



INNOVATIONS IN WOMEN'S MENTAL & REPRODUCTIVE HEALTH

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

References can be found at the end of this presentation



Clinically Proven Effectiveness for:

- ❖ Depression and Anxiety
- ❖ Including in and Around Pregnancy
- ❖ PMS/PMDD & Menopause
- ❖ High or Low Risk Prenatal Vitamin

EnBrace HR Small Gel Cap

INGREDIENTS

“EnBrace HR contains the exact clinically recommended vitamin coenzymes, mineral cofactors and omegas needed to normalize uterine and CNS intracellular methylation for normal mental and reproductive clinical outcomes.”

Towny Robinson, CEO JayMac Pharmaceuticals
Inventor of EnBrace HR

Most Diverse Natural Folates: FDA 15mg DFE

L-Methylfolate Magnesium	7mg
Folinic Acid	2.5mg
Folic Acid	1mg

B Vitamins in their Bioactive Coenzyme Form

B12 (Adenosylcobalamin)	50mcg
B6 (Pyridoxal-5-Phosphate)	25mcg
B1 (Thiamine Pyrophosphate)	25mcg
B2 (Flavin Adenine Dinucleotide)	25mcg
B3 (Nicotinamide Adenine Dinucleotide)	25mcg
Bioperine (B Vitamin Bioenhancer)	25mg

Minerals in their Bioactive Cofactor Form

Magnesium Ascorbate	24mg
Magnesium L-Threonate	1mg
Zinc Ascorbate	1mg
Iron (Ferrous Glycine Cysteinate)	13.6mg

Phospholipid Form – Brain Ready

PS-Omega-3 (Phosphatidylserine, EPA, DHA)	23.3mg
---	--------

Absorption Enhancer

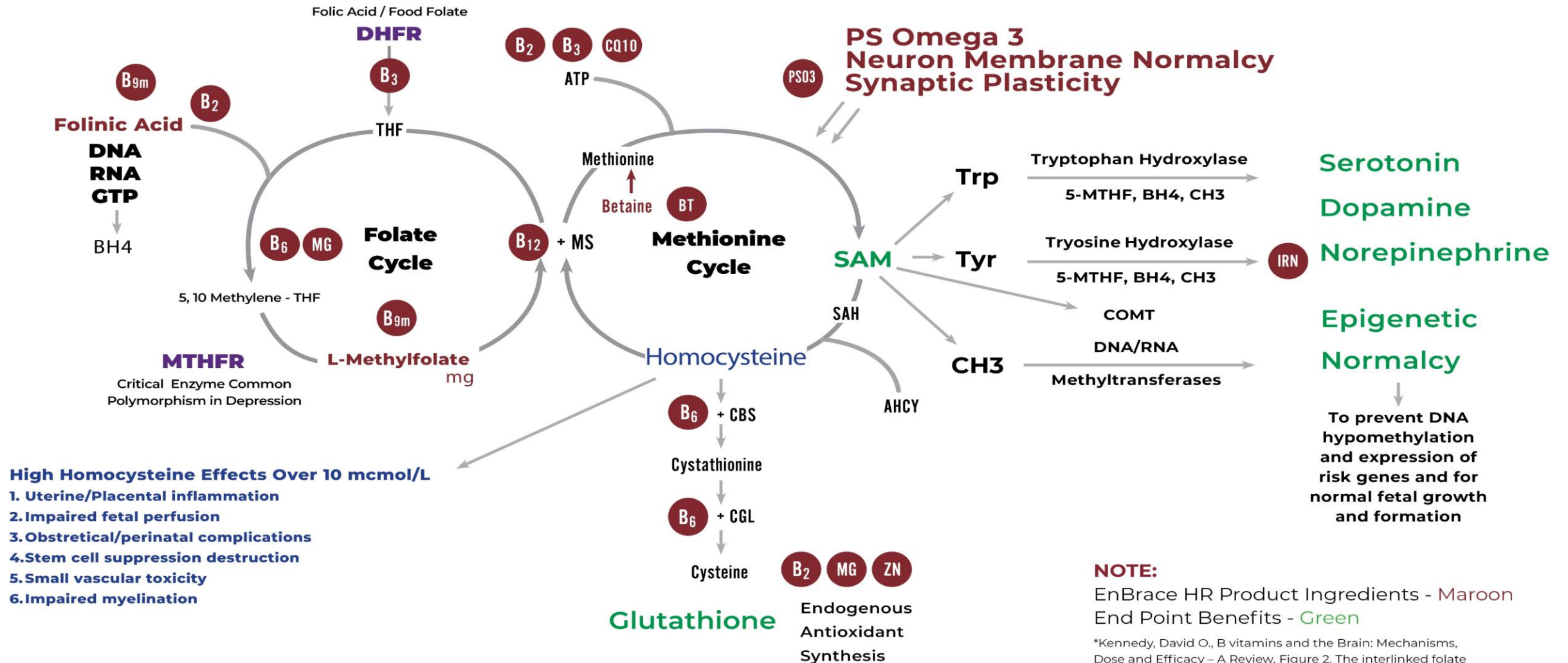
Sodium Citrate	10mg
----------------	------

Energizer

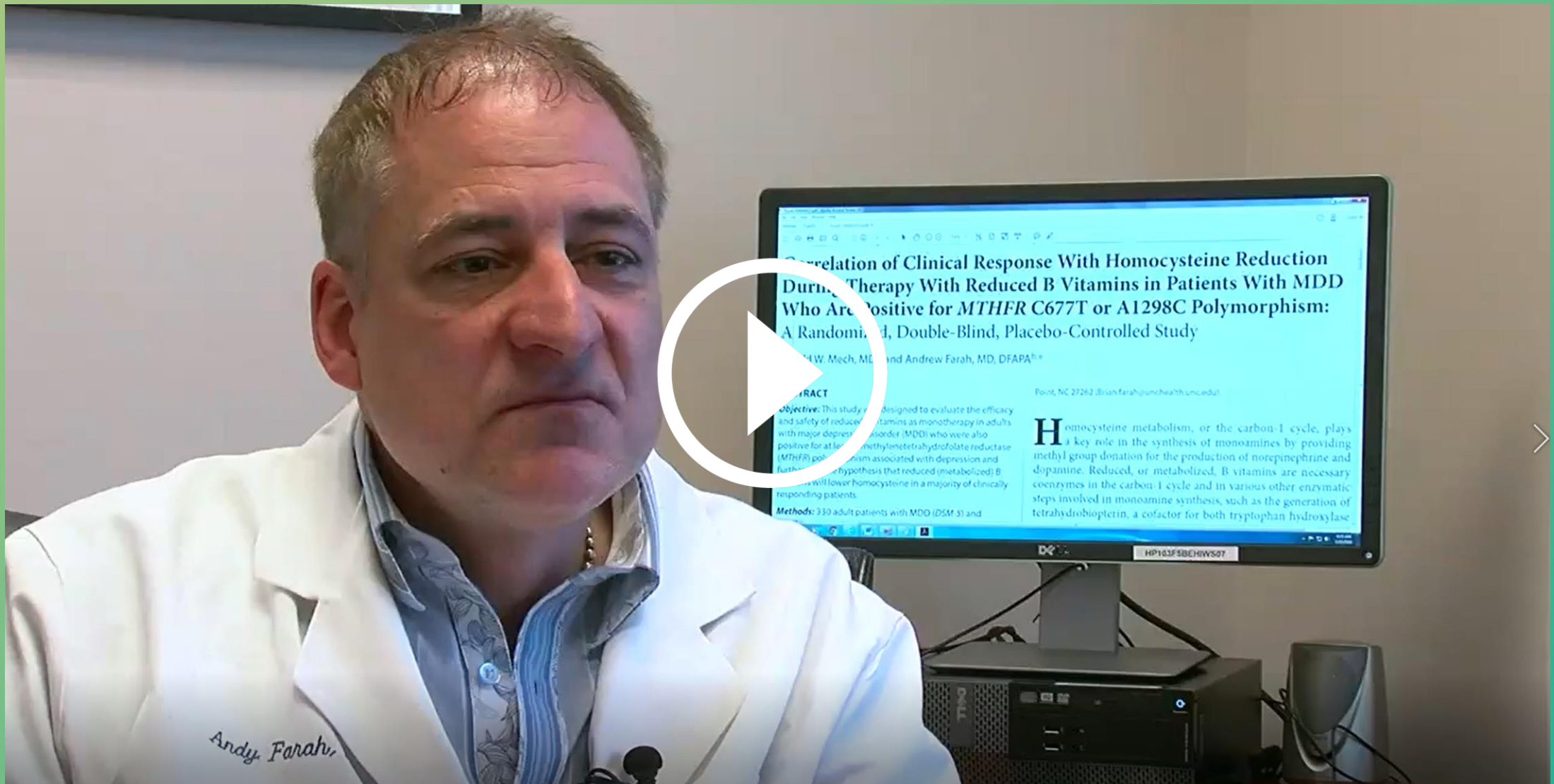
CoQ10	500mcg
-------	--------

Intracellular Biochemical Root Cause Methylation Chart

EnBrace HR Normalizes All Co-Enzyme/Cofactor Deficiencies and Methylation Disruption, No Matter the Cause and Converts to Normal Mental and Reproductive Health Outcomes Based on Well-Controlled Clinical Trials.



CLINICAL STUDY OVERVIEW



Correlation of Clinical Response With Homocysteine Reduction During Therapy With Reduced B Vitamins in Patients With MDD Who Are Positive for MTHFR C677T or A1298C Polymorphism: A Randomized, Double-Blind, Placebo-Controlled Study

David W. Meacham, MD, and Andrew Farah, MD, DFAPA[®]

Point, NC 27262 (Brian.farah@unc.edu)

ABSTRACT

Objective: This study was designed to evaluate the efficacy and safety of reduced B vitamins as monotherapy in adults with major depressive disorder (MDD) who were also positive for at least one methylenetetrahydrofolate reductase (MTHFR) polymorphism associated with depression and further to test the hypothesis that reduced (metabolized) B vitamins will lower homocysteine in a majority of clinically responding patients.

Methods: 330 adult patients with MDD (DSM-5) and

Homocysteine metabolism, or the carbon-1 cycle, plays a key role in the synthesis of monoamines by providing methyl group donation for the production of norepinephrine and dopamine. Reduced, or metabolized, B vitamins are necessary coenzymes in the carbon-1 cycle and in various other enzymatic steps involved in monoamine synthesis, such as the generation of tetrahydrobiopterin, a cofactor for both tryptophan hydroxylase

Andy Farah,

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

... study included women with histories of MDD who were planning antepartum pregnancy. Group 1 participants were well (not in depressive episodes) and planned to continue antidepressant medication during pregnancy. Group 2 participants were depressed at baseline. Primary outcomes included MADRS relapse and depressive symptoms, verified by the Mini International Phobic Interview and the Montgomery-Åsberg Depression Rating Scale (MADRS), respectively. Folate metabolism and inflammation were collected.

Group 1 participants (N=11; well at baseline) experienced no significant decreases in MADRS scores at 12 weeks (27.3%; p=0.005) than expected when compared to historical controls. Group 2 participants (depressed at baseline) experienced significant improvements in MADRS scores (p<0.001), with 50% of participants improving >50% and one improving 33.3%. One adverse event occurred, a hospitalization for perinatal depression.

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

Conclusion

Major Depressive Disorder (MDD) and Major Depressive Episodes (MDEs) in Women: MDD is approximately twice as often in women compared to men.^{1,2} The risk for MDEs during pregnancy and the postpartum period.³ Women often discontinue standard antidepressant medications prior to or during pregnancy for safety concerns.⁴⁻⁶ Few evidence-based alternatives to antidepressant medications for the treatment and prevention of perinatal depression, 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 and folate-related therapies suggest various folate forms including folic acid, folinic acid, and methylfolate may have antidepressant effects.⁷⁻¹² These interconvertible folate forms constitute the one-carbon cycle and are thought to exert an antidepressant effect by impacting neurotransmitter synthesis.¹³ Folate 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.¹⁴⁻¹⁶ Folate methylation may be more readily absorbed in the brain than folate, and methylfolate has potential as an adjunct to antidepressant treatment for MDD.¹⁷⁻²⁴ Folate 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 Folate-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 folinic acid), optimal for a population with high rates of polymorphisms that affect folic acid metabolism.

Methods

Group 1: Well at Baseline; Relapse Prevention Group
Inclusion Criteria:
 • Age ≥18
 • MDD as primary diagnosis
 • Have prescribing clinician
 • Planning to conceive or <28 weeks pregnant at enrollment
Exclusion Criteria:
 • No dose increase of current antidepressant medication
 • Start of new antidepressant medication
 • Currently depressed, as verified by MINI
 • "Depressed", baseline MADRS score ≥15

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
Exclusion Criteria:
 • No dose increase of current antidepressant medication
 • Start of new antidepressant medication
 • Currently depressed, as verified by MINI
 • "Depressed", baseline MADRS score ≥15

Age (years), mean ± SD: 32.8 ± 5.0

Race	%
White/Caucasian	88.24%
Black/African American	11.76%
Native Hawaiian or other Pacific Islander	0
Asian	0
American Indian or Alaska Native	0
Ethnicity	
Non-Hispanic or non-Latina	100%
Hispanic or Latina	0
Marital status	
Married	100%
Separated/Divorced/Widowed	0
Never married/Single	0
Education	
Some high school	0
High school or technical GED	0
Some college or Associate Degree	0
Graduated college (BA, BS)	100%
Master's Degree	100%
Doctoral Degree (PhD, MD, etc.)	0
Employment status	
Full- or part-time work	100%
Homemaker	0
Student	0
Insurance characteristics	
Pregnancy status	
Planning pregnancy/Trying to conceive	100%
Pregnant at enrollment	0
Assisted Reproductive Technology (ART)	0
Use for conception/Attempted conception	100%
No use of ART	0
Pregnancy events during trial	
Became pregnant	100%
Pregnant MDE	0
Outcomes	
Completed	100%
Discontinued	0
Dropouts	0

Adverse Events

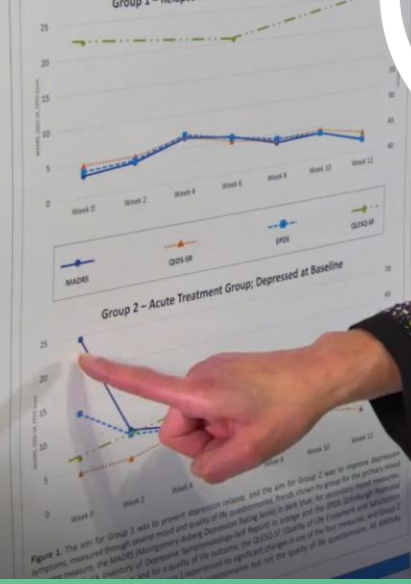
Adverse Event	# of patients
Headache	1
Nausea	1
Constipation	1
Difficulty sleeping	1
Chills/Fatigue	1
Weight gain	1
Joint pain	1
Stomach pain	1
Diarrhea	1
Abdominal pain	1
Upper respiratory tract infection	1
Headache	1
Mental health	1
Depression	1
Anxiety	1
Perinatal depression	1
Postnatal depression	1
Perinatal anxiety	1
Postnatal anxiety	1
Perinatal depression with anxiety	1
Postnatal depression with anxiety	1
Perinatal anxiety with depression	1
Postnatal anxiety with depression	1
Perinatal depression and anxiety	1
Postnatal depression and anxiety	1
Perinatal anxiety and depression	1
Postnatal anxiety and depression	1
Perinatal depression, anxiety, and depression	1
Postnatal depression, anxiety, and depression	1
Perinatal depression, anxiety, and anxiety	1
Postnatal depression, anxiety, and anxiety	1
Perinatal anxiety, depression, and depression	1
Postnatal anxiety, depression, and depression	1
Perinatal depression, anxiety, and depression	1
Postnatal depression, anxiety, and depression	1

Discussion and Conclusions

Results Summary

- We assessed EnBrace HR in two samples of women planning pregnancy to obtain data regarding:
 - Prevention of depressive relapse in women with histories of MDD
 - Acceptability of EnBrace HR to women who were depressed and wanted to avoid the use of an antidepressant during pregnancy

Figure 1. Mood and Quality of Life Outcomes



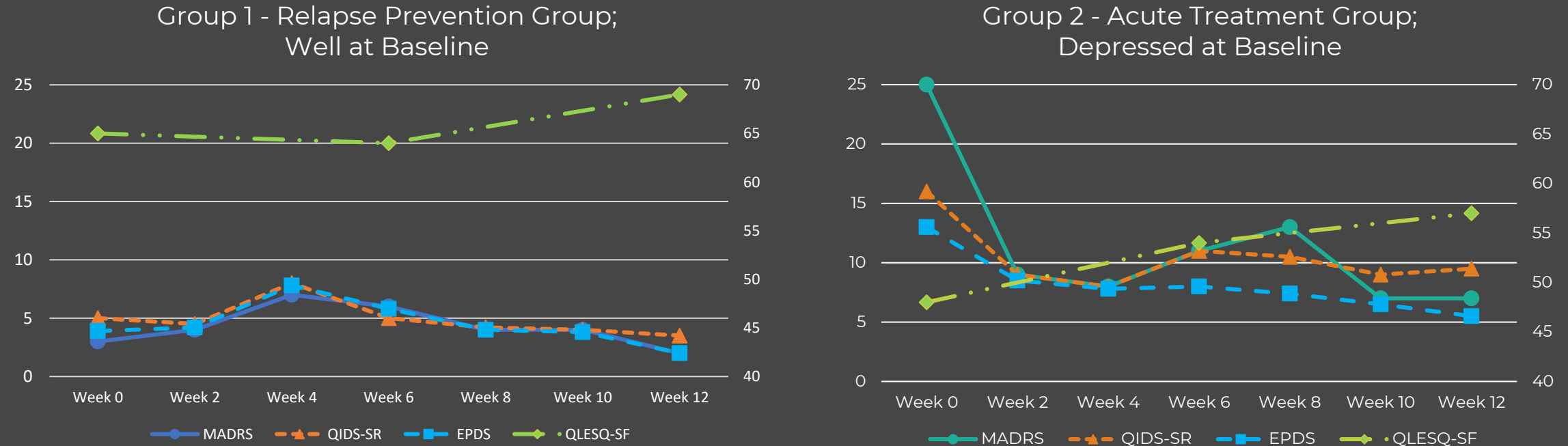
References

Financial Disclosures/Support

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

Menopause

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– Feeling overwhelmed – Hopelessness – Hot Flashes**

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, diuretics, and/or HRT in the prevention or treatment of PMS/PMDD/MENOPAUSE.

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, PMDD, and Menopause 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 female hormonal fluctuations or deficiency”

Andrew Farah, MD

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



Provides the most diverse combination of folates and methylation vitamin coenzymes and mineral cofactors for maximum prevention of NTDs and other birth defects in low or high-risk pregnancies.

An optimal serum folate level for birth defect prevention should be reached 4 weeks prior to conception, 50% of pregnancies are unplanned.

Mechanism of Cellular Action

Normalize impaired cellular “homocysteine/methionine” metabolism disorders that can lead to placental inflammation, impaired fetal perfusion, impaired nucleotide and DNA synthesis and faulty epigenetic expression.

To Prevent or Reduce Risk For:

- ❖ All Neural Tube Defects
- ❖ Congenital Heart & Kidney Disorders
- ❖ Down Syndrome
- ❖ ADHD
- ❖ Autism Spectrum Disorders
- ❖ Orofacial Clefts
- ❖ Drug Related Birth Defects
- ❖ Pregnancy Complications
- ❖ Congenital Structural Malformation

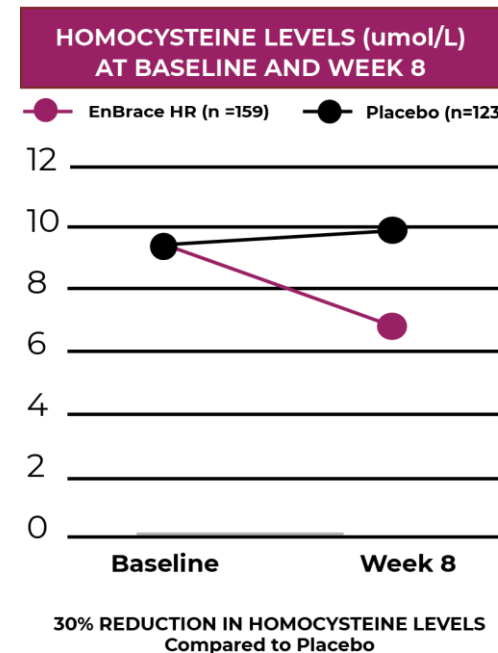
EnBrace HR Helps Eliminate the Risk for Adverse Pregnancy Outcomes, NTDs, and Other Birth Defects Associated with the effects of MTHFR Gene Variant

MTHFR gene variants prevent the production of the enzyme that converts folate to methylfolate leading to high homocysteine and low neurotransmitter production causing negative reproductive and CNS outcomes.

- 60%** of women have the heterozygous form of MTHFR gene variant
- 25%** of women have the homozygous form of MTHFR gene variant
- 50%** of folate related NTDs and other birth defects are linked to MTHFR
- 85%** of depressed and addicted women have an MTHFR gene variant

MTHFR Polymorphisms are Documented Risk Factors for these Adverse Pregnancy Outcomes:

- Miscarriage
- Perinatal/ Post-Partum Depression
- Pre-Term Delivery
- Low Birth Weight
- Pre-Eclampsia
- Placental Inflammation
- Impaired Fetal Perfusion
- Chromosomal Abnormalities



EnBrace HR is proven in a 330 patient, randomized, controlled trial in patients with an MTHFR variant to lower homocysteine 30% compared to placebo group.

Andrew Farah, MD et al.
Journal of Clinical Psychiatry, May 2016

HOW TO PRESCRIBE

STEP 1

USE OUR ONLINE PRESCRIBER FORM

Fill in prescriber and patient information and then hit “submit”

[CLICK HERE](#)

STEP 2

WE WILL OFFER YOUR PATIENT THEIR FIRST 60 DAYS FOR \$60

We will also provide them with the insurance steps and help determine the most cost-effective option moving forward

STEP 3

IF IT'S COVERED ON INSURANCE, WE WILL CONTACT YOUR OFFICE WITH PRESCRIBING INFO

If your patient does not have coverage or has a high co-pay, we will offer our discounted cash-pay option for EnBrace HR. No further action is needed for your office.

References

- 1.Freeman-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*, Feb. 2019
- 2.Farah et.al, Correlation of Clinical Response with Homocysteine Reduction During Therapy With Reduced B Vitamins in Patients With MDD Who Are Positive for MTHFR C677T or A1298C Polymorphism, *Journal of Clinical Psychiatry*, May 2016
- 3.MRC Vitamin Group, Prevention of neural tube defects: Results of the Medical Research Council Vitamin Study, *Lancet*, 1991
- 4.Czeizel et al., Periconceptional Folic Acid and Multivitamin Supplementation for the Prevention of Neural Tube Defects and Other Con-genital Abnormalities, *Clinical and Molecular Teratology*, 2008
- 5.FDA, 21 CFR-101.79- Health Claims: Folate and neural tube defects, CFR Text. 2019
- 6.Kirk E et al., Impact of the MTHFR C677T polymorphism on risk of neural tube defects: case-control study, *BMJ*, 2004
- 7.Ufriend et al., The C677T polymorphism of the methylenetetrahydrofolate reductase gene and idiopathic recurrent miscarriage, *Obstetrics & Gynecology*, April 2002
- 8.MTHFR Living, Preparing for Pregnancy with MTHFR Mutations, Jan. 2014
- 9.Garilli, Bianca ND, MTHFR Mutation: A Missing Piece in the Chronic Disease Puzzle, *Huffington Post*, Summer, 2012
10. Wald et al, Public health failure in the prevention of neural tube defects: time to abandon the tolerable upper intake level of folate,
- 11.Farah et al., The Prevalence and Role of MTHFR Polymorphism in Opiate Dependency, *Journal of Addiction and Therapies*, Feb. 2018
- 12.El-Hadidy et al., Methylene tetra hydrofolate reductase C677T Gene Polymorphism in Heroin Dependence, *Addiction Research & Therapy*, 2015
- 13.Mararwa et al., Prenatal exposure to SSRIs and SNRIs and risk for pulmonary hypertension of the newborn: a systemic review, meta-analysis, *AJOG*, 2018
- 14.Chambers et al., SSRI and Risk of Persistent Pulmonary Hypertension of the Newborn, *The New England Journal of Medicine*, 2011
- 15.Kieviet et al., Use of antidepressants during pregnancy in The Netherlands: observational study into post-partum interventions, *BMC Pregnancy & Childbirth*, 2017
- 16.MGH Center for Women's Health, womensmentalhealth.org, SSRIs and Poor Neonatal Adaptation: How Long do Symptoms Last, 2015
- 17.Liu et al., Antidepressant Use During Pregnancy and Psychiatric Disorders in Offspring, *BMJ*, 2017
- 18.Lugo-Candelas et al., Association Between Brain Structure and Connectivity in Infants and Exposure to SSRIs During Pregnancy, *JAMA Pediatrics*, 2018

References cont'd

20. WebMD. www.webmd.com, pregnancy-and-antidepressants, 2018
21. FDA A Appendix NIH, Antidepressant Drug Labels for Pregnant and Postpartum Women, 2014
22. EnBrace HR PI, FDS Daily Med, Dec. 2018
23. Turgal et al. MTHFR Polymorphisms and Pregnancy Outcome, PMC 6138472, Sept. 2018
24. Duprey Robert P. MTHFR Gene Polymorphism positive treatment-resistant depression, Neuropsychiatry 2019
25. Imbard A, Benoist JF, Blom HJ. Neural tube defects, folic acid and methylation. Int J Environ Res Public Health. 2013
26. Obeid R, Holzgreve W, Pietrzik K. Is 5-methyltetrahydrofolate an alternative to folic acid for the prevention of neural tube defects? J. Perinatal Med, 2013
27. Greenberg JA, Bell SJ, Guan Y, Yu YH. Folic Acid supplementation and pregnancy: more than just neural tube defect prevention. Rev Obstet Gynecol. 2011
28. NIH, Folate Fact Sheet for Professionals, 2022
29. MGH Center for Women's Mental Health, Folic Acid Supplements Before and After Conception: Prevention of Autism, 2022
30. Bjørk M, Riedel B, Spigset O, Veiby G, Kolstad E, Daltveit AK, Gilhus NE. Association of Folic Acid Supplementation During Pregnancy With the Risk of Autistic Traits in Children Exposed to Antiepileptic Drugs In Utero. JAMA Neurol. 2018 Feb
31. Sah AK, Shrestha N, Joshi P, Lakha R, Shrestha S, Sharma L, Chandra A, Singh N, Kc Y, Rijal B. Association of parental methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism in couples with unexplained recurrent pregnancy loss. BMC Res Notes. 2018 Apr
32. MGH Center for Womens' Mental Health Folic Acid and Risk of Perinatal Depression: Is there an Association? 2012
33. Methylenetetrahydrofolate Reductase Polymorphisms and Pregnancy Outcomes, Obstetrics and Gynecology, 2018
34. Zhang L, Sun L, Wei T. Correlation between MTHFR gene polymorphism and homocysteine levels for prognosis in patients with pregnancy-induced hypertension. Am J Transl Res. 2021 Jul