A meta-analysis of arsenic exposure and lung function: Is there evidence of restrictive lung disease?

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Background

Arsenic is a well-established cause of lung cancer. There is also growing evidence of an association between arsenic and non-malignant lung disease.

Identifying whether arsenic-associated lung function deficits resemble restriction may help to illuminate the pathophysiological pathway linking arsenic exposure to chronic lung disease.

The goal of this analysis is to evaluate whether the patterns of association between arsenic exposure and lung function measures from previously published epidemiologic research are suggestive of restrictive deficits.

Methods

Search strategy & data abstraction

- PubMed and EMBASE search until January 2017.
- Screened articles using selection criteria (figure 1) and independently.
- This review followed MOOSE guidelines.

Statistical analysis

Pooled effects were estimated using inverse-variance weighted random-effects models using measure of associations comparing mean lung function level in the highest category of arsenic exposure versus the lowest category for each study (Figure 2).

Sensitivity analyses

- Heterogeneity was calculated using I^2.
- Conducted sensitivity analyses (Table 3) and subgroup (Table 4) using inverse-variance weighted random effects models.

Results

Figure 1. *Study selection criteria*

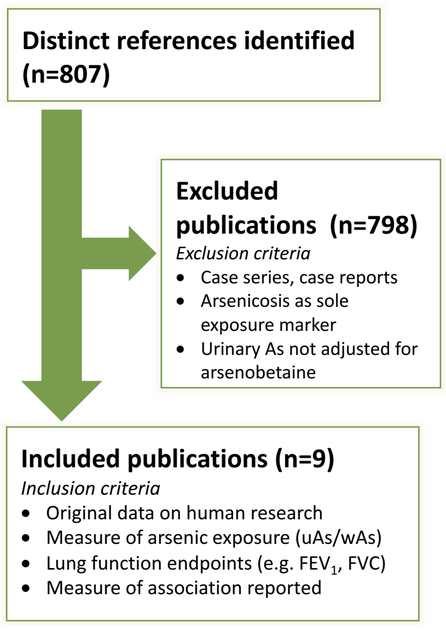
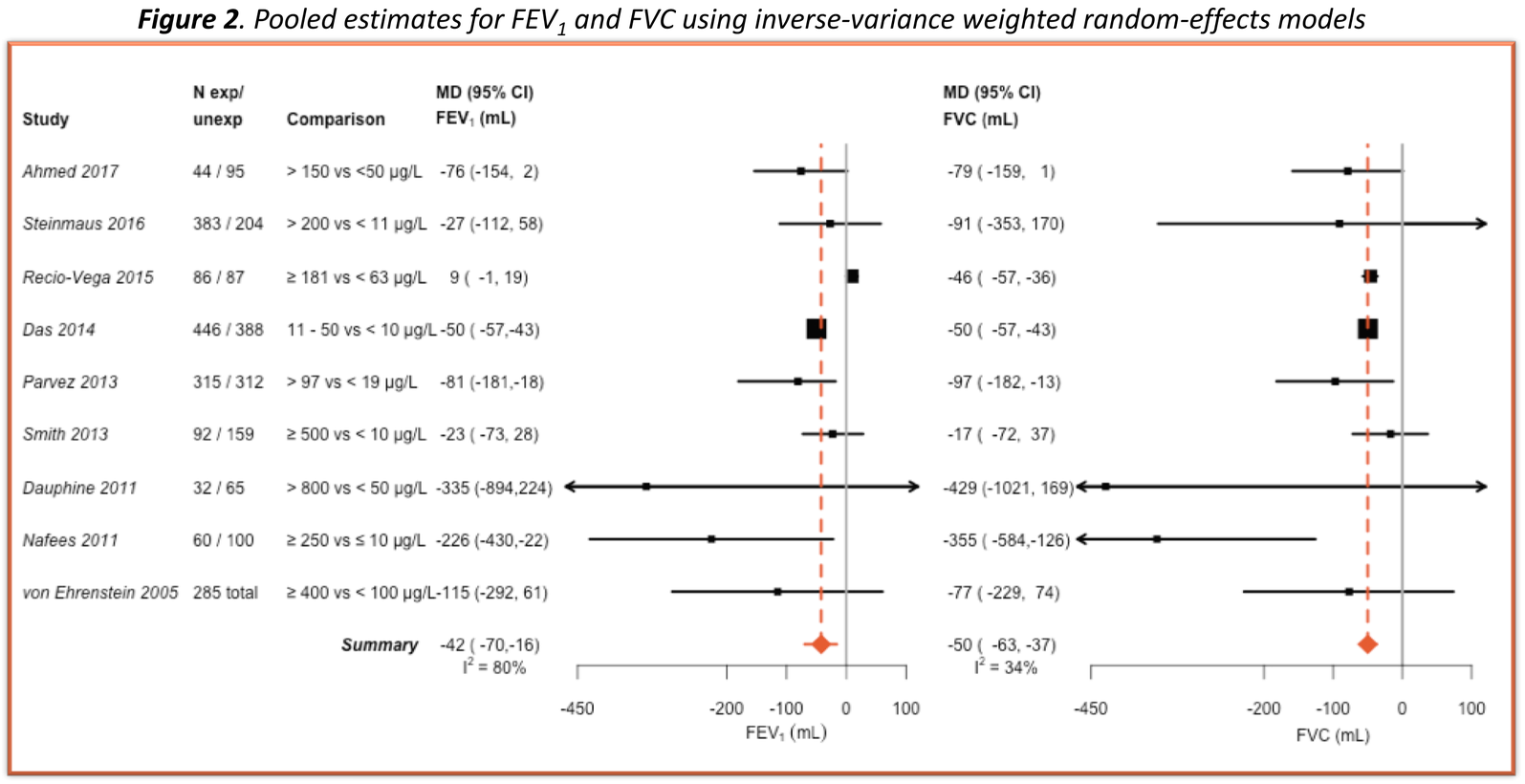


Table 1. *Characteristics of included studies*

Study	Country	N	Men	Age	Exposure (µg/L)	Adjustment variables
Ahmed 2017	Bangladesh	551	48%	8-10	Urine As: ≤50, ≥150	Age, sex, height for age Z-score, SES, season, mom education, micronutrient-group
Steinmaus 2016	Chile	795	51%	<44->49	Water As: <11, 11-200, >200	Age, sex, height, smoking, ethnicity
Recio-Vega 2015	Mexico	358	48%	6-12	Urine As: <63, 63-112, 113-180, ≥181	Sex, BMI, type of water consumed, mom's education
Das 2014	India	834	100%	Avg: 35.3	Water As: <10, 11-50	None
Parvez 2013	Bangladesh	927	48%	37-47	Water As: <19, 19-97, >97	Age, sex, BMI, education, smoking, betel nut, skin lesion
Smith 2013	Bangladesh	650	52%	7-17	Water As: <10, 10-499, ≥500	Age, sex, height, weight, parent education, dad smoking, SES
Dauphine 2011	Chile	97	36%	32-65	Water As: <50, 50-250, >800	Smoking, childhood secondhand smoke, childhood home fuel, edu, occupational air pollution
Nafees 2011	Pakistan	200	46%	≥15	Water As: ≤10, ≥100	Age, sex, height, smoking
von Ehrenstein 2005	India	285	64%	≥20	Water As: ≤100, ≥400	Age, sex, height, smoking

Figure 2. *Pooled estimates for FEV_1 and FVC using inverse-variance weighted random-effects models*



Of the three studies that reported effect estimates for FEV1/FVC, the estimated mean difference was 0.01 (95% CI: -0.005, 0.024).

Table 3. *Sensitivity analyses*

	No. studies	FEV_1 (mL) MD (95% CI)	FVC (mL) MD (95% CI)
Primary analysis	9	-42 (-70, -16)	-50 (-63, -37)
Sensitivity analyses			
Water arsenic	6	-47 (-75, -19)	-62 (-116, -8)
Urinary arsenic	3	-48 (-103, 8)	-47 (-57, -37)
Replacing categorical with continuous[27,16,26]	9*	-26 (-49, -4)	-39 (-66, -11)
Excluding studies without adjustment[22]	8	-41 (-76, -7)	-50 (-63, -37)
Excluding studies with hand-calculated estimates[18,22]	7	-58 (-99, -17)	-70 (-117, -23)

Table 4. *Subgroup analyses*

	No. studies	FEV_1 (mL) MD (95%CI)	FVC (mL) MD (95%CI)
Sex[1,4,7,11]			
Female	4	-8 (-22, 5)	-12 (-31, 7)
Male	4	-67 (-129, -5)	-47 (-102, 7)
		p=0.33	p=0.55
Smoking status[1,4,7,10]			
Smokers	4	-56 (-164, 52)	-50 (-155, 55)
Non-smokers	4	-51 (-97, -5)	-92 (-187, 2)
		p=0.86	p=0.63
Timing of exposure			
Early life[1,4,6,8,10]	5	-14 (-25, -5)	-46 (-56, -36)
Adulthood[3,6,7,11]	4	-66 (-106, -25)	-95 (-172, -19)
		p=0.014	p=0.58

Conclusions

This meta-analysis evaluated the relationship between arsenic exposure and lung function spirometry measures. We identified an inverse association between arsenic exposure and both FEV_1 and FVC, but no association for FEV_1/FVC. These findings show that arsenic exposure may be associated with a restrictive pattern lung disease. However, an obstructive or mixed pattern lung function deficits cannot be entirely ruled out as our analysis is limited by the small number of studies reporting measures of association with FEV_1/FVC. Identifying a specific lung function deficit pattern associated with arsenic exposure, like restriction, and potential effect modifiers, like smoking and sex, can guide future research aimed at understanding relevant pathophysiological pathways and at risk populations.

References

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