

Integrating Evidence Streams – Ozone and Asthma Exacerbation

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Ozone Webinar

Texas Commission on Environmental Quality


March 20, 2015

NAAQS Process for Causal Determination

Step	Description
1	Literature searching
2	Selection of studies for inclusion
3	Consideration of general limitations of each study type
4	Use of modified Bradford Hill aspects to aid in judging causality
5	Evaluate evidence for major health outcome categories
6	Integrate evidence from across disciplines and across health endpoints
7	Weight alternative views on controversial issues
8	Characterize strength of evidence into casual conclusions
9	Assess adversity of effects

Weight-of-Evidence Evaluation Approach

1 Define causal question
Develop study selection criteria



2 Develop and apply criteria for review of
individual studies

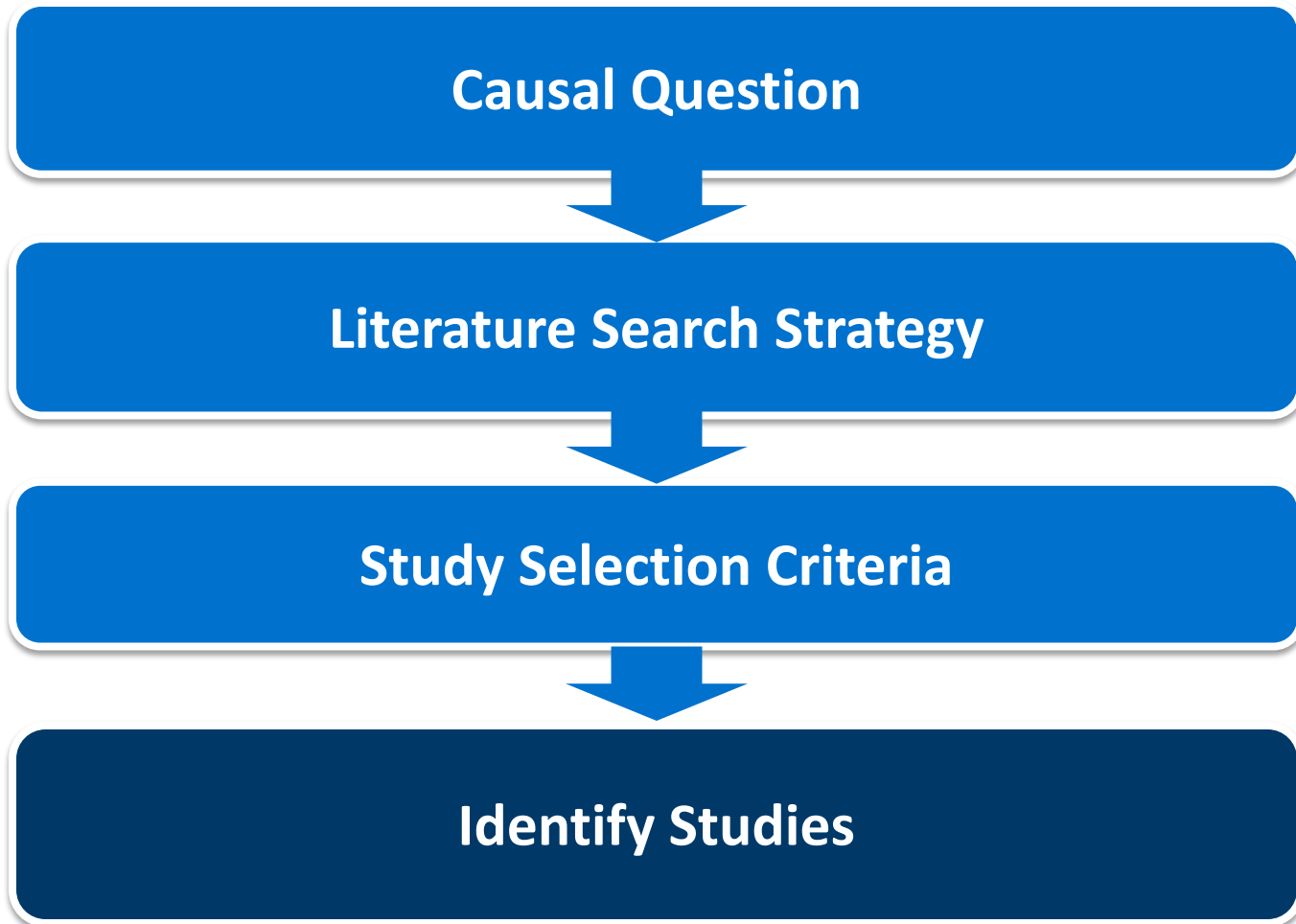


3 Integrate and evaluate evidence



4 Draw conclusions based on inferences

Short-term Ozone and Asthma



Casual Question

**Does short-term
ozone exposure
exacerbate asthma?**

Literature Search

Epidemiology

"ozone"[MeSH Terms] OR "ozone"[All Fields]) AND ("asthma"[MeSH Terms] OR "asthma"[All Fields])

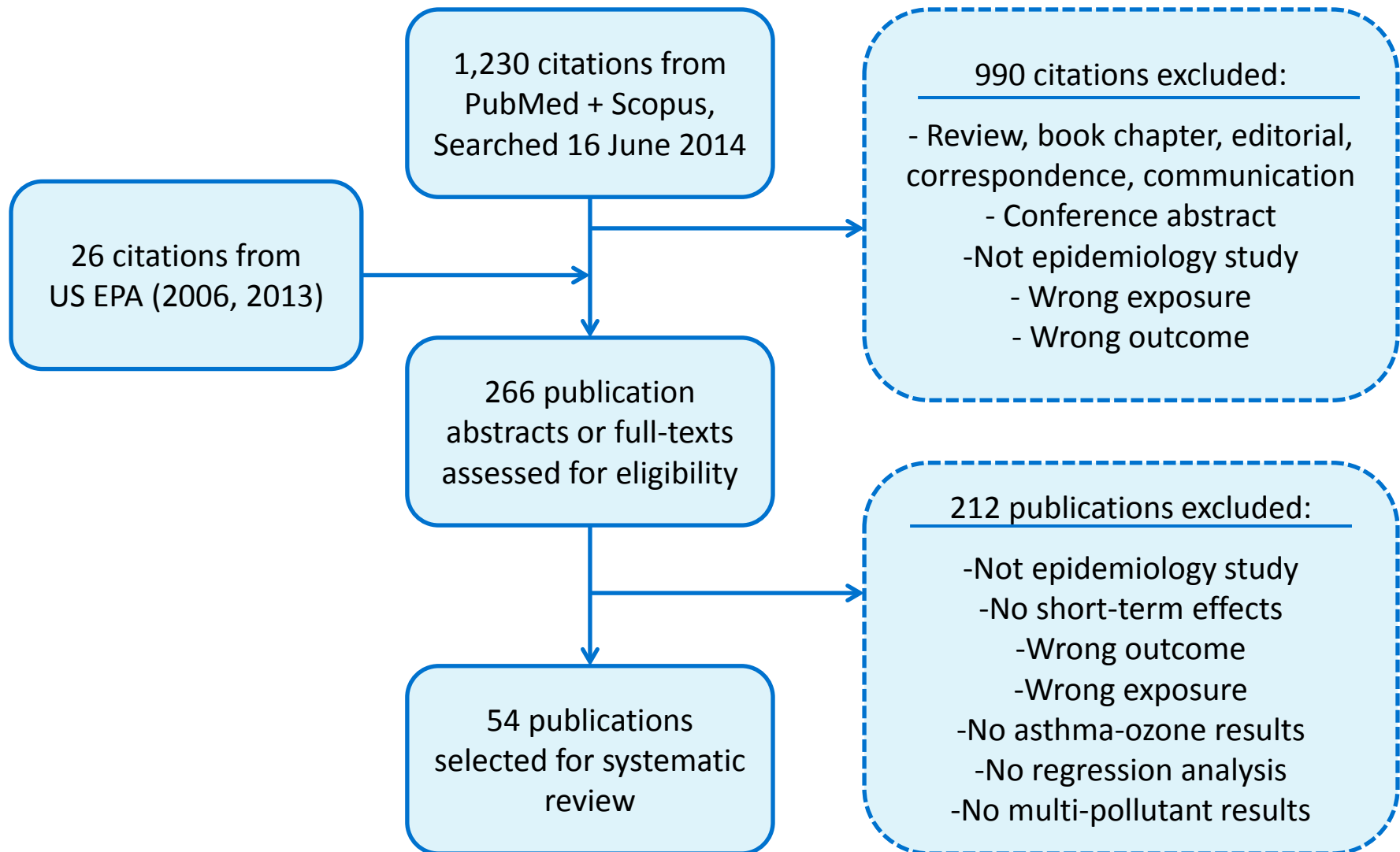
Controlled human exposure

"ozone"[MeSH Terms] OR "ozone"[All Fields]) AND ("asthma"[MeSH Terms] OR "asthma"[All Fields]).

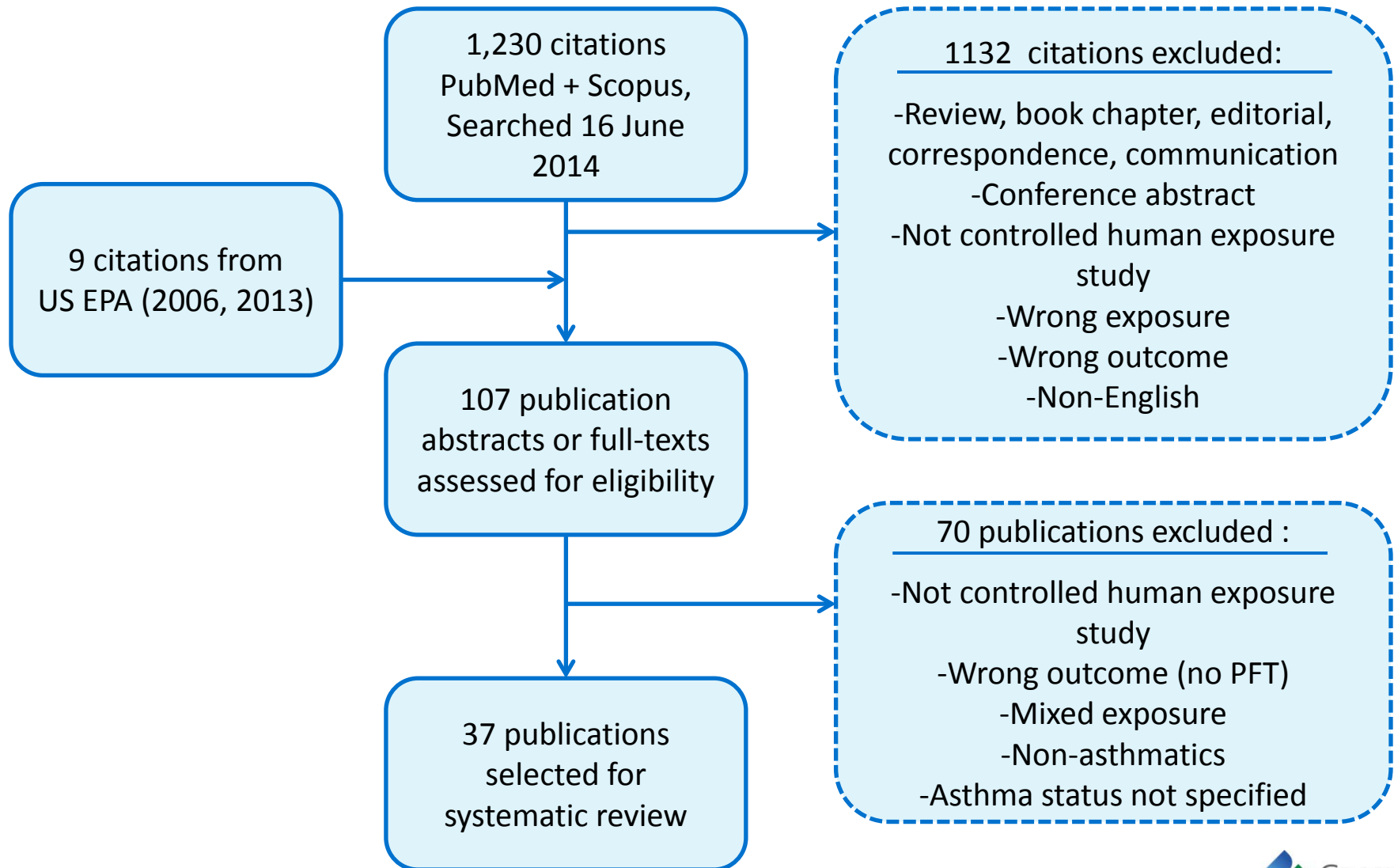
Toxicity/Mode of action

"TITLE-ABS-KEY((rats OR mouse OR mice OR rabbits OR "guinea pigs" OR "guinea pig" OR monkeys OR macaque OR macaques OR primates OR cat OR dogs OR animals)) AND NOT TITLE(("in vitro" OR bioassay OR assay OR therapy OR epidemiology OR epidemiological OR hospital OR emergency OR admissions OR people OR human OR humans OR smokers OR patients)))

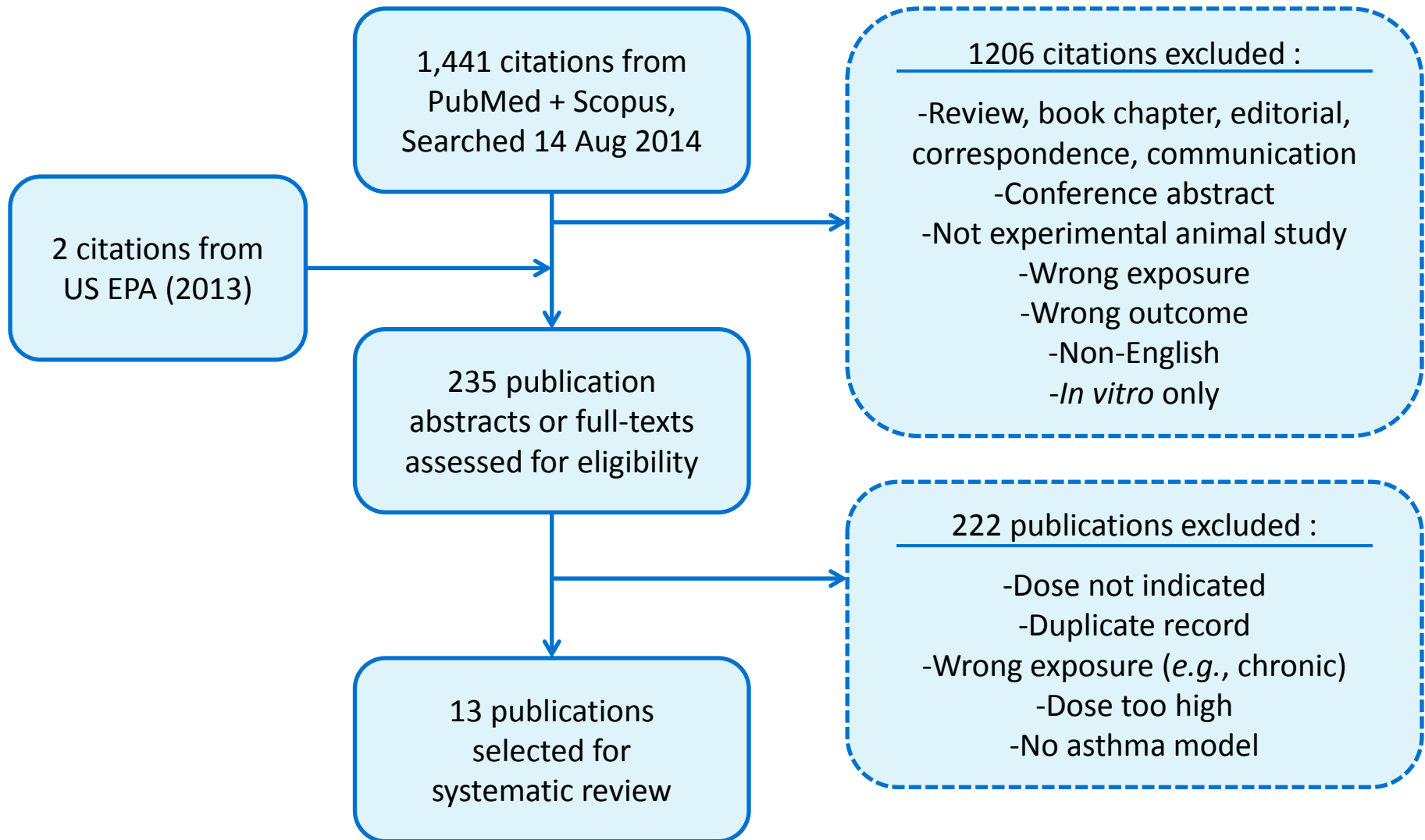
Study Selection: Epidemiology



Study Selection: Controlled Human Exposure



Study Selection: Animal



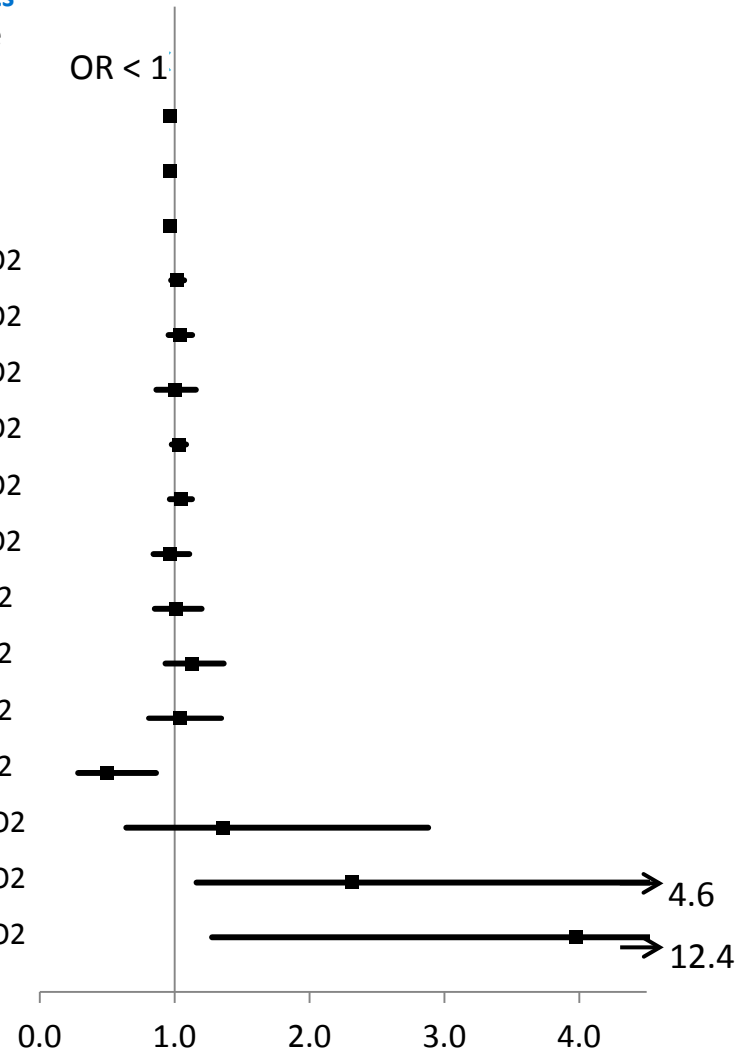
Study Quality Evaluation

Epidemiology	Controlled Human Exposure	Animal
Study design	Selection bias	Randomization
Study size	Blinding	Study size
Selection bias	Exposure method	Exposure monitoring
Exposure assessment	Study design	Experimental animals, housing, and husbandry
Outcome assessment	Smoking	Control groups
Statistical models	Subject inclusion/exclusion criteria	Assay reproducibility
Confounding	Exposure monitoring	Transparent reporting
Adjustment for pollen	Outcome assessment	Statistical methods
Multiple lag times	Data analysis	
Sensitivity analysis	Statistical methods	

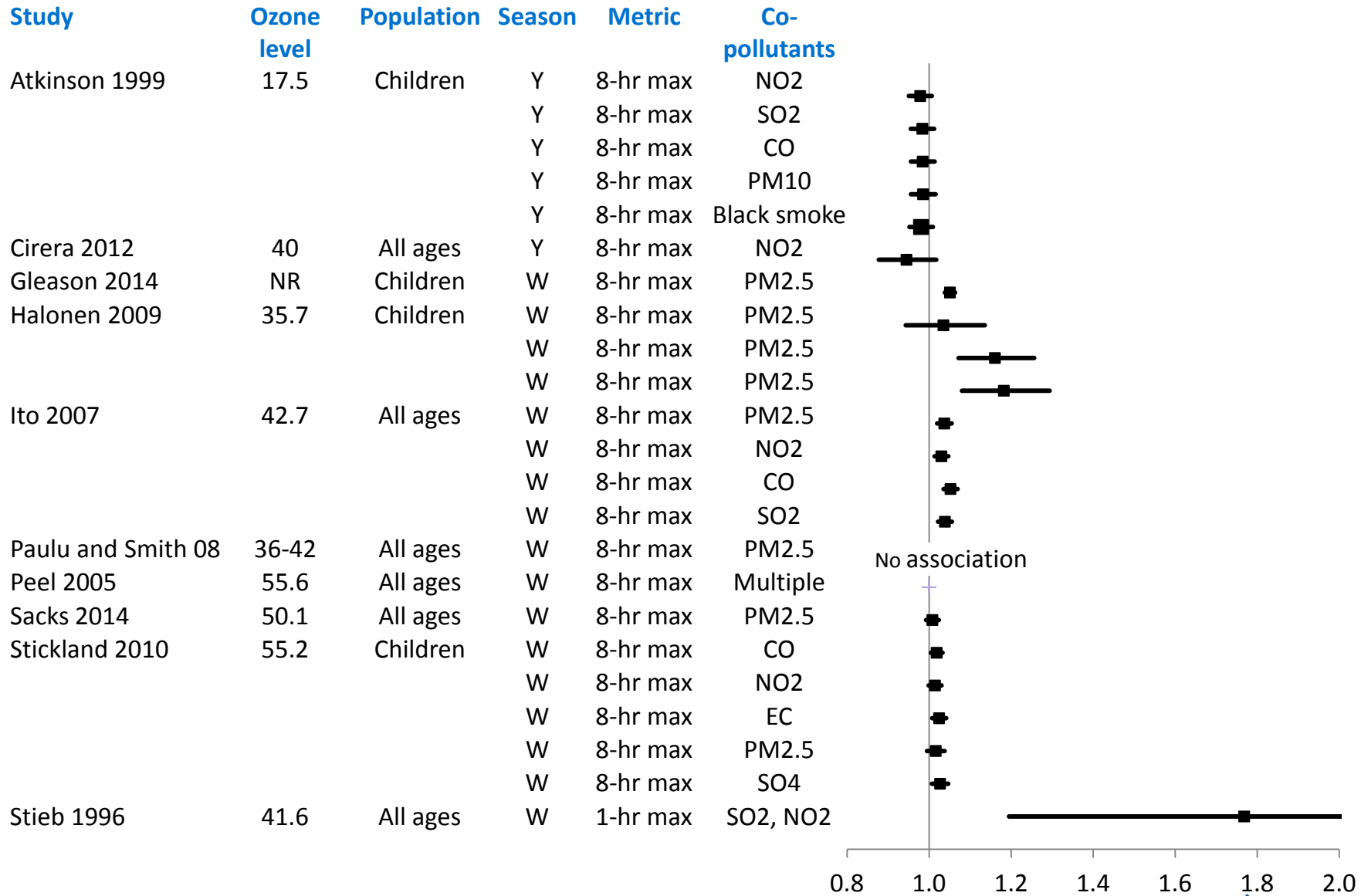
All studies classified as Tier I or Tier II.

Primary Care Visits for Asthma

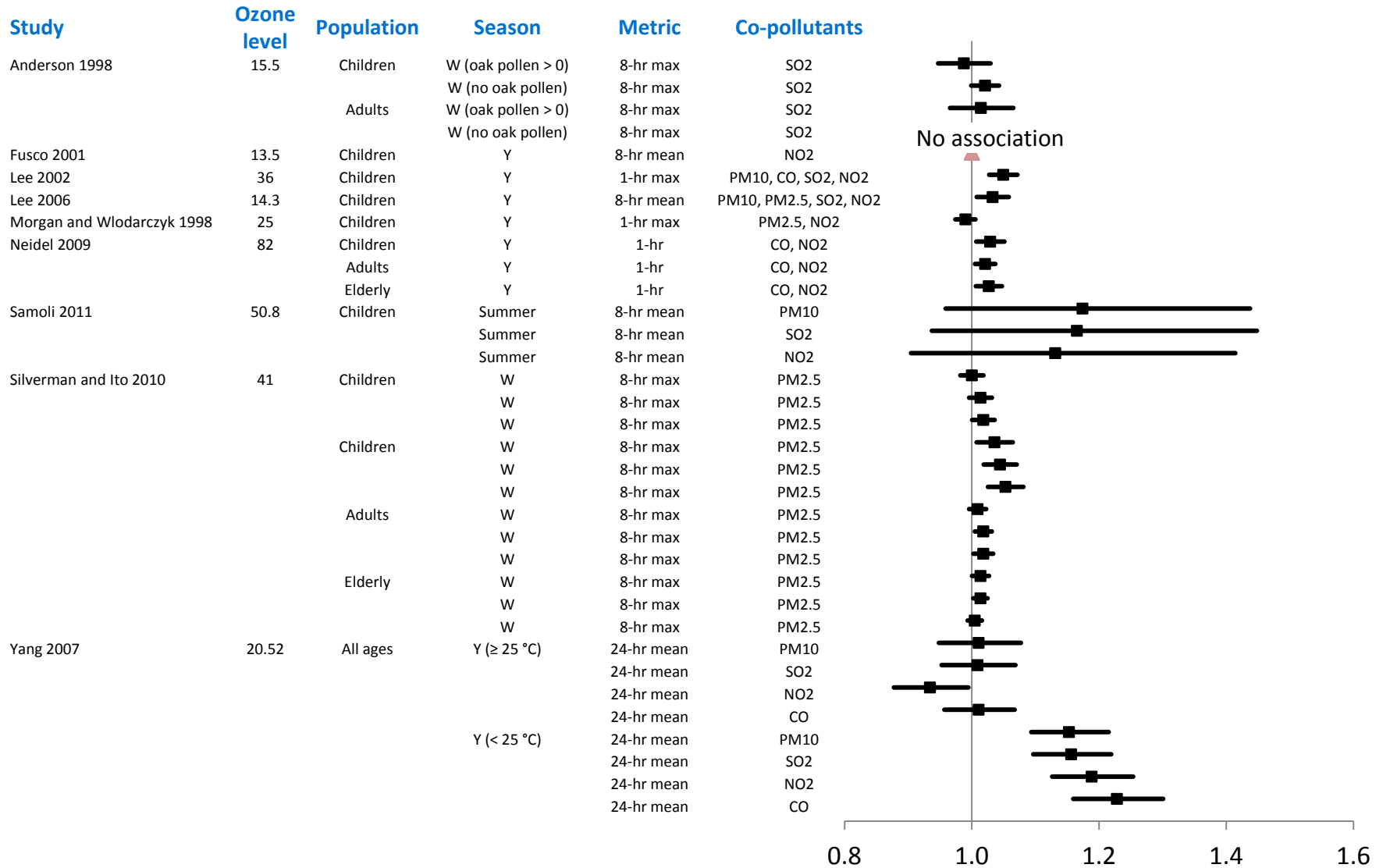
Study	Ozone level	Population	Season	Metric	Co-pollutants
Evans 2014	26.1	Children	Y	24-hr mean	Multiple
Hajat 1999	22.7	Children	Y	8-hr max	NO2
				8-hr max	SO2
				8-hr max	PM10
Lin 2013	52.9	All ages	W	1-hr max	PM10, NO2
			W	8-hr max	PM10, NO2
			W	24-hr mean	PM10, NO2
			C	1-hr max	PM10, NO2
			C	8-hr max	PM10, NO2
			C	24-hr mean	PM10, NO2
Yamazaki 2013	36.2	Children	Spring	24-hr mean	SPM, NO2
	22.5		Summer	24-hr mean	SPM, NO2
	21.5		Fall	24-hr mean	SPM, NO2
	23.0		Winter	24-hr mean	SPM, NO2
Yamazaki 2014	25.7	All ages	C	24-hr mean	PM2.5, NO2
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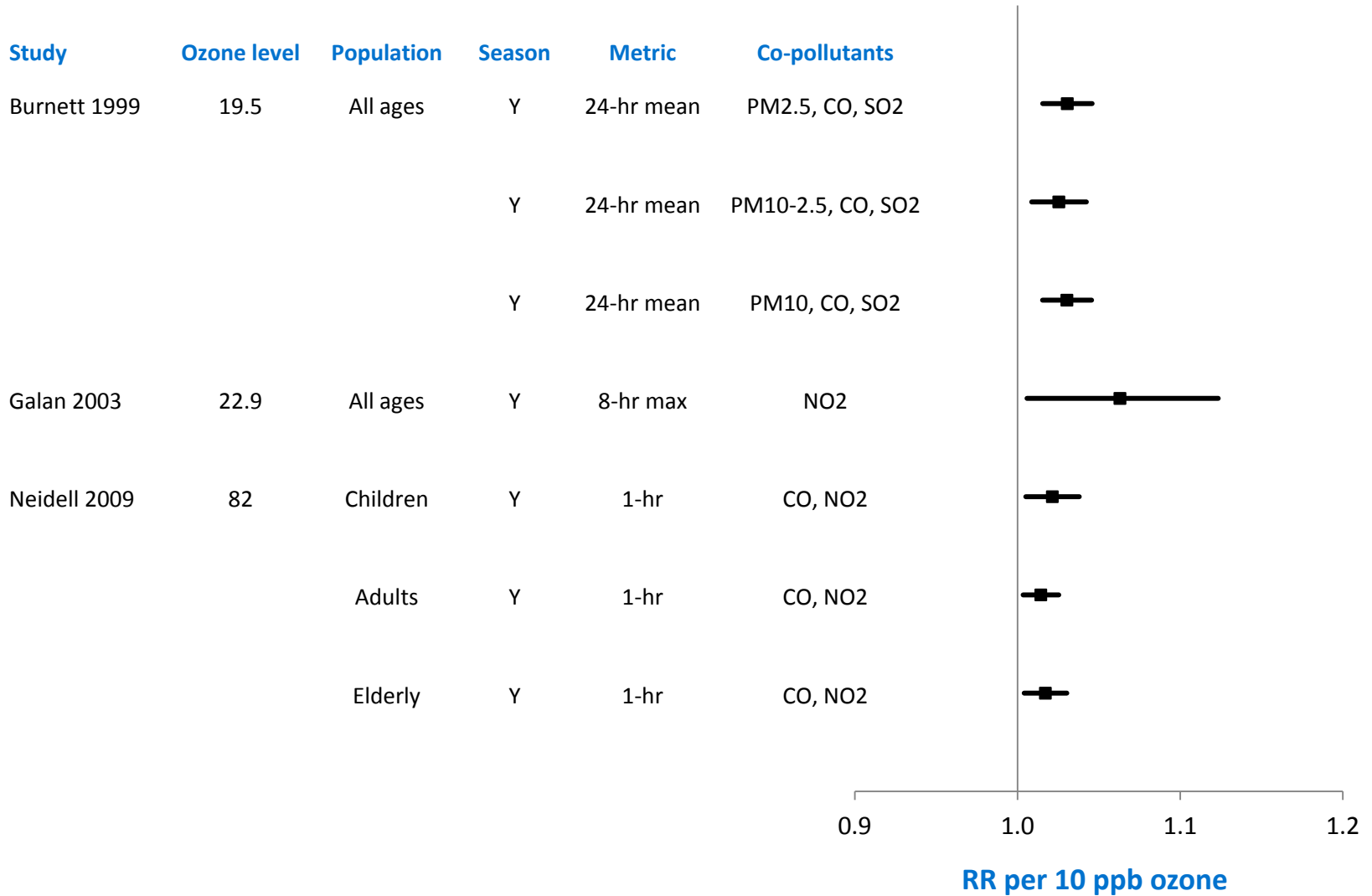
Emergency Room Visits for Asthma



Hospital Admission for Asthma

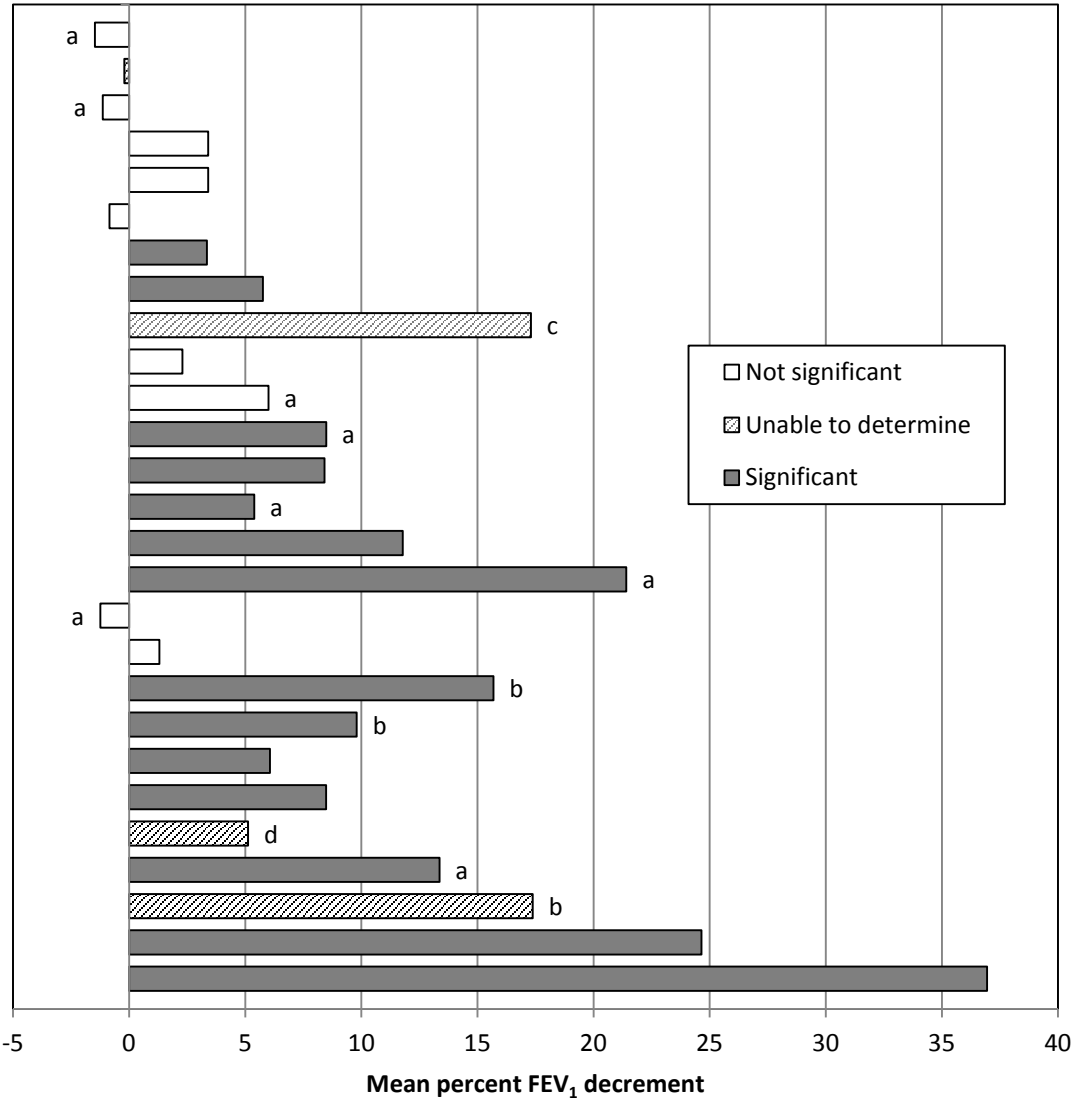


Emergency Room Admission for Asthma



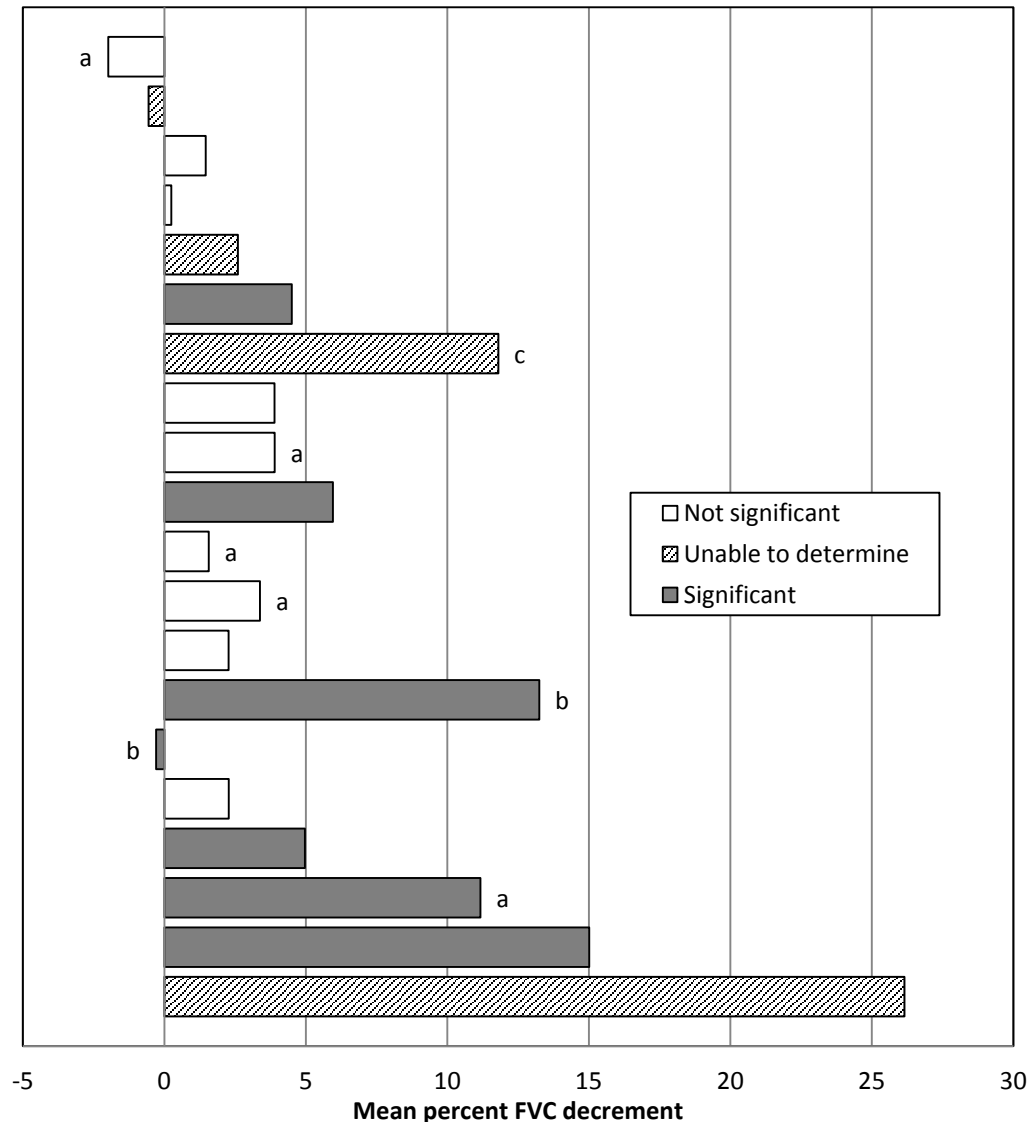
Controlled Exposure Studies – Ozone Exposure and FEV₁ Decrements

Study	n	asthma status	exp (hr)	ozone (ppb)
Jenkins et al., 1999	11	mild	6	100
Ball et al., 1996	12	NR	1	120
Fernandes et al., 1994	15	mild	1	120
Koenig et al., 1985	10	NR	1	120
Koenig et al., 1987	10	NR	1	120
McBride et al., 1994	10	NR	1.5	120
Linn et al., 1994	30	mixed	6.5	120
Balmes et al., 2012	10	mild	4	160
Horstman et al., 1995	17	NR	7.6	160
Koenig et al., 1987	10	NR	1	180
Balmes et al., 1995	14	NR	1	190
Newson et al., 2000	9	mild	2	200
Stenfors et al., 2010	13	persistent	2	200
Jenkins et al., 1999	10	mild	3	200
Nightingale et al., 1999	10	mild	4	200
Scannell et al., 1996	18	mild	4	200
Basha et al., 1994	5	NR	6	200
McBride et al., 1994	10	NR	1.5	240
Vagaggini et al., 1999	7	Intermit't, mild	2	260
Vagaggini et al., 1999	7	persistent, mild	2	260
Vagaggini et al., 2001	11	persistent, mild	2	270
Vagaggini et al., 2007	9	persistent, mild	2	270
Vagaggini et al., 2010	17	stable, mild-mod	2	300
Alexis, 2000	13	mild	2	400
Hiltermann et al., 1995	6	NR	2	400
Kreit et al., 1989	9	mild	2	400
Gong et al., 1997	10	mild	4	400



Controlled Exposure Studies – Ozone Exposure and FVC Decrements

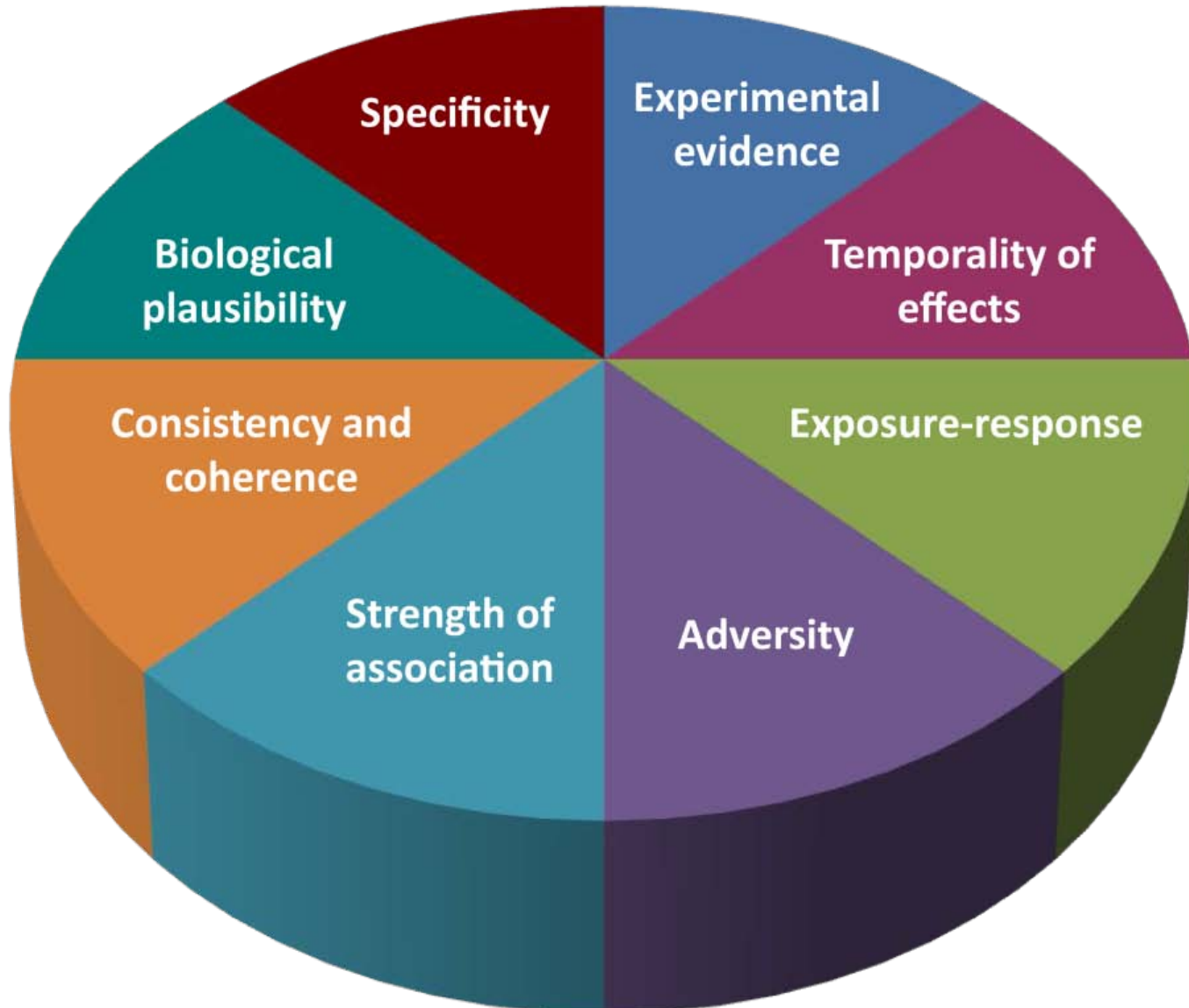
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McBride et al., 1994	10	NR	1.5	240
Vagaggini et al., 1999	7	intermittent, mild	2	260
Vagaggini et al., 1999	7	persistent, mild	2	260
Vagaggini et al., 2001	11	persistent, mild	2	270
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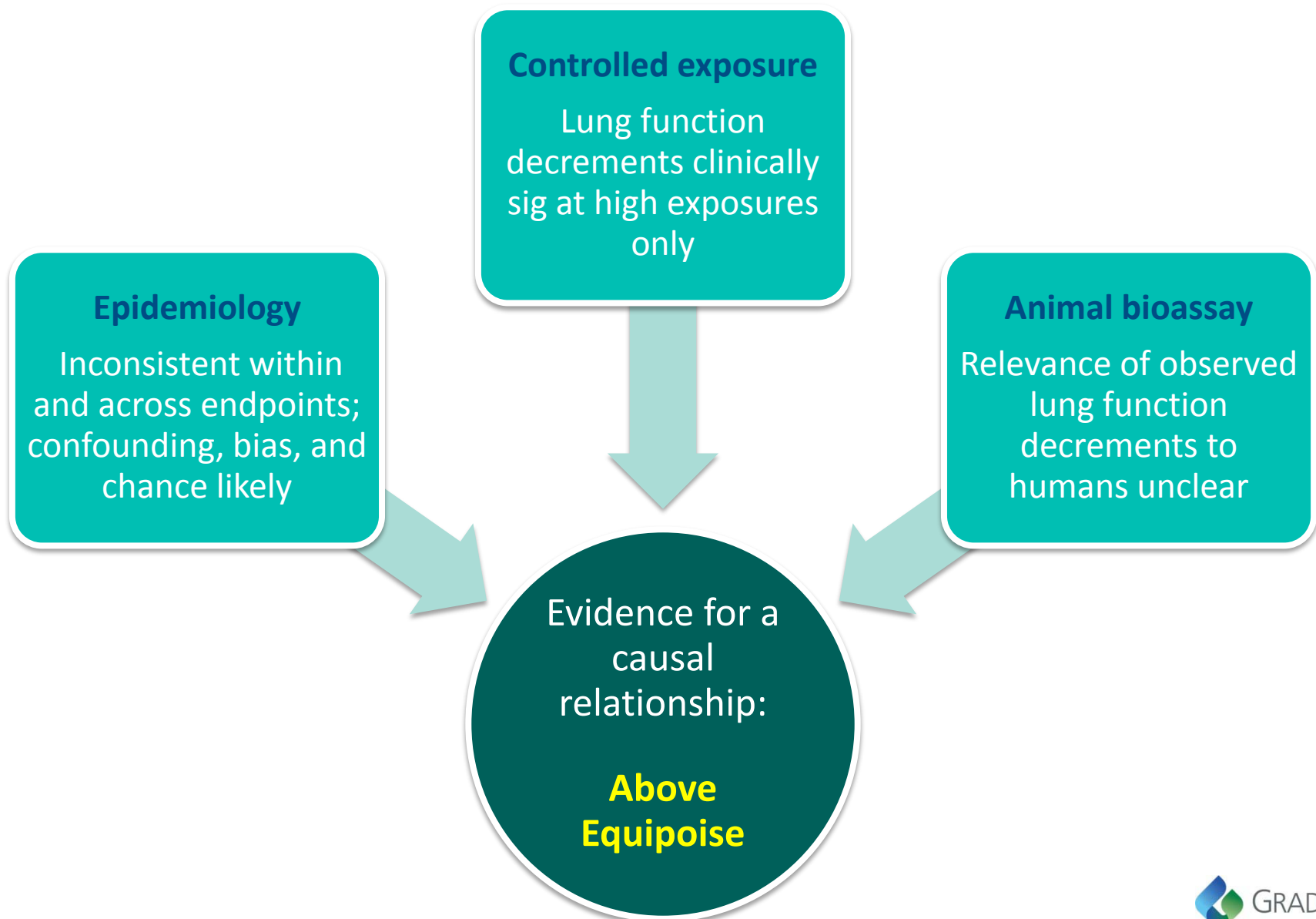
Animal Studies

Study	Ozone (ppb)	AHR	R _L	C	Other
DIRECTION OF ADVERSITY		↑	↑	↓	↕
Larsen et al. (2010)	100	↑			
Schlesinger et al. (2002)	100	↑			sGaw: ↑
Sumitomo et al. (1990)	1000	↑			
Funabashi et al. (2004)	1000		↑	↓	MV, RR, VT: ↑
Groves et al. (2012)	800			↓	
Schelegle and Walby (2012)	1000		↑		RR: ↑ MV, VT: ↓
Yamauchi et al. (2002)	1000		↑	↓	MV: ↓ RR: ↓

Short-term Ozone and Asthma Exacerbation



Short-term Ozone and Asthma Exacerbation



Relevance to the Ozone NAAQS

- Current standard, 0.075 ppm, is max daily 8-hr average.
- Many epidemiology studies conducted outside of the US, in areas with exposures above the NAAQS. Overall, associations inconsistent within and across endpoints; confounding, bias, and chance likely.
- Controlled exposure studies indicate adverse responses at high exposures only.
- Most animal studies conducted at high exposures.

The evidence is insufficient to infer whether ozone exacerbates asthma at exposures below the NAAQS.

Questions?

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