Table 1. Literature Definitions of PNAS With Antidepressant Exposure

Article	Sample and Source	Definition/Measurement of PNAS	Study Type and Results
Costei et al, 2002[11]	n = 55 Women with 3rd trimester paroxetine usage n = 27 Women with 1st or 2nd trimester paroxetine usage n = 27 Control Maternal phone interview performed after delivery of women who called MotherRisk about 3rd trimester paroxetine exposure	Neonatal complications that required prolonged hospitalization	Prospective Neonatal complications: 22% 3rd trimester vs 6% other
Laine et al, 2003[12]	n = 20 Women on 20–40 mg/d of citalopram or fluoxetine for depression or panic disorder n = 20 Control not on any medications Patients referred to study by their PCP	Serotonin Syndrome Scale (blood pressure, HR, temp, myoclonus, restlessness, tremor, shivering, hyperreflexia, incoordination, rigidity) during first 4 days of life Tremor > restlessness > rigidity	Prospective n = 17 SSRI vs n = 9 control OR = 6.9 (95% CI, 1.6–2.92)
Källén 2004[13]	n = 997 Infants of mothers on any antidepressant during pregnancy n = 582,796 Infants not exposed to antidepressants during pregnancy Medical records at delivery and during pediatric exam	Respiratory distress diagnostic codes in Swedish Medical Birth Registry	Prospective Swedish Medical Birth Registry AOR = 2.21 (95% CI, 1.71–2.86)
Oberlander et al, 2004[14]	n = 28 Women on SSRI alone n = 18 Women on SSRI and clonazepam n = 23 Healthy controls Assessment by attending physician	Transient neonatal symptoms that suggest "altered adaptation in the newborn period" (jitteriness, respiratory difficulties, hypoglycemia, lethargy, weak or absent cry, desaturation on feeding)	Prospective PNAS in 30% exposed vs 9% control LR = 5.64 (95% CI, 1.1–25.3)
Levinson-Castiel et al, 2006[15]	n = 60 Women on SSRI alone n = 60 Women not on any medications Finnegan scoring by nurses/physicians at 2 hours, then every 8 hours after meals for 48 hours	NAS; Finnegan > 3	Prospective NAS in 30% exposed vs 0% in control Tachypnea in 12 SSRI vs 0 control Tremor in 37 SSRI vs 11 control
Oberlander et al, 2006[16]	n = 1,451 Women on SSRI and depressed n = 14,234 Women not on SSRI and not depressed 5 Separate administrative sources of medical records	*ICD-9* codes for respiratory distress, jaundice, convulsions, or feeding difficulties	Prospective Respiratory distress in 13.9% exposed vs 7.8% in unexposed
Davis et al, 2007[17]	n = 874 Women using SSRI during pregnancy n = 75,219 Women not using SSRIs Automated health system databases	*ICD-9* codes: convulsions, feeding problems, temperature regulation	Retrospective RR of respiratory distress = 1.97 (95% CI, 1.65–2.35)
Ferreira et al, 2007[18]	n = 76 Women taking SSRI or venlafaxine during pregnancy n = 90 Women not using SSRI/venlafaxine Chart review	Composite of signs and symptoms involving CNS, respiratory, and digestive systems, as well as hypoglycemia and the need for phototherapy—must have at least 1 CNS > respiratory	Retrospective chart review OR = 3.1 (95% CI, 1.3–7.1) for late exposure to SSRIs/venlafaxine Tachypnea in 40.8% exposed vs 15.6% unexposed Shaking in 19.7% exposed vs 6.7% unexposed
Boucher et al, 2008[19]	n = 73 Infants exposed to antidepressant during last 3 weeks of pregnancy n = 73 Infants not exposed to antidepressants during the last 3 weeks of pregnancy Hospital chart review	Categories of symptoms: alertness, muscular tone, neurologic function, GI/feeding, respiratory function, serotonergic/adrenergic activity Tachypnea > tremors > decreased reactivity > feeding difficulties	Case-control (retrospective AE in 78% exposed vs 38% unexposed OR = 7.0 (95% CI, 3.2–15.3) Tachypnea in 43% exposed vs 26% unexposed OR = 2.5 (95% CI, 1.1–5.3) Tremors in 30% exposed vs 3% unexposed
Maschi et al, 2008[20]	n = 200 Infants exposed to antidepressants during pregnancy n = 1,200 Infants not exposed to antidepressants during pregnancy Maternal interviews prior to delivery and 1 month postpartum	Conglomeration of conditions, including respiratory distress, hypoglycemia, jitteriness, lethargy, hypotonia, weak or absent cry, feeding difficulties, neonatal convulsions, and hyperbilirubinemia	Prospective Nonsignificant differences in PNAS symptoms as defined OR = 2.31 (95% CI, 1.14–4.63) for prematurity rate of antidepressant-exposed infants
Galbally et al, 2009[21]	n = 23 Women taking an antidepressant during pregnancy n = 27 Women not taking an antidepressant during pregnancy Maternal questionnaires within 1 week of delivery	Neonatal Abstinence Scoring System (Finnegan): 8 items for CNS, 4 items for GI, 8 items for other; score > 0	Prospective Respiratory distress in 21.7% exposed vs 11.1% control RR = 1.957 (95% CI, 0.52–7.32) Tremor in 56.5% exposed vs 0% unexposed RR = 31.5 (95% CI, 1.98–502.48) Sleeping soon after feeding > tremors > feeding difficulties
Galbally et al, 2017[22]	n = 52 AD n = 230 Control NASS administered by midwives twice a day for 3 days	Neonatal Abstinence Scoring System (Finnegan): 8 items for CNS, 4 items for GI, 8 items for other—score > 0 Sleeping soon after feeding > tremors > feeding difficulties	Prospective 30/31 infants exposed at birth experienced withdrawal symptoms within 5 days of birth (97%) vs 2/11 not exposed at birth (18%)
Rampono et al, 2009[23]	n = 38 Women on SSRI or SNRI n = 18 Women not taking SSRI or SNRI during pregnancy Daily assessment by midwives using NAS scale	NAS; Finnegan > 12 or 3 scores > 8	Prospective NAS in 5% exposed with median Finnegan = 2 on day 1
Zeskind and Stephens, 2004[24]	n = 17 Infants exposed to SSRIs n = 17 Infants not exposed to SSRIs	Behavioral state, startles, tremulousness, motor activity, HRV for 1 hour in between feedings between 14 and 39 hours of age	Prospective Significant differences in tremulousness and behavioral states
Suri et al, 2007[25]	n = 49 Women with MDD taking antidepressant n = 22 Women with MDD not taking antidepressant for > 10 days during the pregnancy or who had discontinued in first trimester n = 19 Healthy controls	Rates of admission to the special care nursery	Prospective Significant differences between groups in rates of SCN admission (21% vs 9% vs 0%)
Suri et al, 2011[26]	n = 33 Women with MDD taking antidepressants n = 16 Women with MDD not taking antidepressants for > 10 days during the pregnancy or who had discontinued in first trimester n = 15 Healthy controls	Apgar scores, special care nursery admissions, BNBAS	Prospective No significant differences between groups on any of the BNBAS clusters
Chambers et al, 1996[27]	n = 228 Women using fluoxetine during their pregnancy n = 254 Women not using fluoxetine during pregnancy Maternal interview perinatally and postpartum + medical records	PNAS defined as jitteriness, tachypnea, hypoglycemia, hypothermia, poor tone, respiratory distress, weak or absent cry, or desaturation on feeding	Prospective 3rd trimester exposure to fluoxetine associated with increased SCN admission RR = 2.6 (95% CI, 1.1–6.9) and PNAS RR = 8.7 (95% CI, 2.9–26.6)
Lund et al, 2009[28]	n = 329 Women treated with SSRI during pregnancy n = 4,902 Women with history of psychiatric illness but no antidepressant treatment n = 51,770 Women with no psychiatric illness Maternal questionnaire during second trimester + midwife assessment at birth	5-min Apgar, NICU admission	Prospective SSRI-exposed had increased risk of NICU admission OR = 2.39 (95% CI, 1.69–3.39) vs control and OR = 2.04 (95% CI, 1.42–2.94) vs +psych/no SSRI SSRI-exposed had increased risk of low 5 min Apgar OR = 4.44 (95% CI, 2.58–7.63) vs control and OR = 6.58 (95% CI, 3.39–12.74) vs +psych/no SSRI
Yang et al, 2017[29]	n = 41 Women exposed to serotonin reuptake inhibitor n = 94 Women diagnosed with depression or bipolar disorder not taking SRI n = 79 Women not taking SRI or diagnosed with mood disorder Finnegan administered by HCP between 2 and 4 weeks of life	Finnegan > 1	Prospective No significant differences—prevalence across all groups ~33% Restless sleep > tremors > nasal stuffiness/sneezing > mottling

Abbreviations: AD = antidepressant, AE = adverse event, AOR = adjusted odds ratio, BNBAS = Brazelton Neonatal Behavioral Assessment Scale, CNS = central nervous system, GI = gastrointestinal, HCP = health care provider, HR = heart rate, HRV = heart rate variability, LR = likelihood ratio, NAS = neonatal abstinence syndrome, NASS = Neonatal Abstinence Scoring System, NICU = neonatal intensive care unit, OR = odds ratio, PCP = primary care provider, PNAS = poor neonatal adaptation syndrome, RR = risk ratio, SCN = special care nursery, SNRI = serotonin-norepinephrine reuptake inhibitor, SRI = serotonin reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.