

“**Depressive disorders occur twice as often in women compared with men.**”

Marlene Freeman, MD

Associate Professor of Psychiatry, Harvard Medical School
Director of Clinical Services, Perinatal and Reproductive Psychiatry Program,
Massachusetts General Hospital

?

“**Sex hormones affect neurotransmitters and shape the adult female brain during hormonal transition periods**”

Frontiers in Neuroscience
Max Planck Institute for Human Cognitive and Brain Sciences



TREATMENT INNOVATIONS IN WOMEN'S MENTAL HEALTH

Women of All Ages and their HCPs Desire Treatment Options Designed to Address their Unique Mental Health Needs Effectively and Safely

EnBrace HR small soft gel
All-Natural & Safe Ingredients
Root Cause Treatment

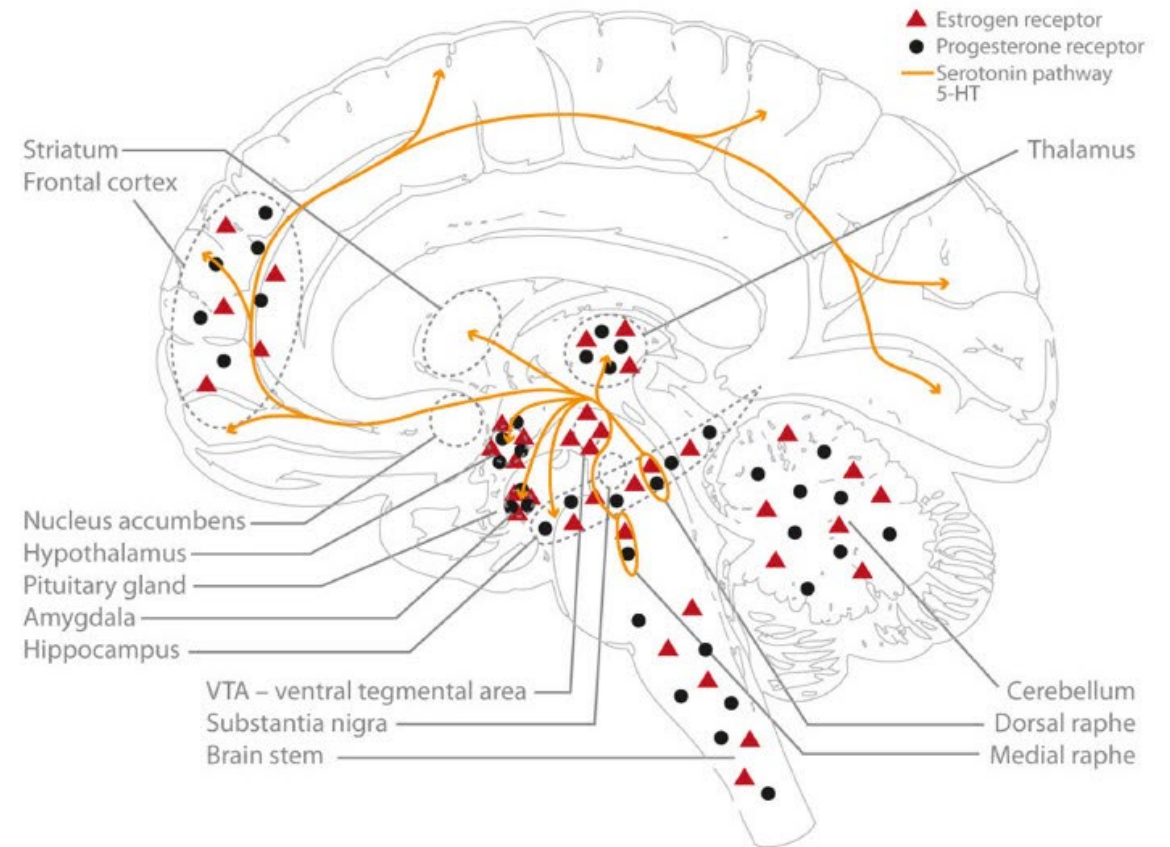
Clinically Proven Effectiveness for:
Major Depressive Disorder
PMS/PMDD & Menopause
Including in and around pregnancy

INTERACTIONS BETWEEN SEX HORMONES AND NEUROTRANSMITTERS

Frontiers in Neuroscience/Neuroendocrine Science, February 2015/Volume 9/Article 37/ Page 4

Interaction between ovarian hormone levels, receptor sites, and circuits, modulate serotonergic functions, levels, and reactivity in females throughout adolescence and adulthood - Affecting mood, memory, emotions, appetite, and cognition.

Serotonergic Pathways



“Promising therapeutic approaches to improve PMS, PMDD, Perimenopausal mood and depressive disorders should include a strategy that increases neurotransmitters by administering dietary coenzymes and mineral cofactors that are the precursors for the monoamines metabolized by MAO-A.”

EnBrace HR Small Gel Cap

INGREDIENTS

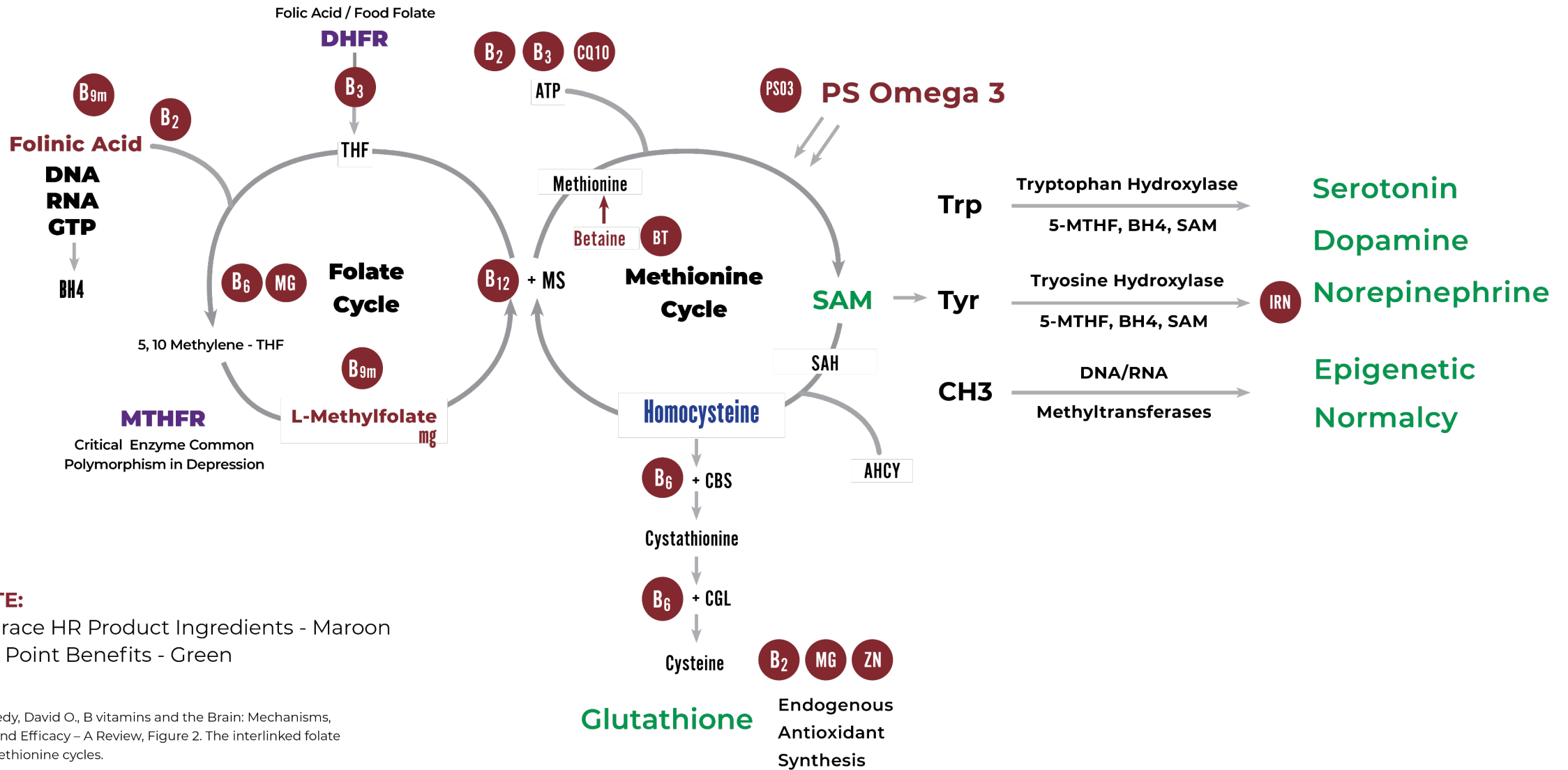
Rx | All Natural | Unique | Bioactive Coenzyme Vitamin Gel Cap

“EnBrace HR contains 5.53 mg. of L-Methylfolate Magnesium and small quantities of other folate derivatives (1mg. folic acid and 2.5mg of folinic acid) optimal for a depressed population with high rates of MTHFR polymorphism that affect folic acid metabolism and high risk of neural tube defects and other birth defects.”

Freeman M. et al: A prenatal Supplement with Methylfolate for the Treatment and Prevention of Depression in Women Trying to Conceive and During Pregnancy, Annals of Clinical Psychiatry, February 2019.

L-Methylfolate Magnesium	7mg
Folinic Acid	2.5mg
Folic Acid	1mg
B12 (Adenosylcobalamin)	50mcg
B6 (Pyridoxal-5-Phosphate)	25mcg
B1 (Thiamine Pyrophosphate)	25mcg
B2 (Flavin Adenine Dinucleotide)	25mcg
B3 (Nicotinamide Adenine Dinucleotide)	25mcg
PS-Omega-3 (Phosphatidylserine, EPA, DHA)	20mg
Magnesium Ascorbate	24mg
Magnesium L-Threonate	1mg
Iron (Ferrous Glycine Cysteinate)	1.5mg
Zinc Ascorbate	1mg
Betaine	500mcg
Citric Acid Monohydrate	1.83mg
Sodium Citrate	3.67mg
CoQ10	500mcg
Piperine (B Vitamin Bioenhancer)	500mcg

METHYLATION CHART

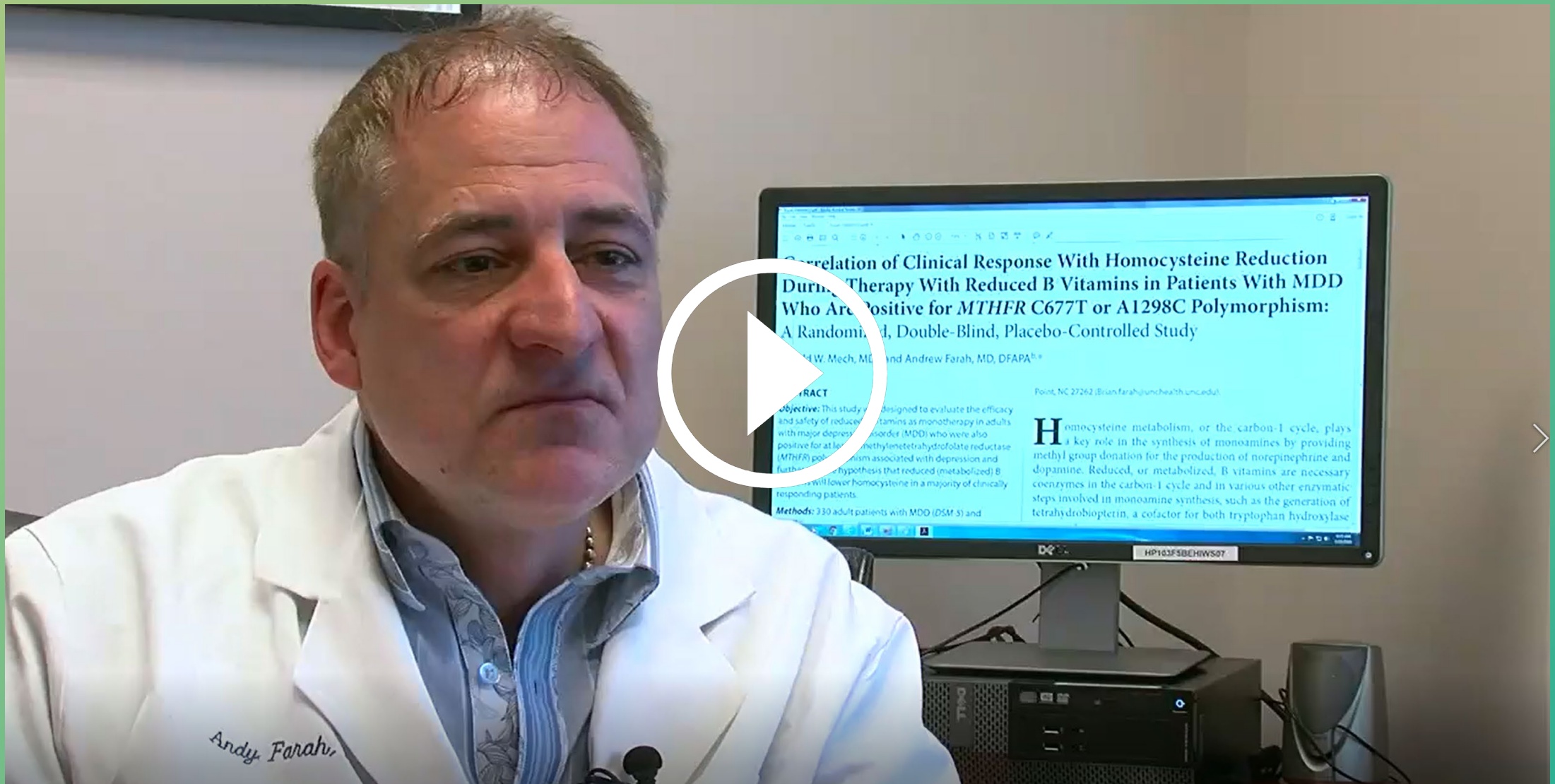


NOTE:

EnBrace HR Product Ingredients - Maroon
End Point Benefits - Green

*Kennedy, David O., B vitamins and the Brain: Mechanisms, Dose and Efficacy – A Review, Figure 2. The interlinked folate and methionine cycles.

CLINICAL STUDY OVERVIEW



THE JOURNAL OF CLINICAL PSYCHIATRY

330 ADULT PATIENT RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED STUDY

OBJECTIVE:

This 8-week study was designed to evaluate the efficacy and safety of EnLyte/EnBrace HR as monotherapy in adults with major depressive disorder (MDD) who were also positive for at least 1 methylenetetrahydrofolate reductase (MTHFR) polymorphism associated with depression and further test the hypothesis that EnLyte/EnBrace HR will lower homocysteine in a majority of clinical responding patients.

MAY 2016

Correlation of Clinical Response With Homocysteine Reduction During Therapy With EnLyte/EnBrace HR in Patients With MDD Who Are Positive for MTHFR C677T or A 1298C Polymorphism - Andrew Farah, MD

1) Mean MADRS Symptom Score of EnBrace HR Versus Placebo



2) 30% Reduction in Homocysteine Levels (Compared to Placebo)

**NO SIDE EFFECT WAS REPORTED AT GREATER RATE
THAN PLACEBO**

ONSET OF ACTION: 2 WEEKS

ENBRACE HR STUDY

regnant <28 weeks. **Group 1** participants were well (not in depressive episodes) and planned pregnancies for pregnancy. **Group 2** participants were depressed at baseline. Primary outcomes included MDD relapse and depressive symptoms, verified with the Mini International Interview and the Montgomery-Åsberg Depression Rating Scale (MADRS), respectively. folic acid metabolism and inflammation were collected.

1 participants (N=11; well at baseline) experienced no significant decreases in MADRS scores of depressive relapse (27.3%; p=0.005) than expected when compared to historical controls. **2** participants (depressed at baseline) experienced significant improvements in MADRS scores (p<0.001), with improving >50% and one improving 33.3%. One adverse event occurred, a hospitalization for safety concerns.^{4,8}

Results suggest EnBrace HR is a well-tolerated intervention with potential efficacy for the treatment of perinatal depression. Larger controlled trials are necessary.

Introduction

Major Depressive Disorder (MDD) and Major Depressive Episodes (MDEs) in Women: MDD occurs approximately twice as often in women compared to men.^{1,2} Women are at a higher risk for MDEs during pregnancy and the postpartum period.³ Many women often discontinue standard antidepressant medications prior to or during pregnancy for safety concerns.⁴⁻⁸

Few evidence-based alternatives to antidepressant medications for the treatment and prevention of perinatal depression exist, leaving pregnant women and clinicians with the clinical dilemma of weighing potential exposure to medication against impact of untreated maternal depression.

Folate and Folate-Related Therapies: Folate, folic acid, and methylfolate may have antidepressant effects.⁹⁻¹³ These interconvertible folate forms constitute the one-carbon cycle and are essential for neurotransmitter synthesis.¹⁴ Methylfolate may exert an antidepressant effect by impacting neurotransmitter synthesis.¹⁵ Methylfolate must be converted to its active form, methylfolate, for use in the body. Polymorphisms in the MTHFR gene may limit the efficacy of folic acid as an intervention targeting MDD.¹⁶⁻¹⁸ Methylfolate may be more readily absorbed in the brain than folic acid, and methylfolate has potential as a neuroprotective agent.¹⁹⁻²² Methylfolate treatment in early trials has been found to induce significant improvement in depressive symptoms both when used as an adjunct to antidepressant therapy and when used as a monotherapy.¹⁹⁻²⁴ Methylfolate related compounds reduce rates of neural tube defects and improve child neurodevelopmental outcomes, conferring benefits and minimizing potential risks of antidepressants during pregnancy.²⁵⁻²⁸

EnBrace HR: EnBrace HR is a prescription prenatal/postnatal dietary management product that contains 5.53 mg L-methylfolate and other folate derivatives (1 mg folic acid, and 2.2 mg folic acid), optimal for a population with high rates of polymorphisms that affect folic acid metabolism.

Methods

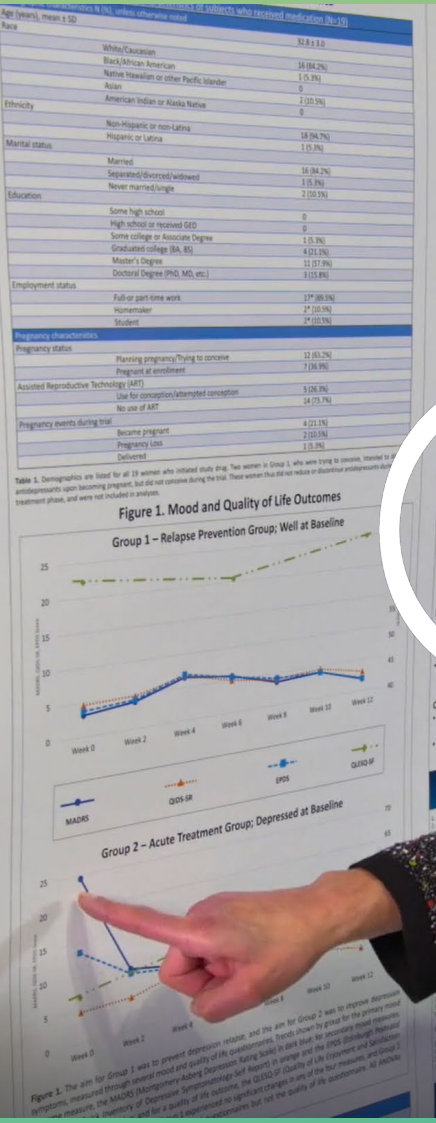
Group 1: Well at Baseline; Relapse Prevention Group

Group 2: Depressed at Baseline; Acute Treatment Group

Inclusion Criteria:

- Age ≥18
- MDD as primary diagnosis
- Have prescribing clinician
- Planning to conceive or <28 weeks pregnant at enrollment
- No dose increase of current antidepressant medication
- Start of new antidepressant medication
- Currently depressed, as verified by MINI
- Depressed, baseline MADRS score ≥15

Primary Outcome: To obtain preliminary data on the efficacy of EnBrace HR for treatment of acute MDEs, and to avoid starting on a higher dose of current antidepressant during pregnancy.



Adverse Events

Adverse Event	n/N (n/N reported)
Cough and throat irritation	1/11 (9.1%)
Difficulty concentrating	1/11 (9.1%)
Difficulty swallowing	1/11 (9.1%)
Headache	2/11 (18.2%)
Heartburn	2/11 (18.2%)
Stomach discomfort	2/11 (18.2%)
Stomach pain	2/11 (18.2%)
Tiredness	1/11 (9.1%)
Weight gain	1/11 (9.1%)
Weight loss	1/11 (9.1%)
Yeast infection	1/11 (9.1%)
Total Adverse Events	15/11 (13.6%)

Discussion and Conclusions

Results Summary

- We assessed EnBrace HR in two samples of women planning pregnancy or during early pregnancy to obtain data regarding:
 - Prevention of depressive relapse in women with histories of MDD
 - Ability to tolerate EnBrace HR while pregnant and postpartum to avoid the use of an antidepressant

Conclusions:

- All participants in Group 1 who were depressed at baseline, experienced a relapse to an MDE (27.3%), a higher relapse rate than historical controls who discontinued antidepressants for pregnancy.
- All participants in Group 2, who were depressed at baseline, experienced a 50% improvement or more in MADRS scores by the end of the study, and 5 of 6 (83.3%) participants achieved remission. One participant in Group 2 relapsed during pregnancy, then again relapsed postpartum.
- We found EnBrace HR was well-tolerated and had no significant adverse events that required hospitalization.

Strengths

- We assessed a novel intervention and treatment in women with perinatal depression during pregnancy.
- We used a validated measure of MDEs and the diagnosis of MDD.
- Other strengths include the use of a validated measure of MDEs and the use of a validated measure of MDEs.

Limitations

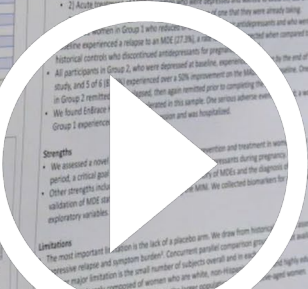
- The most important limitation is the lack of a placebo arm. We draw from historical data and use historical controls to compare our results.
- Concurrent parallel comparison groups were not used.
- Concurrent parallel comparison groups were not used.

References

1. National Institute of Mental Health. Major Depressive Disorder. 2023. <https://www.nimh.nih.gov/health/topics/major-depressive-disorder/index.shtml>

2. Perinatal Depression. 2023. <https://www.nimh.nih.gov/health/topics/perinatal-depression/index.shtml>

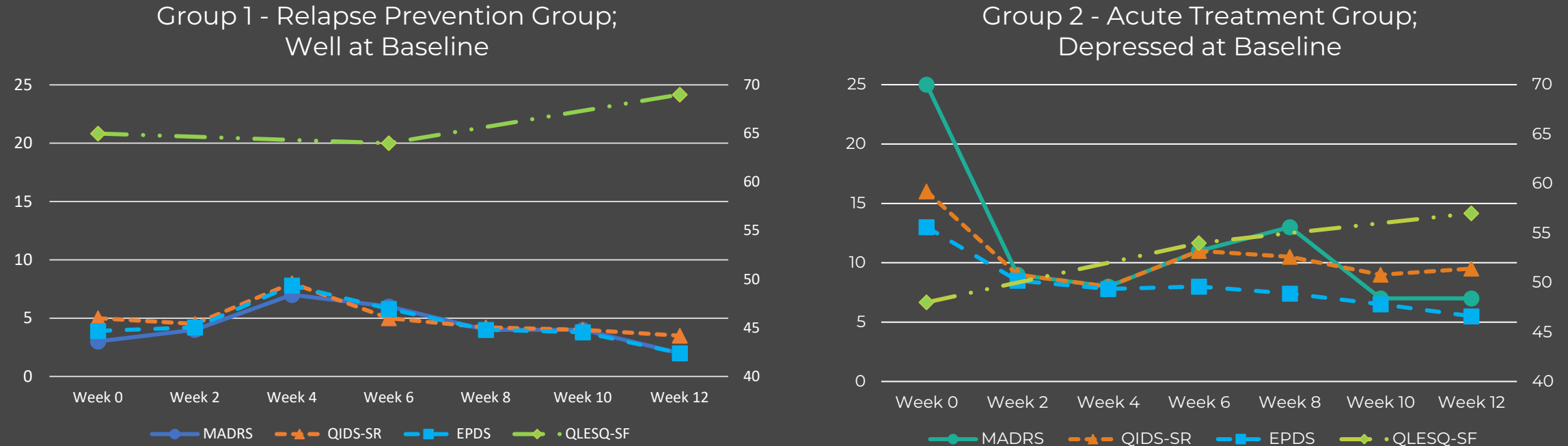
3. National Institute of Mental Health. Major Depressive Disorder. 2023. <https://www.nimh.nih.gov/health/topics/major-depressive-disorder/index.shtml>



EnBrace HR For The Treatment and Prevention of Depression in Women

Trying to Conceive and During Pregnancy

Marlene P. Freeman, MD et al, Annals of Clinical Psychiatry February 2019



CONCLUSION

Study results suggest EnBrace HR is a novel and well tolerated intervention with efficacy for the prevention and treatment of depression among women planning pregnancy and who are pregnant.

Figure 1. The aim for Group 1 was to prevent depression relapse, and the aim for Group 2 was to improve depression symptoms, measured through several mood and quality of life questionnaires. Trends shown by group for the primary mood outcome measure, the MADRS (Montgomery-Asberg Depression Rating Scale) in dark blue; for secondary mood measures, the QIDS-SR (Quick Inventory of Depressive Symptomatology-Self Report) in orange and the EPDS (Edinburgh Postnatal Depression Scale) in light blue; and for a quality of life outcome, the QLESQ-SF (Quality of Life Enjoyment and Satisfaction Questionnaire -Short Form) in green. Group 1 experienced no significant changes in any of the four measures, and Group 2 experienced significant improvements in the mood questionnaires but not the quality of life questionnaire. All ANOVAs indicating significance are reported in Table 3.

PMS

(Premenstrual Syndrome)

Mild/Moderate

Cyclic hormonal changes of the menstrual cycle causes fluctuations of serotonin levels leading to adverse symptomology

– Mayo Clinic –



PMDD

(Premenstrual Dysphoric Disorder)

Severe (DSM-5)

Tension/Anxiety, Depressed Mood – Irritability/Anger – Appetite Changes – Cravings – Insomnia – Social Conflict Withdrawal – Anhedonia – Feeling overwhelmed/ out of control - hopelessness

Biochemical Wellness

EnBrace HR normalizes serotonin levels and is an effective, all-natural, safe, root cause monotherapy option or adjunct to SSRIs, oral contraceptives, NSAIDs, and/or diuretics in the prevention or treatment of PMS/PMDD.

Dietary B Vitamin Intake and Incident of Premenstrual Syndrome. Manson et al. Am J Clin Nutr. 2011

Clinical Result Example

A 17-year-old on Paxil for PMDD experienced side effects and withdrawal symptoms after discontinuing Paxil. She was hesitant to resume antidepressant medications after presenting again with PMDD depression, and a MADRS of 20. The patient elaborated she was “putting on a happy face”. She was prescribed EnBrace HR and within 4 weeks her MADRS dropped from 20 to 6.

Coenzyme Treatment of Childhood and Adolescent Depression: A Case Series. Farah et al. Clinical Psychiatry Vol 7 #5S3:93 April 2021

“For the emotional dysregulation of PMS and PMDD, we turned first-line to the natural, broad spectrum B vitamin coenzymes and mineral cofactor agent, EnBrace HR. This product has provided safe and effective relief for countless patients with these challenging symptoms”

Andrew Farah, MD

Attending Psychiatrist, Novant Health System, Winston-Salem, NC
Medical Director of Strategic Mental Health Interventions

MENOPAUSE

Declining ESTROGEN levels in MENOPAUSE aggravated by MTHFR SNP cause SEROTONIN depletion and HOMOCYSTEINE increases leading to:

EMOTIONAL DYSREGULATION

- Depression Disorders
- Anxiety
- Lack of Motivation
- Aggressiveness
- Difficulty Concentrating
- Fatigue
- Irritability

HOT FLASHES

- Insomnia
- Warmth
- Flushing
- Rapid Heartbeat
- Chills
- Headache
- Night Sweats

LOW BONE MINERAL DENSITY

- Back or Neck Pain
- Loss of Height
- Stooped Posture
- Brittle Bones/Nails
- Receding Gums
- Grip Strength
- Aching Muscles

COGNITIVE DEFICITS

- Working Memory
- Attention
- Reduced Processing Speed
- Reduced Verbal Memory
- Word Retrieval Trouble
- Loss of Train of Thought

*Clinical references available upon request

EnBrace HR restores serotonin levels and reduces high homocysteine and is clinically proven to treat adverse health outcomes in Menopause naturally and safely, alone or adjunctively with HRT, SSRIs or Calcium/D.

HOW TO PRESCRIBE

STEP 1

SUBMIT OUR ELECTRONIC FORM

Visit www.enbracehr.com

- Click "Prescribe Now"
- Fill out the required information
- Click "Submit."

**EnLyte and EnBrace HR will be available in your EMR, but the most cost-effective way to prescribe is by using the "Prescribe Now" button. This ensures your patients receive 60 days for just \$60, and the lowest price available moving forward.*

STEP 2

INFORM YOUR PATIENT

Let your patient know that a friendly customer care representative will contact them shortly to get started on EnBrace HR for just \$1 a day for the first 60 days.

STEP 3

WE TAKE CARE OF THE REST

A representative will contact your patient to arrange the initial **60-day trial for just \$60**, which will typically be shipped the same day.

REFILLS:

Our Medical Food Distributor will handle all refills to ensure uninterrupted care.