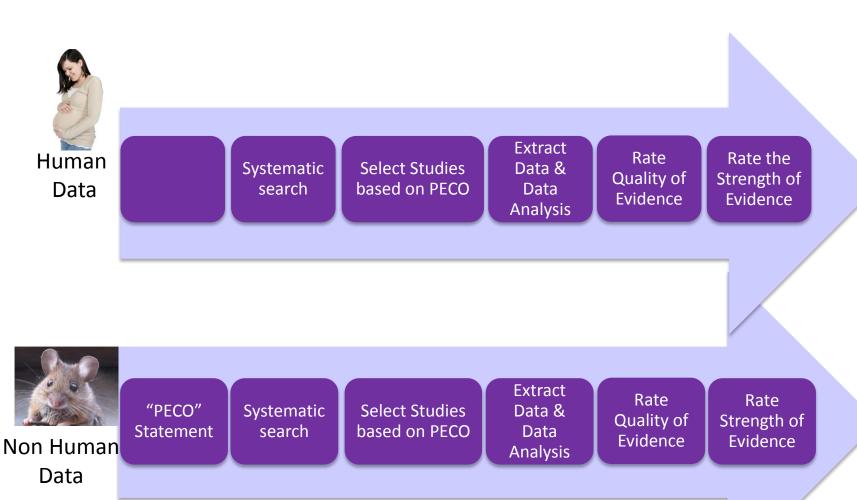


# Pathways to Implementation of the NRC Recommendations

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# Identify evidence more transparently and efficiently



Program on Reproductive Health and the Environment

## **Rate Quality of Evidence**

• Risk of Bias

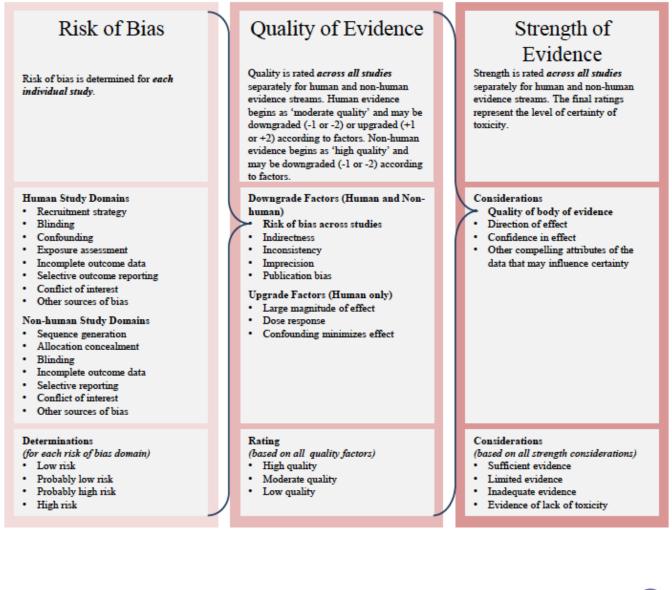


• Rating quality of evidence



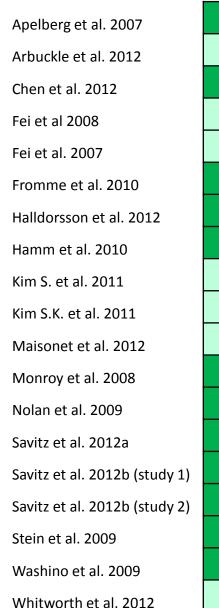
**COLLABORATION®** 

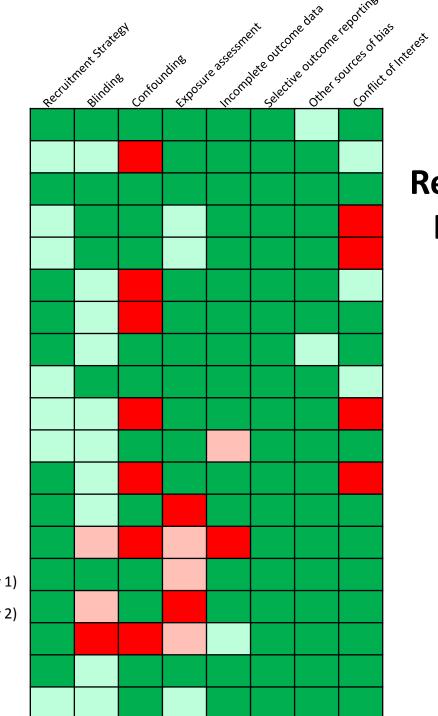
#### Figure 1. Evaluating Study Quality and Strength of Evidence



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#### Lam et al. EHP 2014





#### Results: Risk of Bias Human Evidence N=19

For individual studies (N=19)

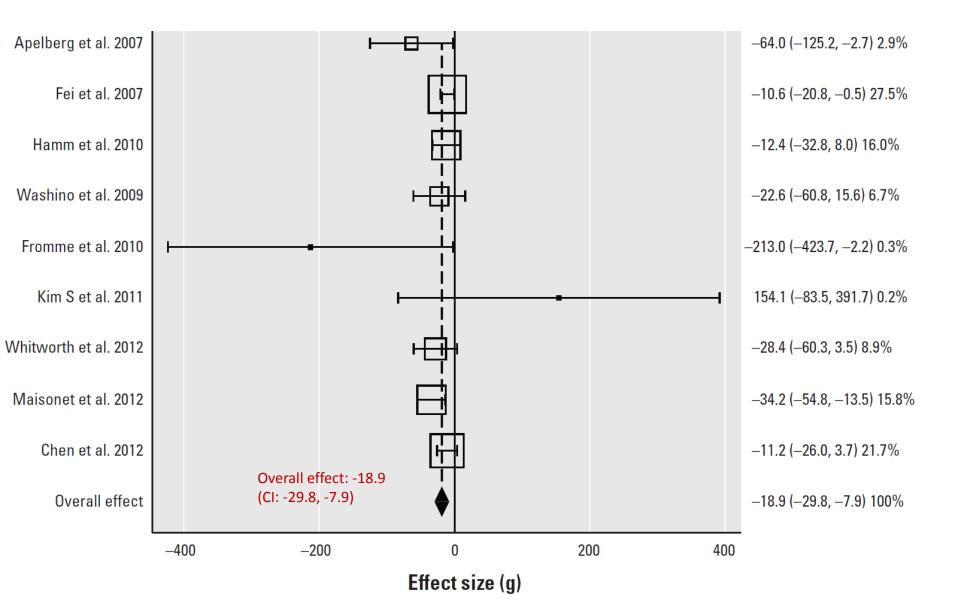
Low risk	
Probably low risk	
Probably high risk	
High risk	
N/A	

## Individual Studies for PFOA & BW

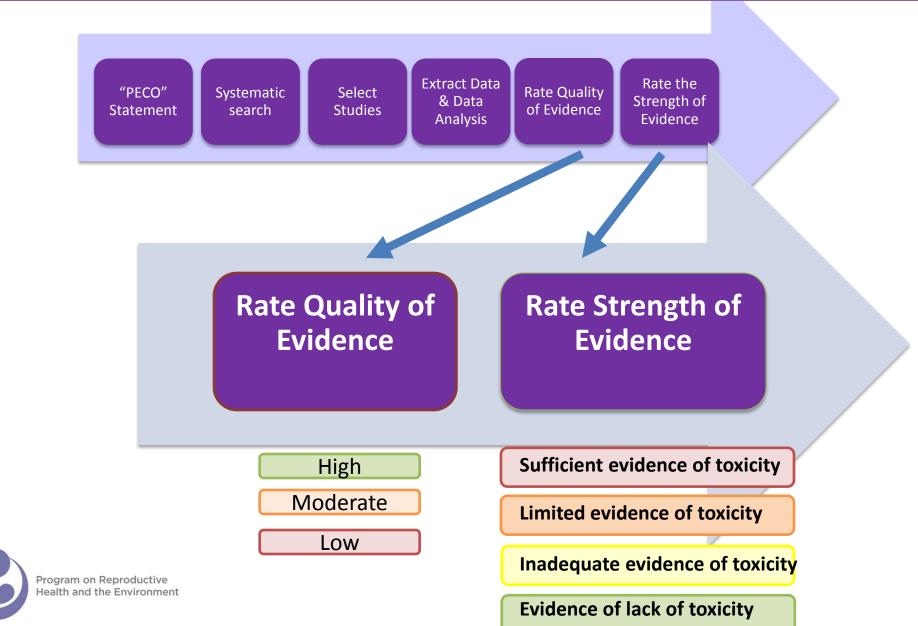
Study	PF0A increase	PFOA range (ng/mL)	Covariates					
Apelberg et al. 2007 Apelberg et al. 2007 Apelberg et al. 2007 Apelberg et al. 2007 Apelberg et al. 2007	In ng/mL In ng/mL 25th to 75th percentile 25th to 75th percentile ng/mL	0.3–7.1 0.3–7.1 1.2–2.1 1.2–2.1 0.3–7.1	ga ga, ma, bmi, race, par, smk, sex, ht, wtg, dia, hyp ga ga, ma, bmi, race, par, smk, sex, ht, wtg, dia, hyp ga, ma			ŀ		
Chen et al. 2012 Chen et al. 2012	In ng/mL ng/mL	geomean(stdev) = 1.84(2.23) geomean(stdev) = 1.84(2.23)	ga, ma, bmi, par, cot, sex, edu, delmode ga, ma				⊨ ei	
Fei et al. 2007 Fei et al. 2007	ng/mL ng/mL	< LLOQ - 41.5 < LLOQ - 41.5	ga, ma, bmi, par, smk, sex, SES, gabd ga, ma, bmi, par, smk, sex, SES, gabd, PFOS				H	
Fromme et al. 2010	ng/mL	0.54-4.20	None				<u> </u>	
Hamm et al. 2010 Hamm et al. 2010 Hamm et al. 2010 Hamm et al. 2010	In ng/mL ng/mL 1st to 2nd tertile (ng/mL) 1st to 3rd tertile (ng/mL)	< LOD-18 < LOD-18 < LOD- < 1.1 to 1.1-2.1 < LOD- < 1.1 to > 2.1-18	ga, ma, race, grav, mwt, matht, smk, sex ga, ma, race, grav, mwt, matht, smk, sex ga, ma, race, grav, mwt, matht, smk, sex ga, ma, race, grav, mwt, matht, smk, sex					
Kim S et al. 2011	ng/mL	0.4–3.23	ga, ma, par				<u>⊢ </u>	
Maisonet et al. 2012 Maisonet et al. 2012 Maisonet et al. 2012	1st to 2nd tertile 1st to 3rd tertile ng/mL	< 3.1 to 3.1–4.4 < 3.1 to > 4.4 1.0–16.4	ga, bmi, par, smk ga, bmi, par, smk ga, bmi, par, smk					
Nolan et al. 2009 Nolan et al. 2009	Low to mid exposure Low to high exposure	NA NA	ga, ga2, ga3, ma, race, sex, SES ga, ga2, ga3, ma, race, sex, SES					
Savitz et al. 2012b, study II Savitz et al. 2012b, study II	25th to 75th IQR (In PFOA) 100 ng/mL PFOA 1st/2nd quintile to 3rd quintile 1st/2nd quintile to 4th quintile 1st/2nd quintile to 5th quintile	1.92 100 ng/mL 3.9- < 8.9 to 8.9 - < 19.6 3.9- < 8.9 to 19.6-53.1 3.9- < 8.9 to 53.1-1897.0	ga, ma, par, edu, smk, exposyr, state ga, ma, par, edu, smk, exposyr, state					
Washino et al. 2009 Washino et al. 2009 Washino et al. 2009	log10PF0A log10PF0A ng/mL	ND-5.3 ND-5.3 ND-5.3	ga ga, ma, bmi, race, par, smk, sex, edu, bsp ma, ga					
Whitworth et al. 2012 Whitworth et al. 2012 Whitworth et al. 2012 Whitworth et al. 2012	ng/mL 1st to 2nd quartile 1st to 3rd quartile 1st to 4th quartile	median (IQR) = 2.2(1.6–3.0) < 1.65 to 1.65–2.24 < 1.65 to 2.25–3.03 < 1.65 to > 3.03	ga, ma, bmi, par ga, ma, bmi, par ga, ma, bmi, par ga, ma, bmi, par					
<ul> <li>β Estimat</li> </ul>	te Δβ Estimate included in me	ta-analysis ■βEstimate tha	at can be used to evaluate dose response	-500	-400	-300	-200 -100 0 100 200 300	400

Change in birth weight (g)

#### Meta-analysis for Birth Weight (n=9 studies)



#### Rate the Quality and Strength of the Evidence



## Summary of Quality of Evidence for PFOA



N/A N/A	
N/A	
NI / A	
N/A	
0	
0	
0	
0	
-1	
e High	
Non-human mammalian	
Evidence Stream	

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9

## Strength of Evidence Human Evidence = "Sufficient"

#### **CRITERIA:**

- 1. Quality of evidence: Moderate
- 2. What is the direction of effect? Decrease in fetal growth with PFOA exposure
- 3. What is the confidence in the effect? A new study would be unlikely to change the certainty in the direction of the effect
- 4. Are there other compelling attributes of the data that influence certainty?

The available evidence includes consistent results from well-designed, well-conducted studies and the conclusions are unlikely to be strongly affected by the results of future studies. A positive relationship was observed between exposure and outcome where chance, bias and confounding can be ruled out with reasonable confidence.

Used criteria and considerations used by IARC, the U.S. Preventive Services Task 269 Force, and U.S. EPA for

Sufficient evidence of toxicity

# Summary of Recommendations for Systematic Review Methods

- 1. Doable!
- 2. Protocol (prespecified approach) is essential
- 3. Apply consistent, systematic approach for evaluating each evidence stream separately, then integrate
- 4. Build off existing methods for a structured, complete and transparent methodology for integrating evidence:

OHAT/ Navigation Guide/GRADE

5. Support infrastructure and research





# Thank you





