

# Ability of Different Flow Rates of Fractional exhaled Nitric Oxide (FeNO) to Discriminate between Asthmatic and Non Asthmatic Subjects: Preliminary Results from the GEIRD Study

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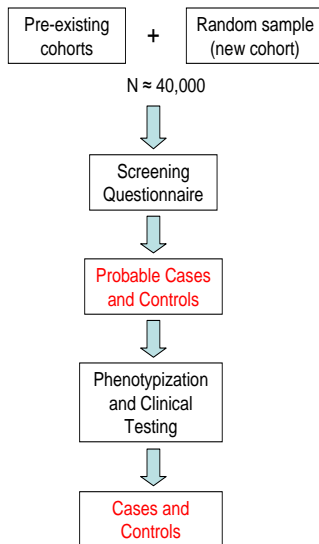
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  3. is flow-dependent (higher at lower flow rates and vice versa)
- ▶ Measurements are normally set up at 50 ml/s, but *the flow rate that better discriminates between asthmatic and non asthmatic subjects is still unknown.*

# Aim

To test the power of different flow rates of FeNO to discriminate between asthmatic subjects and controls.

# GEIRD Study Design



# Cases and Controls - Selection Criteria

**Asthma case:** if a subject

- ▶ has current asthma-like symptoms or had asthma attacks in the last 12 months
- ▶ took respiratory drugs in the last 12 months
- ▶ was positive to the methacoline bronchial provocation test (PD20<1mg)
- ▶ has a pre-bronchodilator  $FEV_1/FVC < LLN$  or  $< 70\%$  and a positive reversibility test

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**Control:** if a subject

- ▶ does not report any respiratory symptoms during the clinical interview
- ▶ does not take respiratory drugs
- ▶ has a  $FEV_1/FVC \geq 70\%$  and  $\geq LLN$  and a  $FEV_1 \geq 70\%$  predicted

# Cases and controls

Asthma cases and controls by cohorts (absolute frequencies and percentages unless stated otherwise):

	<b>Pre-existing Cohorts</b>	<b>New Cohorts</b>	<b>Total</b>
Controls	80 (31.8)	56 (22.2)	116 (46.0)
Cases of Asthma	55 (21.8)	61 (24.2)	136 (54.0)
Total	135 (53.6)	117 (46.4)	252 (100)

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- ▶ Collection time: from April 2008 to July 2009

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- ▶  $p$ -value for curves' comparison → Wald statistics compared to the standard normal distribution [Pepe et al. 2008]

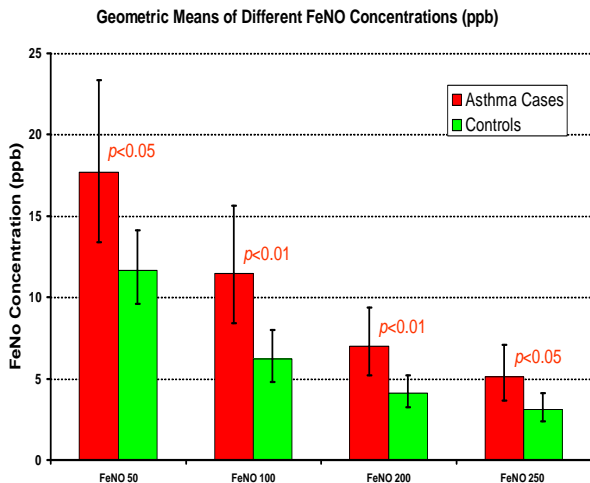
# Results - I

Main characteristics of asthma cases and controls (absolute frequencies and percentages unless stated otherwise):

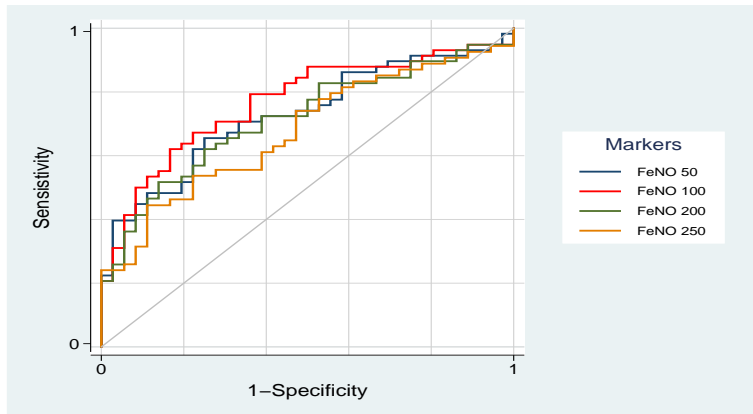
	<b>Cases</b> (n=116)	<b>Controls</b> (n=136)	<b>p-value</b>
Females	58 (50.0)	87 (64.0)	0.03
Age (mean $\pm$ S.D.)	41.3 (0.95)	44.1 (0.79)	0.02
BMI (mean $\pm$ S.D.)	24.6 (0.37)	24.5 (0.37)	0.83
Atopy	93 (80.2)	48 (35.3)	<0.01
<i>Smoking habits:</i>			<0.01
· Non-smokers	52 (44.8)	73 (54.1)	
· Past-smokers	32 (27.6)	38 (28.1)	
· Current smokers	32 (27.6)	24 (17.8)	
Median of cigarettes per day (IQR) <sup>†</sup>	10 (5-17.5)	7 (3-10)	

<sup>†</sup>Current smokers only.

# Results - II



# Results - III ROC Estimation (adjusted)



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## Results - IV

Area under the adjusted ROC curve (95% bootstrapped bias corrected CI) sensitivity and cut-off at a 70% specificity of different FeNO flow rates:

	<b>AUR curve</b>	<b>p-value*</b>	<b>Sensitivity</b>	<b>Cut-Off</b>
FeNO 50	0.73 (0.60, 0.83)	0.2	65%	14.7
FeNO 100	0.77 (0.64, 0.86)	-	67%	10.6
FeNO 200	0.72 (0.59, 0.83)	0.036	62%	6.8
FeNO 250	0.54 (0.35, 0.74)	0.02	54%	5.9

\* using FeNO 100 as reference.

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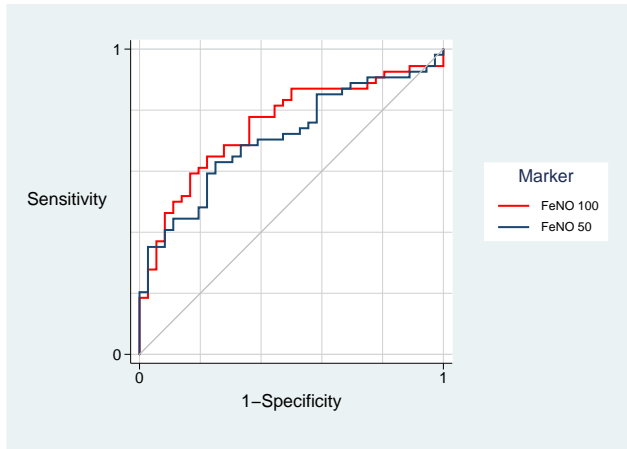
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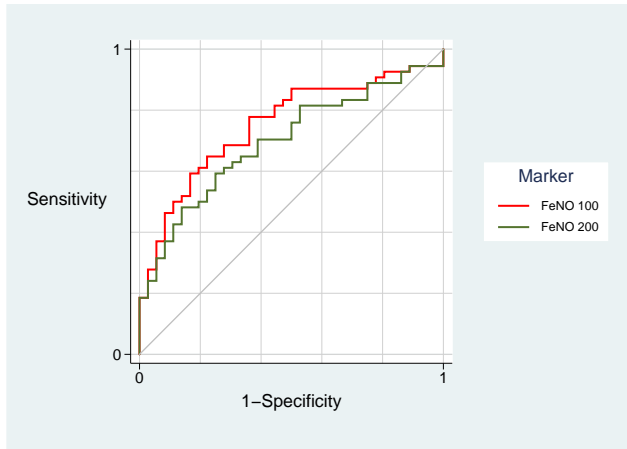
- ▶ best marker (higher AUR): FeNO 100.
- ▶ AUR significant differences: FeNO 100 vs FeNO 200 and FeNO 100 vs FeNO 250.

# FeNO 100 vs FeNO 50



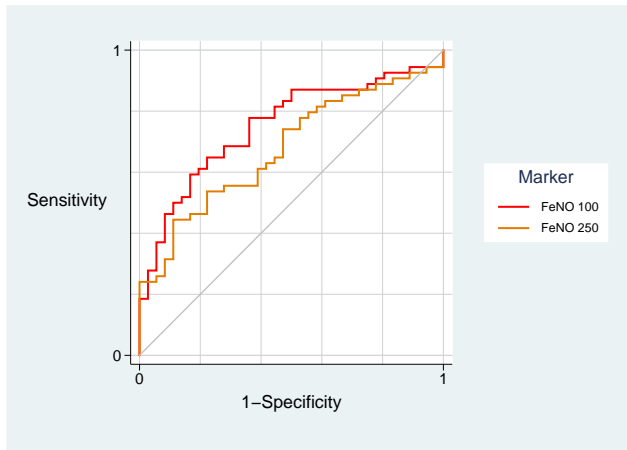
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# FeNO 100 vs FeNO 200



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# FeNO 100 vs FeNO 250



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Area under the ROC curve for FeNO 100 stratified for smoking habits and atopy (adjusted for potential confounders):

<b>Covariates</b>	<b>AUR curve</b>
<i>Smoking Habits*</i>	
Current Smokers	0.70 (0.53, 0.87)
Ex-Smokers	0.55 (0.21, 0.97)
Non Smokers	0.74 (0.55, 0.88)
<i>Atopy*</i>	
Atopic	0.77 (0.62, 0.86)
Non Atopic	0.50 (0.30, 0.68)

\* p-value > 0.05.

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- ▶ **FeNO 50** and **FeNO 100** have a **similar validity** in identifying subjects with current asthma.
- ▶ **FeNO 100** has a statistically significant greater AUR than **FeNO 200** and than **FeNO 250**.

de Marco R, Verlato G, Zanolin ME, Locatelli F, Accordini S, Cazzoletti L, Marcon A, Rava M, Bortolami O, Girardi P, Cappa V, Vesentini R, Braggion M, Nicolis D (*Unit of Epidemiology and Medical Statistics, University of Verona, Italy*); Lo Cascio V, Ferrari M (*Section of Internal Medicine, University of Verona, Italy*); Perbellini L, Olivieri M, D'Amato J (*Unit of Occupational Medicine, Azienda Ospedaliera 'Istituti Ospitalieri di Verona', Italy*); Pignatti P, Trabetti E, Bombieri C, Bettin MD (*Unit of Biology and Genetics, University of Verona, Italy*); Poli A, Nicolis M, Sembeni S (*Unit of Hygiene and Preventive, Environmental and Occupational Medicine, University of Verona, Verona, Italy*); Cerveri I, Corsico AG (*Division of Respiratory Diseases, IRCCS Policlinico 'San Matteo', University of Pavia, Italy*); Marinoni A, Villani S (*Department of Applied Health Sciences, University of Pavia, Pavia, Italy*); Bugiani M, Carosso A (*National Health Service, CPA-ASL 4 Unit of Respiratory Medicine, Turin, Italy*); Rolla G (*Department of Biomedical Sciences and Human Oncology, University of Turin, Italy*); Casali L (*Department of Internal Medicine, Section of Respiratory Disease, University of Perugia, Italy*); Antonicelli L, Bonifazi F (*Department of Internal Medicine, Immuno-Allergic and Respiratory Diseases, Ospedali Riuniti di Ancona, Ancona, Italy*); Pirina P, Fois AG (*Institute of Respiratory Diseases, University of Sassari, Sassari, Italy*)

# Greetings

Thank you for your time!

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