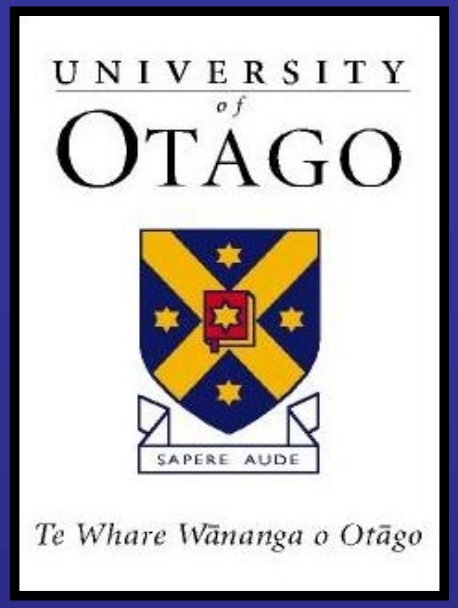


Spirometry and Inflammometry

Professor D. Robin Taylor
Dunedin School of Medicine
University of Otago

Peak flow measurements

- Single measurements useful to assess severity of airflow obstruction if diagnosis of asthma is established
- Single low measurements are non-diagnostic: reduced in BOTH restriction AND obstruction
- Diagnostically helpful if serial measurements are available: look for diurnal variation

Spirometry: technique

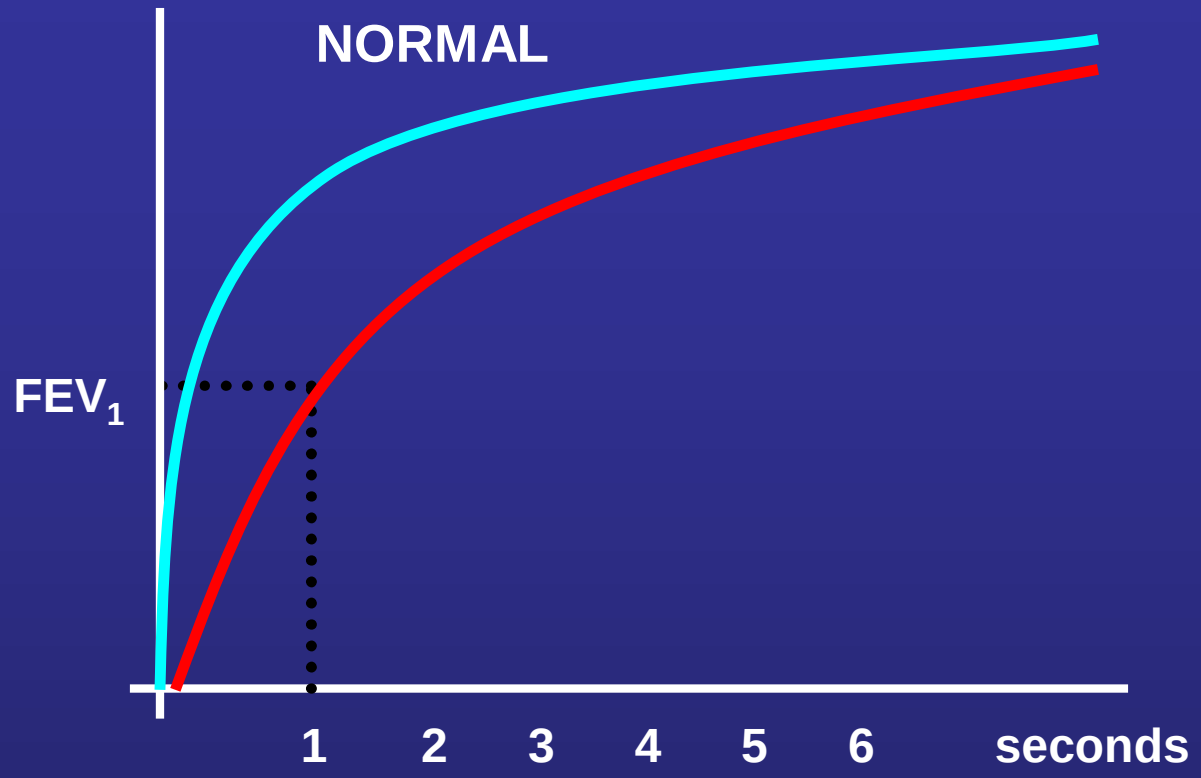
- Effort should be maximal throughout
- A minimum of 6 seconds expiratory time is required.
- Watch for air leakage
- Unsatisfactory tests lead to underestimate of FEV_1 or FVC or both
- Look at the output: visual trace
- Beware of stridor! (abnormal inspiratory limb of FV loop, if this is available)

Spirometry: what to measure?

- Age , sex and height: these determine predicted values
- $FEV_{1:}$ the most robust measurement of lung function. Coefficient of variation = 10%
- Pre-bronchodilator = indication of current severity of obstruction (if obstructed!)
- Post-bronchodilator FEV_1 = for longitudinal comparisons
- FVC (or $FEV_{6)}$
- FEV_1 / FVC ratio: declines with age. Defines obstruction. Use L(ower) L(imit) of N(ormal)
- Change in FEV_1 with time

Reversibility testing

- A change in FEV_1 and >200mL. indicates “reversibility”
- Immediate = change with fast acting beta-agonist (20 minutes)
- Long-term = change with trial of steroid (2-4 weeks)
- Reversibility may not be demonstrable if the spirometric values are within the normal range
- Reversibility may not be demonstrable if the patient is already on treatment (ICS)
- If immediate it confirms the presence of ASM spasm (non-specific)
- If long-term, it confirms oedema / mucus plugging, as well as ASM spasm
- Has no predictive value for long term treatment responsiveness in asthma or COPD in adults

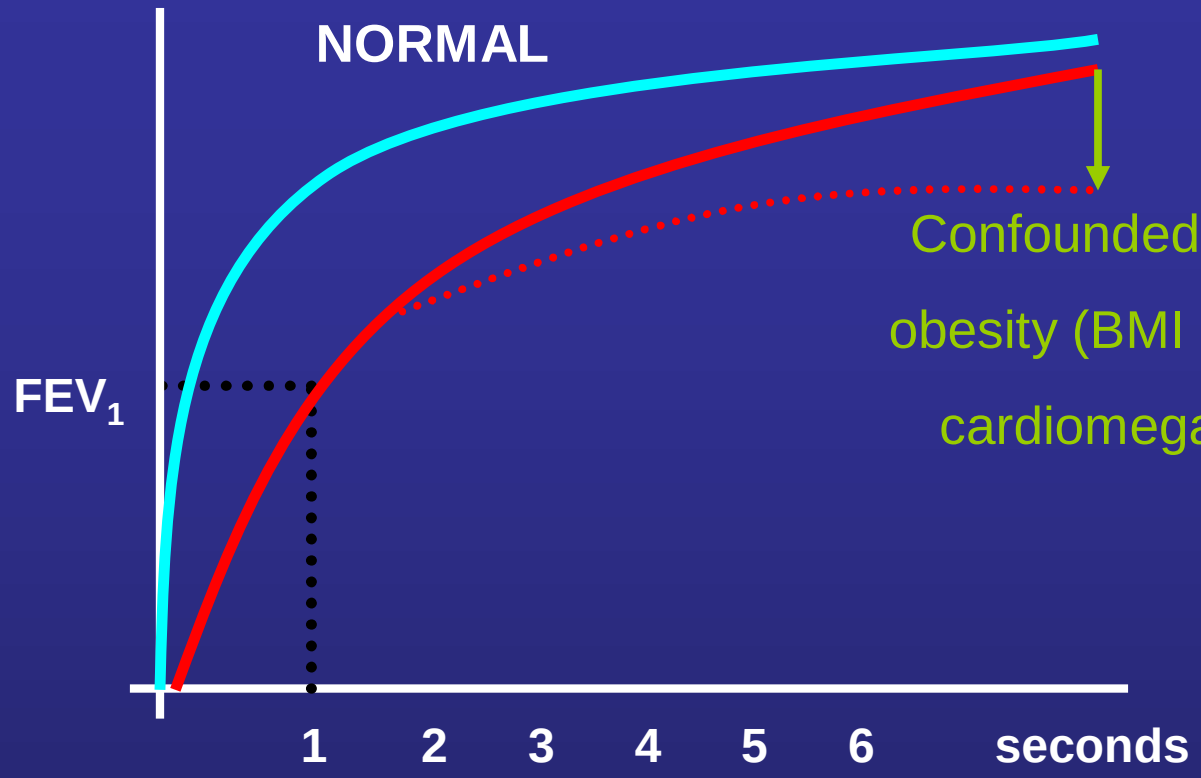


OBSTRUCTED

FEV_1 reduced markedly

FVC reduced minimally

FEV_1 / FVC ratio reduced

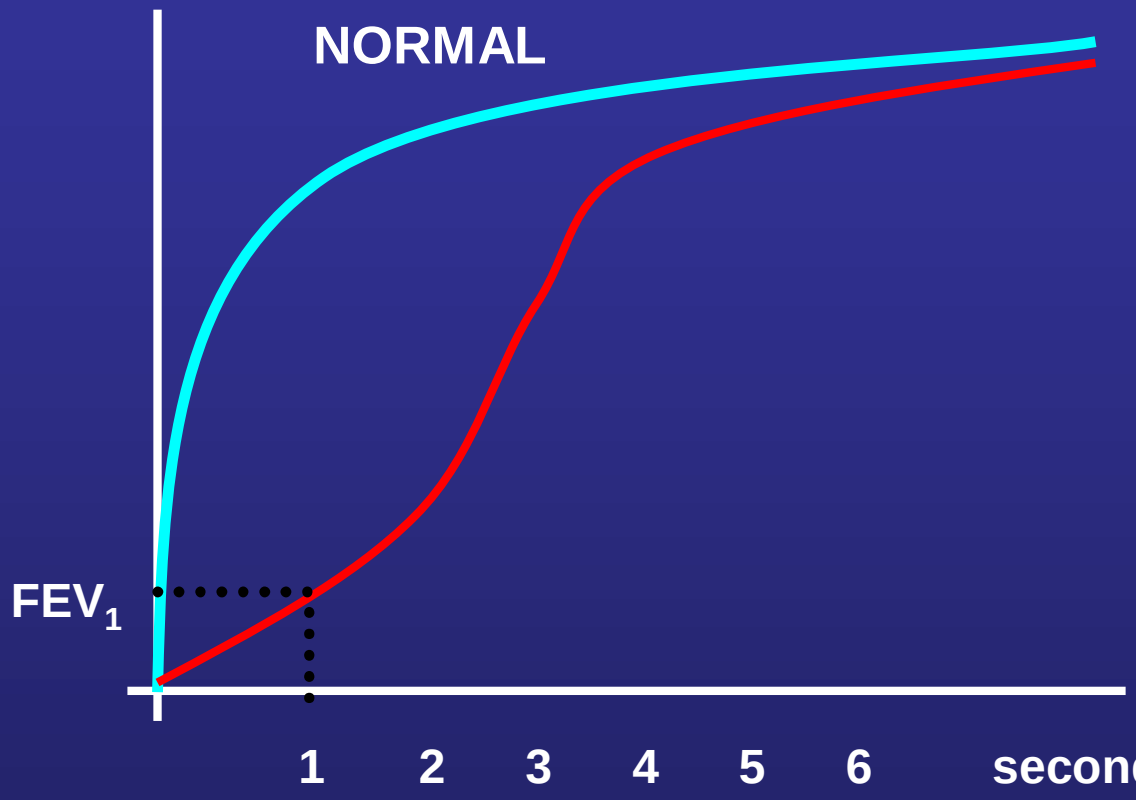


OBSTRUCTED

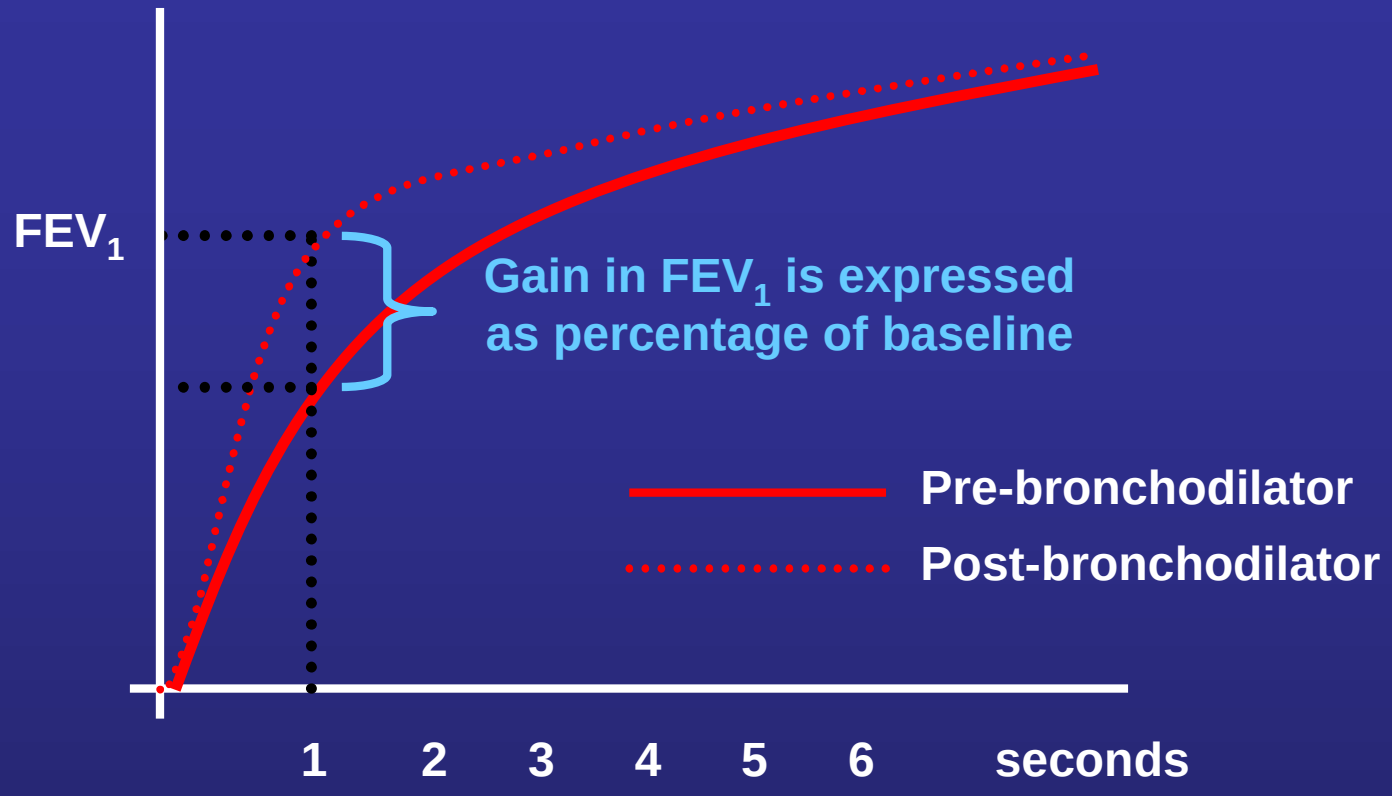
FEV_1 reduced markedly

FVC reduced markedly

FEV_1 / FVC ratio unchanged



ACCELERATING EXPIRATORY EFFORT:
FALSE POSITIVE FOR OBSTRUCTION

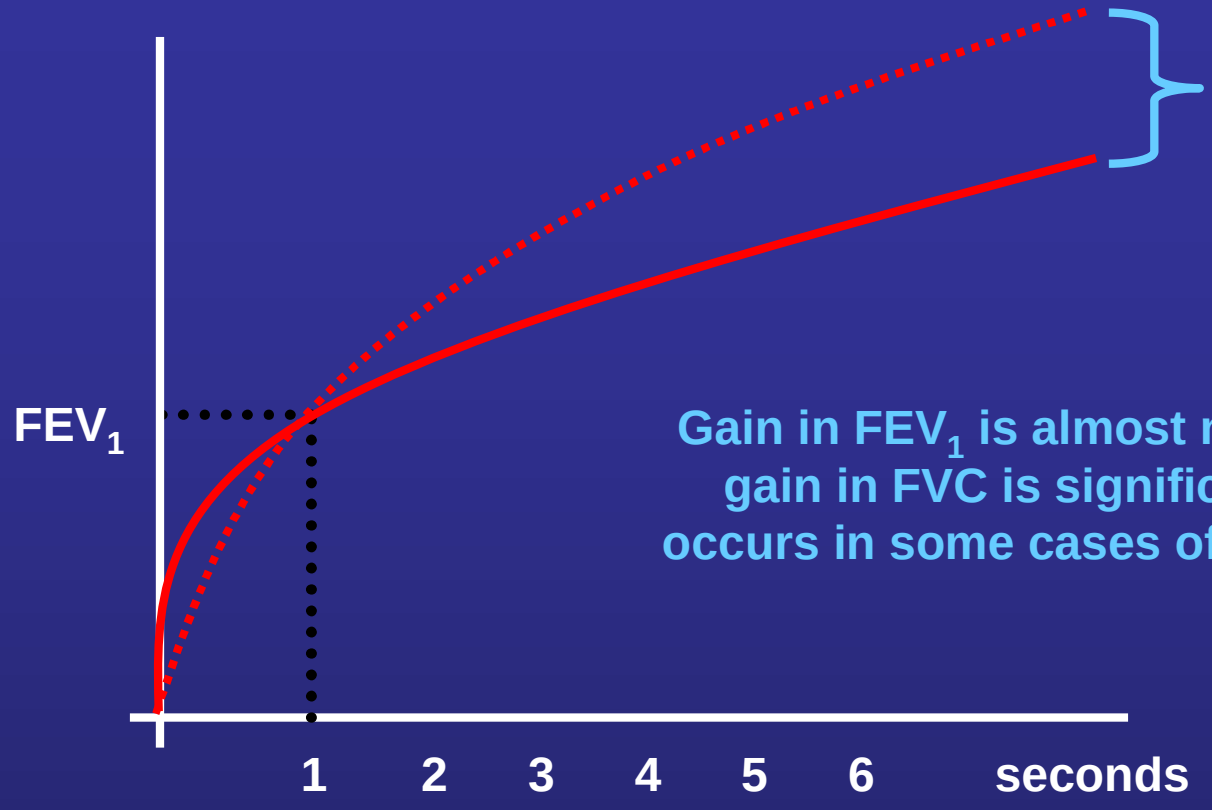


OBSTRUCTED: post-bronchodilator

FEV_1 increased

FVC reduced minimally

FEV_1 / FVC ratio reduced

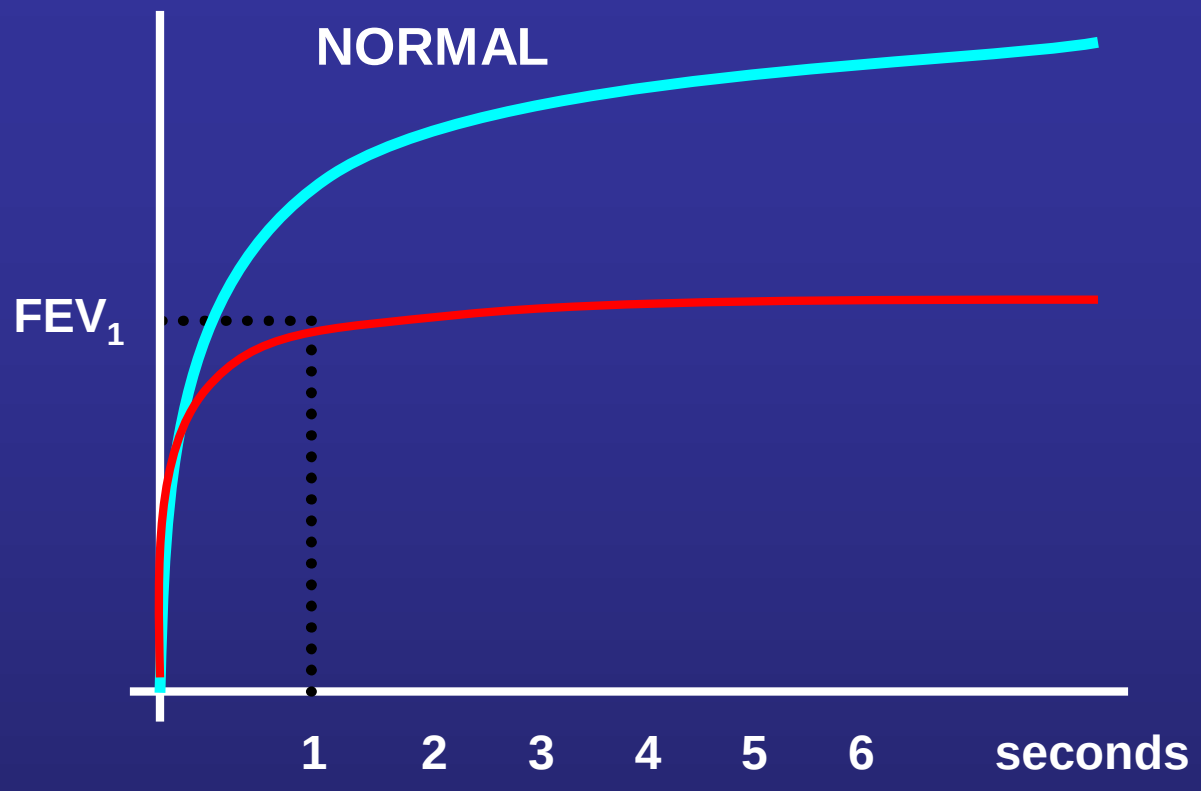


OBSTRUCTED: "volume responder"

FEV_1 reduced markedly

FVC reduced markedly

FVC improves with bronchodilator

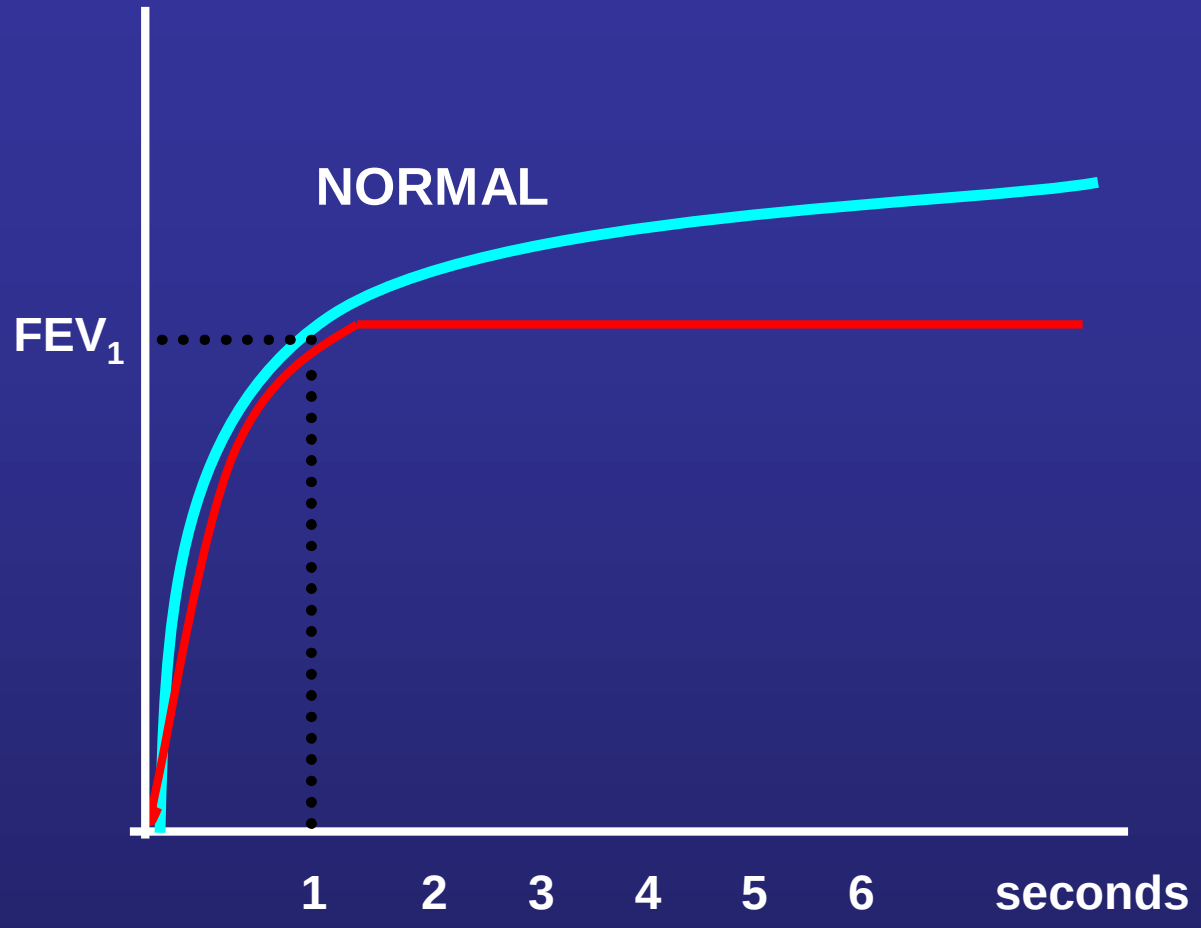


RESTRICTED

FEV_1 unchanged

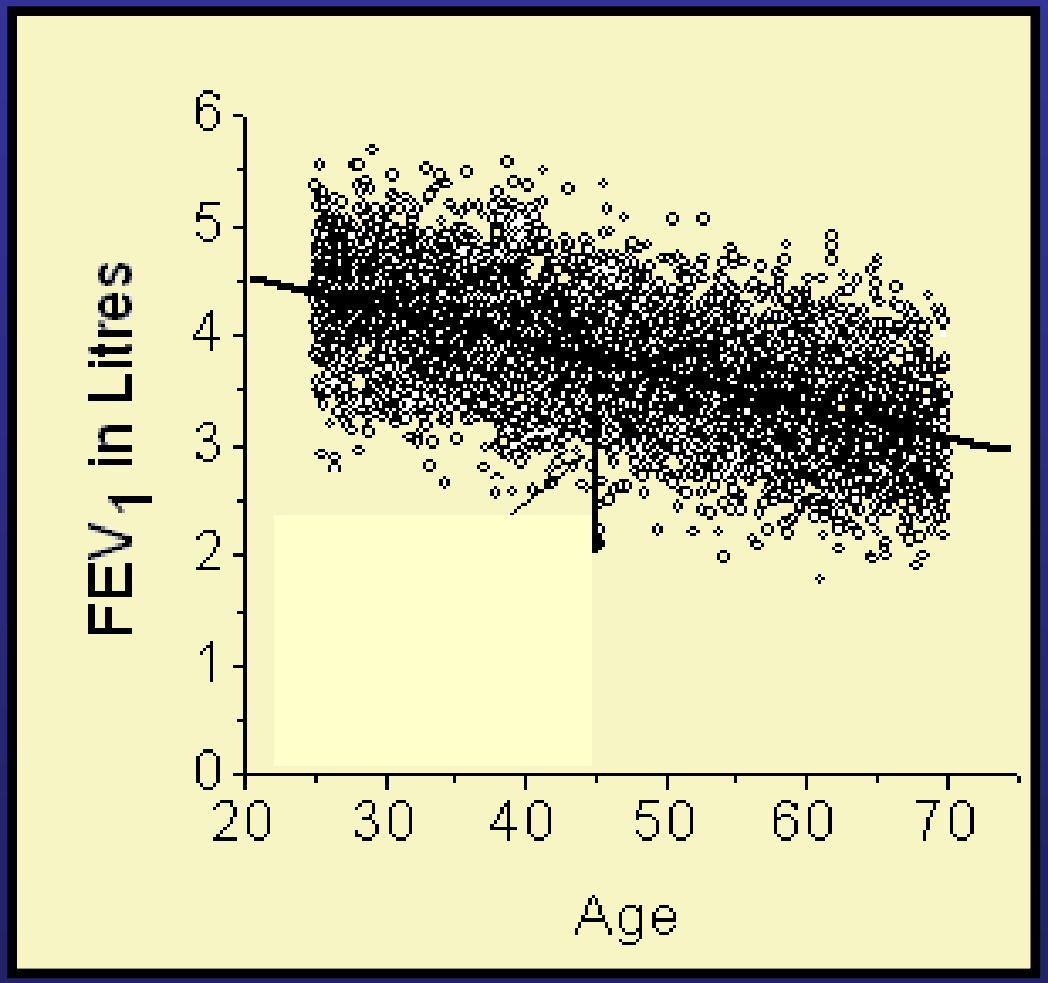
FVC reduced markedly

FEV_1 / FVC ratio increased

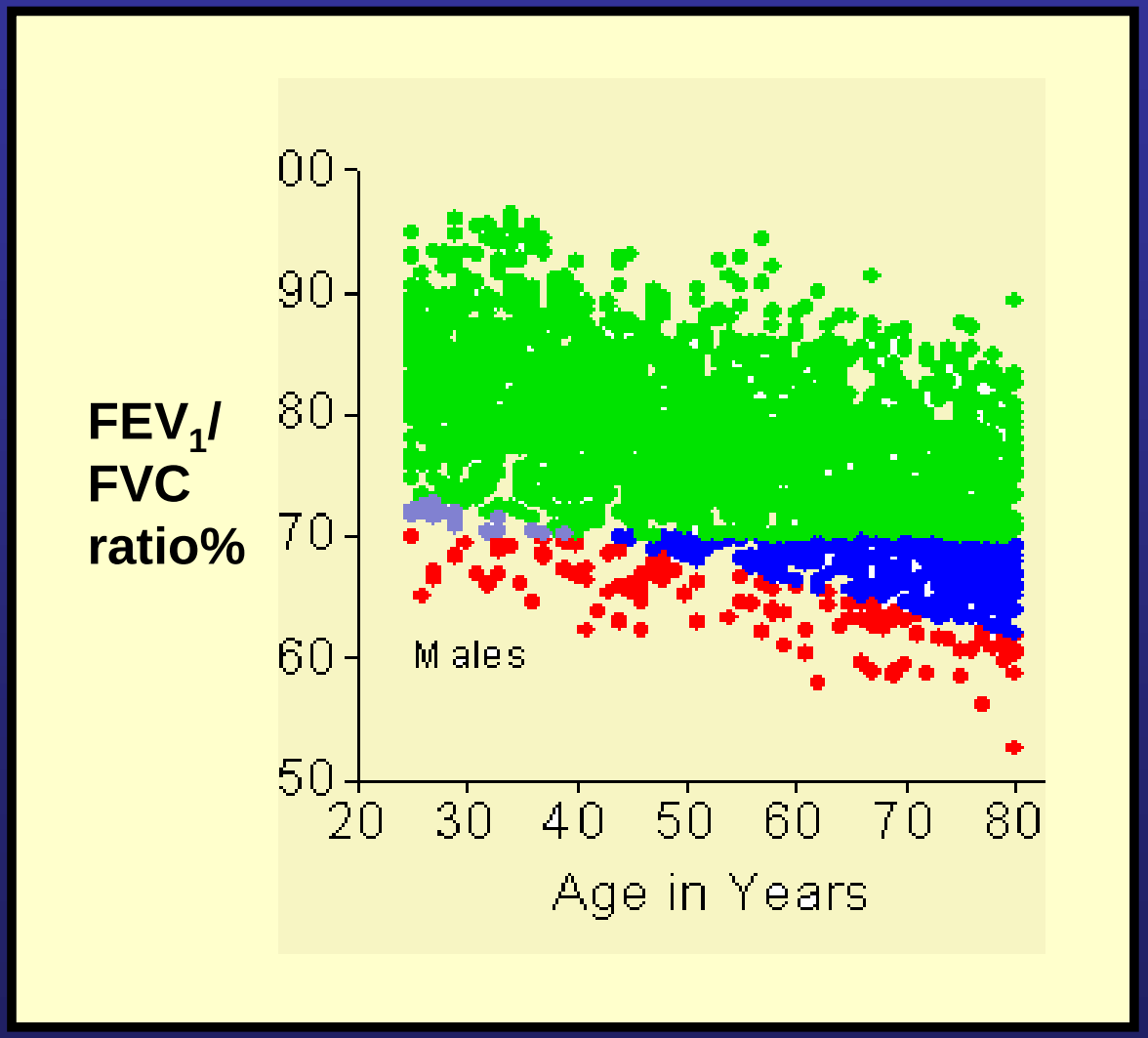


PREMATURE TERMINATION OF EFFORT:
FALSE POSITIVE FOR RESTRICTION

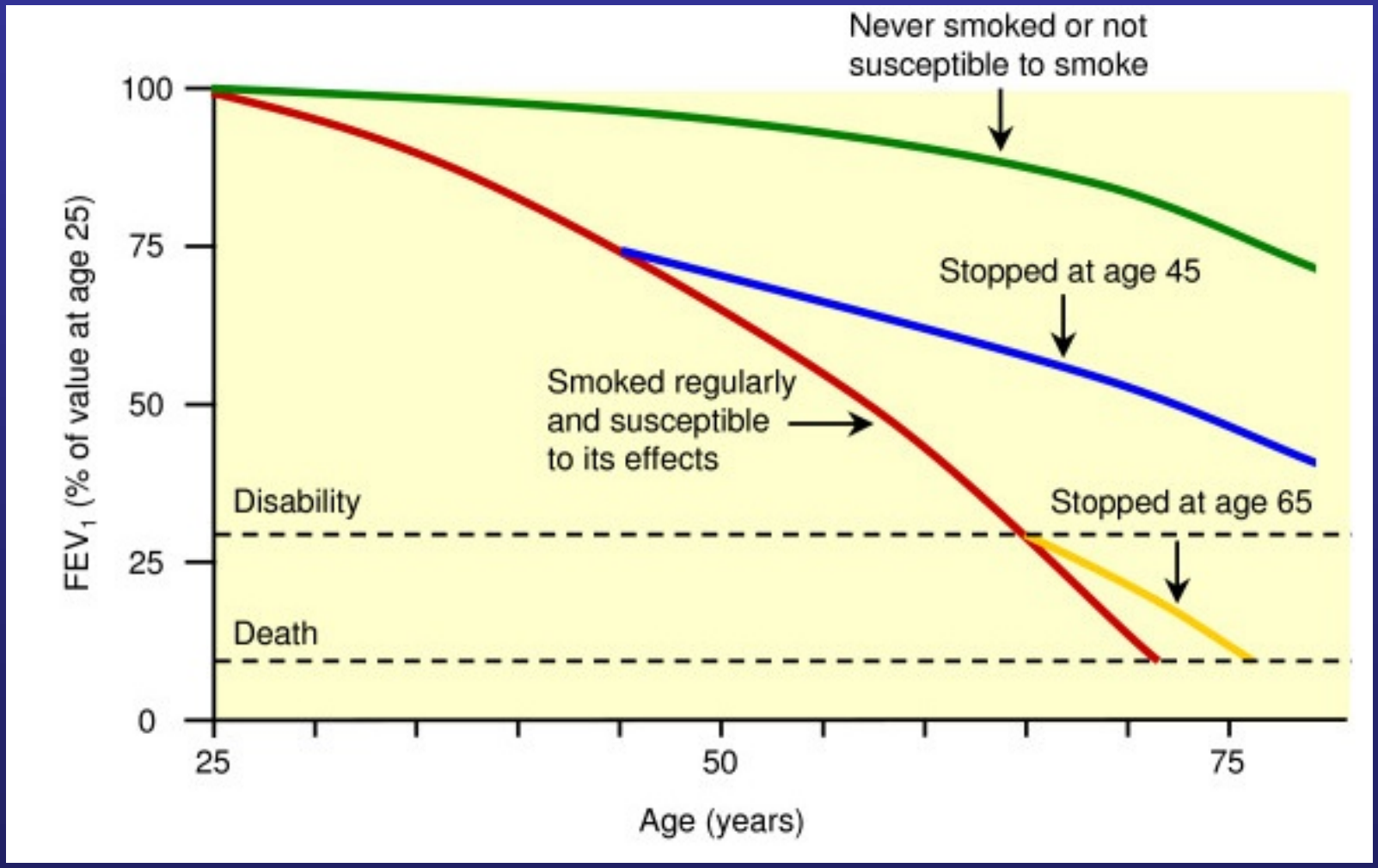
Effect of age on FEV_1



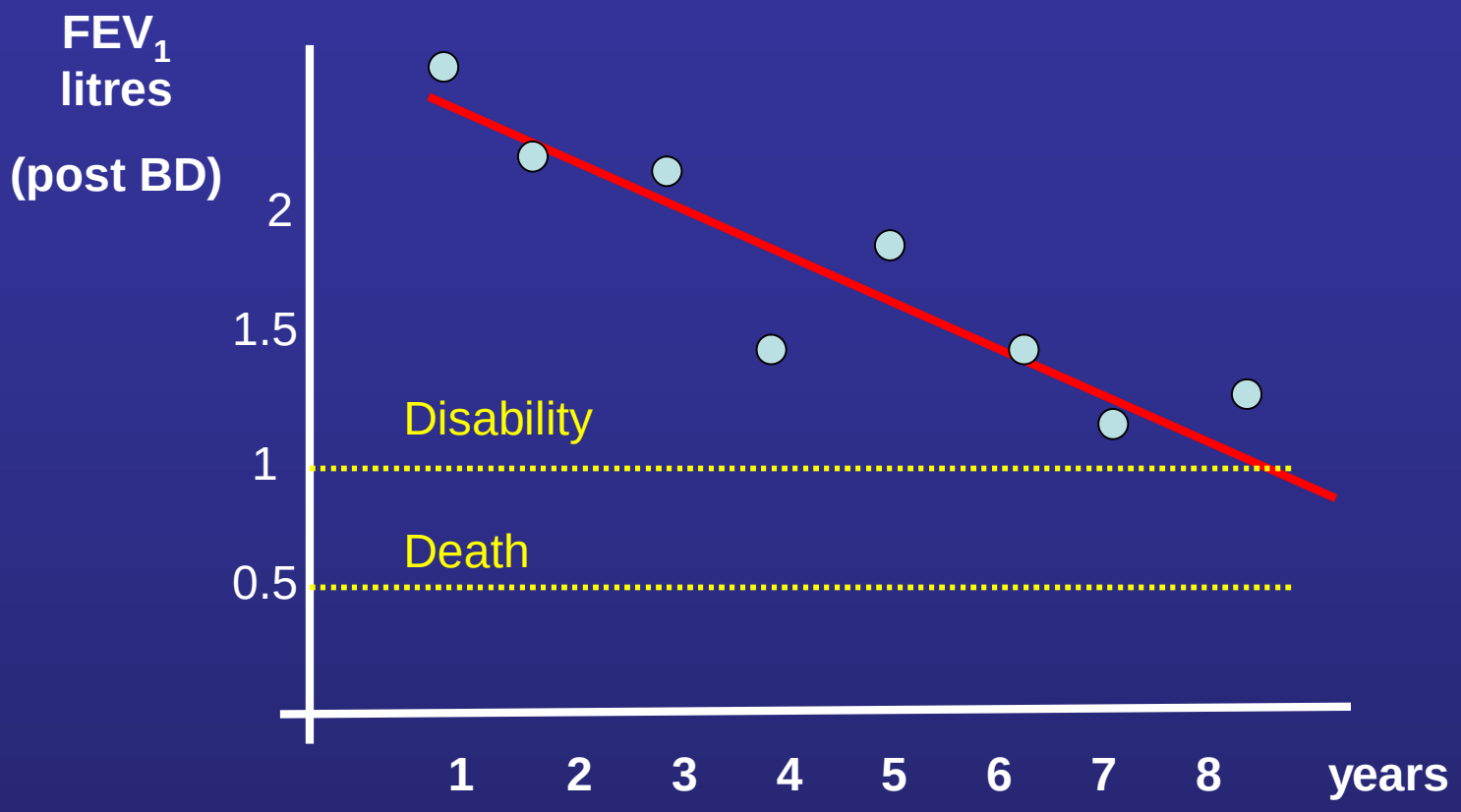
Interpretation of FEV_1/FVC ratio: one size (<70%) doesn't fit all



Decline in lung function in relation to smoking and smoking cessation



Fletcher and Peto



Decline in lung function in non-smoker = 20-30 mL/annum

Decline in lung function with severe COPD = 50-100mL/annum

Minimum of 3 year interval data required to project future trend

GINA definition of asthma

… chronic **inflammatory disorder** of the airways …

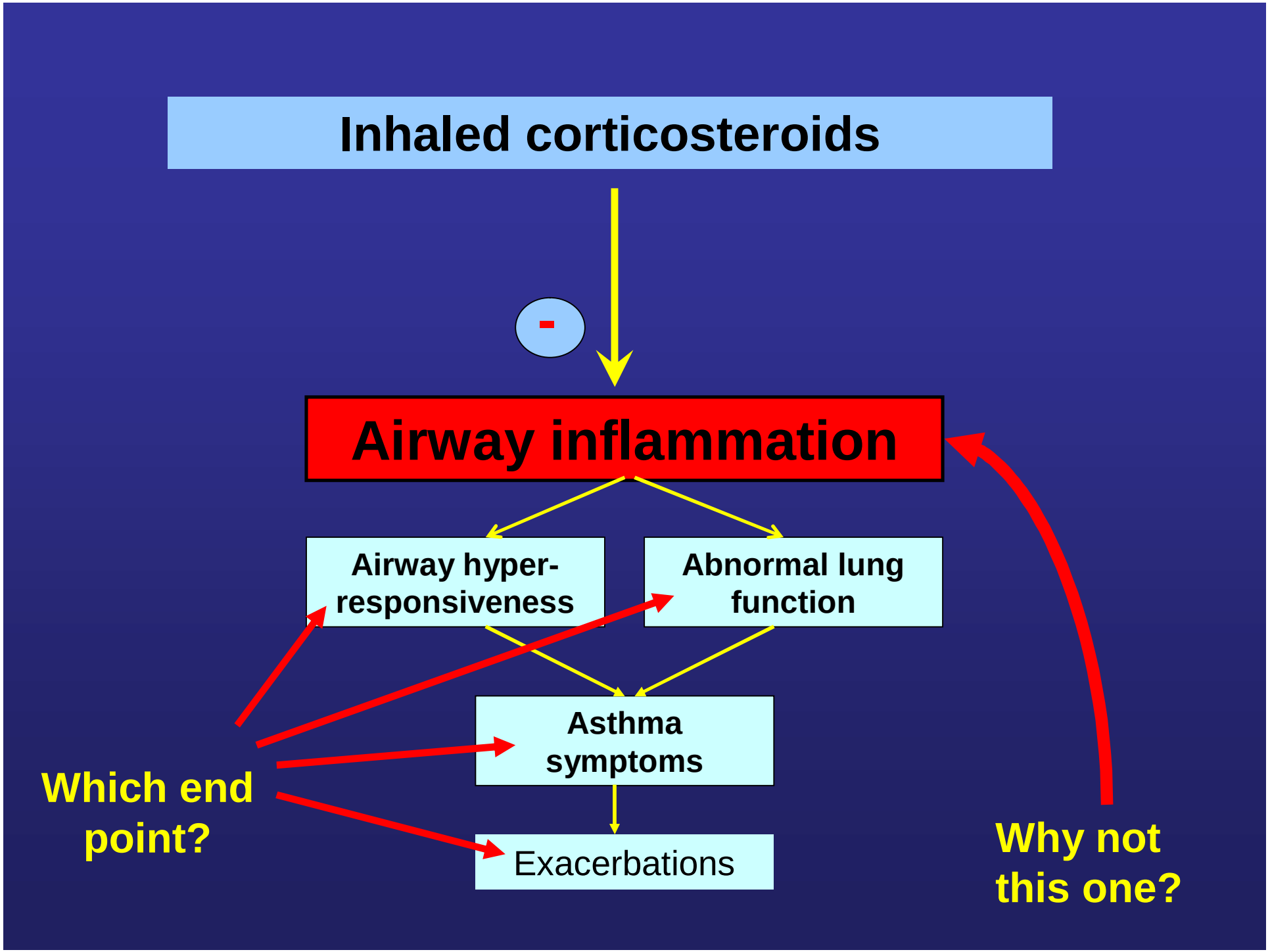
… increase in **airway hyper-responsiveness …**

… recurrent episodes of respiratory symptoms …

… **variable airflow obstruction** …

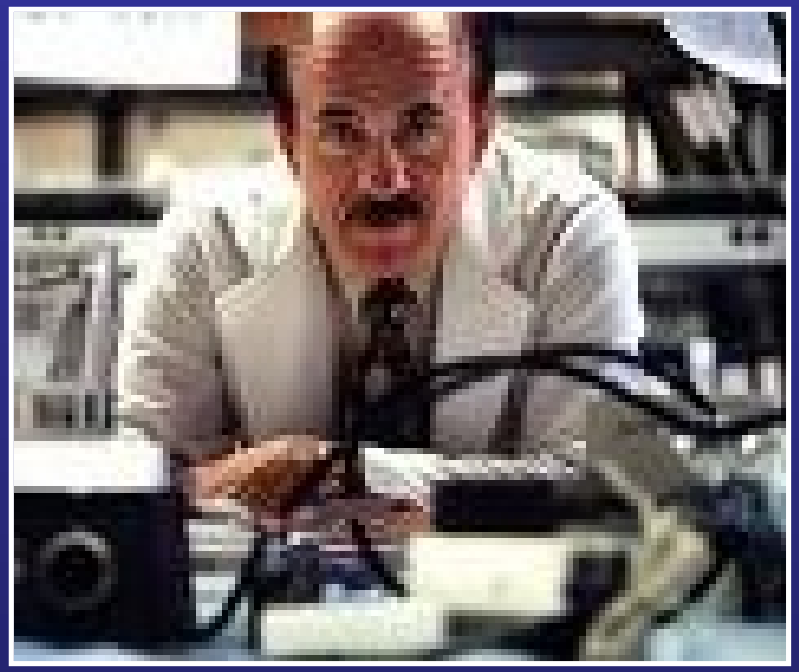
… **reversible** spontaneously or with treatment.

Global **IN**itiative for **A**sthma 2007


Inhaled corticosteroids
-
Airway inflammation
Airway hyper-responsiveness
Abnormal lung function
Asthma symptoms
Exacerbations
Which end point?
Why not this one?

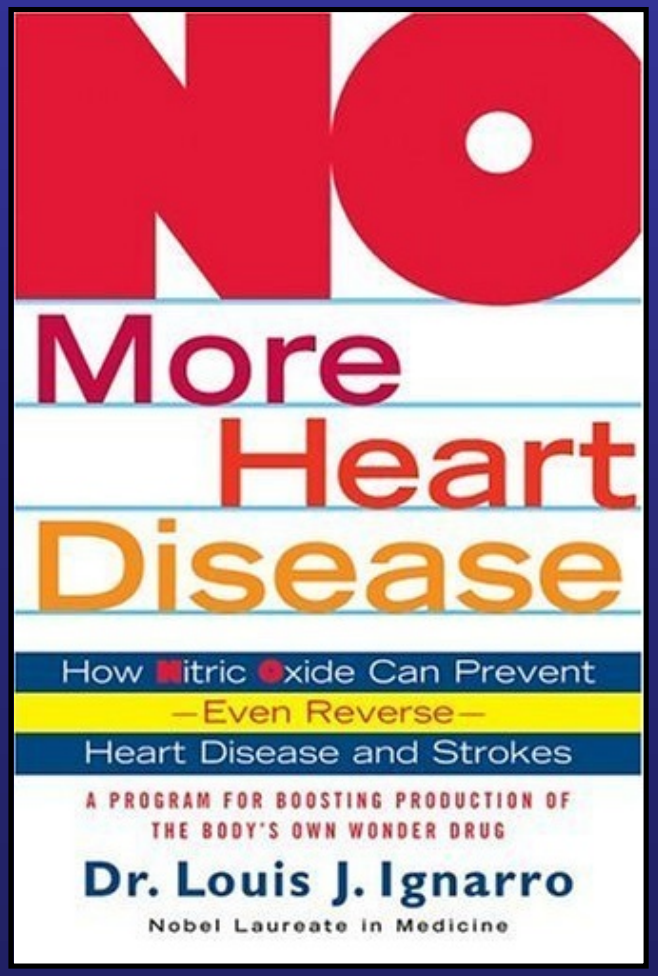
Can you diagnose *steroid responsiveness*?

Nitric oxide: “discovered” in 1988



Louis Ignarro

Nobel Laureate in Medicine
1998



Nitric oxide analysers

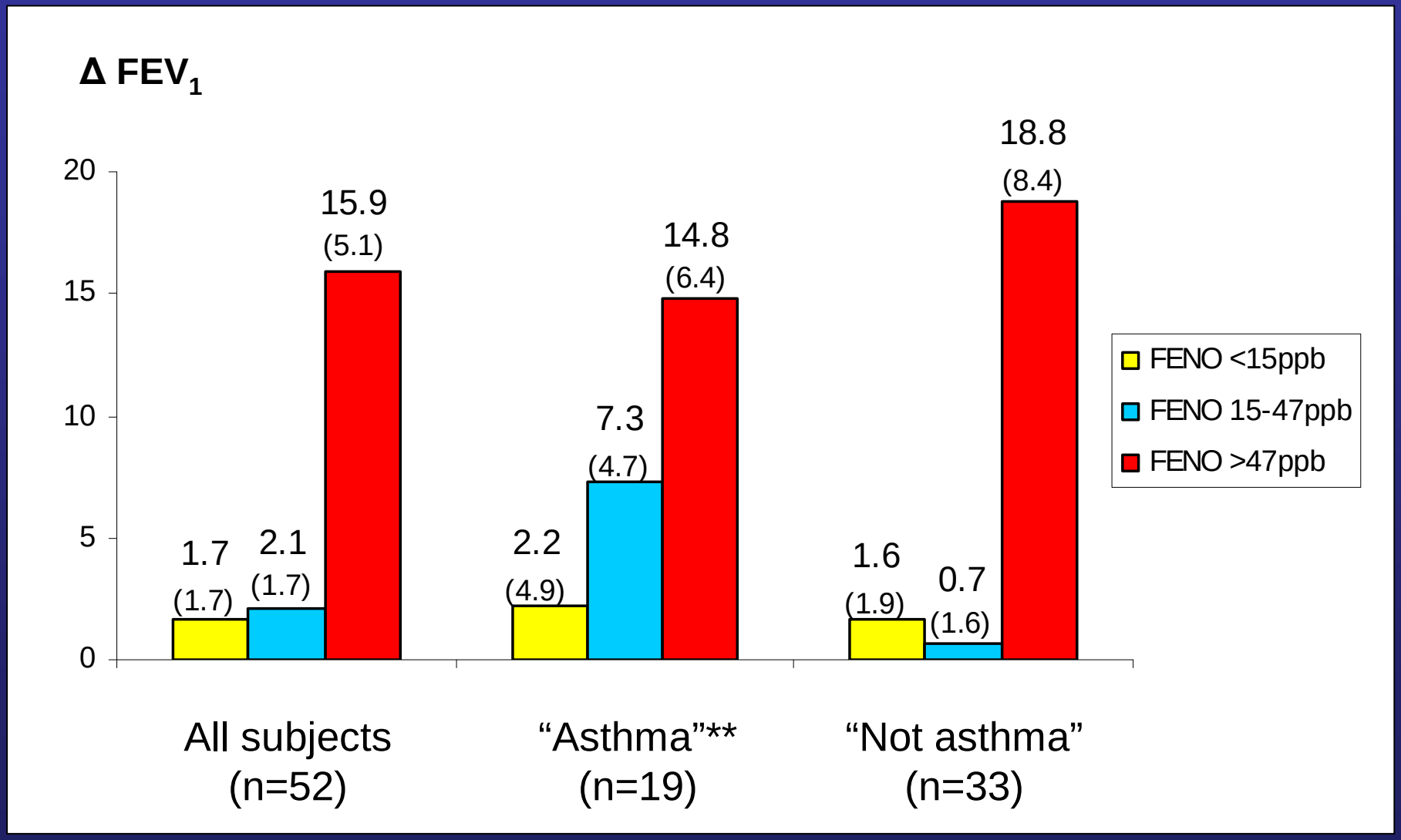
Available devices:

- **F_ENO = fraction of nitric oxide in exhaled air**
- **Ecomedics**

Ecomedics CLD 88 sp

Aerocrine NIOX MINO

Percent change in FEV_1 with fluticasone in relation to baseline F_ENO



** Based on symptoms *plus* either BDR or AHR at presentation

Smith et al. *AJRCCM* 2005

Predicting steroid response: increase in FEV_1 > 12%

Predictor	Cut-point	Sens.	Spec.	PPV	NPV
FE_{NO}	>47ppb*	67	78	47	89
$PD_{20}MCh$	<8umol	58	69	37	84
PEFR var.	>20%	0	97	NA	76
FEV_1% pred	<80%	17	88	29	78
FEV_1 BD response	>12%	8	95	33	78

* Based on ROC curve analysis, not tertiles

Smith et al. AJRCCM, 2005

Predicting success/failure of ICS dose reduction: BHR, sputum eosinophils and FE_{NO}

n = 40 children

ICS dose: 200-500µg/day

Dose reduced by 50% every 8 weeks

30% weaned off ICS

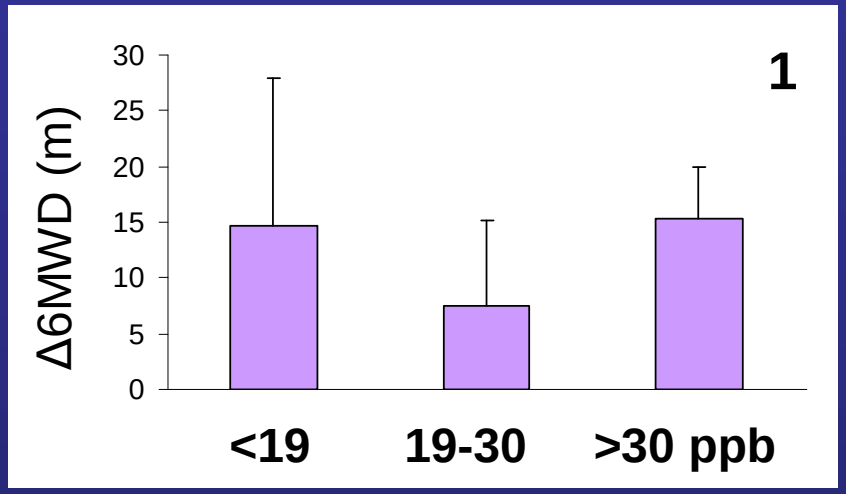
38% lost control

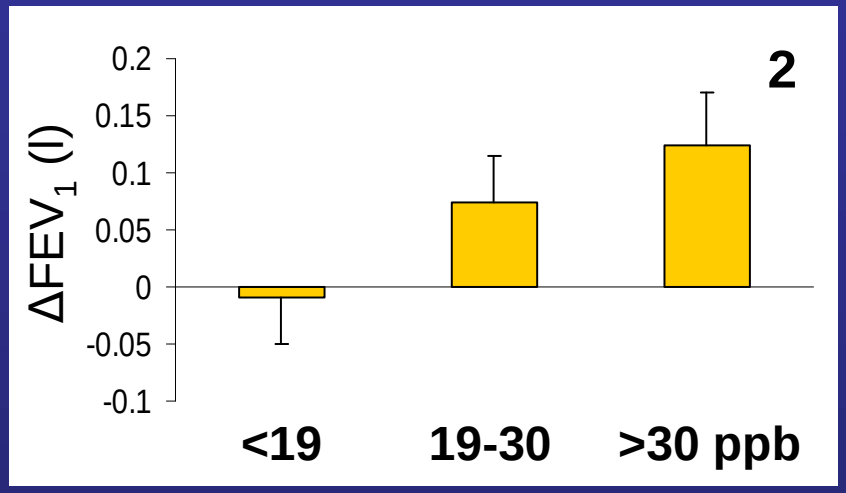
	Sens.	Spec.	PPV	NPV
BHR	63.6	59.5	31.8	84.6
Eosinophils				
>0%	100	51.0	41.0	100
>3%	54.5	84.8	46.1	78.7
F_ENO				
>22ppb	78.6	68.6	44.0	92.5
>35ppb	71.4	82.4	52.6	91.3

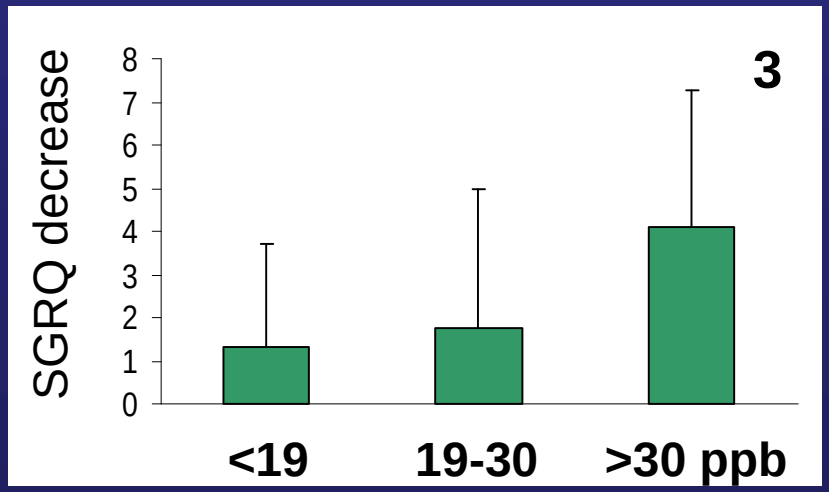
Conclusion: low FE_{NO} (<22ppb) predicted successful reduction / withdrawal of ICS

Zacharasiewicz et al. AJRCCM, 2005

COPD: changes in 6MWD, FEV_1, and SGRQ with steroid, stratified by FE_{NO} tertile







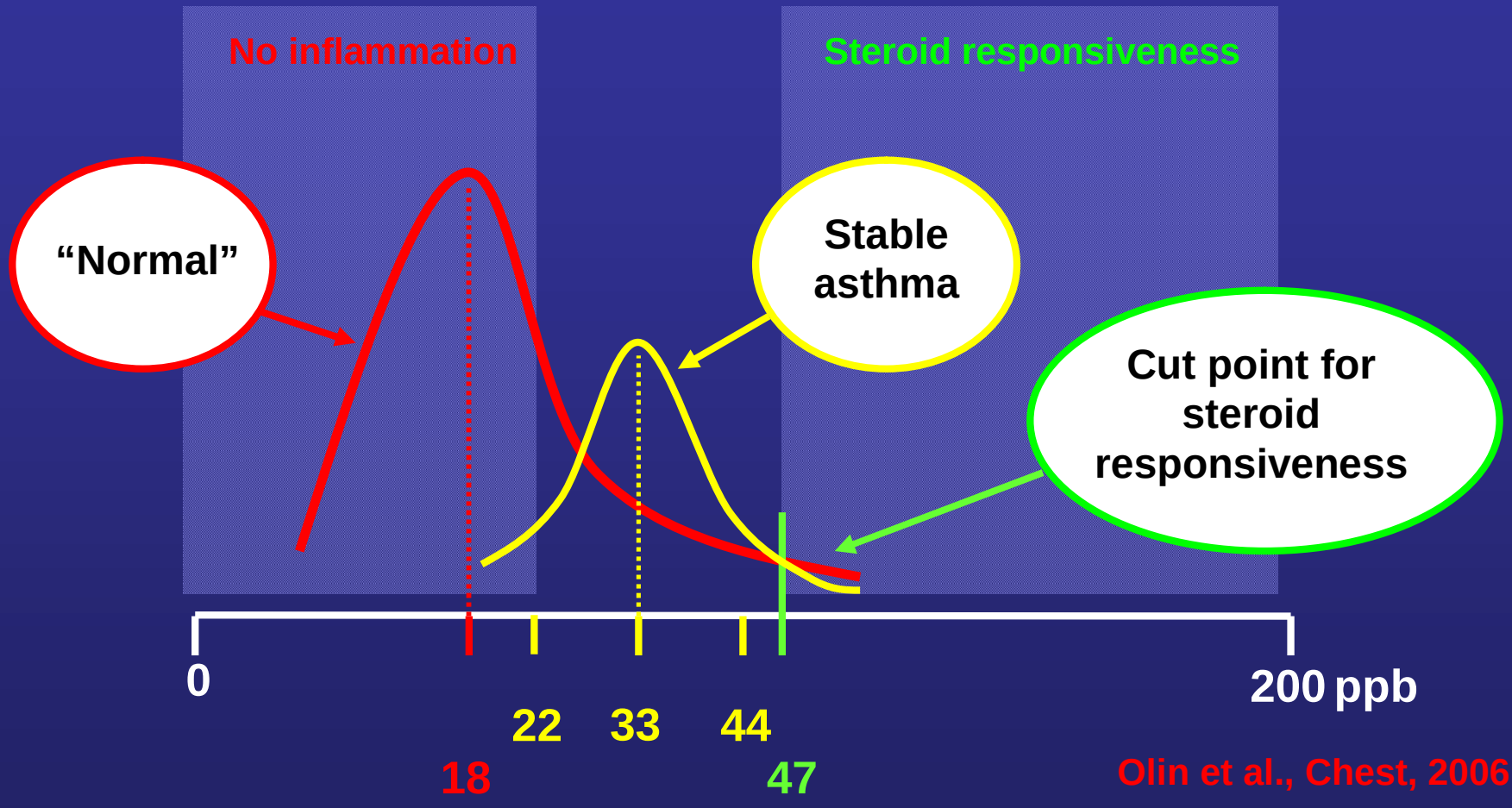
Dummer et al., AJRCCM, 2009

Predictive utility of FE_{NO} for a significant change in FEV_1 with steroid

ΔFEV_1	FE_{NO} cut-point (ppb)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
>0.2 litres	**25**	**71**	**56**	**32**	**87**	**60**
	35	36	79	33	81	69
	50	**29**	**96**	**67**	**82**	**81**
	70	14	98	67	80	79
>20%	**25**	**86**	**55**	**19**	**97**	**58**
	35	57	78	25	93	76
	50	**43**	**95**	**50**	**93**	**89**
	70	14	96	33	90	87

Dummer et al., AJRCCM, 2009

The importance of cut-points when interpreting a biomarker



Figures in yellow = mean and 95% C.I.

Figure in green = optimum cut point

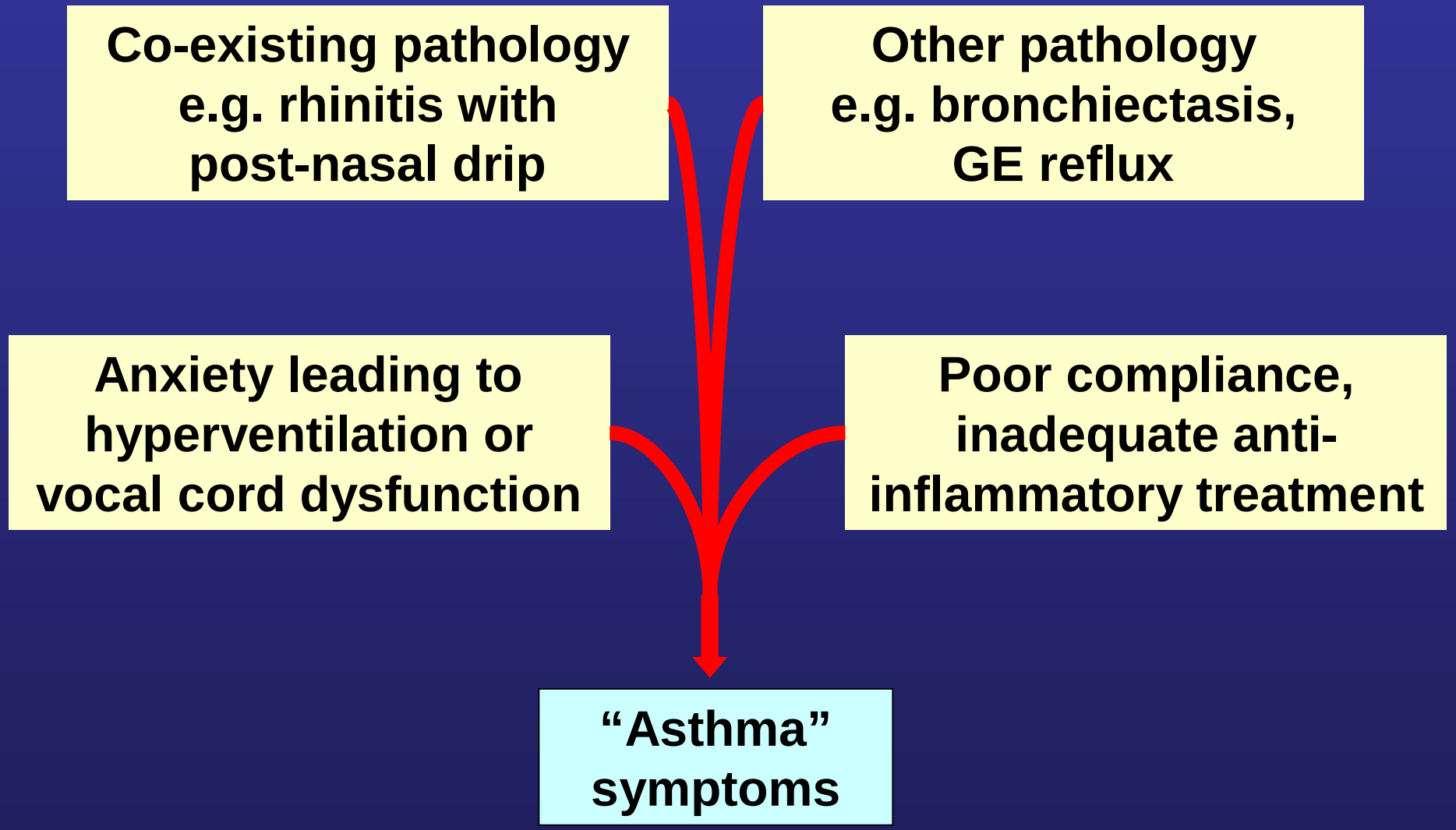
Olin et al., Chest, 2006

Shaw et al., AJRCCM, 2007

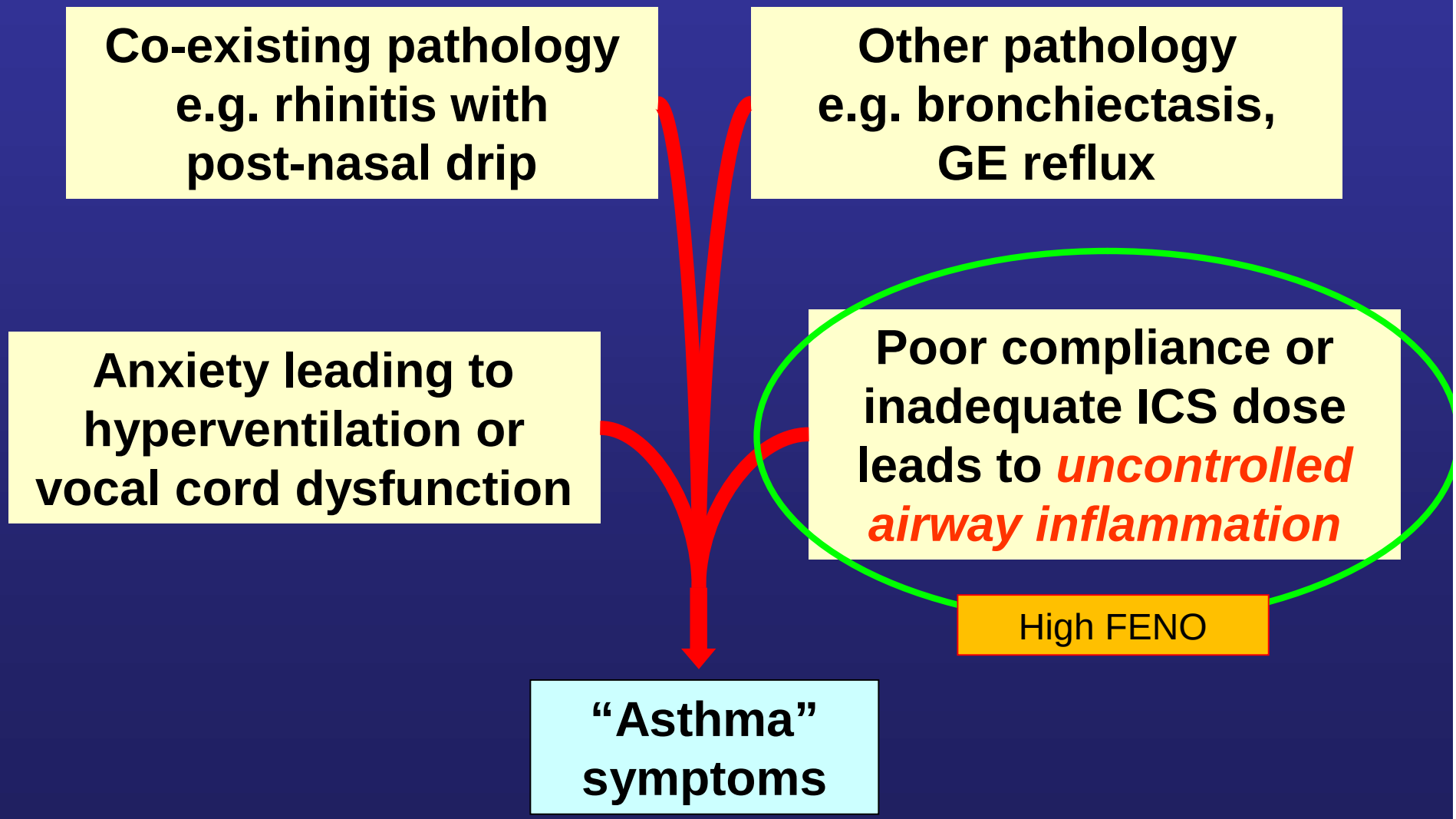
Smith et al., AJRCCM, 2005

Pijnenburg et al., Thorax, 2005

Respiratory symptoms in patients with “asthma”



Respiratory symptoms in patients with “asthma”



Patient K.P., age 34

- Lifelong bronchial asthma, but recent period of instability (4 months).
- High doses of ICS. 4 courses of oral prednisone in 6/12.
- Weight gain over 2 years 80kg. to 98kg. BMI 39.4.
- Coughing precipitates acid reflux; coughing precipitates wheeze.
- Still taking up to 12 puffs salbutamol daily!
- Emotionally labile
- FEV_1 108%; FVC 95%; ratio 89% - *normal*
- **F_ENO 6ppb.**

Patient J.S., age 16

- Asthma since age 2
- BMI 42.0
- Occasional exacerbations, wheezy with exercise
- On fluticasone 250µg 2 puffs b.i.d.
  - **F_ENO 76ppb**
- On fluticasone 250µg 3 puffs b.i.d.
  - **F_ENO 42ppb**
- FEV_1 95%; FVC 128%; ratio 70% - *borderline*
- Mother anxious to reduce dose of ICS

High F_ENO >45ppb
[or rising F_ENO: >60% change]

= uncontrolled steroid-responsive airway inflammation

In an *asymptomatic* patient ……

- No change in ICS dose, but refer to history of individual patient
- Withdrawing ICS is likely to be followed by relapse

High F_ENO >45ppb
[or rising F_ENO: >60% change]

= uncontrolled steroid-responsive airway inflammation

In a *symptomatic* patient ……

- Poor compliance with ICS
  and/or ? poor inhaler technique
- Inadequate ICS dose: likely to respond to increase
- Rarely: truly steroid resistant asthma
- Rarely: pulmonary eosinophilia

Low F_ENO <25ppb

= non-steroid-responsiveness or <u>no</u> airway inflammation

In an *asymptomatic* patient ……..

- Implies adequate dosing and good compliance with therapy
- Reduce dose or withdraw ICS dose altogether

Low F_ENO <25ppb

= non-steroid-responsive or no airway inflammation

In a *symptomatic* patient ……

- Non-eosinophilic asthma, ? neutrophilic probably steroid unresponsive
- Complicating factor e.g. rhinosinusitis GE reflux
- Alternative diagnosis e.g. vocal cord dysfunction , anxiety-hyperventilation, bronchiectasis, cardiac disease

Nitric oxide analysers

Available devices:

- Sievers NOA 280i
- Logan LR2000, LR4000
- Aerocrine NiOX and MINO
- Ecomedics

Ecomedics CLD 88 sp

Aerocrine NIOX MINO

Thank you