(euristic) and U(nconscious) R(isk) E(valuation) M(echanism) for infectious diseases
- HUREM = $R_0 \times CFR$ (as percentage) x prevention efficiency gap (as percentage) x individual weight factor
- $R_0$ = basic reproductive number (can be manipulated by preventative measures, social distancing, and microbe mutation)
- CFR = case fatality ratio, can be varied by effectiveness of available treatment (expressed as a percentage)
- Prevention efficiency gap (1 – proportion of vaccine efficiency, e.g. 0.85, expressed as a percentage – 15%)
- Individual weight factor (perception of vulnerability/invincibility based on objective metrics such as age, chronic diseases, and social milieu, and subjective perception of vulnerability) - ranges from 1 (not at risk) to 3 (very susceptible and vulnerable)
Risk Appraisal in COVID-19

- COVID-19 tends to hover around HUREM value of 1, fluctuating above and below just enough to make us, as individuals and groups, constantly misperceive the risk:

<table>
<thead>
<tr>
<th>COVID-19 Phase</th>
<th>HUREM Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early COVID-19 (early 2020)</td>
<td>2.4 x 2.01 x 1 = <strong>4.824</strong></td>
</tr>
<tr>
<td>Late pre-vaccine COVID-19 (late 2020)</td>
<td>2 x 0.3 x 1 = <strong>0.6</strong></td>
</tr>
<tr>
<td>Vaccine COVID-19 (early 2021)</td>
<td>2 x 0.3 x 0.2 = <strong>0.12</strong></td>
</tr>
<tr>
<td>Delta variant COVID-19 (late 2021)</td>
<td>4 x 0.3 = <strong>1.2</strong> without the vaccine</td>
</tr>
<tr>
<td></td>
<td>4 x 0.3 x 0.6 = <strong>0.72</strong> with the vaccine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HUREM value</th>
<th>Disease Severity and Risk Perception</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>Disease not perceived as a serious threat (flu, cold, etc.)</td>
</tr>
<tr>
<td>&gt; 1</td>
<td>Disease perceived as a serious threat</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>Disease perceived as a very serious threat</td>
</tr>
</tbody>
</table>
What is, actually, our baseline?

- General population is affected without direct involvement with COVID-19
- In Hong Kong general population reported following symptoms without exposure to COVID-19:
  - Depression – 19 percent
  - Anxiety – 14 percent
  - 1 in 4 report deterioration in mental well-being
- In China, self-reported anxiety during opening stages of COVID-19 was 29 percent
- Self-reported symptoms of depression were reported by 37 percent
- In some studies, the incidence of reported sx. reaches 50 percent (Choi, et al. 2020)


Common Neuropsychiatric Symptoms of coronavirus infections

- Neuropsychiatric symptoms of COVID-19 are similar to those of other viral infections, particularly other coronavirus infections.
- With the prevalence of COVID-19, we may see more of the conditions we failed to register during previous, limited outbreaks or failed to attribute to (corona)viruses.

<table>
<thead>
<tr>
<th>SARS and MERS</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia (42 percent)</td>
<td>Anxiety (42 percent)</td>
</tr>
<tr>
<td>Anxiety (36 percent)</td>
<td>Insomnia (40 percent)</td>
</tr>
<tr>
<td>Memory impairment (34 percent)</td>
<td>Depression (31 percent)</td>
</tr>
<tr>
<td>Depression (33 percent)</td>
<td>PTSD (28 percent)</td>
</tr>
<tr>
<td>Confusion (28 percent)</td>
<td>OCD sx. (20 percent)</td>
</tr>
</tbody>
</table>


COVID-19 patients

- Delirium
- Encephalitis
- Neuropsychiatric Sequelae – the implication of P2X7 receptors
- Psychiatric/emotional consequences of the illness
- Psychiatric/emotional consequences of the treatment
- Psychiatric/emotional consequences associated with post-COVID course and recovery
Delirium

- Delirium in hospitalized COVID-19 patients a direct function of severity of the illness
- Reasonable estimates – between 20 and 30 ICU patients, some estimates north of 60
- Comparable to rates of diseases with similar severity and in the similar setting (e.g. ICU)
- Delirium incidence may have been masked by the use of sedation/ventilation
- The implication of the role of P2X7 receptors

C-L Psychiatric care during COVID-19

- Constraints in managing delirium with classic agents (neuroleptics) with concurrent use of HCQ+AZT at one point (QTc prolongation)
- Limitations in managing delirium with alternative agents (e.g. valproate) with concurrent use of RNA-disruptors, such as remdesivir or favipiravir (hepatic injury liability)
- Rise in use of selective α2-adrenergic receptors (e.g. dexmedetomidine) in managing delirium
- Use of α2-adrenergic receptors as a step-down method in managing residual delirium while weaning patients off ventilators (e.g. clonidine)
- Use of interferon and steroids comes with known psychiatric risks
C-L Psychiatric care during COVID-19 – Delirium: next steps

- Exploration of anti-inflammatory agents (IL-6, TNF-α immunomodulators):
  - Tocilizumab – IL-6 inhibitor, preliminarily failed to address depression and improve quality of life and actually worsened all sx (Knight, 2018)
    - Possibly due to failure to simultaneously block IL-1 and TNF, or
    - Due to limited ability to cross the blood-brain barrier
  - Sporadic reports of utility of tocilizumab in delirium in COVID-19 (1 case)
  - Sarilumab – IL-6 inhibitor, sporadically and experimentally used in treatment of COVID-19, significantly better crossing of blood-brain barrier (6x), no reported cases of utility in delirium treatment, likely not as effective in treatment of COVID-19
  - Siltuximab – another IL-6 inhibitor, sporadically and experimentally used in treatment of COVID-19
  - ALL antiinflammatory agents significantly increase the risk for serious infections (IL-1 inhibitors less so)
  - IL-1 inhibitors – anakinra, canakinumab, rilonacept less likely to lead to severe infections, less hepatotoxicity, but have a potential for drug interactions – effect on delirium unknown

https://covidprotocols.org/protocols/therapeutics/
• GM-CSF inhibitors disrupt inflammatory response at different pathways and may be potentially useful in managing the complex delirium cascade:

<table>
<thead>
<tr>
<th>GM-CSF inhibition pathway</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition of the cytokine response</td>
<td>IL-1, IL-6, TNF</td>
</tr>
<tr>
<td>Limiting the chemotaxis</td>
<td>IL-8</td>
</tr>
<tr>
<td>Cell degradation reduction</td>
<td>H2O2, MMPs</td>
</tr>
<tr>
<td>Cellular immune response blunting</td>
<td>T- and B-cells</td>
</tr>
</tbody>
</table>

– Examples include otilimab, gimsilumab, lenzilumab, mavrilimumab, TMJ2
– Actual effect on delirium remains unknown and speculative

Other neuropsychiatric manifestations

- Anosmia and ageusia – common, observed in at least 25 percent cases, most recover in a week
- Rare complications:
  - (Meningo)Encephalitis – direct and autoimmune
  - ADEM (Acute disseminated encephalomyelitis)
  - PRES (Posterior reversible encephalopathy syndrome)
  - Parkinson’s-like symptoms (long-term cognitive loss?)
- Clinical point – worry more about CV incidents (stroke)

Depression

- Like delirium, dependent on the severity of illness, duration of hospitalization, prognosis, isolation, long-term outlook
- Often a part of triad: insomnia, anxiety, depression
- Pervasive fatigue and loss of energy and motivation
- Populations of interest:
  - Pregnant patients with COVID-19
  - Patients with prior history of mood disorders
- Definitive developing area of interest: correlation with inflammatory processes and markers — my best guess are chronic inflammatory symptoms (various body aches and pains, combined with some depression/anxiety, and some cognitive „fog“)

Depression

- Treatment with antidepressants may not be warranted at first
- Focus on psychosocial support, overcoming isolation, and facilitating communication with loved ones (including virtual visitations)
- If treating, make sure delirium (hypovactive is not present), try to address insomnia and anxiety first
- If treating depression, consider SNRI agents
- Keep in mind drug interactions, effects of SSRIs on platelet aggregation
Anxiety

- Present in a considerable proportion of patients (more than 1 in 3)
- Anxiety adversely affected by:
  - Female gender
  - Older age (some studies found the opposite)
  - $O_2$ saturation
  - Existing social support

Anxiety

- Limitations in use of benzos for anxiety due to breathing interference, but benzos are not contraindicated
- 5-HT$_2$ antagonism in some meds can be utilized
- If co-occurring with depression, antidepressants may be considered
- If observed as a part of delirium, SGA with 5-HT$_2$ antagonism should be considered
Traumatic Stress

“Given the very frightening and invasive nature of the Covid-19 critical care experience, the high risk of death and the potential for long-term medical complications, those most severely affected by Covid-19 are likely to be at very high risk of developing trauma and stress-related mental health difficulties.” - COVID Trauma Response Working Group

- Liability for traumatic stress increases with the invasiveness of treatment (ventilation), the length of stay, presence of delirium, and prior traumatic exposure

- COVID-19 ICU patients should be screened for PTSD and traumatic stress sx. at discharge and provided educational material and referral resources

https://www.traumagroup.org/

Traumatic Stress

- Studies place the prevalence of PTSD among severe COVID-19 survivors between 10 and 30 percent
- Prior mental health diagnosis is a strong predictive factor for PTSD
- We are lacking yardsticks at longer-term outcomes post recovery
- It is reasonable to expect that PTSD in COVID-19 survivors plays a significant role in recovery
- Understanding lingering inflammatory processes may be effective in understanding post-COVID-19 trauma processing and emotional well-being


- An amorphous constellation of symptoms that persist in a percentage of COVID-19 survivors beyond customary 4 weeks, with most agreeing that symptom persistence beyond 12 weeks would warrant a ‘long-haul’ label
- About 5 to 6 percent of COVID-19 patients may be experiencing symptoms up to six and even nine months
- Three most common symptoms include shortness of breath, cognitive dysfunction, (brain fog), and fatigue, there are close to 200 various symptoms reported
- Reception in medical community ranges from starting specialized “COVID Rehabilitation Facilities” to brushing patients and their concerns aside
- No definitive treatment, psychosocial interventions, CBT, and medications have been used

Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people, Matthew Whitaker, Joshua Elliott, Marc Chadeau-Hyam, Steven Riley, Ara Darzi, Graham Cooke, Helen Ward, Paul Elliott, medRxiv 2021.06.28.21259452; doi: https://doi.org/10.1101/2021.06.28.21259452

- Some approaches resemble approaches to extreme post-exertional exhaustion, i.e. replenishing depleted nutrients, resolving electrolyte or hormonal imbalances and carefully starting patients on exercise regimens
- Other approaches are similar to approaches Chronic Fatigue Syndrome or Fibromyalgia
- Utilization of inhaled steroids, stimulants, and wakefulness promoting agents (modafinil) has been reported
- SNRIs may be a reasonable choice for individuals with persistent inflammatory and mood symptoms

Scientific American: New Long-Haul COVID Clinics Treat Mysterious and Ongoing Symptoms
Coordinating care among different specialties could help patients with many problems and no proved therapies By Melba Newsome on June 30, 2021
Support for Healthcare Personnel

- Anxiety among healthcare workers precedes that of general public
- Healthcare workers may tend to UNDERESTIMATE and DOWNPLAY the seriousness of a pandemic (this changes if they have small children at home)
- 10 percent develop traumatic stress, more have some symptoms of depression or traumatic stress (up to 50 percent in in China during COVID-19 outbreak in 2020)
- There is a considerable risk for traumatic stress, burnout, demoralization, and moral injury with potentially long-term adverse consequences (including PTSD, depression, substance use)
- Substance use increase can be reported up to three years after the outbreak (SARS, 2003)
- Resilience and support programs can help prevent and provide early treatment for the above complications
Support for HealthCare Personnel

- Four areas were classified as important using factor analysis:
  - health and relationship with the family
  - relationship with friends/colleagues
  - work and
  - spirituality.

- The areas for coping strategies were:
  - clear directives/precautionary measures
  - ability to give feedback to/obtain support from management
  - support from supervisors/colleagues
  - support from the family
  - ability to talk to someone and
  - religious convictions.

- Support from supervisors/colleagues was a significant negative predictor for psychiatric symptoms and PTSD. Work and clear communication of directives/precautionary measures also helped reduce psychiatric symptoms.

Support for HealthCare Personnel

- In some countries (e.g. Singapore), healthcare workers had prior exposure to SARS.
- In comparison to SARS, they report:
  - More than half of them felt safer and better equipped in the current COVID-19 pandemic.
  - Overall, they report experiencing far less stigma and discrimination and positive social cues during COVID-19 than they did during SARS.
  - Being a racial minority and living apart from family were independent predictors of higher distress regardless of prior SARS epidemic experience.
  - Daily exposure to confirmed or suspect COVID-19 cases increased the odds of high IES for healthcare workers without prior SARS experience.
Social Distancing

- Massive, unprecedented ‘experiment’ in the history of humankind
- Imposes significant psychological, social, and economic toll on individuals and communities.
- Prolonged isolation and separation from families and their community can have profound effect on socially isolated individuals.
- We need a better gauge of psychological effects and limitations to such measures.
- Apparently, there was a reason that quarantine, when originally introduced, was limited to 40 days (just under six weeks)
Social Distancing Effects

- Helplessness, loneliness, boredom... combined with anxiety, uncertainty, and non-COVID stressors put a strain on individuals’, families’, and communities’ coping capacities.
- Risk for relapsing or developing anxiety/mood disorders
- Substance use risk
- Abusive behaviors risk
Social Distancing Effects

- When exposed to effects of social distancing, a majority of people experiences it as a considerable inconvenience, imposition, disruption.
- They view it as confinement and experience boredom/depression because of staying home, while feeling helpless.
- Overall, they experience more self-reported psychological problems.
- A subset of people, however, concentrate on the positive sides of staying home and consider it a responsible behavior, an opportunity, and a requirement for feeling safe.
- Those who perceive it as a responsibility or opportunity experience fewer psychological problems.
- In this segment, we are still blind people trying to describe an elephant.

Major Directions for Inquiry

- The effect of social distancing on emotional well-being of general population and sub-populations
- Developing resilience programs for health workers as they bear the brunt of any major disaster or public health event
- Integrating telepsychiatry – telehealth into practice
- Psychoimmunology and immunomodulation
- Focus on inflammatory component and markers
- Research (repurposing) utility of existing drugs
Psychoimmunology and Immunomodulation

- Roles of immune inflammatory response system (IRS) and the compensatory immune-regulatory system (CIRS) have been postulated in etiology/pathology of psychiatric disorders.
- Activation of immune pathways such as ‘cytokine storm’, autoimmunity mediated by cross-reactivity between CNS components and viral particles, and microglial activation can have further neuropsychiatric effects.
- Accelerated use of immunomodulatory drugs to treat COVID-19 allows us to participate in this learning process.

Inflammatory Process and Markers

- Inflammatory processes have been long-implicated as having a role in psychiatric disorders
- Inflammatory processes may play a role in the post-COVID-19 long-term psychiatric sequelae, directing our choice of treatment modalities
- Studying the role of microglial P2X7 receptors in the cascade of inflammatory response, for example, may lead to better understanding of the inflammatory nature of some cognitive and psychiatric symptoms, as well as of neuropathic pain

(Viral) Infections and long-term impairment of well-being

- COVID-19 is an opportunity for investigation of the naturalistic association between viral respiratory infections and (subsequently emerging) psychiatric symptoms
- There are other coronaviruses, such as 229E, NL63, OC43, and HKU1 which freely and commonly circulate among global population; they cause nothing more than a common cold...
- Or do they? Perhaps at this stage we ought to more closely examine the possible relationship between some of the common viruses and some fairly common psychosomatic entities, such as CFS or FM
- Looking from a different perspective, this past season was likely the mildest flu season in modern history; perhaps we ought to study long-term outcomes of such unusually mild flu season and learn from milestones at 15, 20, 25 years?
Fluvoxamine may disrupt cytokine response, thus attenuating the inflammation in COVID-19; also works as a sigma-1 agonist.

Valproate blocks HDAC2 (histone deacetylase 2), which was found to be affected by SARS-CoV-2 viral proteins nsp5 and E. The role of HDAC2 is largely putative and implicated in cell progression.

Haloperidol is an inverse sigma1 agonist and sigma2 agonist. Viral protein Nsp6 interacts with sigma1, while viral protein orf9 interacts with sigma2. Role of sigma receptors in viral proliferation remains unclear at this time.

Chlorpromazine is an inhibitor of clathrin-dependent endocytosis, a key mechanism for the viral entry into the host cells, and also prevents the subsequent viral genome release and replication — there are studies under way to investigate the utility of chlorpromazine in treating COVID-19.


# Challenges of Remote Vs. In-Person Encounter

<table>
<thead>
<tr>
<th>Remote Encounter</th>
<th>In-Person Encounter</th>
</tr>
</thead>
<tbody>
<tr>
<td>May paradoxically appear more immediate (no PPE on the face)</td>
<td>More immediate, but with severe limitations due to PPE</td>
</tr>
<tr>
<td>Safe for provider and patient</td>
<td>Can be made relatively safe for provider and patient</td>
</tr>
<tr>
<td>Requires technology at both ends</td>
<td>Requires high utilization of PPE</td>
</tr>
<tr>
<td>Requires people to operate technology at patient’s end (increasing exposure)</td>
<td>Does not rely on tech/other people (intermediaries, telepresenters)</td>
</tr>
<tr>
<td>May miss key components of physical exam</td>
<td>Allows for physical exam to be performed</td>
</tr>
<tr>
<td>Does not provide authentic experience of a human encounter</td>
<td>Still does not provide authentic experience of a human encounter</td>
</tr>
</tbody>
</table>
Challenges for Mental Health Services in the next phase

- Adjust to the shifts in social proximity/distancing and adopt **flexibility** in providing care by using Telemedicine (e.g. reduction in cancellation of visits even when distancing measures are removed)
- Advocate for our existing patients, particularly those with serious mental illness (SMI) to be provided with adequate access to care
- Advocate for research to understand and protect public mental health during this outbreak and in its aftermath – pertains to both the viral impact and the impact of public health measures
- Advocate for behavioral health experts and behavioral scientists to be given a seat at public health panels – from local communities to WHO
- Convince the scientific community to *redefine epidemiology* as, in part, a *behavioral science*
At this stage, given how little we know about the role emotions, attitudes, and behaviors play in propagating this outbreak, we have to, for a moment, move beyond the ‘traditional’ question that we have been asked as behavioral scientists:

- **How is this pandemic affecting our mind?**
- And reverse the question, asking ourselves, our colleagues, and the entire scientific community:

- **How is our mind affecting and driving this pandemic?**
- By learning answers to this question, we contain the outbreak, save lives, and help future generations
Proactive C-L Psychiatry
Updates Course

Mark Oldham, MD
Assistant Professor of Psychiatry
University of Rochester Medical Center

ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY
Psychiatrists Providing Collaborative Care Bridging Physical and Mental Health
Disclosures – Mark Oldham

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.
Mark Oldham, MD

• Medical Director, PRIME Medicine
  – Proactive Integration of Mental Health Care in Medicine
• Chair, Proactive C-L Psychiatry SIG
• Treasurer, American Delirium Society
• Deputy Editor, *Journal of the ACLP*
Objectives

• **What’s known**: background and principles of proactive CL

• **What’s new**
  – Resources
    • APA Resource Document on Proactive C-L Psychiatry
    • CLP Advocacy Toolkit: Team-based proactive C-L psychiatry
  – Publications
    • Suburban community hospital (Kugler 2020)
    • PRIME Medicine (Oldham 2021)
    • Systematic review of randomized trials (Toynbee 2021)

• **What next**: future outcomes of interest
What’s known

What’s new

What’s next
Proactive C-L psychiatry, in a phrase

An interdisciplinary model of C-L psychiatry that incorporates systematic screening for mental health concerns, early clinical intervention and integration with primary teams with the goal of facilitating efficient care and improved outcomes.
Population impact of psychiatric comorbidity

Medical Inpatients

- 60%
- 40%

Psychiatric comorbidity

Sources: Jansen *PLOS ONE* 2018, Hansen 2001, Bourgeois *Psychosomatics* 2005
<table>
<thead>
<tr>
<th>Psychiatric condition</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental status/delirium</td>
<td>160 (10.1%)</td>
</tr>
<tr>
<td>Dementia</td>
<td>217 (13.6%)</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>592 (37.2%)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>347 (21.8%)</td>
</tr>
<tr>
<td>Psychotic disorder</td>
<td>33 (2.1%)</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>11 (0.7%)</td>
</tr>
<tr>
<td>Psychotropic medication</td>
<td>520 (32.7%)</td>
</tr>
<tr>
<td>Total screens performed</td>
<td><strong>1136 (71.4%)</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total admissions reviewed</td>
<td><strong>1590 (100%)</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values add up to more than 71.4% as categories are not mutually exclusive.

<sup>b</sup> All percentages are relative to total admissions reviewed.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Selected maladaptive features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium</td>
<td>Agitation, restlessness, confusion</td>
</tr>
<tr>
<td>Dementia</td>
<td>Forgetfulness, sundowning, care refusal</td>
</tr>
<tr>
<td>Personality Δ due to TBI</td>
<td>Emotional lability, impulsivity</td>
</tr>
<tr>
<td>Developmental disorder</td>
<td>Nonverbal, oppositional, defiant</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>Hiding food, manipulating weigh-ins</td>
</tr>
<tr>
<td>Substance use disorder</td>
<td>Exaggerating CIWAs, contraband</td>
</tr>
<tr>
<td>Psychotic disorder</td>
<td>Paranoia, cheeking medications</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>Refusing workup, overuse of call button</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>Suicidal, disruptive mania</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>Demanding, hostile, “splitting”</td>
</tr>
<tr>
<td>Munchausen syndrome</td>
<td>Self-injury, deception</td>
</tr>
</tbody>
</table>
General hospital costs of mental illness

**Hospital costs**
- Longer LOS (often 4d+\(^1\))
- Sitters & restraint use
- Poorer outcomes
- Higher readmissions

**Staff costs**
- Lack of training
- Dissatisfaction & distress
- Burnout
- Stigma & implicit bias

**Patient costs**
- Compromised care
- Mistrust of staff
- Reduced quality of life
- Functional decline

\(^1\) Jansen PLOS ONE 2018
Traditional CL Psychiatry

- Mental health care crisis-focused
- Many psychiatric needs unidentified
- Recs chiefly for primary teams
- Liaison role variable

A Modern Approach

- Prevention mindset
- Population approach
- Multidisciplinary teamwork
- Cross-specialty relationships

- Proactive care
- Systematic screening
- Interdisciplinary team
- Integrated care
Academy of Consultation-Liaison Psychiatry

1. Standardized
   - Upon admission
   - Manual vs automated

2. Case review
   - Curbsides
   - Dispo & aftercare plans

3. Corresponding expertise
   - Clinical pathways
   - Shared goals

4. Population health
   - Systematic screening

4. Prevention minded
   - Proactive care

4. Cross-specialty relationships
   - Integrated care

4. Interdisciplinary teamwork
   - C-L team

   - C-L psychiatrist
   - Psychiatric NP
   - Psychiatric SW
   - Other members

1. Population health
   - Systematic screening

2. Prevention minded
   - Proactive care

3. Cross-specialty relationships
   - Integrated care

4. Interdisciplinary teamwork
   - C-L team

1. C-L psychiatrist
   - Psychiatric NP
   - Psychiatric SW
   - Other members
## Modern proactive C-L psychiatry

<table>
<thead>
<tr>
<th>Setting</th>
<th>LOS, overall</th>
<th>LOS, consults</th>
<th>Staff satisfaction</th>
<th>Consult rate</th>
<th>Consult latency</th>
</tr>
</thead>
<tbody>
<tr>
<td>U Rochester&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Medicine</td>
<td>0.2-0.3d</td>
<td>Nursing &amp; physician</td>
<td>5-fold</td>
<td>Similar</td>
</tr>
<tr>
<td>UT Austin&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Community</td>
<td>2d</td>
<td>Nursing</td>
<td>20-fold</td>
<td>1.6d (65%)</td>
</tr>
<tr>
<td>Johns Hopkins&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Medicine</td>
<td>1.8d</td>
<td>Nursing &amp; physician</td>
<td>2-fold</td>
<td>1.2d (35%)</td>
</tr>
<tr>
<td>Stony Brook&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Medicine</td>
<td>1.1d</td>
<td></td>
<td>2-fold</td>
<td></td>
</tr>
<tr>
<td>Brigham &amp; Women’s&lt;sup&gt;5&lt;/sup&gt;</td>
<td>MICU</td>
<td>0.7d</td>
<td></td>
<td>4-fold</td>
<td>4.3d (55%)</td>
</tr>
<tr>
<td>Yale (BIT)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Medicine</td>
<td>0.3d</td>
<td>Nursing</td>
<td>Similar</td>
<td>0.5d (18%)</td>
</tr>
<tr>
<td>Yale (embedded)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Medicine</td>
<td>0.8d</td>
<td></td>
<td>2-fold</td>
<td>1.6d (53%)</td>
</tr>
</tbody>
</table>

What’s known

What’s new

What’s next
• **Resources**
  – APA Resource Document on Proactive C-L Psychiatry
  – CLP Advocacy Toolkit: Team-based proactive C-L psychiatry

• **Publications**
  – Suburban community hospital (Kugler 2020)
  – PRIME Medicine (Oldham 2021)
  – Systematic review of randomized trials (Toynbee 2021)
Special Article

Proactive Consultation-Liaison Psychiatry: American Psychiatric Association Resource Document

• **What is it?**
  – Practical overview of proactive C-L

• **What’s in it?**
  – History
  – Evidence
  – Context*
  – Team members (see Table 2)
  – Opportunities

### Proactive C-L in Practice (see Table 3)
- Yale-New Haven Hospital
- Dartmouth-Hitchcock Medical Center
- University of Rochester Medical Center
- Stony Brook University
- Johns Hopkins Hospital
- University of Pennsylvania
- University of Colorado Hospital
- University of Cincinnati
- Columbia University Irving Medical Center/NY Presbyterian Hospital
Hospital trends

1. **Triple Aim in 2007**
   - Patient experience
   - Population health
   - Per capita costs
   - (Work life of clinicians)

2. **Hospital medicine**
   - “Hospitalist” coined in 1996
   - American Board of Hospital Medicine in 2009

3. **Mid-level practitioners**
   - 2016: 2/3 hospitalist programs
   - 2018: 3/4 hospitalist programs

4. **Integrated care models**
   - CPT codes for care management services

5. **Value-based care**
   - Incentives
APA Resource Document (cont’d)

- Team members
- Team member roles
- Team compositions

<table>
<thead>
<tr>
<th>Table 2: Proactive C-L psychiatry team members</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Team member</strong></td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Attending psychiatrist</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Psychiatric nurse practitioner</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
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<tr>
<td></td>
</tr>
<tr>
<td>Clinical social worker</td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Clinical nurse specialist (optional)</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Service administrator (optional)</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Clinical health psychologist (optional)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Psychiatric and medical trainees (optional)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

C-L = consultation-liaison.
Team-based Proactive C-L Psychiatry

Integrated care meets inpatient C-L psychiatry

Mark Oldham, MD
Medical Director, PRIME Medicine
Assistant Professor of Psychiatry
University of Rochester Medical Center

H. Benjamin Lee, MD
John Romano, Professor and Chair
Department of Psychiatry
University of Rochester Medical Center
CLP Advocacy Toolkit

• Purpose
  – “The Academy has developed executive summaries and slide sets that provide evidence of the importance of including C-L Psychiatry physicians in the delivery of medical care in all settings.”

• Slide set
  – Unmet needs
  – The “business case”
  – Daily operations
  – Future horizons

• Executive summary
  – Slide-by-slide description
Publications

- Suburban community hospital (Kugler 2020)
- PRIME Medicine (Oldham 2021)
- Systematic review of randomized trials (Toynbee 2021)
Embedded psychiatrist in community hospital

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Study</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissions</td>
<td>1531</td>
<td>284</td>
<td>1294</td>
</tr>
<tr>
<td>Psychiatric or substance use</td>
<td>53%</td>
<td>51%</td>
<td>48%</td>
</tr>
<tr>
<td>Consultation rate</td>
<td>1.4%</td>
<td>33%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Consult latency</td>
<td>2.4d</td>
<td>0.8d</td>
<td>2.0d</td>
</tr>
<tr>
<td>Length of stay</td>
<td>5.0d</td>
<td>3.0d</td>
<td>5.0d</td>
</tr>
</tbody>
</table>
Embedded psychiatrist in community hospital
Original Research Article

Proactive Integration of Mental Health Care in Hospital Medicine: PRIME Medicine

Mark A. Oldham M.D. a, Valerie J. Lang M.D., M.H.P.E. b, Justin L. Hopkin M.D. b, Daniel D. Maeng Ph.D. a
PRIME Medicine

Hospital medicine samples
- PRIME: 3 NP/PA units
- Comparison: 2 Resident units

10-mos. pre–post periods
- Baseline: Sept 2017 – June 2018
- Study: Sept 2018 – June 2019

Exclusions
- LOS > 30 days, age < 18, non-ED admission source, expired, eating disorder, left AMA

Outcomes
- Primary
  - Δ in LOS (diff-in-diff)
- Secondary
  - Consult latency & volume
  - Nursing attrition
#### Consultation characteristics & context

<table>
<thead>
<tr>
<th></th>
<th>3 PRIME units</th>
<th></th>
<th>2 Comparison units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-impl.</td>
<td>Implementation</td>
<td>Pre-impl.</td>
</tr>
<tr>
<td></td>
<td>(n = 2555)</td>
<td>(n = 2296)</td>
<td>(n = 1962)</td>
</tr>
<tr>
<td>Consult latency</td>
<td>4.0d</td>
<td>3.8d</td>
<td>2.9d</td>
</tr>
<tr>
<td></td>
<td>n = 40</td>
<td>n = 176</td>
<td>n = 29</td>
</tr>
<tr>
<td>Consult rate</td>
<td>1.6%</td>
<td>7.7%</td>
<td>1.5%</td>
</tr>
<tr>
<td>ED boarding time*</td>
<td>1.6d</td>
<td>1.9d</td>
<td>1.2d</td>
</tr>
<tr>
<td>Dispo, skilled nursing*</td>
<td>7%</td>
<td>16%</td>
<td>6%</td>
</tr>
</tbody>
</table>

*Unavailable for inclusion in regression models
Nurse attrition on PRIME vs comparison units
## Length-of-stay analysis

<table>
<thead>
<tr>
<th></th>
<th>3 PRIME units</th>
<th>2 Comparison units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Implement.</td>
<td>Implementation</td>
</tr>
<tr>
<td><strong>Length of stay</strong></td>
<td>6.6d</td>
<td>6.7d</td>
</tr>
</tbody>
</table>

### Difference-in-difference analysis

- Marginal effects model: **LOS reduction of -4.4% (-0.28 day)**
- Adjusted* regression model: **LOS reduction -2.5% (-0.16 day)**

*Adjusted for age, gender, APR-DRG severity of illness category, multi-morbidity, smoking status, failure-to-thrive, cognitive disorder, mood disorder, psychotic disorder, substance use disorder, & “other mental health condition”
### LOS, regression-adjusted diff-in-diff model

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Observed</th>
<th>Expected</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-intervention (Sept 2017 – June 2018)</td>
<td>6.36</td>
<td>6.36</td>
<td>(reference)</td>
<td></td>
</tr>
<tr>
<td>Intervention (Sept 2018 – June 2019)</td>
<td>6.44</td>
<td>6.59</td>
<td>-0.16</td>
<td>0.08</td>
</tr>
<tr>
<td>Sept – Oct 2018</td>
<td>6.23</td>
<td>6.15</td>
<td>0.09</td>
<td>0.69</td>
</tr>
<tr>
<td>Nov – Dec 2018</td>
<td>6.23</td>
<td>6.43</td>
<td>-0.20</td>
<td>0.049*</td>
</tr>
<tr>
<td>Jan – Feb 2019</td>
<td>6.97</td>
<td>7.09</td>
<td>-0.12</td>
<td>0.53</td>
</tr>
<tr>
<td>March – April 2019</td>
<td>6.41</td>
<td>6.51</td>
<td>-0.10</td>
<td>0.11</td>
</tr>
<tr>
<td>May – June 2019</td>
<td>6.39</td>
<td>6.79</td>
<td>-0.41</td>
<td>0.03*</td>
</tr>
</tbody>
</table>
Take-homes from PRIME Medicine

• No more than modest LOS reduction

• Consider hospital context & workflow
  – ED boarding times & SNF placements
  – Geriatric syndromes & older adults
  – Concurrent med-psych unit

• Consult characteristics
  – Consult rate increased greater than 5-fold
  – Consult latency unchanged
  – Favorable trend in nurse attrition
Review article

The effectiveness of inpatient consultation-liaison psychiatry service models: A systematic review of randomized trials

Mark Toynbee¹,¹, Jane Walker¹,¹, Felix Clay², Laura Hollands¹, Maike van Niekerk¹, Eli Harriss³, Michael Sharpe¹,³

¹ Psychological Medicine Research, University of Oxford Department of Psychiatry, Warneford Hospital, Oxford, UK
² Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK
³ Bodleian Health Care Libraries, University of Oxford, Oxford, UK
Inpatient C-L psychiatry effectiveness

• **Objective**
  – Systematic review of randomized trials of inpatient C-L on outcomes, LOS, & healthcare costs

• **Article selection**
  – Search Ovid Medline, Ovid Embase, Ovid PsycINFO, EBSCO CINAHL
  – ~16k titles & abstracts reviewed
  – ~500 full papers reviewed
  – 8 papers included

• **Eligibility for randomization in included studies**
  – Positive for some combination of depression, confusion, anxiety, or pain \((n = 5)\)
  – Positive for “probable psychiatric illness” \((n = 2)\)
  – Patients with a safety sitter \((n = 1)\)
Inpatient C-L psychiatry effectiveness

• **Results**
  – Most recent included study: 2007
  – Half of studies in geriatric populations
  – All primary outcomes negative
  – Two secondary outcomes positive
    • Reduced depression scores
    • Higher satisfaction with care
What to make of these findings?

• These “models” could simply be ineffective

• Methodological shortcomings in prior studies
  – Were recruited patients likely to benefit?
  – Uncertain quality of C-L psychiatry delivery
  – Possible contamination bias in comparator arms
  – Limited power due to sample sizes

• More rigorous studies are needed
Outcomes of interest to be explored further

• Financial impact beyond reduced length of stay
  – Cost of sitters & security
  – Cost of nursing turnover
  – Re-admission rates
  – Enhanced RVU
• Satisfaction: providers, nurses, patients, families
• Medical staff burnout
• Medical staff performance
• Patient symptoms, functioning, and outcomes
• Care quality: injuries (patients & staff) and falls
• Handoff to outpatient providers (vertical integration)
Many questions remain

• Which elements of proactive C-L are ‘required’ and for which benefits?
• Are there more effective ways of operationalizing the principles of proactive C-L?
• What other principles have yet to be articulated?
• Which patient-specific factors (e.g., age, population) and hospital contexts (e.g., critical care, surgery) might experience differential benefits from different ways of delivering proactive C-L?
• What factors are associated with successful implementation and delivery of proactive C-L models?
Greetings from the Proactive C-L Psychiatry SIG!
Proactive C-L SIG page on ACLP website

Proactive C-L Psychiatry SIG – Resources

Home > ACLP Special Interest Groups (SIGs) > Proactive C-L Psychiatry SIG > Proactive C-L Psychiatry SIG – Resources

Proactive C-L Psychiatry SIG – Resource Center

- Launching a Proactive C-L Psychiatry Service Resource Packet
- Materials
- Publications and Articles
- Previous ACLP Presentations
Proactive C-L Psychiatry
Updates Course

Mark Oldham, MD
Assistant Professor of Psychiatry
Medical Director, PRIME Medicine
Treasurer, American Delirium Society
Deputy Editor, Journal of the ACLP

ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY
Psychiatrists Providing Collaborative Care Bridging Physical and Mental Health
Chronic Pain for the CL Psychiatrist: A Brief Review and Recent Updates

Xavier Jimenez, MD, FAACLP
Director, CL Psychiatry
Long Island Jewish Medical Center (Northwell)

ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY
Advancing Integrated Psychiatric Care for the Medically Ill
Disclosures

- No relevant financial/commercial disclosures to report.
COURSE OBJECTIVES

- Appreciate role for CL Psychiatry in assessing and managing chronic pain
- Review neurobiology and behavior psychology of chronic pain
- Explore treatment options, with emphasis on psychopharmacology
My journey...

- Psychodynamically-informed/behaviorally-interested CL psychiatrist interested in atypical medical presentations (abnormal illness behavior, somatoform/conversion disorders, factitious disorders, primary/secondary gain, personality disorders, covert/complex trauma, etc) but also cleaning up polypharmacy/delirium/addiction

- Invited to run a chronic pain department despite no pain mgmt training; quickly appreciated CL psychiatry is well-prepared for the work
  - Eventually became pain and addiction boarded

- Offered biopsychosocial evals/treatment of patients in 3 settings:
  - CL setting (“Pain-Psych” consults blending psych, pain, addiction)
  - Admission to and during chronic pain IOP (medical oversight, detox/meds, etc)
  - Individual outpatient cases for ongoing detox/med mgmt
CL Psychiatrists managing pain???

- Firstly, the target is more so **chronic** pain...
- Secondly, we can recognize/manage psych comorbidities when others cannot
- Thirdly, we are adept at psychopharmacology and detox (highly relevant)
- Fourthly, within psychiatry, we are best equipped at translating pain/neurological/medical phenomena
Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

The function of pain is to protect us against injury and create a pain “memory” so we don’t repeat a potentially harmful action.

The intensity of pain that we experience is based not only on the information between the body part and the brain, but also upon our emotional/psychological reaction to the event.
Chronic Pain as a cross-section only...

- Failure of most pain management: a cross-sectional, focal approach
- Patient presents with pain, and natural approach is to assess/treat in that moment
  - Numeric Rating Scale: 0-10/10 approach
  - Emphasis becomes acute relief
  - Acute relief = analgesics
  - Only “true” analgesics = opioids
  - Back to square one...
- Consider a broader understanding of pain
Chronic Pain ≠ Acute Pain

- Chronic Pain = Pain lasting greater than 3-6 months from acute incident, insult, injury, etc
- Acute pain resolves with the expected healing process.
- Chronic pain is maintained by something unexpected...
Mechanisms

- Complex processes and comorbidities
  - Biological: ongoing neural enhancement, *central sensitization*, comorbid diseases, physical deconditioning, etc
  - Psychological: catastrophizing, avoidance, comorbid depression, anxiety, insomnia, stress, addiction, etc
  - Social: unemployment, disability status, family effects, enabling, etc

- Complex problem requiring biopsychosocial balancing...
Pain Psychology: Pain as Experience

- **Pain Experience (or perception)** = physiology + psychology
- Central diagnostic/treatment question:
  - How much of the **pain experience** is due to physiological disturbance versus psychological disturbance?
    - If predominantly physiological: nerve blockade, neuroanatomical interventions, medications, etc.
    - If predominantly psychobehavioral: behavior modification, psychotherapy, psychiatric management, coping strategies, etc.
Pain as threat

- Pain experienced as visceral threat to bodily integrity
- Activates vigilance and worry
- Leads to cascade of psychological features
- But the patient is here for pain, not psychology!
- So *pain psychology* needs to be relevant to their *pain experience*.
Neurological Pain Signaling “Modes”

- Control state (normal)
  - Warns against repeat painful simulation

- Suppressed
  - Permits continued stimulation despite painful injury (e.g. marathon runner, boxer, ... borderline self-injury?)

- Sensitive
  - Exaggerated response to benign stimuli, excessive protection against further damage (e.g. anxiety, severe avoidance... somatic PTSD?)

- Reorganized (pathological)
  - Changes, death/restructuring/rewiring (irreversible?)
Central Sensitization

- Central sensitization (CS) involves abnormal and intense enhancement of pain in the central nervous system, characterized by both allodynia and hyperalgesia.
  - Hyperalgesia: excessive pain sensation caused by stimulus mean to cause pain (e.g. light bump hurts excessively/for prolonged state)
  - Allodynia: pain sensation caused by stimulus not meant to cause pain (e.g. light touch/clothes activates pain)

- Windup: progressive increase in pain perception with second-order neural response to repetitive stimulation (more often than every 3 seconds) of peripheral C fibers – AKA temporal summation

Woolf, 2011; Staud et al, 2007
Sensitization of CNS/brain

- Repeated hits/traumas sensitize brain structures exacerbating pain experience
- PTSD model: pain/injury/trauma activates amygdala, results in hypervigilance (so more attention directed at pain), sympathetic output (adrenergic fuel to the fire), and avoidance (to escape intolerable sensation)
- Strong neurobiological similarities in PTSD and chronic pain (central sensitization)

Moeller-Bertram et al, 2014
Academy of Consultation-Liaison Psychiatry

PAIN

Sensory Cortex

Sensory Thalamus

Shortcut

Amygdala

Presentation of PAIN

PAIN BEHAVIORS, PHYSIOLOGIC EFFECTS, SNS OUTPUT...

FINAL SUMMATIVE PAIN EXPERIENCE
Chronic Pain Treatment: Functional Restoration and Rehabilitation

- Emphasis on chronic *management*
- Target is *not cure*, but rather is *rehabilitation*
  - Medical (pharmacological, graded detox, proper psychiatric dx/tx, education)
  - Physical (reconditioning, graded exposure to movement, aerobic work, diversion, occupational tx)
  - Psychological (coping, relaxation, biofeedback, counseling, family, dynamic/process groups, communication, emotional awareness, desensitization)
- Management of all three (not just one or two legs of the stool!)
Pain psychopharmacology

- Pharmacological creativity (and off-label use) is the norm, not the exception
- Remove barriers first: benzos, opioids, MJA
- SNRIs
  - Duloxetine, Venlafaxine, Milnacipran, etc
- TCAs
  - Amitriptyline, Nortriptyline, Doxepin, etc
- Anticonvulsants
  - Gabapentinoids (Gabapentin, Pregabalin), Topiramate, Lamotrigine, Valproate, Carbamazepine, Oxcarbamazepine
- Antipsychotics
  - Atypicals mostly, low-dose (receptor heterogeneity)
- Sympathetic modulators
  - Prazosin, Clonidine (for sympathetically-maintained syndromes: PTSD, complex regional pain syndrome)
- Buprenorphine-Naloxone (Suboxone)
First (opioids), do no/less harm...

- Avoid chronic opioid therapy
  - Cite conventional concerns: dependence/addiction, risk of death
  - But more so, cite patient-centered concerns: opioid-induced hyperalgesia (“opioids are obstacle to pain management”), CNS suppression (falls, cognitive, depression, fatigue), systemic (GI, immune, endocrine), social/logistical (stigma, costly, time-consuming)

- Risk mitigation: CDC guidelines

- Method?
  - Complicated blend of MI, “neurovalidation,” pharmacology, and TIME...

  CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Dowell et al, 2016
No shortcuts...

- Hard recognition
- Time-consuming
- Requires specialized consultation, communication, and resources
Impact of Guidelines

Goldstick et al, 2021
Second (benzos), continue to do no/less harm...

- Avoid chronic benzodiazepine therapy
  - Safety: risk of overdose dramatically higher when co-administered with opioids
  - Worse outcomes
    - Benzos predict opioid use better than dose pain itself!
    - N = 17,074
    - Linked to Norwegian Prescription Database during 2004–2007
    - OR for moderate-high prescription frequency of opioids for previous BZ users was 7.7
    - Benzodiazepine users had more disability, CV disease and reported musculoskeletal pain

Skurtveit, 2010
Avoid chronic benzodiazepine therapy
- Danish Health Survey 2010 + Danish health and socio-economic registers
  - N = 13,281 individuals analyzed
  - Patients on chronic opioid therapy had 12.5 x the odds of being prescribed long-term BZs as did pain patients not receiving opioids
- Cross sectional study
  - N = 229 patients entering pain rehabilitation
  - BZ use was associated with:
    - Worse mood, pain, and function
    - Authors speculated that BZ effect was due to impaired mood, coping, cognition, ability to tolerate pain

Hojsted et al, 2013;
Third, do no/less harm...

- Cannabis/CBD efficacy in pain is meager (at best), yet harms are known and certain

- Counterpoints
  - Chronic Pain is complicated (most cannabis studies: short duration/small sample sizes, cross-sectional outcome measures, exclude psychiatric/substance use patients, etc)
  - Impact on cognition/motivation (impacts true rehabilitation/behavioral activation)
  - Not all “cannabis” is the same (semantics matter: cannabis ≠ medical marijuana ≠ CBD ≠ THC ≠ synthetic MJA ≠ other; but do non-medically trained, psychiatric/substance use populations really know the difference?
  - Youth/psychiatric at risk (evidence from medical cannabis dispensaries: younger patients used more cannabis, had higher rates of using “when bored,” and had higher rates of dependence than older patients; also high use among young men with low SES and psych/substance use disorders; add this to old evidence on serious psych disorders (schizophrenia, depression, bipolar disorder) unfolding in youth after cannabis exposure.

Jimenez, 2018; Mücke et al, 2018.
CS/Chronic Pain Psychopharmacology

- Anxiolytic
  - Benzodiazepines
  - \(\beta\)-blockers
  - AEDs
  - Neuroleptics?

- Analgesic
  - NSAIDs
  - Local anesthetics
  - Topicals
  - Antiarrhythmics
  - Opioids

- Antidepressant
  - TCAs
  - SNRIs
  - SSRIs
  - Bupropion
Antidepressant-Responsive Pain

- Neuroma
- Post-herpetic neuralgia
- Diabetic neuropathy
- Complex Regional Pain Syndrome
- Temporomandibular Joint d/o
- Fibromyalgia
- Low Back Pain

- Migraine
- Tension headache
- Phantom limb pain
- Thalamic/central pain
- Irritable Bowel Syndrome
- Vulvodynia
- Arthritis (?)
Descending Pain Inhibition

- Attention, expectations, excitement all modulate pain
- Dorsolateral funiculus (contralateral corticospinal and spinothalamic tracts)
  - Electrical / opioid stimulation of DLF → analgesia
  - Analgesia antagonized by coadministered 5-HT and NE antagonists
- SSRIs thus (mostly) ineffective in pain mgmt.

Hayashida and Obata, 2019
Tricyclic Antidepressants

<table>
<thead>
<tr>
<th>Tertiary Amine TCAs</th>
<th>Reuptake Mechanism*</th>
<th>Sedation</th>
<th>Hypo-Tension</th>
<th>Seizures</th>
<th>Weight</th>
<th>Cardiac</th>
<th>Initial/Max Dosing (for MDD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>5HT &gt; NE</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>25-75mg/200mg daily</td>
</tr>
<tr>
<td>Clomipramine (Anafranil)</td>
<td>5HT &gt; NE</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>25mg/250mg daily</td>
</tr>
<tr>
<td>Doxepin (Sinequan)</td>
<td>5HT = NE</td>
<td>++++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>50-75mg/300mg nightly</td>
</tr>
<tr>
<td>Imipramine (Tofranil)</td>
<td>5HT = NE</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>50-100mg/200mg daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Amine TCAs</th>
<th>Reuptake Mechanism</th>
<th>Sedation</th>
<th>Hypo-Tension</th>
<th>Seizures</th>
<th>Weight</th>
<th>Cardiac</th>
<th>Initial/Max Dosing (for MDD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desipramine (Norpramin)</td>
<td>NE &gt; 5HT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>100-200mg/300mg daily</td>
</tr>
<tr>
<td>Maprotiline (Ludiomil)</td>
<td>NE &gt; 5HT</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>25mg-50mg/225mg nightly</td>
</tr>
<tr>
<td>Nortriptyline (Pamelor)</td>
<td>NE &gt; 5HT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>25-50mg/150mg daily</td>
</tr>
</tbody>
</table>

*Tertiary amine TCAs tend to preferentially inhibit serotonin reuptake (resulting in greater synaptic serotonin levels), whereas secondary amine TCAs tend to preferentially inhibit norepinephrine reuptake (resulting in greater synaptic norepinephrine levels). 5HT = serotonin; NE = norepinephrine; MDD = major depressive disorder.

Schneider et al, 2019
<table>
<thead>
<tr>
<th>Indication</th>
<th>Medication(s)</th>
<th>Initial/Max Dosing</th>
<th>Dose Rate/Limits</th>
<th>Side Effect Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache/Migraine</td>
<td>Amitriptyline</td>
<td>10–25mg/100mg nightly</td>
<td>Individualized: 10–25mg increase every 5–14 days; assess for tolerability/side effects</td>
<td>Dry mouth/secretions: pilocarpine 5mg 2-3/day</td>
</tr>
<tr>
<td>Neuropathic Pain</td>
<td>Amitriptyline</td>
<td>25–50mg/150mg nightly (vs divided into twice daily doses if frequent pain/symptom flares)</td>
<td></td>
<td>Constipation: stool softeners such as docusate sodium or senna glycoside</td>
</tr>
<tr>
<td>Chronic Low Back Pain</td>
<td>Amitriptyline, Maprotiline</td>
<td>25–50mg/150mg nightly</td>
<td>Amitriptyline side effects (dry mouth, orthostasis) often limit dose escalation above 100mg; Nortriptyline vs Maprotiline may be considered (better tolerated at higher doses)</td>
<td>Weight gain: consider augmenting with metformin 500-1000mg daily or topiramate 50-100mg/day</td>
</tr>
<tr>
<td>Fibromyalgia/Chronic Widespread Pain</td>
<td>Amitriptyline, Nortriptyline, Maprotiline</td>
<td>25–50mg/150mg nightly (vs divided into twice daily doses if frequent pain/symptom flares)</td>
<td></td>
<td>Seizures, QT interval prolongation, active suicidal risk, and/or orthostasis/falls: discontinue TCA</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome</td>
<td>Amitriptyline, Nortriptyline</td>
<td>10-25mg/100mg nightly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclic Vomiting Syndrome</td>
<td>Amitriptyline, Nortriptyline</td>
<td>25–50mg/100mg nightly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Pelvic Pain/Interstitial Cystitis/Nocturia</td>
<td>Amitriptyline, Nortriptyline, Imipramine</td>
<td>10-25mg/100mg nightly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>Amitriptyline, Maprotiline, Doxepin</td>
<td>25–50mg/150mg nightly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Serotonin-Norepinephrine Reuptake Inhibitor

- High promise/potential
  - Combining efficacy of tricyclic antidepressants (older) for pain with safe side effect profile of SSRIs (newer)
  - But efficacy questionable...
  - Conclusion: Duloxetine/Milnacipran not significantly better than placebo

Welsch et al, 2018
Serotonin-Norepinephrine Reuptake Inhibitor

- Venlafaxine (Effexor)
- Duloxetine (Cymbalta)
- Milnacipram (Savella)
- Desvenlafaxine (Pristiq)
- Levomilnacipram (Fetzima)

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Suggested Dose for Neuropathic Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary-Amine TCAs</strong></td>
<td></td>
</tr>
<tr>
<td>Desipramine</td>
<td>10-25 mg/day; titrate up to 300 mg/day</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10-150 mg/day</td>
</tr>
<tr>
<td><strong>Tertiary-Amine TCAs</strong></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10-25 mg/day; titrate up to 150 mg/day</td>
</tr>
<tr>
<td>Imipramine</td>
<td>10-150 mg/day</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>60-120 mg/day</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Initially 37.5-75 mg/day; mean dose 225 mg/day; max 375 mg/day</td>
</tr>
</tbody>
</table>

max: maximum; SNRI: serotonin-norepinephrine reuptake inhibitor; TCA: tricyclic antidepressant.
A word about SNRIs...

- Cymbalta: its in the water!
- Think more creatively, especially at an academic tertiary care hospital
- Cymbalta: OK for depression, mediocre for anxiety, OK for pain. Reasonable for depressed + mild-to-moderate pain cases
- NOT reasonable for other psychiatric concerns and/or severe pain cases (most of our cases in busy tertiary care centers)
- Instead, look at the psychiatric priority
### Chronic Pain and Psych Comorbidity

**DEPRESSION**
- Spinal pain 2%-56%,
- Fibromyalgia 21%-83%,
- Pelvic pain 19%-22%
- Abdominal pain 9%-54%,
- Arthritis 3%-39%

**ANXIETY**
- Spinal pain 1%-26%,
- Neuropathic pain 5%-27%,
- Fibromyalgia 18%-60%
- Pelvic pain 12-41%,
- Abdominal pain 21%-51%,
- Arthritis 1%-35%

Hooten, 2016
A word on SSRIs...

- Don’t forget them!
- High safety profile
- When dosed appropriately, excellent anxiolytics (better than Cymbalta!)
- If problem is predominantly anxiety/panic/PTSD/hypervigilance, do you even need analgesia?
  - Dose aggressively (e.g. Prozac/Paxil 20mg x 2 weeks, then up to 40mg x 4 weeks)
  - Avoid “ginger”/overly-cautious dosing
    - These are anxious patients – they need results!
Bupropion?

- Modest impact on neuropathic pain
- Average decrease in numeric pain score on bupropion was 1.7 compared to placebo
- No role in chronic pain (except if dealing with severe depression, fatigue, etc).

Shah and Moradimehr, 2010
Anticonvulsant-Responsive Pain

- Trigeminal/cranial neuralgias
- Paroxysmal pain
- Lightning pains – MS
- Post-herpetic neuralgia
- Diabetic neuropathy
- Vascular headache
- Fibromyalgia
- Plexopathy

- Myelopathy
- Phantom limb pain
- Thalamic/central pain
- Traumatic neuropathy
- Tumor invasion/compression

Dosenovic et al, 2018
- Na+ Channel Blockers
- GABAergic Agents
- Mixed action

Dosenovic et al, 2018
**Gabapentin (Neurontin)**

- **MOA**
  - Binds to α2δ subunit of Ca++ channels → reduces membrane Ca density → decreased glutamate/substance P release
  - Supraspinally activates descending noradrenergic system via inhibition of presynaptic GABA

- **Evidence:** Postherpetic neuralgia, diabetic neuropathy, migraine prophylaxis, spinal cord injury, Guillain Barre, lumbar canal stenosis, HIV neuropathy, fibromyalgia, alcohol/benzo/opiate, sedative withdrawal, anxiety/PTSD, insomnia, etc

- **Use:** TID +/- PRN dosing.
  - Max dose 3600mg/day (rest is excreted renally)
  - Dose clinically (assess for effect; use alcohol effects as guide → “cheap date?”)

- **Problems**
  - Cleared renally, adjust dose or avoid in CKD
  - Sedation (but short half-life/duration), confusion in elderly
  - Rare (though increasing) dependence/addiction/abuse), rare/no drug-drug interactions

Dosenovic et al, 2018
Pregabalin (Lyrica)

- **MOA**
  - Similar to gabapentin; anxiolytic, analgesic, anticonvulsant

- **Use**
  - Postherpetic neuralgia, diabetic neuropathy, fibromyalgia
  - Failed in LBP and sciatica
  - Dose: 50 BID/TID, increase gradually (2 weeks) to 150 BID/TID.
  - Max 600mg/day

- **Problems**
  - Sedation
  - Delirium/AMS
  - Swelling, peripheral edema
  - Weight gain
  - Rare withdrawal encephalopathy
  - Minimal hepatic metabolism/protein binding
  - Monitor in CKD/ESRD

Dosenovic et al, 2018
Topiramate (Topamax)

- **MOA**
  - blocks voltage-gated Na+ channels
  - Increases GABA activity (GABA-A)
  - AMPA glutamate receptor blockade

- **Use**
  - Migraine prophylaxis, chronic low back pain (other neuropathic pains?)
  - Dose: 50mg/day to 300mg/day

- **Problems**
  - Weight loss
  - Renal calcifications (watch out in renally impaired or hx of nephrolithiasis)
  - Cognitive slowing (“Dopamax”) – 15%, dose dependent
  - Dizziness, somnolence, mood effects

Will et al, 2018
Carbamazepine (Tegretol)

- Older, more complex
  - Auto-induces metabolism, requires monitoring (myelosuppression, hepatic burden), drug-drug interactions

- Effective
  - Indicated: trigeminal / glossopharyngeal neuralgia
  - Paroxysmal pains (tabes dorsalis, MS)
  - Diabetic neuropathy, post-herpetic neuralgia, phantom limb pain, fibromyalgia
  - Wiffen, 2014

- Ineffective in central post-stroke pain – only 5/15 responded

Wiffen, 2014
Oxcarbamazapine (Trileptal)

- Minimal CYP 450 interactions (compared to CBZ)
- Doesn’t induce its own metabolism
- No liver/heme monitoring needed
- Hyponatremia risk
- Inhibits high-frequency nerve firing
- Relieves trigeminal neuralgia refractory to CBZ
- Effective: neuropathic pain
- Ineffective: diabetic neuropathy

Dosenovic et al, 2018
Lamotrigine (Lamictal)

- **MOA**
  - Slows recovery of voltage-gated Na+ channels
  - Decreased repetitive firing
  - Decreased glutamate release

- **Use**
  - Mixed results for traumatic/trigeminal neuralgia, HIV neuropathy, fibromyalgia, etc
  - + use in post-stroke central pain

- **Difficulties**
  - Rash/Stevens-Johnson’s syndrome (1/1000; children: 1/50)
    - Usually “warning rash”
    - Slow titration – start low/go slow; no rush, no rash
    - More likely if combined with other anticonvulsant
    - Effective pain dose ranges: 200-400mg/day

Wiffen, 2013
Valproic Acid (Depakote)

- **MOA**
  - GABA transaminase inhibition

- **Use**
  - Migraine prophylaxis vs acute abortion (500mg IV x 1)
  - Mixed neuropathic pain

- **Problems**
  - Platelet suppression
  - Acute liver injury/hyperammonemia
  - Toxicity: check trough, aim between 50-150

Dosenovic et al, 2018
Lithium?

- Classically, effective in chronic cluster headaches
- Equally effective as methysergide and ergotamine
- Strong anti-suicidal effects; important in refractory/unrelenting chronic pain with SI

Tfelt-Hansen and Jensen, 2012
Antipsychotics

- Dopamine antagonists
- Typical (first generation) and atypical (second generation)
- Atypicals have heterogeneous receptor action (5HT, histamine, Ach, etc)
- For pain: dosing much under that used in psychosis/bipolar disorder
- Consider comorbidities (mood/anxiety/sleep disorder)
  - Ex: Olanzapine (Zyprexa) 5-10mg daily (2.5 BID, or 2.5 AM and 5 HS, etc); Quetiapine (Seroquel) 25mg PO TID
  - Problems (dose dependent): weight gain/metabolic syndrome; QTc prolongation
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Pain Syndrome</th>
<th>Study Design</th>
<th>n</th>
<th>Efficacy</th>
<th>Measure</th>
<th>Limitations</th>
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</thead>
<tbody>
<tr>
<td>Kiser et al</td>
<td>2001</td>
<td>Fibromyalgia</td>
<td>Case series</td>
<td>2</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
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<tr>
<td>Rico-Villademoros et al</td>
<td>2005</td>
<td>Fibromyalgia</td>
<td>Case series</td>
<td>25</td>
<td>Effective</td>
<td>CGI</td>
<td>High dropout rate, side effects</td>
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<tr>
<td>Freedenfeld et al</td>
<td>2006</td>
<td>Fibromyalgia</td>
<td>Retrospective</td>
<td>51</td>
<td>Effective</td>
<td>BPI</td>
<td>Study design, side effects</td>
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<tr>
<td>Rozen</td>
<td>2001</td>
<td>Headache, cluster</td>
<td>Case series</td>
<td>5</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
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<tr>
<td>Silberstein et al</td>
<td>2002</td>
<td>Headache, migraine</td>
<td>Retrospective</td>
<td>50</td>
<td>Effective</td>
<td>Headache severity, frequency</td>
<td>Study design</td>
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<td>Bober and Star</td>
<td>2005</td>
<td>Headache, atypical</td>
<td>Case report</td>
<td>1</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
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<tr>
<td>Hill et al</td>
<td>2008</td>
<td>Headache</td>
<td>RCT</td>
<td>87</td>
<td>Effective</td>
<td>VRS, VAS</td>
<td>Equal response/effect as droperidol</td>
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<tr>
<td>Khojainova et al</td>
<td>2002</td>
<td>Cancer pain (mixed)</td>
<td>Case series</td>
<td>8</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
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<tr>
<td>Gorski et al</td>
<td>2003</td>
<td>Chronic pain (mixed)</td>
<td>Case series</td>
<td>3</td>
<td>Effective</td>
<td>Patient report, decreased opiate use</td>
<td>Sample size, uncontrolled, heterogeneous syndromes</td>
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<tr>
<td>Gick et al</td>
<td>2004</td>
<td>Glossodynia</td>
<td>Case report</td>
<td>1</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
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</table>

Jimenez et al, 2018
### Quetiapine

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Syndrome</th>
<th>Study Design</th>
<th>n</th>
<th>Efficacy</th>
<th>Measure</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Hidalgo et al</td>
<td>2007</td>
<td>Fibromyalgia</td>
<td>Case series</td>
<td>35</td>
<td>Ineffective (pain)</td>
<td>CGI, FIQ</td>
<td>Uncontrolled</td>
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<tr>
<td>Krymchantowski et al</td>
<td>2011</td>
<td>Migraine</td>
<td>Case series</td>
<td>29</td>
<td>Effective</td>
<td>Patient report</td>
<td>High dropout rate, side effects, uncontrolled</td>
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<tr>
<td>Potvin et al</td>
<td>2012</td>
<td>Fibromyalgia</td>
<td>RCT, DB</td>
<td>51</td>
<td>Ineffective</td>
<td>CGI, FIQ</td>
<td></td>
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<tr>
<td>McIntyre et al</td>
<td>2014</td>
<td>Fibromyalgia (with MDD)</td>
<td>RCT, DB</td>
<td>120</td>
<td>Effective</td>
<td>HAM-D, CGI, BPI, FIQ</td>
<td>Primary endpoint MDD treatment</td>
</tr>
</tbody>
</table>

### Risperidone

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Syndrome</th>
<th>Study Design</th>
<th>n</th>
<th>Efficacy</th>
<th>Measure</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe-Bornstein et al</td>
<td>2002</td>
<td>Chronic pain (with MDD)</td>
<td>Case series</td>
<td>2</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled, primary endpoint MDD treatment</td>
</tr>
</tbody>
</table>

### Aripiprazole

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Syndrome</th>
<th>Study Design</th>
<th>n</th>
<th>Efficacy</th>
<th>Measure</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kasahara et al</td>
<td>2011</td>
<td>Chronic pain, mixed</td>
<td>Case series</td>
<td>4</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
</tr>
<tr>
<td>Fei et al</td>
<td>2012</td>
<td>Chronic pain, mixed</td>
<td>Case series</td>
<td>5</td>
<td>Effective</td>
<td>Patient report</td>
<td>Sample size, uncontrolled</td>
</tr>
</tbody>
</table>

### Ziprasidone

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Syndrome</th>
<th>Study Design</th>
<th>n</th>
<th>Efficacy</th>
<th>Measure</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calandre et al</td>
<td>2007</td>
<td>Fibromyalgia</td>
<td>Case series</td>
<td>32</td>
<td>Ineffective</td>
<td>CGI, FIQ, PSQI</td>
<td>Uncontrolled</td>
</tr>
</tbody>
</table>

Other atypical antipsychotic studies in pain syndromes (less efficacy than olanzapine)
Sympathetic Modulators

- Adrenergic system implicated in many pain syndromes (e.g. CRPS/RSD) as well as comorbidities (PTSD/anxiety/panic)
- Heightened sympathetic nervous system results in increased attention/vigilance to pain, poor sleep (unrefreshed to deal with pain), and kinesiophobia (avoidance of movement 2/2 fear).
- Consider Propranolol, Clonidine, etc.
  - Clonidine PO vs patch; good for anxiety/cravings/insomnia
- Prazosin for nightmares – good in PTSD; FDA approved (1-10mg QHS, assess response, slowly titrate as needed) – watch for hypotension, orthostasis/falls
Suboxone (buprenorphine-naloxone)?

- 1 (small) study showed promise

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Patient Population</th>
<th>Study Duration</th>
<th>N</th>
<th>Route and Dose</th>
<th>Comparator</th>
<th>Scale</th>
<th>Mean/Median Pain Score</th>
<th>Outcome and Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neumann et al(^9)</td>
<td>2013</td>
<td>Chronic nonmalignant pain related to the spine or a large joint</td>
<td>6 mo</td>
<td>54</td>
<td>Average daily sublingual dose of buprenorphine/naloxone was 14.93 mg/3.73 mg</td>
<td>Oral methadone (20–60 mg, divided 3–4 times daily)</td>
<td>NRS</td>
<td>5.5 ± 1.9 after 6 mo compared to initial visit (6.3 ± 1.2)</td>
<td>There was significant difference in pain relief for both buprenorphine and methadone treatment groups ((P = .043))</td>
</tr>
</tbody>
</table>

Aiyer, 2018
Suboxone (buprenorphine-naloxone)?

- N= 37 with CNCP and OUD on full agonist opioid (mean MED 300mg+) to Suboxone

- Are we just treating a variant of opioid use disorder?

Schellekens et al, 2021
Conclusions/Summary

- Chronic Pain ≠ Acute Pain...
  - Consider biopsychosocial targets
- Consider actual summative pain experience (fear? Anger? Depression?)
- Understand pathophysiology: central sensitization, PTSD, pain psychology ABCs
- What is the tx priority? Psychiatric?
- Explore psychopharmacological options with creativity and confidence
- Pair your interventions with physical and psychological rehabilitative efforts (including iCPRP). Refer intelligently.
- “Neurovalidate” the patient, employ MI, etc...
References

References

References


References

ACLP Updates Course 2021

Perinatal Psychiatry and Women's Health: Updates in the Time of COVID-19, Health Disparities, and Maternal Mortality

ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY
Advancing Integrated Psychiatric Care for the Medically Ill
Priya Gopalan, MD FAACLCP
Associate Professor of Psychiatry and OB-GYN
Medical Director, Psychiatry Consultation-Liaison Service
Chief of Psychiatry, Magee-Womens Hospital
CLP 2021
Disclosure: Priya Gopalan, MD

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.
Objectives

- Appreciate recent trends in maternal morbidity and mortality
- Acknowledge clinical challenges associated with medication discontinuation
- Discuss COVID-19 effects on women's mental health
- Recognize health care disparities in women's health and perinatal health
- Review novel, rapid-acting antidepressant medications in perinatal care
Maternal Mortality/Morbidity

Figure 4. Leading Underlying Causes of Pregnancy-Related Deaths*

- Hemorrhage: 14.0%
- Cardiovascular and Coronary Conditions: 14.0%
- Infection: 10.7%
- Cardiomyopathy: 10.7%
- Embolism: 8.4%
- Preeclampsia and Eclampsia: 7.4%
- Mental Health Conditions: 7.0%

* CDC Foundation Report from Nine MMRCs

1) **Pregnancy-related death:** CDC defines pregnancy-related death as “the death of a woman while pregnant or within one year of the end of a pregnancy – regardless of the outcome, duration, or site of the pregnancy – from any cause related to or aggravated by the pregnancy or its management.” An example of pregnancy-related death would be a maternal death from a complication of eclampsia.²

2) **Pregnancy-associated but not related death:** CDC defines pregnancy-associated but not related death as “the death of a woman while pregnant or within one year of termination of pregnancy from any cause, which is not a cause of pregnancy or illness exacerbated by pregnancy.”² An example of pregnancy-associated but not related death is maternal death from a motor vehicle accident.
Figure 11. Leading Causes of Pregnancy-Associated Deaths in Pennsylvania, 2013 – 2018 (N=547)

- **Neoplasm**: 13 (2%)
- **Other symptom, sign and lab abnormality**: 14 (3%)
- **Circulatory System**: 24 (5%)
- **Indirect OB Deaths**: 27 (5%)
- **Intentional Self-harm**: 41 (8%)
- **Assault**: 44 (8%)
- **Transportation Accident**: 55 (10%)
- **Other Pregnancy related**: 62 (11%)
- **Direct OB Deaths**: 72 (13%)
- **Accidental Poisoning**: 162 (30%)

**Total Counts**

Note: Numbers rounded to the nearest whole.

Data Source: DOH Bureau of Health Statistics & Registries
Ms. A is a 28 year old female G2P1 who you see after an admission to the obstetrical hospital after a positive pregnancy test. She presents to you at approximately 10 weeks gestation. She reports to you that this was an unplanned, wanted pregnancy and that she has limited supports.
Ms. A has no significant past medical history. She has a psychiatric history significant for postpartum depression after her last pregnancy and one other depressive episode in her teenage years. She denies use of alcohol, cocaine, heroin, and marijuana.
You refer Ms. A to a perinatal psychiatry clinic for counseling due to her psychiatric risk factors. As you are wrapping up the visit, she mentions that she had actually been on fluoxetine 40 mg daily prior to pregnancy, but stopped 2 weeks prior due to concerns around medication use in pregnancy.
5x ↑ risk of relapse with discontinuation

50% of discontinuers depressed by 2nd trimester

- Cohen et al. JAMA 2006
Lithium
Study of 25 pregnant patients with ADHD and no change in antidepressant dosing.

- Baker et al. Journal of Attention Disorders 2020
Ms. A was restarted on fluoxetine 40 mg daily. She sees your colleague at 30 weeks’ gestation and states that her depression has recurred and she is very worried about postpartum depression. She notes that her first postpartum period with her now-3 year old was very difficult, and she had significant challenges with bonding with her newborn. She wants to do anything to avoid this scenario but is also worried about dose increases.
Medication Titration

- Total of 367 pregnant women
- 38 on antidepressants at beginning of pregnancy but discontinued by end of 2nd trimester
- 180 used antidepressants continuously
- Among continued users, 46 modified antidepressant dosage
Medication Titration

- Adjusted for confounders including maternal depression/anxiety before pregnancy
- Compared to non-users, discontinued 5.95x more at risk of depression in the 2nd half of pregnancy (95%CI: 1.54-23.02)
- Continued users without dosage changes 4.59x more at risk of depression in 2nd half of pregnancy (95%CI: 1.44-14.64)
191 unique studies; 195,751 unique mother-child dyads

Maternal perinatal depression/anxiety associated with poor offspring development

- Social-emotional
- Cognitive
- Language
- Motor
- Adaptive behavior

Findings extended beyond infancy, into childhood and adolescence

- Rogers et al.  
  JAMA Pediatrics 2020
Academy of Consultation-Liaison Psychiatry

Bowers and Yehuda, Nature 2015; https://www.nature.com/articles/npp2015247
Window of Opportunity
Case Control Studies

- Not depressed
  - Not on medications
- Depressed mothers
  - Not on medications
- Depressed mothers
  - On medications
In the majority of studies, when underlying confounders are accounted for, the associations disappear!
At her next visit, Ms. A shares that her depression has improved, but she has experienced increased anxiety around the COVID-19 pandemic. She wonders if there is a connection between COVID-19 and increased depression or anxiety and notes that her pregnant friends are similarly struggling.
Prevalence of depression symptoms in US adults during the Coronavirus Disease 2019 (COVID-19) Pandemic

- 8.5% before COVID-19 to 27.8% during

Women more likely to have depression symptoms than men

<table>
<thead>
<tr>
<th></th>
<th>Pre-Pandemic</th>
<th>Pandemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>10.1%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Men</td>
<td>6.9%</td>
<td>21.9%</td>
</tr>
</tbody>
</table>

The impact of the COVID-19 pandemic on the perinatal mental health of women

- Patient Health Questionnaire Anxiety-Depression Scale (PHQ-ADS)
- 288 completed
- 34.4% anxiety and 39.2% depression symptomatology
- Rates much higher than pre-pandemic (3.1% pre-pandemic mental health concerns)
• Review of 23 studies
• 20,569 participants
• Prevalence rates of anxiety, depression, psychological distress, and insomnia
Review article

Health risks and outcomes that disproportionately affect women during the Covid-19 pandemic: A review

Jade Connor\textsuperscript{a,*}, Sarina Madhavan\textsuperscript{a}, Mugdha Mokashi\textsuperscript{a}, Hanna Amanuel\textsuperscript{a}, Natasha R. Johnson\textsuperscript{a,b}, Lydia E. Pace\textsuperscript{a,c,d}, Deborah Bartz\textsuperscript{a,b,d}
% who say that are very or somewhat worried about the following

- They or someone in their family will get sick from COVID-19
- They will lose income due to workplace closure or reduced hours because of COVID-19
- They would put themselves at risk of exposure to COVID-19 because they can't afford to stay home and miss work
- They will not be able to afford testing or treatment for COVID-19 if they need it
- Their investments such as retirement or college savings will be negatively affected by COVID-19
- COVID-19 has had a negative impact on their mental health

COVID-19 and Trauma

Alarming trends in US domestic violence during the COVID-19 pandemic

Brad Boserup, PhD; Mark McKenney, MD, MBA; Adel Elbuli, MD, MPH

- Review of police data from stay-at-home orders
- Jefferson, AL; Portland, OR; San Antonio, TX; NYC, NY
COVID-19 and Trauma

PERCENT INCREASE IN DOMESTIC VIOLENCE 2020

Jefferson, Alabama
Portland, Oregon
San Antonio, Texas
New York City
Ms. A is admitted for induction of labor at 39 weeks gestation. She reports to you on arrival that her depression remains improved, but she has a couple of concerns for you. First, she asks you about health care disparities with postpartum depression.
Compared to white women, a Black woman is

69% more likely to die from CAD

352% more likely to die from HTN

12x more likely to die from pregnancy- and childbirth-related causes

https://www.pcdc.org/covid-19-disparities-new-york-testimony/?creative=440829519542&keyword=covid-19%20disparities&matchtype=b&network=g&device=c&gclid=Cj0KCQiAw_H-BRD-ARIsALQE_2ObQxu0u-ur6D6Zq5eH4ShcH4_PL0ZiuyAgcNbGcbBW4k5p89sQXNYaAj4xEALw_wcB
2010–2014: 41,000 deaths from breast cancer each year

Breast cancer mortality 41% higher in black women

Source: CDC’s National Program of Cancer Registries and the National Cancer Institute’s Surveillance, Epidemiology, and End Results Program.

Abbreviation: AAPC=Average annual percentage change

https://www.cdc.gov/mmwr/volumes/65/wr/mm6540a1.htm#F1_down
Black mothers are much more likely than White mothers to suffer from PMADs like postpartum depression.

Risk factors include:

- Lack of access to high-quality medical care
- Higher risk of pregnancy and childbirth complications
- Lack of social support
- Gaps in medical insurance
- Financial barriers, including lack of PTO
- Unsafe neighborhoods
- Increased stress
- Exposure to trauma
US Black/Latina women have a much higher prevalence of postpartum depression (PPD) compared to White mothers. The prevalence is 35-67% compared to 10-15%.

Risk factors include:
- Lack of access to high-quality medical care
- Higher risk of pregnancy and childbirth complications
- Lack of social support
- Gaps in medical insurance
- Financial barriers, including lack of PTO
- Unsafe neighborhoods
- Increased stress
- Exposure to trauma
Health Care Disparities

- BIPOC identified at ↓ rates for perinatal mood and anxiety disorders
- Screening tools designed for white women
- Fear of repercussions
  - CYF disproportionately removes Black children from homes
  (https://www.childwelfare.gov/pubpdfs/racial_disproportionality.pdf)
**Table 2**

Outcomes for low-income white, black, and Latina women who initiated treatment for postpartum depression within six months of delivery

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Whites (N=13,001)</th>
<th>Blacks (N=13,416)</th>
<th>Latinas (N=3,154)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initiated care for postpartum depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>1,120</td>
<td>558</td>
<td>162</td>
</tr>
<tr>
<td>%</td>
<td>9</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>AOR</td>
<td>.43</td>
<td>.39–.48</td>
<td>.59</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.001</td>
<td></td>
<td>.49–.69</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Type of care initiated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any antidepressant</td>
<td>1,069</td>
<td>546</td>
<td>159</td>
</tr>
<tr>
<td>%</td>
<td>95</td>
<td>96</td>
<td>98</td>
</tr>
<tr>
<td>AOR</td>
<td>1.34</td>
<td>.79–2.26</td>
<td>2.62</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.01</td>
<td></td>
<td>.50–8.59</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any mental health outpatient visit</td>
<td>1,056</td>
<td>553</td>
<td>157</td>
</tr>
<tr>
<td>%</td>
<td>94</td>
<td>97</td>
<td>97</td>
</tr>
<tr>
<td>AOR</td>
<td>2.19</td>
<td>1.23–3.92</td>
<td>1.81</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.01</td>
<td></td>
<td>.71–4.60</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>730</td>
<td>316</td>
<td>89</td>
</tr>
<tr>
<td>%</td>
<td>65</td>
<td>56</td>
<td>55</td>
</tr>
<tr>
<td>AOR</td>
<td>.66</td>
<td>.53–.81</td>
<td>.67</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.001</td>
<td></td>
<td>.48–.94</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Medication refill</td>
<td>471</td>
<td>124</td>
<td>43</td>
</tr>
<tr>
<td>%</td>
<td>44</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>AOR</td>
<td>.37</td>
<td>.29–.47</td>
<td>.43</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.001</td>
<td></td>
<td>.29–.63</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Second mental health outpatient visit</td>
<td>395</td>
<td>236</td>
<td>59</td>
</tr>
<tr>
<td>%</td>
<td>37</td>
<td>43</td>
<td>38</td>
</tr>
<tr>
<td>AOR</td>
<td>1.20</td>
<td>.96–1.50</td>
<td>1.10</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.001</td>
<td></td>
<td>.77–1.57</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continued care</td>
<td>386</td>
<td>179</td>
<td>42</td>
</tr>
<tr>
<td>%</td>
<td>35</td>
<td>32</td>
<td>26</td>
</tr>
<tr>
<td>AOR</td>
<td>.81</td>
<td>.65–1.02</td>
<td>.67</td>
</tr>
<tr>
<td>95% CI</td>
<td>&lt;.10</td>
<td></td>
<td>.46–.99</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

\(a\) Odds ratios and 95% confidence intervals are from logistic regression models, all of which included an intercept term and controlled for age at delivery, drug dependency, high-risk pregnancy, cesarean delivery, preterm delivery, and diabetes. All outcomes were evaluated within an acute treatment phase of 120 days after initiation.

\(b\) Evaluated within an acute treatment phase of 120 outpatient days after initiation, which was indicated by receipt of an antidepressant medication or mental health outpatient visit in the six months after delivery.

\(c\) Attained by either a second outpatient visit or a refill of a prescription for antidepressant medication.

\(d\) At least three antidepressant prescription refills or three outpatient visits during the acute treatment phase.

**BIPOC women less likely to initiate postpartum mental health treatment (9% white; 4% Black; 5% Latina; \(p<0.001\))**

Mary Peeler MD, MPH, Munish Gupta MD, Patrice Melvin MPH, Allison S. Bryant MD, MPH, Hafsatou Diop MD, MPH, Ronald Iverson MD, MPH, Katherine Callaghan ... (show all authors)

[+ ] Author affiliations, information, and correspondence details

Accepted: July 20, 2020 Published Online: November 12, 2020
• 1710 deliveries
  • 89.3% (n = 1527) non-Hispanic white
  • 3.3% (n = 57) non-Hispanic Black
  • 7.4% (n = 126) Hispanic
Significant differences ($P < .001$) in use of MOUD during pregnancy by race/ethnicity

- 88.9% (n = 1357) of non-Hispanic white women receiving any MOUD
- 75.4% (n = 43) non-Hispanic Black women
- 77.0% (n = 97) of Hispanic women

Non-Hispanic Black and Hispanic women more likely to receive methadone than buprenorphine ($P < .001$)
Telepsychiatry in Peripartum Mothers

- Shore et al. Psychiatric Services 2020
  - Telepsychiatry in integrated care (OP)
  - 96% treatment engagement
  - Low ED utilization rates, high breastfeeding rates in depressed moms

- Nair et al. J Telemed Telecare 2018
  - Meta-analysis of 8 studies
  - Improved depression scores with outpatient telepsychiatry
Ms. A has a spontaneous vaginal delivery with no complications. When you see her 6 weeks later, she tells you she has been having had difficulty with low mood, anhedonia, hopelessness, and some difficulty with bonding with her baby. She has remained on her fluoxetine and continued psychotherapy. She asks you about new medications she’s heard about: brexanolone and zuranolone.
**F.D.A. Approves First Drug for Postpartum Depression**

The medication works quickly, within 48 hours. But it’s an expensive infusion and requires a stay in a medical center.
- Mechanistically driven neurosteroid treatment
- Rapid ↓ symptoms in postpartum women with moderate to severe MDD
- 60-hour infusion
- Requires medical hospitalization to monitor for excessive sedation and loss of consciousness (REMS)
Phase 2 studies showed early 60-hour and sustained 30-day reduction in HAM-D scores (12 points)

Larger phase 3 studies show a 2.5-5.5 point separation

Not consistently confirmed by secondary instruments (EPDS, PHQ-9)
• 4% in Phase 3 trials with loss of consciousness
• Potent GABA-A agonist
• Requires hospital to monitor for excessive sedation, loss of consciousness
• Requires enrollment in Risk Evaluation and Mitigation Strategies (REMS)
Hot off the Presses
Multisite phase 3, double-blind, randomized, outpatient, placebo-controlled clinical trial; 153 randomized patients

Zuranolone 30 mg PO QHS x 2 weeks

Significant day 15 HAMD-17 score improvements from baseline vs placebo (−17.8 vs −13.6; 95% CI, −6.9 to −1.5; p = .003)

Differences in HAMD-17 scores observed day 3 (difference, −2.7; 95% CI, −5.1 to −0.3; p=.03)

Sustained through day 45 (difference, −4.1; 95% CI, −6.7 to −1.4; p = .003)
A phase 1 double-blind, placebo-controlled study of zuranolone (SAGE-217) in a phase advance model of insomnia in healthy adults

Amy Bullock | Handan Gunduz-Bruce | Gary K. Zammit | Min Qin | Hailong Li | Abdul J. Sankoh | Christopher Silber | Stephen J. Kanes | Jeffrey Jonas | James Doherty
FDA NEWS RELEASE

FDA approves new treatment for hypoactive sexual desire disorder in premenopausal women

For Immediate Release: June 21, 2019

The U.S. Food and Drug Administration today approved Vyleesi (bremelanotide) to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women.
Bremelanotide

- Peptide which acts as a melanocortin receptor agonist
- Injected under skin of abdomen or thigh at least 45 minutes before sexual activity
- Women using bremelanotide reported improvements in sexual desire scores compared with women receiving a placebo (25% vs. 17%)
- 40% experienced nausea with first injection
Ms. A sees you again 3 years later in the hospital after the delivery of her third child. She tells you at that time that she did receive brexanolone after her last pregnancy with good effect and an intensive outpatient program brought her to symptom remission. She has had no depressive symptoms since including during her third pregnancy, when she was able stay on her SSRI and in therapy.
Questions?

Dr. Priya Gopalan: gopalanpr@upmc.edu