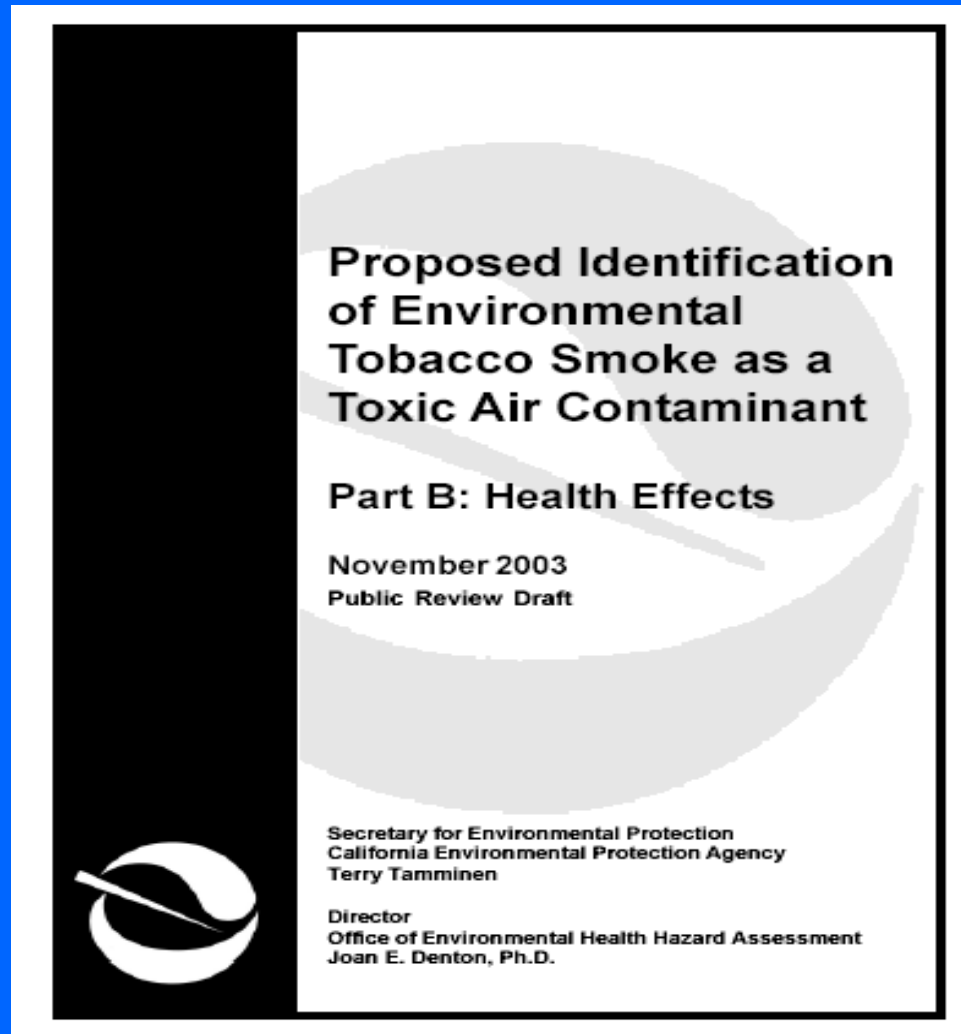


ETS: Health Effects



Effects Causally Associated with ETS Exposure

- **Developmental Effects**
 - **Fetal Growth: LBW and decrease in birthweight**
 - **Sudden Infant Death Syndrome (SIDS)**
- **Respiratory Effects**
 - **Acute LRTI in children (*e.g.*, pneumonia)**
 - **Asthma in children and adults**
 - **Chronic respiratory symptoms in children**
 - **Eye and nasal irritation in adults**
 - **Middle ear infections in children**
- **Carcinogenic Effects**
 - **Lung, nasal sinus, and breast cancer**
- **Cardiovascular Effects**
 - **Heart disease morbidity and mortality**
 - **Altered vascular properties**



Effects with Suggestive Evidence of a Causal Association with ETS Exposure

- **Developmental Effects**
 - Spontaneous abortion, preterm delivery, IUGR
 - Adverse impact on cognition and behavior
 - Allergic sensitization
- **Respiratory Effects**
 - Exacerbation of cystic fibrosis
 - Decreased pulmonary function growth
 - Chronic respiratory symptoms in adults
- **Carcinogenic Effects**
 - Cervical cancer
 - Brain cancer and lymphomas in children



Chemical compounds in tobacco smoke for which IARC found sufficient evidence of carcinogenicity in animals and/or humans

Aliphatic hydrocarbons	Aldehydes	acetamide
butadiene	acetaldehyde	acrylonitrile
Aromatic hydrocarbons	formaldehyde	4-aminobiphenyl
benzene	Nitrogen Compounds	<i>ortho</i> -anisidine
benz[a]anthracene	4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)	hydrazine
benzo[b]fluoranthene		1,1-dimethylhydrazine
benzo[j]fluoranthene	N'-nitrosodimethylamine	2-naphthylamine
benzo[k]fluoranthene	N-nitrosodiethylamine	2-nitropropane
benzo[a]pyrene	N-nitrosodi-n-propylamine	<i>ortho</i> -toluidine
dibenz[a,h]anthracene	N-nitrosodi-n-butylamine	urethane
dibenzo[a,e]pyrene	N-Nitroso-N-methylethylamine	Halogen compounds
dibenzo[a,h]pyrene		DDT
dibenzo[a,i]pyrene	N'-nitrosornicotine	vinyl chloride
dibenzo[a,l]pyrene	N-nitrosodiethanolamine	Inorganic elements
indeno[1,2,3-cd]pyrene	N-nitrosopyrrolidine	arsenic
5-methylchrysene	N-nitrosopiperidine	cadmium
naphthalene	dibenz[a,h]acridine	chromium VI
catechol	dibenz[a,j]acridine	lead
	7H dibenzo[c,g]carbazole	nickel



Calculation of Attributable Risks and Excess Cases Associated with ETS (SIDS example)

- $A = p(R-1)/[p(R-1)+1]$ (Lilienfeld & Lilienfeld, 1980)
- $p = 11.4\%$ children 1-17 yrs exposed to ETS at home (California Tobacco Survey; DHS 2001)
- $R = \text{SIDS OR} = 1.94 (1.55; 2.43)$ (Anderson and Cook, 1997)
- $A = 0.114(1.94-1)/[0.114(1.94-1)+1] = 0.097$
- SIDS deaths in CA in 2000 = 222 (CA DHS, 2001)
- Excess death attributable to ETS = 21
($222 \times 0.097 = 21$)



Attributable Risks Associated with ETS

	Conclusion OEHHA 1997		Conclusion OEHHA 1997		Conclusion Update		Conclusion Update	
Outcome	Excess # in CA		Excess # in US		Excess # in CA		Excess # in US	
Pregnancy LBW	1,200	2,200	9,700	18,600	1,577		24,253	
PTD					1,943		29,590	
Cardiac death	4,200	7,440	35,000	62,000	1,713	5,483	22,669	69,553
Lung cancer: Death	360		3000					
Incidence					411	1,514	7,564	26,473
Asthma children					Episodes		Episodes	
New cases	960	3,120	8,000	26,000	29,424	46,695	438,933	669,295
Exacerbation	48,000	120,000	400,000	1,000,000				
Lower respiratory illness	18,000	36,000	150,000	300,000	N/A		N/A	
Otitis media visits	78,600	188,700	700,000	1,600,000	51,690		789,712	
SIDS	120		1,900 2,700		21		431	

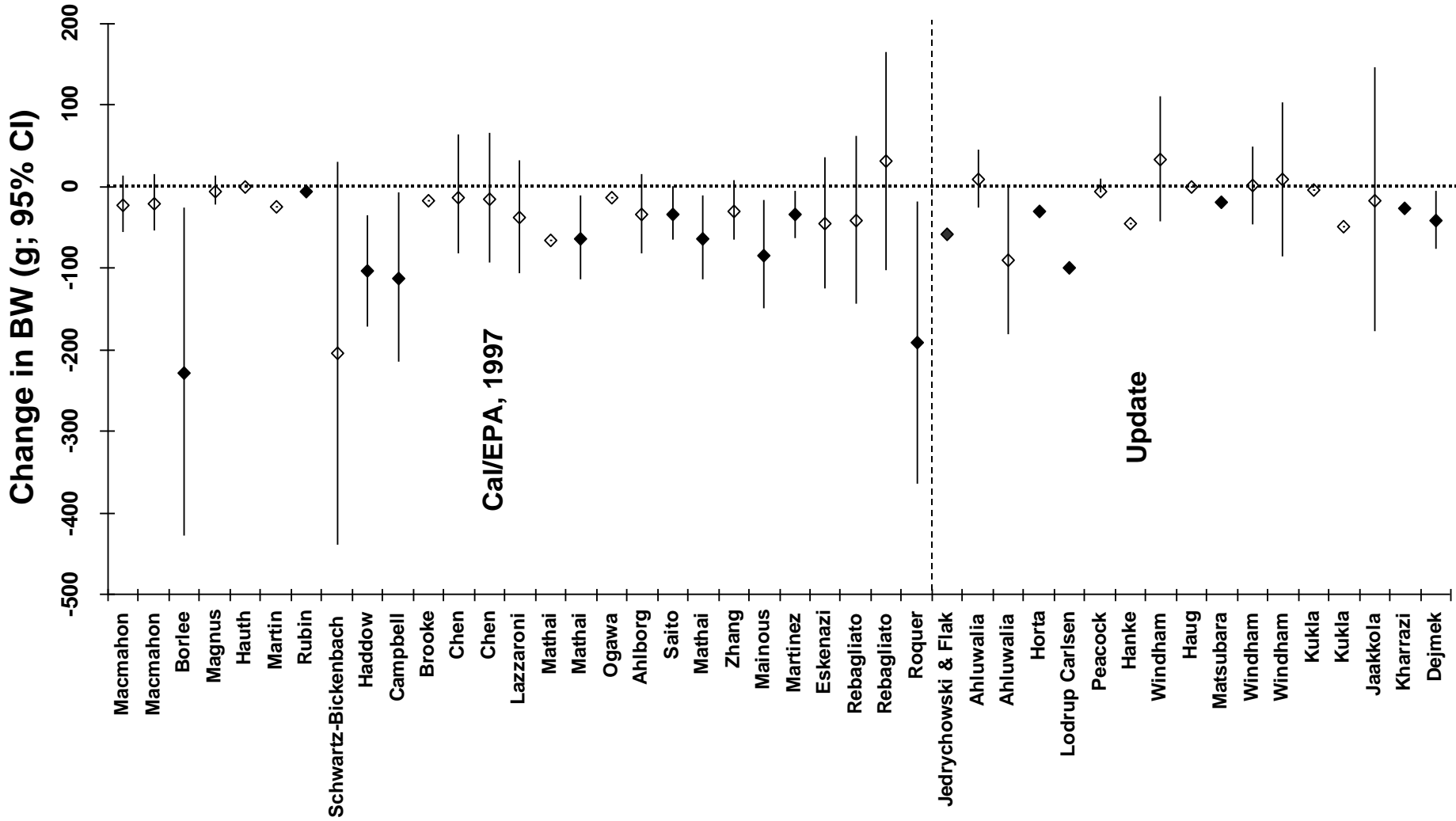


Developmental Toxicity 1: Perinatal Manifestions

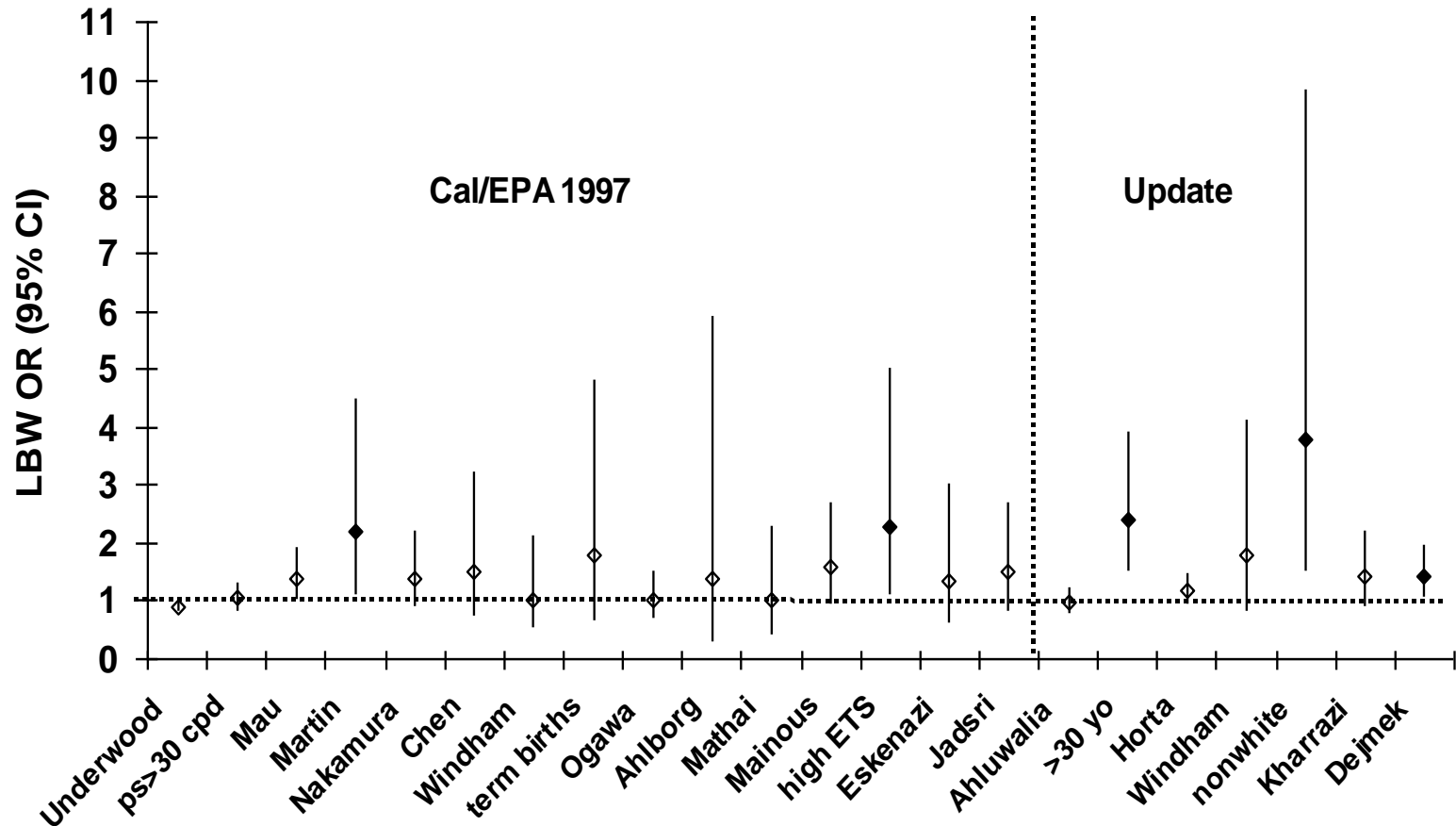
Out come	# Studies 1997	# Studies Update	Findings: OEHHA 1997 Evidence of causal association	Findings: Update Evidence of casual association
BW	24	15	Conclusive	Conclusive (strengthened)
LBW	13	9	Conclusive	Conclusive (strengthened)
PTD	6	4	Suggestive	Suggestive (strengthened)
IUGR	5	7	Suggestive	Suggestive (strengthened)
SAB	5	2	Inconclusive	Inconclusive
Malformations	5	6	Inconclusive	Inconclusive



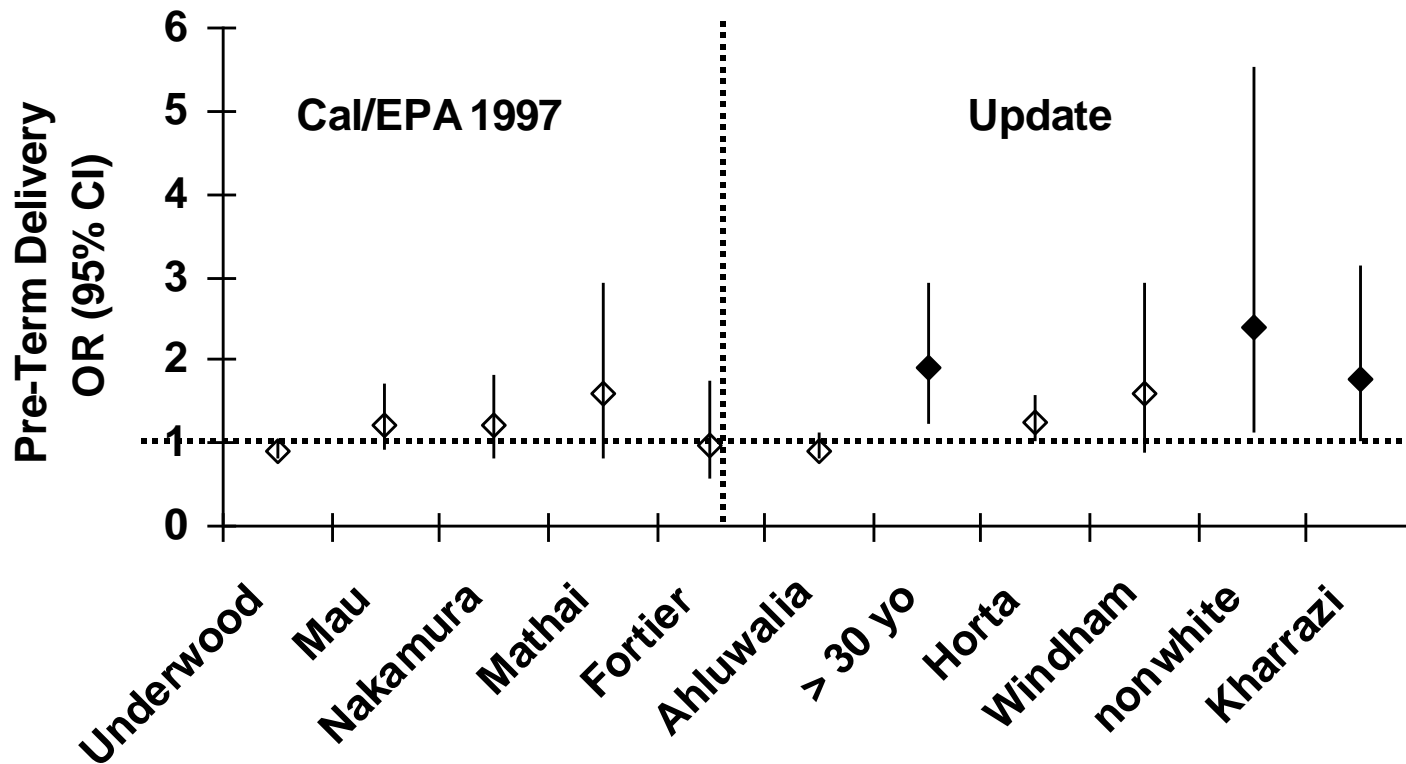
Effects of ETS on Birth Weight



ETS and Risk of Low Birth Weight



ETS and Risk of Preterm Delivery



Prospective study of maternal serum cotinine and birth outcomes. (Kharrazi 2001; n=2815)

Central Valley, state of the art laboratory, cotinine measured at 15-19 weeks

Maternal cotinine

Change in birth weight

< 1.0 ng/ml

-30 g

>1.0 ng/ml

-100 g

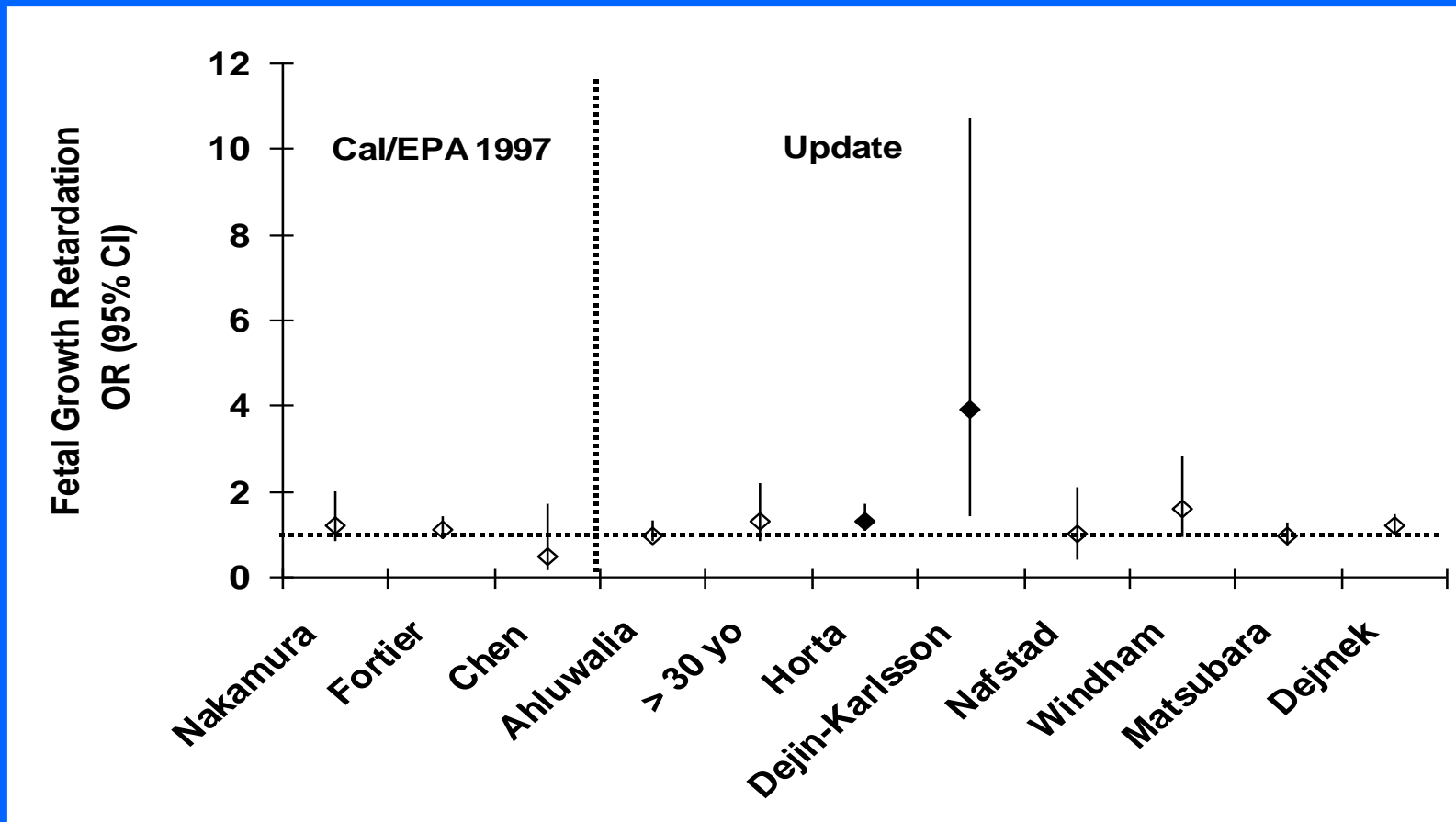
>0.05 ng/ml

OR adverse outcome
1.36 (1.07; 1.72)

preterm delivery 1.78 (1.01; 3.13)



ETS and Risk of Fetal Growth Retardation (IUGR, SGA)



SIDS and Postnatal Development

Outcome	# Studies 1997	# Studies Update	Findings: OEHHA 1997 Evidence of causal association	Findings: Update Evidence of causal association
SIDS	10	9	Conclusive	Conclusive (strengthened)
Cognition and Behavior	11	3	Suggestive	Suggestive
Postnatal physical development	5	0	Inconclusive	Unchanged
CNS changes	0	2	Not assessed	Suggestive (animal model)
Cardiovascular Hematological Immune	0	6	Not assessed	Suggestive

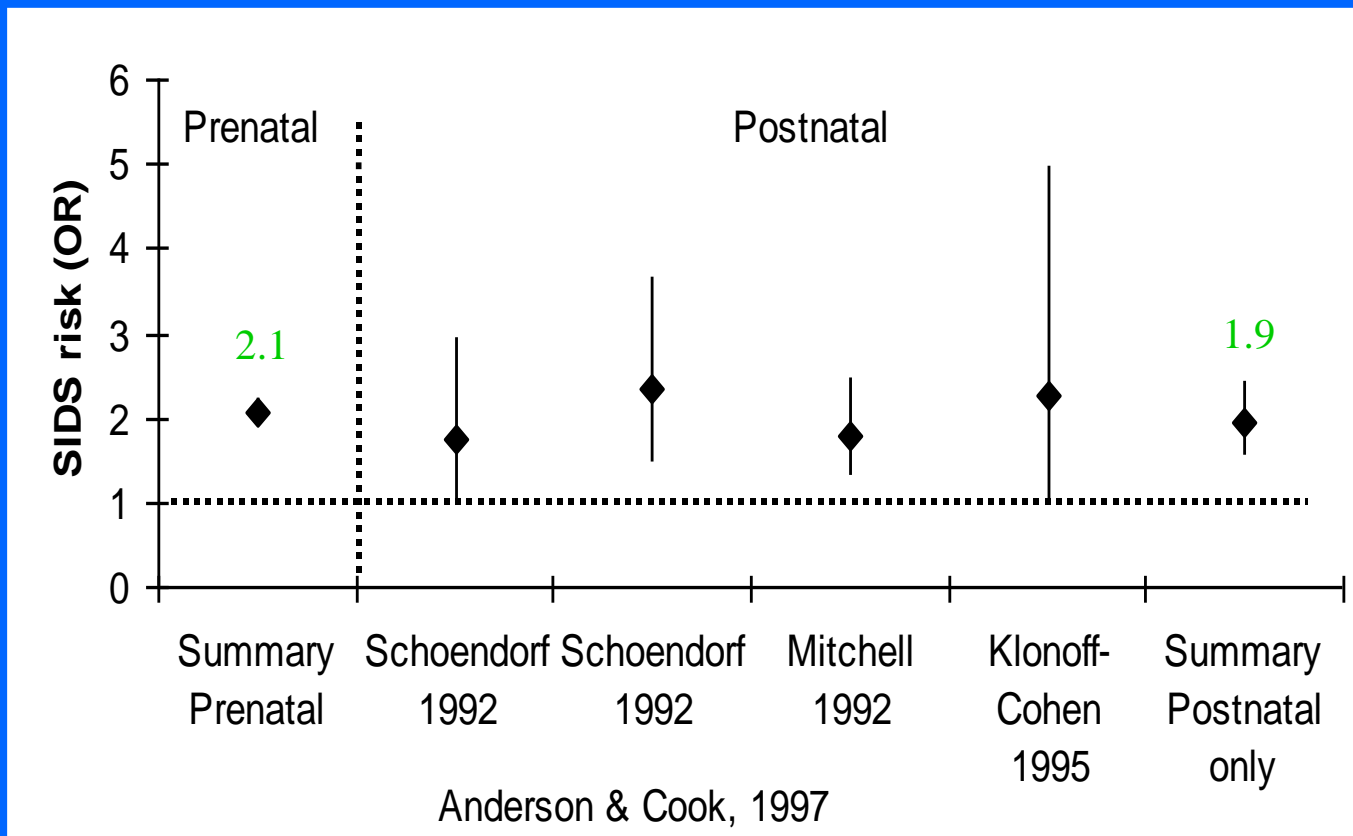


What is SIDS?

- **SIDS is the sudden unexplained death of an infant under one year of age.**
- **It is the leading cause of death in infants between 1 month and 1 year of age**
- **In California in 2000 there were 222 SIDS deaths out of 2,884 infant deaths from all causes.**
- **Excess SIDS deaths attributable to ETS = 21**



SIDS Risk from Maternal Smoking Pre- and Postnatal; Postnatal Only



Reproductive Health Effects

Outcome	# Studies 1997	# Additional Studies in Update	Finding OEHHA 1997 Evidence of causal association?	Findings Update Evidence of causal association?
Fertility or fecundability	8	5	Inconclusive	Suggestive
Lower age at Menopause	2	1	Inconclusive	Inconclusive
Menstrual cycle Disorders	0	3	Inconclusive	Suggestive
Male reproductive dysfunction	0	1	Inconclusive	Inconclusive



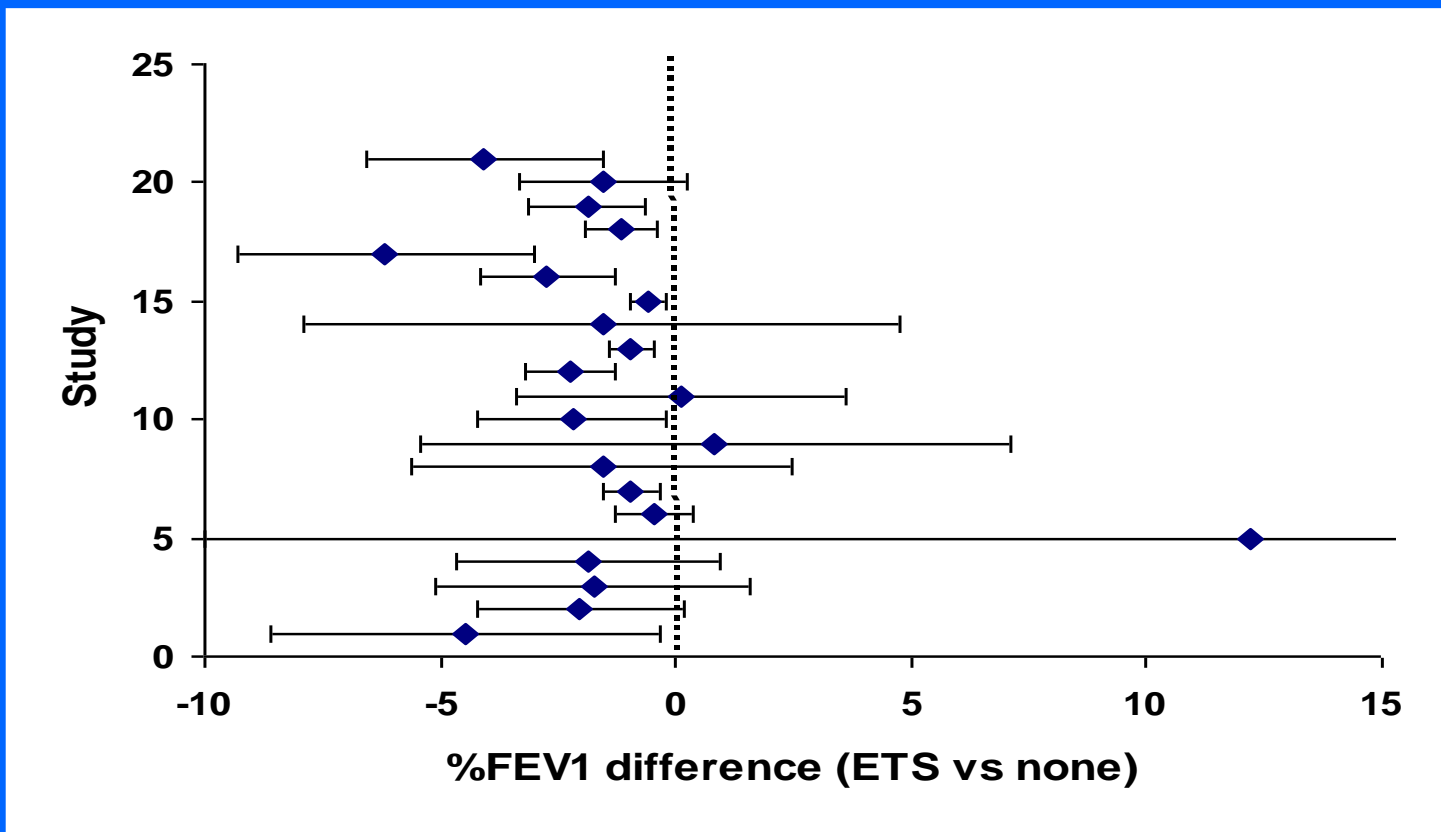
Respiratory Health Effects

Out come	# Studies 1997	# Studies Update	Findings: OEHHA 1997 Evidence of causal association	Findings: Update Evidence of casual association
Asthma (child) exacerbation (adult)	8 4	12 8	Conclusive Suggestive	Conclusive Conclusive
Respiratory illness	0	6	Conclusive	Conclusive
Otitis media ± infusion	22	7	Conclusive	Conclusive
Sensory irritation and annoyance	18	15	Conclusive	Conclusive
Asthma (child) induction (adult)	37 2	28 9	Conclusive Suggestive	Conclusive Conclusive
Lung (child) development	8	6	Suggestive	Suggestive
Respiratory (child) symptoms (adult)	6	4	Conclusive Suggestive	Conclusive Suggestive (strengthened)



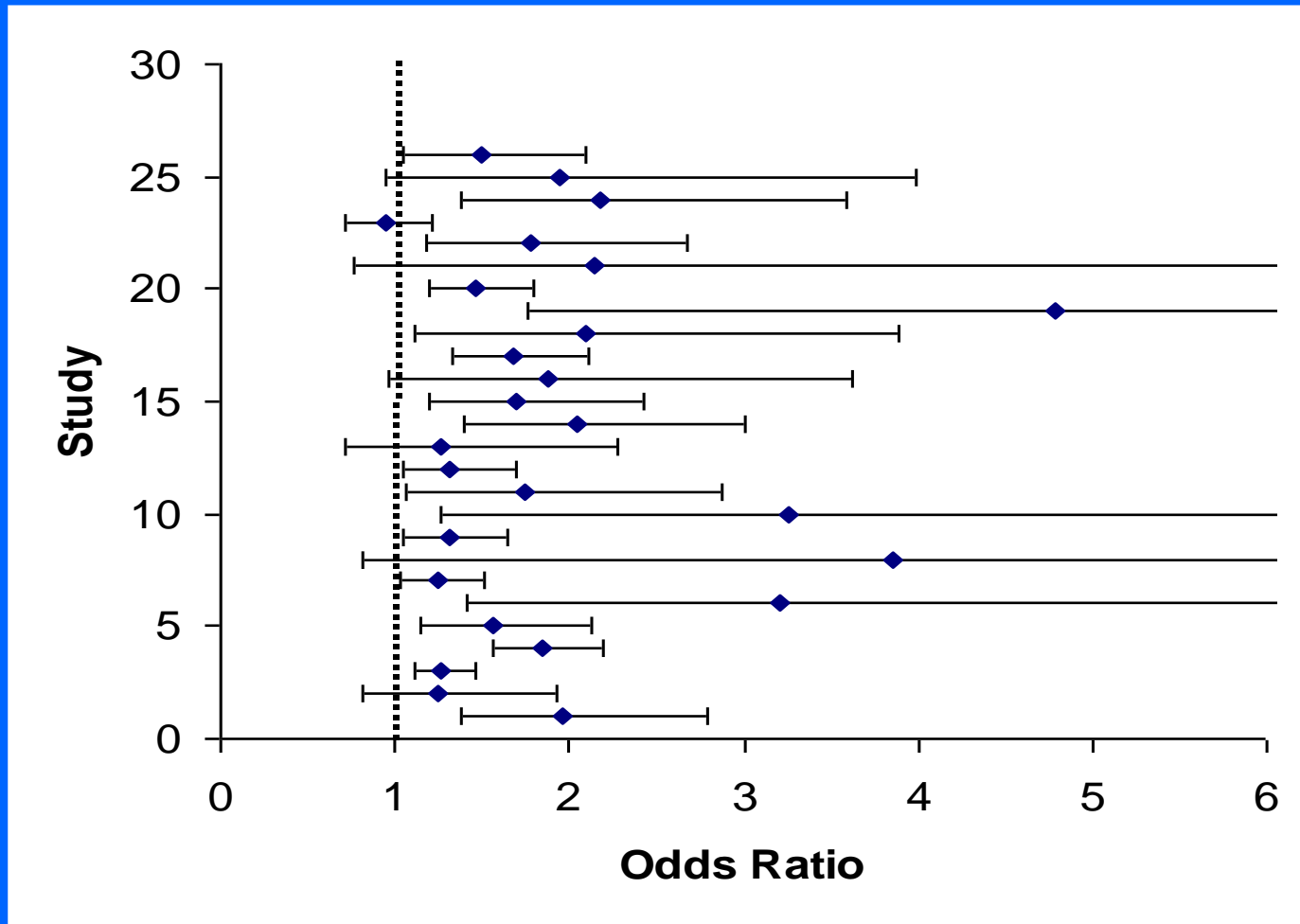
FEV₁ Decreased in School Children with ETS Exposure (Cook et al. 1998)

Meta-analysis of 21 studies



Effects of Either or Neither Parent Smoking on Respiratory Illness

Meta-analysis of 38 studies (Strachan and Cook, 1997)



Meta-analysis of 13 studies of ETS and lower respiratory tract infections (LRT) in children.

Li et al. 1999	Pre/postnatal Overall	LRT 1.93 (1.66; 2.25)	ETS associated with LRT mainly in younger kids. Postnatal only data from Chinese studies where mothers didn't smoke.
	0 2 yrs old	1.71 (1.33; 2.20)	
	0 6 yrs old	1.57 (1.28; 1.91)	
	3 6 yrs old	1.25 (0.88; 1.78)	
	Postnatal only	2.13 (1.52; 3.00)	



Doctor Consultations for Respiratory Symptoms by Number of Smokers

10,402 children ages 8-13 years in Hong Kong (Data fr. Peters *et al.*, 1998)

Household smokers	Cough OR (95% CI)	Phlegm OR (95% CI)	Wheeze OR (95% CI)	Any symptom OR (95% CI)	
None	1	1	1	1	
One	1.15 (1.01; 1.32)	1.26 (1.02; 1.54)	1.04 (0.76; 1.41)	1.15 (1.01; 1.31)	Cost 13% higher
Two or more	1.33 (1.08; 1.64)	1.33 (0.97; 1.83)	1.57 (1.02; 2.43)	1.38 (1.14; 1.67)	Cost 28% higher
Trend by # smokers	P < 0.01	P < 0.05	NS	P < .001	



ETS

Carcinogenic Effects



Outcome	# Studies 1997	#Additional Studies in Update	Findings OEHHA 1997 Evidence of causal association?	Findings Update Evidence of causal association?
All cancers Adult	5	0	Suggestive	Unchanged*
Childhood Mother (smoker)	7	5	Inconclusive	Inconclusive
Father (smoker)	1	5	Inconclusive	Suggestive
Lung	19	17	Conclusive	Conclusive (strengthened)
Breast	4	13	Inconclusive	Conclusive
Nasal sinus	3	3	Conclusive	Conclusive (strengthened)
Cervical	4	0	Suggestive	Unchanged
Bladder	2	0	Inconclusive	Unchanged
Stomach	1	2	Inconclusive	Inconclusive
Brain Adult	3	0	Inconclusive	Unchanged
Brain Children	10	12	Inconclusive	Suggestive**
Leukemia Childhood	8	6	Inconclusive	Inconclusive
Lymphomas	6	4	Inconclusive	Suggestive (in children)



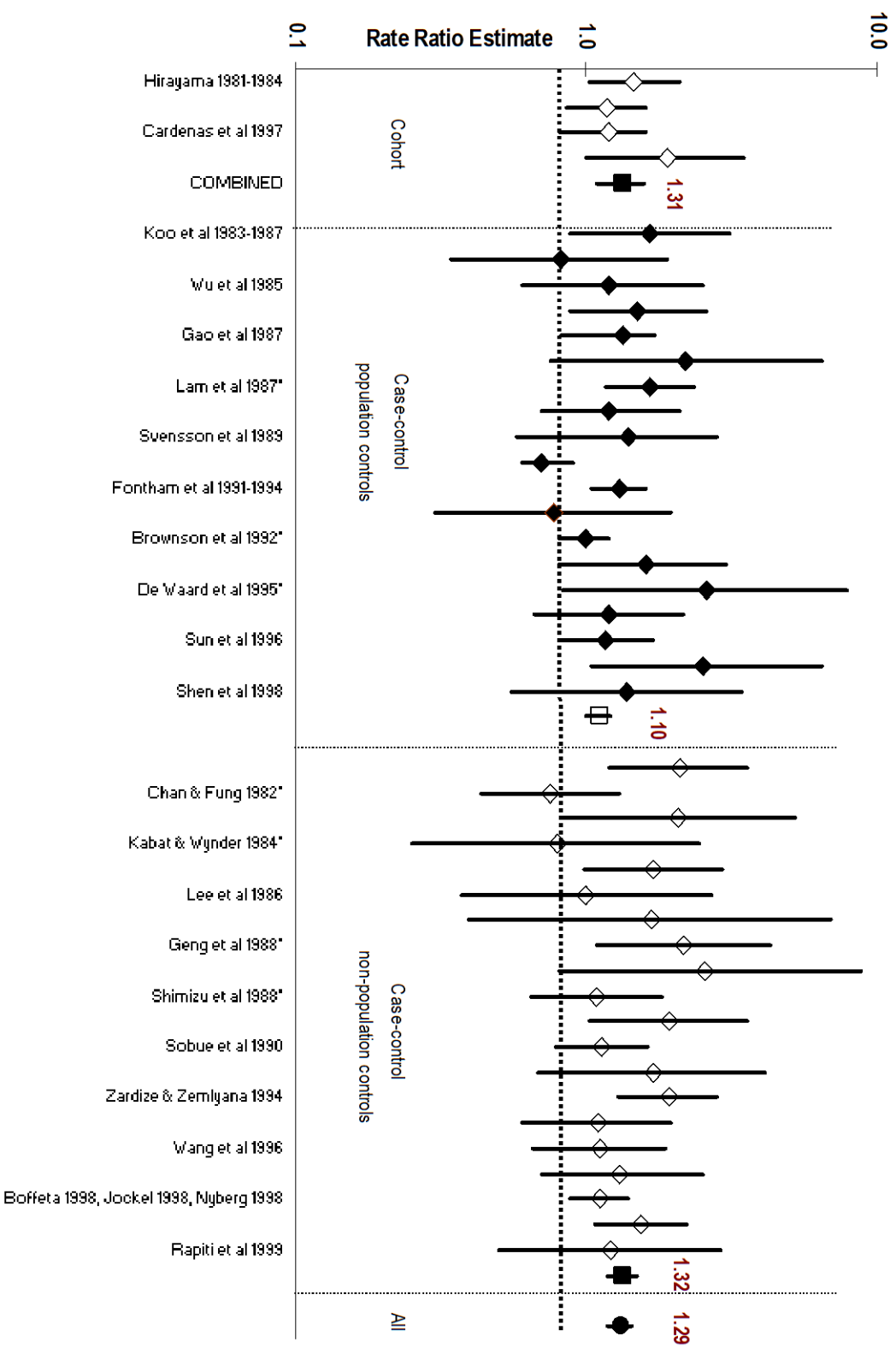
Lung Cancer

- Consistently report elevated and often significant risk estimates (particularly for women married to smokers)
- Several recent studies provided evidence of positive increasing trends with increased exposure
- Misclassification of exposure in the “unexposed” populations in some studies by not measuring lifetime exposure results in biasing results to the null



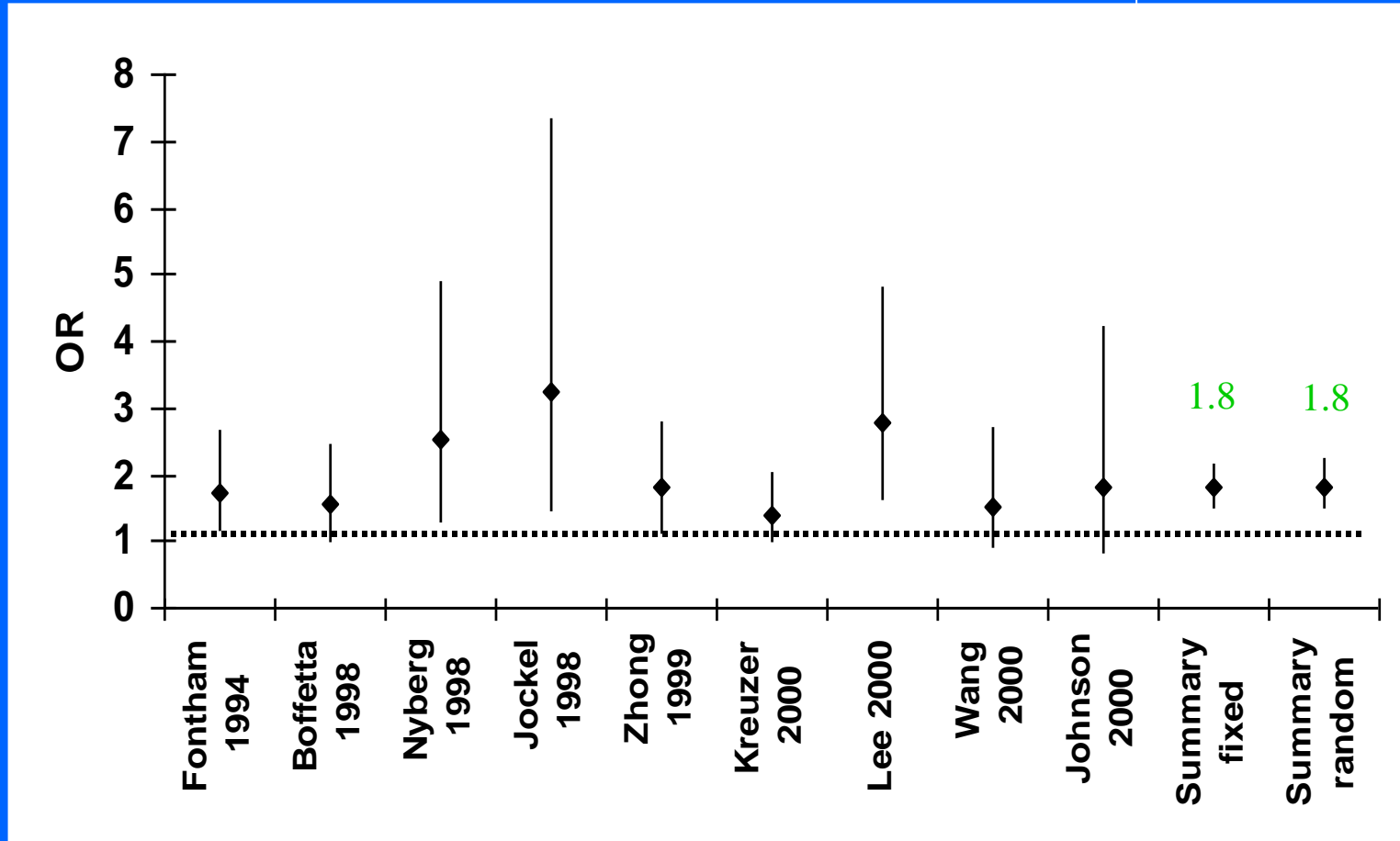
Lung Cancer Meta-analysis

(Based on Data from Taylor *et al.*, 2000)



ETS and Lung Cancer Risk in Never Smokers

Population-based studies that include quantitative adult lifetime residential and occupational assessment of ETS exposure (based on Johnson 2000)



OEHHA 1997

Problems Determining Breast Cancer Association with ETS

- The effect seen in active smokers was comparable to (or weaker than) those noted in passive smoking
 - Active smokers are also passive smokers
- No dose response trends were evident in the data
- There was uncertainty about the suggestion that tobacco smoke may effect the risk of breast cancer only in certain susceptible groups of women

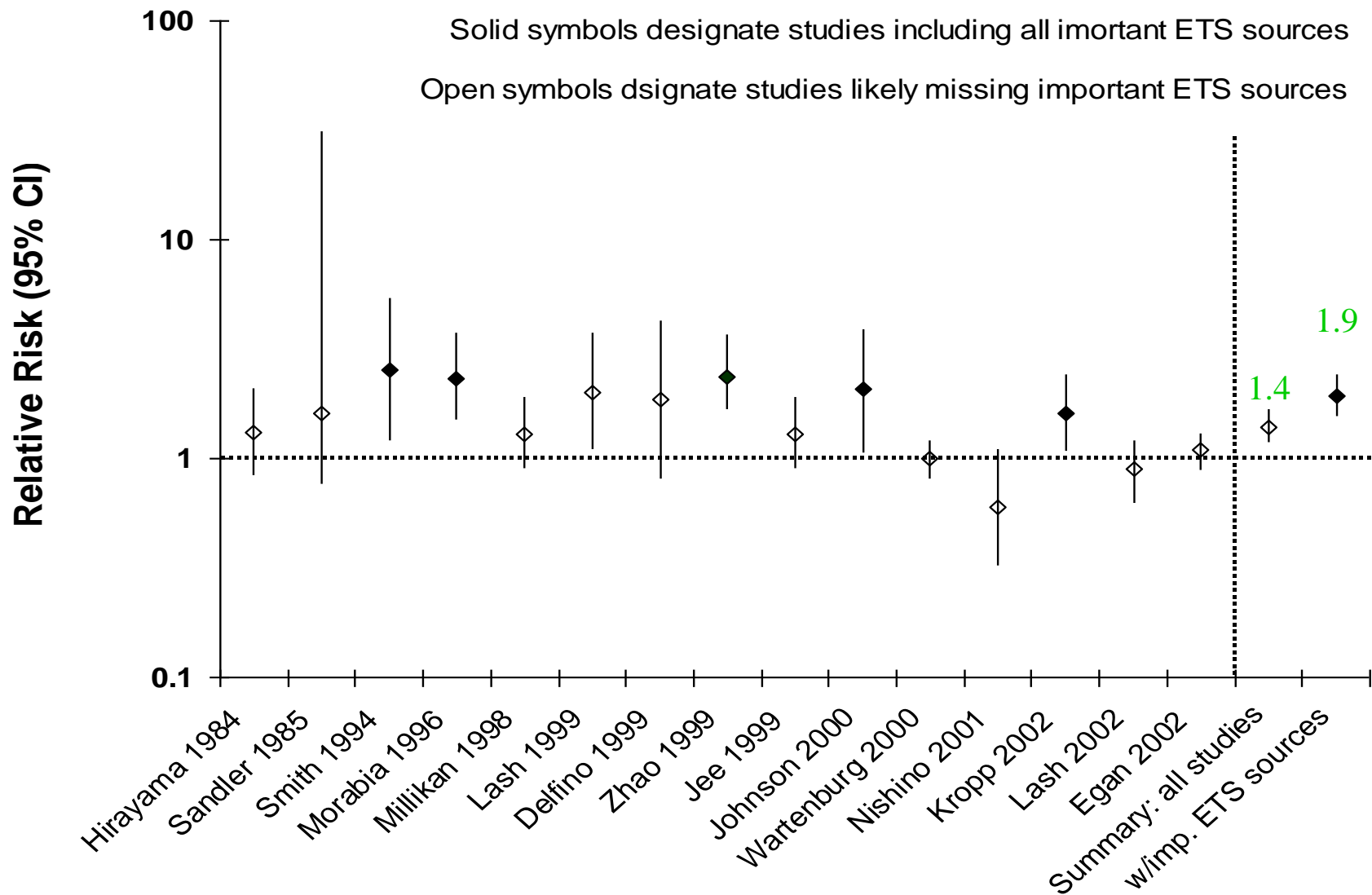


Hypothesis Examined in Literature That May Help Explain Earlier Finding

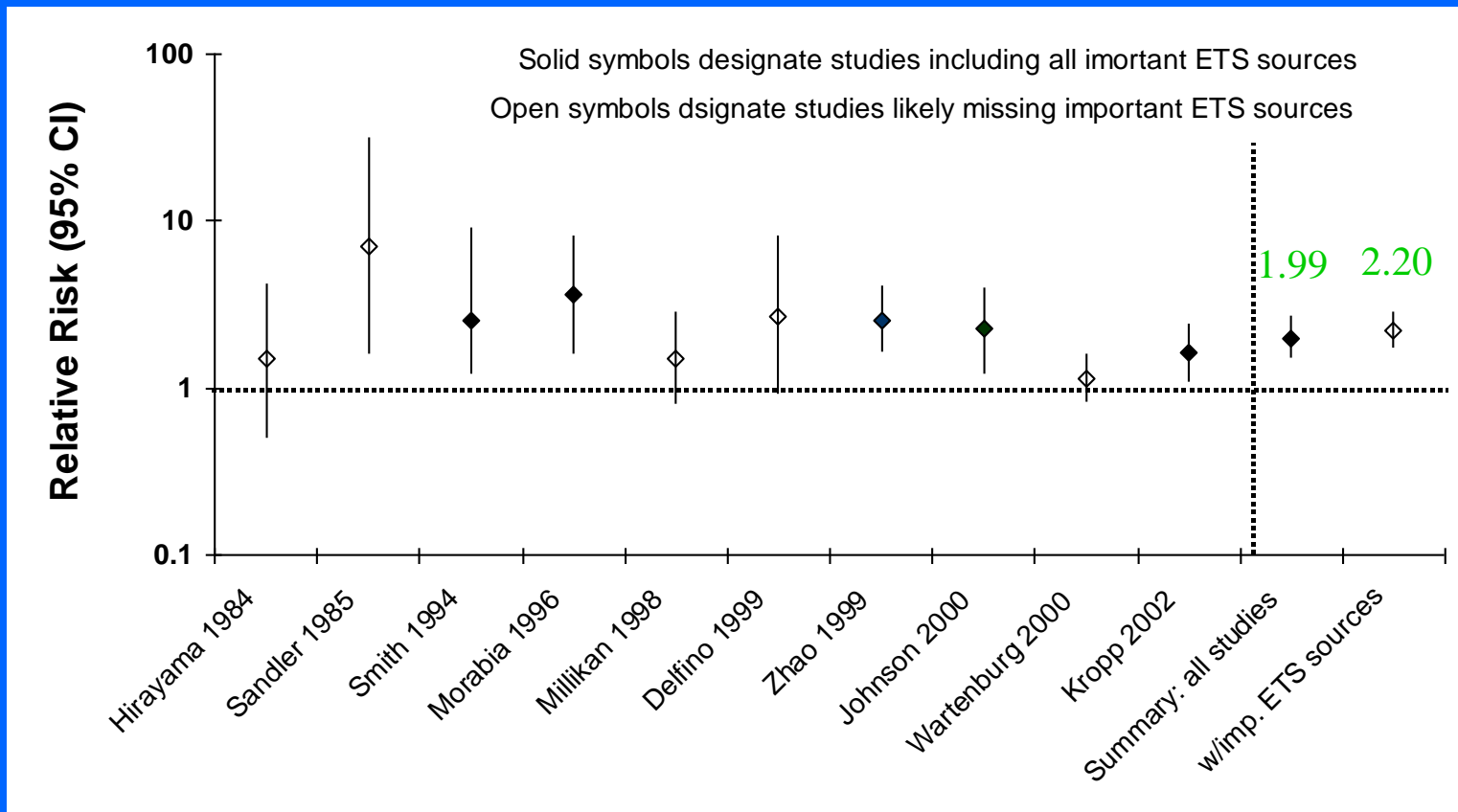
- Causal preventive effects from current active smoking
 - (eg. anti-estrogenicity) may obscure any overall association between smoking and breast cancer.
- Risk similar for active/passive exposure
 - Need unexposed cohort
- Sensitive subpopulations
 - Polymorphisms
 - windows of susceptibility (ie. Before 1st preg.)
- Exposure > 30 to 40 yrs.
 - Difficult to find as women smokers less common earlier in century



Summary estimates for passive smoking and overall breast cancer risk



Summary risk estimates for ETS and premenopausal breast cancer



Cardiovascular Health Effects

Outcome	# Studies 1997	# Studies Update	OEHHA 1997 Evidence of causal association?	Findings Update Evidence of causal association?
CHD	18	8	Conclusive	Conclusive (strengthened)
Altered vascular properties	6	8	Suggestive	Suggestive (strengthened)
Exercise tolerance	4	0	Suggestive	Unchanged
Stroke	0	1	Not assessed	Suggestive

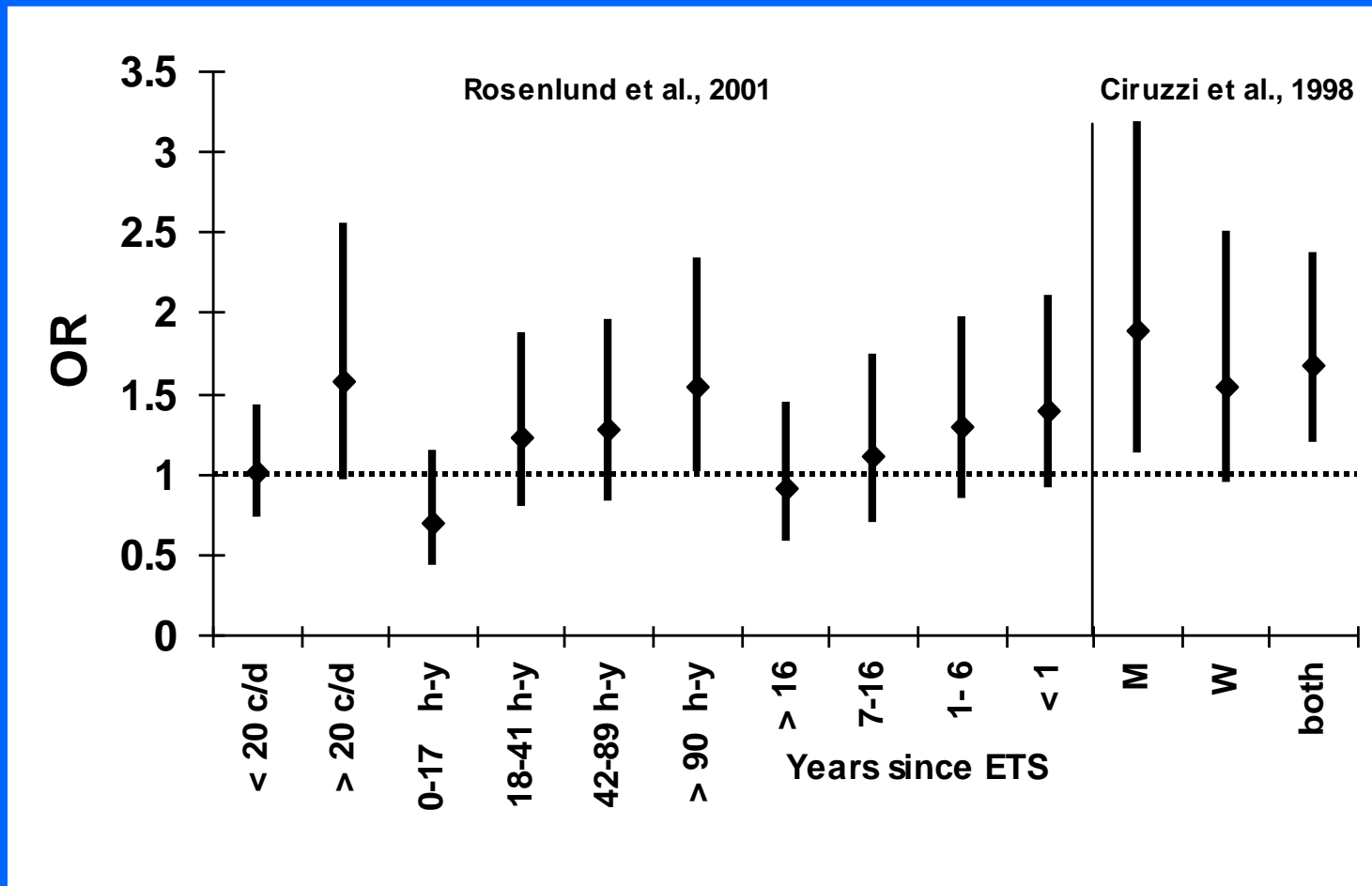


ETS Cardiovascular Effects

- **Multiple insults – Interrelated effects**
 - Myocardial infarction
 - Endothelial dysfunction
 - Thickening of the carotid wall
 - Loss of arterial elasticity
 - Promotion of plaque formation
- **Blood changes**
 - Decreased HDL Cholesterol
 - Decreased anti-oxidant capacity
 - Increased oxidized lipids
 - Increased platelet activation
 - Increased fibrinogen levels
 - Decreased oxygen carrying capacity
- **CVD risk of 20-50%**
- **Ischemic stroke risk of 70- 90%**



Risk of Myocardial Infarction



Future Actions

End of April —————> **Respond to public comments**

Early May —————> **Revise report**

June/July —————> **SRP meeting**

Summer —————> **ARB public Hearing**

