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## Physician perceptions of risk regarding mood disorders and pharmacological management during pregnancy: What is current practice?

Laura G. Hendon

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PHYSICIAN PERCEPTIONS OF RISK REGARDING  
MOOD DISORDERS AND PHARMACOLOGICAL  
MANAGEMENT DURING PREGNANCY: WHAT IS  
CURRENT PRACTICE?

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MOOD DISORDERS AND PHARMACOLOGICAL  
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CURRENT PRACTICE?

A  
THESIS

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Graduate School of Biomedical Sciences  
in Partial Fulfillment  
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for the Degree of  
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by

Laura Godfrey Hendon, MA  
Houston, Texas

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**Physician perceptions of risk regarding mood disorders and pharmacological management during pregnancy: What is current practice?**

Publications No. \_\_\_\_\_

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Mood disorders are the most common form of mental illness and one of the leading causes of morbidity worldwide. Major depressive disorder and bipolar disorder have a lifetime prevalence of 16.2% and 4.4%, respectively. Women comprise a substantial proportion of this population, and an estimated 500,000 pregnancies each year involve women with a psychiatric condition. Management with psychotropic medications is considered standard of care for most patients with mood disorders. However, many of these medications are known human teratogens. Because pregnant women with mood disorders face a high risk of relapse if unmanaged, the obstetrician faces a unique challenge in providing the best care to both mother and baby.

It has been suggested that many obstetricians overestimate the teratogenic risks associated with psychotropic medications, while concurrently underestimating the risks associated with unmanaged mood disorders. This may be due a knowledge gap regarding the most current teratogen information, and lack of official management guidelines. Therefore, the purpose of this study is to determine the current knowledge base of obstetricians regarding the teratogenic effects of common psychotropic medications, as wells as to capture current management practices for pregnant women with mood disorders.

A total of 117 Texas obstetricians responded to a survey regarding teratogen knowledge and management practice. It was common for respondents to encounter women who disclose both having a mood disorder and taking a psychotropic medication during

pregnancy. Many respondents did not utilize up-to-date drug counseling resources, and were unaware of or over-estimated the teratogenic risks of common medications used to treat mood disorders. Finally, many respondents reported wanting to refer pregnant patients with mood disorders to psychiatrists for co-management, but are reportedly restricted in doing so due to accessibility or insurance issues.

This study demonstrates that there is a knowledge gap among obstetricians regarding the teratogenicity of common psychotropic medications utilized to manage a patient population they frequently encounter. Further, obstetricians have vastly different risk perceptions of these medications, resulting in various management approaches and recommendations. Future research should focus on establishing standard practice guidelines, as well as better accessibility to psychiatric services for pregnant women.

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## **BACKGROUND**

Psychiatric disorders are one of the leading causes of morbidity in the world. Mood disorders or affective disorders are the most common form of mental illness and include major depressive disorder and bipolar disorder or manic-depressive illness, (Craddock & Forty, 2006). Major depressive disorder (MDD) is defined as one or more incidences of persistent depression accompanied by symptoms such as insomnia, fatigue, and suicidal ideation that last more than two weeks (Marchesi, Bertoni, & Maggini, 2009). Bipolar disorder (BPD) is characterized by alternating episodes of major depression and either mania (bipolar I disorder) or hypomania (bipolar II disorder). Mania is an elevated mood state characterized by irritability, feelings of grandeur, and an increase in goal-directed behavior (Benazzi, 2007).

Individuals with mood disorders have high incidences of comorbid mental conditions such as anxiety disorder and obsessive-compulsive disorder (Kessler, Merikangas, & Wang, 2007). Further, it is widely recognized that among all types of mental illness, the highest incidences of comorbid substance abuse and suicide are found in mood disorders (Bertolote, Fleischmann, De Leo, & Wasserman, 2004; Tohen, Greenfield, Weiss, Zarate, & Vagge, 1998). The 2004 National Comorbidity Survey Replication estimates a lifetime prevalence of 16.2% for MDD and 4.4% for BPD (Kessler, et al., 2007). Women comprise a substantial proportion of this population. While BPD has an equal prevalence between genders (Burt & Rasgon, 2004), MDD is twice as common in women (Kessler, 2003) and is the leading cause of female disease-related disability worldwide (Lopez & Mathers, 2006).

## **Mood disorders and pregnancy**

The management of women with mood disorders presents unique challenges to the health care provider, especially the obstetrician (Burt & Rasgon, 2004). Most individuals with MDD and BPD are diagnosed during their reproductive years. The average age of onset is 32 years old for MDD and 18 and 20 years old for type I and type II BPD, respectively (Kessler, et al., 2007). The American College of Obstetricians and Gynecologists (ACOG) estimates that more than 500,000 pregnancies each year involve women with psychiatric conditions (ACOG, 2008). Between 14 and 23% of pregnant women are affected by a depressive disorder during pregnancy (Yonkers et al., 2009). In addition, as much as 20% of the pregnant population will experience either the relapse of a previous psychiatric condition or the onset of new symptoms during pregnancy (Frieder, Dunlop, Culpepper, & Bernstein, 2008). A 2002 survey of 14,549 pregnant woman in the United States found an 8.4% and 2.8% incidence of MDD and BPD, respectively, during pregnancy and postpartum (Vesga-Lopez et al., 2008). It is possible that our current approximation of the incidence of MDD during pregnancy is an underestimate, as women with MDD are less likely to present for prenatal care (Bennett, Einarson, Taddio, Koren, & Einarson, 2004) or may lack an official diagnosis at presentation. Indeed, as many as 70% of women report depressive symptoms during pregnancy (ACOG, 2008).

While post-partum depression is now widely recognized and treated, the incidence and impact of mood disorders during pregnancy is just beginning to be evaluated (Yonkers, et al., 2009; Yonkers et al., 2004). A 2004 meta-analysis of 19,284 pregnant patients found that the rate of MDD in the second and third trimesters of pregnancy is nearly double that of the normal female population (Bennett, et al., 2004). Bennett and colleagues recognize that

typical symptoms of pregnancy can be difficult to separate from those of MDD, however, they report success using validated questionnaires such as the Beck Depression Inventory. Mood disorders have serious clinical effects on pregnancy. Depressive episodes during gestation are associated with an increased risk for pre-eclampsia, pre-term birth, and low birth weight infants (Wisner, 2010). Overall, affected women have poorer pregnancy outcomes, higher rates of post-partum mental illness, and an increased risk for substance abuse and lack of prenatal care (Frieder, et al., 2008; Wisner, 2010).

### **Accessibility and utilization of mental health resources**

It is estimated that up to 40% of individuals with mental health problems initially present for care to their primary care physician (Smalley et al., 2010). Coupled with the average age of onset for mood disorders, it is therefore likely that many women present symptoms for the first time to their obstetrician/gynecologist. Perhaps even more common is the pregnant woman taking a psychotropic medication originally prescribed by a primary care physician, but not receiving any long-term professional management or surveillance by a psychologist or psychiatrist. Obstetricians may play an important role in identifying pregnant women with mood disorders and referring them to psychiatric care for symptom management, cognitive behavioral therapy, and recommendations on drug therapy during pregnancy.

However, it is estimated that only 25-35% of pregnant women with a mood or anxiety disorder receive mental health treatment (M. V. Smith et al., 2009). In fact, pregnant women are less likely than non-pregnant women to receive psychiatric care (Vesga-Lopez, et al., 2008). The management of women with mood disorders may be

restricted by both accessibility to and utilization of mental health care resources. A recent study of 315 pregnant women referred for mental health services found that only 35.6% (n=112) actually attended a mental health appointment and only 6% followed up with long-term care (M. V. Smith, et al., 2009). Obstetricians and physicians in certain communities may not even have the option to refer to a mental health care provider in the first place. It is estimated that over one-half of the counties in the United States lacks a psychologist or psychiatrist (Smalley, et al., 2010). Indeed, the third highest overall area and number one specialty area of healthcare service shortage in rural America is psychiatry (MacDowell, Glasser, Fitts, Nielsen, & Hunsaker, 2010). In addition to accessibility, individuals with mood disorders face additional challenges in obtaining proper care, including inadequate insurance coverage, high cost of treatment, unavailability of generic drugs for many commonly prescribed psychotropics, under-recognition or misdiagnosis of symptoms, and fear of cultural or societal stigmatization (Bhugra & Flick, 2005).

A recent case study of a young woman with type I bipolar disorder who successfully managed her illness through two pregnancies suggests the “key treatment components” for mood disorder management during pregnancy include an intimate and long-term relationship with a psychiatrist, access to excellent perinatal care and monitoring, and familial and financial support (Burt, Bernstein, Rosenstein, & Altshuler, 2010). This array of resources is not available to many patients.

Further studies are needed on the availability and utilization of mental health care resources by pregnant women, as well as an evaluation of the referral patterns of obstetricians who treat women with mood disorders.

## **Pharmacological treatment of mood disorders and pregnancy risks**

In addition to cognitive behavioral therapy, pharmacological therapy is also considered standard of care in the treatment of moderate to severe mood disorders. Common medications for the management of MDD and BPD include selective serotonin reuptake inhibitors (SSRIs), anti-epileptic drugs (AEDs) that act as mood stabilizers, and atypical antipsychotics (ACOG, 2008). While effective, many of the drugs in these classes are known human teratogens or associated with adverse neurobehavioral outcomes in the fetus (Frieder, et al., 2008). Obstetrician knowledge of the teratogenicity of these medications is imperative, as ACOG estimates that one-third of all pregnancies are exposed at some point in gestation to a psychotropic medication (2008).

### *Selective serotonin reuptake inhibitors (SSRIs)*

SSRIs were discovered in the 1980s, and quickly gained popularity due to their effectiveness in treating depression and lack of negative side effects in comparison to older tricyclic antidepressants (Louik, Lin, Werler, Hernandez-Diaz, & Mitchell, 2007). SSRIs are now the most widely prescribed drugs in the treatment of MDD, and an estimated 13% of women are exposed to them during pregnancy (Yonkers, et al., 2009). Some of the most common SSRIs in clinical use include citalopram (Celexa®), escitalopram (Lexapro®), fluoxetine (Prozac®), paroxetine (Paxil®), and sertraline (Zoloft®). The current data regarding the risk for specific birth defects related to SSRI exposure is conflicting and lacks reproducibility (Yonkers, et al., 2009). For example, two similar case-control studies published concurrently in *The New England Journal of Medicine* reported significantly discrepant results in evaluating the teratogenicity of SSRIs (Alwan, Reefhuis, Rasmussen,

Olney, & Friedman, 2007; Louik, et al., 2007). Alwan and colleagues analyzed 9622 cases and 4092 controls from the National Birth Defects Prevention Study and found an association between SSRI use in pregnancy and the incidence of anencephaly, craniosynostosis, and omphalocele, but not congenital heart defects (2007). In contrast, Louik and colleagues' evaluation of data from the Slone Epidemiology Center Birth Defects Study (9849 cases and 5860 controls), found no association between maternal SSRI use and anencephaly, craniosynostosis, omphalocele, or congenital heart defects overall, but a significant association with the use of paroxetine and right ventricular outflow tract obstruction defects (Louik, et al., 2007).

The association between prenatal exposure to paroxetine and heart defects was first widely reported in a 2007 study of the Swedish Medical Birth Register (B. A. Kallen & Otterblad Olausson, 2007). This study reported a 1.5 to 2-fold increased risk for cardiac malformations in infants exposed to paroxetine and thus raised concern about the safety of SSRIs during pregnancy in general (ACOG, 2008; B. A. Kallen & Otterblad Olausson, 2007). However, this risk was calculated from retrospective analyses of birth and insurance registries and attempts to replicate this finding in large cohort studies have been unsuccessful (Yonkers, et al., 2009). The overall risk for structural abnormalities due to SSRIs is still considered low at 2 per 1,000 births (ACOG, 2008).

Transient neonatal "withdrawal" symptoms consisting of irritability, tachypnea, hypoglycemia, temperature instability, and seizures have been described in newborns exposed to SSRIs (Chambers, Johnson, Dick, Felix, & Jones, 1996; Costei, Kozer, Ho, Ito, & Koren, 2002; Oberlander, Warburton, Misri, Aghajanian, & Hertzman, 2008). However, these symptoms typically resolve within two weeks and no long-term neurobehavioral

outcomes have been observed in children or adults that were exposed in utero (Gentile & Galbally, 2010). The use of SSRIs has also been associated with low birth weight and preterm babies, but these outcomes are also seen in offspring of women with MDD not exposed to medication (ACOG, 2008; Yonkers, et al., 2009).

Currently, ACOG recommends that women avoid taking paroxetine during pregnancy, and physicians should consider monitoring those pregnancies exposed in the first trimester to the drug with fetal echocardiography (2008). There are no established guidelines for the use of other SSRIs during pregnancy. ACOG suggests physicians take an “individualized” approach to outlining treatment plans, and consider both the potential risks of the medication and the severity of maternal illness when managing women with MDD (2008).

#### *Anti-epileptics (AEDs)*

In contrast to SSRIs, the teratogenicity of several AEDs is firmly established from studies in the epileptic population. It is estimated that 45,000 children have been exposed to AEDs in the United States alone (Kluger & Meador, 2008). Valproic acid (Depakote®) is one of the oldest and most effective AEDs used as a mood stabilizer in BPD. However, VPA is considered the most teratogenic anti-convulsant on the market (Ornoy, 2006). An increased incidence of spina bifida in infants exposed to VPA in utero was first observed in the early 1980s (Bjerkedal et al., 1982; Dalens, Raynaud, & Gaulme, 1980; Gomez, 1981). Since then, numerous studies have reported an association between VPA exposure and multiple major anomalies including cardiac, skeletal, craniofacial, and limb defects (Kluger & Meador, 2008).



A 1992 prospective cohort study of 300 women found that 9.4% of pregnancies exposed to VPA had a major malformation, including six cases of spina bifida (6.3%) (Omtzigt et al., 1992). Similarly, an evaluation of the 3,441 women in the North American Antiepileptic Drug Pregnancy Registry found that those exposed to VPA during pregnancy had a 7.3 relative risk to have a baby with a major congenital malformation in comparison to women taking other AEDs during pregnancy (Wyszynski et al., 2005). Further, birth registries in Finland and the United Kingdom (UK) found a 4.6% and 6.2% incidence of major malformations, respectively, in those pregnancies exposed to VPA (Artama, Auvinen, Raudaskoski, Isojarvi, & Isojarvi, 2005; Morrow et al., 2006). Six children exposed to VPA in the Finland study (7%) and seven in the UK study (1%) had spina bifida (Artama, et al., 2005; Morrow, et al., 2006). Overall, a 1-2% risk for neural tube defects and up to a 10% risk for any major congenital malformation is typically quoted to patients receiving counseling for pregnancies exposed to VPA (Kluger & Meador, 2008; Ornoy, 2009).

There is a known dose-dependent relationship between VPA and an increased incidence of birth defects. Adverse pregnancy outcomes are unlikely to occur in women receiving less than 1,000 mg a day (J. Smith & Whitehall, 2009). The incidence of birth defects, including NTDs, is considered increased above the background when daily doses reach 1,400 mg or higher (Ornoy, 2009; J. Smith & Whitehall, 2009). While VPA is a known folic acid antagonist, no studies of VPA have demonstrated a decrease in the rate of neural tube defects after supplementing with 4-5 mg/day of folic acid (Ornoy, 2009).

In addition to congenital anomalies, VPA exposure is associated with other risks. DiLiberti and colleagues first described a unique pattern of dysmorphic facial features and mental impairments in a group of seven children exposed to VPA in utero (1984). Features

of what is now termed “fetal anticonvulsant syndrome” or “anti-epileptic drug (AED) syndrome” are often seen in children exposed to AEDs in utero (Ornoy, 2009). Facial findings include a smooth, long philtrum with thin upper lip, midface hypoplasia, flat nasal bridge, small anteverted nose, down-turned angles of the mouth, and thin arched eyebrows (DiLiberti, et al., 1984; J. Smith & Whitehall, 2009). Children with features of AED syndrome often have other congenital anomalies and cognitive delays. It is unknown the exact percentage of children exposed to VPA in utero that develop AED syndrome. A study by Kini and colleagues found that of 274 children exposed to AEDs, 47% were correctly identified by dysmorphologists as being exposed based on their unique facial features (Kini, Adab, Vinten, Fryer, & Clayton-Smith, 2006).

Many children exposed to VPA will also have developmental delays and learning problems. Some studies have reported lower verbal intelligence quotient scores (J. Smith & Whitehall, 2009). An association between VPA exposure and the development of autistic spectrum disorder (ASD) has been frequently reported (Ornoy, 2006). A 2005 study found that the incidence of ASD, including pervasive developmental disorder and Asperger syndrome, is about 20 times higher in those exposed to VPA than in the general population. Of 56 children exposed to VPA in utero, 8.9% met a DSM-IV diagnosis of ASD (Rasalam et al., 2005). Finally, about 20% of infants exposed to VPA in utero will experience withdrawal symptoms after birth, similar to the transient neonatal withdrawal response seen with SSRI exposure (J. Smith & Whitehall, 2009). When VPA use during pregnancy cannot be avoided, the lowest effective dose possible prescribed in 2-3 divided doses is considered the best course of treatment (Ornoy, 2009).

In addition to VPA, the AED carbamazepine (Tegretol®) is also considered teratogenic due to an association with neural tube defects and syndromic facial features (Dodd & Berk, 2006). A 1991 meta-analysis of 984 pregnancies exposed to carbamazepine found 9 cases of spina bifida, suggesting an approximately 1% risk for neural tube defects (Rosa, 1991). More recently, the United Kingdom Pregnancy Registry reported an overall 2.3% malformation rate for pregnancies exposed to carbamazepine (n=700) (Kaplan, 2004). Multiple congenital anomalies including cardiac defects, skeletal malformations, cleft lip and palate, and brain anomalies have also been reported in exposed infants (Ornoy, 2006).

Based on current knowledge of VPA and carbamazepine in the epileptic population, these medications are not recommended as first-line therapy in the treatment of BPD in women of reproductive age. Lamotrigine (Lamictal®), introduced in the late 1990s, is not believed to be associated with an increased risk for birth defects (Cunnington, Ferber, & Quartey, 2007) and is currently considered the safest BPD treatment option during pregnancy (ACOG, 2008). Pooled data from studies performed from 2003 to 2007 suggests a 2.6% incidence of major malformations following first-trimester exposure to lamotrigine, which is below the universal 3-5% background risk for birth defects in any pregnancy (Newport et al., 2008). Among these studies, the pooled risk for orofacial clefts was 0.34% (Newport, et al., 2008). A recent study of the Australian Register of Antiepileptic Drugs in Pregnancy found the incidence of birth defects in pregnant women who took lamotrigine (n=243), carbamazepine (n=302), and valproic acid (n=224) to be 4.9%, 5.3%, and 15.2%, respectively (Vajda et al., 2010). The incidence of birth defects related to lamotrigine was similar to that of women who did not take an AED during pregnancy (Vajda, et al., 2010). While further studies are needed, Newport and colleagues felt that lamotrigine was effective

in managing bipolar disorder during pregnancy. In their study of 26 women with type II BPD, the incidence of new episodes during pregnancy was only 30% in women who took lamotrigine compared to 100% who completely discontinued treatment during pregnancy (Newport, et al., 2008).

### *Second-generation antipsychotics*

The use of second-generation (atypical) antipsychotics such as aripiprazole (Abilify®), clozapine (Clozaril®), and risperidone (Risperdal®) to manage the acute manic episodes of bipolar disorder is becoming more common (Dodd & Berk, 2006). Unlike the original (typical) antipsychotics, this group is associated with less adverse effects in the mother and is considered more effective in managing psychosis (Einarson & Boskovic, 2009). Typical antipsychotics have been in use for over 40 years (ACOG, 2008), and their effects on the developing fetus have been widely studied (Reis & Kallen, 2008). In contrast, there is little data regarding the potential teratogenicity of atypical antipsychotics (Einarson & Boskovic, 2009) which were not introduced until the mid-1990s (McKenna et al., 2005). One of the largest studies of exposures to antipsychotics was a 2008 analysis of the Swedish Birth Registry by Reis and Kallen. This population-based study looked at 460 women who took typical antipsychotics and 101 women who took atypical antipsychotics during pregnancy for the treatment of a psychiatric disorder. There was a slightly increased risk for birth defects (odds ratio of 1.5) in pregnancies exposed to typical antipsychotics, particularly atrial and ventral septal heart defects (Reis & Kallen, 2008). However, there was no increased risk for congenital malformations in the group exposed to atypical antipsychotics, suggesting a lack of teratogenicity in this new class (Reis & Kallen, 2008). In a similar

case-control study of 151 pregnancies exposed to atypical antipsychotics, there was no significant increase in birth defects in the exposed group (McKenna, et al., 2005). However, there was a significant increase in the incidence of low birth weight babies in pregnancies exposed to antipsychotics (10%) compared to controls (2%) (McKenna, et al., 2005). The rate of therapeutic abortions was also significantly higher in the exposed group (9.9%) than in controls (1.3%). Of note, a significant increase in maternal weight gain has been observed in women exposed to atypical antipsychotics (McKenna, et al., 2005). Indeed, Reis and Kallen found that women exposed to these drugs were two times more likely to develop gestational diabetes (2008).

Overall, atypical antipsychotics are considered safer for pregnancy than the common mood stabilizers. While further studies are needed, current data suggest they are not associated with an increased risk for birth defects (Dodd & Berk, 2006). However, antipsychotics are rarely used as monotherapy in BPD and are often combined with another mood stabilizer like VPA (Dodd & Berk, 2006). Thus, physicians must consider the combined teratogenicity of the two agents when assessing risk to the pregnancy. In general, polytherapy is associated with poor birth outcomes (Dodd & Berk, 2006). ACOG recommends the use of a single medication at a higher dose rather than multiple medications to manage psychiatric disease (2008).

## **Unmanaged mood disorders and pregnancy**

### *Symptom recurrence*

The risks associated with pharmacological management of mood disorders during pregnancy must be weighed against the risks associated with discontinuing treatment.

Pregnancy is no longer considered to have a “protective” effect on women (Kloos, Kegelmeyer, Young, & Kostyk, 2010), and studies suggest it is a dangerous time for women with mood disorders to discontinue treatment. Viguera and colleagues observed a 50% recurrence of symptoms within two weeks in women with BPD who discontinued treatment during pregnancy (2007). Further, women who stopped pharmacological therapy experienced a new episode four times sooner than those women who maintained treatment (Viguera, et al., 2007). Another study found that 68% of women who discontinued medication during pregnancy experienced a recurrence of MDD symptoms, compared to 26% of patients who continued pharmacological therapy (Cohen et al., 2006). A recent review article suggests women with MDD face an estimated 50-75% risk of relapse when discontinuing medication (Frieder, et al., 2008).

### *Outcomes of unmanaged episodes*

Unmanaged mood disorders during pregnancy affect the fetus and the mother. Premature birth, low birthweight, and fetal growth restriction are associated with untreated depression during pregnancy (ACOG, 2008). Mood episodes during pregnancy are also associated with an increased risk for substance abuse, and a higher incidence of post-partum psychosis, which itself is linked to higher rates of suicide and infanticide (Frieder, et al., 2008). Infants of mothers with unmanaged depression are more likely to present with increased irritability, decreased attentiveness, and increased cortisol levels compared to infants of non-depressed women (Yonkers, et al., 2009). Further, offspring of women with untreated depression are more likely to have behavioral and emotional problems that require psychiatric care later in life (ACOG, 2008). Children of women who were depressed during

pregnancy are more likely to have developmental delays, irrespective of whether their mothers experienced post-partum depression (Alwan, et al., 2007).

### **Current management guidelines**

The treatment of pregnant women with mood disorders raises difficult questions about who is the primary patient in the mother-fetus pair. Left to weigh the risks and benefits of pharmacological treatment during pregnancy, obstetricians often find themselves between a “teratologic rock and clinical hard place” (Cohen, Friedman, Jefferson, Johnson, & Weiner, 1994). While no explicit guidelines exist for the management of mood disorders during pregnancy, recent recommendations suggest that a detailed assessment of each woman’s illness history, including frequency and severity of episodes, should be performed before decisions about maintenance therapy are made (Yonkers, et al., 2004).

### *APA and ACOG recommendations*

The American Psychiatric Association (APA) and the American College of Obstetricians and Gynecologists (ACOG) recently published a report regarding the management of depression during pregnancy. The report outlines the risks associated with both antidepressant use and unmanaged MDD during pregnancy, but does not offer explicit guidelines as to how these cases should be handled. Rather, it generally states that proper management is dependent on case-by-case factors such as severity and duration of illness, and response to different forms of treatment (Yonkers, et al., 2009). As an example of the report’s relative ambiguity, the authors respond to the “frequently asked question” of

“should women who are being treated with paroxetine prior to conception switch to an alternative SSRI?” with:

the decision to continue or change medication is a collaborative one between the physician and the patient, and there is no universal ‘best answer’ for all women... the clinician should review data regarding paroxetine as outlined in the preceding sections, and document the discussion and the woman’s questions carefully in the medical record (Yonkers, et al., 2009).

In addition to this 2009 report, ACOG also published a practice bulletin extensively reviewing the risks associated with the most commonly used psychiatric medications, as well as general clinical considerations for managing each psychiatric disease (ACOG, 2008). These guidelines were extensively referenced in the previous overview of commonly used psychotropics.

#### *Adherence to guidelines*

While some guidelines for managing pregnant women with mood disorders currently exist, they are not widely followed. It is estimated that a large proportion of women with mood disorders are advised by their physicians to completely stop taking medication when they discover they are pregnant (Einarson & Boskovic, 2009; Viguera, et al., 2007). This common practice may be due to concerns of medical liability in the rare event of an adverse pregnancy outcome (Koren, 2001; Koren & Levichek, 2002; Webster & Freeman, 2001; Wisner, 2010). In addition to physician-recommended discontinuance, many pregnant women independently decide to stop taking prescribed medications due to fear of possible teratogenicity. A study of 1793 pregnant women found that 7 out of 10 women chose not to



take a medication of any type during pregnancy because they felt it was unsafe (Nordeng, Ystrom, & Einarson, 2010).

### **Teratology perceptions and information sources**

Fueling physician concern for adverse outcomes and the general practice of discontinuing medications may be misinformation about the actual teratogenic risks associated with the use of psychotropics during pregnancy (Koren & Levichek, 2002). There is a widely accepted 3-5% background risk for birth defects with any pregnancy (Polifka, Faustman, & Neil, 1997), and it is estimated that less than 1% of birth defects are due to prescription drug exposures (Webster & Freeman, 2001). However, numerous studies have demonstrated that physicians and their patients often overestimate the teratogenicity of medications used during pregnancy (Koren & Levichek, 2002; Pole, Einarson, Pairaudeau, Einarson, & Koren, 2000; Webster & Freeman, 2001).

#### *Overestimation of risk*

One study found that women exposed to medications well classified as non-teratogenic estimated their risk for birth defects to be as high as 24% (Koren, Bologa, Long, Feldman, & Shear, 1989). Further, in a recent Norwegian risk perception questionnaire of pregnant women taking prescription drugs, 87% of women exposed to antidepressants during pregnancy (n=100) overestimated the teratogenicity of these medications (Nordeng, et al., 2010). However, only 12% of these women overestimated their risk after receiving appropriate drug counseling (Nordeng, et al., 2010). This emphasizes the need for a well-informed health care professional to provide accurate information to anxious women who

may overestimate their risk prior to consultation. Indeed, 78% of women in the Norwegian study acquired their drug information directly from a physician, suggesting this group is often the first and only educational resource for most patients (Nordeng, et al., 2010).

However, a study of data from the Canadian teratology information Motherisk Program found that women referred directly from physicians did not have more accurate teratology risk perceptions than self-referred women (Koren & Levichek, 2002). The authors note their experience with numerous cases in which physicians suggested terminations of pregnancies in spite of “clear information on fetal safety” (Koren & Levichek, 2002). This suggests physicians themselves are misinformed or misinterpret (or both) available teratogen information.

### *Outdated risk figures*

These misperceptions could be due to the pervasiveness of risk figures from the original studies of these medications. For example, a 1974 study of birth defects in babies exposed to lithium, a mood stabilizer commonly used to manage BPD, found a 400-fold increase in the incidence of a rare heart defect called Ebstein’s anomaly (Cohen, et al., 1994). Since then, multiple epidemiological surveys, cohort studies, and case-control studies have failed to replicate this finding (Jacobson et al., 1992; B. Kallen & Tandberg, 1983; Sipek, 1989; Zalstein, Koren, Einarson, & Freedom, 1990). These studies report a 1.2-7.7 risk ratio for cardiac defects in babies exposed to lithium, a significantly lower risk than previously estimated (Cohen, et al., 1994). It is possible that many physicians still quote these older risk figures and may not be aware of current teratology data. While teratology information services in Canada and Italy report that the two drug classes most

frequently queried are SSRIs and AEDs (De Santis et al., 2008; Einarson, Park, & Koren, 2004), physicians comprise less than 10% of phone calls (De Santis, et al., 2008). A study by the Canadian Motherisk Program found that physicians most commonly obtain teratology information from 1) the *Physicians Desk Reference (PDR)*, 2) textbooks, 3) peer-reviewed journals, and 4) colleagues; sources that may not contain the most up-to-date information (Einarson, et al., 2004).

### *FDA drug classes*

In addition to outdated risk figures, physicians may also find themselves confused by the current United States Food and Drug Administration (FDA) pregnancy risk categories. The current FDA drug classification system was created in 1979 with the goal of helping physicians make informed decisions about prescribing, continuing, or discontinuing medications during pregnancy based on published teratology and reproductive risk data (Doering, Boothby, & Cheek, 2002). Drugs are classified into one of five categories (A, B, C, D, and X) based on their risk to the developing fetus, with somewhat of an increasing risk from categories A to D, while drugs in category X are contraindicated in pregnancy (Erdeljic, Francetic, Makar-Ausperger, Likic, & Radacic-Aumiler, 2010). FDA drug categories are required information in package inserts on all medications manufactured after 1979, but are not available on 60% of the drugs in the *PDR* because the regulations did not apply to drugs already on the market (Sannerstedt et al., 1996).

The current FDA drug categories have faced intense criticism since their implementation (Doering, et al., 2002; Erdeljic, et al., 2010). In general, physicians feel that the information provided is “not sufficient to make informed decisions adequately about

drug therapy in pregnant women and women of childbearing potential” (Doering, et al., 2002). The two most significant problems with the current labeling system are that physicians incorrectly perceive 1) a gradation of risk that increases across the categories (from A to X), and 2) that drugs in the same category carry the same level and types of risks (Doering, et al., 2002). Further, the labeling system does not provide information on the possible negative effects on the developing fetus of the condition associated with the drug (e.g. the risks associated with maternal seizures on an anti-epileptic drug label).

The biggest limitation of the current FDA categorization system is the overall lack of human data regarding the teratogenicity of medications, largely due to the ethical restrictions prohibiting case-control studies, and the small nature of available retrospective studies and case reports (Doering, et al., 2002). Erdeljic and colleagues feel that relying solely on the FDA drug categories in patient counseling can lead to an inappropriate discontinuation of medication, an increase in elective terminations of healthy pregnancies, and an overall increase in maternal anxiety (2010). A recent study of 1076 pregnant Croatian women evaluated the concordance between clinical pharmacologists’ assessment of medication exposures during pregnancy and the current FDA drug categories. Risk assessments provided by the pharmacologists agreed with the FDA categories in only 28% of cases (Erdeljic, et al., 2010). Further, those risk estimates provided by the expert professionals were more accurate than those of the drug classes.

The FDA recognizes the limitations of its current system, and announced in May 2008 that they plan to replace the A, B, C, D, X system with an easier to use “narrative” guide on pregnancy risks, available studies, and clinical recommendations (Feibus, 2008). However, these changes have yet to be implemented.

### *Teratology information resources*

While the FDA drug class are a less than ideal resource for teratogen counseling, multiple other text and online sources of teratogen information are currently available to physicians. The *Physicians Desk Reference (PDR)* is a popular reference book and contains information on drug labeling and product safety, and is described as “the most trusted and commonly used drug information resource” (PDRNetwork, 2010). The *PDR* is essentially an anthology of prescription drug package inserts (Doering, et al., 2002). In an increasingly technology-reliant clinical setting, many physicians today utilize electronic information resources on personal digital assistants (PDAs) such as Epocrates, a physician-compiled information database that contains a drug guide, formulary information, and drug interaction tool (Epocrates, 2011). Peer-reviewed web sites are also convenient physician resources. The Organization of Teratology Information Specialists (OTIS) is a non-profit teratology information service that offers counseling to both physicians and patients in North America regarding exposures during pregnancy via both local and national call centers (OTIS, 2010). OTIS also offers free patient-friendly drug fact sheets for many common medications and exposures encountered during pregnancy. Finally, the web site Reprotox offers physicians detailed reviews of available literature regarding the teratogenicity of numerous medications (Reprotox, 2011).

### **Study objective**

Given that many physicians appear to rely on out of date or unreliable information, we hypothesize that obstetricians currently quote inaccurate risk figures to women taking psychotropic medications during pregnancy. We hypothesize that regardless of their

knowledge of these medications, most obstetricians overestimate the teratogenic risk to the developing fetus, and this greatly impacts their recommendations during pregnancy.

Therefore, the aim of this study is to determine the current knowledge base of obstetricians regarding the teratogenic effects of mood stabilizer, anti-psychotic, and anti-depressant use during pregnancy, and whether these perceived risks influence their recommendations during pregnancy management. This study will evaluate whether obstetricians are up-to-date on current teratology data related to mood disorder treatment, as well as how physicians perceive the risks associated with these medications. This study will also investigate which teratology information resources obstetricians utilize in patient counseling, if any. Finally, this project also hopes to elucidate current obstetrician referral and management patterns for women with mood disorders. The ultimate goal of this study is to capture the current standard of practice in managing pregnant women with mood disorders, as well as further the ongoing dialogue of the importance of education and awareness of psychiatric illness during pregnancy.

## **MATERIALS AND METHODS**

### **Survey design**

A 26-item questionnaire was designed to assess obstetricians' medical background, experience, and opinions regarding the pharmacological management of women with mood disorders during pregnancy. The questionnaire was divided into four parts: demographics, experience and referral patterns, teratogen knowledge and perceptions, and situational vignettes.

The questionnaire contained fill-in-the-blank, multiple choice, and ranking questions. Space was available for additional comments at the end of each of the two situational

vignettes. The survey was written in English and was intended to take the respondent less than 15 minutes to complete. The questionnaire was anonymous, and no personal identifiers were requested or recorded. All responses were kept completely confidential. The questionnaire was approved by the Institutional Review Board at the University of Texas Health Science Center at Houston Graduate School of Biomedical Sciences (IRB# HSC-MS-10-0374). A copy of the survey may be found in Appendix 1.

### **Population**

The study population was comprised of all registered members of the Texas Association of Obstetricians and Gynecologists (TAOG) as of May 2010. Members of TAOG are obstetrician/gynecologists or gynecologists only that typically practice in the state of Texas. Those physicians with non-Texas addresses were not excluded from the study (n=10). A database of members containing names and mailing addresses was supplied directly by TAOG. Eleven hundred and four active, retired, and physicians in residency comprised the list according to TAOG. Three of the physician listings did not have complete mailing addresses and were excluded from the study. Therefore, 1101 physicians were surveyed in total.

### **Survey Administration**

The questionnaire was administered in two separate waves. The first wave of questionnaires was distributed to the entire study population (n=1101) on September 16, 2010. A cover letter explaining the purpose of the study, its benefits and limitations, and completion instructions was included at the beginning of each survey (see Appendix 1).

Each survey was packaged with a self addressed stamped envelope (SASE). Each SASE was numbered on the inside flap from 1 to 1101, and these numbers corresponded to a numbered but de-identified database of physician addresses. The purpose of this numbering system was to allow anonymous tracking of which surveys were returned so that original responders could be excluded from a second wave of mailing.

A Microsoft Excel database was created to track which numbered SASEs containing the completed questionnaires had been returned. Those anonymous “numbers” that had not returned a questionnaire by November 1, 2010 (n= 835) were mailed a second questionnaire November, 24, 2010.

Questionnaires returned to the principal investigator were coded and entered into a Microsoft Excel 2007 database. Each entry was reviewed twice for accuracy. Collection of both first and second wave questionnaires ended Friday, January 14, 2011.

### **Statistical Analysis**

Response data was analyzed using Small Stata Version 11.0 (StataCorp, LP, College Station, Texas). Basic summary statistics were performed on all questions with the exception of the fill-in-the-blank sections. Descriptive charts and graphs were created using Microsoft Excel 2007. The two-sample Wilcoxon rank-sum (Mann-Whitney) test was used to analyze responses to most questions by three binary categories: age (<50 or  $\geq$ 50 years), gender, and primary practice (academic or private practice). A p-value cut-off of 0.05 or less was designated for statistical significance. For analysis of Part II Question 6, a probability test was utilized to determine statistical significance because physician responses were not mutually exclusive. For those association graphs comparing obstetrician-quoted



risk figures and obstetricians' perceptions of these figures, Fisher's Exact test was utilized to determine statistical significance.

### **Reclassifications**

Responses that were left blank were coded as missing data. Responses were coded as "Don't know" only if that option was specifically checked by the responder, or hand-written in on a question where "Don't know" was not an available answer. Otherwise, these responses were coded as missing data. Responses that were hand written and could be logically placed in an available category were reclassified appropriately. However, if a response was at all ambiguous or not easily reclassified, it was coded as missing data. Comments hand-written into the margins of pages not designated for additional comments were grouped with those comments written in Part IV. Only questionnaires that had at least one non-demographic full section completed were included in statistical analysis. However, surveys that did not have a completed demographics section were included. Nine returned questionnaires were excluded because the responder reported he or she practiced gynecology only.

## **RESULTS**

### **Survey Response**

The database provided by TAOG included 1101 physicians with addresses. Of the 1101 surveys distributed in the first mailing, 261 (24%) were returned by the post office to the University of Texas Health Science Center at Houston. One hundred and seventy-four (66%) of those surveys returned were excluded from statistical analysis due to the following: no forwarding address (n=153), respondent not actively practicing obstetrics (n=19), or a blank survey (n=2). Those categorized as no longer practicing included physicians who were retired, deceased, or practiced gynecology only. Of the 261 surveys returned, 87 were included for statistical analysis, for a first mailing response rate of 10% (87/1101-261).

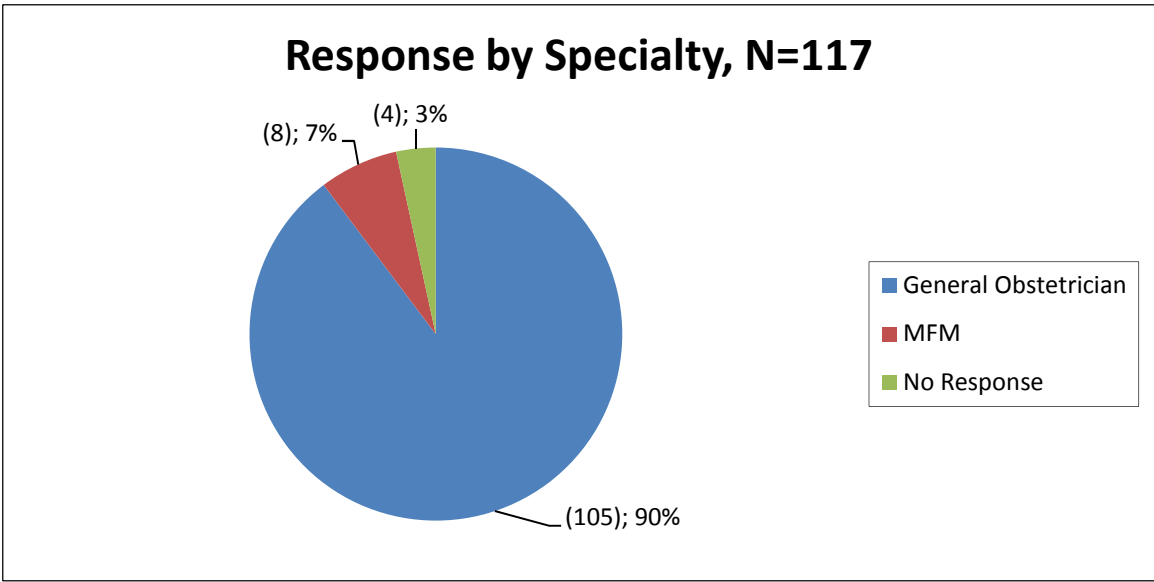
For the second wave of distribution, 840 previous non-respondents were mailed the survey again. Of these, 102 (14%) were returned. Seventy-two (70%) of these surveys were excluded from statistical analysis due to the following: no forwarding address (n=57), respondent not actively practicing obstetrics (n=13), or a blank survey (n=2). Of the 102 surveys returned, 30 were included for analysis, for a second mailing response rate of 4% (30/840-72). The total response rate for both distributions was 13.6% (117/1101-174-72).

In total, 117 surveys were included for statistical analysis in this study. Respondents were selective in which questions they chose to answer, which resulted in different total response numbers for each question. The three categories by which responses were stratified during statistical analysis did not have equal numbers due to selective answering: age (n=113), gender (n=113), and primary practice (n=109). Throughout this section, percentages are derived from a total survey number of 117, unless otherwise noted. The

number of missing responses is noted for each question analyzed. The terms “obstetrician” and “physician” are used interchangeably.

**Part I: Demographics**

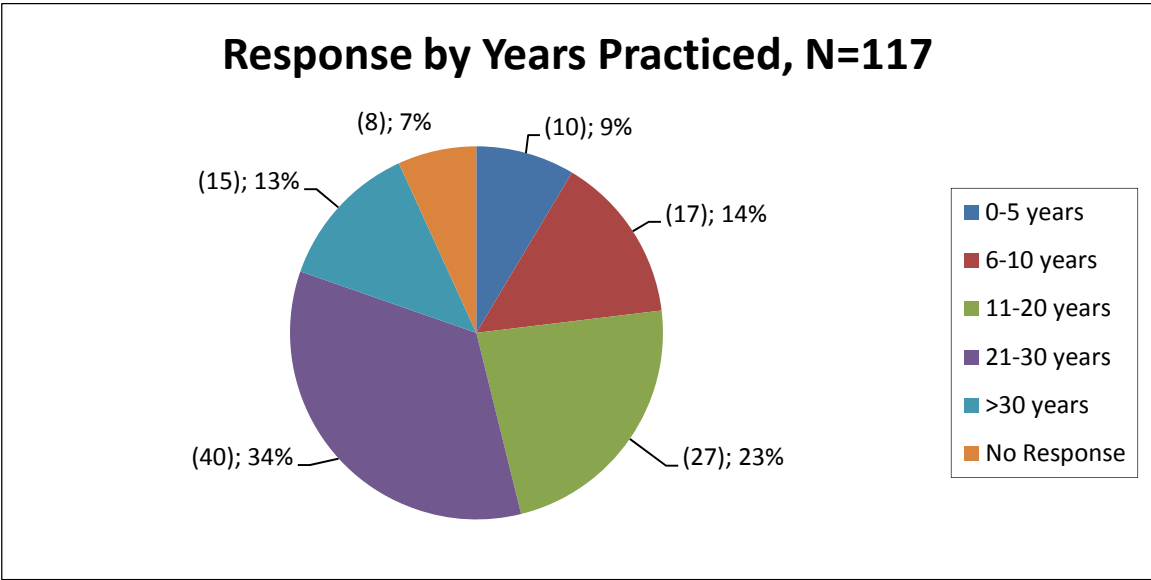
One hundred and five (90%) respondents were general obstetricians, 8 (7%) were maternal fetal medicine specialists (specified under “Subspecialty Ob/gyn”), and 4 (3%) did not indicate their area of practice. One of the general obstetricians was also boarded in psychiatry (Figure 1).



**Figure 1:** Survey response by area of specialty.

Twenty-three percent (n=27) of physicians reported practicing obstetrics between 0 and 10 years. Fifty-seven percent (n=67) reported practicing between 11 and 30 years. Thirteen percent (n=15) reported practicing over three decades. Eight respondents did not indicate how long they had been practicing obstetrics (Figure 2).

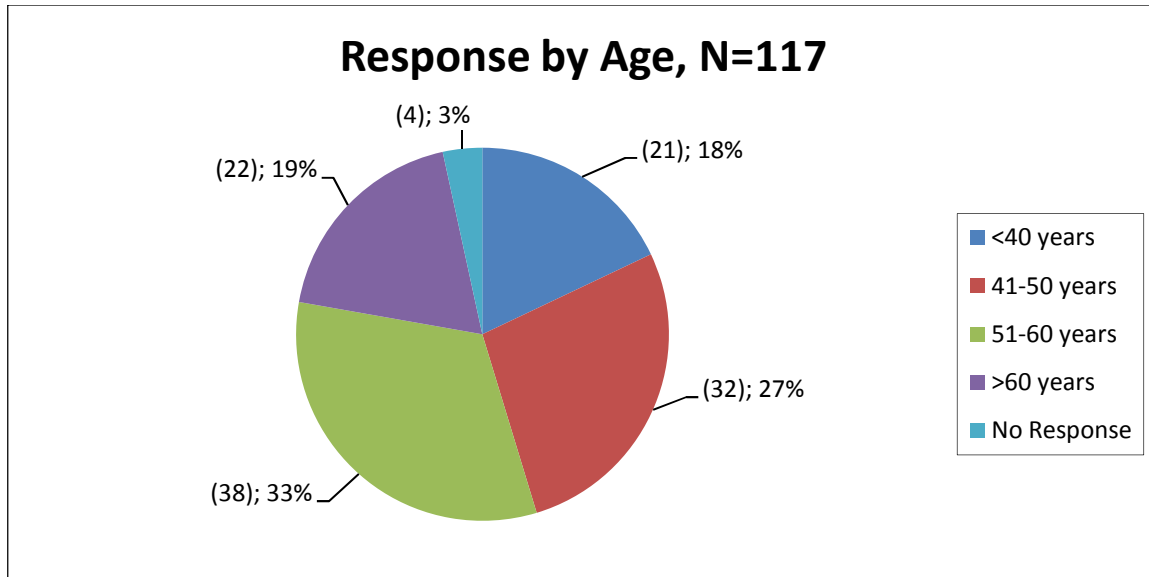
The mean years practiced was 20.11 years, with a range of 0 to 52 years. The median years practiced was 21 years.



**Figure 2:** Survey response by years in practice.

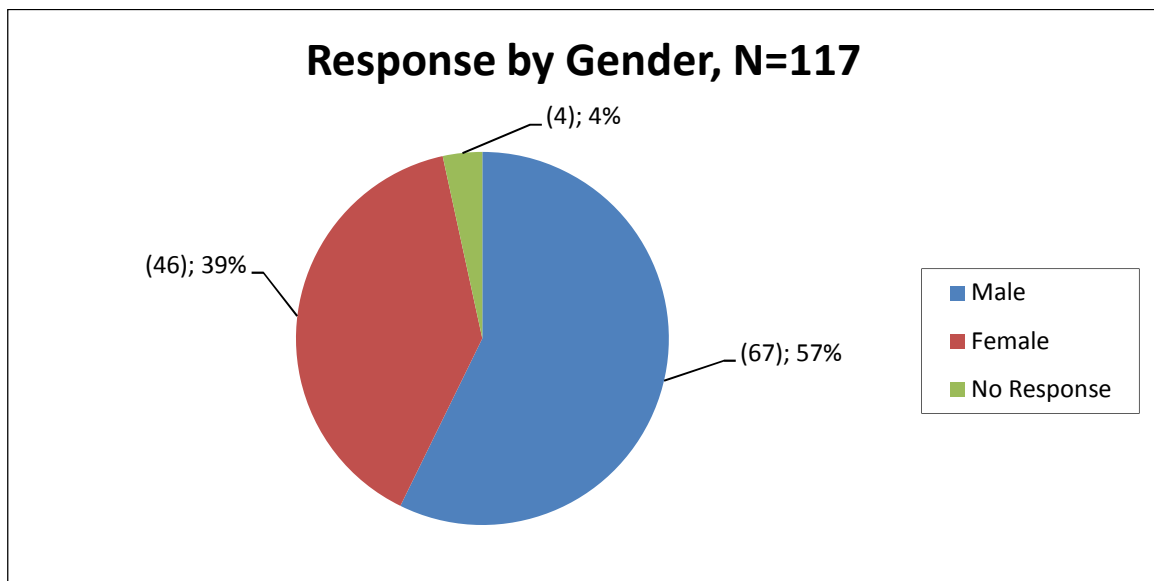
The majority of respondents, 60% (n=70), were between the ages of 41 and 60. Nineteen percent (n=22) were over the age of 60 and 18% (n=21) were at or below the age of 40. Three percent (n=4) did not indicate their age (Figure 3).

The mean age of respondents was 51.9 years old, with a range of 25 to 82 years old. The correlation coefficient for years practiced and age of respondent was 0.95.



**Figure 3:** Survey response by age.

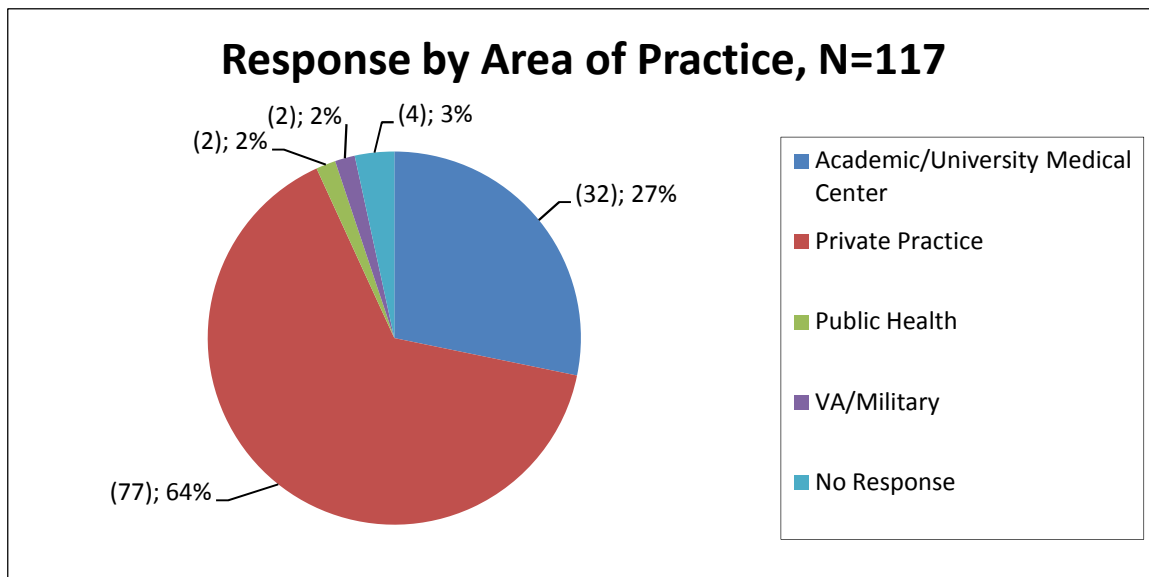
Fifty-seven percent (n=67) of respondents were male, 39% (n=46) were female, and 4% (n=4) did not specify their gender (Figure 4).



**Figure 4:** Survey response by gender.

In response to Part I Question 6 (Appendix 1), the majority of obstetricians (64%) reported working in a private practice setting. Twenty-seven percent (n=32) reported working in an academic or university medical center setting. Two percent (n=2) reported practicing in a Veterans Affairs or military practice, and two percent (n=2) reported practicing in public health. Three percent (n=4) did not specify their area of practice.

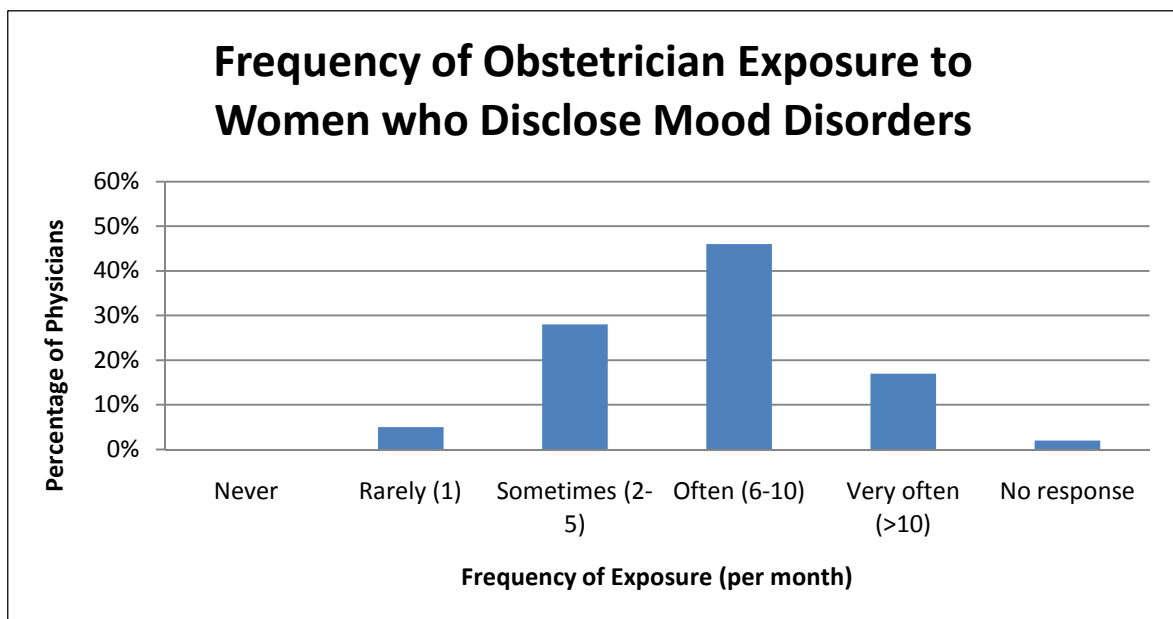
Four respondents originally selected “Other” for their primary practice setting, and wrote in additional information. These respondents were reclassified as follows: “hospital based clinic” and “multidisciplinary group” were designated as private practice, while “underserved clinic” and “community hospital” were designated as public health. These four reclassifications are included in the total category percentages as mentioned above and shown below (Figure 5). Individuals who selected one of the four main practice categories but wrote in more detail about their practice (e.g. multidisciplinary clinic) were still classified by one of the four categories they had originally selected.



**Figure 5:** Survey response by area of practice.

## Part II: Experience/Referral Patterns

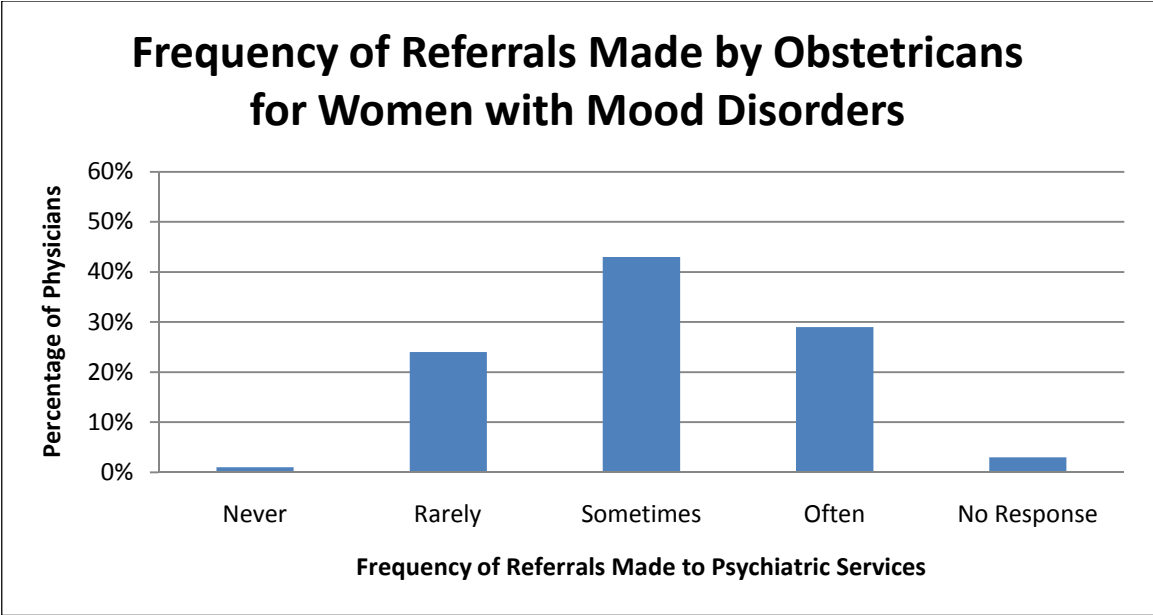
Obstetricians were asked how frequently they see women who disclose having a mood disorder (depression or bipolar disorder). Seventeen percent (n=20) reported they see women with mood disorders “very often,” or greater than 10 times per month. Forty-six percent (n=54) see women with mood disorders “often” or about 6-10 times per month, while 28% (n=33) see these women “sometimes” (2-5 times per month). Five percent (n=6) reported seeing women with mood disorders “rarely,” while no one reported “never” seeing these patients (Figure 6). Four obstetricians (2%) did not respond to this question.



**Figure 6:** Obstetrician-reported frequency of exposure to women who disclose having a mood disorder (per month).



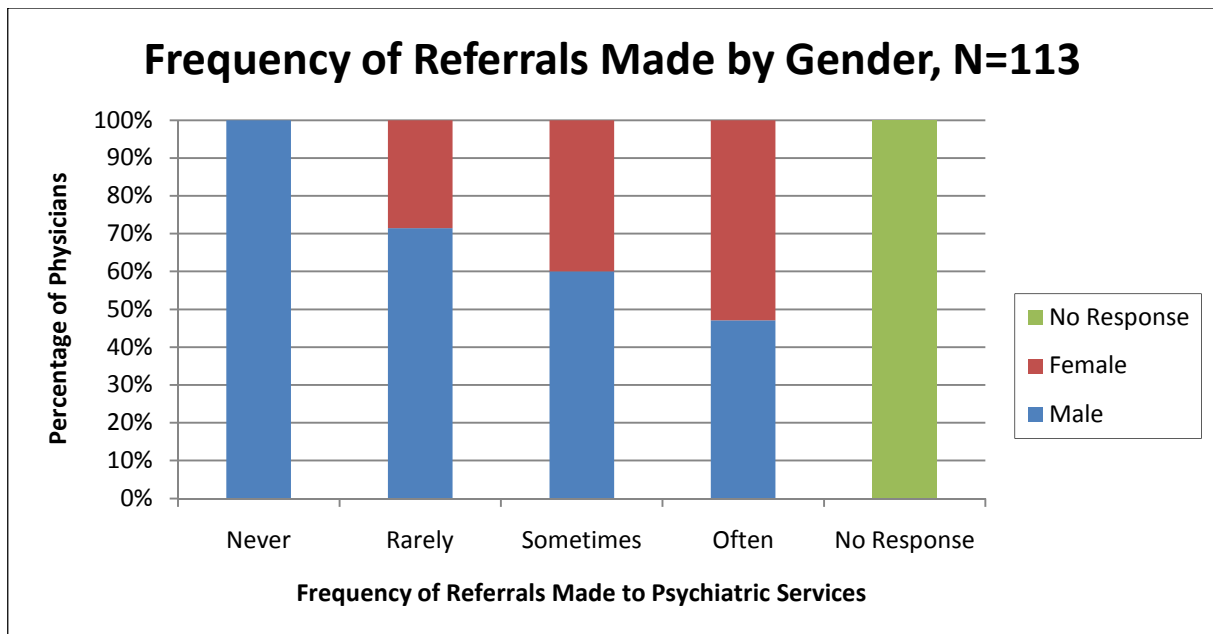
Obstetricians were asked how frequently they refer women who disclose having a mood disorder to psychiatric services. Twenty-nine percent (n=34) reported they “often” refer women, while 43% (n=43) reported they “sometimes” refer. Twenty-nine percent (n=34) reported they “rarely” refer, and one (1%) obstetrician reported “never” referring to psychiatric services (Figure 7). Four obstetricians (2%) did not respond to this question.



**Figure 7:** Obstetrician-reported frequency of referrals made to psychiatric services for women who disclose having a mood disorder.

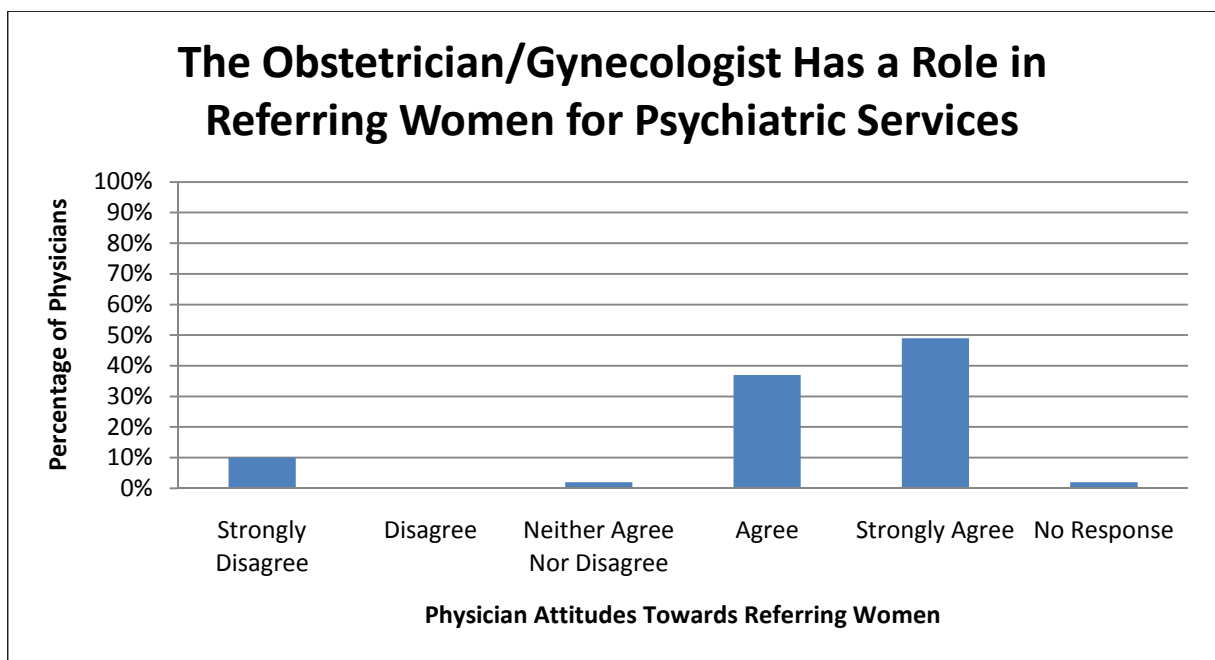
The frequency of referrals made to psychiatric services by obstetricians was significantly different by gender ( $p=0.039$ ), (Figure 8). Overall, women reported referring these patients on a more frequent basis. Thirty-nine percent (18/46) of responding women reported they “often” refer compared to 24% (16/67) of responding men. In contrast, 30% (20/67) of responding men reported “rarely” referring these patients, compared to only 17% (8/46) of responding women.

There was no significant difference in frequency of referrals made when stratified by age ( $p=0.779$ ) or practice ( $p=0.070$ ). There was no significant relationship between the frequency of physician exposure to women disclosing mood disorders and the frequency of referrals made ( $p=0.74$ ).



**Figure 8:** Obstetrician-reported frequency of referrals made to psychiatric services for women who disclose having a mood disorder stratified by gender (n=113).

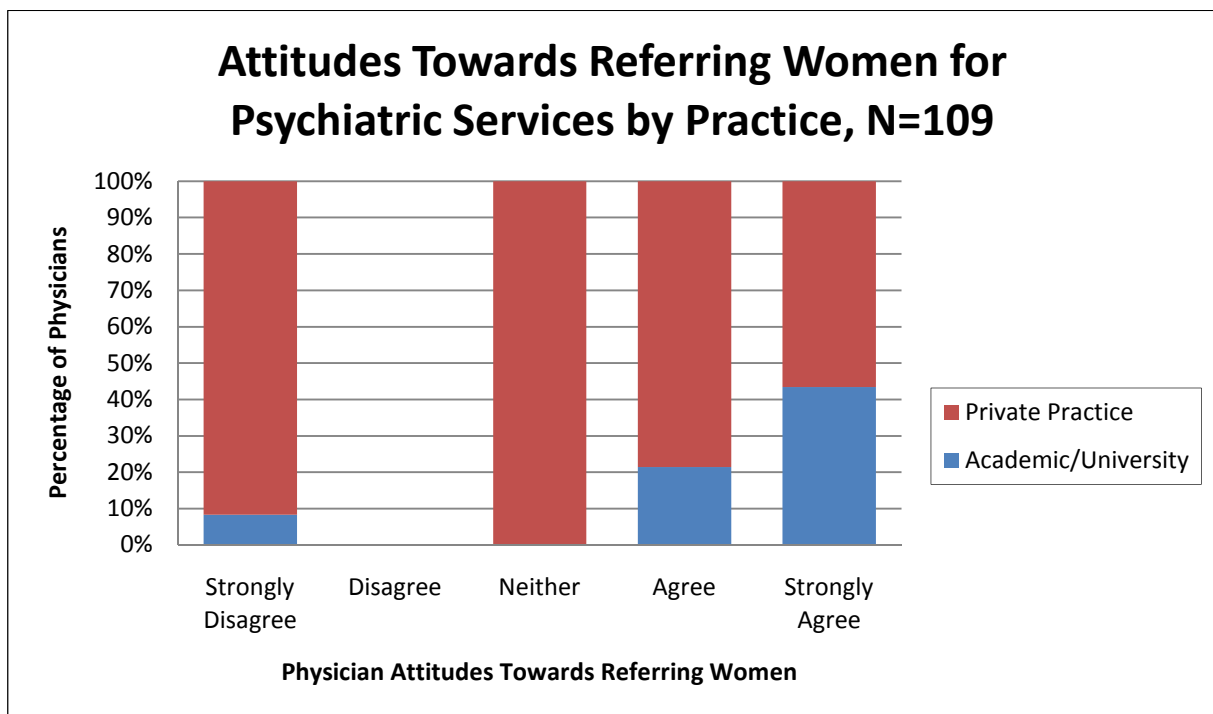
Obstetricians were asked to indicate their level of agreement with the following statement: “The obstetrician/gynecologist has a role in referring women for psychiatric services.” Forty-nine percent (n=57) and 37% (n=44) of respondents “strongly agree” and “agree,” respectively, that obstetricians have a role in the referral process. Two percent (n=2) neither agreed nor disagreed with the statement. Ten percent (n=10) of obstetricians “strongly disagreed” with the statement (Figure 9). Two obstetricians (2%) did not respond to this question.



**Figure 9:** Obstetrician attitudes towards the following statement: “The obstetrician/gynecologist has a role in referring women for psychiatric services.”

Attitudes towards referring women for psychiatric services were significantly different between those obstetricians in private practice and those in an academic or university setting ( $p=0.002$ ). Those in private practice were more likely to strongly disagree or be indifferent towards the statement (Figure 10). Fourteen percent (11/76) of respondents in private practice selected “strongly disagree,” compared to only 3% (1/33) of those in academia. By contrast, 70% (23/33) of respondents in the academic setting “strongly agreed,” while only 39% (30/76) in private practice chose that response.

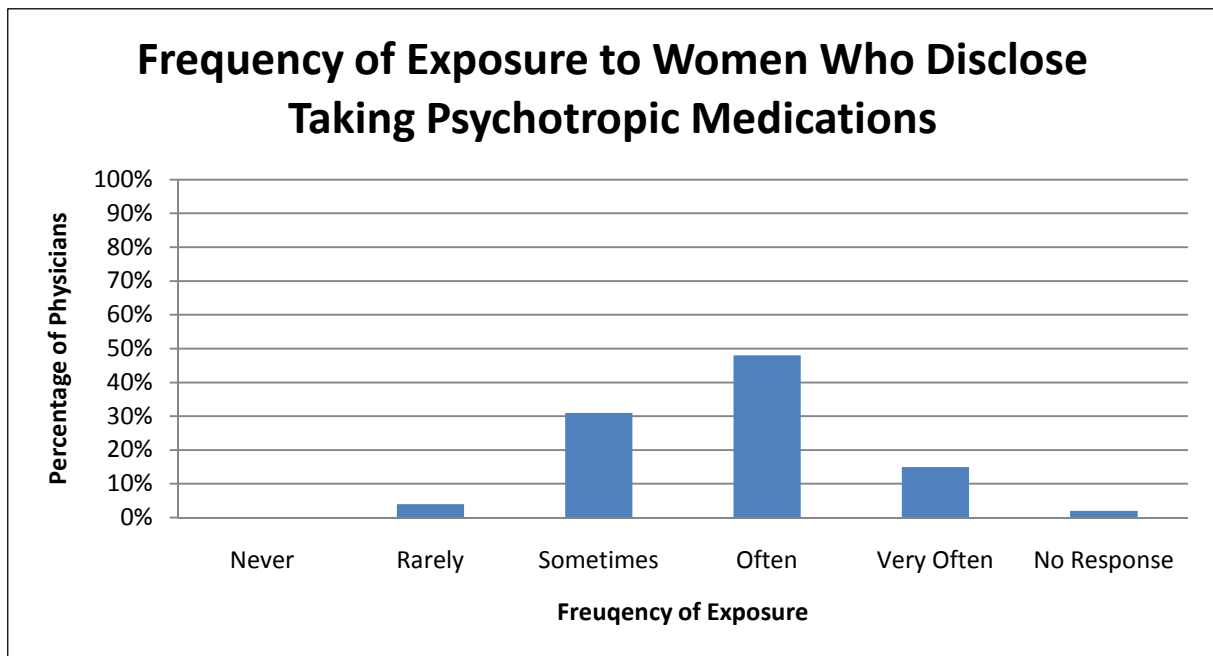
There was no significant difference in attitudes when stratified by age ( $p=0.623$ ) or gender ( $p=0.749$ ).



**Figure 10:** Obstetrician attitudes towards referring women for psychiatric services stratified by obstetrician area of practice.

Obstetricians were asked how often they see women who disclose taking a psychotropic medication (e.g. SSRIs, anti-convulsants, anti-psychotics). More than half of the respondents reported seeing women who disclose this information “very often” (n=18, 15%) or “often” (n=56, 48%). Nearly a third (n=36, 31%) reported being exposed to women who disclose taking psychotropics “sometimes,” while 5% (n=4) reported this “rarely” happens to them. Two obstetricians (2%) did not respond to this question (Figure 11).

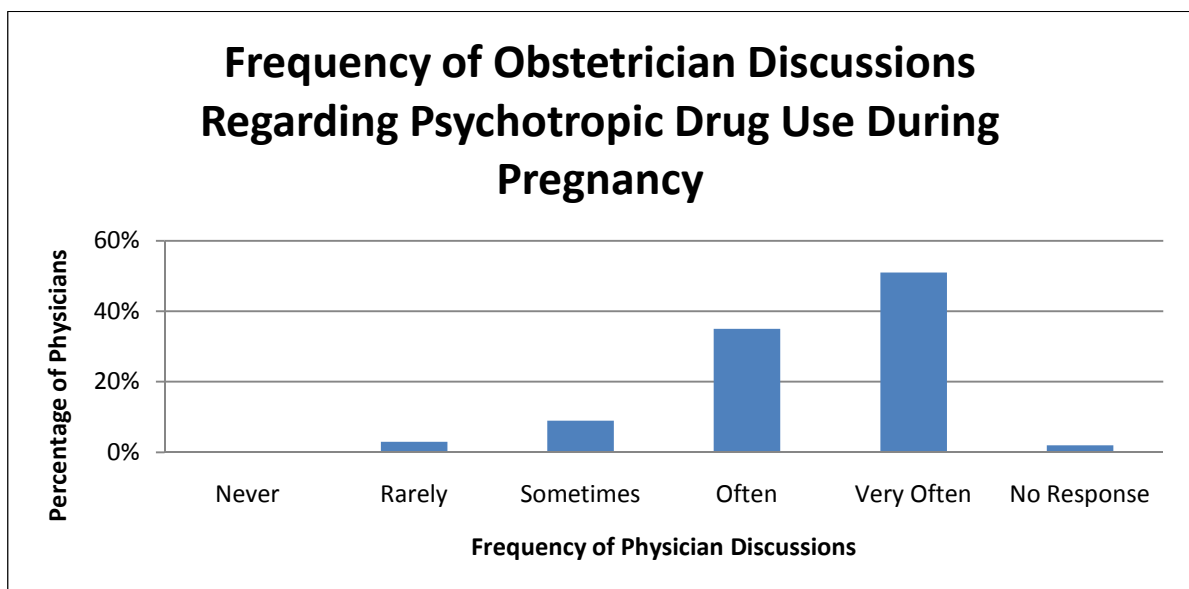
There was no significant difference in the frequency of exposure when stratified by age (p=0.918), gender (p=0.406), or practice (p=0.980).



**Figure 11:** Obstetrician-reported frequency of exposure to women who disclose taking a psychotropic medication.

Obstetricians were then asked how often they discuss psychotropic medications with their patients after patients disclose taking them. About half (51%, n=60) of obstetricians reported discussing these medications “very often.” Thirty-five percent (n=41) reported doing this “often.” Nine percent (n=10) and 3% (n=4) reported discussing these drugs “sometimes” and “rarely,” respectively. Two physicians (2%) did not respond to this question (Figure 12). There was no significant difference in the frequency of discussions when stratified by age ( $p=0.411$ ), gender ( $p=0.129$ ), or practice ( $p=0.112$ ).

Of those respondents who reported they “often” and “very often” (n=74) see women with who disclose taking medications, 41% (n=31) discuss these medications with their patients “often” and 53% (n=39) discuss them “very often.” Only 1% (n=1) reported “rarely” discussing the drugs. Among those who see these women “sometimes” (n=36), 72% (n=26) reported talking about these medications either “often” or “very often.” Further, among those who “rarely” see these patients (n=5), 100% (n=5) also reported discussing psychotropics either “often” or “very often.”

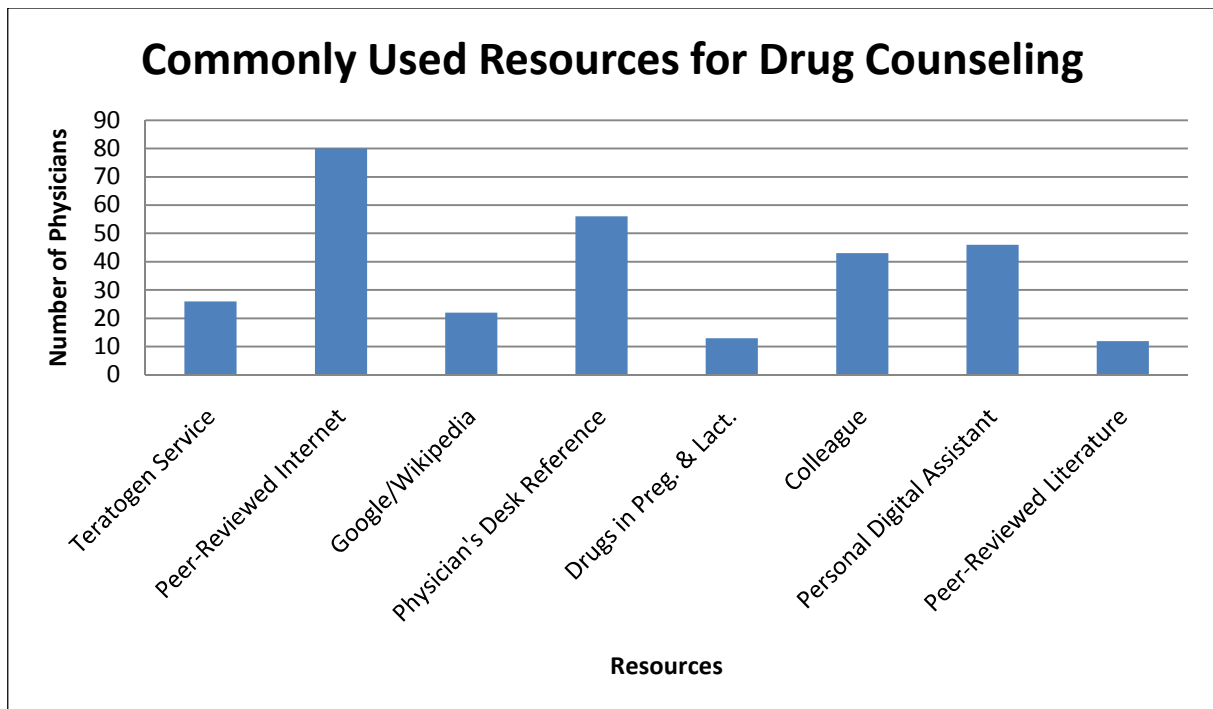


**Figure 12:** Obstetrician-reported frequency of discussions with patients regarding psychotropic drug use during pregnancy.

In Part II Question 6, obstetricians were presented with a list of six commonly used teratogen information resources including the following: “Teratogen information services (e.g. OTIS),” “Peer-reviewed internet source (e.g. ACOG website, Reprotox),” “Google and/or Wikipedia,” “Physician’s Desk Reference,” “Colleague,” and “PDA software (e.g. Epocrates).” Respondents also had the option of selecting “Other” and specifying any additional resources that were not listed. Respondents were instructed to check as many sources that applied to them.

Based on the high frequency with which they appeared in the “Other” category, two new physician resources were added: “Drugs in Pregnancy and Lactation” and “Peer-Reviewed Literature.” The first of the two new categories included any variation on the name of the *Drugs in Pregnancy and Lactation* textbook by Briggs and colleagues (e.g. “Briggs,” “Drugs in Pregnancy Book,” etc.). The second new category included the responses marked as “Other” that specified peer-reviewed literature sources such as journal articles or other textbooks, and these responses were reclassified into “Peer-Reviewed Literature.” Respondents who marked “Other” and wrote that they referenced a colleague such as a MFM, genetic counselor, or perinatologist were reclassified as “Colleague” regardless of whether they selected that category or not. Along that same logic, those respondents who marked “Other” and wrote in an obvious member of the original eight categories without selecting that original category were reclassified into that category. For example, if a respondent selected “Other: UPTODATE website,” this was reclassified as “Peer-Reviewed Internet.”

Figure 13 shows the frequency each resource was used by obstetricians to discuss medication use during pregnancy. “Peer-reviewed internet sources” (n=81) and “Physician’s Desk Reference” (n=56) were the most commonly chosen resources. “Personal Digital Assistant software” and “Colleague” were selected 43 and 46 times, respectively. The less commonly chosen sources were “Teratogen information services” (n=26) and “Google and/or Wikipedia” (n=22). The two new categories, “Drugs in Pregnancy and Lactation” and “Peer-Reviewed Literature” were cited 13 and 12 times, respectively (Figure 13). Twenty percent (n=23) of respondents only selected one resource. Fifty-six percent selected either two (n=32), or three (n=34) resources. Twelve percent (n=14) selected four, while less than 10% selected 5 or more resources.

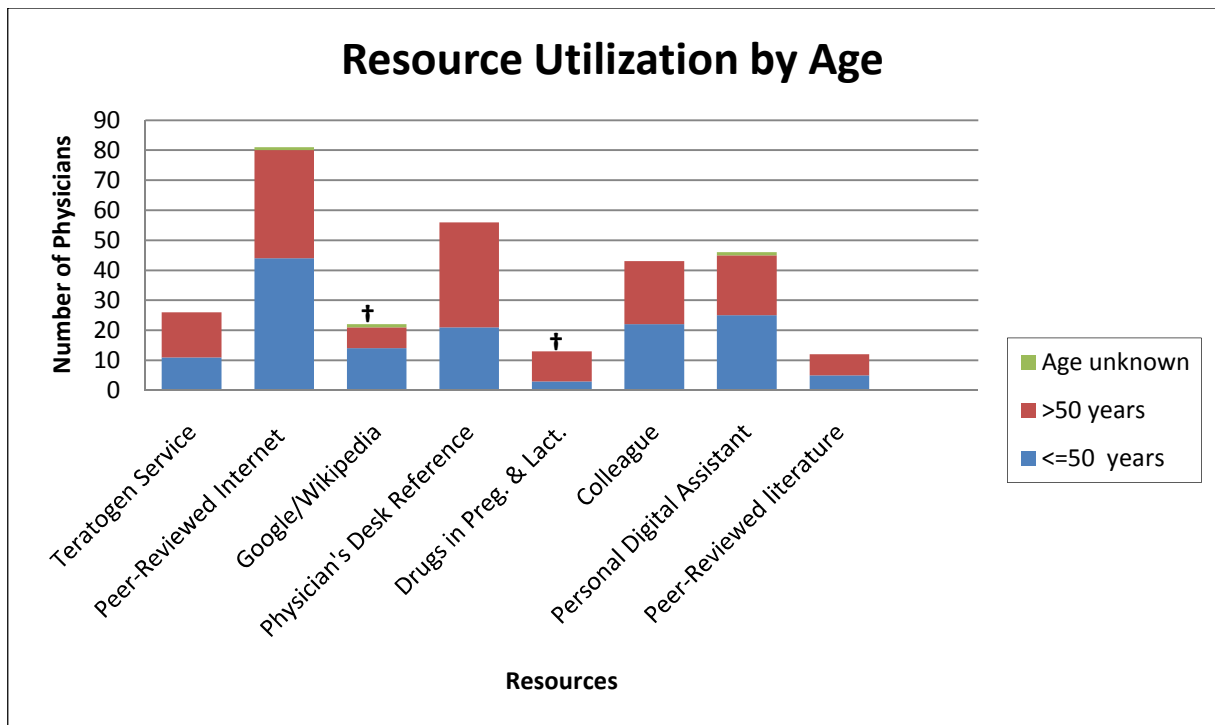


**Figure 13:** Resources commonly used by obstetricians to provide drug counseling.



There were notable trends in the types of resources used by obstetricians depending on their age (Figure 14). “Google and/or Wikipedia” was selected twice as often by obstetricians under the age of 50 (n=14), as those above the age of 50 (n=7), (p=0.07). In contrast, “Drugs in Pregnancy and Lactation” was selected three times as often by obstetricians over the age of 50 (n=10), compared to those below the age of 50 (n=3), (p=0.08).

There was no significant difference in the use of the other resources when stratified by age: “teratogen service” (p=0.63), “peer-reviewed internet” (p=0.15), “Physician’s Desk Reference” (p=0.15), “colleague” (p=0.59), “personal digital assistant” (p=0.25), and “peer-reviewed literature” (p=0.71).

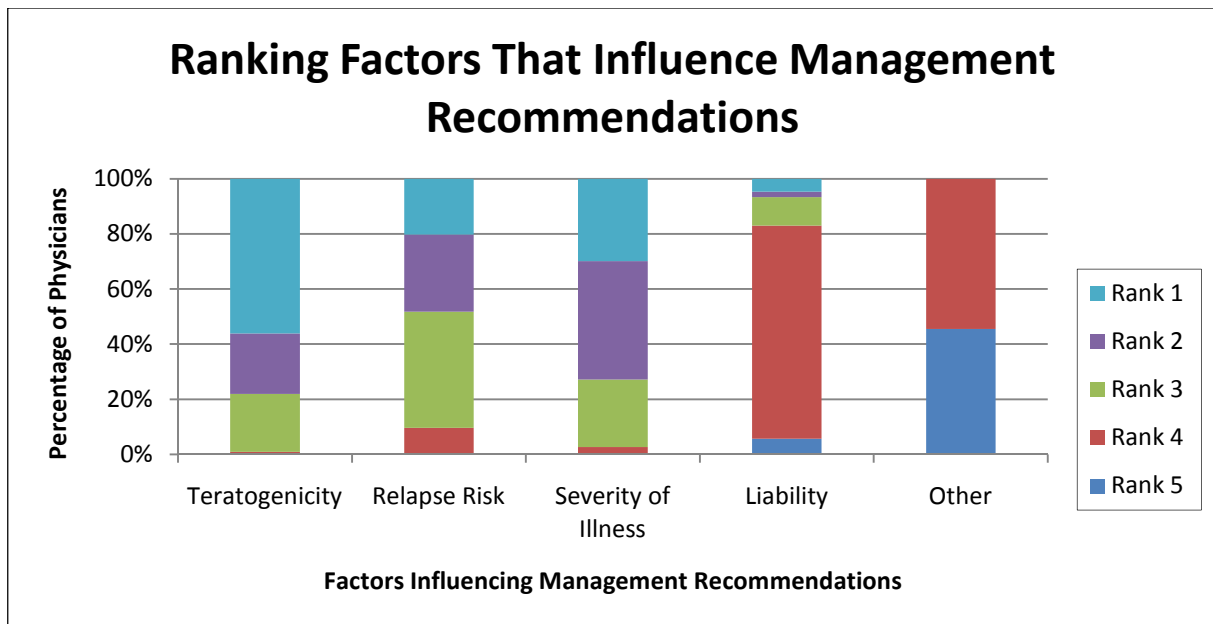


**Figure 14:** Obstetrician utilization of common drug counseling resources stratified by age. †Denotes those resources with notable, although not statistically significant, differences between age groups.

In Part II Question 7, obstetricians were asked to rank four different factors, from most contributory (1) to least (5), regarding how they influenced their recommendations for pharmacological management during pregnancy. These factors were “teratogenic risk to the fetus,” “risk of relapse in mother if discontinued,” “severity of maternal illness,” and “medical liability.” The “Other” option was available as a write-in option for respondents to list any additional factors that may influence their recommendations.

Many obstetricians did not rank in a mutually exclusive and non-overlapping sequential “1, 2, 3...” order. For example, some respondents gave all four factors equal ranks of “1.” Individuals who gave equal ranks to more than one category were coded as such. For example, if a respondent ranked the first two factors both “1,” they were coded as “1” and “1” each. However, the next lowest category they ranked was coded as “3” and not “2.” For example, consider the following response: “Teratogenic risk to fetus”(1), “Risk of relapse in mother if discontinued” (2), “Severity of maternal illness” (1), “Medical liability” (3), “Other” (4). This would be coded as “1, 3, 1, 4, 5,” respectively. Many respondents left different factors blank after ranking only a few, and these were coded as missing data.

Fifty-one percent (n=64) of respondents who ranked “Teratogenic risk to fetus” chose it as the most contributory factor (Rank 1) influencing their decision-making. The most common factor to be given Rank 2 was “Severity of Maternal Illness” (n=49; 45% of respondents for that category). “Risk of relapse in mother if discontinued” was most commonly given Rank 3 (n=48; 43% of respondents for that category). The least contributory factor (Rank 4) most commonly selected was “Medical liability” (n=82; 80% of respondents for that category). Eleven obstetricians ranked “Other” factors that influenced their decisions, either at Rank 4 or 5 (Figure 15). Examples of “Other” factors include the following: “cost,” “side effects,” “lack of available counseling,” and “intellectual capability of the mother.” A full list of “Other” factors respondents listed is located in Appendix 2.

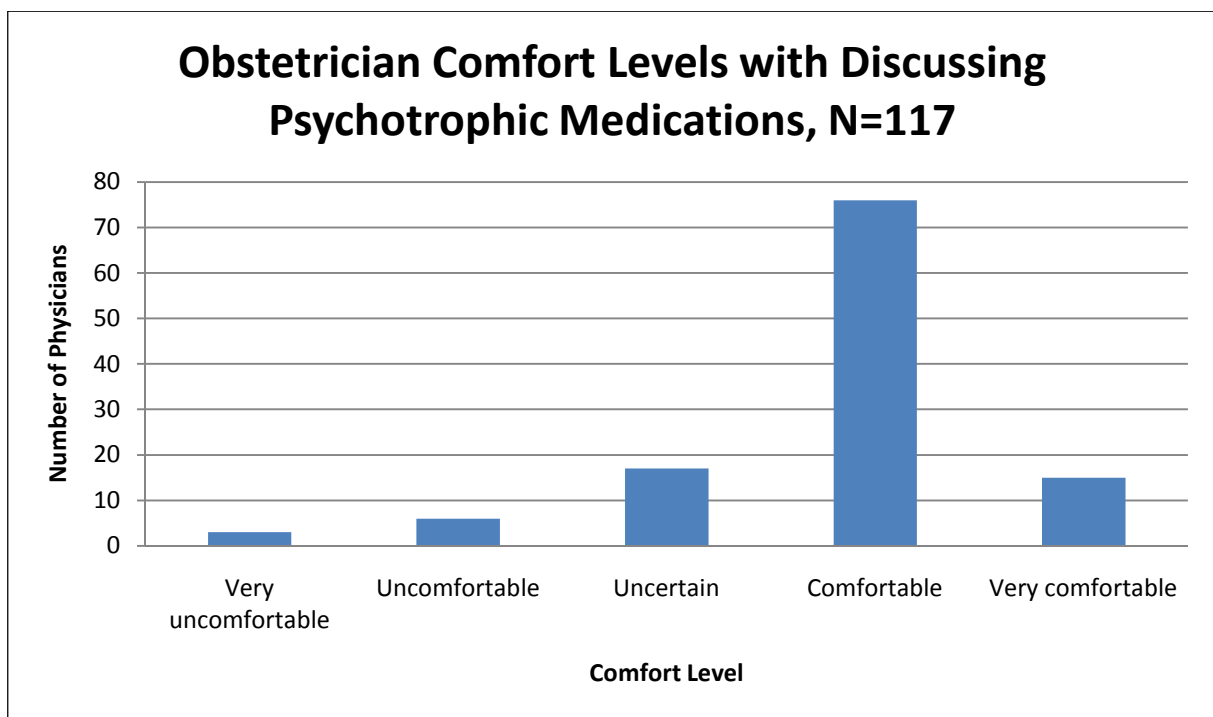


**Figure 15:** Obstetrician rankings of those factors that influence their recommendations regarding pharmacological management during pregnancy. Rank 1 is most contributory while rank 4 or 5 is least contributory.

### **Part III: Teratogen Knowledge/Perceptions**

In Part III, a series of five paired questions was utilized to assess obstetricians' knowledge of accurate teratogenic risk figures associated with common psychotropic medications (e.g. SSRIs, anti-psychotics), as well as obstetricians' perceptions of these risks. In this section a few respondents did not select an available answer but wrote in their own answer next to the question. This typically occurred with those questions requesting a specific risk figure. If the hand-written response could be logically placed in an available category, the answer was reclassified. For example, if a responder wrote the incidence of structural birth defects was "7%" for exposure to SSRIs *in utero*, this could easily be placed in the "5-10%" answer category. However, if the response was at all ambiguous or not easily reclassified, it was coded as missing data. Those individuals who wrote in "I don't know" or similar statements were reclassified as "Don't know" if the question had that category available. Otherwise, these responses were coded as missing data.

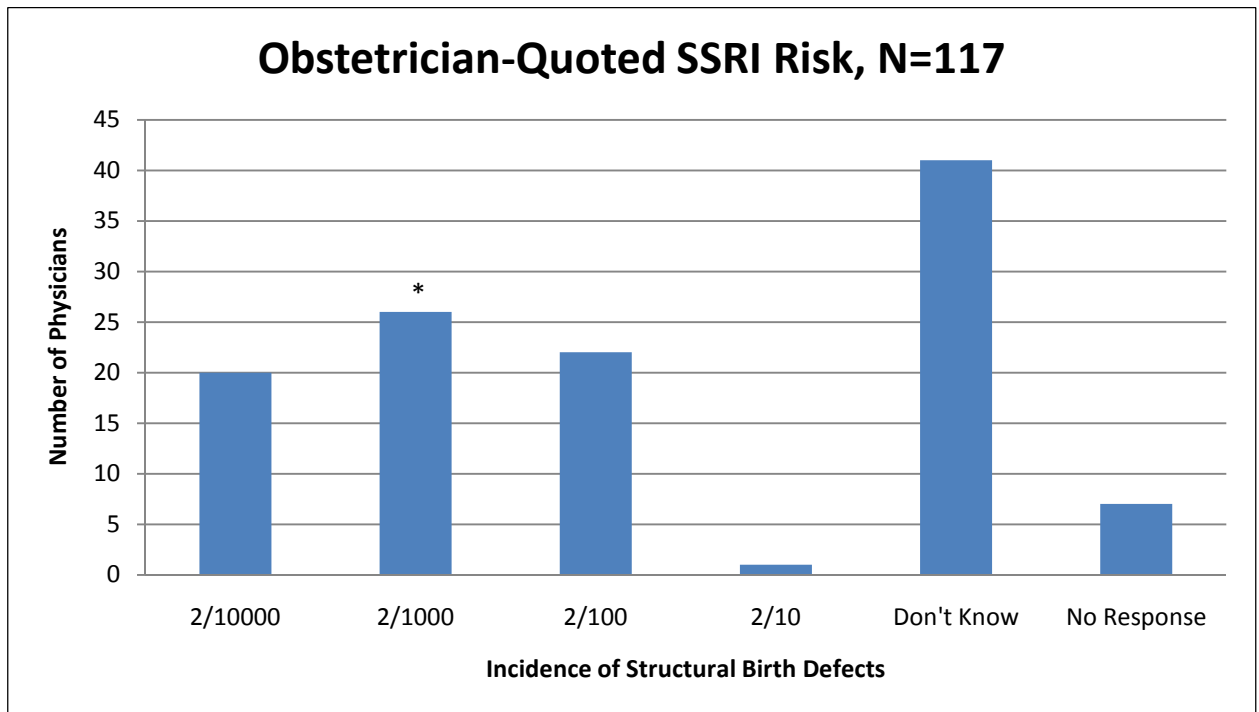
Obstetricians were asked how comfortable they are discussing the teratogenicity of medications used to manage mood disorders with their patients. Sixty-four percent (n=76) reported feeling “comfortable” and 12% (n=15) reported feeling “very comfortable,” while 14% (n=17) were “uncertain.” Five (n=6) and 2% (n=3) reported feeling “uncomfortable” or “very uncomfortable,” respectively, when having these discussions (Figure 16). There was no significant difference in comfort level when stratified by age ( $p=0.607$ ), gender ( $p=0.523$ ), or practice ( $p=0.421$ ).



**Figure 16:** Obstetrician-reported level of comfort when discussing the teratogenicity of psychotropics with their patients.

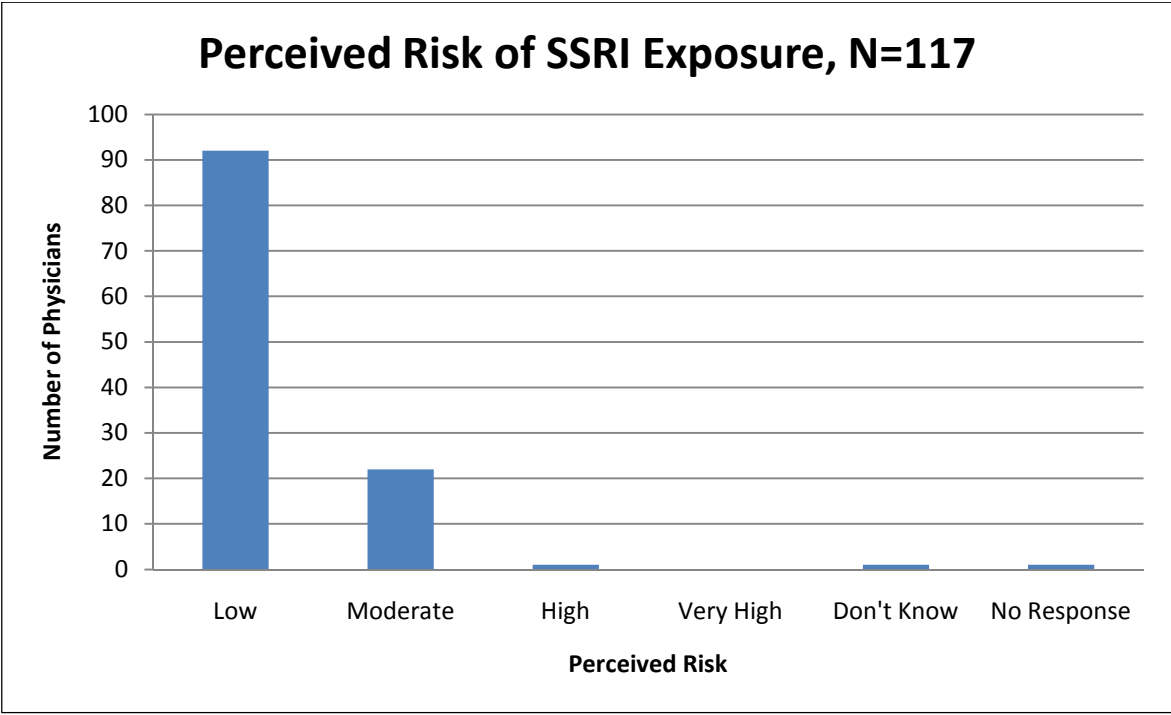
Obstetricians were asked what incidence of structural birth defects they quote to patients taking selective serotonin reuptake inhibitors (SSRIs) during pregnancy. Of those who responded (n=110), the majority (n=41; 37%) selected “Don’t Know.” Twenty-four percent (n=26) selected the correct value of 2/1000. Eighteen percent (n=20) underestimated the risk at 2/10,000, while 20% (n=22) and 1% (n=1) overestimated the risk at 2/100 and 2/10, respectively (Figure 17).

There was no statistically significant difference in quoted risk when stratified by age (p=0.356), gender (p=0.927), or practice (p=0.293). Twenty-four percent (8/33) of obstetricians from academia and 24% (18/76) of obstetricians from private practice selected the correct answer. Nineteen percent (10/53) of obstetricians at or below the age of 50 selected the correct answer, compared to 18% (11/60) above the age of 50.



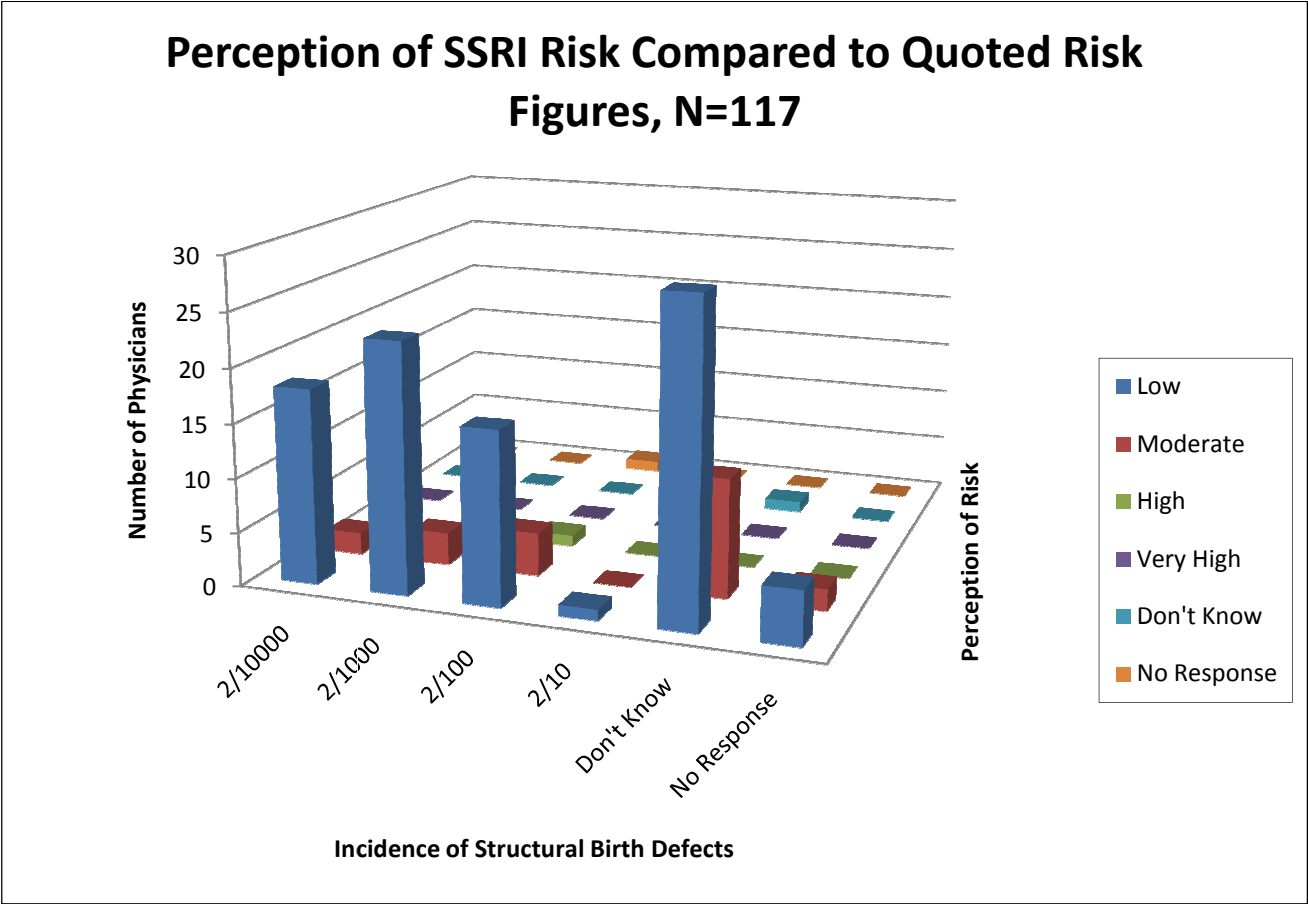
**Figure 17:** Obstetrician-quoted incidence of structural birth defects due to *in utero* SSRI exposure. \*Denotes the correct answer.

Obstetricians were next asked how they perceive the risks associated with taking SSRIs during pregnancy. Of those who responded (n=116), the majority (n=92; 79%) felt the risk was “low.” Nineteen percent (n=22) felt the risk was “moderate,” while only 1 responder (less than 1%) thought the risk was “high.” No obstetricians felt the risk for structural birth defects was “very high” (Figure 18). There was no significant difference in SSRI risk perception when stratified by age (p=0.836), gender (p=0.071), or practice (p=0.887).



**Figure 18:** Obstetrician perceptions of the risk for structural birth defects associated with SSRI exposure.

There was no significant association between quoted risk figures for SSRI exposure, and obstetricians' perceptions of these risks ( $p=0.455$ ). Regardless of the exact risk number quoted, the majority of respondents felt the risk was low. Figure 19 shows the obstetrician-quoted risk figures plotted against obstetrician perceptions of these risks.

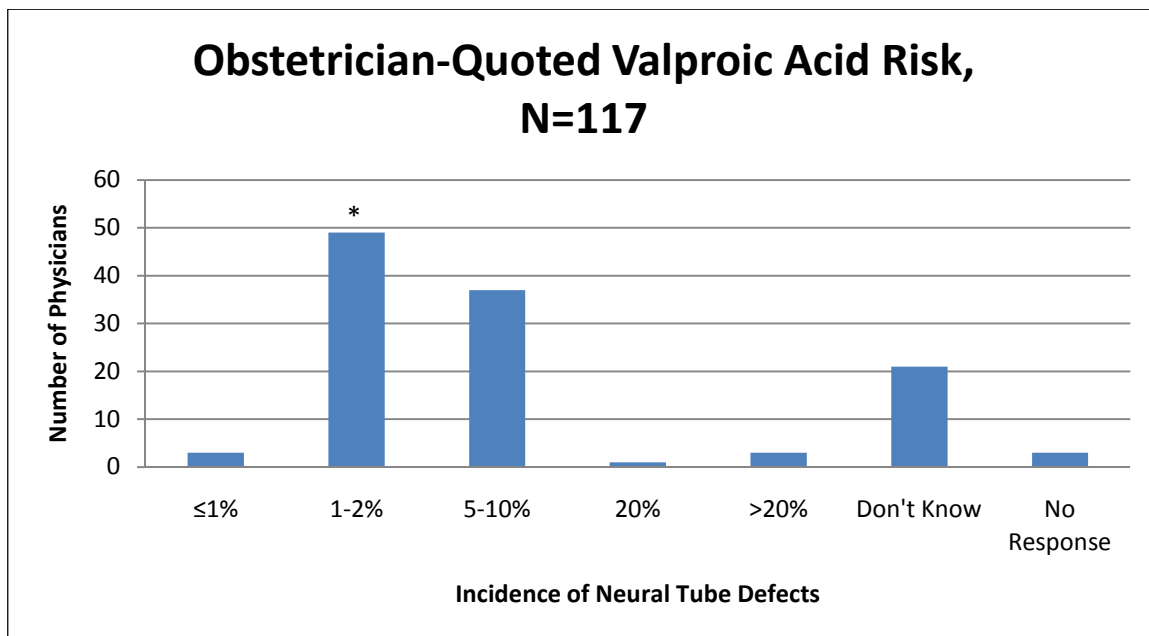


**Figure 19:** Obstetrician-quoted incidence of structural birth defects compared to obstetrician perception of risk regarding SSRI use during pregnancy.



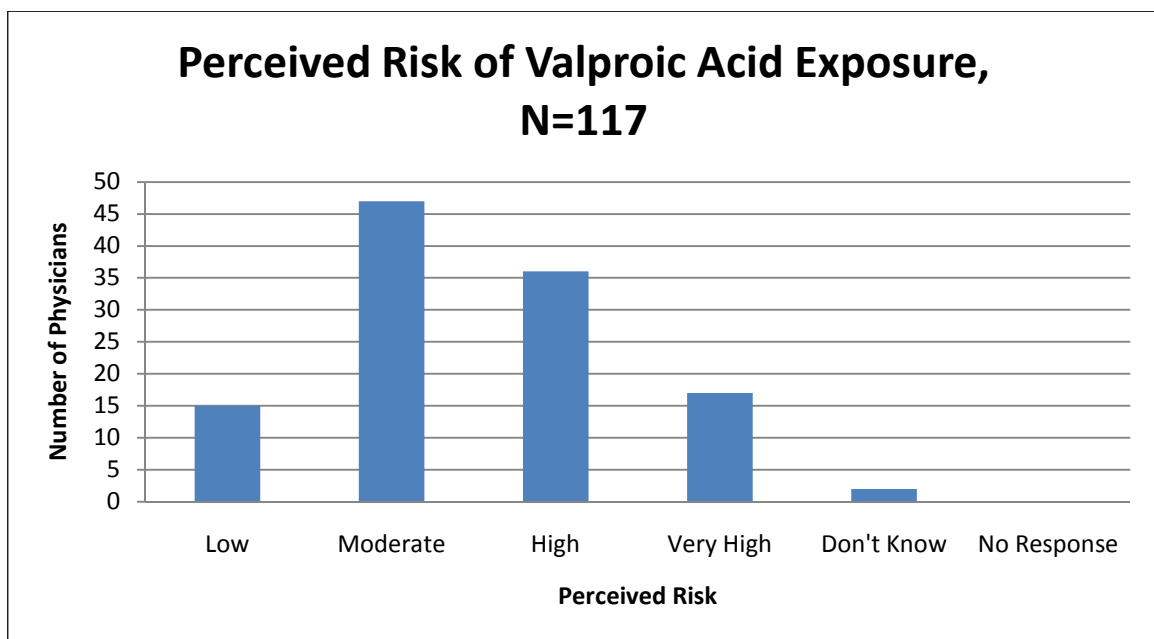
Obstetricians were also asked what incidence of neural tube defects they quote to patients taking valproic acid (Depakote®) during pregnancy. Of those who responded (n=114), the majority (n=49; 43%) selected the correct incidence of 1-2%. Thirty-two percent (n=37) of respondents overestimated the incidence at 5-10%. Four respondents (4%) overestimated the incidence at 20% or higher. Only 3% (n=3) of obstetricians underestimated the risk, while 18% (n=21) of obstetricians selected “Don’t Know” (Figure 20).

There was no statistically significant difference in quoted risk when stratified by age (p=0.328), gender (p=0.930), or practice (p=0.557). Forty-five percent (15/33) of obstetricians from academia and 42% (32/76) of obstetricians from private practice selected the correct answer. Forty-five percent (24/53) of obstetricians at or below the age of 50 selected the correct answer, compared to 40% (24/60) above the age of 50.



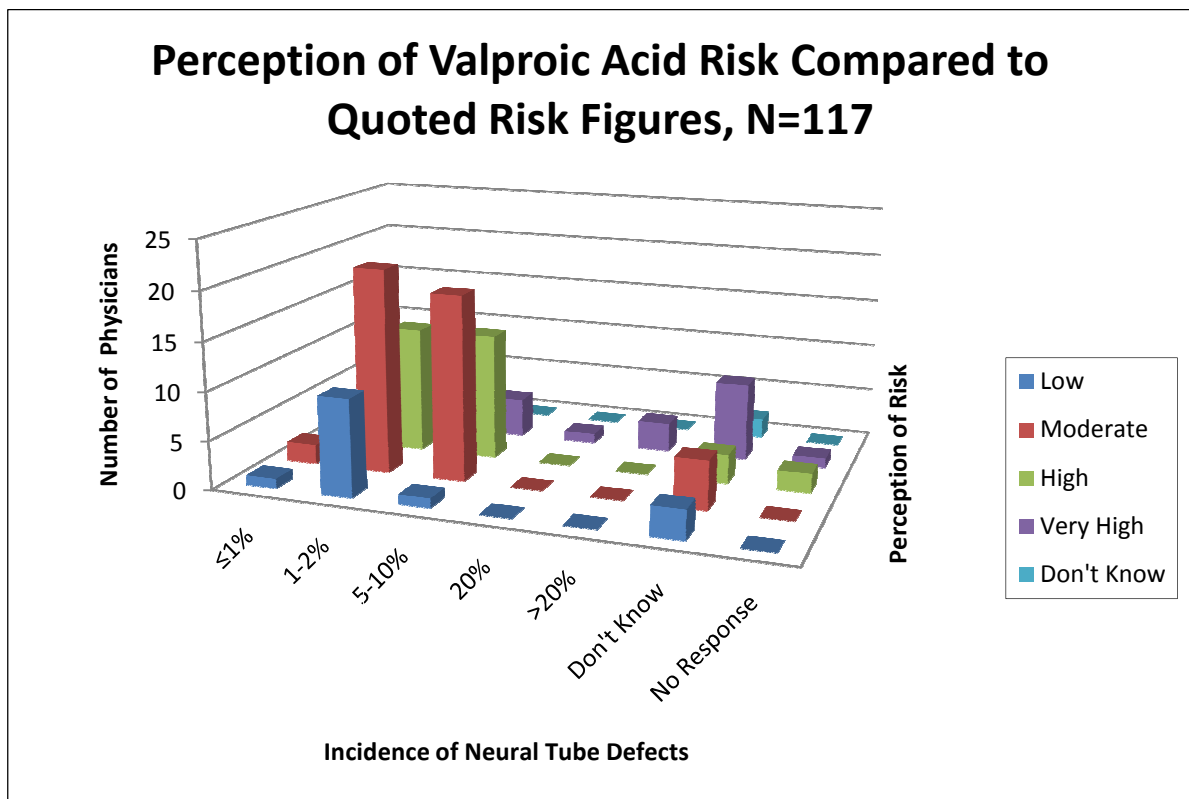
**Figure 20:** Obstetrician-quoted incidence of structural birth defects due to *in utero* valproic acid exposure. \*Denotes the correct answer.

Obstetricians were next asked how they perceive the risk for neural tube defects associated with taking valproic acid during pregnancy. Of those who responded (n=115), the majority (n=47; 40%) felt the risk was “moderate.” Thirty-one percent (n=36) felt the risk was “high,” and 15% (n=17) felt the risk was “very high.” Thirteen percent (n=15) of respondents felt the risk was “low” (Figure 21). There was no significant difference in the perceived risk of valproic acid exposure when stratified by age (p=0.255), gender (p=0.257), or practice (p=0.340).



**Figure 21:** Obstetrician perceptions of the risk for neural tube defects associated with valproic acid exposure.

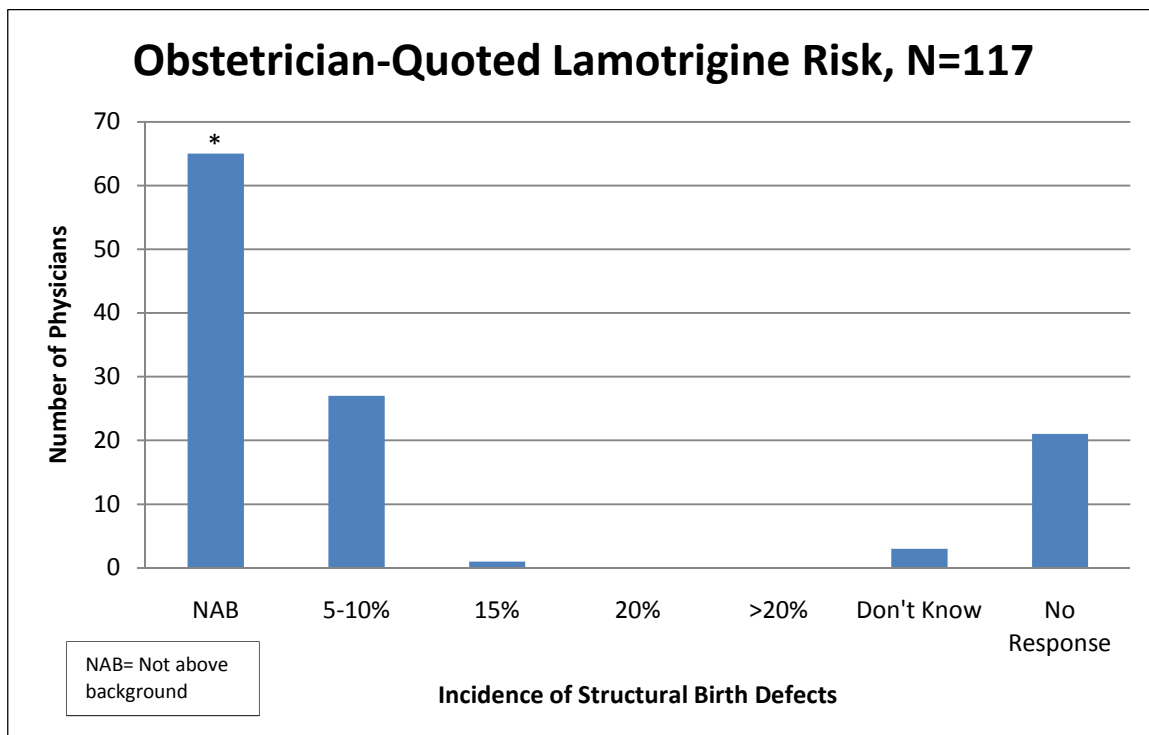
There was not a significant association between quoted risk figures for valproic acid exposure, and obstetricians' perceptions of these risks ( $p=0.067$ ). However, there was a wide variation in risk perception for the same categories. For example, 49 respondents chose a 1-2% incidence of neural tube defects. Twenty percent ( $n=10$ ) felt the risk was “low,” 43% ( $n=21$ ) felt the risk was “moderate,” 26% ( $n=13$ ) felt the risk was “high,” and 10% ( $n=5$ ) felt the risk was “very high.” Similar differences in risk perception for the same risk figure can be seen in other incidence categories (e.g. 5-10% category). In addition, respondents who selected an incidence of 5-10% were more likely to perceive this as a “moderate” or “high” risk, compared to those who selected the lower incidence of 1-2%. In general, as the risk quantification increases, those obstetricians perceiving the risk as “low” decreases (Figure 22).



**Figure 22:** Obstetrician-quoted incidence of neural tube defects compared to obstetrician perception of risk regarding valproic acid use during pregnancy.

Obstetricians were asked what incidence of birth defects they quote to patients taking lamotrigine (Lamictal®) during pregnancy. Of those who responded (n=96), the majority (n=65, 68%) selected the correct answer, “Not increased above the background.” Twenty-eight percent (n=27) of obstetricians selected 5-10%, and only one obstetrician chose 15%. No one selected a birth defect incidence of 20% or higher. Twenty-one obstetricians did not respond to this question (Figure 23).

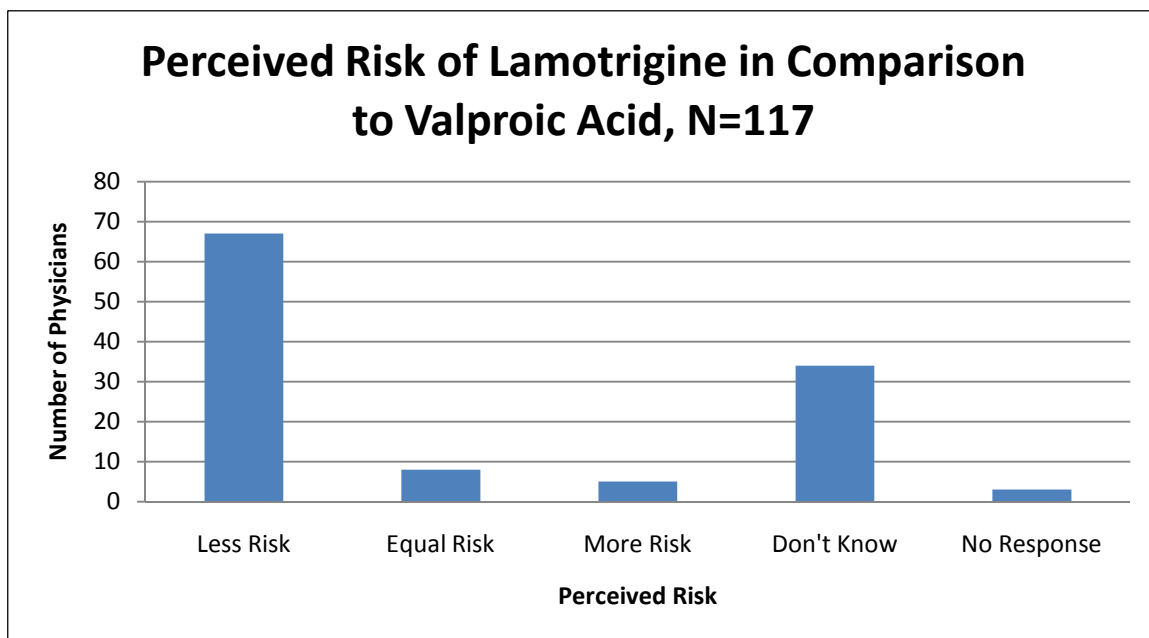
There was no statistically significant difference in quoted risk when stratified by age (p=0.113), gender (p=0.069), or practice (p=0.718). Sixty-one percent (20/33) of obstetricians from academia and 55% (42/76) of obstetricians from private practice selected the correct answer. Fifty-five percent (29/53) of obstetricians at or below the age of 50 selected the correct answer, compared to 58% (33/60) above the age of 50.



**Figure 23:** Obstetrician-quoted incidence of birth defects due to *in utero* lamotrigine exposure. \*Denotes the correct answer.

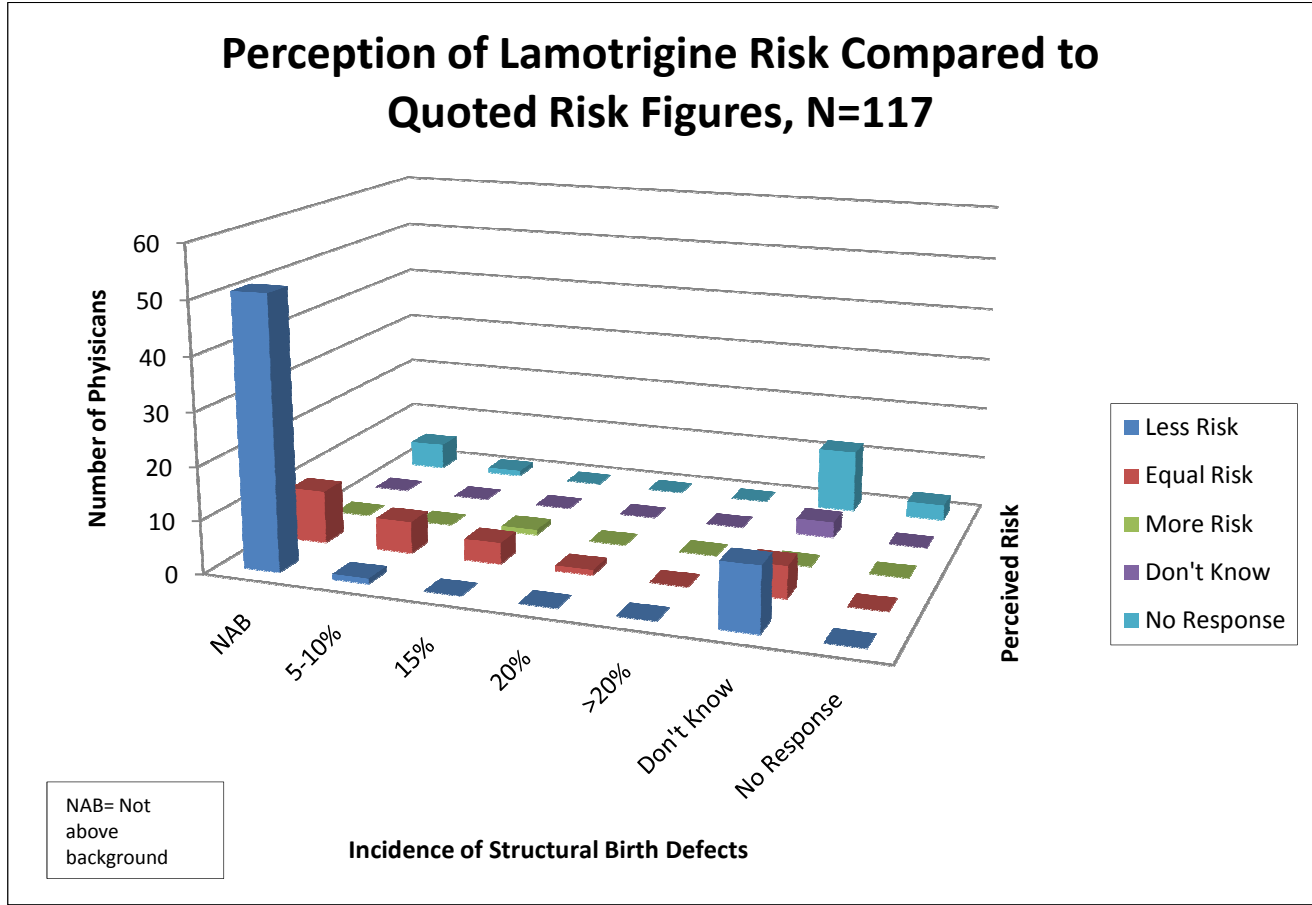
Obstetricians were next asked how they perceive the risk associated with taking lamotrigine during pregnancy in comparison with the risk associated with valproic acid. Of those who responded (n=114), 59% (n=67) felt that lamotrigine has “less risk than valproic acid.” Seven percent (n=8) felt that lamotrigine has the same risk as valproic acid, while 4% (n=5) felt that lamotrigine has “more risk than valproic acid.” Thirty percent (n=34) of respondents selected “Don’t know” (Figure 24).

There was no significant difference in the perceived risk of lamotrigine exposure when stratified by age (p=0.108), gender (p=0.766), or practice (p=0.867).



**Figure 24:** Obstetrician perceptions of the risk for birth defects associated with lamotrigine use during pregnancy, in comparison to valproic acid.

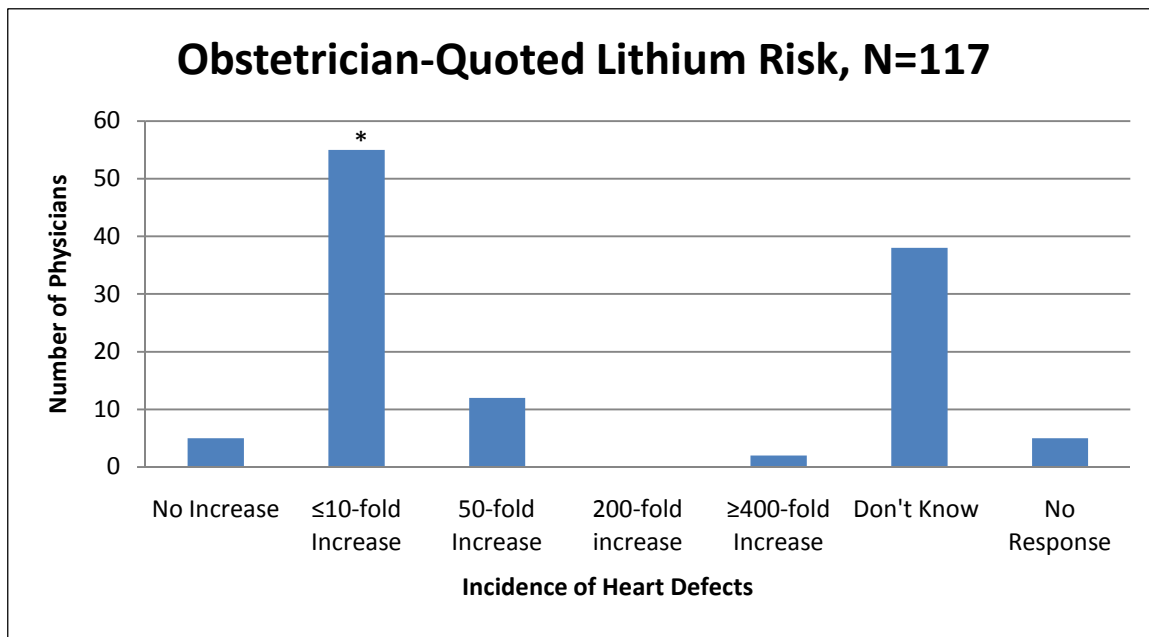
There was a significant association between quoted risk figures for lamotrigine exposure, and obstetricians' perceptions of these risks ( $p<0.001$ ). Of the 66 respondents who chose a risk “not increased above the background,” 77% ( $n=51$ ) thought this qualification was of less risk than valproic acid. However, 15% ( $n=10$ ) thought this qualification was equal to the risk associated with valproic acid. Of the 33 respondents who selected “Don’t know” for the risk figure associated with lamotrigine, 36% ( $n=12$ ) felt the risks associated with the two drugs are equal, while 36% ( $n=12$ ) reported that did not know how they felt about the comparison. Figure 25 shows the obstetrician-quoted risk figures plotted against obstetrician perceptions of these risks.



**Figure 25:** Obstetrician-quoted incidence of birth defects compared to obstetrician perception of risk regarding lamotrigine use during pregnancy.

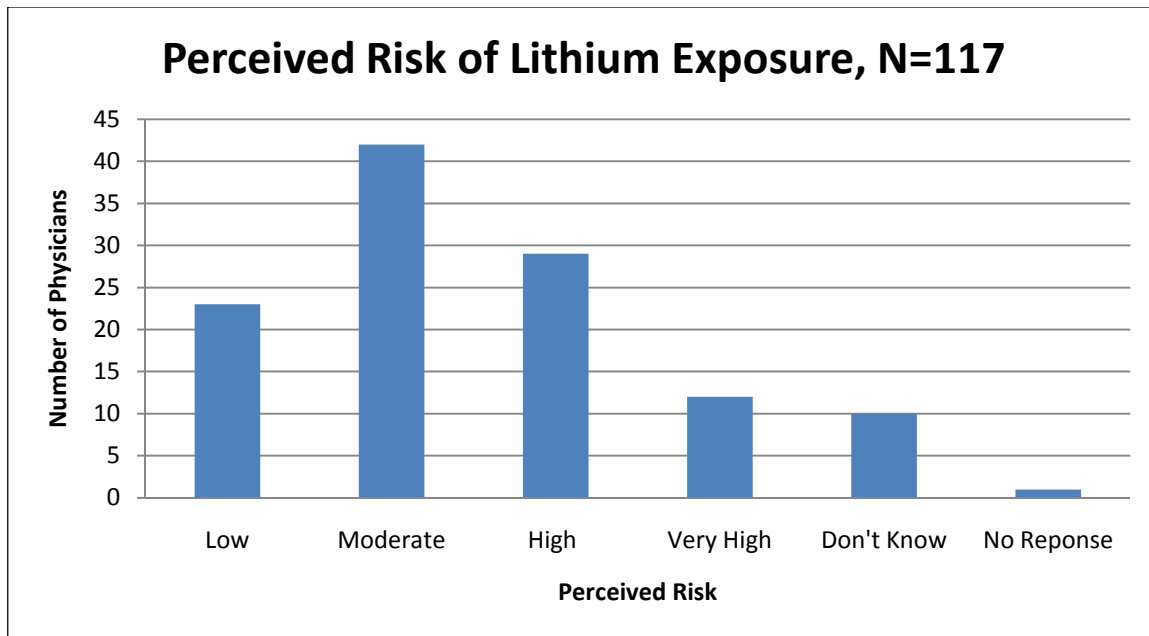
Obstetricians were asked what incidence of congenital heart defects they quote to patients taking lithium during pregnancy (in relation to the background risk of heart defects). Of those who responded (n=112), 49% (n=55) selected the correct value of “less than a 10-fold increase” in the incidence of heart defects. Thirty-four percent (n=38) selected “Don’t know.” Four percent (n=5) of respondents underestimated the risk associated with lithium use (“no increase”), while 13% (n=14) overestimated the incidence of heart defects. Of note, two obstetricians (2%) selected a “greater than 400-fold increase” in the incidence of heart defects (Figure 26).

There was no statistically significant difference in quoted risk when stratified by age (p=0.219), gender (p=0.975), or practice (p=0.112). Sixty-one percent (20/33) of obstetricians from academia and 45% (34/76) of obstetricians from private practice selected the correct answer. Forty-seven percent (25/53) of obstetricians at or below the age of 50 selected the correct answer, compared to 58% (29/60) above the age of 50.



**Figure 26:** Obstetrician-quoted incidence of congenital heart defects due to *in utero* lithium exposure. \*Denotes the correct answer.

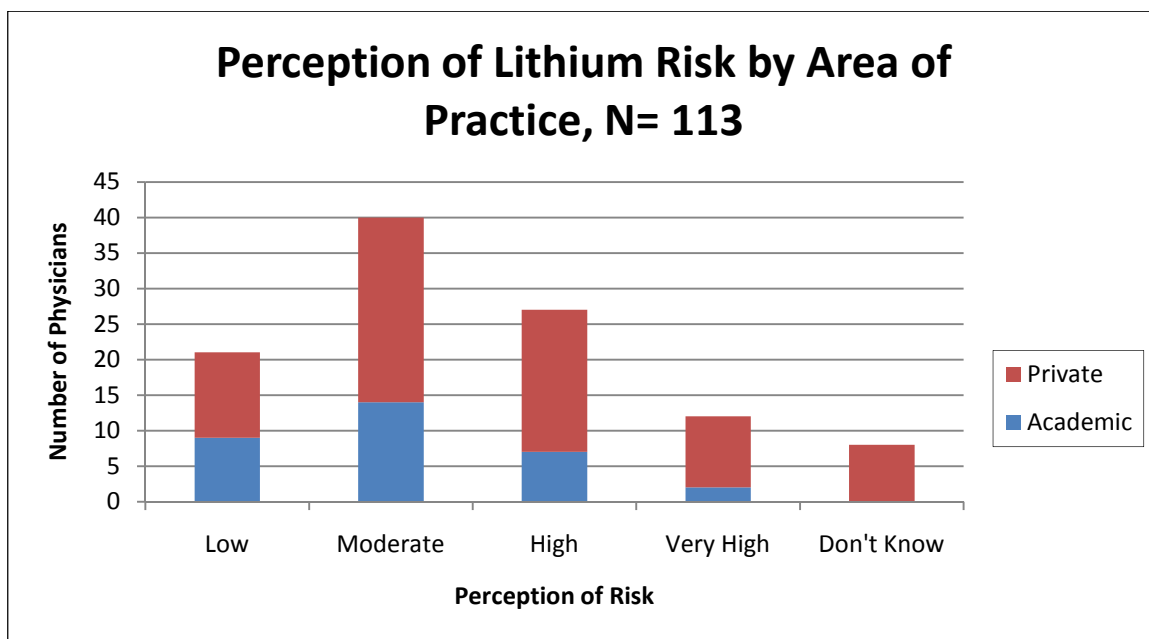
Obstetricians were next asked how they perceived the risk for heart defects associated with taking lithium during pregnancy. Of those who responded (n=116), 36% (n=42) felt the risk was “moderate,” while 25% (n=29) felt the risk was “high.” Ten percent (n=12) of respondents felt the risk was “very high.” Only 10 obstetricians (8%) responded “Don’t Know” (Figure 27).



**Figure 27:** Obstetrician perceptions of the risk for congenital heart defects associated with lithium use during pregnancy.

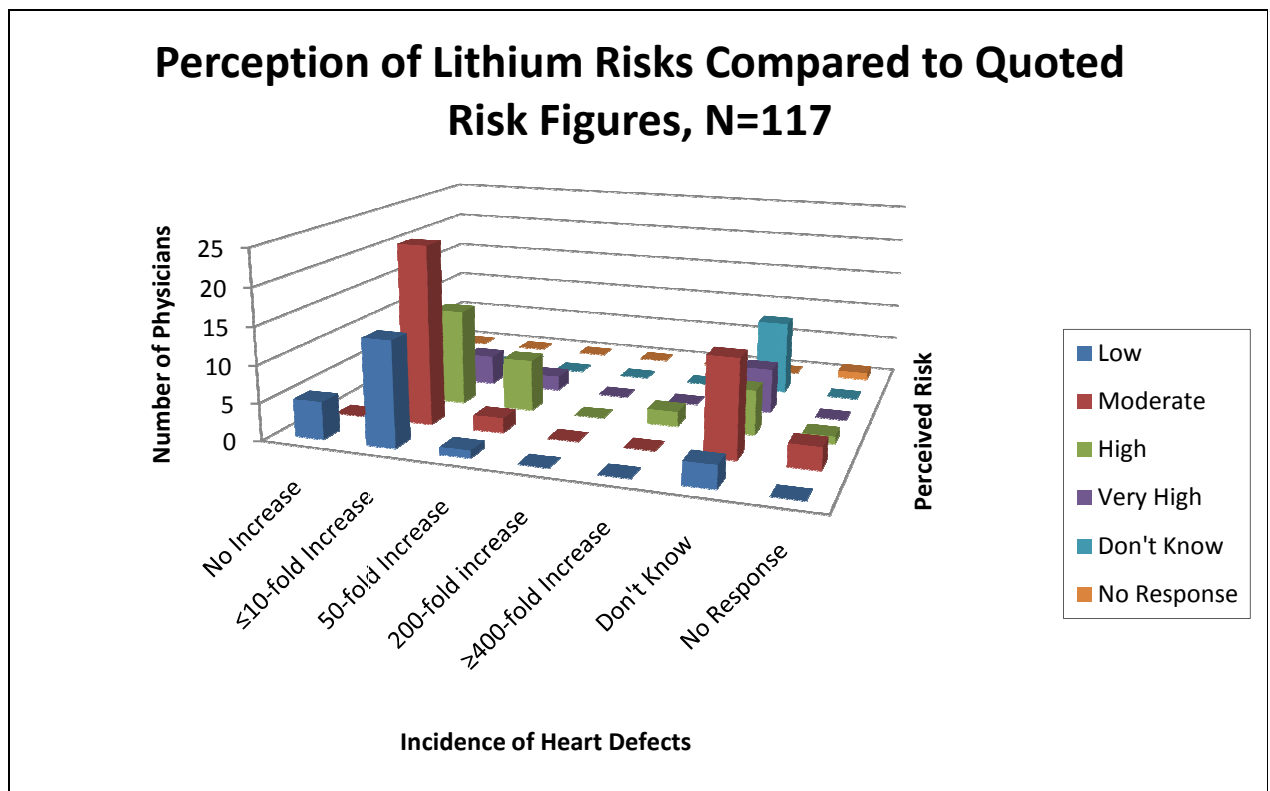


There was no significant difference in the perceived risk of lithium exposure when stratified by age ( $p=0.424$ ) or gender ( $p=0.495$ ). However, there was a significant difference in the perceived risk of lithium when stratified by area of practice ( $p=0.014$ ). Of those obstetricians who selected a risk perception of “high” ( $n=27$ ), 74% ( $n=20$ ) were in private practice while the remaining 26% ( $n=7$ ) practiced in an academic setting. In addition, of those who selected a risk perception of “very high” ( $n=12$ ), 83% ( $n=10$ ) were in private practice while 17% ( $n=2$ ) were in academia (Figure 28).



**Figure 28:** Obstetrician perceptions of the risk for congenital heart defects associated with lithium use during pregnancy stratified by area of practice.

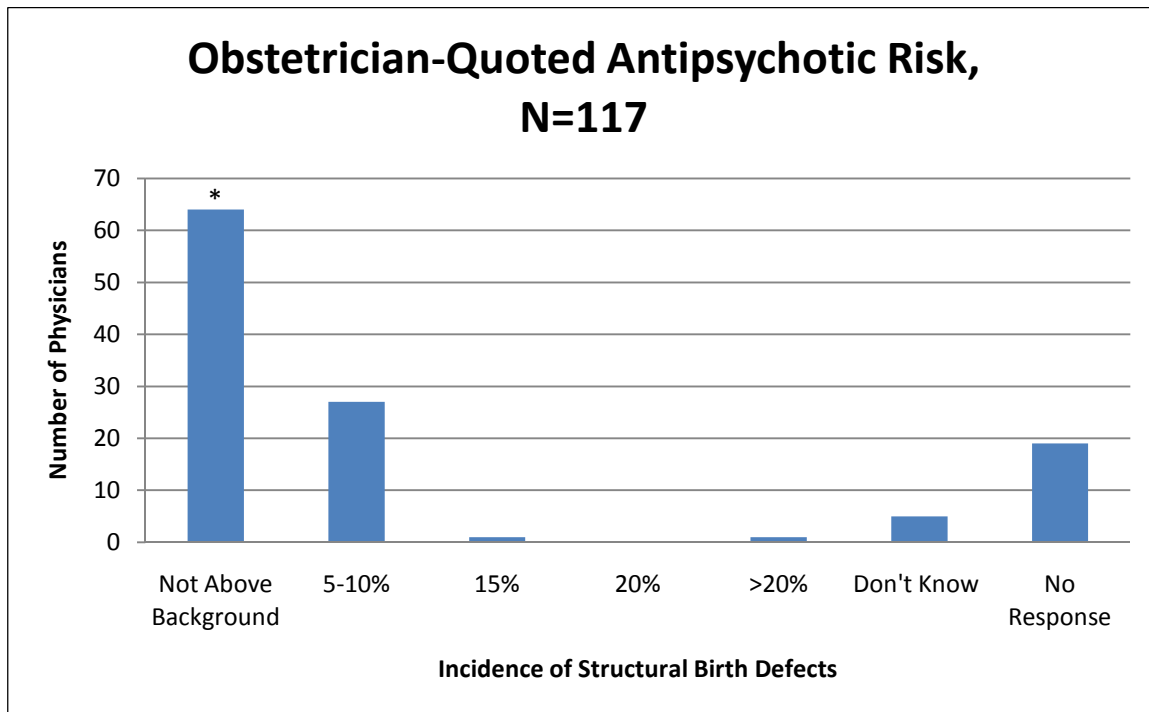
There was a significant difference between quoted risk figures for lithium exposure, and obstetricians' perceptions of these risks ( $p=0.002$ ), (Figure 29). Fifty-five respondents chose an incidence of "less than a 10-fold increase." However, these respondents perceived this incidence differently. Twenty-five percent ( $n=14$ ) felt the incidence was "low," while 44% ( $n=24$ ) felt the incidence was "moderate." Twenty-four percent ( $n=13$ ) felt the incidence of heart defects was "high," and 7% ( $n=4$ ) felt it was "very high." Similar variations in perception were associated with those 38 obstetricians who were not able to select an exact incidence (e.g. those who chose "Don't know"). However, individuals who selected a "less than 10-fold increase" were more likely to perceive the risk as low, compared to those who selected "Don't know." Individuals who were not able to quantify a risk ("Don't know") were more likely to perceive the risk as "high" or "very high."



**Figure 29:** Obstetrician-quoted incidence of congenital heart defects compared to obstetrician perception of risk regarding lithium use during pregnancy.

Obstetricians were asked what incidence of birth defects they quote to patients taking second-generation antipsychotics (e.g. aripiprazole, clozapine, risperidone) during pregnancy. Of those who responded (n=98), 65% (n=64) selected the correct incidence of “not increased above the background.” Twenty-eight percent (n=27) overestimated the incidence at 5-10%. One physician each selected an incidence of 15% and greater than 20% (1% each), (Figure 30).

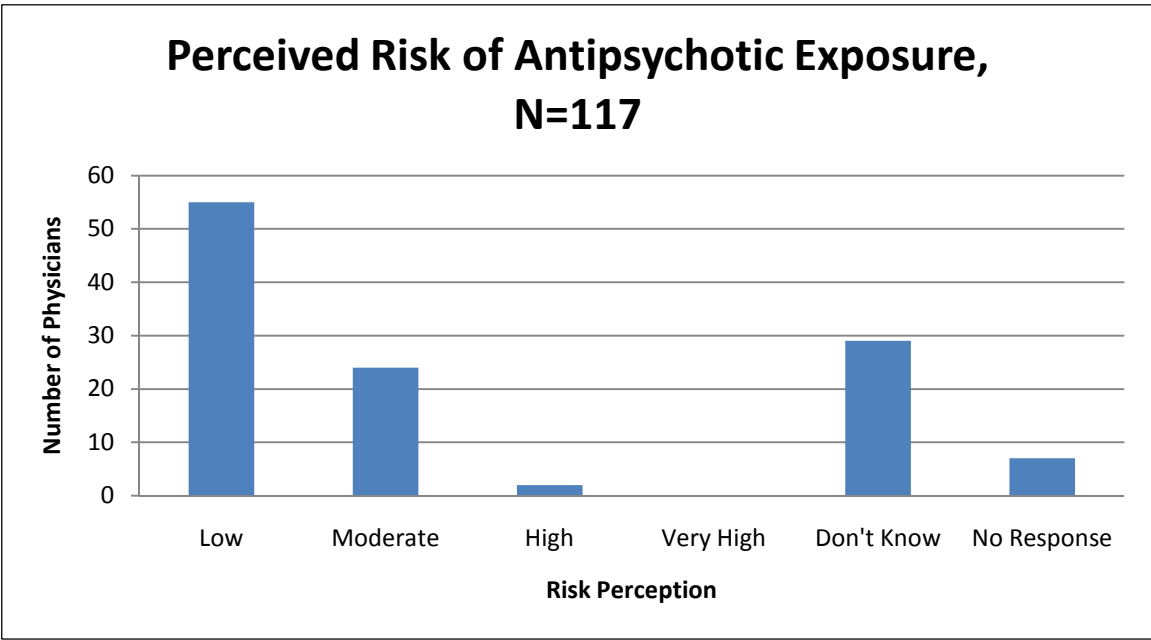
There was no statistically significant difference in quoted risk when stratified by age (p=0.056), gender (p=0.066), or practice (p=0.343). Fifty-five percent (18/33) of obstetricians from academia and 55% (42/76) of obstetricians from private practice selected the correct answer. Forty-nine percent (26/53) of obstetricians at or below the age of 50 selected the correct answer, compared to 60% (36/60) above the age of 50.



**Figure 30:** Obstetrician-quoted incidence of birth defects due to *in utero* second-generation antipsychotic exposure. \*Denotes the correct answer.

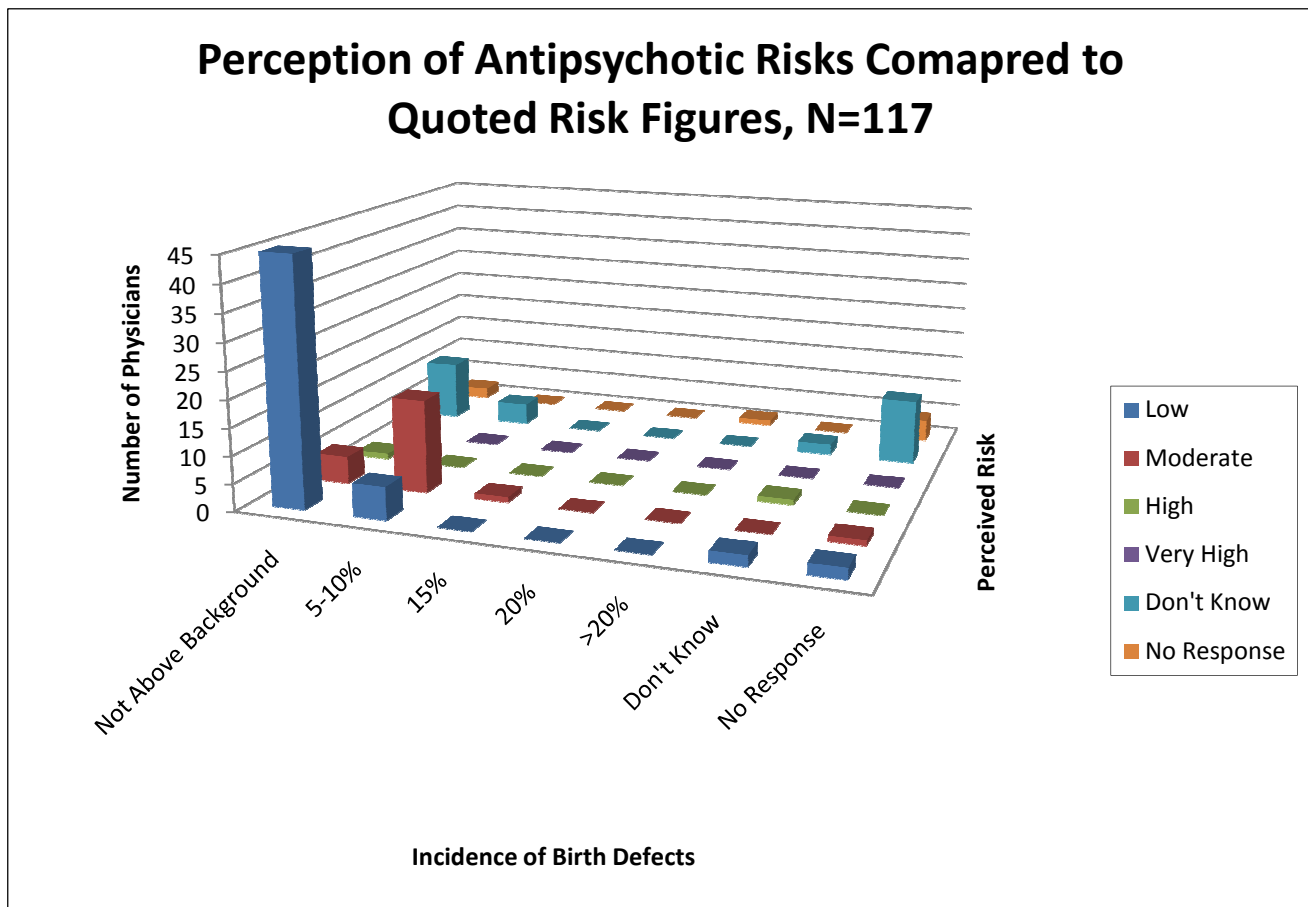
Obstetricians were next asked how they perceived the risk for birth defects associated with taking second-generation antipsychotics during pregnancy. Of those who responded (n=100), the majority (55%, n=55) thought the risk was “low.” Twenty-nine percent (n=29) of respondents selected “Don’t know.” Twenty-four percent (n=24) of obstetricians felt the risk was “moderate,” while only 2% (n=2) felt the risk was “high” (Figure 31).

There was no statistically significant difference in perceived risk when stratified by age (p=0.684), gender (p=0.170), or practice (p=0.717).



**Figure 31:** Obstetrician perceptions of the risk for birth defects associated with second-generation antipsychotic use during pregnancy.

There was a significant association between quoted risk figures for second-generation antipsychotic exposure, and obstetricians' perceptions of these risks ( $p < 0.001$ ). Sixty-four respondents quantified that the incidence was “not increased above the background.” However, these respondents perceived this incidence differently. Seventy percent ( $n=45$ ) of these respondents thought that qualification was “low,” 8% ( $n=5$ ) thought it was “moderate,” and 2% ( $n=1$ ) thought it was “high.” Twenty-four percent ( $n=11$ ) were uncertain how to perceive that incidence (e.g. selected “Don’t know). Figure 32 shows the obstetrician-quoted risk figures plotted against obstetrician perceptions of these risks.



**Figure 32:** Obstetrician-quoted incidence of birth defects compared to obstetrician perception of risk regarding second-generation antipsychotic use during pregnancy.

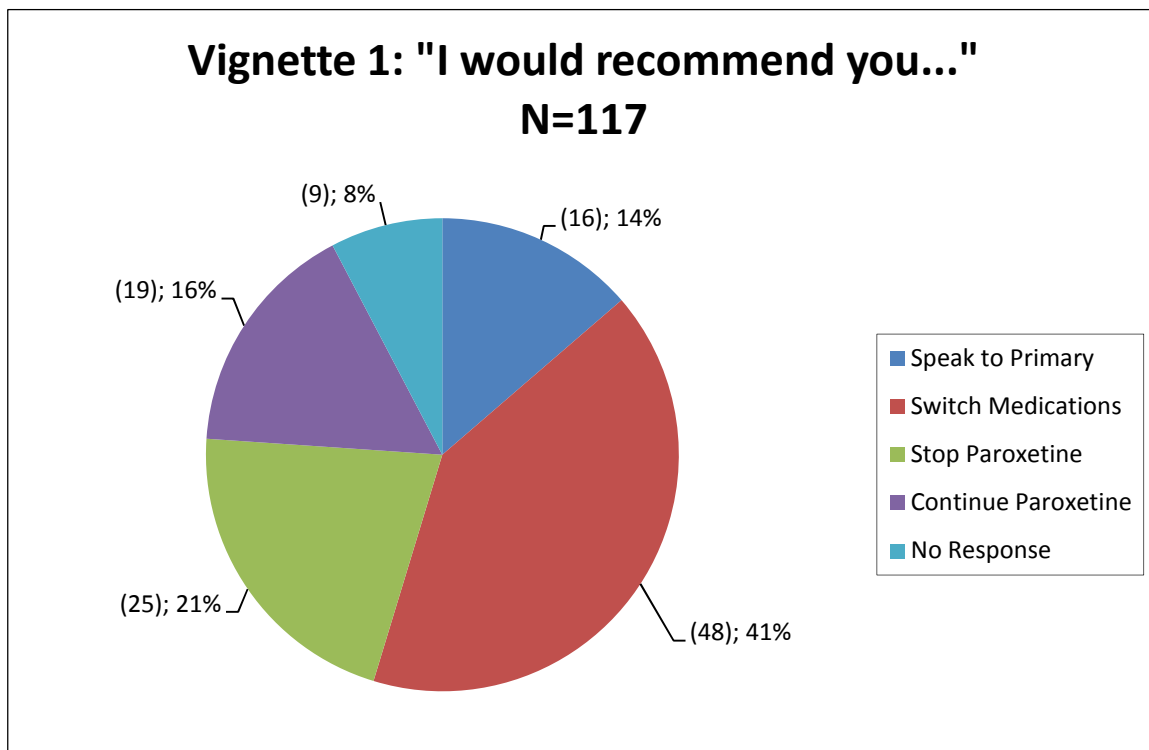
#### **Part IV: Situational Vignettes**

In Part IV, obstetricians were asked to evaluate two different situational vignettes and answer two questions for each- what recommendations they would make to the patient and what (if any) referrals they would make to another provider. Respondents had the option of filling in a particular specialist they would refer to if that option was not listed. These “Other” specialists are listed in detail in Appendix 3. At the end of each situational vignette, responders also had the option of writing in additional comments.

A detailed description of each vignette can be found in Appendix 1.

Figure 33 shows the distribution of obstetricians' recommendations in response to Vignette 1. Of those who responded (n=108), the majority (n=48; 44%) would recommend that the patient “switch to a different SSRI, because paroxetine is associated with an increased risk for birth defects.” Twenty-three percent (n=25) would recommend the patient “stop taking paroxetine (gradually, in decreased doses) for the remainder of the pregnancy.” Eighteen percent (n=19) would recommend the patient “continue taking paroxetine as (her) primary care physician prescribed,” while 15% (n=16) would recommend the patient “speak with (her) primary care physician before making changes to (her) pharmacological management.”

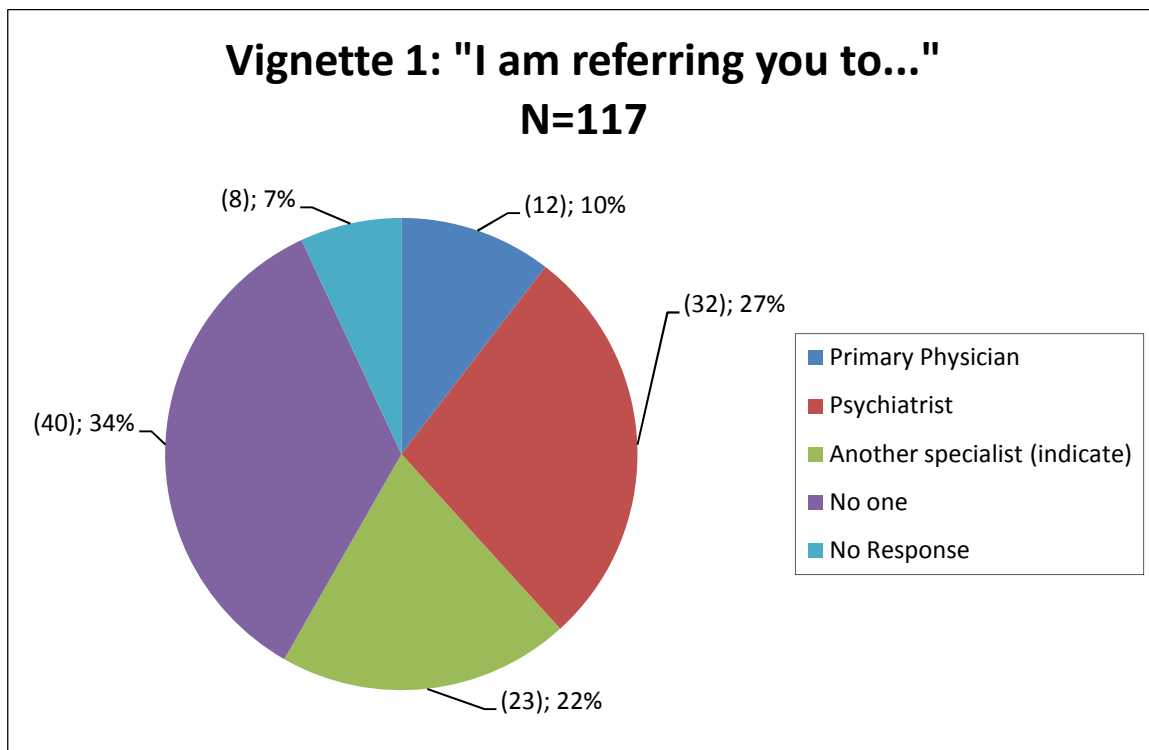
There was no statistically significant difference in recommendations when stratified by age (p=0.77), gender (p=0.36), or practice (p=0.897).



**Figure 33:** Obstetrician recommendations in response to Vignette 1.

Figure 34 shows the distribution of obstetricians' choice of referrals in response to Vignette 1. Of those who responded (n=109), the majority of obstetricians (37%; n=40) felt comfortable managing the case alone and did not feel a referral was necessary. Twenty-nine percent (n=32) would refer the patient to “a psychiatrist to discuss whether or not to continue taking paroxetine.” Twenty-one percent (n=23) would recommend the patient see “another specialist to co-manage the pregnancy.” Of these “Other” specialists, a maternal fetal medicine specialist was the most common response (n=12). Eleven percent (n=12) of obstetricians would refer the patient to her “primary care physician to re-discuss paroxetine.”

There was no statistically significant difference in referrals made when stratified by age (p=0.46), gender (p=0.11), or practice (p=0.33).

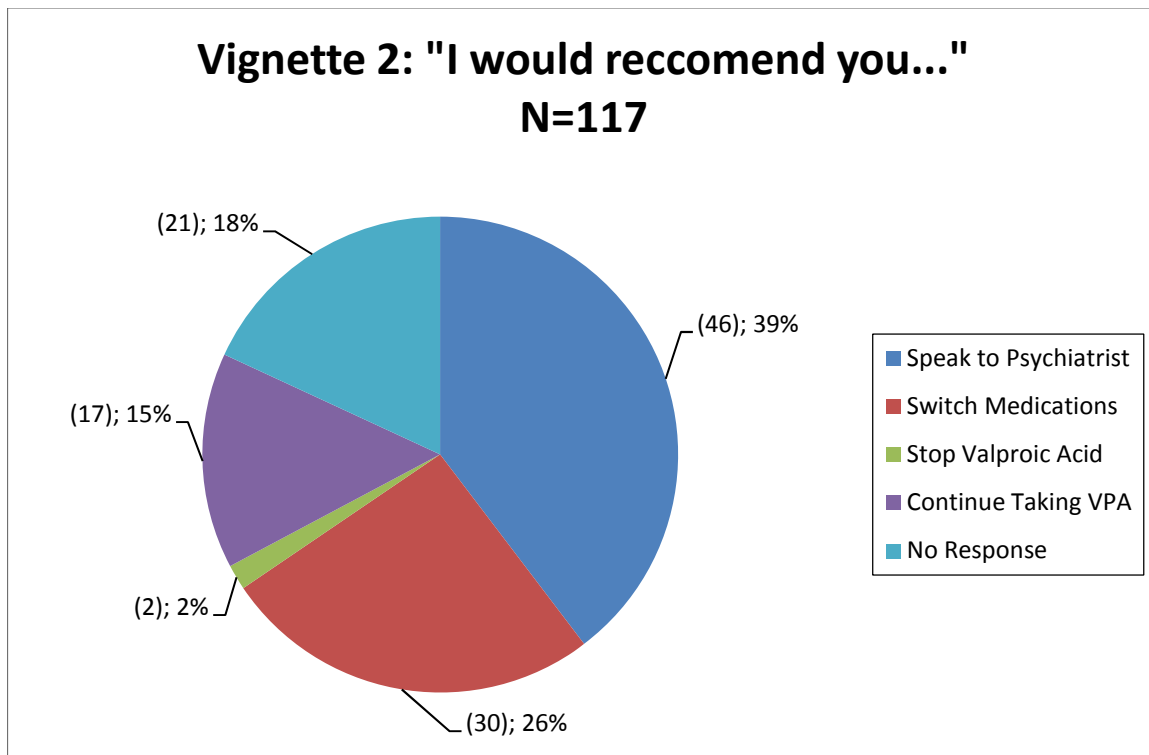


**Figure 34:** Obstetrician referrals in response to Vignette 1.



Figure 35 shows the distribution of obstetricians' recommendations in response to Vignette 2. Of those who responded (n=96), the majority (n=46; 47%) would recommend the patient "speak with (her) psychiatrist before making changes to (her) pharmacological regimen." Thirty-one percent (n=30) would recommend the patient "switch to a different mood stabilizer, because valproic acid is associated with an increased risk for birth defects," while 18% (n=17) would recommend the patient "continue taking valproic acid as your psychiatrist recommended." Only 2% of respondents (n=2) recommended that the patient "stop taking valproic acid." Twenty-one obstetricians did not respond to this question.

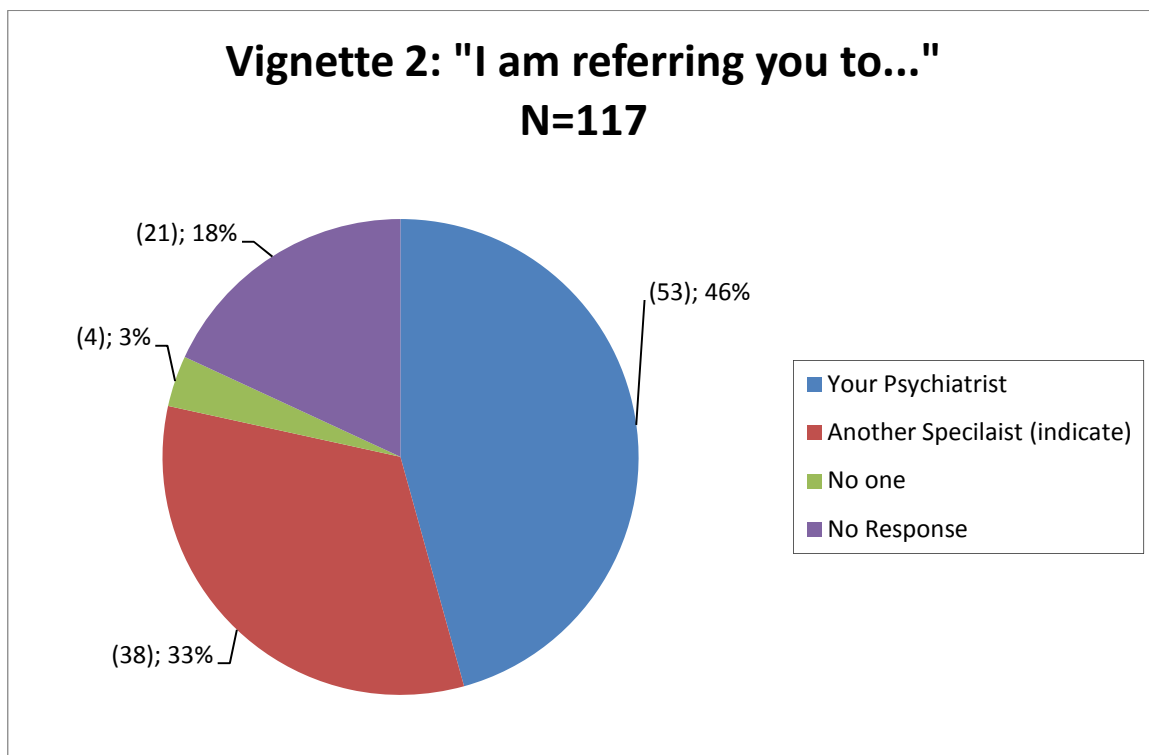
There was no significant difference in recommendations when stratified by age (p=0.817), gender (p=0.054), or practice (p=0.701).



**Figure 35:** Obstetrician recommendations in response to Vignette 2.

Figure 36 shows the distribution of obstetricians' choice of referrals in response to Vignette 2. Of those who responded (n=96), the majority of obstetricians (55%; n=53) would refer the patient to her "psychiatrist to re-discuss taking valproic acid." Forty percent (n=38) would refer that patient to "another specialist to co-manage the pregnancy." Of these "Other" specialists, a maternal fetal medicine specialist was the most common response (n=30, 79%). Only 4% of obstetricians (n=4) felt comfortable managing the case alone. Twenty-one obstetricians did not respond to this question.

There was no statistically significant difference in referrals made when stratified by age ( $p=0.586$ ), gender ( $p=0.386$ ), or practice ( $p=0.317$ ).



**Figure 36:** Obstetrician referrals in response to Vignette 2.

## **DISCUSSION**

In this study, Texas obstetricians were asked about their experience with women who disclose having mood disorders, their referral patterns and counseling methods for these women, and their knowledge base and opinions regarding the use of different psychotropic medications (e.g. SSRIs, AEDs) during pregnancy. Due to the increasing prevalence of mood disorders in the general population, and the widespread use of psychotropic medications to treat them, it was hypothesized that the average obstetrician frequently encounters women with depression or bipolar disorder taking psychotropics during pregnancy. Further, due to a lack of explicit management guidelines, and the variable and often discordant array of available drug safety information, it was thought that many obstetricians incorrectly counsel their patients regarding the teratogenicity of these medications. In turn, it was hypothesized that this practice could lead to adverse pregnancy outcomes. The ultimate purpose of this study was to capture the current knowledge base and practice recommendations of obstetricians treating women taking psychotropic medications for mood disorders during pregnancy.

### **Study Population**

Over half (57%) of respondents were male, most (60%) were between the ages of 41-60, and most (57%) had practiced between 11-30 years. The vast majority indicated they practiced general obstetrics (90%). While the overall study population is not a particularly heterogeneous group, it likely represents an accurate sample of those individuals who currently practice obstetrics in Texas. In general, most respondents were in their 50s, had

been practicing for at least 20 years, typically practiced in a private setting, and were most often male.

### **Exposure and Referral Patterns**

The majority (46%) of respondents indicated they see women who disclose having a mood disorder “often” or “very often” (17%). Notably, only 5% reported seeing these women “rarely,” and no one reported they “never” see these types of patients. It can be concluded from this response that it is most likely common for obstetricians to encounter women with mood disorders in their practice.

Most (43%) respondents indicated they “sometimes” refer these women to psychiatric services. However, almost one-third reported that they “rarely” refer women who disclose mood disorders to mental health providers, suggesting a missed opportunity to refer for psychiatric care during pregnancy, especially if the patient does not currently have a mental health care provider and the obstetrician is her primary physician. Female respondents were more likely than male respondents to report referring women to psychiatric providers ( $p=0.039$ ). While it could be suggested that female physicians might be more “in tune” to the emotional and physical challenges of pregnancy, the significance of this difference is most likely due to the small sample size of the study ( $n=117$ ).

While almost one-third of respondents reported that they “rarely” refer to psychiatric services, 86% either “agreed” or “strongly agreed” that the obstetrician “has a role in referring women for psychiatric services.” This suggests discordance between how obstetricians feel and how they actually practice. It is possible barriers to the referral process exist, such as availability of psychiatrists in the area, willingness of these

psychiatrists to see pregnant women, and lack of insurance coverage for mental health services. Indeed, the majority of comments made at the end of this survey were related to obstetricians' desire to refer their patients for psychiatric evaluations, but their reported inability to do so due to various challenges. One respondent wrote:

The issue is not if psychiatric consultation is needed, rather, the availability of timely and adequate consultation. The vast majority of psychiatrists in private practice refuse to see and/or treat pregnant patients. Few take Medicaid and getting appointments in county clinics is never timely... I would prefer to have all of these patients seen by a psychiatrist, but that is not possible.

While no known studies have ever documented that psychiatrists are unwilling or even refuse to see pregnant patients, this was a very frequent concern of respondents. It is possible psychiatrists are less familiar with pregnancy, and uncomfortable managing a clinical situation that could result in a teratogenic exposure. One obstetrician wrote:

I rarely have my OB patients see psych. I manage with MFM. There are several reasons for this: 1) often takes a while to get an appt with psych and time is important, 2) often find psych not comfortable with this discussion, 3) rarely do psych docs follow-up with me, send letters, phone calls, etc.

An additional barrier to psychiatric care listed was cost and insurance coverage. Many private insurance companies have limited coverage for psychiatric services, and psychiatry is not covered by Medicaid. One obstetrician commented, "Most of my patients do not have access to psychiatry either because of insurance or cost reasons; very few in network and limited access to Medicaid." In addition, many respondents commented that psychiatric providers are not even available in their communities. This is not surprising, considering

many of these surveys were distributed to rural cities in East and West Texas, and that psychiatry is the leading subspecialty area in America that lacks adequate healthcare service coverage (Smalley, et al., 2010).

Respondents in private practice were more likely to “strongly disagree” with the statement “the obstetrician has a role in referring women for psychiatric services” ( $p=0.002$ ). It is possible that those in private practice feel more “specialized” in their practice and are less focused on extraneous, non-obstetrical issues compared to someone in academic medicine who typically practices within an easily accessible community of various specialty providers. Again, however, the small sample size of this study, and the low number of respondents who selected “strongly disagree” ( $n=10$ ), should be considered as a possible explanation of this finding.

Most respondents reported seeing women who disclosed taking a psychotropic medication, such as an SSRI, AED, or atypical antipsychotic, “often” or “sometimes.” Notably, only 5% reported “rarely” seeing women who disclose taking these medications. This suggests that not only is it common for obstetricians to see women who disclose they have a mood disorder, but it is also common for these women to be taking medications to manage these conditions. Once women disclose taking these types of medications, a majority of respondents either “very often” or “often” discuss these medications with their patients. Most of the respondents (64%) reported feeling “comfortable” discussing the teratogenicity of these medications with their patients, while only 7% reported feeling “uncomfortable” or “very uncomfortable” with these discussions.

Based on the responses of this study population, it can generally be concluded that is common for the obstetrician to be exposed to women who disclose both having a mood

disorder and taking a psychotropic medication. In addition, about two-thirds of obstetricians reported referring these types of patients for outside psychiatric services. Finally, most obstetricians feel they have a role in this referral process.

### **Counseling Resources**

The majority of respondents reported they provide drug counseling or information of some type to their patients. One goal of this study was to determine what types of resources obstetricians use to obtain teratogen information for their patients. “Peer-reviewed internet sources,” such as ACOG’s website (n=81), and the text “Physician’s Desk Reference” (n=56) were the two most commonly selected resources. Obstetricians also reported using “Personal digital assistant software” and “Colleagues” frequently.

While electronic resources such as peer-reviewed websites and PDA software likely provide the most up-to-date teratogen information available, textbooks such as the *Physician’s Desk Reference (PDR)* and *Drugs in Pregnancy and Lactation*, however well-respected, are limited in their ability to provide the most current drug safety information. A new *PDR* is typically published yearly, while the most updated edition of *Drugs in Pregnancy and Lactation* is from 2008. The teratogenicity of numerous psychotropics is continuously being researched, and new data emerges daily for many medications as more observational studies and case reports are published. Further, many of these texts reference the unclear and often misinterpreted FDA drug classification system, which is itself in the process of being redesigned (Feibus, 2008). Therefore, obstetricians are not using the best resources to obtain correct teratogen information.

Notably, very few respondents reported utilizing “teratogen information services” (n=26) such as the teratogen hotline OTIS. Teratogen call centers are perhaps one of the most accurate and easily accessible resources available to all physicians, yet they have a history of being under-utilized (De Santis, et al., 2008). One respondent wrote at the end of his survey, “I wish there were a resource with updated counseling info.” This suggests that perhaps obstetricians are not aware of the variety of teratogen counseling resources available to them.

### **Factors that Influence Recommendations**

Integral to understanding current practice regarding the management of pregnant women taking psychotropic medications is identifying those factors that most influence obstetricians in their decision-making process. When respondents were asked to rank four factors, “Teratogenic risk to the fetus” was most frequently given the highest rank, and “Severity of maternal illness” was most commonly given Rank 2. While both the pregnant woman and the fetus are under the care of the obstetrician, these responses suggest that the health of the fetus and any teratogenic risk a medication might pose to that fetus is the most important factor to this population when making management recommendations. Indeed, the “Risk of relapse in mother if discontinued” was typically ranked low (Rank 3 or 4) by respondents. It could be interpreted that the obstetrician ultimately feels the most responsibility towards the fetus in this complicated situation. However, most respondents did rank “Severity of maternal illness” as the second most contributory factor in their decision-making process. A possible explanation is that obstetricians highly value the health and care of the mother with a mood disorder; however, they underestimate the risks



associated with discontinuing psychotropic medications mid-pregnancy, while concurrently overestimating the teratogenic risks to the fetus.

Almost all respondents ranked “Medical liability” as the least contributory factor to their management recommendations, a finding not unexpected given the stigma associated with valuing such an issue. However, it is likely that in our litigation-friendly society, this is a serious (albeit unspoken) concern of many obstetricians. Indeed, advertisements for law firms recruiting women who took drugs such as Depakote® and Paxil® during pregnancy and had a child with complications or birth defects have been aired on television stations nationwide.

Eleven respondents listed “Other” factors they consider when managing women taking psychotropic medications during pregnancy, and these were always given ranks of either 4 or 5. Two respondents cited the availability of a psychiatrist’s input as being important to their management plan. Others focused their attention on the maternal state, with such concerns as “inability to wean off medications,” “side effects,” and “intellectual capability of the mother.” The remaining respondents listed “cost,” “other risks to the baby,” and “trimester” as factors that influence their decision making. These responses suggest that maternal, fetal, and environmental factors all contribute to a very complicated decision-making process for the obstetrician encountering pregnant women taking psychotropics.

## **Teratogen Knowledge and Perceptions**

### *Selective serotonin reuptake inhibitors (SSRIs)*

The majority of respondents (37%) selected “Don’t Know” when asked what incidence of structural birth defects they quote to women taking SSRIs during pregnancy. The highest number of respondents who actually selected a numerical value (n=69) selected the “correct” risk of 2/1000 (38%). One-third of those selecting a value overestimated the risks associated with SSRIs, while 29% underestimated the risk. These results suggest that the majority of obstetricians do not know the incidence of structural birth defects associated with SSRIs. Further, almost as many obstetricians who chose an answer overestimated the risk (33%) as got it correct (38%).

There was no significant difference in quoted risk when responses were stratified by age ( $p=0.356$ ) or area of practice ( $p=0.293$ ). An equal number of respondents from private practice and an equal number of respondents from academia selected the “correct” answer. Almost an equal number of respondents below and above the age of 50 selected the “correct” answer. One might expect physicians over the age of 50 to be less accurate in their risk counseling if they typically use less updated sources of information (e.g. textbooks). It is also notable that an equal percentage of providers in private practice (24%) selected the correct answer as those in academia (24%). It was suspected that those in academic medicine would be more likely to report the correct risk figure, as they are more frequently exposed to continuing education opportunities and the results of ongoing research. These results suggest that an obstetrician’s area of practice does not affect his or her awareness of current teratogen information.

Despite the wide variability in the actual risk figures obstetricians reported quoting to their patients, almost all respondents felt the risk associated with SSRI use was low (79%) or moderate (19%). Thus, regardless of what figure obstetricians quoted, they still felt the overall risk to the fetus due to SSRI exposure was low. Further, only one obstetrician selected “Don’t know” in how they perceived the risk of SSRIs, compared to two-thirds of respondents in the first question. This suggests that even if respondents could not select an actual risk figure, they still felt the risk was “low.”

#### *Valproic acid (Depakote®)*

In contrast to the question regarding SSRI exposure, the majority of respondents (43%) did report quoting the “correct” 1-2% incidence of neural tube defects to pregnant patients taking valproic acid. However, one-third of respondents overestimated the risk to be 5-10%, and 4 respondents even selected an incidence of greater than 20%. Only 18% of respondents reported not knowing the incidence. These results suggest that obstetricians are more familiar with the risks associated with the use of valproic acid during pregnancy than those associated with SSRI use during pregnancy. This may be related to the length of time valproic acid has been on the market (circa 1967), as well as the pervasiveness of numerous studies on its safety. However, 35% overestimated the incidence of neural tube defects, suggesting that many obstetricians may be quoting incorrect risk figures to their patients.

The majority of respondents (40%) felt the risk for neural tube defects due to valproic acid exposure was “moderate,” and 31% felt the risk was “high.” Fifteen percent even felt the risk was “very high.” This data suggests that, in general, respondents felt valproic acid was a “riskier” drug than SSRIs. There was not a significant difference

( $p=0.067$ ) between quoted risk figures for valproic acid exposure and how obstetricians perceived those risk figures. However, in this study many respondents selected the same risk figure, but reported feeling very differently about it. For example, perception of the 1-2% incidence for neural tube defects encompassed the entire spectrum, from “low” to “very high.” Similar variations in perception were also present in the “5-10%” and “Don’t know” risk categories. Therefore, each individual provider may use the same risk figure to make very different treatment recommendations based on their personal perception of the drug’s risk. In addition, as obstetricians’ risk quantifications increased, their perception of risk also increased.

#### *Lamotrigine (Lamictal®)*

Similar to valproic acid, respondents were relatively well-informed about the teratogenicity of lamotrigine, another antiepileptic medication. The majority of respondents (68%) selected the “correct” answer- that the incidence of structural birth defects due to lamotrigine is “not increased above the background.” However, almost one-third of respondents felt the risk for birth defects was as high as 5-10%. Again, there was no significant difference when the responses were stratified by age ( $p=0.113$ ) or area of practice ( $p=0.718$ ). Notably, 18% of the total number of surveys analyzed in this study (21/117) did not have a response for this question. It is possible this lack of response was due to lack of familiarity with the drug lamotrigine, a less commonly prescribed antiepileptic drug than valproic acid.

Obstetricians were asked to compare how they felt about the risks associated with lamotrigine in comparison to the risks associated with valproic acid. Most respondents

(59%) felt there was less risk associated with lamotrigine, while only 4% felt there was more risk with this drug. Notably, only 2% of the total population did not respond to this question, a drastic increase in response rate compared to the previous question. One possible explanation for this finding is that even if obstetricians were unfamiliar with lamotrigine and its associated risks, they still thought or assumed it to have less risk to the developing fetus than valproic acid.

There was a significant ( $p < 0.001$ ) difference between quoted risk figures for lamotrigine exposure, and obstetrician's perceptions of these risks. Again, respondents who selected the same risk figure (e.g. "Not increased above the background), felt very differently about this risk when comparing it to valproic acid. The entire spectrum, from "less risk" to "more risk," was represented. This would provide another example of a psychotropic that is viewed very differently depending on the personal perceptions of the providing obstetrician.

### *Lithium*

The incidence for congenital heart defects, particularly Ebstein's anomaly, due to *in utero* lithium exposure is a commonly overestimated risk (Cohen, et al., 1994). In this study, however, the majority of respondents (49%) reported that they quote patients a "less than 10-fold increase" in the incidence of heart defects, which is the "correct" response. Only 13% overestimated the risk, and only 2 respondents reported they use the original risk figure of "greater than a 400-fold increase." However, a large proportion of respondents (34%) selected "Don't know," suggesting that many obstetricians are not aware of the exact risks associated with lithium use during pregnancy.

There was a significant difference between quoted risk figures for lithium exposure, and obstetricians' perceptions of these risks ( $p=0.002$ ). While the majority of obstetricians selected a "less than 10-fold increase," respondents felt very differently about this risk. Thirty-six percent felt the risk was "moderate," 25% felt the risk was "high," and 10% felt the risk was "very high." Again, it is possible this wide variability in perception among providers could lead to very different management recommendations for patients. It is also possible that while obstetricians are aware of more accurate lithium risk data, the negative stigma surrounding lithium use during pregnancy presented decades ago may have a lasting impression on their risk perceptions.

Notably, while 34% of respondents reported they did not know the exact numerical risk associated with lithium exposure, only 8% did not know how they perceived the risk associated with lithium exposure. This suggests that while respondents may have been unable to quantify the risks associated with this lithium, most still possessed a qualifiable risk perception of the drug.

There was a significant difference in how respondents perceived the risks associated with lithium exposure when stratified by area of practice ( $p=0.014$ ). Obstetricians in private practice were more likely to classify lithium's risk as "high" ( $n=20$  in private practice versus  $n=7$  in academia) or "very high" ( $n=10$  in private practice versus  $n=2$  in academia). It is possible obstetricians in private practice are less exposed to women taking lithium and therefore perceive it as more dangerous. However, it is much more likely this significance is an artifact of the small sample size of the study.

### *Second-generation antipsychotics*

Due to their recent emergence on the market, it was hypothesized that obstetricians' knowledge of second-generation antipsychotics would be less than that of the other psychotropics discussed. However, the majority (65%) of respondents selected the "correct" answer that this class is thus far not associated with any significantly increased risk for birth defects above the background. Twenty-eight percent of respondents did overestimate the incidence at 5-10%.

Most respondents (55%) perceived the risks associated with *in utero* exposure to second-generation antipsychotics as "low." Notably, almost one-third of respondents (29%) selected "Don't know" regarding how they perceive the risk. This is an almost three-fold increase in the number of respondents who chose "Don't know" compared to the first question, which is unusual. This is the only question pair in which respondents appear to be better able to provide a quantified risk figure for a medication than to provide a qualified risk perception.

Again, there was a significant difference between quoted risk figures and how obstetricians perceived these risks ( $p < 0.001$ ). While the majority of respondents thought the risk associated with second-generation antipsychotic use was "not increased above the background," they had variable perceptions of this risk (from "low" to "very high"). This again highlights how different individuals can look at the same risk figure and interpret it very differently.

### *Overall Knowledge and Perceptions*

In assessing this population's knowledge base of the teratogenicity of five different types of psychotropics, the majority of respondents who actually selected a numerical answer did select the "correct" figure. However, in all five sets anywhere from 5 to 37% of respondents selected "Don't know" when asked for a specific risk figure. When combined with those who selected incorrect answers, the majority of obstetricians did not select the correct answer. This suggests a significant knowledge gap in the field of obstetrics regarding the teratogenicity of most medications used to treat mood disorders.

If respondents were unable to select an exact numerical risk figure for a medication, they were typically still able to qualify that risk in terms of "high" versus "low." However, there were widely discrepant perceptions of the same numerical risk figures among responders for all but one set of questions. This finding suggests that personal perception and interpretation of teratogenic risks may play an important role in how obstetricians make management recommendations for this patient population. If so, explicit practice guidelines for managing women taking psychotropic medications during pregnancy may be critical for uniform risk assessment and equal treatment of individuals in this population.

### **Situational Vignettes**

In the last part of the survey, respondents were given two different situational vignettes and asked to indicate what, if any, recommendations they would make for the patient in the scenario, and who, if anyone, they would refer the patient to for further care. Respondents had the opportunity to write-in a provider they would refer to if it was not



already listed. The purpose of these vignettes was to attempt to capture obstetricians' current practice and referral patterns in two very different clinical situations.

### *Vignette One*

In the first clinical scenario, the majority of respondents (44%) would recommend the patient “switch to a different SSRI” because of the increased risk for birth defects associated with paroxetine. Notably, 23% of respondents would recommend the patient “stop taking paroxetine” for the remainder of the pregnancy. Only 15% recommended the patient “speak with (her) primary care physician” before changing her drug regimen. This suggests that obstetricians feel it is within their scope of practice to make pharmacological regimen changes for pregnant patients with moderate depression, even changes as drastic as complete cessation of SSRI use for the remainder of the pregnancy. In fact, one respondent wrote they feel comfortable with recommending cessation because “I find pregnant women are motivated to do well off medication.”

In addition to feeling it is within their practice to make pharmacological regimen changes for this patient, 37% of respondents indicated they would manage the case alone and did not feel a referral to another provider was necessary. About one-third of respondents thought the patient should see a psychiatrist to see if taking paroxetine was necessary, while 20% felt a specialty consultation, typically with a maternal fetal medicine specialist, was warranted. Therefore, over one-half of respondents did not feel comfortable managing this case alone. This is striking considering the majority of respondents (79%) reported earlier that they felt the risk for structural birth defects associated with SSRI exposure was “low.” However, only 24% of respondents reported the correct incidence of

structural birth defects associated with SSRI use. This suggests discordance between how obstetricians think and feel about a medication's teratogenicity, and how they actually practice.

It is possible the slightly elevated risk for congenital heart defects and the recent negative publicity surrounding paroxetine could contribute to those obstetricians who feel more comfortable consulting a specialty provider. Overall, the responses to this vignette demonstrate a wide variety of practice and management recommendations among obstetricians.

### *Vignette Two*

In contrast to the responses to the first vignette, 47% of obstetricians would recommend the patient in the second clinical situation speak with her psychiatrist first before changing her pharmacological regimen. One third of respondents would recommend the patient switch to a different mood stabilizer because of the risks associated with valproic acid. Notably, only 2% of respondents would recommend the patient stop taking valproic acid completely. This response is in stark contrast to the first vignette, in which 23% of obstetricians recommended drug cessation. These results suggest obstetricians are far less comfortable making recommendations for patients with bipolar disorder or for patients taking high doses of valproic acid, or both.

Indeed, most respondents were uncomfortable with managing this case alone. The majority selected that they would either refer the patient to a psychiatrist to discuss taking valproic acid (46%), or to another specialist to co-manage the pregnancy (33%). This suggests that while obstetricians reported they were comfortable providing drug counseling

to their pregnant patients, some indications or medications may reside outside their “comfort zone.” Many respondents wrote in their reasoning for referring the patient to an outside provider. The most common concern was for structural birth defects due to valproic acid exposure during the period of organogenesis, so many respondents recommend maternal fetal medicine consults and increased ultrasound surveillance. Notably, only one respondent recommended the patient also see a genetic counselor to better understand the teratogenic exposure and pregnancy options.

In general, obstetricians were far less comfortable with the second situational vignette. This is apparent when one considers that 40 out of 113 (35%) respondents felt comfortable managing the first situational vignette alone, compared to only 4 of 90 (4%) respondents for the second clinical scenario. There are multiple components of the second vignette that could have contributed to respondents’ discomfort. First, antiepileptic medications like valproic acid were typically perceived as “riskier” than SSRIs by respondents. In addition, the patient in the second vignette was taking a dosage of valproic acid that is sufficiently high enough, based on established research, to possibly cause birth defects. Differences in the social aspects of the two vignettes may have also affected responses. The first patient was an older, college-educated multiparous woman who only reported minor symptoms of depression. In contrast, the second patient was a young woman with an unplanned pregnancy who did not fill out her intake forms and reported manic episodes. Finally, the general perception of bipolar disorder being a more severe mood disorder than depression also likely played a significant role in obstetricians’ discomfort with the second vignette.

## **Strengths and Limitations**

This study provided direct insight into the accuracy of the general obstetrician in providing psychotropic risk figures to pregnant women with mood disorders. Equally as important, this survey elicited how providers feel about the risks associated with certain medications, which undoubtedly factors into their practice recommendations. In addition, the current practice of obstetricians managing this subset of women in the state of Texas was captured via responses to the situational vignettes. This information could help better define how obstetricians are actually managing the ever-growing population of pregnant women with mood disorders. Ultimately, this study and others like it could increase awareness of the necessity for accurate drug counseling in this patient population, as well as the need for official practice guidelines.

This study was limited by a small sample size ( $n=117$ ), and overall low response rate (13.6%). In addition, the study population was mostly comprised of middle-age men in private practice. Further, the results of this study reflect the thoughts and opinions of obstetricians in the state of Texas only. It is possible that cultural, regional, and religious viewpoints may have impacted respondents' answers. Therefore, the results of this study may not be entirely representative of all obstetricians in the United States. Finally, this study was limited by selective answering on the part of the respondent.

## **Overall Conclusions and Future Directions**

Four main conclusions can be drawn from the results of this study. First, it is common for the general obstetrician to encounter women who disclose both having a mood disorder and taking a psychotropic medication during pregnancy. Second, many

obstetricians are either not aware of or under-utilize up-to-date drug counseling resources, as well as the services of educated providers such as genetic counselors and teratogen hotlines. Third, many obstetricians are unaware of or over-estimate the teratogenic risks of many medications used to treat mood disorders. And finally, many obstetricians want to refer pregnant patients with mood disorders to psychiatrists for co-management, but are reportedly restricted in doing so due to accessibility or insurance issues.

The main goal of this study was to capture the current practice of obstetrician-provided drug counseling and management for pregnant women with mood disorders. It appears that many practicing obstetricians have conflicting views on how to manage women with mood disorders and are unaware of the teratogenic potential of various medications used to treat mood disorders. Thus, a future direction would be to distribute this survey on a larger scale (e.g. American College of Obstetricians and Gynecologists). This would provide a greater quantity and diversity of data to better define current practice throughout the country. General practice guidelines and educational materials could then be developed. An ongoing dialogue regarding the best management of pregnant women with mood disorders is vital to the goal of ultimately providing the best healthcare possible for both mother and baby.

## APPENDIX ONE

### **Survey Regarding Physician Risk Perceptions of the Pharmacological Management of Pregnant Women with Mood Disorders**

The purpose of this survey is to assess obstetricians' medical background, experience, and opinions regarding the pharmacological management of women with mood disorders during pregnancy. For purposes of this study, we define a mood disorder as either major depressive disorder or bipolar disorder. In addition to multiple choice questions, this survey has two situational vignettes through which we hope to better understand current practice regarding this topic. Space is available for additional comments should you find this necessary.

Completion of this anonymous survey is voluntary and for research purposes only. It should take less than 15 minutes to complete this survey. All responses are completely confidential, and you will not be personally identified in any reports or publications of this study. Data will be summarized and presented as part of a thesis project at The University of Texas Graduate School of Biomedical Sciences at Houston. By completing and submitting the questionnaire, you are implying consent to have your answers used and shared among collaborators for this study. There is no financial compensation for taking this survey.

Although the results of this study will be useful for doctors, other health professionals and future pregnant women, there may be no direct benefit to you for participating in this study. You can refuse to answer or skip any questions or stop taking the survey at any time. If you decide to participate in the study, it is very important that you answer as honestly as you can to the questions that are asked.

This survey has been approved by the UTHSC-H Institutional Review Board (HSC-MS-10-0374). If you have any questions or concerns, please contact Laura Hendon, MA or Kate Wilson, MS, CGC at 713-560-6463.

Thank you very much for your input regarding this important issue.

Sincerely,

Dr. Manju Monga, MFM  
UT Physicians  
Thesis Committee Member

Kate L. Wilson, MS CGC  
UT Health Science Center  
Thesis Committee Chair

Laura Hendon, MA  
GSBS  
Principal Investigator



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### Part I: Demographics

1. Do you currently practice obstetrics as a(n):
  - ☐ Generalist Ob/gyn
  - ☐ Subspecialty Ob/gyn (Specify subspecialty): \_\_\_\_\_
2. Are you also boarded in Psychiatry?
  - ☐ Yes
  - ☐ No
3. How long have you practiced obstetrics (beyond your residency or fellowship)? \_\_\_\_\_
4. What is your current age? \_\_\_\_\_
5. What is your gender?
  - ☐ Male
  - ☐ Female
6. What is your primary practice setting?
  - ☐ Academic/University Medical Center
  - ☐ Private practice
  - ☐ Public health
  - ☐ VA/military
  - ☐ Other (Specify): \_\_\_\_\_

### Part II: Experience/Referral Patterns

1. How often do you see women who disclose they have a mood disorder (depression or bipolar disorder)?
  - ☐ Never
  - ☐ Rarely (1 a month)
  - ☐ Sometimes (2-5 a month)
  - ☐ Often (6-10 a month)
  - ☐ Very often (more than 10 a month)
2. How often do you refer these women to psychiatric services?
  - ☐ Never
  - ☐ Rarely
  - ☐ Sometimes
  - ☐ Often



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3. Select the box that reflects your attitude to the following statement:

The obstetrician/gynecologist has a role in referring women for psychiatric services.

- ☐ Strongly disagree
- ☐ Disagree
- ☐ Neither agree nor disagree
- ☐ Agree
- ☐ Strongly Agree

4. How often do you see women who disclose taking psychotropic medications (e.g. SSRIs, anti-convulsants, anti-psychotics) during pregnancy?

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Very often

5. How often do you discuss the medications with these patients?

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Very often

6. From where do you obtain information to discuss these medications? Check all that apply.

- ☐ Teratogen information services (e.g. OTIS)
- ☐ Peer-reviewed internet source (e.g. ACOG website, Reprotox)
- ☐ Google and/or Wikipedia
- ☐ Physician's Desk Reference
- ☐ Colleague
- ☐ PDA software (e.g. Epocrates)
- ☐ Other: (Specify): \_\_\_\_\_

7. Rank the following factors, from most contributory (1) to least (4 or 5), regarding how they influence your recommendations for pharmacological management during pregnancy.

- \_\_\_ Teratogenic risk to fetus
- \_\_\_ Risk of relapse in mother if discontinued
- \_\_\_ Severity of maternal illness
- \_\_\_ Medical liability
- \_\_\_ Other (Specify): \_\_\_\_\_



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### Part III: Teratogen Knowledge/Perceptions

1. How comfortable are you discussing the teratogenicity of medications used to manage mood disorders?

- ☐ Very uncomfortable
- ☐ Uncomfortable
- ☐ Uncertain
- ☐ Comfortable
- ☐ Very comfortable

2. When you counsel women taking selective serotonin reuptake inhibitors (SSRIs) during pregnancy, what incidence of structural birth defects do you quote?

- ☐ 2/10,000
- ☐ 2/1,000
- ☐ 2/100
- ☐ 2/10
- ☐ Don't know

3. What is your perception of the risk of SSRIs in pregnancy?

- ☐ Low
- ☐ Moderate
- ☐ High
- ☐ Very high
- ☐ Don't know

4. When you counsel women taking valproic acid (Depakote) during pregnancy, what incidence of neural tube defects do you quote?

- ☐  $\leq 1\%$
- ☐ 1-2%
- ☐ 5-10%
- ☐ 20%
- ☐  $> 20\%$
- ☐ Don't know

5. What is your perception of the risk of valproic acid in pregnancy?

- ☐ Low
- ☐ Moderate
- ☐ High
- ☐ Very high
- ☐ Don't know



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6. When you counsel women taking lamotrigine (Lamictal) during pregnancy, what incidence of birth defects do you quote?

- ☐ Not increased above the background
- ☐ 5-10%
- ☐ 15%
- ☐ 20%
- ☐ >20%

7. What is your perception of the risk of lamotrigine in pregnancy?

- ☐ Less risk than valproic acid
- ☐ Equal risk as valproic acid
- ☐ More risk than valproic acid
- ☐ Don't know

8. When you counsel patients taking lithium during pregnancy, what incidence of heart defects (including Ebstein's anomaly) do you quote?

- ☐ No increase
- ☐ ≤10-fold increase
- ☐ 50-fold increase
- ☐ 200-fold increase
- ☐ ≥400-fold increase
- ☐ Don't know

9. What is your perception of the risk of lithium in pregnancy?

- ☐ Low
- ☐ Moderate
- ☐ High
- ☐ Very high
- ☐ Don't know

10. When you counsel women taking second-generation antipsychotics (e.g. aripiprazole, clozapine, risperidone) during pregnancy, what incidence of birth defects do you quote?

- ☐ Not increased above the background
- ☐ 5-10%
- ☐ 15%
- ☐ 20%
- ☐ >20%



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11. What is your perception of the risk of second-generation antipsychotics when taken alone in pregnancy?

- ☐ Low
- ☐ Moderate
- ☐ High
- ☐ Very high
- ☐ Don't know



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#### Part IV: Situational vignettes

1. A G2P1 28 year-old Caucasian female is being seen in your clinic for the first time for standard prenatal care. She is currently 8 weeks pregnant. She discloses on her intake form that she has depression and takes 30 mg of paroxetine (Paxil) a day. During the appointment, the patient reports that she has had depression "off and on since college," but started taking Paxil two years ago at the advice of her general physician. She is not managed by a psychiatrist or a psychologist. Since taking Paxil, your patient reports that her moods have improved and she feels "happier" about her life. She is currently worried that taking Paxil during her pregnancy might "hurt the baby," but also voices fear about "losing control" of her moods if she stops taking the medication.

Chose which statement *best describes* what you would recommend to the patient.

##### "I would recommend that you..."

- ☐ speak with your primary care physician before making changes to your pharmacological regimen.
- ☐ switch to a different SSRI because paroxetine is associated with an increased risk for birth defects.
- ☐ stop taking paroxetine (gradually, in decreased doses) for the remainder of your pregnancy.
- ☐ continue taking paroxetine as your primary care physician prescribed.

Chose which referral you would *most likely* make.

##### "I am referring you to..."

- ☐ your primary care physician to re-discuss paroxetine.
- ☐ a psychiatrist to discuss whether or not to continue taking paroxetine.
- ☐ another specialist to co-manage your pregnancy. (Please indicate which type of specialist) \_\_\_\_\_.
- ☐ no one. I feel comfortable managing your case.

*Additional Comments:* \_\_\_\_\_



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2. A G1P0 21 year-old Caucasian female is being seen in your clinic for the first time for standard prenatal care. She is currently 12 weeks by LMP. She does not complete her new patient questionnaire. During the session she is visibly agitated and seems uncomfortable. She tells you the pregnancy was "an accident." She discloses that she has bipolar disorder and has been taking 1000 mg of valproic acid (Depakote) daily since she was 16. She reports that she called her psychiatrist's office when she discovered she was pregnant four weeks ago, and he recommended she continue taking her medication until she was able to speak to a "special doctor" about the pregnancy and taking the medication.

Chose which statement *best describes* what you would recommend to the patient.

**"I would recommend that you..."**

- ☐ speak with your psychiatrist before making changes to your pharmacological regimen.
- ☐ switch to a different mood stabilizer, because valproic acid is associated with an increased risk for birth defects.
- ☐ stop taking valproic acid (gradually, in decreased doses) for the remainder of your pregnancy.
- ☐ continue taking valproic acid as your psychiatrist prescribed.

Chose which referral you would *most likely* make.

**"I am referring you to..."**

- ☐ your psychiatrist to re-discuss taking valproic acid.
- ☐ another specialist to co-manage your pregnancy. (Please indicate which type of specialist) \_\_\_\_\_
- ☐ no one. I feel comfortable managing your case.

*Additional Comments:* \_\_\_\_\_



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## **APPENDIX TWO**

### **Responses to Survey Part II: Question 7**

“Other” factors that influence obstetrician recommendations for pharmacological management during pregnancy:

- need for OB psy contact in pregnancy- best Rx
- nothing really, I just care about medical liability when making these decisions
- inability to successfully wean off or psychiatrists recommendation
- accepting conditions during pregnancy
- cost
- side effects
- other risks to the baby
- lack of available counseling
- intellectual capability of mother
- trimester

## **APPENDIX THREE**

Responses to Survey Part IV: Questions 1 and 2

“Other” specialists to co-manage the pregnancy:

### *Vignette 1*

- Psychiatrist, MFM
- Psychiatrist (n=4)
- MFM (n=13)
- MFM or Geneticist
- Perinatology
- Psychologist (n=3)

### *Vignette 2*

- Psychiatrist (n=3)
- MFM (n=30)
- Perinatologist
- MFM or genetic counseling

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## **VITA**

Laura Godfrey Hendon was born in Macon, Georgia on December 27, 1983. She grew up outside of Washington, D.C. in Manassas, Virginia, and later moved to Jackson, Mississippi at 13. She is the daughter of Steven Godfrey, Sr. and Kathy Godfrey. She has an older brother Steven. After completing high school at Northwest Rankin High School in Brandon, Mississippi, she attended the University of Mississippi in Oxford, Mississippi. She graduated magna cum laude in 2006 with a Bachelor of Science in Biology, and was also a member of the Sally McDonnell Barksdale Honors College. Laura continued her education at Washington University in Saint Louis, where she earned a Master of Arts degree in Biomedical Sciences with an emphasis in Molecular Genetics and Genomics in 2008. She then moved back to Jackson, Mississippi, where she worked as a Genetic Counseling Assistant for two years at the University of Mississippi Medical Center. Laura married her husband, Andrew, in 2009. In August 2009 she entered the University of Texas Health Science Center at Houston, where she earned the degree of Master of Science in Genetic Counseling in May 2011.