Improving maternal psychiatric health at Northwell Health

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Outline of today's webinar

Recent initiatives to improve maternal (perinatal) psychiatric health at Northwell Health

1) Education and training
   - Perinatal psychiatry education and training for clinical staff and trainees

2) Prevention
   - ROSES preventative counseling/education intervention

3) Treatment and referral
   - Collaboration with Northwell Health Solutions: integrated care in OBGYN practices
   - Women's Behavioral Health Center and Women's Unit at Zucker Hillside Hospital

4) Research and the novel FDA-approved antidepressant for postpartum depression (brexanolone/Zulresso)

Perinatal depression is common, under-diagnosed and undertreated

Approximately 11.5% of women giving birth suffer from perinatal depression (Gavin NI et al, 2005; Ko JY et al. MMWR Morb Mortal Wkly Rep. 2017;66:153-158; Centers for Disease Control and Prevention, Births and Natality. https://www.cdc.gov/nchs/fastats/births.htm)

U.S. Preventative Services Task Force (USPSTF) and American Psychiatric Association (APA) recommend screening for depression in pregnant and postpartum women (JAMA 2016; APA position statement 2018;)

ACOG recommends screening women at least once during perinatal period for depression and anxiety symptoms using a standardized, validated tool, if antenatal screening is done, then additional screening should occur during the comprehensive postpartum visit (ACOG Committee Opinion #757, NOV 2018 Obst Gynecol)

30.8% of women with PPD are identified in clinical settings; 15.5% receive treatment; 6.3% receive adequate treatment; 3.2% achieve remission (Cox EQ et al, 2016)

Maternal suicide is leading cause of direct maternal mortality in the first postpartum year with 1 in 7 deaths due to suicide (Chesney E et al,2014; Johannsen BM et al,2016; MBRACE UK Maternal Report, 2017)

There are validated screening tools to differentiate symptoms; clinical diagnosis must follow screening

Patient Health Questionnaire-9 (PHQ-9)

- Designed for MDD, but commonly used to detect symptoms of PPD (Kroenke K et al 2001)
- Cut-off of **≥10** (0.85 sensitivity, 0.89 specificity); cut-off of **≥15** (0.62 sensitivity, 0.96 specificity) (Manea L et al 2012)

Edinburgh Postnatal Depression Scale (EPDS)

- 10- item self-report validated in antepartum and postpartum periods (Cox JL et al 1987)
- Assesses depressive, anxiety and anhedonia symptoms
- Cut-off of **≥13** for major depression (0.86 sensitivity, 0.78 specificity) (Gaynes et al, 2005; Matthey S et al 2006)
- In women with EPDS score **>11**, 31.4% had MDD, 13.1% had bipolar disorder, 60.8% had anxiety disorder (of which 17.6% had OCD, 5.2% with dysthymia, 11.8% somatoform disorder, 4.6% with current substance abuse) (Lydsodottir, LB et al, 2014)

Mood disorder questionnaire (MDQ) is 5 minute self-report that screens for bipolar I, bipolar II and bipolar NOS
https://www.integration.samhsa.gov/images/res/MDQ.pdf

Anxiety disorders: Unlike PND, there are no comparable screening recommendations for perinatal anxiety disorders; May use EPDS-3 (Q3,4,5) subscale, score ≥5 requires further evaluation (Matthey S. 2008)

Growing evidence base for psychotherapies in perinatal depression

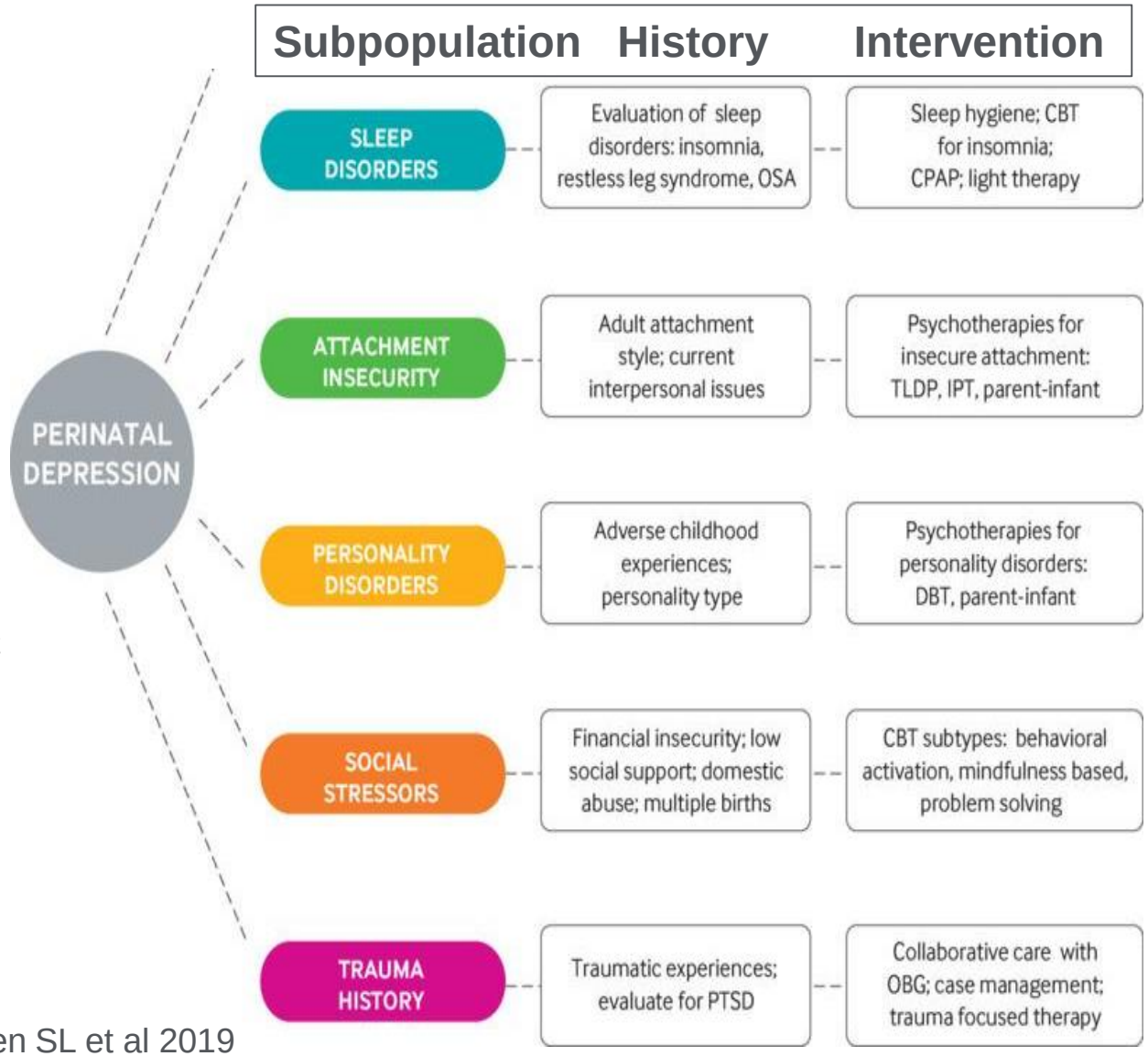
Psychotherapies are recommended as monotherapy for mild unipolar perinatal depression

Interpersonal psychotherapy (IPT) (Reay R et al, 2012; Grote NK et al, 2010; Spinelli MG & Endicott J 2003; O'Hara MW et al, 2000; Klier CM et al, 2001; Stuart S & O'Hara MW 1995)

Cognitive behavioral therapy (CBT) (Milgrom J et al, 2016; Milgrom J et al, 2015; Ammerman RT et al, 2013; Le HN et al, 2011;Chabrol H et al, 2002)

Mindfulness-based CBT (Dimidijian S et al, 2016; Dimidijian S et al, 2014; Goodman JH 2014)

Peer support and group psychotherapies (Dennis CL et al 2009; Dennis CL 2003; Chen CH et al 2000; Honey KL 2002; Milgrom et al 2005)



Johansen SL et al 2019

Antidepressants are effective and indicated for moderate/severe perinatal unipolar depression

Antidepressants are first line treatment with some are supported by RCT data in postpartum women.

- Fluoxetine
- Paroxetine
- Sertraline

Zulresso (brexanolone IV) is the first and only FDA approved antidepressant for adult unipolar perinatal depression.

In women who are treatment-resistant (partial response or lack of response) to SSRI or SNRIs, there is data supporting the use of a TCA (nortriptyline)

Frieder, Fersh, Hainline, Deligiannidis, 2019

Education and Training

- Perinatal psychiatry education and training for clinical staff and trainees

Perinatal Psychiatry Education and Training

Perinatal Mood and Anxiety Disorder (PMAD) screening, diagnosis, treatment and triage/referral

Zucker School of Medicine:

- Introduction to PMADs (screening, differential diagnosis and treatment)- 1st year medical students
- PMAD treatment (risk/benefits/alternatives to treatment)- 2nd year medical students
- PMAD clinical rotations in ambulatory and research perinatal psychiatry- 3rd and 4th year medical students

Hofstra-Northwell Graduate School of Nursing: Nurse Practitioner Program

- Introduction to PMADs (screening, differential diagnosis and treatment)- Family Practice NP students
- Introduction to PMADs (screening, differential diagnosis and treatment)- Psychiatric Mental Health NP students

Northwell Health Residency Programs

- Adult Psychiatry Residency: Perinatal psychiatry resident tracks (clinical, educational and research)
- Ob-Gyn Residency at LIJMC: Introduction to PMADs (screening, differential diagnosis and treatment)

Northwell Health Continuing Medical Education Series (Grand Rounds and other trainings)

- Departments of Psychiatry and Ob-Gyn across health system (Huntington Hospital, Lenox Hill, Crouse, Long Island Jewish, North Shore University Hospital, etc.)

Prevention

- ROSES preventative counseling/education intervention

USPSTF recommends providing interventions aimed at preventing perinatal depression in at-risk women (JAMA, Feb 2019)

The USPSTF recommended “that clinicians provide or refer pregnant and postpartum persons who are at increased risk of perinatal depression to counseling interventions (B recommendation)” after finding convincing evidence that cognitive behavioral therapy (CBT) and interpersonal therapy (IPT) are effective in preventing perinatal depression.

Women who would benefit:

- History of depression
- Current depressive symptoms
- Socioeconomic risk factors e.g. low income, young or single parenthood

ROSE (Reach Out, stay Strong, Essentials for mothers of newborns) is an EBM based intervention developed at Brown University (Dr. Carolyn Zlotnick) that **reduces the risk of perinatal depression in low income women by 50%** and has been tested in community prenatal settings with racially and ethnically diverse low-income pregnant women. (Crockett K et al 2008; Phipps MG et al, 2013; Zlotnick C et al 2016; Zlotnick C et al 2006)

- ROSE is associated with increased breastfeeding duration (median days breastfed 54 v 21) Kao JC et al 2015

ROSE (Reach Out, stay Strong, Essentials for mothers of newborns)

ROSE is a 5 session course

- Four 1-1.5 hour prenatal classes that can be split into shorter sessions
- One postnatal phone check-in

ROSE program outline:

- Session 1: signs/symptoms of baby blues and perinatal depression
- Session 2: stress management skills, managing the transition to motherhood, identifying positive supports
- Session 3: teaches types of interpersonal conflicts common around childbirth and role plays techniques for resolving them
- Session 4: skills for resolving interpersonal conflicts, setting goals
- Postpartum booster: reinforces previous sessions, reviews resources

(Crockett K et al 2008; Phipps MG et al, 2013; Zlotnick C et al 2016; Zlotnick C et al 2006)

In NY state, ROSE is considered preventative counseling for high risk mothers and, as defined by Medicaid Prenatal Care Standards, the provider can be an MD, NP or PA. There are CPT, charge and revenue codes that can be used to bill for these interventions.

Treatment and referral

- Collaboration with Northwell Health Solutions: integrated care in OBGYN practices

Integrated Behavioral Health Program at Health Solutions

Northwell Health Solutions has a Behavioral Health (BH) Care Management Team that works with primary care, pediatrics and in 2020 expanded to work with Northwell Health Physician Partner OB practices to integrate BH care.

The Integrated Behavioral Health Program is an evidence-based model in which a Behavioral Health Care Manager, Primary Care Provider/OBGYN/Pediatrician, and Consulting Psychiatrist work as a team to manage patients' depression and improve overall wellness

Enrolled practices screen all patients for depression and anxiety.

An embedded BH care manager conducts initial and follow up assessments with referred patients, provide treatment recommendations to physicians and will refer patients to a higher level of BH care if needed.

The physician/NP assesses patients and initiate psychotropic medication as indicated.

The psychiatrist at Health Solutions supervises and supports the embedded BH care manager at each affiliated practice.

Integrated Behavioral Health Program at Health Solutions

Provides targeted treatment interventions which are adjusted based on clinical outcomes following EBM algorithm. All patients enrolled in the integrated care program are entered into a registry where depression/anxiety scale scores and treatment responses are tracked.

- Medication management, prescribed by the OB/GYN, with advice from consulting psychiatrist
  - Depression
  - Anxiety

- Short term psychotherapy
  - 6-8 sessions of individual/possibly group therapy
  - Cognitive behavioral therapy/problem solving therapy/motivational interviewing

- Care management
  - Symptom monitoring
  - Psychoeducation
  - Outreach
  - Linkage to additional services

Integrated Behavioral Health Program at Health Solutions

Consulting psychiatrist: telepsychiatry pilot

Consults for:

- Diagnosis clarification
- Medication management
- Bridging to outside clinical behavioral health services

Perinatal psychopharmacology curbside consults to Health Solutions BH psychiatrists

- Antepartum vs. lactation pharmacotherapy choices
- Pharmacotherapy dosing guidance re: peripartum drug metabolism changes

Training to OBGYN practices affiliated with Health Solutions BH Integrated Care Program

- Perinatal Mood and Anxiety Disorder (PMAD) screening, diagnosis, and treatment trainings focused on practice needs to compliment training on integrated care provided by Health Solutions

Women’s Behavioral Health Center and Women’s Unit at Zucker Hillside Hospital

Northwell Health℠

Short-term treatment through the Zucker Hillside Women's Behavioral Health Center may benefit a wide range of women, including:

Adult (18+) women who are:

- planning pregnancy (pre-conception consultation)
- seeking one-time medication consultation
- looking for treatment to maintain mood stability during perinatal period
- struggling with miscarriage or birth loss
- with psychiatric symptoms during pregnancy/postpartum/lactation (up to 1 year of delivery)
- seeking diagnosis/treatment recommendations for premenstrual dysphoric disorder (consultation)

For information and appointments, the referring clinician and the patient should call our WARMLINE: 516-470-4MOM (4666)- catchment area is NYC/Nassau/Suffolk counties

The warmline is for NON-URGENT clinical referrals. Women in crisis should be evaluated in the nearest ER.

Treatment and interventions at the Zucker Hillside Women's Behavioral Health Center

Initial telephone assessment
Standardized rating scales
Comprehensive evaluation for medication/therapy
Short-term individual therapy
Interpersonal therapy (IPT)
Cognitive behavioral therapy (CBT)
Supportive psychotherapy
Group therapy
Marital therapy/Couples therapy
Medication management
Parent-child bonding coaching

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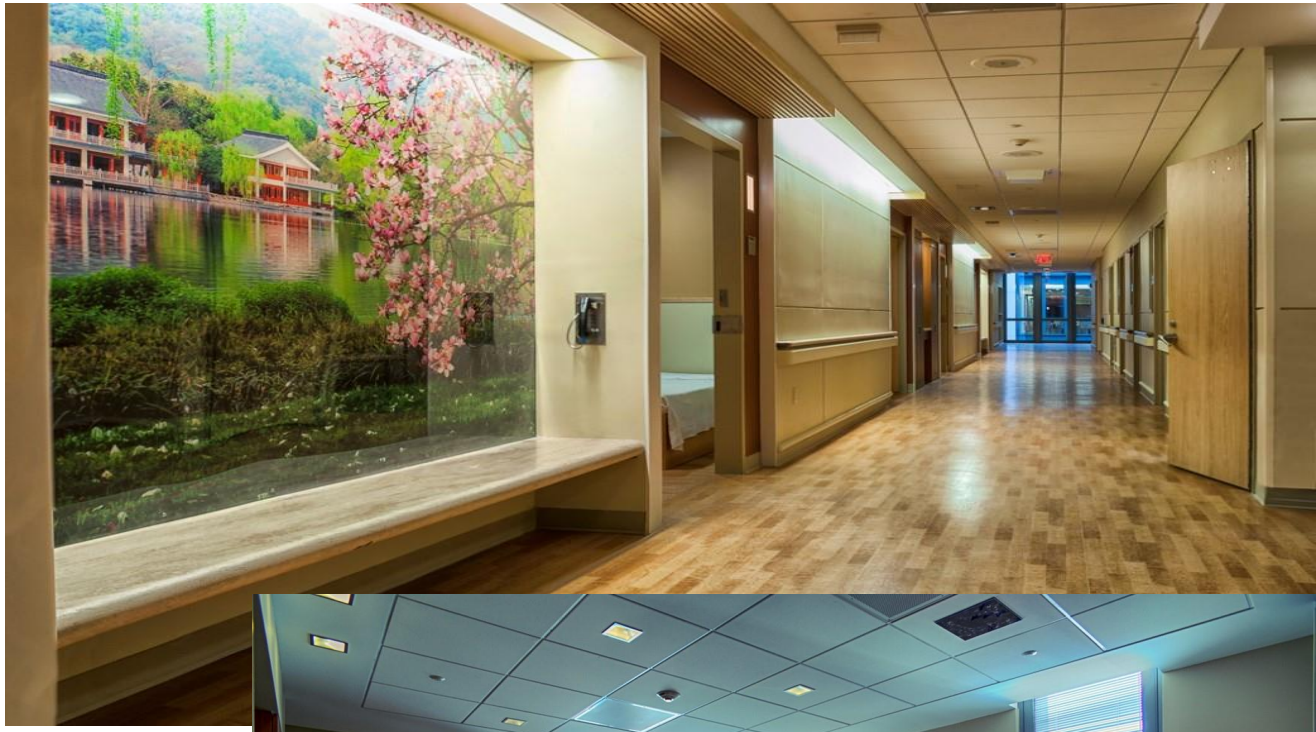
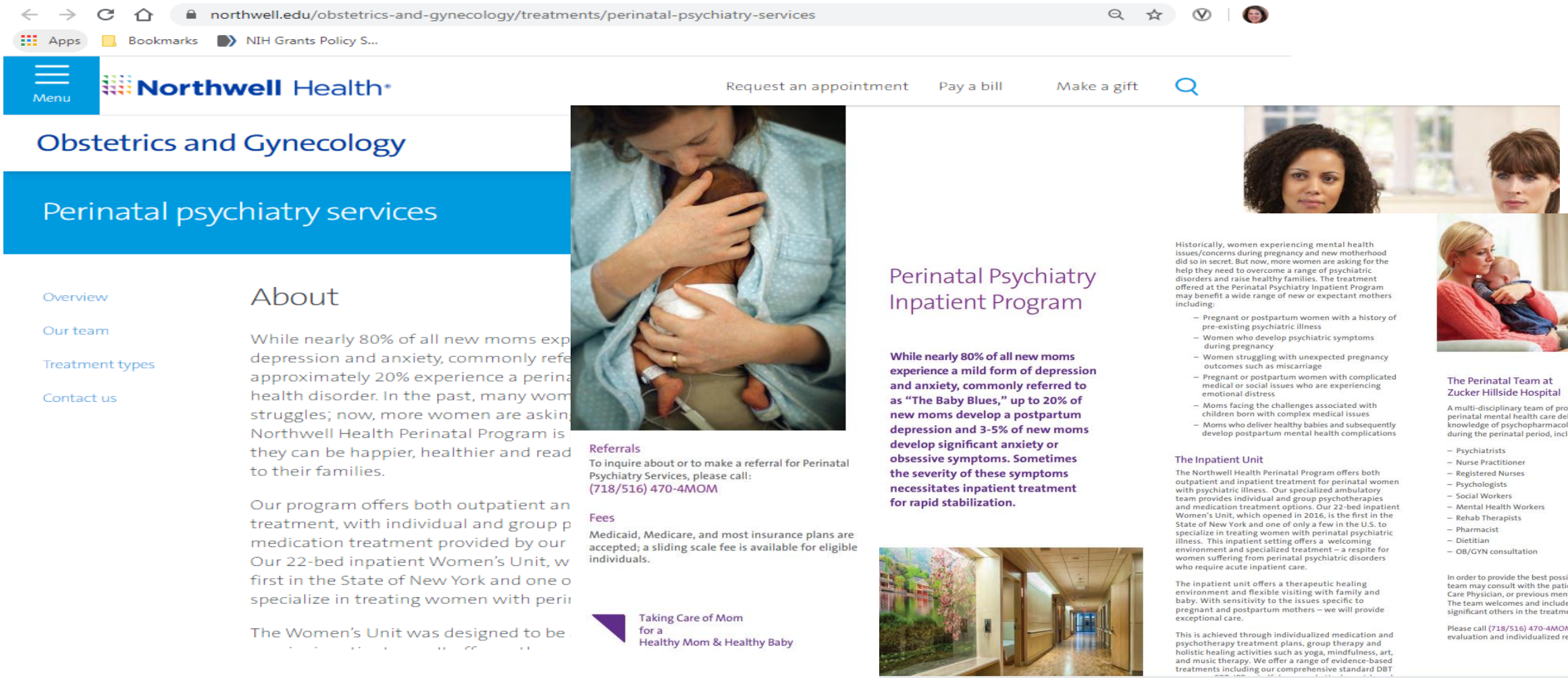
ZHH has the largest dedicated Women's Unit (2W) that provides inpatient psychiatric care to perinatal women in the U.S.

- For women with perinatal mood and psychotic disorders who require acute inpatient care
- All female-staff, trained in perinatal psychiatry
- Led by 2 perinatal psychiatrists
- OB-GYN consultation
- Private GYN exam room on the unit
- Hospital-grade Medela breast pumps
- Comfort room: meditation, yoga
- Laundry room, exercise equipment, community living room and eating areas
- Private family room for infant/family visits



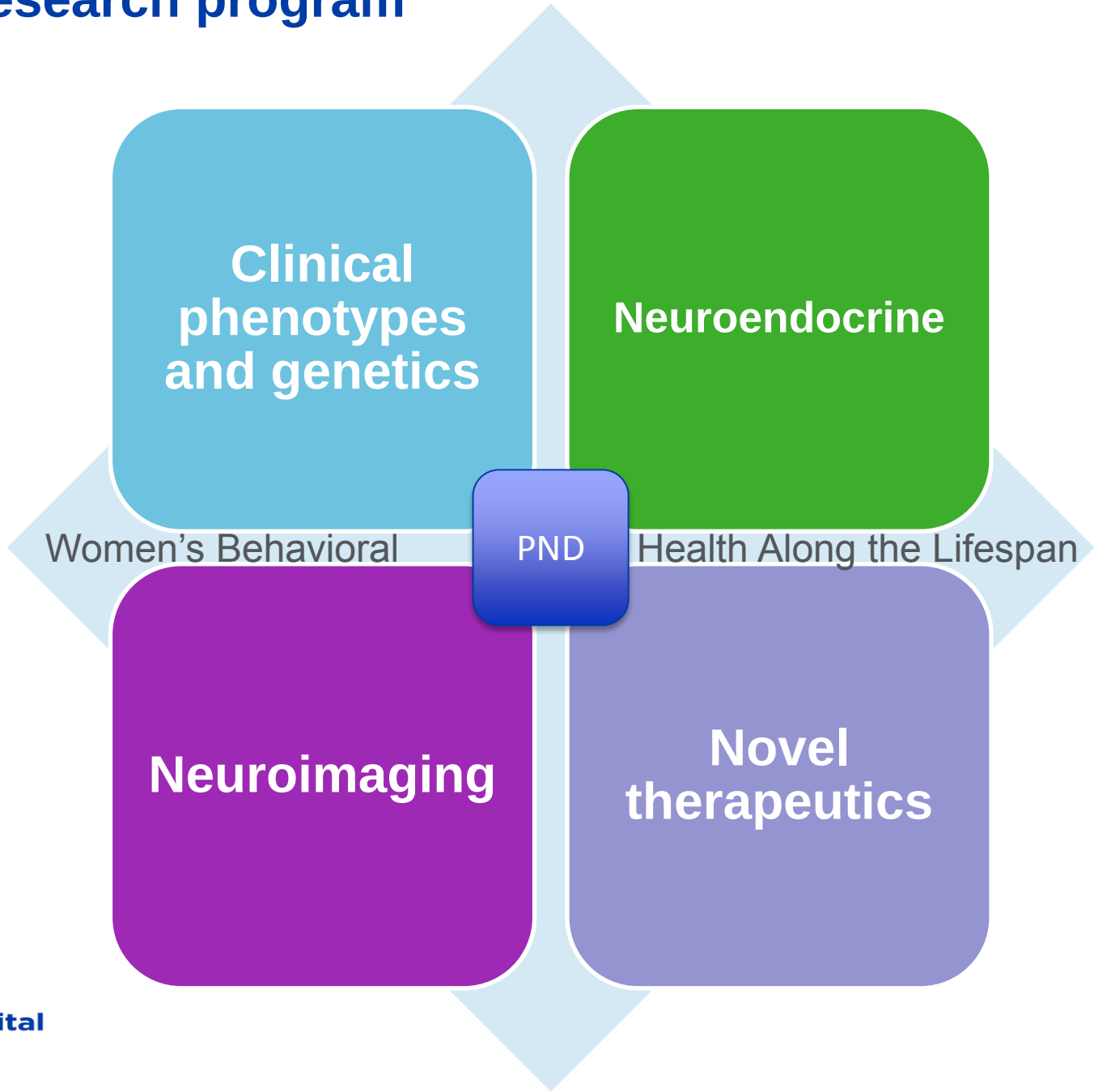
New outpatient and inpatient PDF brochures for printing and distribution are available at Northwell OBGYN and Psychiatry websites

https://www.northwell.edu/obstetrics-and-gynecology/treatments/perinatal-psychiatry-services



Research and the novel FDA-approved antidepressant for PPD (i.e. brexanolone/Zulresso)

Overview of our research program



Novel antidepressant for the treatment of postpartum depression

Neuroactive steroids (NAS) are progesterone metabolites (break-down products) which are important for normal brain functioning and they help to balance the stress brain circuit during acute and chronic stress. (Gunn BG et al, 2015)

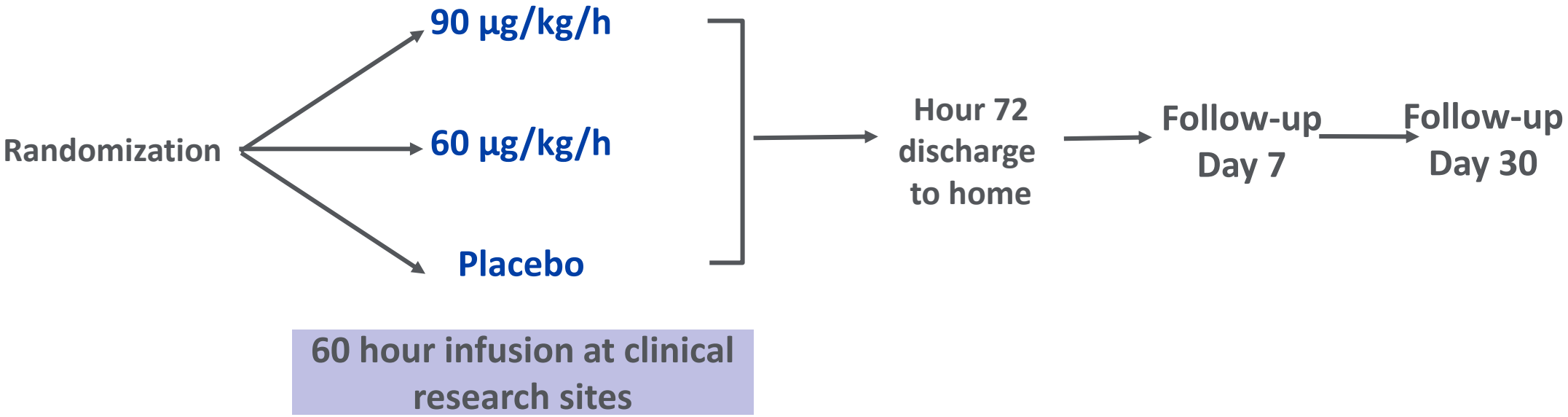
NAS such as allopregnanolone are made in the body (brain, ovaries, adrenal glands) and are modulators of $GABA_A$ receptors ($GABA_A$Rs).

NAS are pharmacologically distinct from benzodiazepines which also bind $GABA_A$Rs at different sites.

Brexanolone/Zulresso (synthetic allopregnanolone) is 1st FDA-approved medication for PPD

- -new antidepressant class
- -60 hr. peripheral IV infusion (schedule IV)
- -rapid acting (hours) (Kanes S et al. Lancet 2017; Meltzer-Brody S et al. Lancet 2018)
- -first-line treatment for moderate or severe PPD

Phase 2/3 double-blind, placebo-controlled RCTs of 60h synthetic allopregnanolone (brexanolone) injection for moderate-severe PND



Kanes S et al. *Lancet* 2017
Meltzer-Brody S et al. *Lancet* 2018

Integrated data from 202A, 202B and 202C brexanolone vs. placebo RCTs

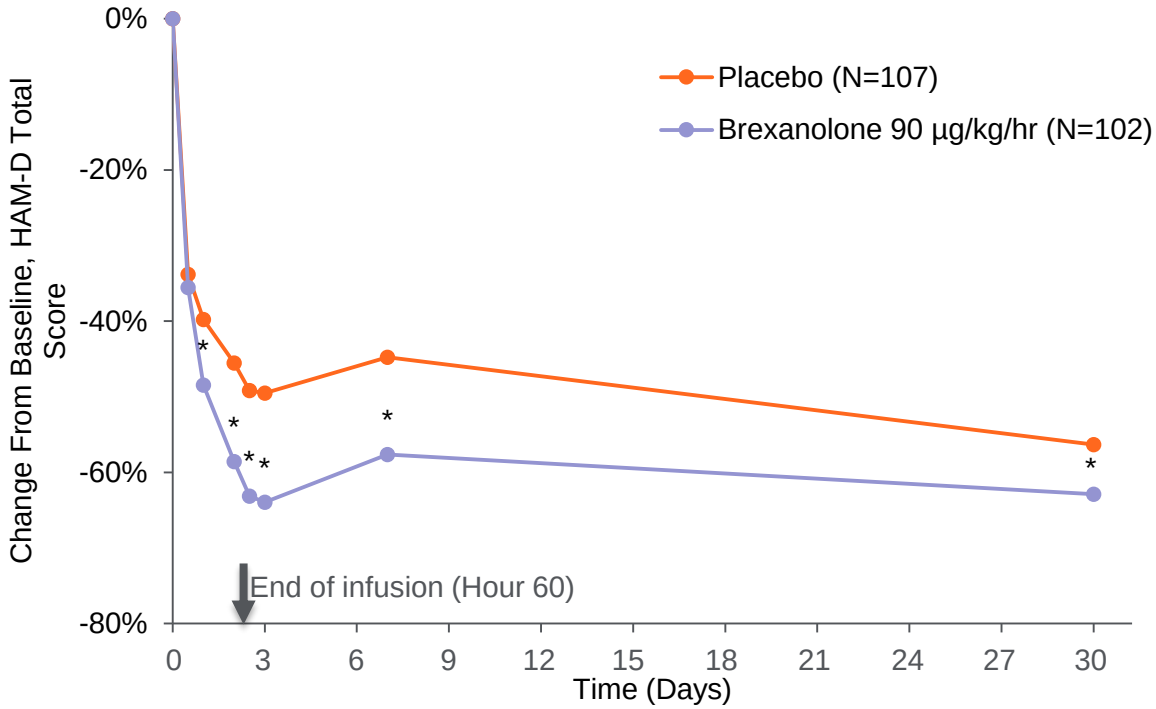


Figure 3: **Percentage change from baseline in mean HAM-D total score in the integrated BRX90 study population**

p values were calculated by two-sided *t* test. BRX90=brexanolone injection 90 µg/kg. *p<0·05 *vs* placebo. Source: Meltzer-Brody S. et al. *Lancet*, 2018

Adverse events across all placebo-controlled RCTs of brexanolone injection

Adverse Reactions in Placebo-Controlled Studies in Patients with PPD Reported in ≥ 2% of Brexanolone Injection-Treated Patients and Greater than Placebo-Treated Patients

	Placebo (n=107)	Maximum dosage 60 µg/kg/hour (n=38)	Maximum dosage 90 µg/kg/hour (Recommended dosage) (n=102)
Cardiac Disorders			
Tachycardia	-	-	3%
Gastrointestinal Disorders			
Diarrhea	1%	3%	2%
Dry mouth	1%	11%	3%
Dyspepsia	-	-	2%
Oropharyngeal pain	-	3%	2%
Nervous System Disorders			
Dizziness, presyncope, vertigo	7%	13%	12%
Loss of consciousness	-	5%	3%
Sedation, somnolence	6%	21%	13%
Vascular Disorders			
Flushing, hot flush	-	5%	2%

Source: Prescribing information; FDA Zulresso REMS website;

Excessive sedation and sudden LOC Black Box
In clinical studies, brexanolone caused sedation and somnolence that required dose interruption or reduction in some patients during the infusion (5% of brexanolone-treated patients compared to 0% of placebo-treated patients).

Some patients were also reported to have LOC or altered state of consciousness during the brexanolone injection infusion (4% of the brexanolone-treated patients compared with 0% of the placebo-treated patients).

All patients with loss of or altered state of consciousness recovered with dose interruption.

Brexanolone (Zulresso) was FDA-approved in March 2019; can only be prescribed at certified facilities through a **Risk Evaluation and Mitigation Strategy (REMS)** safety program

In summary

- Perinatal mood and anxiety disorders are common, underdiagnosed and undertreated.
- Screening for unipolar and bipolar perinatal depression is recommended in both antepartum and postpartum periods
- Current effective psychotherapies and pharmacotherapies are underutilized but can be very effective.
- Brexanolone (Zulresso) for the treatment of unipolar postpartum depression is a promising new pharmacological approach to treatment.
- Initiatives aimed at education (screening/differential diagnosis/treatment/referral), developing new WBH clinicians, integrated care programs, specialized treatment center development and research will help fill current gaps in women's behavioral health care.

Thank you!

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