

## **Bupropion for Major Depressive Disorder and Smoking Cessation in Pregnancy. A Systematic Literature Review**

### **Authors:**

SALLY LAMBERT<sup>1</sup>, ADRIAN DUNLOP<sup>1,2</sup>

<sup>1</sup>*Drug and Alcohol Clinical Services, Hunter New England Local Health District,* <sup>2</sup>*School of Medicine & Public Health, University of Newcastle, NSW*

Presenter's email: [Adrian.Dunlop@hnehealth.nsw.gov.au](mailto:Adrian.Dunlop@hnehealth.nsw.gov.au)

**Introduction and Aims:** Bupropion is an antidepressant re-purposed to support nicotine cessation. Both nicotine use and depressive disorder are high prevalence disorders in pregnancy, with known adverse maternal and fetal outcomes. This review evaluates the effectiveness of bupropion for smoking cessation and depression in pregnancy and on birth outcomes following bupropion exposure during pregnancy.

**Method:** A systematic literature review was performed in February 2018 for published clinical studies investigating bupropion use in pregnancy

**Results:** Ten studies reported on adverse fetal outcomes: negative findings include a slightly elevated risk of ventricular septal defect and a slightly elevated risk of left outflow tract heart defects, however, most studies found no elevated risk of malformations. One study reported increased risk of ADHD with bupropion, another no adverse associations related to birthweight and prematurity, however did report an increased rate of spontaneous abortion. Four studies measured effectiveness for nicotine cessation in pregnant women, all found indicators that smoking was reduced, but none found an association with sustained tobacco abstinence. While there were no studies primarily measuring the effectiveness of bupropion for depression for pregnant women, one small study (n=56), did show promising results.

**Conclusions:** Overall, the literature comprised of small sample size studies which utilised different methodologies and included multiple variables, making between group comparison difficult. Only (three Studies were randomised controlled trial n=156). Future prospective controlled cohort studies may be able to determine the causality and temporality of observed fetal malformations, and larger randomised controlled trials may elucidate effectiveness of bupropion as an intervention for smoking cessation and depression in pregnant women.

**Implications for Practice:** While there are possible risks with its use in pregnancy, bupropion may be considered for smoking cessation during pregnancy where other approaches (e.g. Nicotine replacement therapy) have failed or are not clinically appropriate and the benefits outweigh the risks.

**Disclosure of Interest Statement:** No grants were received and there were no conflicts of interest in the development of this study.

### **References:**

Chung TK, Lau TK, Yip AS, Chiu HF, Lee DT. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. *Psychosom Med* 2001; 63: 830–834

Coleman T, Chamberlain C, Davey MA, Cooper SE, Leonardi-Bee J. Pharmacological interventions for promoting smoking cessation during pregnancy. *Cochrane Database Syst Rev* 2015:CD010078.

Sullivan PM, Dervan LA, Reiger S, et al. Risk of congenital heart defects in the offspring of smoking mothers: a population-based study. *J Pediatr*. 2015;166(4):978–984.e2

Marinescu I, Foarfa MC, Pirlog MC, et al. Prenatal depression and stress-risk factors for placental pathology and spontaneous abortion. *Rom J Morphol Embryol*. 2014;55(suppl 3):1155–1160.

Jarde A, Morais M, Kingston D, et al. Neonatal outcomes in women with untreated antenatal depression compared with women without depression: a systematic review and meta-analysis. *JAMA Psychiatry*. 2016;73(8):826–837.

De Long NE, Barra NG, Hardy DB, Holloway AC. Is it safe to use smoking cessation therapeutics during pregnancy? *Expert Opin Drug Saf* 2014;13:1721-31.

Louik C, Lin AE, Werler MM, Hernández- Díaz S, Mitchell AA. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *N Engl J Med* 2007;356:2675-83.

Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM; National Birth Defects Prevention Study. Use of selective serotonin-re-uptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med* 2007;256:2684-92.

Benowitz NL, Dempsey DA, Goldenberg RL, et al. The use of pharmacotherapies for smoking cessation during pregnancy. *Tob Control* 2000;9(Suppl 3):III91-4.

Berard A, Ramos E, Rey E, Blais L, St-Andre M, Oraichi D. First trimester exposure to paroxetine and risk of cardiac malformations in infants: the importance of dosage. *Birth Defects Res B Dev Reprod Toxicol* 2007;80:18-27.

Cole JA, Modell JG, Haight BR, Cosmatos IS, Stoler JM, Walker AM. Bupropion in pregnancy and the prevalence of congenital malformations. *Pharmacoepidemiol Drug Saf* 2007;16:474-84.

Thyagarajan V, Clifford CR, Wurst KE, et al. Bupropion therapy in pregnancy and the occurrence of cardiovascular malformations in infants. *Pharmacoepidemiol Drug Saf*. 2012;21(11):1240–1242

GlaxoSmithKline Bupropion Pregnancy Registry. Final report: 1 September 1997 through 31 March 2008. Registry Report. Wilmington, NC, 2008.

Einarson A, Choi J, Einarson T, et al. Incidence of major malformations in infants following antidepressant exposure in pregnancy: results of a large prospective cohort study. *Can J Psychiatry*. 2009;54(4):242–246.

Boshier A, Wilton LV, Shakir SA. Evaluation of the safety of bupropion (Zyban) for smoking cessation from experience gained in general practice use in England in 2000. *Eur J Clin Pharmacol* 2003; 59(10): 767-73.

Figuroa R. Use of antidepressants during pregnancy and risk of attention-deficit/hyperactivity disorder in the offspring. *J Dev Behav Pediatr*. 2010 Oct;31(8):641-8

Nanovskaya TN, et al. Bupropion sustained release for pregnant smokers: a randomized, placebo-controlled trial. *Am J Obstet Gynecol*. 2017 Apr;216(4):420.e1-420.e9.

Stotts AL, et al. Randomized, controlled pilot trial of bupropion for pregnant smokers: challenges and future directions. *Am J Perinatol*. 2015 Mar;32(4):351-6.

Chan B, Einarson A, Koren G. Effectiveness of bupropion for smoking cessation during pregnancy. *J Addict Dis* 2005;24:19-23.

Chisolm MS, et al. The relationship between antidepressant use and smoking cessation in pregnant women in treatment for substance abuse. *Am J Drug Alcohol Abuse* 2010;36: 46-51.