

# Fetal HAP Exposure and Lung Development: Evidence from GRAPHS

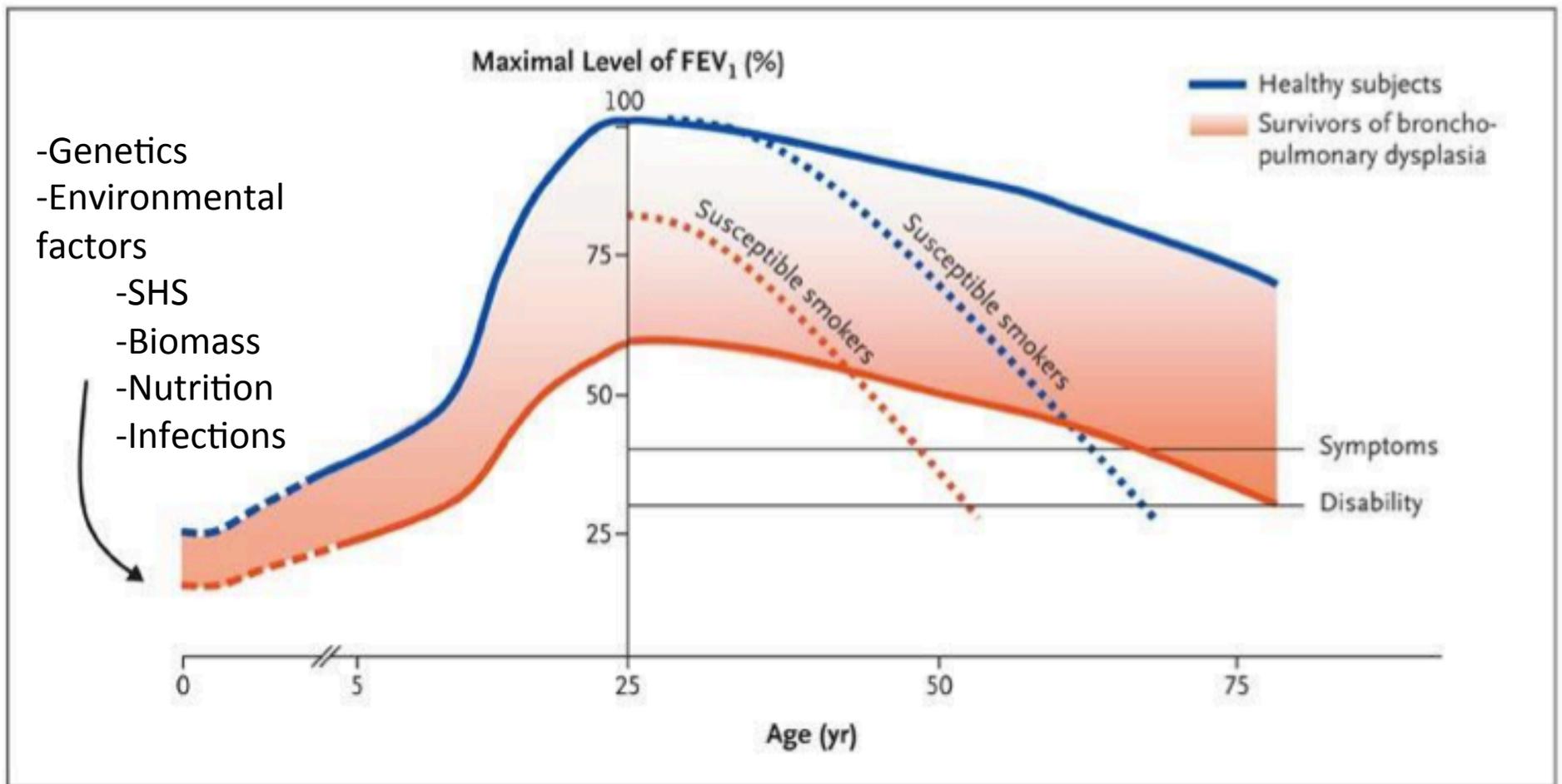
Alison Lee, Darby Jack, and Kwaku  
Poku Asante on behalf of the  
GRAPHS team

Point of departure:

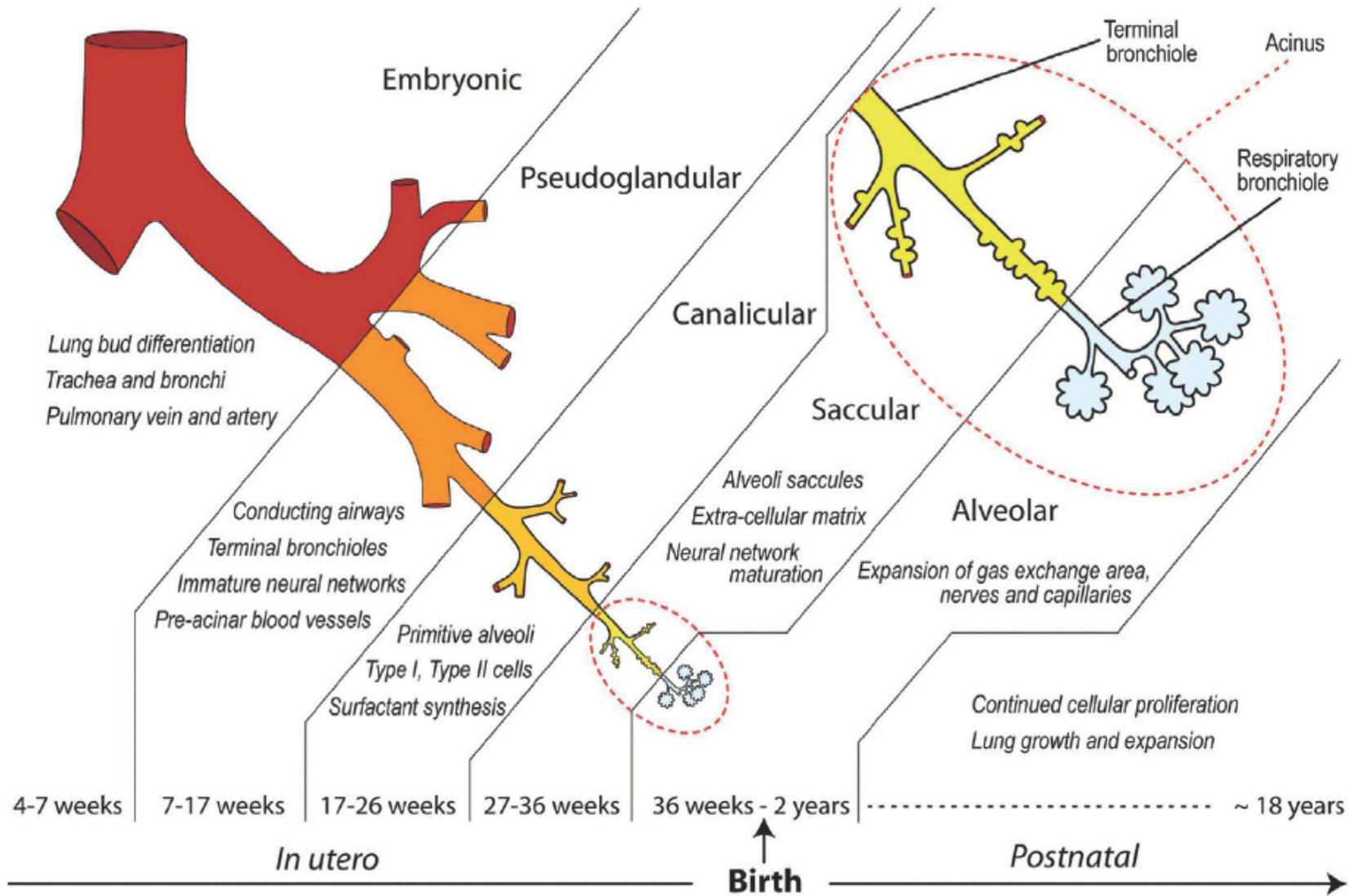
**“The most important adverse exposure for chronic obstructive lung diseases in childhood is maternal tobacco smoking”**

Duijts et al European J of Epi 2014

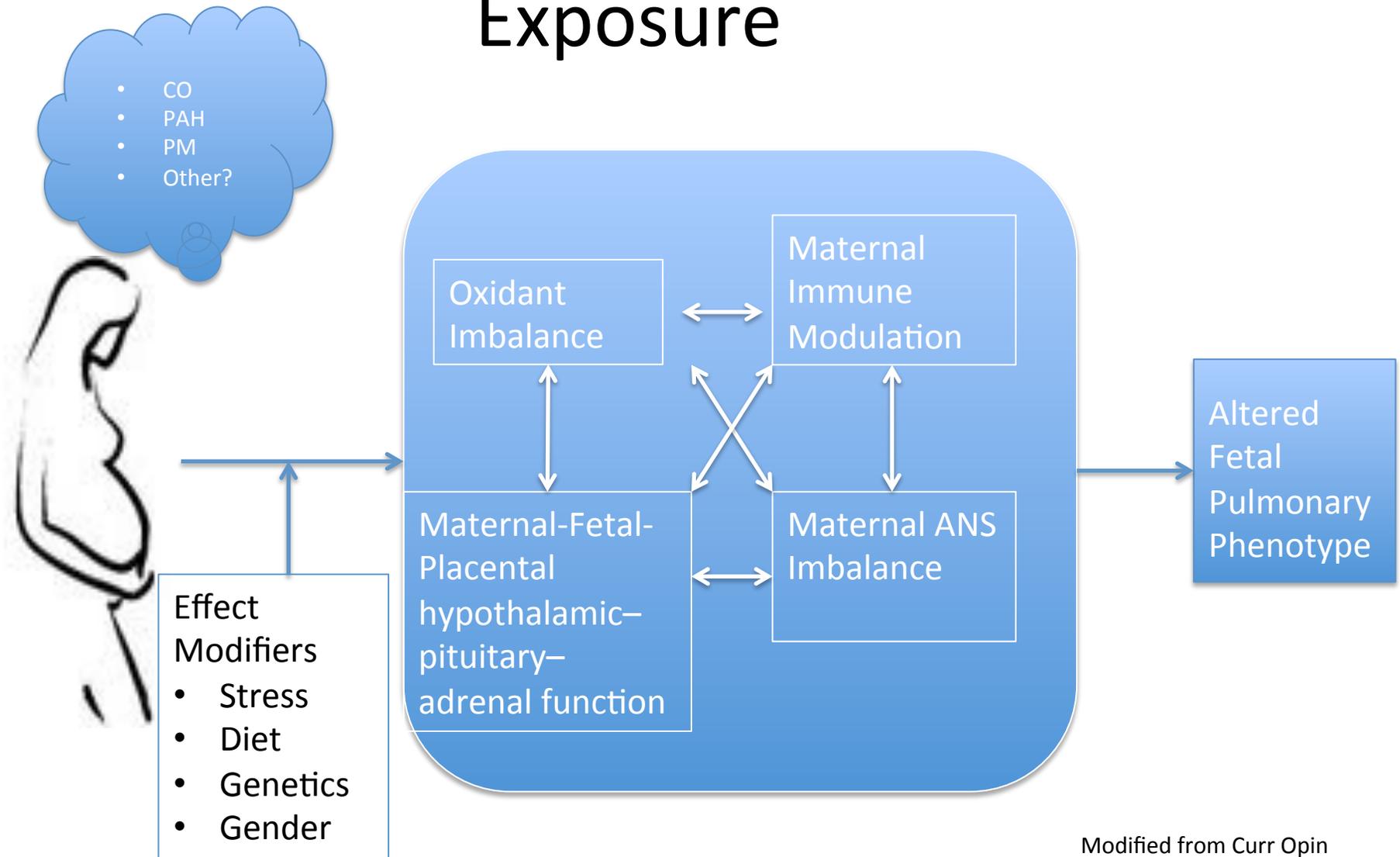
# Natural History of FEV1



# Fetal Respiratory Development



# Conceptual Model of *in utero* HAP Exposure



# Parameters of interest

- **Tidal volume** (TV) size of breath (in mL) at rest/normal breathing Hypothesized to **decrease** with exposure
- **Respiration rate** (RR) is the number of breaths per minute. Hypothesized to **increase** with exposure.
- **Minute ventilation** (MV)  $RR \times TV$ : hypothesized to **increase**
- $t_{PTEF}:t_E$  (TFV ratio) time to reach tidal peak expiratory flow as a ratio of total expiratory time. Reduced when flow limitation exists. Hypothesized to **decrease** with exposure
- **Compliance** (“stiffness”) of the respiratory system ( $C_{rs}$ ) is a measure of tissue and airways elasticity. Hypothesized to **decrease** with exposure
- **Resistance** of the respiratory system ( $R_{rs}$ ) as a measures of airways size. We hypothesize that resistance will **increase** with exposure.

## TVF ratio and compliance decreased with fetal tobacco smoke exposure

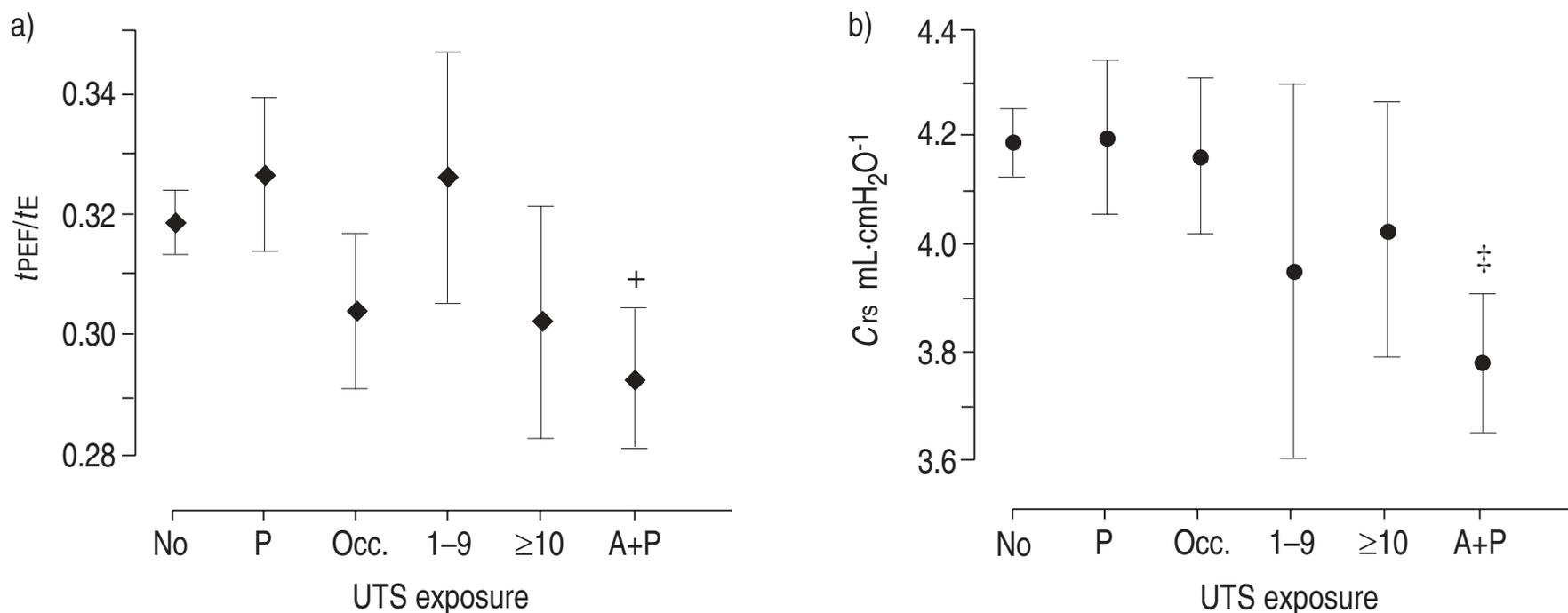
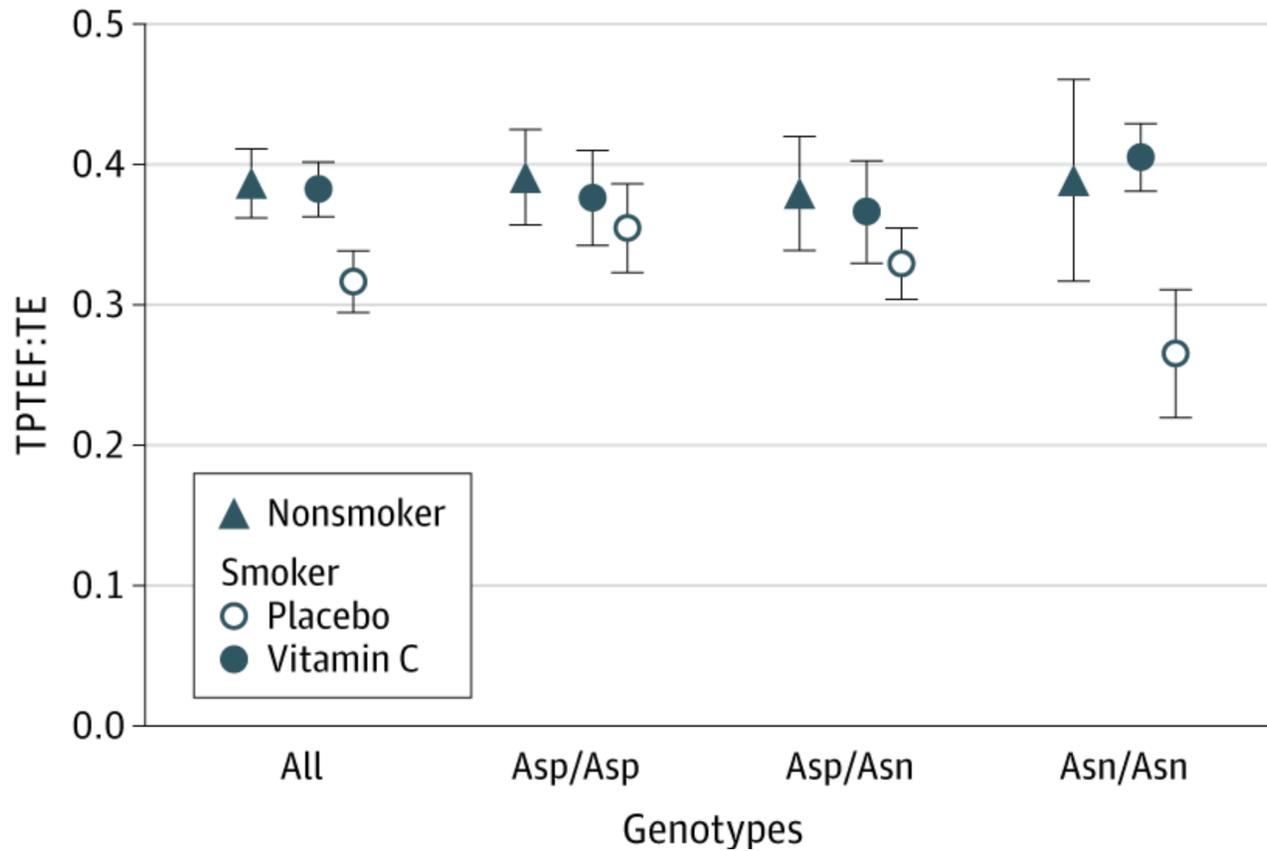


Fig. 1. — a)  $t_{PEF}/t_E$ ; and b)  $C_{rs}$  in newborn babies in relation to maternal smoking. Values are presented as mean and 95% confidence interval. No: no active or passive maternal smoking; P: daily passive (but not active) maternal exposure to tobacco smoke in the household; Occ.: occasional maternal smoking ( $\pm$ passive smoking); UTS: uterine tobacco smoke exposure; 1–9: maternal active (but not passive) smoking of 1–9 cigarettes·day<sup>-1</sup>;  $\geq 10$ : maternal active (but not passive) smoking of  $\geq 10$  cigarettes·day<sup>-1</sup>; A+P: both active and passive daily smoking.  $t_{PEF}/t_E$ : ratio of time to reach peak expiratory flow to total expiratory time;  $C_{rs}$ : compliance of the respiratory system. +:  $p=0.04$ ; ‡:  $p<0.005$ , compared to nonexposed group.

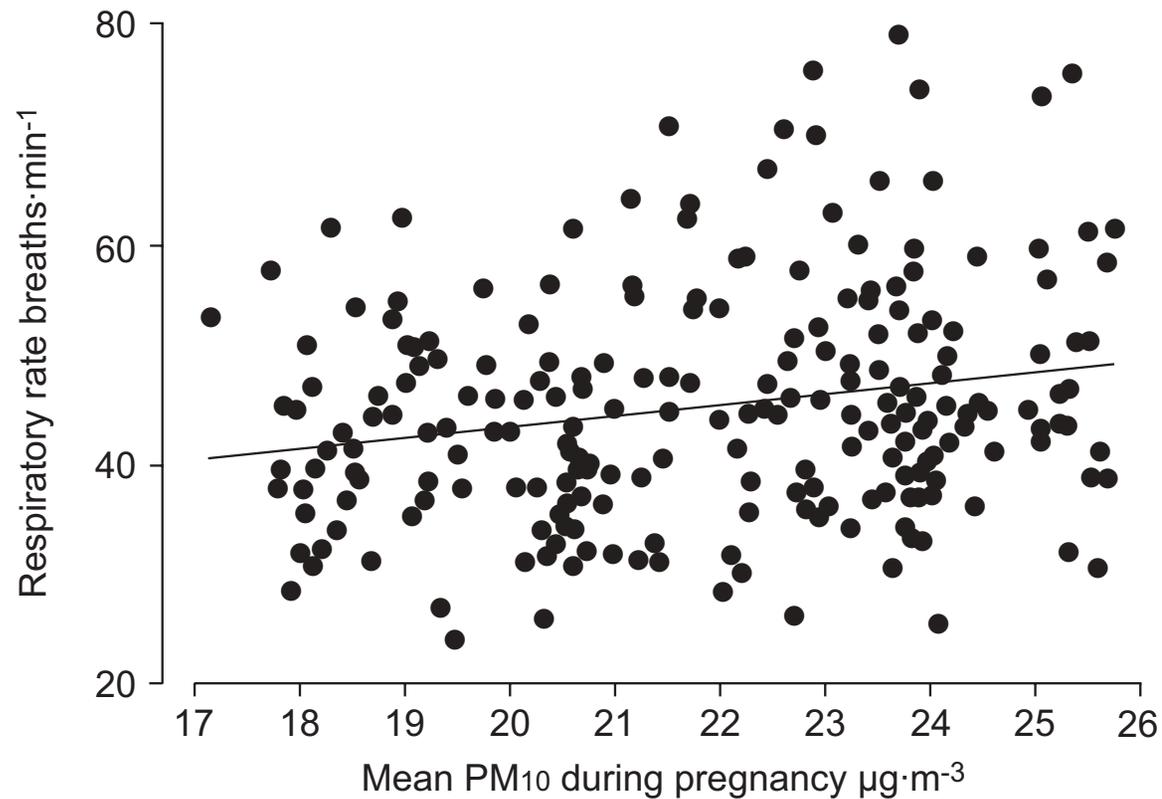
From: **Vitamin C Supplementation for Pregnant Smoking Women and Pulmonary Function in Their Newborn Infants: A Randomized Clinical Trial**

JAMA. 2014;311(20):2074-2082. doi:10.1001/jama.2014.5217

TFV ratio decreased with fetal exposure to tobacco smoke



## Respiratory rate increased with PM10 exposure in a prospective birth cohort

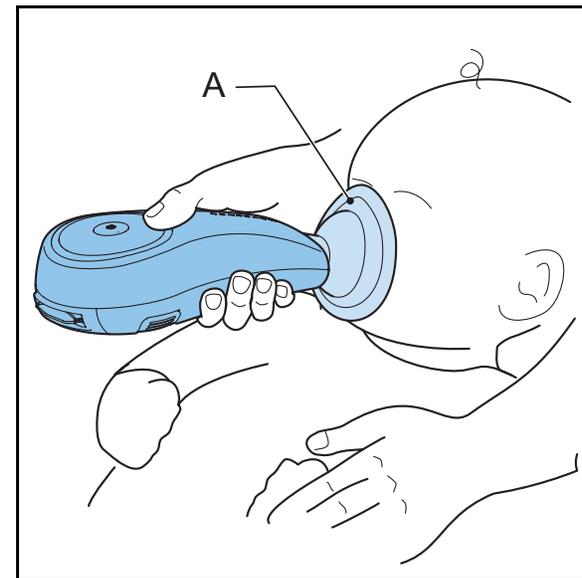


**FIGURE 2.** Individual respiratory rate at 5 weeks of age plotted against mean concentration of particles with a 50% cut-off aerodynamic diameter of 10 μm (PM<sub>10</sub>) during pregnancy. An increase from the lowest to the highest quartile of pre-natal PM<sub>10</sub> exposure was associated with a change in respiratory rate from 42 to 48 breaths·min<sup>-1</sup>.

# Single occlusion technique

- The airway is occluded for a brief period (400 – 1500 milliseconds) after maximal inhalation.
- Compliance and resistance of the respiratory system are inferred by measuring flow and pressure during and after this occlusion period
  - During occlusion, there is no airflow and pressures can equilibrate, so the airway opening pressure reflects the pressure within the alveoli.
  - After occlusion, the infant's exhalation is relaxed and prolonged, making it possible to calculate the compliance ( $C_{rs}$ ) and the ( $R_{rs}$ ) of the airway.

  
WHISTLER

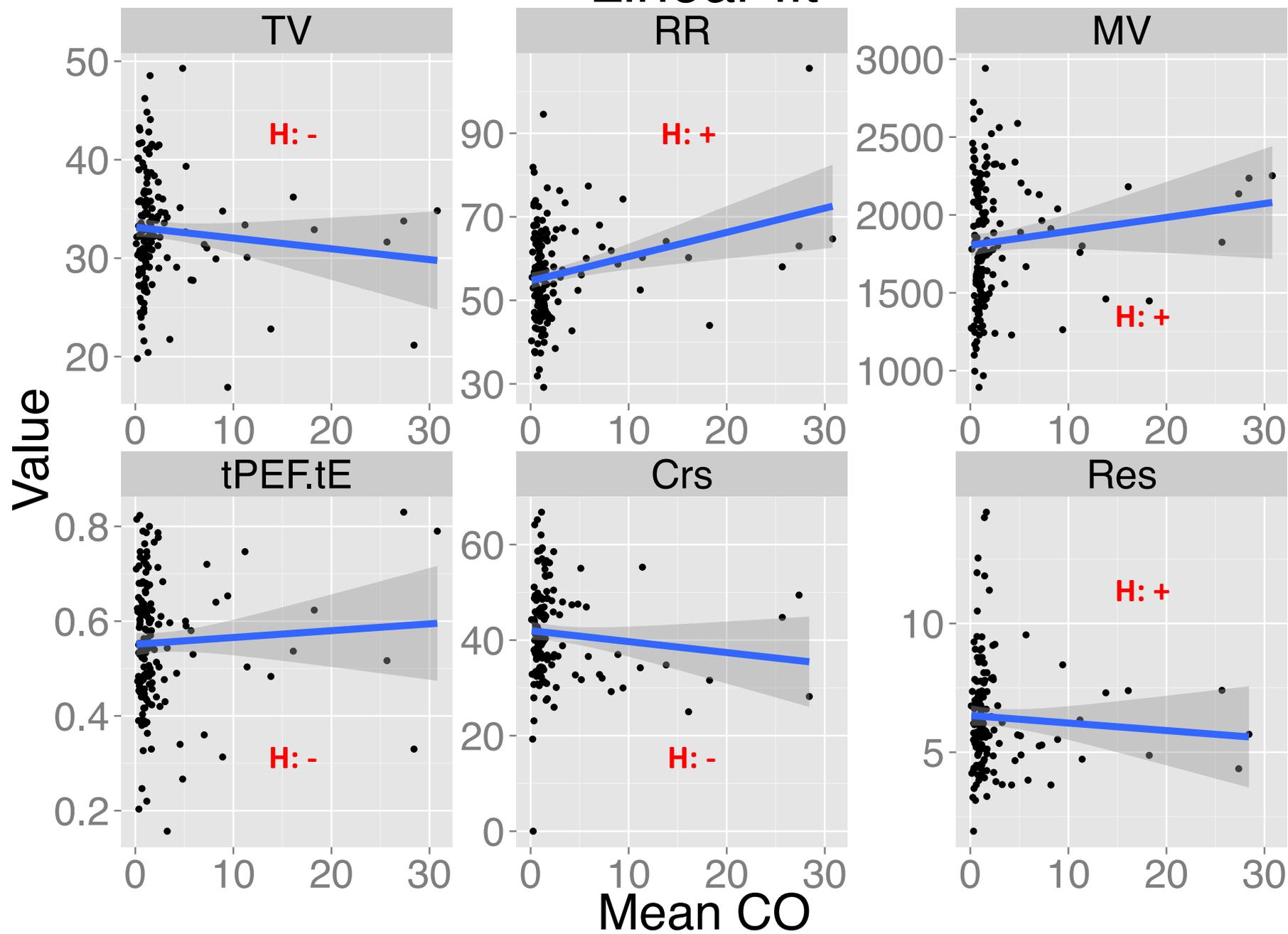


# Infant Lung Function Testing in GRAPHS

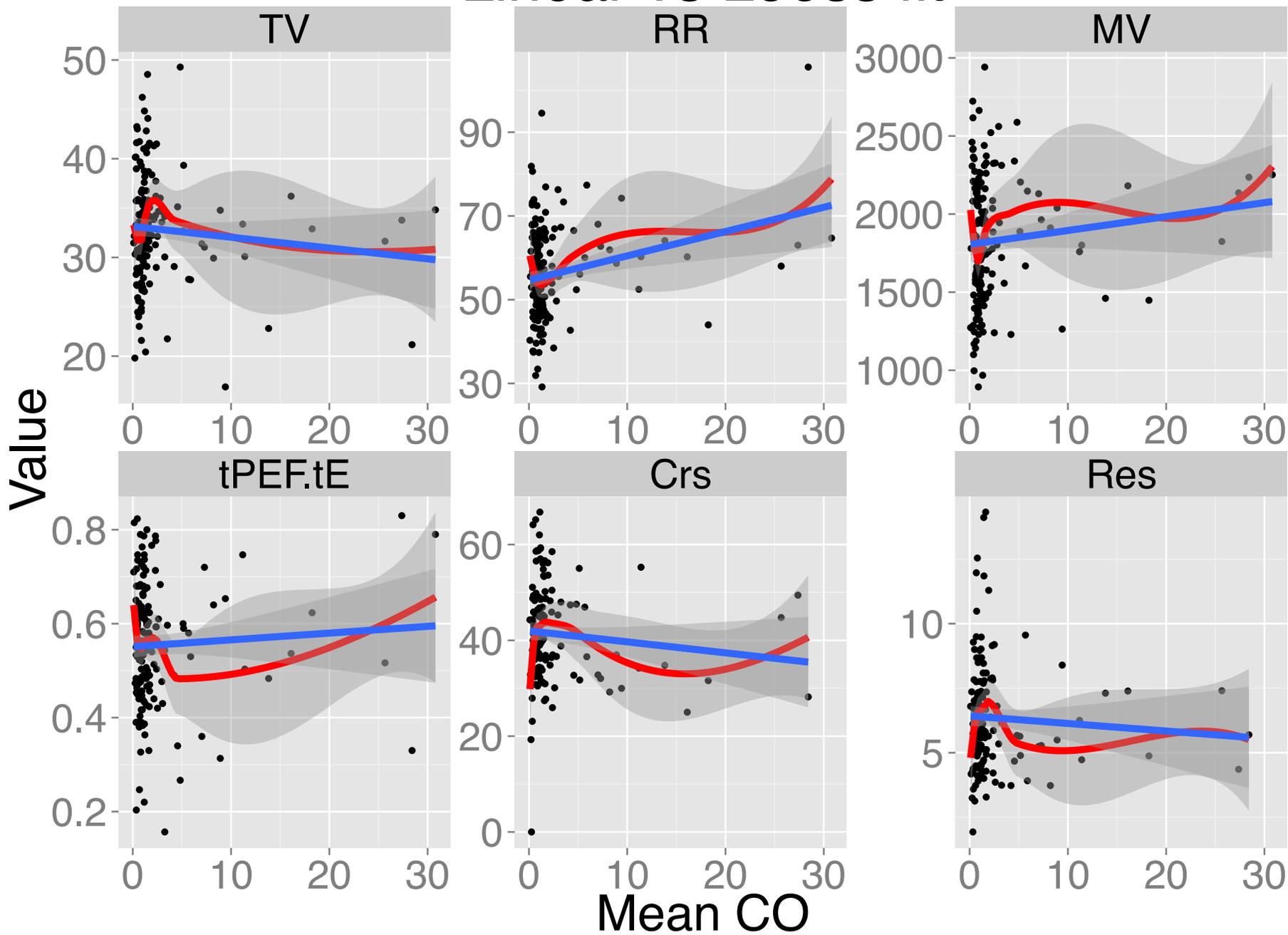
- Lung function at 1 month at Kintampo Hospital
- Infant is asleep
- High success rate

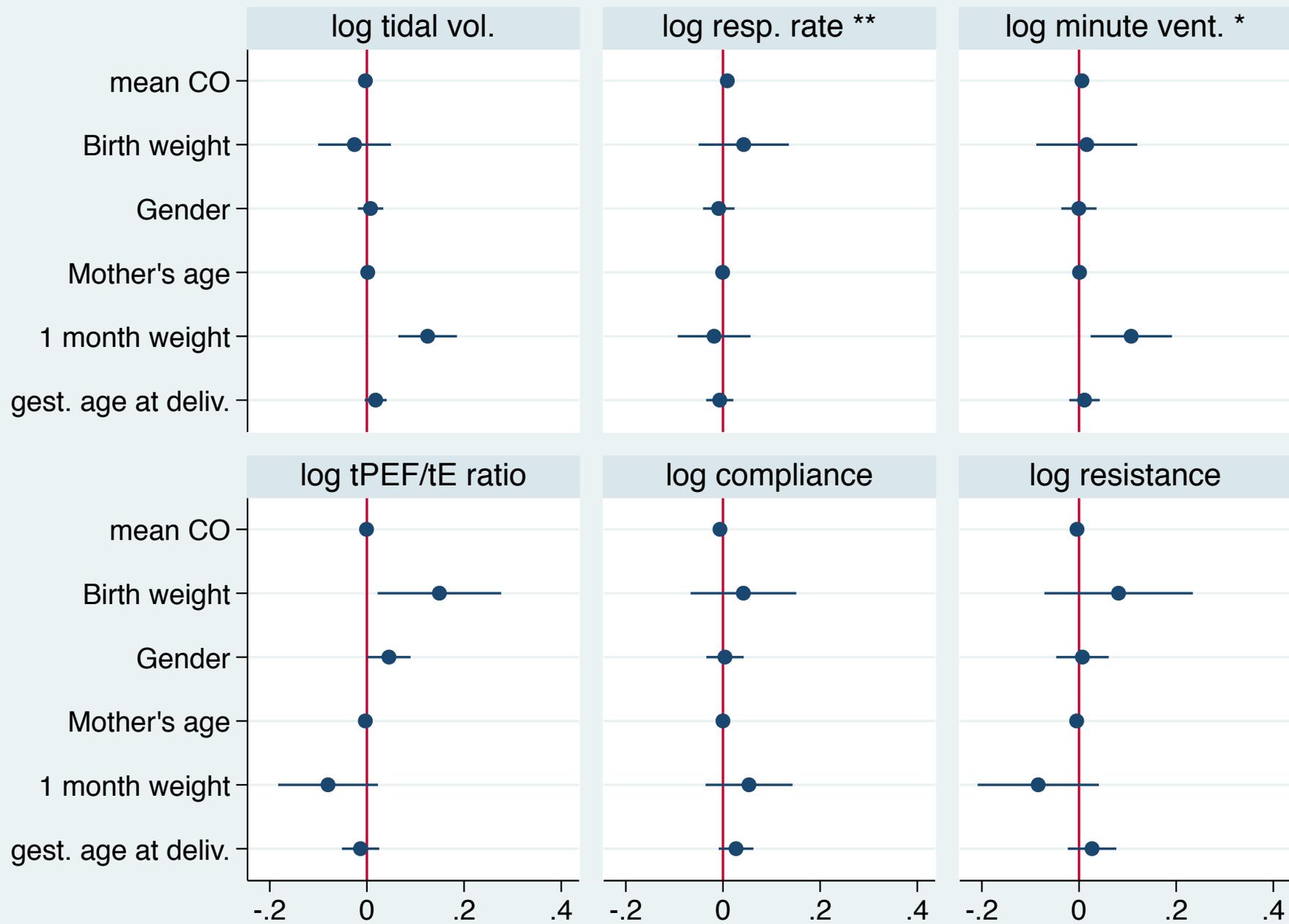


# Linear fit



# Linear vs Loess fit





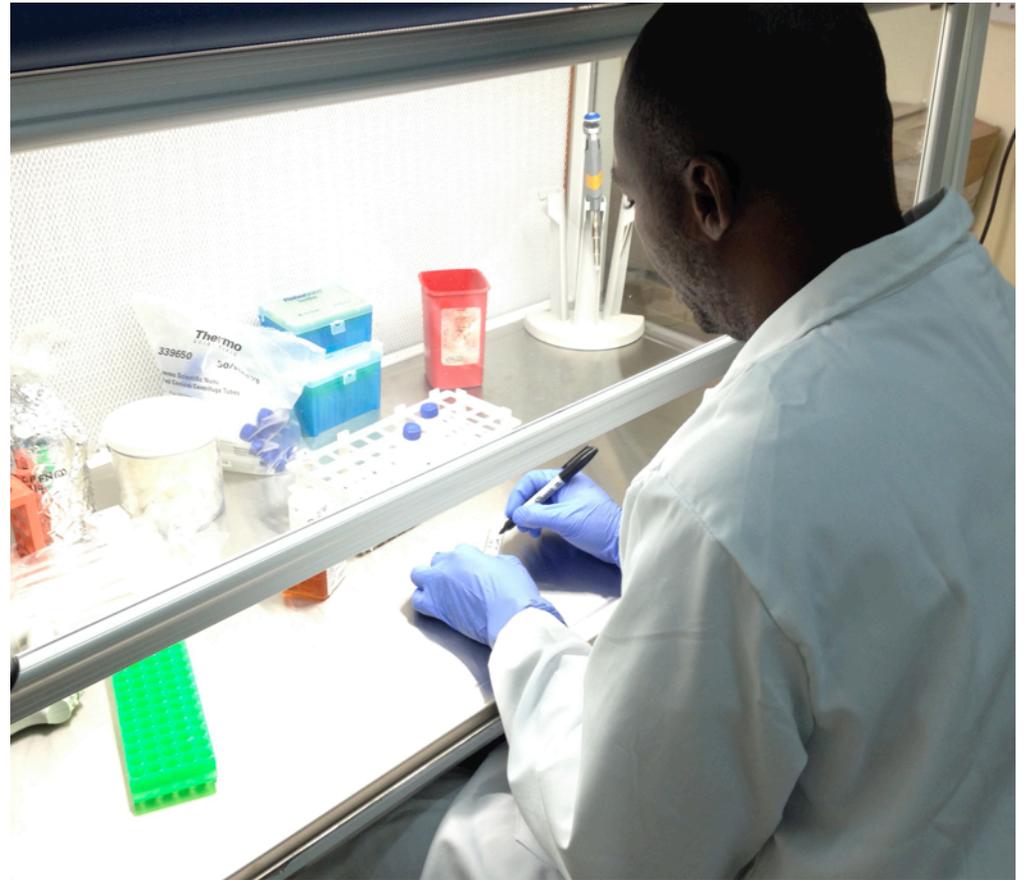


# Next steps

- More data! Results presented comprise about half of our target sample.
- Models for PM (need filter weights)
- Additional covariates for adjusted estimates?
- Alternative specifications?

# Cord Blood – mechanisms and confounders

- Plasma → Pro-oxidant / anti-oxidant analyses
- CBMCs (cord blood mononuclear cells) → immune function
- Plasma → nutritional status
- CBMC Pellet/placenta → epigenetics
- All samples + whole blood, serum → banking



# acknowledgements

- Study participants
- KHRC
- NIEHS
- GACC
- Thrasher Fund
- Chest Foundation and Respiratory Health Association, Clinical Research Grant in Women's Lung Health