Integration of Mental Health & Substance Use Disorder Treatment in Obstetrics Care

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Disclosures

Conflict of Interest

- SAGE Advisory Board
  - Zulresso (Brexanolone) for ppd

- Funding
  - NIH/NIDA: 5UG1DA013727
  - NIH/NIDA: R34 DA046730
  - NIH/NIDA: U54DA016511
  - HRSA: U66 RH31458
  - SAMHSA: TI080221
  - American Foundation of Suicide Prevention 8D477-01
  - Duke Endowment 8868-SP, 8563-SP
Overview

- Integrated Behavioral Health
  - Background
  - Evidence
  - Implementation

*Note: Number of pregnancy-related deaths per 100,000 live births per year.
Opioid Overdose Deaths

1999-2015
Prescription Opioid-Related Deaths
- Increased 471% in women
  [218% in men]

Synthetic Opioid-Related Deaths
- Increased 850% in women

2002-2013
Heroin Use
- Increased 100% in women,
  [50% in men]

Figure 1. Age-adjusted drug overdose death rates: United States, 1999–2016

1 Significant increasing trend from 1999 to 2016 with different rates of change over time, p < 0.001.
2 2016 rate for males was significantly higher than for females, p < 0.001.

NOTES: Deaths are classified using the International Classification of Diseases, Tenth Revision. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. The number of drug overdose deaths in 2016 was 63,632. Access data table for Figure 1 at:

Suicide

2000-2015
30% increase in suicide overall
2nd leading cause of death age 10-34
4th leading cause of death age 35-54

2000-2016
50% increase in suicide in women
21% increase in suicide in men

1 Significant increasing trend from 2000 through 2016 with different rates of change over time, p < 0.001

NOTES. Suicides were identified using International Classification of Diseases, 10th Revision, underlying cause of death codes: U03, X60-X84, and Y87.0.

Age-adjusted death rates were calculated using the direct method and the 2000 standard population.

Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db309_table.pdf#1

Maternal self-harm deaths: an unrecognized and preventable outcome

Kimberly Mangla, MD; M. Camille Hoffman, MD, MSCS; Caroline Trumpff, PhD; Sinclaire O’Grady, BA; Catherine Monk, PhD

National Rates of Maternal Deaths due to Suicide or Drug Use:
• Largely Unknown due to lack of or inadequate measurement
• ~14-30%
Maternal self-harm deaths: an unrecognized and preventable outcome

Kimberly Mangla, MD; M. Camille Hoffman, MD, MSCS; Caroline Trumpff, PhD; Sinclaire O'Grady, BA; Catherine Monk, PhD
Screen All Pregnant & Postpartum Women for MH & SUDs
When to Screen All Pregnant & Postpartum Women for Depression?

Screen for depression & anxiety symptoms:
- at least 1 during the perinatal period\(^1\)
- during comprehensive postpartum visit\(^1\)

“Clinical staff in obstetrics and gynecology practices should be prepared to initiate medical therapy, refer patients to appropriate behavioral health resources when indicated, or both.”

Why Screen All Pregnant & Postpartum Women for Depression?

• Peripartum Depression is Common
  • 1 in 7 women experience peripartum depression
  • 1 in 3 low income
  • 1 in 5 women experience peripartum anxiety

Why Screen All Pregnant & Postpartum Women for Depression?

• Peripartum Depression Persists

• 46% of women who screen positive for depression early postpartum, continue to have elevated depressive symptoms at 1-year.

Risks of Untreated Peripartum Depression

• **Women**
  – Severity of illness/Suicide
  – Poor health habits
  – Relationships

• **Obstetric/Fetal**
  – C-section
  – LBW (OR 1.96)
  – PTB (OR 1.56)

• **Child Development**
  – Less likely to breastfeed
  – Child Development:
    • Sleep, mother-infant bonding, communication, cognition, fine motor, behavioral, academics, psychiatric
In comparison to children of parents without PPD, children of parents with PPD are significantly more likely to:

- **3 Weeks**: Infant behaviors (difficulty sleeping, demanding, difficult to comfort)
- **4 Months**: Unintentional injury
- **6 Months**: Impaired mother-infant bonding
- **12 Months**: Delay in communication skills
- **18 Months**: Delay in cognitive and fine motor development
- **4 Years**: Emotional, conduct, and behavioral difficulties
- **6 Years**: Attenuated growth
- **10 Years**: Psychological difficulties
- **18 years**: Adolescent depression

Of the 30 studies providing data on the impact of PPD on children, 29 reported the long-term negative impact of maternal PPD on the physical and mental development of children. EPDS=Edinburgh Postnatal Depression Scale.

Peripartum Depression

• Impact on child health and development
• Behavioral problems in kids 3-4 years old
  – 4-fold increased risk
• Poor academic performance-middle school
  – 2-fold increased risk
• Depression in adolescents
  – 7-fold increased risk

What is the Cost
Peripartum Mood & Anxiety?

• Mathematica Analysis
• Annual Cohort of Mother-Child Dyad
  • followed pregnancy- five years
• Estimated cost 1 year:
  $14.2 Billion
  $32,000 per Mother-Child Dyad

The California Health Care Foundation, the Perigee Fund, and the Zoma Foundation
Prevention of Postpartum Depression

• Grade B Evidence

• Interventions for Prevention of PPD
  • Refer all at risk pregnant and postpartum women to counseling interventions

• Most Effective Counseling Interventions:
  – Cognitive Behavioral Therapy
  – Interpersonnel Psychotherapy

Past Month Substance Use among Pregnant Women

Illicit Drugs:
- 2015: 109K, 4.7%
- 2016: 143K, 6.3%
- 2017: 194K, 8.5%
- 2018: 128K, 5.4%

Tobacco Products:
- 2015: 319K, 13.9%
- 2016: 239K, 10.6%
- 2017: 334K, 14.7%
- 2018: 271K, 11.6%

Alcohol:
- 2015: 214K, 9.3%
- 2016: 187K, 8.3%
- 2017: 261K, 11.5%
- 2018: 233K, 9.9%

Marijuana:
- 2015: 78K, 3.4%
- 2016: 111K, 4.9%
- 2017: 161K, 7.1%
- 2018: 111K, 4.7%

Opioids:
- 2015: 19K, 0.8%
- 2016: 26K, 1.2%
- 2017: 32K, 1.4%
- 2018: 22K, 0.9%

Cocaine:
- 2015: 1K, <0.05%
- 2016: 2K, 0.1%
- 2017: 8K, 0.4%
- 2018: *

* Estimate not shown due to low precision.
+ Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.
Tobacco Use in Pregnancy

Obstetric, fetal, and newborn risks

- Ectopic Pregnancy\(^1\)
- Miscarriage\(^2\)
- Placental abruption\(^3\)
- Low birth weight\(^4-6\)
- Prematurity\(^7,8\)
- Stillbirth\(^9-12\)
- Sudden Infant Death Syndrome

Horne et al. 2014\(^1\); Pineles, Park, and Samet 2014\(^2\); Salihu and Wilson 2007\(^3\); Cnattingius 2004; Quesada et al. 2012; Salihu and Ion and Bernal 2015; Salihu and Wilson 2007\(^7,8\); Cnattingius 2004; Forray 2016; Salihu and Wilson 2007; Tikkanen et al. 2006\(^9\).
Tobacco Use in Pregnancy

- Low birth weight
- Prematurity
- ADHD
- Developmental delays
- Cognitive problems
- Behavioral problems
- School achievement
- Smoking

Alcohol Use in Pregnancy

Obstetric, fetal, and newborn risks
- Birth defects
- Preterm birth
- Low birth weight
- Small for gestational age
- Motor dysfunction
- Developmental delay
- Intellectual disability

(CDC, 2011; APA, 2013)
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* Estimate not shown due to low precision.

Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.
Prevalence of Past Month Cannabis Use

Prevalence of Past Month Daily/Near Daily Cannabis Use

Prevalence of Perinatal Opioid Use Disorder
Per 1,000 Delivery Hospitalizations in US 1999-2014

National prevalence of OUD increased 333%,
1.5 cases (1999) to 6.5 cases (2014) per 1,000 delivery Hx
Av. Yr. increase of 0.4 per 1,000 delivery Hx/Yr

<table>
<thead>
<tr>
<th>Condition</th>
<th>Delivery Hospitalizations with Opioid Abuse or Dependence</th>
<th>Delivery Hospitalizations without Opioid Abuse or Dependence</th>
<th>Multivariable Odds Ratio* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>60,994</td>
<td>20,456,485</td>
<td></td>
</tr>
<tr>
<td>Died during hospitalization</td>
<td>20 (0.03)</td>
<td>1,311 (0.006)</td>
<td>4.6 (1.8–12.1)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>24 (0.04)</td>
<td>1,873 (0.01)</td>
<td>3.6 (1.4–9.1)</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>4,157 (6.8)</td>
<td>431,032 (2.1)</td>
<td>2.7 (2.4–2.9)</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>2,315 (3.8)</td>
<td>215,057 (1.1)</td>
<td>2.4 (2.1–2.6)</td>
</tr>
<tr>
<td>Length of stay &gt;7 days</td>
<td>1,837 (3.0)</td>
<td>235,738 (1.2)</td>
<td>2.2 (2.0–2.5)</td>
</tr>
<tr>
<td>Preterm</td>
<td>10,538 (17.3)</td>
<td>1,506,941 (7.4)</td>
<td>2.1 (2.0–2.3)</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>2,736 (4.5)</td>
<td>564,410 (2.8)</td>
<td>1.7 (1.6–1.9)</td>
</tr>
<tr>
<td>Transfusion</td>
<td>1,205 (2.0)</td>
<td>208,073 (1.0)</td>
<td>1.7 (1.5–1.9)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>727 (1.2)</td>
<td>124,607 (0.6)</td>
<td>1.5 (1.3–1.8)</td>
</tr>
<tr>
<td>Premature rupture of membranes</td>
<td>3,499 (5.7)</td>
<td>778,157 (3.8)</td>
<td>1.4 (1.3–1.6)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>22,130 (36.3)</td>
<td>6,768,679 (33.1)</td>
<td>1.2 (1.1–1.3)</td>
</tr>
<tr>
<td>Severe preeclampsia or eclampsia</td>
<td>722 (1.2)</td>
<td>289,668 (1.4)</td>
<td>0.8 (0.7–0.9)</td>
</tr>
<tr>
<td>Anesthesia complications</td>
<td>20 (0.03)</td>
<td>3,123 (0.02)</td>
<td>2.1 (0.8–5.3)</td>
</tr>
<tr>
<td>Cerebrovascular complications</td>
<td>37 (0.06)</td>
<td>5,079 (0.02)</td>
<td>2.0 (0.9–4.4)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>273 (0.4)</td>
<td>79,169 (0.4)</td>
<td>1.3 (1.0–1.7)</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>1,866 (3.1)</td>
<td>589,811 (2.9)</td>
<td>1.1 (0.9–1.2)</td>
</tr>
</tbody>
</table>

Statistically significant values are indicated in bold.

* Adjusted for age group, race, primary payer, previous cesarean section, multiple gestation, and maternal preexisting conditions shown in table 1.

(Maeda, 2014)
Neonatal Abstinence Syndrome (NAS)

• Median rate NAS
  • Overall
    • 7.1 per 1,000 births
  • Mental health shortage areas:
    • 14.0 per 1,000
  • Highest 10 year unemployment rate:
    • 20.1 per 1,000
Peripartum Treatment “Cascade”

Cox et al., 2016; J Clin Psych

Dx Tx Adaquate Tx Remission

Antenatal
Postpartum
Peripartum Treatment “Cascade”

Absence of screening

Absence of training in assessment, diagnosis or treatment

Lack of access to treatment providers

Poor access to treatment; long wait times

Women do not want to go to treatment

Cox et al., 2016; J Clin Psych
Integrated Care

• Systematic coordination of general, behavioral, mental health and addiction care with the goal of improving clinical outcomes and patient experience, and reducing costs.

• Large spectrum of integration
  – Coordinated
  – Co-Located
  – Integrated
### SAMHSA 6 Levels of Integrated Care

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Behavioral Health, Primary Care and Other Healthcare Providers Work:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level 1</strong></td>
<td>Minimal Collaboration</td>
<td>In separate facilities, where they:</td>
</tr>
<tr>
<td></td>
<td>Have separate systems</td>
<td>■ Have separate systems</td>
</tr>
<tr>
<td></td>
<td>Communicate about cases only rarely and under</td>
<td>■ Communicate about cases only rarely and under compelling circumstances</td>
</tr>
<tr>
<td></td>
<td>compelling circumstances</td>
<td>■ Communicate, driven by provider need</td>
</tr>
<tr>
<td></td>
<td>May never meet in person</td>
<td>■ May never meet in person</td>
</tr>
<tr>
<td></td>
<td>Have limited understanding of each other’s roles</td>
<td>■ Have limited understanding of each other’s roles</td>
</tr>
</tbody>
</table>

| **Level 2** | Basic Collaboration at a Distance             | In separate facilities, where they:                                 |
|             | Have separate systems                          | ■ Have separate systems                                             |
|             | Communicate periodically about shared patients | ■ Communicate periodically about shared patients                    |
|             | Communicate, driven by specific patient issues | ■ Communicate, driven by specific patient issues                    |
|             | May meet as part of larger community           | ■ May meet as part of larger community                               |
|             | Have limited understanding of each other’s roles| ■ Have limited understanding of each other’s roles                   |

| **Level 3** | Basic Collaboration Onsite                    | In same facility not necessarily same offices, where they:          |
|             | Have separate systems                          | ■ Have separate systems                                             |
|             | Communicate regularly about shared patients    | ■ Communicate regularly about shared patients                       |
|             | Communicate, driven by need for each other’s   | ■ Communicate, driven by need for each other’s services             |
|             | services and more reliable referral            | ■ More reliable referral                                            |
|             | May meet occasionally to discuss cases due to  | ■ May meet occasionally to discuss cases due to close proximity     |
|             | close proximity                                 | ■ Close proximity                                                  |
|             | Feel part of a larger yet non-formal team      | ■ Feel part of a larger yet non-formal team                         |

| **Level 4** | Close Collaboration Onsite with Some System Integration | In same space within the same facility, where they:                   |
|             | Share some systems, like scheduling or medical records | ■ Share some systems, like scheduling or medical records            |
|             | Communicate in person as needed                  | ■ Communicate in person as needed                                   |
|             | Collaborate, driven by need for consultation and coordinated plans for difficult patients | ■ Collaborate, driven by need for consultation and coordinated plans for difficult patients |
|             | Have regular face-to-face interactions about some patients | ■ Have regular face-to-face interactions about some patients        |
|             | Have a basic understanding of roles and culture   | ■ Have a basic understanding of roles and culture                   |

| **Level 5** | Close Collaboration Approaching an Integrated Practice | In same space within the same facility (some shared space), where they: |
|             | Actively seek system solutions together or develop work-a-rounds | ■ Actively seek system solutions together or develop work-a-rounds |
|             | Communicate frequently in person                | ■ Communicate frequently in person                                   |
|             | Collaborate, driven by desire to be a member of the care team | ■ Collaborate, driven by desire to be a member of the care team        |
|             | Have regular team meetings to discuss overall patient care and specific patient issues | ■ Have regular team meetings to discuss overall patient care and specific patient issues |
|             | Have an in-depth understanding of roles and culture | ■ Have an in-depth understanding of roles and culture                 |

| **Level 6** | Full Collaboration in a Transformed/ Merged Integrated Practice | In same space within the same facility, sharing all practice space, where they: |
|             | Have resolved most or all system issues, functioning as one integrated system | ■ Have resolved most or all system issues, functioning as one integrated system |
|             | Communicate consistently at the system, team and individual levels | ■ Communicate consistently at the system, team and individual levels |
|             | Collaborate, driven by shared concept of team care | ■ Collaborate, driven by shared concept of team care                   |
|             | Have formal and informal meetings to support integrated model of care | ■ Have formal and informal meetings to support integrated model of care |
|             | Have roles and cultures that blur or blend       | ■ Have roles and cultures that blur or blend                           |
Collaborative Care- Primary Care

- 1990s; 80 RCTs
- Reduce MDD Sx
- Decreases Stigma
- Increase provider & patient satisfaction
- Improves clinical workflow/efficiency
- Reduces costs
- CMS/Billing Codes
Integrated Care - Ob/Gyn

Systematic review 21 articles

At least 1 of 11 components of integrated behavioral health
Integrated Behavioral Health

Feasible

- Screen
- Diagnosis
- Refer

Feasibility

Screening
- EPDS cut-off = 9-13, n=15 (refs 32-37, 40, 42, 44-50)
- PHQ-9 cut-off = 10, n=6 (refs 35, 41, 43, 46, 51-52)
- BDI n=2 (ref 38, 39)

Diagnostic Assessment
- MINI n=4 (refs 32, 34, 51-52)
- SCL-20 n=4 (refs 38-39, 51-52)
- SCID n=3 (refs 40-, 44 49)
- BDI-II n=1 (ref 49)
- DASS n=1 (ref 44)
- Unspecified interview approach n=4 (refs 33, 41, 45, 50)

Referral Rate
- 11-100% (non-emergency)
## Integrated Behavioral Health

### Effective Tx
- Started
- Sustained
- Effective

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Treatment Initiation</th>
<th>n=15 (refs 32-33, 38-39, 41-51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental health services encounter (e.g., psychotherapy, education, counseling) with varied specialists (e.g., advisors, LCSWs, psychologists, and psychiatrists) (12-98%), n=11 (refs 32, 33, 38-39, 42-45, 47-48, 50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacotherapy (15-87%), n=4 (refs 33, 46-47, 50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Support groups or classes (46%), n=1 (ref 33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combinations (15-98%), n=4 (refs 41, 43, 49, 51)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment Sustainment</th>
<th>n=5 (refs 32, 46-47, 51-52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment plan completion (55%), n=1 (ref 32)</td>
<td></td>
</tr>
<tr>
<td>IPT/medication management sessions (84-93%), n=1 (ref 51)</td>
<td></td>
</tr>
<tr>
<td>Mental health visits (59-100%), n=3 (refs 46-47, 52)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment Efficacy</th>
<th>n=5 (refs 36, 44, 46, 51-52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom improvement n=4 (refs 36, 44, 51-52)</td>
<td></td>
</tr>
<tr>
<td>Symptom remission n=2 (refs 46, 51)</td>
<td></td>
</tr>
<tr>
<td>Maternal/child outcomes n=0</td>
<td></td>
</tr>
</tbody>
</table>
Integrated Behavioral Health

Acceptable

- Patients
- Providers
- Staff

Acceptability

**Patient Satisfaction***
- n=10 (refs 32-34, 36, 39, 40, 42-43, 51-52)
  - Comfortable talking about mood/found discussion supportive (97-99%)
  - Appreciate provider concern about mood (96%)
  - Positive opinion of intervention staff (91-100%)
  - Care satisfaction (62-98%)

**Provider Improvement***
- n=7 (refs 33, 35-37, 40, 43, 49)
  - Depression treatment confidence
  - Use of validated tools
  - Discussion after positive screen
  - Referral to community resources

**Practice Staff Acceptance***
- n=6 (refs 33, 35-37, 43, 47)
  - Improved treatment knowledge and skills
  - Increased screening and validated tool use
  - Familiarity with programs
  - High program utilization
Integrated Behavioral Health

Sustainable

- Start-up expense
- 1.4 FTE NP
- 0.6 FTE Admin

Intervention Costs/Resources
n=3 (refs 35, 44, 51)

- Byatt et al.: $8.38/woman/year plus start-up administrative expenses and community capacity building (ref 35)
- Grote et al.: $1,117/woman (ref 51)
- Harvey et al.: 1.4 FTE senior-level mental health nurse and 0.6 FTE administrative staff (ref 44)
Integrated or Collaborative Care- Ob Care

- Limited Ob data
- CMS/Billing Codes
  - SC Medicaid does not support
- Leverage existing resources
Birth Outcomes Initiative
Mental Health and Substance Use Screening- SBIRT

- **SCREENING** quickly assesses the frequency and severity of substance use, identify the appropriate level of treatment.

- **BRIEF INTERVENTION** focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.

- **REFERRAL TO TREATMENT** provides those identified as needing more extensive treatment with access to specialty care.
**Screening:**
- Substance Use
- Domestic Violence
- Mental Health (Past, Present)

**Brief Intervention:**
- Assessment
- Motivational Interviewing
  - [increase likelihood of accessing tx]

**Referral to Treatment:**
- Follow up
  - [ensure accessed treatment]
**SBIRT INTEGRATED SCREENING TOOL**

* Fax the COMPLETED form to the patient’s plan and referral site and keep a copy in patient file.

<table>
<thead>
<tr>
<th>Practice name</th>
<th>Group NPI</th>
<th>Individual NPI</th>
<th>Screening provider’s name</th>
<th>Phone no.</th>
</tr>
</thead>
</table>

### PATIENT INFORMATION

- **Patient’s last name:**
- **First:**
- **Middle:**
- **Language:**
- **Race:**
- **Expected due date:**
- **Phone no.:**
- **Street address:**
- **Member ID no.:**

### PROVIDER INFORMATION

- **Screening information**

#### PATIENT SCREENING INFORMATION

<table>
<thead>
<tr>
<th>Parents</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did any of your parents have a problem with alcohol or drug use?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Did any of your friends have a problem with alcohol or other drug use?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Partner</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your partner have a problem with alcohol or drug use?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Violence</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you feeling at all unsafe in any way in your relationship with your current partner?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emotional Health</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the last few weeks, has worry, anxiety, depression or sadness made it difficult for you to do your work, get along with people or take care of things at home?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Past Life</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past, have you had difficulties in your life due to alcohol or other drugs, including prescription medications?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Present</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past month, have you drunk any alcohol or used other drugs?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>1. How many days per month do you drink?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>2. How many drinks on any given day?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>3. How often did you have 4 or more drinks per day in the last month?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>4. In the past month have you taken any prescription drugs?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smoking</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you smoked any cigarettes in the past three months?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

#### ADVICE FOR BRIEF INTERVENTION

<table>
<thead>
<tr>
<th>Y</th>
<th>N</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you state your medical concern?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Did you advise to abstain or reduce use?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Did you check patient’s reaction?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Did you refer for a future assessment?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

#### CONFIDENTIAL SBIRT REFERRAL INFORMATION

- **Patient referred:**
- **Date of referral appointment (DD/MM/YY):**
- **Date screened:**
- **Patient refused referral:**
- **Referral not warranted:**
- **Patient requested assistance:**

### Follow up

- Communicate with Ob Team
- Screening information
- Referral and Tx Progress

---

*Adapted from Institute for Health & Recovery, (2015)*
Screening

- Program is briefly introduced [brochure provided]
- Women provide verbal consent & cell phone number
- Cell phone number entered in web-based system
- Patient receives text immediately and survey to be completed in office while waiting
Screening

- Self-report, as opposed to in-person interviews yield higher rates of reporting substance use & depression.
- + Screens = EDPS, NIDA, AA
  - Increase specificity of screens
- Categorize patients according to needs to optimize time and workflow

Screening

- Algorithm classifies women into clinical categories and priority for assessment and intervention:
  - Low Risk
  - Risk Factors for Depression
  - Positive Depression Screen
  - Substance Abuse High/Low Risk
  - Domestic Violence Risk
Brief Intervention & Referral to Treatment

- Care Coordinator Contacts Patient
- Assessment
- Creates Care Plan
- Motivational Interview/Referral Services
- Follow-Up with Patient
- Care Coordinator provides summary of screen, assessment and plan to provider via EHR.
Brief Intervention & Referral to Treatment

• Reduce the need for training and re-training
• Increase the reach of experts in MI, care coordination & mental health
• Patient connects with one care coordinator
Referral to Treatment
Program Enrollment

Where a women enters care:

- Prenatal care at obstetricians office
- Delivery at hospital
- Postnatal care at obstetricians office
- Well-child visits at pediatricians office
Follow-up Screenings

- Enroll anytime
- Each trimester of pregnancy
- Months 1, 3, 6, 9, 12, 15, 18 postpartum
Virtual Collaborative Ob Care

Evaluation

- Improve detection
- Reduce sx
- Decreases Stigma
- Increase provider & patient satisfaction
- Improve clinical workflow/efficiency
- Reduces costs
- CMS/Billing Codes
Summary

Key takeaways

PMADs are the #1 complication of pregnancy and childbirth

Untreated PMADs in the U.S. are costly and have multigenerational consequences

Half of perinatal women with a diagnosis of depression do not get the treatment they need

Nationally, PMADs affect up to 1 in 7 pregnant and postpartum women

An estimated $14.2 billion for all births in 2017
Acknowledgements

• Collaborators
  • Katie Cristaldi, MD
  • Dee Ford, MD
  • Donna Johnson, MD
  • Kathleen Brady, MD, PhD
  • Roger Newman, MD
  • Jimmy McElligott, MD
  • Lisa Boyars, MD
  • Rubin Aujla, MD
  • Claire Smith, MD
  • Edie Douglas, MPH
  • Lauren Shipley, BA
  • Savanna Lee, BA

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  • NIH/NIDA/ORWH
  • HRSA
  • SAMHSA
  • American Foundation of Suicide Prevention
  • Duke Endowment
Thank you

Connie Guille
Email: guille@musc.edu
Summary

**Text Based Screening in Ob Office**

**Brief Intervention**
Remote Care Coordinator

**Referral to Treatment**
Telemedicine/ Office or Home
Follow up

**Communicate with Ob Team**
Screening information
Referral and Tx Progress
Health

First drug specifically for postpartum depression is approved

The new medication must be taken intravenously over 60 hours.
Brexanolone

- Beta-cyclodextrin, IV formulation of allopregnanolone\(^1,2\)
  - Symptom improvement: 24 hours; remission: 3 days
- Mechanism\(^1,2\)
  - Modulation of GABA-A receptors
- Logistics\(^1,2\)
  - 60-hour IV infusion in healthcare facility
  - Continuous pulse ox, q2 hour mentation checks
- Side Effects\(^1\)
  - Blackbox warning: sedation, loss of consciousness
- Cost\(^1\)
  - $34,000 per patient

1. “Brexanolone (Zulresso) for Postpartum Depression,” 2019, 73-74
2. Meltzer-Brody, Colquhoun & Riesenberge, et. al., 2018, 1058-1070
Brexanolone

How does it work?

Figure 2. Bhati, (n.d.)
Efficacy of brexanolone injection in post-partum depression: Two multicentre, double-blind, randomized, placebo-controlled, phase 3 trials
Purpose

• Objective
  o To assess the efficacy and safety of Brexanolone in the treatment of postpartum depression

• Endpoints
  o Primary – change from baseline in the mean 17-item Hamilton Rating Scale for Depression (HAM-D) total score at 60 hr post-infusion
  o Secondary – mean HAM-D score change from baseline at 30 days after infusion
  o Secondary – comparison of adverse effects among treatment and placebo groups
METHODS
Study Design

- Randomized, double-blind, placebo-controlled
  - 30 clinical research centers
- Randomization:
  - Study 1 (Mean HAM-D $\geq$ 26)
    Brexanolone 90 ug/kg vs. Brexanolone 60 ug/kg vs. placebo
  - Study 2 (Mean HAM-D 20-25)
    Brexanolone 90 ug/kg vs. placebo
- Each patient received 60 hrs continuous infusions
- Repeated assessments of HAM-D
- Adverse effects recorded
Study 1
Needed 40 patients/group to achieve 90% power to detect a difference of 9

Study 2
Needed 50 patients/group to achieve 90% power to detect a difference of 8
Population

**Inclusion Criteria**
- Females aged 18-45 yo
- Negative UPT & reliable contraception
- ≤6mo postpartum
- Onset of PPD in the third trimester to 4 weeks postpartum
- Good health
- Discontinued breastfeeding
- If on antidepressant, must be stable dose

**Exclusion Criteria**
- ESRD on dialysis
- Allergy to pregnanolone or progesterone
- Hgb <10
- PMH schizophrenia, schizoaffective, attempted suicide
- Drug or alcohol abuse
- Recent ECT
RESULTS
Results – Demographics

• Well-balanced baseline characteristics
  o Mean age: 27-28 yo
  o Race: white (62%), African American (35%), Hispanic (17%)
  o Onset of depression: Similar across all groups, generally within 4 weeks PP
  o Antidepressants at baseline: 22% across both studies
Results

- **Primary Endpoint: 60 hrs**
  - Significant reduction in HAM-D scores at the end of 60 hours among both studies

- **Secondary Endpoint: 30 d**
  - Study 1 - Significant reduction in HAM-D scores at 30 days among both treatment groups

**Study 1**

- **BRX60 (M [SE])**
  - Mean change [95% CI]
  - 19.5 [1.2]
  - -5.5 [-8.8,-2.2]

- **BRX90 (M [SE])**
  - 17.7 (1.2)
  - Mean change [95% CI]
  - -3.7 [-6.9,-0.5]

- **Placebo (M [SE])**
  - 14.0 [1.1]
  - Mean change [95% CI]
  - -12.1 [0.8]

**Study 2**

- **BRX90 (M [SE])**
  - 14.0 [0.8]
  - Mean change [95% CI]
  - -2.5 [-4.5,0.5]

- **Placebo (M [SE])**
  - -12.1 [0.8]
Results

- Secondary Endpoint: Adverse effects
  - Similar across all groups

<table>
<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=43)</td>
<td>BRX60 (n=38)</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any adverse event</td>
<td>22 (51%)</td>
<td>19 (50%)</td>
</tr>
<tr>
<td>Severe adverse event</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Adverse event leading to discontinuation of study treatment</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Adverse events in three or more patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>7 (16%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (2%)</td>
<td>6 (16%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>3 (7%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Infusion site pain</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (7%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>0 (0%)</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

*Data are n (%). Treatment-emergent adverse events were defined as an adverse event with onset after the start of study drug, or any worsening of a pre-existing medical condition or adverse event with onset after the start of study drug. Treatment-emergent adverse events were coded according to the Medical Dictionary for Regulatory Activities version 19.1 or later. BRX60 = brexanolone injection 60 μg/kg per h. BRX90 = brexanolone injection 90 μg/kg per h.*

*Table 3: Treatment-emergent adverse events*
Blackbox Warning

• Loss of consciousness
  o Study 1
    • BRX60 – 1 of 38 (3%)
  o Study 2
    • BRX90 – 1 of 51 (2%)
  o Across both studies
    • 5 total patients with excessive sedation
DISCUSSION
Discussion

• PPD is common
• High morbidity & mortality
• Brexanolone shows efficacy in the treatment of moderate-severe depression
  o Quick onset and response
    o 3 days vs 6-8 weeks with SSRIs
  o Some durability at 30 days

5. Stewart & Vigod, 2016, 2177-2186
6. Brummelte & Galea, 2016, 153-166
Limitations

• Large placebo response
  o Consistent with most other MDD studies

• Mean change in HAM-D Score 2.5-5.5 points
  o Consistent with most other MDD studies

• Access
  o Healthcare facility
  o Social support
  o 60 hour monitoring
  o Cost/Insurance coverage
Conclusions

• Brexanolone: novel MOA
• Safety and efficacy moderate-severe postpartum depression
• Quick response
But,
• Access/Insurance coverage
• Longitudinal studies are needed
References

315 of 1220 participants (26.3%) met reference standard criteria for positivity.

The single-item screening questions from the NIDA Quick Screen showed high specificity (0.99) for all substances, but very poor sensitivity (0.10-0.27).

The 5Ps showed high sensitivity (0.80-0.88) but low specificity (0.35-0.37).

The CRAFFT, SURP-P and 5Ps had the highest area under the curve (AUC) for alcohol (0.67, 0.66 and 0.62, respectively)

The WIDUS had the highest AUC for illicit drugs and opioids (0.70 and 0.69, respectively).

Ondersma SJ et al., Addiction. 2019 Sep;114(9):1683-1693.
Screening: Which Measure to Use?

• Universal Screening: ACOG, AAP, AMA, CDC
• N=1220 racially, ethnically and socio-economically diverse pregnant women
  – Substance Use Risk Profile-Pregnancy (SURP-P)
  – CRAFFT (acronym for five-item screener with items related to car, relax, alone, forget, friends and trouble), 5Ps (parents, peers, partner, pregnancy, past)
  – Wayne Indirect Drug Use Screener (WIDUS)
  – National Institute on Drug Abuse (NIDA) Quick Screen.
  – Participants later provided a urine sample and completed a calendar recall-based interview regarding substance use

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Ondersma SJ et al., Addiction. 2019 Sep;114(9):1683-1693.
Screening

Drug toxicology is **NOT** recommended for universal screening because it has limitations and should only be considered if there is a clinical indication and with consent.
Edinburgh Postnatal Depression Scale

- Review Item 10
- Total Score w/ Reverse Scoring
- High Probability of Peripartum Depression Diagnosis
  - EDPS score of >13
    - Sensitivity: 0.80
    - Specificity: 0.90
  - If borderline, repeat in 2 weeks
  - EDPS score of >10
    - 20% will have suicidal ideation
**Patient Health Questionnaire (PHQ-9)**

For each statement, please mark the response which best represents how often have you been bothered by any of the following problems over the \textbf{PAST 2 WEEKS}?

<table>
<thead>
<tr>
<th>Statement</th>
<th>Not at all</th>
<th>Less than half the days</th>
<th>More than half the days</th>
<th>Nearly everyday</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little interest or pleasure in doing things.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling down depressed or hopeless.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble falling asleep, staying asleep or sleeping too much.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling tired or having little energy.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor appetite or overeating.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling badly about yourself- or that you are a failure or that you have let yourself or your family down.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble concentrating on things such as reading the newspaper or watching TV.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moving or speaking so slow that others could have noticed. Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoughts that you would be better off dead or hurting yourself in some way.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you have experienced any of these problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all
- Somewhat difficult
- Very difficult
- Extremely difficult

If you have comments or questions regarding this survey please email us at \texttt{intern.health@yale.edu}
Patient Health Questionnaire (PHQ-9)

- High probability DSM-5 Depression Diagnosis:
  - Add up all items
  - Cut off score: PHQ > 10
  - 88% sensitivity and 88% specificity

- Severity of Symptoms:
  - Add up all items (including outside shaded area)
    - 5-9 = Mild Depression
    - 10-14 = Moderate Depression
    - 15-19 = Moderate Severe Depression
    - 20+ = Severe Depression

(Kroenke et al., 2001)
Patient Health Questionnaire (PHQ-9)

- **Severity of Symptoms:**

<table>
<thead>
<tr>
<th>PHQ-9 Score</th>
<th>Depression Severity</th>
<th>Proposed Treatment Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>None-Minimal</td>
<td>None</td>
</tr>
<tr>
<td>5-9</td>
<td>Mild</td>
<td>Monitor, repeat at follow-up</td>
</tr>
<tr>
<td>10-14</td>
<td>Moderate</td>
<td>Psychotherapy and Pharmacotherapy</td>
</tr>
<tr>
<td>15-19</td>
<td>Moderate-Severe</td>
<td>Psychotherapy and Pharmacotherapy</td>
</tr>
<tr>
<td>20+</td>
<td>Severe</td>
<td>Pharmacotherapy, Psychotherapy and Referral to Psychiatrist</td>
</tr>
</tbody>
</table>

(Kroenke et al., 2001)
Peripartum Depression

• Completed Screen
  EDPS: review item 10; Score 10/13 +
  PHQ-9: review item 9; Score 10 +

• Assessment & Diagnosis