NBDPN Data Call Template for a Multistate Project with Examples

Project Title: _____ Interpregnancy Interval and Prevalence of Selected Birth Defects_____

Principal Investigator name, title, affiliation, address and email:_____Jane Doe, PhD, Director,

Birth Defects Monitoring Program, 250 Washington St., Boston, MA 02108, jane.doe@state.gov_

Lead program contact name, affiliation, address, and email: ___Zane Smith, Birth Defects Monitoring Program, 250 Washington St., Boston, MA 02108, Zane.smith@state.gov___

Initial Request Date:_____4/11/22_____

Funding source(s), if applicable:_____No outside funding_____

Program Project Investigators/Study Personnel Contact Information and Backup Contact information

Provide contact information below for the lead study contact, principal investigator, and any co-investigators at your site involved in the study, as well as their level of access to confidential data below:

Note: At the time of initial participation and at least once a year thereafter, participating programs will be asked to review the list of study personnel with their contact information and level of data access and provide updates as needed.

Name, Degree, and Title	Email	Phone numbers(s)	Affiliation and address	Role in study	Access to confidential data (including unsuppressed small cell counts?) Y/N
Zane Smith, MPH, Epidemiologist	Zane.smith@state.gov	O: 444-444-4444	MA Birth Defects Monitoring Program, 250 Washington St., 5th Floor, Boston, MA 02108	Study Lead	Y
Jane Doe, PhD, Director	Jane.doe@state.gov	O: 555-555-5555 C: 222-222-2222	MA Birth Defects Monitoring Program, 250 Washington St., 5th Floor, Boston, MA 02108	Principal Investigator	Y
Jean Day, ScD, Postdoctoral Fellow	Jean.Day@state.gov	C: 333-333-3333	MA Birth Defects Monitoring Program, 250 Washington St., 5th Floor, Boston, MA 02108	Co-investigator	Y

Note: Any personnel with confidential access must have completed human subjects training, with proof submitted as part of IRB application.

Key requirements for participation

Note: This section should include the most important requirements for study data to help programs quickly determine whether they can participate.

Please include here a brief list of the criteria that states must meet in order to be able to participate, such as:

- ***Study years: At least 3 consecutive years within 2015-2018***
- ***Data structure: individual or aggregate: Individual, line level data***
- ***Required defect(s):*** *(List in Appendix if needed)* ***See Appendix 1***
- ***Estimated deadline for data submission: 9/1/2022***
- ***Number of years of follow-up,*** *if applicable: N/A*
- ***Data Sources:*** *(List all data sources for Numerator and Denominator (live births). Examples: Vital Records, Birth Defects program, National Death Index, etc.):* ***MA Birth Defects Monitoring Program, Vital Records***
- ***Birth Outcomes for cases: Live births and stillbirths***

Study Proposal

Introduction/Background

Include a brief description of the research question/What is known and not known, including references and description of the public health impact/importance of the question:

Short interpregnancy intervals (IPI), typically defined as those less than 6 or 12 months, have been consistently identified as a risk factor for a number of adverse pregnancy outcomes including low birth weight, preterm birth, and small-for-gestation age (1). Short IPIs have also been associated with a modest increase in the overall risk for any major congenital malformation and sub-analyses by system revealed increases in cardiovascular and musculoskeletal defects, specifically (2). Utilizing such overly broad outcomes could potentially obscure larger increases in risk for specific defects. Separate studies identified an increased risk for neural tube defects (3) and gastroschisis (4). In contrast, another study reported an inverse association between short IPI and cleft palate (5), but it has been suggested that this association may be an artifact of classification errors in the operationalization of the interpregnancy intervals, specifically using categories of IPI that were too wide (6). Some investigators attribute the higher risk of adverse outcomes to factors related to short IPI, such as maternal socioeconomic and lifestyle characteristics; however, evidence from studies that have controlled for such factors suggest that the results are not completely explained by confounding (1). The nutritional depletion hypothesis has been proposed as an explanation specific to short interpregnancy intervals. It postulates that between closely spaced pregnancies there is insufficient time for repletion of nutritional reserves needed to support fetal development in the subsequent pregnancy (7, 8, 9). During pregnancy and lactation, maternal stores of important micronutrients, such as vitamins A, B_6, B_{12}, D_3, zinc, and folate decline during pregnancy, and while most have been shown to rebound relatively shortly after delivery, vitamin D_3 and folate may take several months (10, 11). Certain subpopulations, including teenagers and black women, may require longer intervals to replenish nutrient stores between pregnancies (7, 12).

Pooling of data from multiple states within the National Birth Defects Prevention Network (NBDPN) will provide enhanced numbers allowing for assessment of risks for a wide range of specific defects in relation to interpregnancy interval.

Study Objectives

Primary aim: *If you are hypothesis-testing, please state the hypothesis*

- To evaluate the relationships between interpregnancy interval and the occurrence of specific major congenital malformations

Secondary aim(s) (if applicable): *If you are hypothesis-testing, please state the hypothesis*

- To evaluate the relationships between interpregnancy interval other adverse outcomes, such as preterm birth, low birth weight, and small-for-gestational age

- To evaluate the compatibility of observed associations with the nutritional depletion hypothesis

Study Design and Data Collection/Study Population

For Primary Aim I and Secondary Aim 1

All live births and fetal deaths identified through vital statistics and birth defects surveillance data occurring between 2010 and 2018 born to mothers who had at least one previous pregnancy. Cases will include births with any of the birth defects of interest listed in **Appendix 1.**

Live births and stillbirths to mothers with at least one previous pregnancy should be identified as those in which the following birth or fetal death certificate data fields sum to greater than zero: Number of Previous Live Births Now Living, Previous Live Births Now Dead and Number of Other Pregnancy Outcomes (includes spontaneous and induced losses and ectopic pregnancies).

We acknowledge that the range of birth defects monitored differs between states. Each participating state must provide a list of the birth defects used to identify births without congenital malformations.

NOTE: This study does not require linkage of records for consecutive births to the same mother, since all requested information can be obtained directly from a birth certificate or from the birth defects registry.

Detailed Study Inclusion and Exclusion Criteria:

Note: Detailed variable information and variable coding, including defects required are provided in Appendices.

1. Case information, including birth outcomes requested, and coding system used

ICD-9-CM	ICD-10-CM	CDC/BPA

2. ***Provide Appendices Listing Defects and Other Variables Requested.*** *Please note any of the requested defects that your state does not collect on the accompanying Data Submission Questionnaire Form.*

3. *Inclusion criteria (list below):*

   Live births to those in 2015-2018 who had at least 1 prior live birth

4. *Exclusion criteria (list below):*
   Nonlive births, Those without a prior pregnancy resulting in live birth

5. Data Sources: Vital Records and Birth Defects Registry records—linkage optional

6. **List of Variables required for cases (Attach in Appendix if necessary):** *Please note any variables not collected in your state program or not available during the requested time period in the accompanying Data Submission Questionnaire Form.* See Appendix 1 for birth defects and Appendix 2 for covariates.

7. **List of Variables required for denominator/controls (Attach in Appendix if necessary):** See Appendix 2 variables described as source BC.

8. Requested Data Structure (Line level or aggregate, separate numerator and denominator files, etc.)

   Line level data are requested.

9. Time period of data requested (birth cohort years) and follow-up time period, if applicable:
   Requested years are 2015-2018, but any consecutive 3 year period within these years is acceptable.

If for some reason, participating programs cannot meet the above requirements, differences should be noted on the Data Questionnaire that accompanies the data submission.

Analysis Plan

Predictor Variable(s): Interpregnancy Interval

Interpregnancy interval will be calculated as the time period in completed weeks between the more recent of either the Date of Last Live Birth and the Child Date of Birth, minus the Obstetric Estimate of Gestation (in completed weeks) using information from birth certificate information provided by participating states. If the Obstetric Estimate of Gestation is missing then gestational age based on last menses will be used. If the day is missing for the end the previous pregnancy, then the 15th of the month will be used to compute interpregnancy interval.

Interpregnancy interval will be separately evaluated as a continuous and a categorical predictor of each of the outcomes of interest. Consistent with the literature, we will look at intervals less than 6 months, 6-11 months, 12-17 months, 24-59 months, and greater than or equal to 60 months relative to intervals of 18-23 months.

Outcomes of Interest

Birth Defects

The defects to be included in the project are itemized in Appendix 1 and include defects from the NBDPN national prevalence estimates project (13, 14) among live births and stillbirths. We provide both the CDC/BPA codes and the ICD-9 and ICD-10 codes for the requested defects, along with comments regarding relevant exclusions and inclusions for the defects of interest.

Other Outcomes

In addition to the selected birth defects, we are also interested in examining the relationship between interpregnancy interval and other pregnancy outcomes. Birth weight and gestational age will be assessed as continuous outcomes and will also be dichotomized to assess low birth weight and preterm, respectively. Low birth weight will be defined as a birth weight less than 2500 grams. Preterm will be defined as a gestational age less than 37 weeks. Small-for-gestational age will be defined as birth weight below the 10th percentile for gestational age on the basis of a sex-specific standard. We plan to derive the standard using all nonmalformed singleton births from 2010-2018 to mothers with at least one previous live birth from participating centers.

Analysis Plan

We will describe the counts and prevalence of each outcome over the range of interpregnancy intervals during the years provided. Prevalence will be evaluated by categories of IPI for each birth defect overall and evaluated by maternal age at prior live birth, state/program, and race.

Stratified analysis will be conducted to evaluate whether maternal race, maternal age or other covariates modify the relationships between short interpregnancy interval and the occurrence of each adverse pregnancy outcome. Prevalence ratios and 95% confidence for short and long IPI compared to IPI of 18-23 months will be calculated using generalized linear models.

Sensitivity analyses will be performed to look at those missing data on date of last live birth, limiting to active surveillance programs, and limiting to states with no more than 10% missing IPI information.

Documentation of status of IRB approval

See attached approval letter from the MA Department of Public Health IRB.

Data submission method

Please describe secure file transfer method requested and note what types of files participating programs can submit. (N/A if not applicable).

Unless different arrangements are made, all participating states will submit their data using the Massachusetts Secure File Transfer system, Interchange, which requires an invitation to enroll. Transferred files are automatically deleted after 14 days. Data should be submitted either as SAS datasets or in Excel files.

How will data be stored securely? Brief description of where and how data will be stored by lead state.

After being received through the Interchange Secure File Transfer system or other secure transfer, data will be stored on a secure server at the Massachusetts Department of Public Health. Data will be stored in a directory with restricted access so that only authorized study personnel may access the data. Network access is protected by requiring a user to login to an Active Directory system with a username and password. Access to directories and files are restricted by user membership to network security groups. Network security group access is granted only if a user is affiliated with a research study or group. When a user is not affiliated with a research study or group, access is denied or removed. We do not anticipate any need for paper copies with identifying information; however, if the need for paper copies arises, they will be kept in locked cabinets, and only authorized study personnel will have access to the files.

Data Destruction Plan

All study files will be deleted from the network 10 years from the study start date (estimated 9/1/2022) or 3 years following publication of the data, whichever comes first. This 3-year holding period after publication will allow any questions regarding the published data to be answered. In addition to deleting files, access to the restricted folders will be revoked at the same time that the files are deleted.

Anticipated Study Start and End dates

Anticipated Start Date: Analysis will begin once all data from participating states has been received, estimated to be April 2023.

Anticipated End Date: We anticipate data analysis to be completed by April 2024.

List of other participating programs, if known: TX, AZ

***Lead Program Primary Contact Information for Data Submission Questions (name, address, phone, email)**

Zane Smith, 250 Washington St., Boston, MA 02108, 444-444-4444, Zane.smith@mass.gov

List any other lead program contact information below, if applicable (for example, Vital Records contact or IRB contact):

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Detailed description of Case Data with required formats should be provided in Appendices.

REFERENCES

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Appendix Examples below.

Appendix 1. Birth Defects Requested (Line Level data)				
Birth Defects	**ICD-9-CM Codes**	**ICD-10 CM codes**	**CDC BPA Codes**	**Notes**
Anencephalus	740.0 – 740.1	Q00.0–Q00.1	740.000 – 740.100	
Spina bifida without anencephalus	741.0-741.9 without 740.0 – 740.1	Q05.0–Q05.9, Q07.01, Q07.03 w/o Q00.0–Q00.1	741.000 – 741.990 without 740.000 – 740.100	
Encephalocele	742.0	Q01.0–Q01.9	742.000 – 742.090	
Anotia/microtia	744.01, 744.23	Q16.0, Q17.2	744.010, 744.210	Exclude Type I microtia as per NBDPN "Abstractor's Instructions"
Common truncus	745.0	Q20.0	745.000 – 745.010	
Transposition of great arteries	745.10 – 245.12, 745.19		745.100 – 245.120, 745.190	
Tetralogy of Fallot	745.2	Q21.3	745.200 – 745.210, 746.840, 747.310	Include pulmonary artery atresia with septal defect (BPA code 747.31, "tetralogy with pulmonary atresia")
Hypoplastic left heart syndrome	746.7	Q23.4	746.700	
Total anomalous pulmonary venous return	747.41	Q26.2	747.420	
Tricuspid atresia	746.1	Q22.4	746.100	Exclude stenosis only
Cleft palate without cleft lip	749.0	Q35.1–Q35.9	749.000 – 749.090	
Cleft lip with and without cleft palate	749.1, 749.2	Q36.0–Q36.9, Q37.0–Q37.9	749.100 – 749.290	

Esophageal atresia/ tracheoesophageal fistula	750.3	Q39.0–Q39.4	750.300 – 750.350	
Rectal and large intestinal atresia / stenosis	751.2	Q42.0–Q42.9	751.200 – 751.240	
Reduction deformity, upper limbs	755.20 – 755.29	Q71.0–Q71.9	755.200 – 755.290	
Reduction deformity, lower limbs	755.30 – 755.39	Q72.0–Q72.9	755.300 – 755.390	
Reduction deformities, total (including unspecified limb)	755.20 – 755.4	Q73.0–Q73.8	755.200 – 755.490	
Diaphragmatic hernia	756.6	Q79.0, Q79.1	756.610 – 756.617	Exclude eventration of the diaphragm, as per NBDPN "Abstractor's Instructions"
Gastroschisis	756.79, 756.73 (as of 10/1/2009)	Q79.3	756.710	If your state uses ICD-9 codes, please indicate if you have another method to distinguish between gastroschisis and omphalocele. If not, do not report.
Omphalocele	756.79, 756.72 (as of 10/1/2009)	Q79.2	756.70	If your state uses ICD-9 codes, please indicate if you have another method to distinguish between gastroschisis and omphalocele. If not, do not report.
Down syndrome	758.0	Q90.0–Q90.9	758.00 – 758.09	
Trisomy 13	758.1	Q91.4–Q91.7	758.10 – 758.19	
Trisomy 18	758.2	Q91.0–Q91.3	758.20 – 758.290	

APPENDIX 2: Individual level data elements for infants and mothers to be included in "Call for Data"				
Variable	Source (C=Created, BC=birth certificate)	Variable name	Variable type	Notes
Random ID	C	C_ID	Char	Pos 1-2 = 2-digit state code Pos 3-4 = 2-digit birth year Pos 5-11 = Sequential number (e.g., NY00001). Other means accepted, such as birth year and cert number
Maternal Resident State at Child's Birth	BC	STATE	Char	2 letter US postal abbreviation
Child Sex	BC	SEX	Num	1=male 2=female 3=undetermined 9=unknown
Child Date of Birth	BC	CHILD_DOB	Date	MM/DD/YYYY
Maternal Age at Birth	BC	MOM_AGE	Date	Years (Month and year of mother birth can be provided instead)
Maternal Race	BC	MRACE	Num	1= white 2= black 3= American Indian/Alaska nativ 4=Chinese 5=Japanese 6=Hawaiian 7=Filipino 8=Korean 10=Asian Indian 11=Vietnamese 12=Other Asian/Pacific Islanders 88=multiple race 99=other/unknown

APPENDIX 2 cont.: Individual level data elements for infants and mothers to be included in "Call for Data"				
Maternal Hispanic Ethnicity	BC	METHN	Num	1= not Spanish/Hispanic/Latina 2= Hispanic – Mexican, Mexican American, Chicana 3= Hispanic – Puerto Rican 4= Hispanic – Cuban 5= Hispanic – Other Spanish/Hispanic/Latina 9= unknown
Maternal Education	BC	MEDUC	Num	1= <12th grade, no HS diploma 2= HS diploma or GED 3= Some college, no degree 4= Associate degree 5=Bachelor's degree 6= Master's degree 7= Doctorate or Professional degree
Mothers height	BC	MOM_HT	Num	Inches 8888 = refused 9999 = unknown
Mother's pre-pregnancy weight	BC	MOMWT	Num	Pounds 8888 = refused 9999 = unknown
Previous Live Births Now Living (not including this child)	BC	LBLIVE	Num	888=refused 999=unknown
Previous Live Births Now Dead (not including this child)	BC	LBDEAD	Num	888=refused 999=unknown

APPENDIX 2 cont.: Individual level data elements for infants and mothers to be included in "Call for Data"				
Date of Last Live Birth	BC	DLLBTH	Date	MM/DD/YYYY 99/DD/YYYY = missing month MM/99/YYYY = missing day MM/DD/9999 = missing year
Date Last Normal Menses Began	BC	LMP	Date	MM/DD/YYYY 99/DD/YYYY = missing month MM/99/YYYY = missing day MM/DD/9999 = missing year
Average number of Cigarettes Smoked Daily Prior to Pregnancy	BC	PRESMK	Num	8888=refused 9999=unknown
Average number of Cigarettes Smoked Daily During Pregnancy	BC	DURSMK	Num	8888=refused 9999=unknown
Delivery Payment Method	BC	PAY	Num	1=private insurance 2=public/Medicaid 3=self-pay 9=other/unknown
Maternal Diabetes	BC	MDIAB	Num	0=none 1=pre-pregnancy 2=gestational 3=non-specific 9=unknown
Maternal Hypertension	BC	MHBP	Num	0=none 1=chronic pre-pregnancy 2=gestational 9=unknown

APPENDIX 2 (continued): Individual level data elements for infants and mothers to be included in "Call for Data"				
Pregnancy Resulted from Infertility Treatment	BC	FERTGATE	Num	1=yes 2=no 9=unknown
Fertility enhancing drugs, artificial insemination, or intrauterine insemination used	BC	TRTFERT	Num	1=yes 2=no 9=unknown Only applicable if FERTGATE = 1.
Assisted reproductive technology (e.g., in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT))	BC	ARTPROC	Num	1=yes 2=no 9=unknown Only applicable if FERTGATE = 1.
Obstetric Estimate of Gestation	BC	GA_CLIN	Num	weeks 99=unknown
Gestational age, based on LMP	BC	GA_LMP	Num	weeks 99=unknown
Birth weight (grams)	BC	BWT_GM	Num	grams 9999=unknown
Plurality	BC	PLURAL	Num	1= singleton 2= twin 3= triplet 4= quadruplet Etc. 999 = unknown

APPENDIX 2 (continued): Individual level data elements for infants and mothers to be included in "Call for Data"				
Birth Defects Code	BDR	BD_DX1 - BD_DX24	Char	Up to 24 codes with each code left-justified OPTIONAL Use 6 spaces per code with no decimals; leave trailing blanks Leave blank for non-malformed OPTIONAL (only include for linked records)
Birth Defects Verbatim Diagnosis	BDR	BDTXT1 – BDTXT24	Char	Verbatim birth defect diagnosis separate column for each unique defect. Leave blank for non-malformed OPTIONAL (only include for linked records)
Coding system utilized	BDR	CODSYS	Num	1= ICD-9 2=BPA 3=ICD10
Program Ascertainment Type	BDR	SURVtype	Num	1=Active, 2=Passive, 3=Other