7. SELECTION OF OUTCOME AND EXPOSURE MEASURES

To guide the selection and prioritization of exposure and outcome measures, 28 hypotheses were developed based on the input from multiple federal agencies and scientific experts. The criteria for these core hypotheses were that they be scientifically compelling, have important public health implications, be feasible to test, and clearly justify the need for a prospective birth cohort study of 100,000. These hypotheses can be found in Appendix A. Although it is expected that many other scientific questions will be investigated, the core hypotheses have served as guidelines for prioritization of measures.

Due to the breadth of the National Children's Study, each contact between the participant and NCS personnel must capture information pertinent to multiple exposure and outcome domains. Thus, the length of time a measure takes to administer is an important issue with respect to overall participant burden and retention. Also for these reasons, measures that are generally perceived as invasive or uncomfortable are less likely to be included in the full protocol. Each of the procedures, measurements, and assessments associated with the NCS must meet the criteria for "minimal risk" as defined in the Code of Federal Regulations [§45 CFR 46.102(i)]. In addition, the NCS is committed to minimizing even minimal risks.

7.1 Exposures, Outcomes, Mediators, and Confounders

To some degree, the categorization of certain measurements as an outcome, an exposure, a potential mediator, or a confounder is arbitrary because a factor that is an exposure in one hypothesis may be a mediator, confounder, or outcome for another. For example, childhood obesity can be considered an outcome related to fetal growth and maternal glucose tolerance and also a risk factor for subsequent development of diabetes or cardiovascular disease. For consistency, this document categorizes outcomes and exposures as they are presented in the NCS hypotheses while acknowledging the fluidity inherent in many of the areas. For a more in-depth discussion of mediators and confounders see the Statistical Analysis Plan (Chapter 10).

7.2 Overview of Measures

As described previously, the NCS will engage in a continual process of planning the protocol measures to ensure they reflect the best science and technology available. Protocol development will continue as the children age and new scientific data become available. Specific measurements for each new wave of data collection will begin approximately two years before the measures are needed in the field.

Assessment of exposures and outcomes will utilize tools suitable for a large-scale, longitudinal, multi-site, geographically dispersed epidemiologic study. In general, measurements used successfully in other large studies of child health are most likely to be included in the NCS because they have a record of past performance and will facilitate the comparison of NCS results to those from other studies. However, some novel or less frequently used tools may provide important high-quality data and are included where appropriate for the entire cohort, while others may be more suitable for focused adjunct studies.

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7.2.1 Organization of Rationale for Measures Chapters and Appendices

The rationale for outcome and exposure measurement strategies is presented in Chapters 8 and 9. The domains of exposures and outcomes described in these chapters extend from birth to age 21. There is more specificity, however, relating to assessments through infancy since protocol development is still ongoing. These chapters are supported by Appendices E through I, which contain detailed information about the domains of measurement at each participant contact through child age 24 months.

Chapter 8 describes the rationale for measurement strategies with regard to each of the seven priority outcome areas: pregnancy; neurodevelopment and behavior; child health and development; asthma; obesity and growth; injury; and reproductive development.

Chapter 9 describes the rationale for measurement strategies with regard to chemical exposures, physical exposures and environment, psychosocial environment, biological exposures, and genetics.

7.2.2 Overview of Measures Related to Specific Hypotheses

As mentioned previously, the NCS core hypotheses served as guidelines for the selection of outcome and exposure measurement domains. Consequently, in conceptualizing the relation between the outcome and the exposure measurement domains, it is helpful to think about their connections within these core hypotheses. Table 7-1 presents the 28 core hypotheses across the top of the table organized by priority outcome area. Domains of exposures and covariates are listed down the side. For each hypothesis, the exposures and covariates central to that hypothesis are indicated in the table.

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Table 7-1. Measures by Hypotheses

Control Cont			Pi	regnancy Ou	ıtcomes		Neurode	velopment	and Behavi	or	Ch	nild Health	and Devel	opment				Asthma	a				Obesity	y and Grov	vth			Injury	Reproduct Developme
Section		. e. l		1	tive dism and	Onpersistent Pesticides and Poor leurobehavioral and Cognitive Skile		Environment Interactions and	and Perinatal Infection and	amily Influences on Child Health and	npact of Neighborhood and communities on Child Hears.	mpact of Media Exposure on Child	ocial Institutions and Child Health and	nfluences on Healthy Development	natal Maternal Stress and Genetics	oor, Outdoor Air Pollution, oallergens and Asthma Rist.	tary Antioxidants and Asthma	cial Environmental influences on the disparities	Exposure to Components and isk of Asthmoganisms Decra			Insulin Res Growth Res	eastfeeding Associated with Lower sulin Resistant Lower	Whole Grains, High Glycemic Index	anetics, Environmental Exposures, and	Peated Mild Traumatic	thavioral Exposures, Genetics, and	ints and Resiliency to Traumatic	nental Agents
Manufactor Section of Manufactor Section Manufa		40 2	2 2 2	2002	1 < 6	< <	/ L Z	70 14	16.00	11. 12	1=0	- 1	00 12	-	14.0	1 = 4	ū	() to	<u> Ш </u>	ш = 0	0 2	10 %	ш с =		0 -	- E - Z	# O Q	V 1	<u>T</u>
Provide the column Provide State Provide	Questionnaire - Mother																												
Separate	HH Composition and Demographics		С	С		С		С	С	N	С	С	С		С	С		С	С	N	С	С	С	С		С		N	С
Section Sect	Parental Stress		С				С	N		N	N			N														N	
Part	Maternal Exhaustion *Prop							С																					
Mathematic Mat	Social Support							N							С			-											
March Marc	Family Process							N		N	С							N								N		С	
March Approxime March March March March March March Approxime March	Health Behaviors	С	С					С				С		N	С	С											С		_
Name Materians Against Market	Diet and Toxicants through food					N											N		N		С	С	N	N	N				С
Charles Char	Media Use									С		N	С																
March Anthone Members March Anthone Marc	Maternal Mental Health & Cognition					С		N		N		С	С	N													N	N	
Case	Parenting Style							N		N		С		N													N	N	
Magnificance Magn	Maternal / Paternal Attachment					N		N		N			N	N															
March Marc	Child Care									N	N	N	N	N															
Header Construction	Neighborhood									С	N		С															N	
Consistent Problem Consist	Public Policy													N														N	
Post of the content	Housing Characteristics				С	С	С	С	С		С					N	С	С	С	С									С
The contribution C	Occupation / Hobbies				N	N	С	С	С						N	N	С	N	N	N			С	С	N	С			N
Tend Antals/ Frontier (resident fame)	Appliance and Product Use				N	N	С	С	С							N	С	N	N	N			С	С		С			N
Family Enginement (Industration only)	Use of medicines	С					N	С	N								С		С				С	С			С		
First Modical Hastory	Time and Activity (mother / resident father)				N	N	С	С	С			С				N	С	N		N	С	С	С	С		С			N
Child Temperament Emotional Regulation N N N N N N N N N N N N N N N N N N	Family Environment (observation only)							N		N				N													N	С	
California Frenchard Fendoral Regulation	Brief Medical History	N	N	N		С	N		N	N	N	N	С		N	N	N	N	N	N	N	N	N	N	N	N	N	N	С
Scoid Completence Pethaloring Scoid	Child Language Development					N		N		N			N	N															
Social Compensor / Behavior / Problems	Child Temperament / Emotional Regulation							N		N				N													N	С	
Child Aufsirn Screening	Socio-Emotional Functioning					N				N	N	N	N	N															
Adaptive Behavior Questionnaire - Child N N N N N N N N N N N N N N N N N N N	Social Competence / Behavior Problems													N														С	
Neoratal Neuro-behavior	Child Autism Screening					N		N		N																	N		
No.	·							N		С																	N		
Ceneral Cognitive Ability	Questionnaire - Child																												
Cognitive Processes	Neonatal Neuro-behavior	N		N		N	N				N			N															
Cognitive Processes N	General Cognitive Ability					N				N	N	N	N	N															
Language Development N	General Motor Development					N				N	N	N	N	N														N	
Infant Emotion	Cognitive Processes					N	N			N	N	N	N													N	N	N	
Parent-Child Interaction N <td>Language Development</td> <td></td> <td></td> <td></td> <td></td> <td>N</td> <td></td> <td></td> <td></td> <td>N</td> <td>N</td> <td>N</td> <td>N</td> <td>N</td> <td></td> <td>N</td> <td></td>	Language Development					N				N	N	N	N	N														N	
Attachment Status N	Infant Emotion					N		N		N																	N	N	
Sensory Function N	Parent-Child Interaction							N		N				N													N	N	
Questionnaire - Father Image: Company of the company of	Attachment Status					N				N	N	N	N	N														N	
Demographics N C C N <t< td=""><td>Sensory Function</td><td></td><td></td><td></td><td></td><td>N</td><td></td><td></td><td></td><td>N</td><td>N</td><td>N</td><td>N</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>	Sensory Function					N				N	N	N	N																
Paternal Mental Health and Cognition C N N N C C N N N N Social Support Experiences with Target Child	Questionnaire - Father																												
Social Support Experiences with Target Child N C N C C C C C C C C C C C C C C C C	Demographics									N	С		С															N	
Experiences with Target Child	Paternal Mental Health and Cognition					С		N		N		С	С	N													N	N	
	Social Support							N		С				N	С			С									С		

 \overline{N} = Needed for Analysis C = Confounder/Covariate *Prop = Proposed measure

Table 7-1. Measures by Hypotheses (continued)

		Pi	regnancy Ou	tcomes		Neurodey	velonment	and Behavi	or	Ch	ild Health a	and Devel	onment				Asthm	a				Ohesit	y and Grov	wth			Injury	Reproductive Development
	Birth Defects from Impaired Glucose	Increased Risk of Preferm Birth from Inflammation	s of riction, hildren	tive idism and	ticides and Po		Gene Environment Interactions and	Prenatal and Perinatal Infection and	Family Influences on Child Health and	Impact of Neighborhood and Communities on Child Heats.	Impact of Media Exposure on Child	Social Institutions and Child Health and	Development	Prenatal Maternal Stress and Genetics in	Indoor, Outdoor Air Pollution, Aeroaliergens and Asthma Di	Dietary Antioxidants and Asthma Risk	Social Environmental influences on	to Components and	ental Exposure and Ge	Obesity and Insulin Resistance from Impaired Maternal Glucose Ma.	Obesity and Insulin Resistance form	10	is, High Glycemic Index	S, and	Repeated Mild Traumatic Brain Injury and	pu	aumatic	Hormonally Active Environmental Agents and Reproductive Development
Questionnaire - Father continued																												
Parenting Style							N		N		С		N													N	N	
Paternal Attachment					N		N		N			N	N															
Child Care									N	N	N	N																
Tobacco Product Use, Alcohol Use, Illicit Drug Use and Prescription Drug Abuse (5.10)																												
Use of Medicines and Alternative Medicines																												
Brief Medical History																											N	
Occupation / Hobbies				N	N										N		N	N	N					N				N
Family Process							N		N	С		С	N				N					С			N	N		
**Subdomains are shown if they are a confounder/covariate only.																												
Environmental																												
Indoor air																						_	_	_				
PM2.5 - ETS, Pb, Cd, Mn	С	С	С		С	С				+					N	С	N		N					_				N
PM10 - PAHs, pesticides	С	С	С	N	N	С	N,C	С							N		N		N						С			
VOCs					С	С		С							N				N						С			
Aldehydes & Ketones							С			+					N	С	С		N			_	_	_				
NO2 Hg					_	_	_	_							N	С	N		N					_	_			
O3				N	С	С	С	С																С	С			
co										+					N	С	N N		N 					_				
House dust					С					+					N	С	N		N									
Allergens, endotoxin															N	С	N		N									
Mold															N	С	N		N									
Metals - Pb, Cd, Mn, As					С	С	С								N		IN IN		IN .									N
Pesticides: OPs, Carbamates, Pyrethroids				N	N	c	С	С																	С			N .
Pesticides: OCs				N		С	С	С																	С			
Drinking water																												
Disinfection Byproducts (DBPs) - HAA9	С	С	С	С				С																				
VOCs	С	С	С		N,C	N,C	N,C	С							N										С			
Metals - Pb, Cd, As			С	С	С	С	С	С																	С			N
Nitrate	N,C	N,C	N,C	N,C																								
Perchlorate				N																								N
Pesticides: OPs, Carbamates, Pyrethroids				N	N	С	С	С																	С			
Pesticides: Atrazine																												N
Pesticides: OCs				N																								
Soil																												
Metals - Pb, Cd, Mn, As						С	С																					N
Pesticides - OPs, Carbamates, Pyrethroids				N	N	С	С	С																	С			
Near CCA treated wood - Cr+6 (as total), As					N	С	С	С																	С			
Visual assessment		С		N	N,C	С		С							N,C	С	N,C			С	С				С			N
Noise survey														С														
Indoor/Outdoor measurements																												

C = Confounder/Covariate

Table 7-1. Measures by Hypotheses (continued)

J		P	regnancy Ou	romes		Neurode	/elonment	and Behavi	ior	Ch	ild Health a	and Develo	onment				Asthma	a				Ohesity	and Grov	vth			Injury	Reproductive Development
	Sirth Defects from Impaired Glucose	erm Birth from	ors of striction, children	ve ism and	icides and Poor		Gene Environment Interactions and	Prenatal and Perinatal Infection and	Family Influences on Child Health and	mpact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child	Social Institutions and Child Health and	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Rise	Dietary Antioxidants and Asthma Risk	Social Environmental influences on	Posure to Components and S of Microganisms had		Obesity and Insulin Resistance from	isity and Insulin Res auterine Growth Res	er	c Index	res, and	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	and	ncy to Traumatic	Hormonally Active Environmental Agents
Environmental - Continued																												
Community air																												
PM2.5								С							N	С	N		N									N
PM10 - PAHs				N	N	С	С	С							C		IN		IN						С			N
0.				- N	IN										N	С	N		N									
NO _x , SO ₂															N	С	N		N									
Pollen (non-NCS data collection)										С				С	N		N		N									
Outdoor water samples at homes	С	С	С	N	N	С		С						U	С		N N	N	N					С	С			N
Community water systems (non-NCS data collection)				- N	IN .													T N										N
Hg				N	С	С	С	С																С	С			
Perchlorate				N	U																			-				N
Pesticides				N	N	С	С	С																	С			N
Nitrate	С	С	С	IN .	IN	- C																						N
Physical Exam - Mother																												
Anthropometric									С	С	С									С	С	С	C					С
Ultrasound			N						U		C									N	N	C	C					
Physical Exam - Father			IN																	N	N							
Anthropometric									С	С	С									С	С	С	С					С
Blood Pressure									С	C																		- U
Physical Exam - Child																												
Anthropometric									N	N	N									N	N	N						
Blood Pressure									N	N	N									N	N	N N						
Dysmorphology/Physical Exam	N		N						- N	N																		
Physical Activity	N		IN						С	N N	С									С	С		С					
- trystalling									U		C												C					
Biospecimen Collection - Mother																												
Blood																												
Endocrine Panel																												
Cortisol	С						С	N						N												С		
Cortisone	c						C	N						N												c		
Cortisorie Corticotropin releasing hormone (check volume)	С						С	N						N												С		
Cortisol binding globulin	c						С	N						N												С		
CRH binding protein	С						С	N						N												С		
Reproductive								14						.,														
Estriol	С						С	N						N												С		
Estradiol	С						С	N						N												С		
Progesterone	С						С	N						N												С		
Infection/Inflammation/Biological								14						.,														
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N			N	N		N							N			N	N									
cytokines/interleukins		N			IV	N N		N							IN			N N	N N									
Ig types and subtypes and org specific		N				N		N											N									
Rubella (IgM antibody)		N			С	N		N										N										

Table 7-1. Measures by Hypotheses (continued)

		Pı	regnancy Ou	tcomes		Neurode	velopment a	and Behavi	or	Chi	ild Health a	and Devel	opment				Asthma	ı			Obesity	and Grov	vth			Injury	Reproductive Development
	Birth Defects from Impaired Glucose	Increased Risk of Pretern Birth from Inflammation Exposure to Medical	includes of includes include includes inchildren.	Maternal Subclinical Hypothyroidism and	Nonpersistent Pesticides and Poor	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Heath and	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Rist	Dietary Antioxidants and Asthma Risk	Social Environmental influences on	Early Exposure to Components and the Risk of Microganisms Decreases Environmental Exposure and Components and Environmental Exposure and Componental Exposure and Componental Exposure and Component Action and Component A	en ty and Insulin red Maternal G	Obesity and Insulin Resistance form	Breastfeeding Associated with Lower Insulin Resistant Cower	Fiber, Whole Grains, High Glycemic Index	Genetics, Environmental Exposures, and	Repeated Mild Traumatic Brain Injury and	Behavioral Exposures, Genetics, and Agression	Antecedents and Resiliency to Traumatic	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Mother (continued)																											
Syphilis (Ig)		N			С	N		N										N									
Varicella (Ig)		N			С	N		N										N									
Herpes Simplex 1&2 (Ig)		N			С	N		N										N									
Hepatitis Profile (a and b) Medical Records (Ig)		N			С	N		N										N									
Toxoplasmosis (toxoplasma gondii) (Ig)		N			С	N		N										N									
IgE (cat, dog, cockroach, dust mite, fungi, mouse/rat urine)		N				N		N							N			N N									
CRP		N			С	N		N										N									
Heat Shock proteins		N			С	N		N										N									
Homocysteine and folate (fasting?) serum or red cells (prenatal vitamin influence)		N			С	N		N								N		N									
Cells T-cell subsets for Th-type *Prop		N			С	N		N										N									
thyroid (TSH and free t4)				N																							
Fasting N3-N6 Fatty Acids *Prop																N											
Antioxidant (vit A/E/Carotenoids)																N											
Vitamin C																N											
%carb deficient transferrin (alcohol)	С	С																							С		С
Glucose Metabolism																			AND THE RESIDENCE OF THE PERSON OF THE PERSO								
Fasting C-peptide *Prop	N																		N								
Fasting Glucose	N																		N								
HgbA1C	N																		N								
Insulin like Growth Factor *Prop	N																		N								
Fasting Insulin	N																		N								
Fasting lipids (included in chemical volume)	N																		N								
Genetic Tests																											
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)					N													N									
Gene Expression (RNA)					N													N								N	
Epigenetic changes (genomic DNA)					N													N									
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	С		С										N	N	N	С	С	С		N		
Cryopreserved PBMCs	N				N	С		С										N	N	N	С	С	С		N		
Cell lines *Prop	N				N	С		С											N	N	С	С	С		N		
mitochondrial DNA *Prop	N				N	С		С											N	N	С	С	С		N		
Chemical Exposures																											
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)				N	С																						N
Lead, Mercury, Cadmium (3 mL bld)				N	С																				С		N
Combination of dioxins/furans and all other chemicals (excluding metals)				N	С																						N
Stored Samples																											

C = Confounder/Covariate

Table 7-1. Measures by Hypotheses (continued)

Misperime Collection: More (positions)	The state of the s		P	regnancy Out	tcomes		Neurode	velopment	and Behav	ior	Chi	ild Health a	and Develo	opment				Asthm	a				Obesity	y and Grov	wth			Injury	Reproductive Development
Manufacture		rth Defects from Impair	Increased Risk of Pretern Birth from Inflamman	Increased risk of fetal growth restriction, technologies in children.	ism /e	الله الله	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child	Social Institutions and Child Health and	Influences on Healthy Development	ss and	olluti	and Asthma	88	1005	ronmental Expo action and Asth	Insulin ernal G	Obesity and Insulin Resistance form	eastfeeding Assites of Obesity is	Whole Grain Pesity, Insu	Genetics, Environmental Exposures, and	Repeated Mild Traumatic Brain Injury and	Behavioral Exposures, Genetics, and Agression	Antecedents and Resillency to Traumatic	Hormonally Active Environmental Agents and Reproductive Development
Second S	Biospecimen Collection - Mother (continued)																												
Mache of the section	Serum	N	N		N	N	N		N						N	N	N		N	N	N								N
Marie Mari	Plasma	N	N		N	N	N		N						N	N	N		N	N	N								N
Marie Mari	RBCs (folate and fatty acids)	N	N		N	N	N		N						N	N	N		N	N	N								N
Name		N	N		N	N	N		N						N	N	N		N	N	N								N
Common C	Buccal Cells *Prop																												
Name	Nails																												
Note 1	Organic Hg (ethyl, methyl)				N	С																							N
Extra control of the	Hg inorganic				N	С																							N
Series	Hair																												
Part Segretary S	Cd				N	С																							N
Count of the principle	cotinine	С	С		N	N		С							С	N	С										С		С
Company Comp	Hg inorganic				N	С																							N
Services Ser	Organic Hg (ethyl, methyl)				N	С																							N
Control Cont	nicotine	С	С		N	N		С							С	N	С										С	С	С
March Marc	Saliva																												
Seesal Nation Seesal Natio	Cortisol	С						С	N						N												С		
## Approximation of the Control of t	storage	С						С	N						N												С		
Expressives Call Caylorium, Cargonium, Cargo	Breast Milk																												
Chemical Exposuration Chem	Antioxidants: Vit C/E/ Beta Carotene																N						N						
Decining furnity: Organization of Pesticides; PCBs																	N						N						
Pesticides Positificant land land land land land land land land	Chemical Exposures																												
PEDEC (trosen) filtere retardant	Dioxins/furans; Organochlorine Pesticides; PCBs					С																			N				N
Perchiorate						N																			N				N
Metals: Manganese and others Manganese and others C C C C C C C C C	PBDE (frozen) flame retardant					С																			N				N
phytoestrogens N	Perchlorate					С																			N				N
MTBE methyl tertiary butyl ether (fuel additive) N	Metals: Manganese and others					С																			N				N
Bisphenol A	phytoestrogens					N																			N				N
Urine	MTBE methyl tertiary butyl ether (fuel additive)					N																			N				N
Illicit Drug Panel						N																			N				N
alcohol marker 'Prop C C C C C Antioxidants N N N M M M M M M M M M M M M M M M M N N M	Urine																												
Antioxidants N N N Image: Control of the control o	Illicit Drug Panel	С	С																								С		С
Catecholamine C N N N C C C C C N N N N C C N <	alcohol marker *Prop	С	С																								С		С
Cortisol C N N N N N C Symptomatic bacteriuria N <th< td=""><td>Antioxidants</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>N</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>	Antioxidants																N												
Asymptomatic bacteriuria N <td>Catecholamine</td> <td>С</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>С</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>N</td> <td></td> <td>С</td> <td></td> <td></td>	Catecholamine	С						С							N												С		
Fertility Monitor Image: Control of Specific Organisms Proposed N Image: Control of Specific Organisms Proposed N Image: Control of Specific Organisms Image: Control of Specific Organisms Prop N </td <td>Cortisol</td> <td>С</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>С</td> <td>N</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>N</td> <td></td> <td>С</td> <td></td> <td></td>	Cortisol	С						С	N						N												С		
Pregnancy Test Kit N	Asymptomatic bacteriuria		N				N		N										N										
PCR for identification of specific organisms *Prop N N N N	Fertility Monitor																												
	Pregnancy Test Kit																												
Chemical Exposures	PCR for identification of specific organisms *Prop		N				N		N										N										
	Chemical Exposures																												

N = Needed for Analysis C = Confounder/Covariate *Prop = Proposed measure

Table 7-1. Measures by Hypotheses (continued)

3 31 · · ·			roance	laan		News	volon	and Daline	ior	0.	ild Hackt	and David	onmant.				Agelon					Ohari	and Co	dh.			laiue -	Reproductive
		P	regnancy Ou	comes		Neurode	reiopment :	and Behavi	IOF	Ch	ild Health	and Devel	opment	.s	1	1	Asthma		1 ~	. –	T	Obesity	and Grow	nn b	9	.	Injury .ల	Development
	Birth Defects from Impaired Glucose	creased Risk of Pretern Birth from flammarine Exposure to Madicial	creased risk of fetal growth restriction, or through assisted fence.	aternal Subclinical Hypothyroidism an	onpersistent Pesticides and Poor	ilitie	Gene Environment Interactions and	Penatal and Perinatal Infection and	imily Influences on Child Health and	ipact of Neighborhood and	npact of Media Exposure on Child	ocial Institutions and Child Health and	fluences on Healthy Development	ess and Genetics	r Pollution, Asthma Pier		Social Environmental influences on	rly Expo oducts o	teraction and Asthma and Gene hildren	oesity and Insulin Resistance from Paired Maternal Glucose Metabolic	besity and Insulin Resistance form	eastfeeding Associated with Lower sulin Resistance	Fiber, Whole Grains, High Glycemic Inde	Genetics, Environmental Exposures, an	Repeated Mild Traumatic Brain Injury an Neurocognitive Developmen	Behavioral Exposures, Genetics, and Agression	ntecedents and Resiliency to Traumati	ormonally Active Environmental Agent and Reproductive Development
Disanceiman Callection Mather continued	<u>a</u> 2	1555	<u> </u>	% ≥	ŽŽ	ΔŽ	0 0	Ē	ш <u>а</u>	ਵ ਹ	= <u>I</u>	ŭ ŭ	=	<u> </u>	EĄ	۵	0 %	<u> </u>	<u> </u>	5 5	0 5	<u> </u>	<u>ii.</u> ie	Q F	ŘŽ	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	4 3	Ĭ
Biospecimen Collection - Mother continued PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium				N	N																							N
PAH (may be storage issues); requires separate analysis (3-4 ml)				N	N										N													N
ICP/MS urine screen *Prop				N	С																							N
cotinine	С	С		N	N		С							С	N	С										С		С
Phytoestrogens				N	N											N												N
Storage	С	N		N	N	N	С	N						N	N	N		N								С		N
Vaginal Swabs																												
Chlamydia		N				N		N										N										
Bacterial Vaginosis		N				N		N										N										
Cultures antibodies		N				N		N										N										
Cultures cytokines		N				N		N										N										
Cultures metalloproteinase		N				N		N										N										
Group B Strep		N				N		N										N										
Gonorrhea		N				N		N										N										
Placenta																												
Cultures antibodies and cytokines		N				N		N										N										
Pathology		N				N		N																				
Chemical Contaminants				N	N										N													N
Umbilical Cord																												
Cultures antibodies and cytokines		N				N		N										N										
Pathology		N				N		N																				
Chemical Contaminants				N	N										N													N
Biospecimen Collection - Child																												
Blood (NOTE: Because of the limited blood draw volume for the child, samples will be stored for future analysis. Final protocol for analytes will be decided in the future.)																												
Infection/Inflammation/Biological																												
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N			N	N		N		N				N	N		N	N	N					N				N
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)				N	С																			N				N
Stored Samples																												
Serum	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Lavender Top	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Guthrie Card at birth	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Buccal Cells *Prop																												
Hair																												
Cd				N	С																			N				N
cotinine	С	С		N	N		С							С	N	С								N		С		С

C = Confounder/Covariate

Table 7-1. Measures by Hypotheses (continued)

Tuble / 1. Mediates by Hypotheses (continued	´ [Reproductive
		Pi	regnancy Ou	1_	_	Neurode	/elopment	and Behav	ior	Chi	Id Health a	and Develo	pment		- 1	- 1	Asthma			1	Obesity /	and Grow	vth	17	, /	Injury	Development
	Birth Defects from Impaired Glucose	Increased Risk of Pretern Birth from Inflammation Exposure to Madic trom	Increased risk of fetal growth restriction, technologies in children	5 129	Nonpersistent Pesticides and Poor	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and	Prenatal and Perinatal Infection and	Family Influences on Child Health and	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Pier.	Dietary Antioxidants and Asthma Risk	Social Environmental influences on	Early Exposure to Components and Products of Microoganisms Decreases Environmental Exposure and Gene Children	ity and Insulin	Obesity and Insulin Resistance form	Breastfeeding Associated with Lower Insulin Resieved	Fiber, Whole Grains, High Glycemic Indep	Genetics, Environmental Exposures, and	Repeated Mild Traumatic Brain Injury and	Behavioral Exposures, Genetics, and Agression	Antecedents and Resiliency to Traumatic	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Child continued																											
Hg inorganic				N	С																		N				N
Organic Hg (ethyl, methyl)				N	С																		N				N
nicotine	С	С		N	N		С							С	N	С		N					N		С	С	С
Saliva																											
Cortisol	С						N							N					С	С	С	С	N		N		С
storage	С						N							N					С	С	С	С	N		N		С
Urine																											
Chemical Exposures																											
PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium				N	N								C		N			N					N				N
PAH (may be storage issues); requires separate analysis (3-4 ml)																											
ICP/MS urine screen *Prop				N	N										N N			N					N				N
cotinine				N	С										N 								N 		+		N
Phytoestrogens	С	С		N	N 		С							С	N	C							N 		С		<u> </u>
Storage		С		N N	N N	N	С							С	N	N N	N	N		N	С	С	N N		С		N N
Meconium	С			N	N	N	C							C	N	N	N	N	N	N	C		N		C		N
Cotinine	С	С		N	N		С							С	N	С							N		С		С
Organophosphate Metabolites	C	<u> </u>		N N	N N		C							C	N	C							N N		C		N
				N	N																		N				N
Cord Blood	С						N							N					С	С	С	С	N		N		
Cortisol	С						N N							N N					C	С	С	С	N N		N		C C
Cortisone							N N							N N					C	С	С	С	N N		N		
Conticotropin releasing hormone	С						N N							N N					С	С	С	С	N N		N		С
Cortisol binding globulin	С						N N							N N					C	С	С	C	N N		N		C C
CRH binding protein	C						N							N					C	C	C	C	N		N		C
Reproductive Estriol	С						N							N					С	С	С	С	N		N		С
Estradiol	С						N N							N N					С	С	С	С	N		N		C
Progesterone	С						N							N					С	С	С	С	N		N		С
Infection/Inflammation/Biological							N							N					-			U	- N		I N		
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N		N	N	N		N		N				N	N		N	N					N				N
cytokines/interleukins		N				N		N		N				N	N		N	N					N				
IgE (cat, dog, cockroach, dust mite, fungi, mouse/rat urine)		N				N		N	N	N				N	N	N	N	N									
Ig types and subtypes		N				N		N	N	N				N	N	N	N	N									
N3-N6 Fatty Acids								С								N			С	С	С	С					
Antioxidant (vit A/E/Carotenoids)								С								N			С	С	С	С					
Vitamin C								С								N			С	С	С	С					
Lymphocyte Subsets Th status (processing difficult)																											
Glucose Metabolism																											
Glucose	N								N	N									N	N	N	N	N				
HgbA1C	N								N	N									N	N	N	N	N				
Insulin like Growth Factor	N								N	N									N	N	N	N	N				

C = Confounder/Covariate

Table 7-1. Measures by Hypotheses (continued)

Tuble 7 1. Measures by Hypotheses (continue		Pı	regnancy Ou	tcomes		Neurode	velopment	and Rehav	ior	Ch	ild Health a	and Devel	onment				Asthma					Ohesity	and Grow	rth.			Injury	Reproductive Development
	Glucose			. Z	and Poor	skills	ons and	tion and	Health and		on Child	d Health and	lopment	and Genetics in	lution, ma Rici	sthma Risk	nces on	8	osure and Gene hma and Wheezing in	Resistance from Ucose Metabolica	nce form	15	Index	S, and	rain Injury and	Pu	umatic	t s
	Birth Defects from Impaired Metabolism	Increased Risk of Pretern Birth from Inflammation	Increased risk of fetal growth restriction, technologies.	Maternal Subclinical Hypothyroidism a	Nonpersistent Pesticides a Neurobehavioral and Cogn	Prenatal Infection and Neurodevelopmental Disab	Gene Environment Interact	Prenatal and Perinatal Infe Schizophrenia	Family Influences on Child	Impact of Neighborhood an Communities on Child Hos	Impact of Media Exposure Health and Development	Social Institutions and Chil	Influences on Healthy Deve	Prenatal Maternal Stress ar Childhood Asthma	Indoor, Outdoor Air Polluti	Dietary Antioxidants and Asthr	Social Environmental influasthma disparities	rily Exposure to (oducts of Microo e Risk of Asthma	Interaction and Asthma and	Obesity and Insulin Resista Impaired Maternal Glucose	Obesity and Insulin Resistance form	Breastfeeding Associated with Lower Insulin Resistance	Fiber, Whole Grains, High Glycemic and Obesity, Insulin Resistance	Genetics, Environmental Es Type I Diabetes	Repeated Mild Traumatic Brain Inju	Behavioral Exposures, Gen Agression	Antecedents and Resiliency to Tra	Hormonally Active Environmental Agen and Reproductive Development
Biospecimen Collection - Child continued																												
Insulin	N								N	N										N	N	N	N	N				
lipids (included in chemical volume)	N								N	N										N	N	N	N	N				
Genetic Tests																												
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)					N								N											N				
Gene Expression (RNA)					N		N						N									С	С	N		N	N	
Epigenetic changes (genomic DNA)					N		N															С	С	N		N		
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	С	N	С												N	N 	С	С	N		N		
mitochondrial DNA *Prop	N				N	С	N	С												N	N	С	С	N		N		
Chemical Exposures lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds (4 mL Serum)				N	С								С											N				N
Lead, Mercury, Cadmium (3 mL bld)				N	С								С											N		С		N
Stored Samples																												
Serum	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Plasma RBCs	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Guthrie Card	N	N		N	N	N	N	N	N	N				N 	N	N 	N	N	N	N	N 	N	N	N		N		N
	N N	N N		N N	N N	N N	N N	N N	N N	N N				N N	N N	N N	N N	N N	N N	N N	N N	N N	N N	N N		N N		N N
Lavender Top Whole blood storage PCR	N	N		N	N	N	N	N	N	N				N	N N	N	N		N	N	N	N	N N	N		N		N
Biospecimen Collection - Father	- 1	- 1		14				- 14	- 1					14		.,,	N	N			- 14	- 1		- 1		, N		, ,
Blood																												
Genetic Tests																			N									
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)													N/C						N									
Gene Expression (RNA)													N/C						N								N	
Epigenetic changes (genomic DNA)																			N									
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	С		С											N	N	N	С	С	С		N		
Cryopreserved PBMCs	N				N	С		С											N	N	N	С	С	С		N		
Cell lines *Prop	N				N	С		С												N	N	С	С	С		N		
mitochondrial DNA *Prop	N				N	С		С												N	N	С	С	С		N		
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)					С																							
Lead, Mercury, Cadmium (3 mL bld)					С																							
Combination of dioxins/furans and all other chemicals (excluding metals)					С																							
Stored Samples																												
Serum					N																					N		
Plasma					N N	N		N N																		N N		
<u> </u>					N	IN		N																		IN		

C = Confounder/Covariate

Table 7-1. Measures by Hypotheses (continued)

		P	regnancy Ou	ıtcomes		Neurode	velopment	and Behavi	or	Ch	ild Health	and Deve	lopment				Asthma					Obesity	and Grov	vth			Injury	Reproductive Development
	Birth Defects from Impaired Glucose	Increased Risk of Pretern Birth from Inflammarica.	sk of fetal growth restriction, hassisted to thildren	Pothyroidism and	des and Poor Cognitive Star	sulls a	Gene Environment Interactions and	Prenatal and Perinatal Infection and	Family Influences on Child Health and	Impact of Neighborhood and Communities on Child Heath.	Impact of Media Exposure on Child	Social Institutions and Child Health and	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma D	: / V	ental influences o	Early Exposure to Components and the Risk of Alkicroganisms.	na Xposure and Gene	Obesity and Insulin Resistance from	Obesity and Insulin Resistance form		ndex	es, and	Repeated Mild Traumatic Brain Injury and	and	Traumatic	ntal Agents
Biospecimen Collection - Father continued																												
RBCs (folate and fatty acids)					N	N		N					_													N		
Lavender Top					N	N		N					_													N		
Buccal Cells *Prop																												
Nails													_															
Organic Hg (ethyl, methyl)					С																							
Hg inorganic					С																							
Hair																												
Cd					С																							
cotinine					N																							
Hg inorganic					С																							
Organic Hg (ethyl, methyl)					С																							
nicotine					N																						С	
Saliva																												
Cortisol	С						С							N												С		
storage	С						С							N												С		
Urine																												
Chemical Exposures																												
PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium					N																							
PAH (may be storage issues); requires separate analysis (3-4 ml)					N																							
ICP/MS urine screen *Prop					С																							
cotinine					N		С																					
Phytoestrogens					N																							
Storage					N		N																					
Semen																												
Quality (home collection)																												

N = Needed for Analysis C = Confounder/Covariate *Prop = Proposed measure