Supplementary Materials

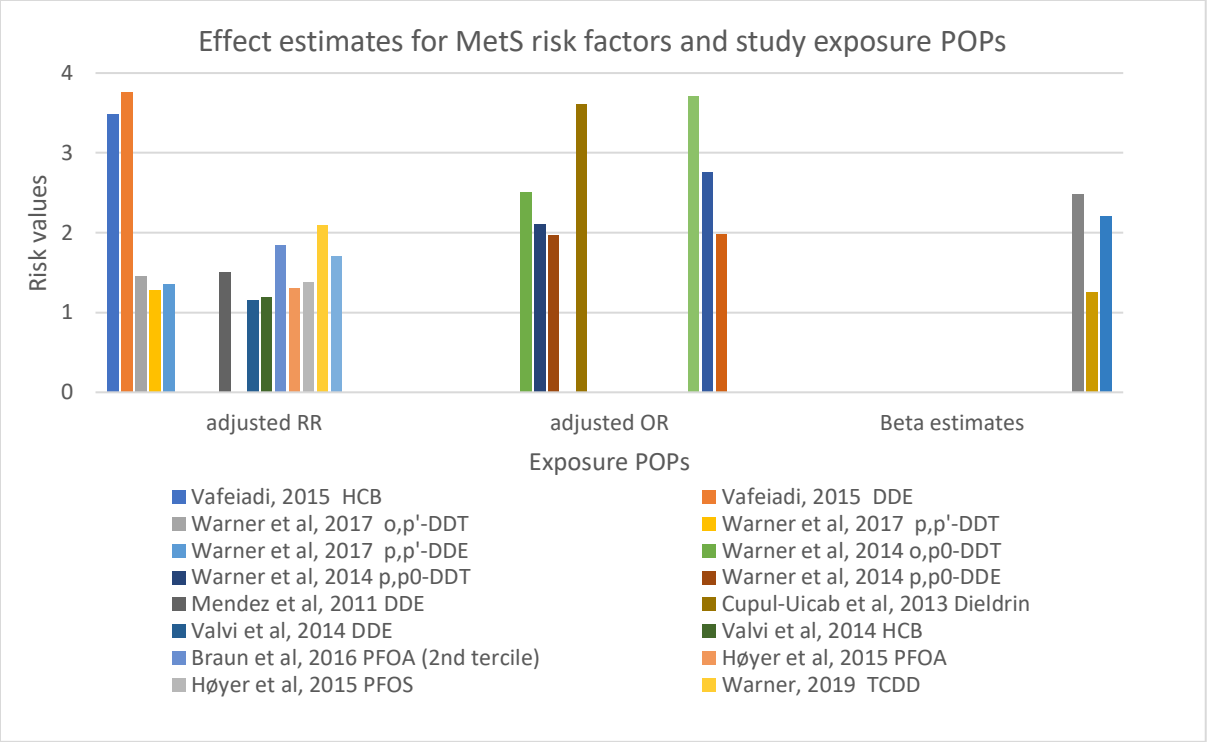

Figure 1.0 Effect estimates for MetS risk factors and exposure POPs per study

Table 2.0 Characteristics and results summaries of studies included in review

First Author, Year	**Country**	**Study Participants: No. of Subjects, Characteristics, Time of gestation at enrollment**	**Baseline Year**	**Follow-up Period after birth Years(y), months (m)**	**Exposure, Measured Chemicals**	**Outcome: Measurement on child**	**Adjustment**	**Results Relative Risk (RR) / Odds Ratio (OR) (95% Confidence Interval)**	**Limitations**
Vafeiadi, 2015	Greece	689 Mother-Child pairs First trimester	2007	4 y	PCB congeners (118, 138, 153, 156, 170, and 180), HCB, DDT and DDE, and BDE-47	Obesity as BMI z-score using IOTF definitions, blood Pressure, central adiposity as WC ≥ 90th percentile for age and sex	Maternal: prepregnancy BMI, age at birth, parity, education, smoking during pregnancy, breastfeeding duration. Child: birth weight & BMI	HCB and obesity RR=8.14 (1.85, 35.81); HCB and abdominal obesity RR= 3.49 (1.08, 11.28); DDE and abdominal obesity RR= 3.76 (1.70, 8.30).	1) Lack of postnatal exposure measurement at other time points. 2) socioeconomics as unmeasured covariates 3)lack of multiple comparisons since some outcomes are inter-correlated
Warner, 2019	Italy	611 offspring Sevesco Second Generational Study Mothers	2014	Average of 23.7 y (range: 2-39yrs)	TCDD	Overweight as BMI ≥25kg/m2 and <30kg/m2, Obese as ≥30 kg/m2; #MetS	Maternal age at explosion, age at pregnancy, smoking during pregnancy, BMI, hypertension family history. Child: age, sex, and smoking. Primary wage-earner education.	In sons only, maternal TCDD was associated with increase risk of metabolic syndrome adj-RR=2.09 (1.09, 4.02).	1) participation rate of 66.4% 2) reliance on a modeled estimate of maternal TCDD at the time of pregnancy is likely a source of exposure misclassification

Fleisch, 2017	U.S.A.	665 Mother-Child pairs, Mothers part of Project Viva in Boston, Massachusetts, 9.6 (median) weeks gestation	1999-2002	7.7 y	PFASs (PFOA, PFOS, PFNA, PFHxS, and PFDeA)	Leptin, adiponectin, fasting insulin and glucose levels, ₸HOMA-IR	Maternal: age, education. Child: age, sex, & race/ethnicity. Neighborhood census tract at mid-childhood (median household income, percent below poverty).	No evidence of adverse effect of early-life PFAS exposure on metabolic function in mid-childhood. Children with higher PFAS concentrations had lower insulin resistance.	1) Generalizability is limited to study's' cohort
Manzano-Salgado, 2017	Spain	1,154 Children at 6 months, 1,230 Children at 4y, 1,086 Children at 7y	2003–2008	7 y	PFHxS, PFOS, PFOA, PFNA	Overweight as BMI z-score ≥85th percentile, WC, BP. Only at 4y: HDL-C,LDL-C, TGs, ##Cardiometabolic-risk (CM-risk)	Maternal: region of residence, country of birth, parity, prepregnancy BMI, previous breastfeeding, age at follow-up. Child: age & sex	Prenatal PFAS concentrations were not associated with individual outcomes or the combined CM-risk score.	1)Fasting blood samples were inconsistent per study regions 2)lipid levels only measured in subset of sample at 4y 3) CM-Risk score doesn't include glucose homeostasis 4) possible interaction between PFOA and BMI z-scores at 4y & 7y with longer breastfeeding duration

Warner, 2017	U.S.	240 child-mother pairs Gestation at <20 wks CHAMACOS cohort	1999-2000	12 y	o,p′-DDT, p,p′- DDT, and p,p′-DDE - samples taken at 26 weeks gestation (n = 215) or delivery (n = 25)	Overweight as BMI-z scores between ≥85th and <95th percentile, obese as BMI-z-scores ≥95th percentile, increased WC as≥ 90th percentile	Maternal: prepregnancy BMI, years in the U.S. at childbirth, puberty age	At 12 years, boys only Obesity and o,p'-DDT RR=1.46 (1.07, 1.97), obesity and p,p'-DDT RR=1.28 (1.01, 1.64), Obesity and p,p'-DDE RR=1.35 (0.98, 1.87). In 12y old boys only: Increased WC and o,p'-DDT RR=1.53 (1.53, 2.10), increased WC and p,p'-DDT RR=1.36 (1.05, 1.76),increased WC and p,p'-DDE RR=1.39 (0.97, 1.98)	1) Limited number of children with anthropometric measures. 2) No collection of comprehensive dietary and physical activity data
Warner, 2014	U.S.	261 child-mother pairs Gestation at <20 wks CHAMACOS cohort	1999-2000	9 y	o,p′-DDT, p,p′- DDT, and p,p′-DDE - samples taken at 26 weeks gestation (n = 242) or delivery (n = 19)	Overweight as BMI-z scores between >85th and <95th percentile, obese as BMI-z-scores ≥ 95th percentile, WC, percent body fat	Maternal prepregnancy BMI, time in the U.S. at birth	Boys only- overweight/ obese: o,p0-DDT, adj OR = 2.5 (1.0, 6.3), p,p0-DDT, adj OR = 2.1 (1.0, 4.5), p,p0-DDE, adj OR = 1.97, (0.94, 4.13). Increased WC odds: o,p′-DDT adj OR= 1.98 (0.95, 4.11), p,p′-DDT adj OR = 2.05 (1.10, 3.82)	1) Limited number of children with anthropometric measures. 2) Percentage of body fat not standardized for age or sex.

Tang-Péronard, 2014	Faroe Islands	539 child-mother pairs Singleton births	November 1997-March 2000	5-7y	PCBs and DDE Maternal blood collected at 34 wk gestation. Breast milk collected 4–5 d after parturition.	Overweight as WC >62.12 cm in boys and> 61.86 cm in girls, obesity as WC > 69.53 cm in boys and > 69.70 cm in girls	Maternal: BMI, age, & parity,	Estimates for PCBs in 4th quartile and WC in girls with normal weight mothers = 1.25 (0.04, 2.45) P=0.04; Estimate for PCBs in 4th quartile and WC in girls with overweight mothers= 2.48 (1.10, 3.85) P=0.001. Estimate for DDE and WC in girls with overweight mothers= 2.21 (0.84, 3.56). No associations seen in boys.	**1)** Seafood diet not taken into account.
Tang-Péronard, 2015	Faroe Islands	520 child-mother pairs Singleton births	November 1997-March 2000	5y & 7y	PCBs, DDE, & HCB - Collected at 34 wks gestation. Breast milk collected 4-5d after parturition.	Non-fasting Insulin levels, Leptin	maternal age, parity, prepregnancy BMI, BMI at 5y of age, time of day blood sampling	Girls only- PCBs 4th quartile and high non-fasting insulin OR=3.71 (1.36, 10.010); DDE 4th quartile and high non-fasting insulin OR=2.75 (1.09, 6.90); HCB 4th quartile and high non-fasting insulin OR=1.98 (1.06, 3.69) compared to lowest quartile.	Fasting blood samples not collected

Høyer, 2015	Greenland and Kharkiv (Ukraine)	1,023 mother–child pairs Singleton births INUENDO cohort	May 2002-February 2004	5-9y	PFOA, PFOS -Blood sample taken at a mean (± SD) gestational of 24 ± 10 weeks	Overweight BMI z-score > 1 SD, **WHtR > 0.5 high risk	Maternal: age at birth, parity, smoking, education, prepregnancy BMI, country of residence. Child: age and sex.	WHtR >0.5 and PFOA adj. RR=1.30 (0.97, 1.74), WHtR > 0.5 and PFOS adj. RR=1.38 (1.05, 1.82)	Inconsistent measuring equipment used, large number of missing data, possible exposure misclassification
Mendez, 2011	Spain	518 child-mother pairs First trimester of pregnancy	2004-2006	14 months	DDE, HCB, β-HCH, & PCBs (118, 138, 153, & 180).	Overweight as BMI z-scores ≥1.44, corresponding to the 85th percentile	gestational age, breast-feeding at 6m, firstborn; maternal: smoking, education, age at delivery	DDE was associated with elevated BMI at 14 months RR = 1.50 (1.11, 2.03)	1) BMI-z scores and growth were used and no direct measures of adiposity were used. 2) maternal exposure measurements were taken only in early pregnancy 3) modest sample size 4) short follow-up time
Cupul-Uicab, 2013	U.S.	1,915 children Collaborative Perinatal Project Maternal samples collected at 3rd trimester & delivery Singleton live-births	1959-1965	7y	β-HCH, p,p´-DDE, p,p´-DDT, dieldrin, heptachlor epoxide, HCB, transnonachlor, oxychlordane, & PCBs congeners	Overweight as BMI z-scores >90th percentile, obese as BMI z-scores >97th percentile	Maternal: race, education, socioeconomic index, prepregnancy BMI, smoking. Child birth order, child's age	Obesity with dieldrin exposure OR= 3.6 (1.3, 10.5) for the fourth quintile and 2.3 (0.8, 7.1) for the highest quintile. Overweight and BMI were not associated with DDE, DDT, HCB, or PCB exposure	1) Interactions (i.e., exposure with maternal smoking and child's sex) were not replicated in the present study. 2)Only high levels of exposure were measured in this study (lower levels of not measured)

					(28, 52, 74, 105, 118, 138, 153, 170, 180, 194, & 203)				
Valvi, 2012	Spain	344 child-mother pairs 20w gestation	1997-1998	6-7y	Umbilical cord blood -DDE, DDT, HCB, & PCBs congeners (28, 52, 101, 118, 138, 153, 180)	Overweight BMI z-score ≥ 85th percentile	Child: birth weight. Maternal: pregnancy BMI, smoking during pregnancy, parity, education, social class, age, breast-feeding duration.	Overweight and PCB exposure in 3rd tertile RR=1.70 (1.09, 2.64), overweight and DDE exposure in 2nd tertile R= 1.67 (1.10, 2.55). Associations between overweight and PCB and DDE exposure were stronger in girls than in boys.	1) Small sample size 2) cord blood lipid concentrations only in a subgroup of children (n = 90), and thus OC concentrations were not lipid adjusted.
Valvi, 2014	Spain	1285 child-mother pairs First-trimester	2003-2008	6m & 14m	DDE, HCB, & PCB congeners (153, 138, 180)	Overweight as BMI z-score ≥85th percentile	Maternal: serum lipid content, country of origin, social class, age at delivery, prepregnancy BMI, smoking during pregnancy. Infant: sex, exact age at 6-	At 14m of age- Overweight and DDE RR=1.15 (1.03, 1.28), overweight and HCB RR=1.19 (1.05, 1.34).	1) BMI and weight as indirect measures of total body fat 2) exposure dilution may differ among infants

							month exam. Gestational age, exclusive breastfeeding duration.		
Braun, 2016	U.S.	204 child-mother pairs 16+/- 3 wk gestation	March 2003-Januar y 2006	8y	Maternal blood samples at 16-26wk gestation -PFOA, PFOS, PFNA, & PFHxS	Overweight/ obesity as BMI z-scores ≥85th percentile, WC, body fat percentage	Urinary BPA, breastfeeding duration, weekly gestational weight gain. Maternal: age, race, education, parity, employment, marital status, depressive symptoms, BMI at 16 wks gestation, fruit/vegetable consumption, fish consumption, prenatal vitamin use, serum cotinine concentrations. Child: age,	PFOA 2nd tercile and overweight/obesity adj. RR=1.84 (0.97, 3.50); PFOA 3rd tercile and overweight/obesity adj. RR=1.54 (0.77, 3.07)	1) limited adiposity measurements 2) small sample size

WC: waist circumfernece, IOTF: International Obesity Task Force, SBP: systolic blood pressure, DBP: diastolyc blood pressure, WHtT: Waist-to-height ratio

#MetS defined as:presence of three or more of the following: (1) WC≥80 cm (female) or≥ 94 cm (male); (2) elevated TGs≥ 150 mg/dL or current use of TGs treatment; (3) HDL-C <50 mg/dL (female) or <40 mg/dL (male) or current use of HDL-C reducing treatment; (4) SBP≥ 130 mmHg, DBP≥ 85 mmHg, or current use of antihypertensive medication; (5) fasting glucose≥ 100 mg/dL or current use of diabetes med-ication.
Cardiometabolic risk defined as: the sum of the standardized z -scores for WC, BP, and the mean of the HDL-C and TG z-scores, with HDL-C multiplied by− 1
**WHtR high risk for cardiometabolic morbidity
Ŧ insulin resistance by calculating the HOMA-IR as [fasting glucose (mg/dL) × fasting insulin (mU/L))/405]

Table 3.0 Summary of effect estimates per study and POPs

Study	**Exposure chemical**	**Adj. RR**	**Adj. OR**	**Beta estimates**	**Major POP Category**	**Outcome measurement**
Vafeiadi, 2015	HCB	3.49			OC	Abdominal obesity
	DDE	3.76			OC	Abdominal obesity
Warner et al, 2017	o,p'-DDT	1.46			OC	overweight/obesity only in boys
	p,p'-DDT	1.28			OC	overweight/obesity only in boys
	p,p'-DDE	1.35			OC	overweight/obesity only in boys
Warner et al, 2014	o,p0-DDT		2.5		OC	overweight/obesity only in boys
	p,p0-DDT		2.1		OC	overweight/obesity only in boys
	p,p0-DDE		1.97		OC	overweight/obesity only in boys
Mendez et al, 2011	DDE	1.5			OC	overweight
Cupul-Uicab et al, 2013	Dieldrin		3.6		OC	obesity
Valvi et al, 2014	DDE	1.15			OC	overweight
	HCB	1.19			OC	overweight
Braun et al, 2016	PFOA	1.84			PFASs	overweight/obesity
Høyer et al, 2015	PFOA	1.30			PFASs	Waist-to-height-ratio
	PFOS	1.38			PFASs	Waist-to-height-ratio
Warner, 2019	TCDD	2.09			Dioxin	Met Syn
Valvi et al, 2012	PCBs	1.7			PCBs	overweight
Tang-Péronard, 2015	PCBs		3.71		PCBs	Insulin only in girls
	DDE		2.75		OC	Insulin only in girls
	HCB		1.98		OC	Insulin only in girls
Tang-Péronard, 2014	PCBs#			2.48	PCBs	WC
	PCBs*			1.25	PCBs	WC
	DDE#			2.21	OC	WC
Fleisch, 2017	PFASs	Not sig			PFASs	fasting insuling
Manzano-Salgado, 2017	PFASs	Not sig			PFASs	Cardiometabolic risk

HCB: Hexachlorobenzene, DDE: Dichlorodiphenyldichloroethylene, DDT: Dichlorodiphenyltrichloroethane, PFOA: Perfluorooctanoic acid, PFOS: Perfluorooctanesulfonic acid, TCDD: 2,3,7,8-Tetrachlorodibenzodioxin, PCBs: Polychlorinated biphenyls
#Overweight mothers
*****Normal weight mothers