Study Design in the Study of Adverse Birth Outcomes: Clinic-Based Versus Representative Samples

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To understand the predictors and antecedents of birth outcomes and related biological processes, it would be advantageous to study these in representative samples of pregnancies with rich measurement of clinical procedures such as ultrasound examination, behavioral (e.g., dietary, physical activity), psychosocial factors (e.g., anxiety, perceived stress) and biological specimens data. However, this is never possible. Researchers must make difficult design choices, sacrificing strength in some domains for strength in others. The proposed paper assesses the relative strengths and weaknesses of a clinic-based versus representative sample of births for furthering our understanding of adverse birth outcomes. It uses the Pregnancy, Infection and Nutrition (PIN) Study as a starting point. PIN is a prospective cohort study of risk factors for adverse birth outcomes based in North Carolina. It recruited 2006 women before 20 weeks' gestation through UNC Hospital prenatal clinics between January 2000 and August 2005. Women younger than 16 years, who didn't speak English, and who had multiple gestations or a chronic disease condition were excluded from the study. We compare the PIN data to 90,000 birth records obtained from the NC State Center for Vital Statistics for five counties between 2000 and 2005, the same area and years that the clinic sample delivered.

We begin our assessment with a consideration of quality of measurement. We matched 83.7% (n=1680) of the PIN participants to the birth records, based on mother's name, street address, date of birth, and gender of the child. Table 1 shows level of agreement for variables collected by both. Among the sociodemographic data collected in PIN and reported on the birth certificate, age, maternal race, maternal education, all had excellent (ICC or kappa > 0.90) agreement and marital status and parity had very good agreement. With regard to health behaviors, reporting of pounds of gestational weight gained and smoking had very good or excellent agreement, whereas alcohol consumption had poor agreement. With respect to pregnancy outcomes, gestational age, birth weight, and preterm birth had excellent agreement, and pregnancy induced hypertension had good agreement, but reporting of anemia and gestational diabetes had poor agreement. Because of the way the data were collected, PIN is arguably a better source than the birth certificates. As a further point, the birth certificates are limited to just a few measures and outcomes.

The PIN study is superior with respect to measurement, but there are questions about the degree to which descriptive results based on these data can be generalized. Savitz et al. (2005) have already published an assessment of a previous PIN cohort delivering between 1996 and 2000. Marked differences were found in social and demographic characteristics between the PIN sample and birth records. PIN women were more likely to be black, younger, have lower education, be unmarried, have a previous adverse birth outcome, enter prenatal care later, and smoke; however, preterm birth was lower among PIN women compared to area women. Even though PIN and area women had distinct social and demographic characteristics, the association between risk factors of age, education, marital status, prior adverse birth outcome, prenatal care entry, and smoking with preterm birth had the same magnitude of effect and direction of association among PIN and area women. Savitz et al. qualitatively assessed the differences in individual characteristics and compared the estimates for predictors of preterm birth between the PIN and area women. We will directly estimate the bias between the two samples and provide a correction if bias exists.

There is a clear trade-off with respect to quality of measurement and the degree to which results can be generalized to a larger population of interest. What are the implications for the analysis of potential determinants of birth outcomes? To answer this question, we specify a two stage model in which we first estimate the likelihood of being in the PIN study, and then conditional on this, we estimate the predictors of prepregnancy body mass index (continuous), glucose tolerance (continuous), bacterial vaginosis (yes/no), gestational diabetes mellitus (yes/no), 2nd semester anemia (yes/no), gestational hypertension (yes/no) and pre-eclampsia (yes/no). Each of these was collected as part of the PIN study and either are not obtained on the birth record or not reported reliably. Each is itself an important predictor of adverse birth outcomes. We will also estimate a two-stage model of birthweight controlling for gestational age and adjusting for covariates of maternal age, race, Hispanic ethnicity, education, marital status, birth order, month entered prenatal care, weight gain, smoking status and pregnancy-induced hypertension.

To identify the two-stage model, we will create three distance and differential distance measures using geocoded birth records and use them to predict who is in the PIN sample in the first stage equation. We hypothesize that two strong reasons that women sought prenatal care and delivered at UNC hospitals were (1) UNC was the closest hospital to their home and/or (2) UNC is a tertiary care hospital. Women with a known risk factor for adverse birth outcomes might be referred to UNC Hospitals from smaller hospital in the five county area and beyond. To pursue these ideas, we use three distance measures: (1) distance to UNC Hospital, (2) the differential distance between the UNC and another tertiary care hospital in the are, and 3) the differential distance between UNC and the closest hospital. The estimation and evaluation of the two-stage model will speak directly to potential for bias if inferences are based on the PIN sample and provide a correction if such a bias exists.

References:

Savitz DA, Dole N, Kaczor D, Herring AH, Siega-Riz AM, Kaufman J, Thorp JM Jr. Probability samples of area births versus clinic populations for reproductive epidemiology studies. Paediatr Perinat Epidemiol. 2005 Jul;19(4):315-22.

TABLE 1. COMPARISONS OF INFORMATION IN PIN VS BIRTH RECORD

	For categorical variables: Prevalence [N(%)] For continuous variables: Mean [Mean(StdDev)]		N	CORRELATIONS
	BIRTH RECORDS	**PIN**		
MATERNAL DEMOGRAPHICS AND HEALTH BEHAVIORS				
Maternal Age, *years*	29.74 (5.67)	29.01 (5.66)	1685	Spearman: 0.9951 ICC: 0.99208
Maternal Education, *years*	14.97 (3.07)	15.52 (2.97)	1677	Spearman: 0.9386 ICC: 0.92942
Maternal Race	White NH: 1186 (70.47) Black NH: 366 (21.75) Hispanic: 131 (7.78)	White NH: 1179 (76.56) Black NH: 356 (23.12) Hispanic: 5 (0.32)	1683	% Agreement: 96.61 Kappa: 0.9253
Maternal Marital Status	Married: 1291 (76.62) Not Married: 394 (23.38)	Married: 1226 (72.93) Not Married: 455 (27.07)	1681	% Agreement: 95.60% Kappa: 0.8833
Parity, *number of previous live births*	1.42 (1.53)	0.80 (0.96)	1635	Spearman: 0.7785 ICC: 0.69199
Maternal Weight Gain, *pounds*	32.86 (12.67)	33.71 (13.10)	1557	Spearman: 0.8187 ICC: 0.70245
Maternal smoking	Non-smoker: 1499(89.12) Smoker: 183 (10.88)	Non-smoker: 1299(89.28) Smoker: 156 (10.72)	1453	% Agreement: 96.15% Kappa: 0.7869
Maternal smoking, *# of cigarettes smoked*	0.98 (3.59)	0.73 (2.80)	1453	Spearman: 0.8055 ICC: 0.94368
Maternal alcohol consumption	Non-drinker: 1661(98.58) Drinker: 24 (1.42)	Non-drinker: 762 (52.26) Drinker: 696 (47.74)	1458	% Agreement: 53.77% Kappa: 0.0330
Maternal alcohol consumption	Drink<5/wk: 1684 (99.94) Drink≥5/wk: 1 (0.06)	Drink<5/wk: 1450 (99.52) Drink≥5/wk: 7 (0.48)	1,457	% Agreement: 99.59% Kappa: 0.2491
MAJOR PREGNANCY EVENTS				
Gestational age, *weeks*	38.35 (2.39)	38.38 (2.40)	1685	Spearman: 0.9015 ICC: 0.93994
Birth Weight (continuous)	3276.47 (626.98)	3284.80 (626.64)	1679	Spearman: 0.9851 ICC: 0.98468
Birth Weight (categorical - <1500g, 1500-2499g, ≥2500g)	<1500: 30 (1.78) 1500-2499: 125 (7.42) ≥2500: 1530 (90.80)	<1500: 32 (1.90) 1500-2499: 115 (6.82) ≥2500: 1538 (91.28)	1685	% Agreement: 98.99% Kappa: 0.9392
Birth Weight among term births (continuous)	3417.39 (465.21)	3424.28 (466.61)	1462	Spearman: 0.9804 ICC: 0.97819
Birth Weight among term births (categorical - <1500g, 1500-2499g, ≥2500g)	<1500: 0 (0.0) 1500-2499: 33 (2.25) ≥2500: 1433 (97.75)	<1500: 1 (0.07) 1500-2499: 29 (1.98) ≥2500: 1436 (97.95)	1466	% Agreement: 99.59% Kappa: 0.9027
Anemia (BR: at any time during pregnancy; PIN: during the 3rd trimester)	Anemic: 150 (8.90) Not Anemic: 1535 (91.10)	Anemic: 455 (27.73) Not Anemic: 1186 (72.27)	1641	% Agreement: 74.16% Kappa: 0.1854
Gestational Diabetes	Diabetes: 54 (3.20) No Diabetes: 1631(96.80)	Diabetes: 64 (3.90) No Diabetes: 1579(96.10)	1643	% Agreement: 93.79% Kappa: 0.0889
Preg induced Hypertension-Eclampsia	PIH-Eclamp: 147 (8.96) No PIH-Eclamp: 1493 (91.04)	PIH-Eclamp: 173 (10.53) No PIH-Eclamp: 1470 (89.47)	1600	% Agreement: 94.56% Kappa: 0.6973
Preterm	Preterm: 217 (12.88) Full-Term: 1468 (87.12)	Preterm: 219 (13.00) Full-Term: 1466 (87.00)	1685	% Agreement: 97.98% Kappa: 0.9104