

The inherent variability of asthma: implications for diagnosis and assessing response to treatment

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INTRODUCTION

- Asthma diagnostic guidelines emphasise the importance of objective testing.
- With limited access to tests, many clinicians utilise “response to treatment” in diagnostic decision making.
- Asthma is characterised by temporal variability and symptoms may improve without treatment.

AIMS

To assess between-visit variability in:

- 1. Airway inflammation (FeNO)**
- 2. Symptoms (ACQ)**
- 3. Lung function (FEV₁)**

in adults and children presenting with suspected asthma, and to explore the implications of temporal variability for diagnosis.

METHODS

- **Recruitment:** Rapid Access Diagnostics for Asthma (**RADicA**) is a prospective cohort study that recruited from primary care practices across Greater Manchester. Participants aged 3-69 yrs with asthma symptoms and no recent inhaled corticosteroid use, a <10 pack year smoking history and no known lung disease were recruited.
- **Tests:** Participants completed **baseline assessments** at two time-points, **Visit 1 and Visit 2**, 48 hours - 6 weeks apart and without change in treatment including: 1) FeNO, 2) FEV₁ and 3) ACQ-5. Participants were classified into “Asthma” or “Not-asthma” groups.
- **Analysis:** Between-visit variability was assessed by determining the proportion of participants demonstrating the minimal clinically important difference (MCID) between visits.
 - **MCID: FeNO = 20%; FEV₁ = 200mls; ACQ = 0.5**

RESULTS

- 228/345 participants were classified as having asthma. 63% of adults, and 71% of children.

1. Spontaneous improvement occurred between visits

Participants with between-visit improvement >MCID				
Test	Adults: Asthma	Adults: Non-asthma	Children: Asthma	Children: Non-asthma
FeNO	39%	33%	46%	52%
Median change (IQR), ppb	1 (-10-19)	0 (-9-7)	-2 (-20-13)	3 (-3-26)
FEV₁	21%	19%	11%	15%
Median change (IQR), mL	-30 (-162.5 -80)	-45 (-57.5-50)	0 (-110-60)	-35 (-145-60)
ACQ	40%	36%	48%	38%
Median change (IQR), points	-0.4 (-1.2- 0.4)	-0.2 (-1.0-0.2)	-0.4 (-1.0-0.6)	-0.2 (-1.0-0.5)

Table: Between-visit improvement >MCID (%) and median change (IQR) in FeNO, FEV₁ and ACQ.

2. Additional diagnoses from repeating FeNO:

- **Visit 1:** FeNO was above the diagnostic threshold in:
 - **39% of asthmatic adults** (>50 ppb) &
 - **41% of asthmatic children** (>35 ppb)
- **Visit 2:** repeat FeNO identified **additional diagnoses:**
 - **14 adults (12%) & 10 children (16%).**
- FeNO was highly variable between visits in both adults and children (Figure).

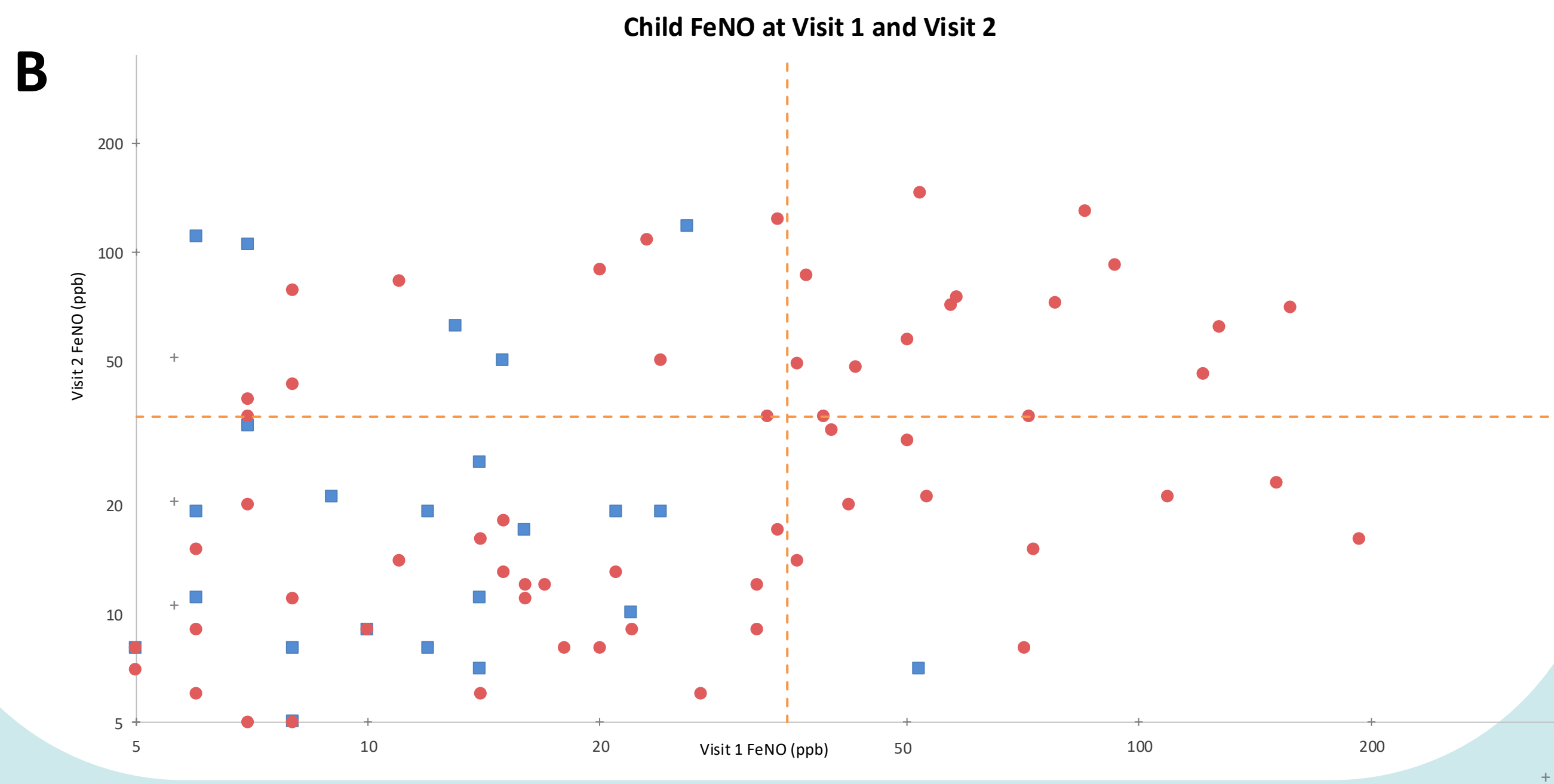
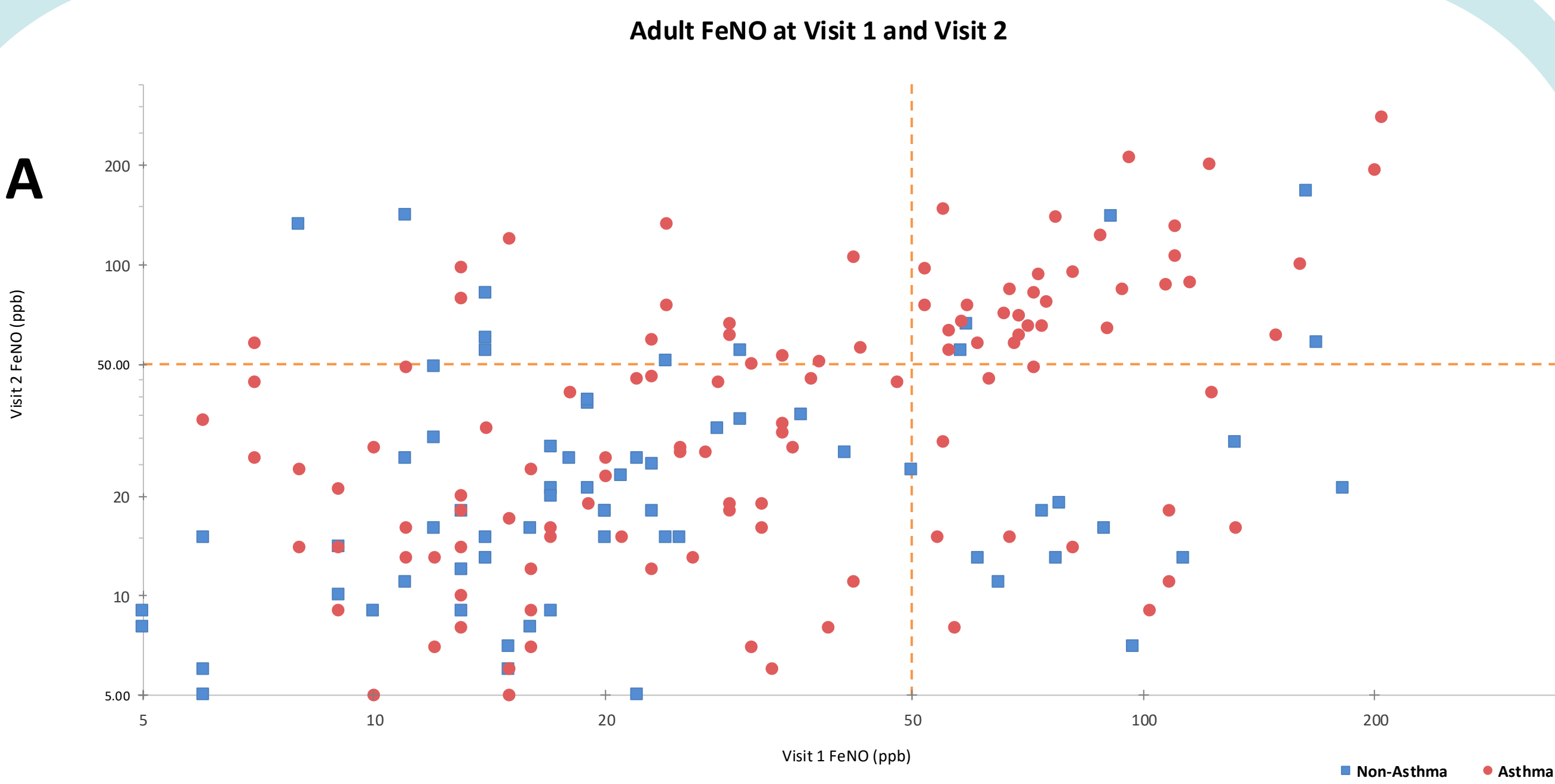


Figure: FeNO measurements from visit 1 and visit 2 in symptomatic adults (A) and children (B). Dotted lines represent diagnostic cutoffs (50ppb adults; 35ppb children).

CONCLUSION

1. Spontaneous improvement in asthma symptoms between visits:

- ✓ Inflammation, symptoms and lung function commonly improve spontaneously between visits in people with suspected asthma, regardless of their diagnosis.
- Therefore, assessing “response to treatment” should be used with caution in the diagnosis of asthma.

2. Repeat FeNO may improve diagnostic yield

- ✓ Repeating FeNO without treatment change can increase diagnoses
- This could reduce the number of referrals for bronchial challenge testing where the resources to deliver this are limited