Associate Professor Jeffrey Garrett

Respiratory Physician
Department of Respiratory Services
Middlemore Hospital

Saturday, August 10, 2019 (Room 11)

16:30 - 17:30 WS #136: Masterclass in Asthma Management
17:35 - 18:30 WS #146: Masterclass in Asthma Management (Repeated)

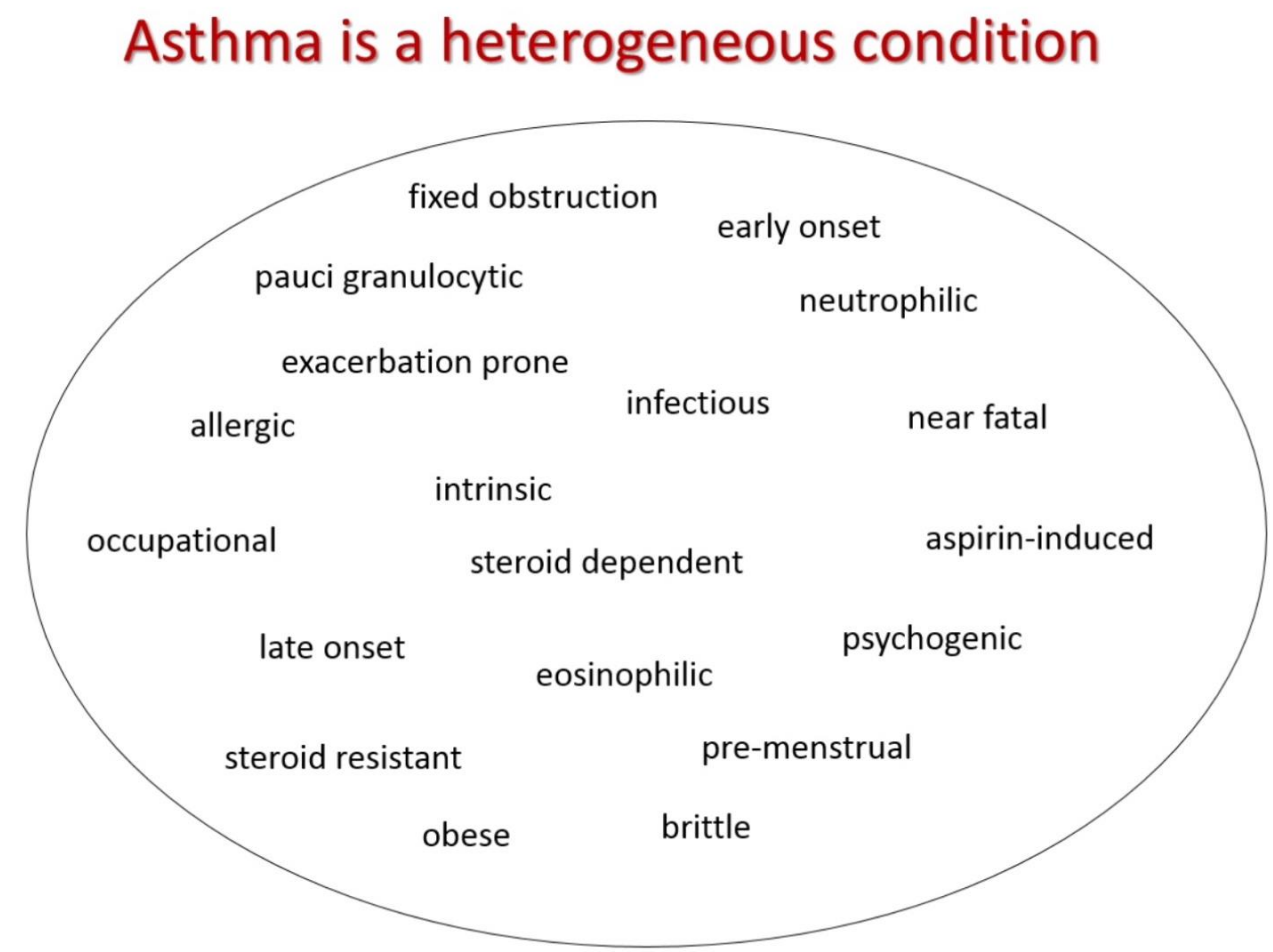
Masterclass in Asthma management-importance of biomarkers, inhaler choice, inhaler technique and adherence.

Jeff Garrett

PERSONALISED (PRECISION) MEDICINE

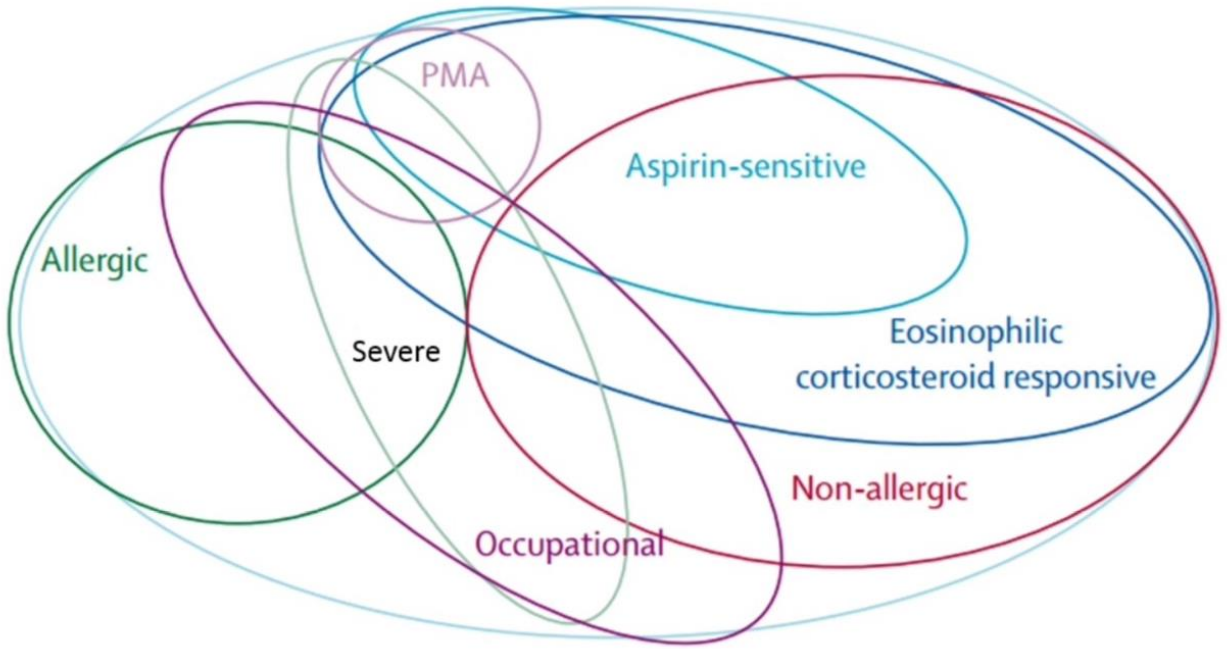
- “The practice of tailoring treatment to individual patients based on their predicted response or risk of disease”
- “Precision Medicine requires a different type of clinical trial that focuses on individual , not average, responses to therapy”

Asthma-A heterogeneous Condition



Asthma Phenotypes

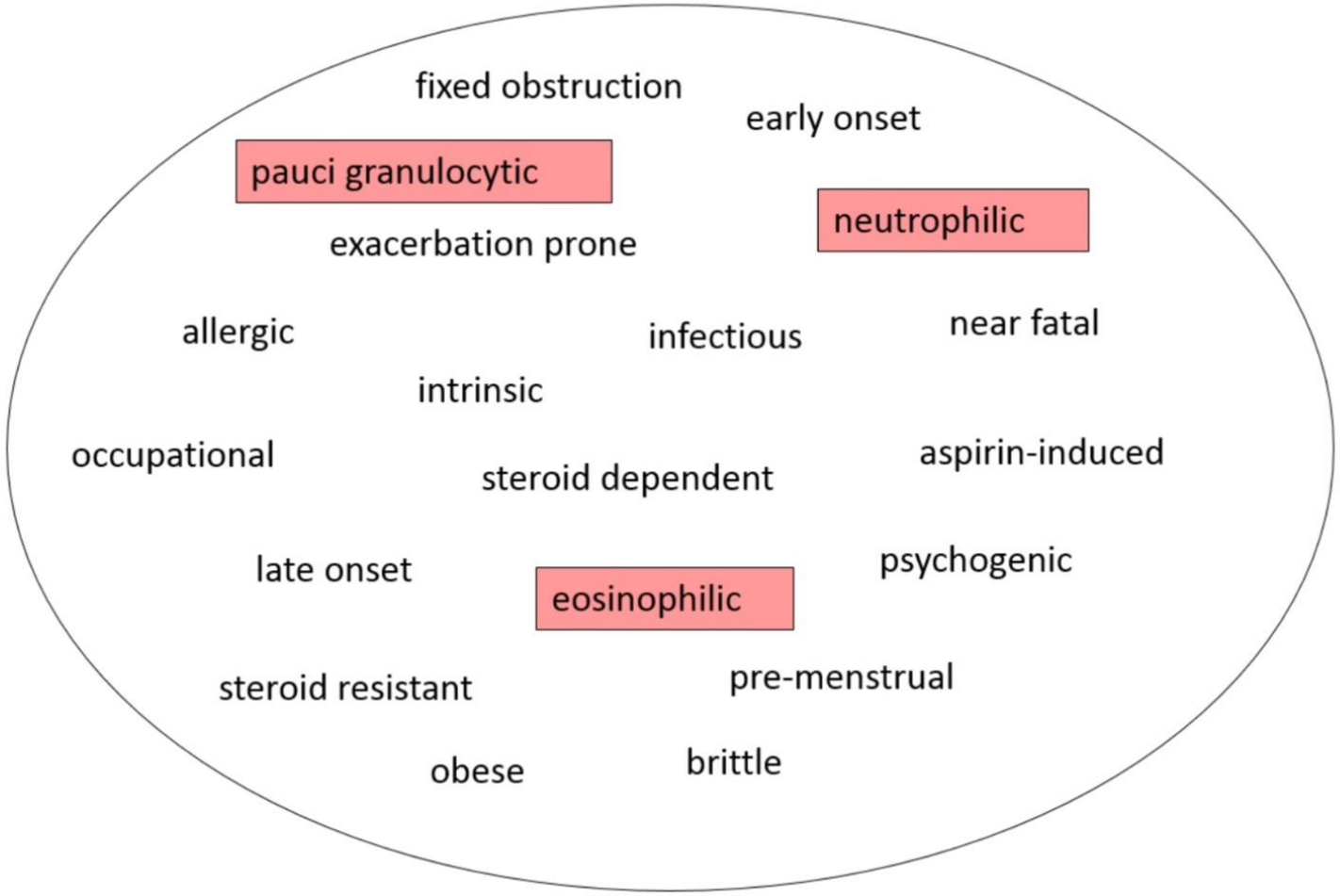
Phenotyping asthma by triggers



Wenzel SE. Lancet 2006

Inflammatory Phenotypes

Phenotyping asthma by type of inflammation



Asthma history

Phenotyping history

- Trigger based phenotypes
  - Allergic *vs* non-allergic asthma
  - Aspirine-exacerbated asthma

- Clinical phenotypes
  - Early onset vs late onset asthma
  - Mild *vs* severe asthma

- Biomarker based phenotypes
  - Eosinophilic *vs* non-eosinophilic

Definitions

FDA

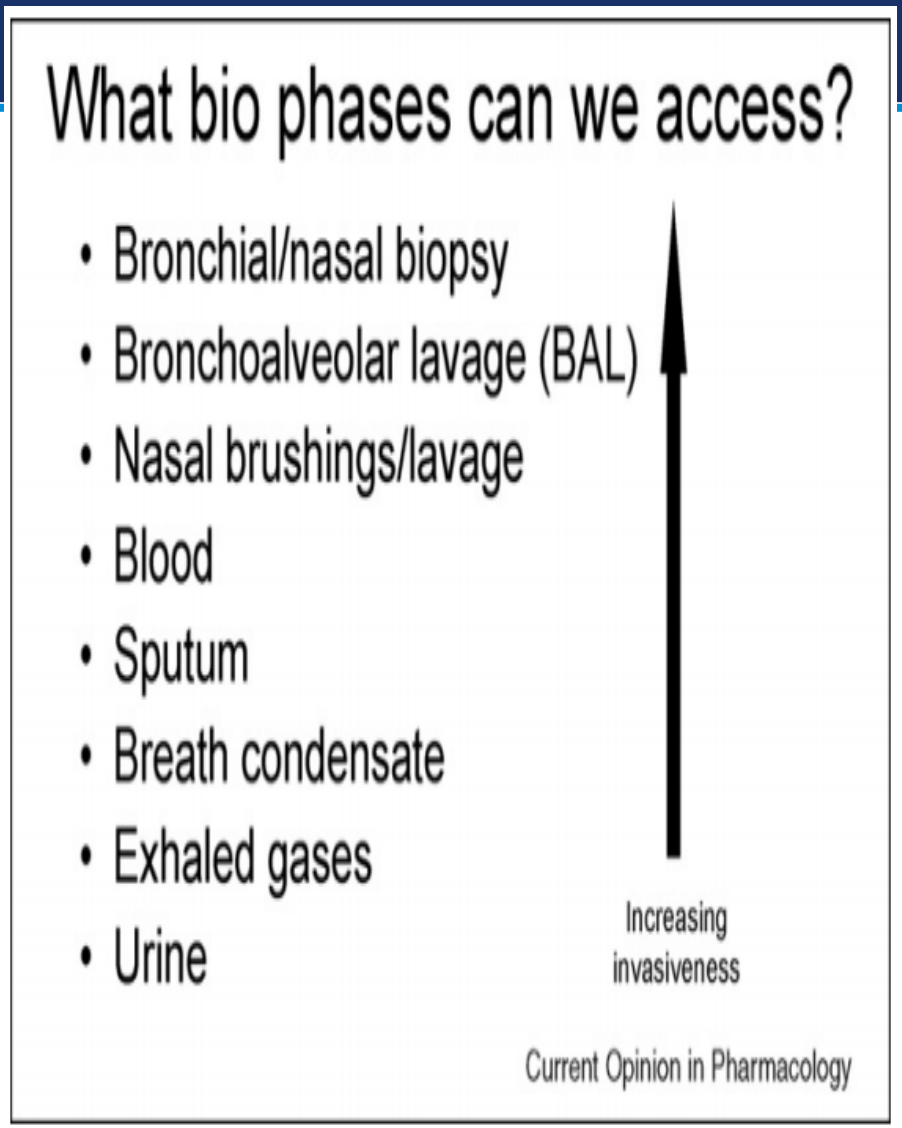
A biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or biological responses to a therapeutic intervention.

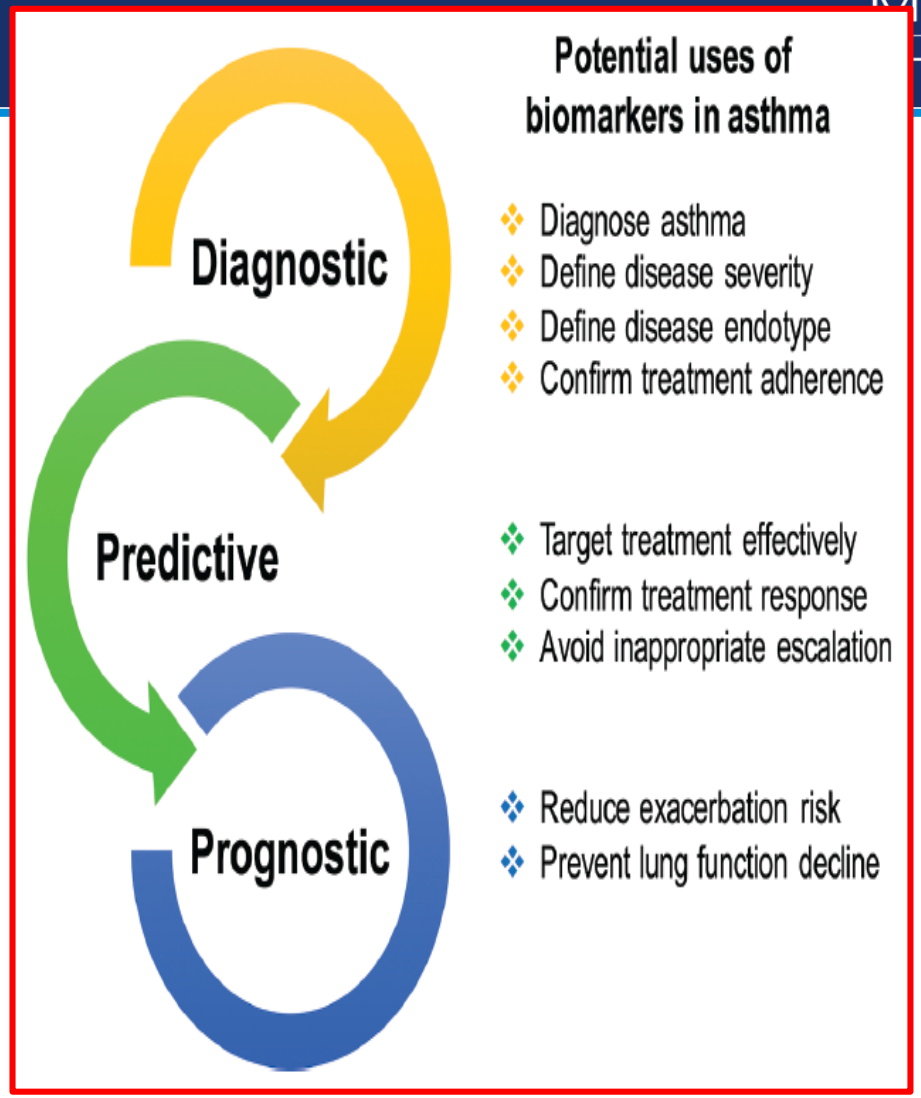
EMA

Biomarkers are tests that can be used to follow body processes and diseases in humans and animals. They can be used to **predict how a patient will respond to a medicine** *or* **whether they have, or are likely to develop, a certain disease**.

https://www.fda.gov/Drugs/NewsEvents/ucm424545.htm;
http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000349.jsp

Sampling and potential uses of biomarkers in asthma





Snell M et al, Curr Opin Pharmacol 2008; 8(3): 222-35; Fricker M et al, Respirology 2017; 22: 430-42

Airway Inflammation

- Underlying pathology in asthma/bronchitis
- No good test to measure degree of airway inflammation
- Biomarker measurement:

  bronchoscopy: BAL/bronchial biopsy

  induced sputum*

  exhaled nitric oxide (eNO)*

  blood eosinophil level

**Have fulfilled criteria to be used as a biomarker*

Inflammatory subtypes in asthma: Assessment and identification using induced sputum

SIMPSON JL, SCOTT R, BOYLE MJ, GIBSON PG. *Respirology* 2006; **11**: 54–61

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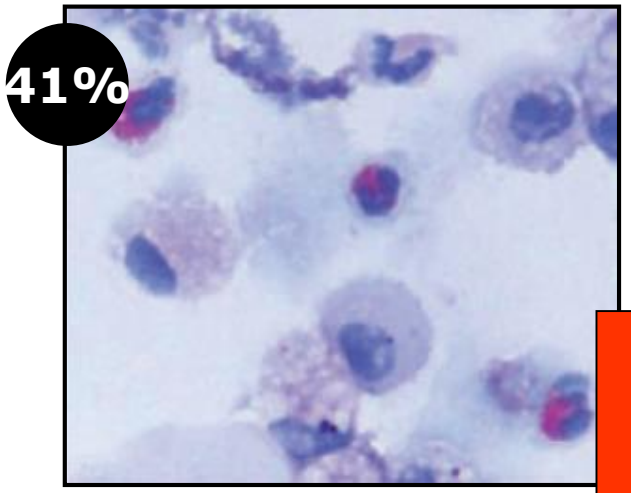
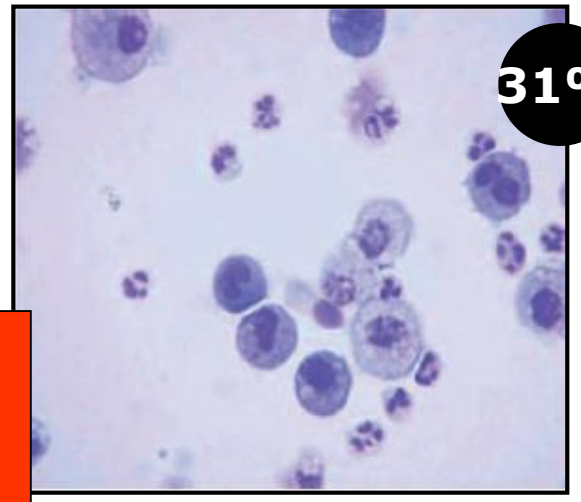


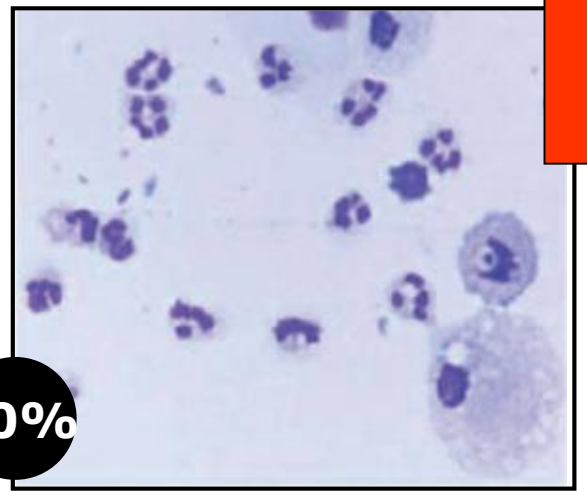
Eosinophilic



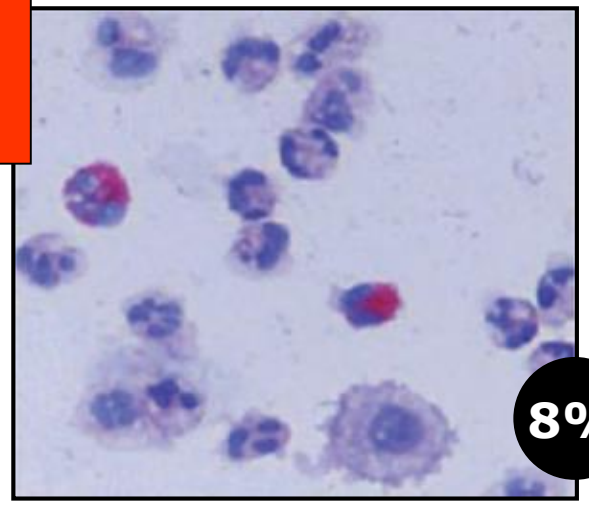
Paucigranulocytic

eosinophils
> 1.01%

neutrophils
> 61%



Neutrophilic



Mixed

Utility of Biomarkers – Using eosinophils to target and maximise therapy

- The use of information gathered from measures of airway inflammation to guide assessment and treatment.

- Success with induced sputum eosinophil counts. (Gold standard)

Predicts steroid responsive disease

Pavord 1999
Pizzichini 1999
Brightling 2000
Green 2002

A rise in counts measured longitudinally predicts subsequent loss of asthma control

Jatakanon 2000
Deykin 2004

Management protocols aimed at titrating steroid therapy to maintain normal counts lead to superior asthma control

Green 2002
Jayaram 2005
Chlumsky 2006

The JAMA Network

From: **Comparison of Physician-, Biomarker-, and Symptom-Based Strategies for Adjustment of Inhaled Corticosteroid Therapy in Adults With Asthma: The BASALT Randomized Controlled Trial**

JAMA. 2012;308(10):987-997. doi:10.1001/2012.jama.10893

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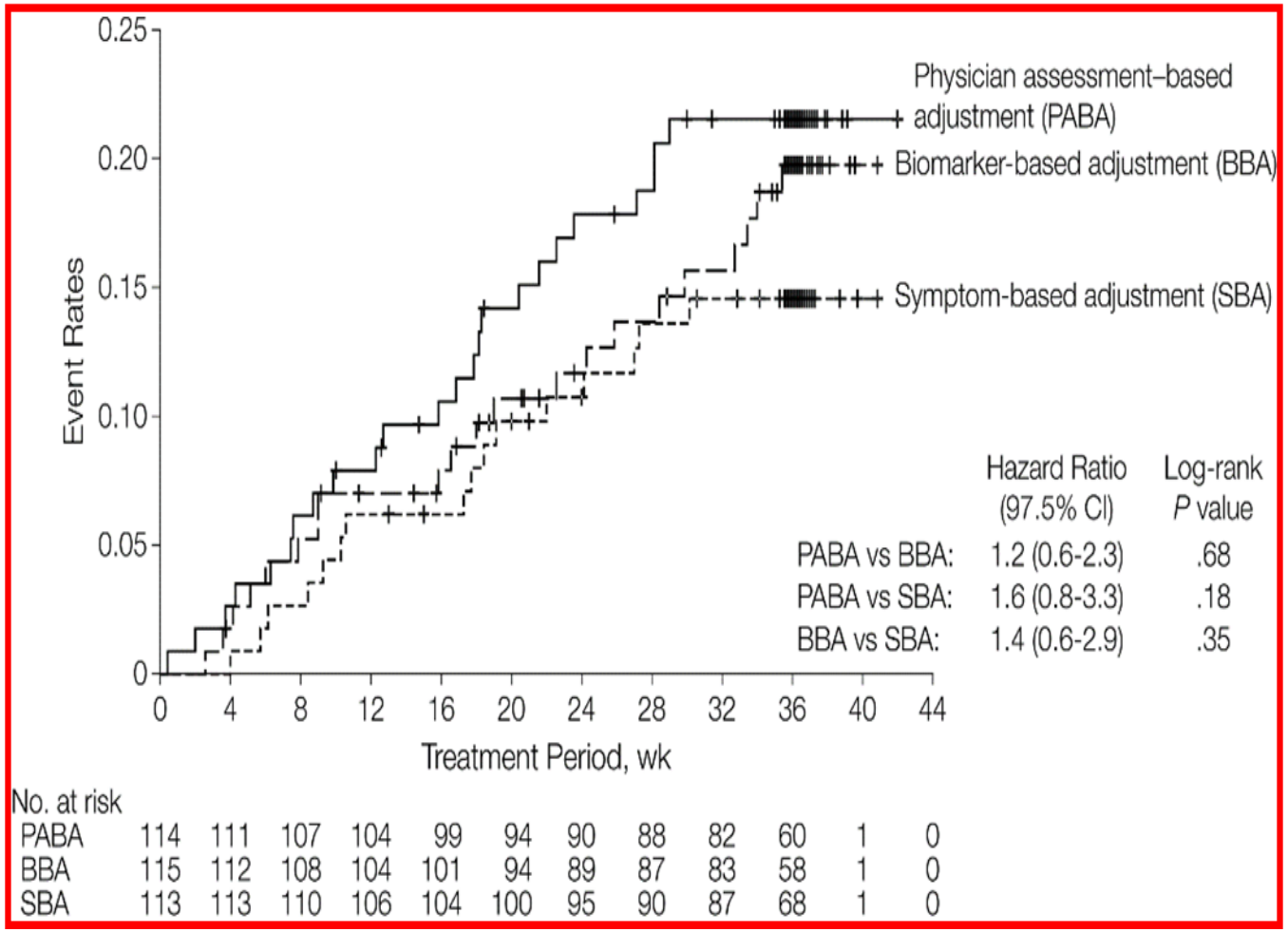
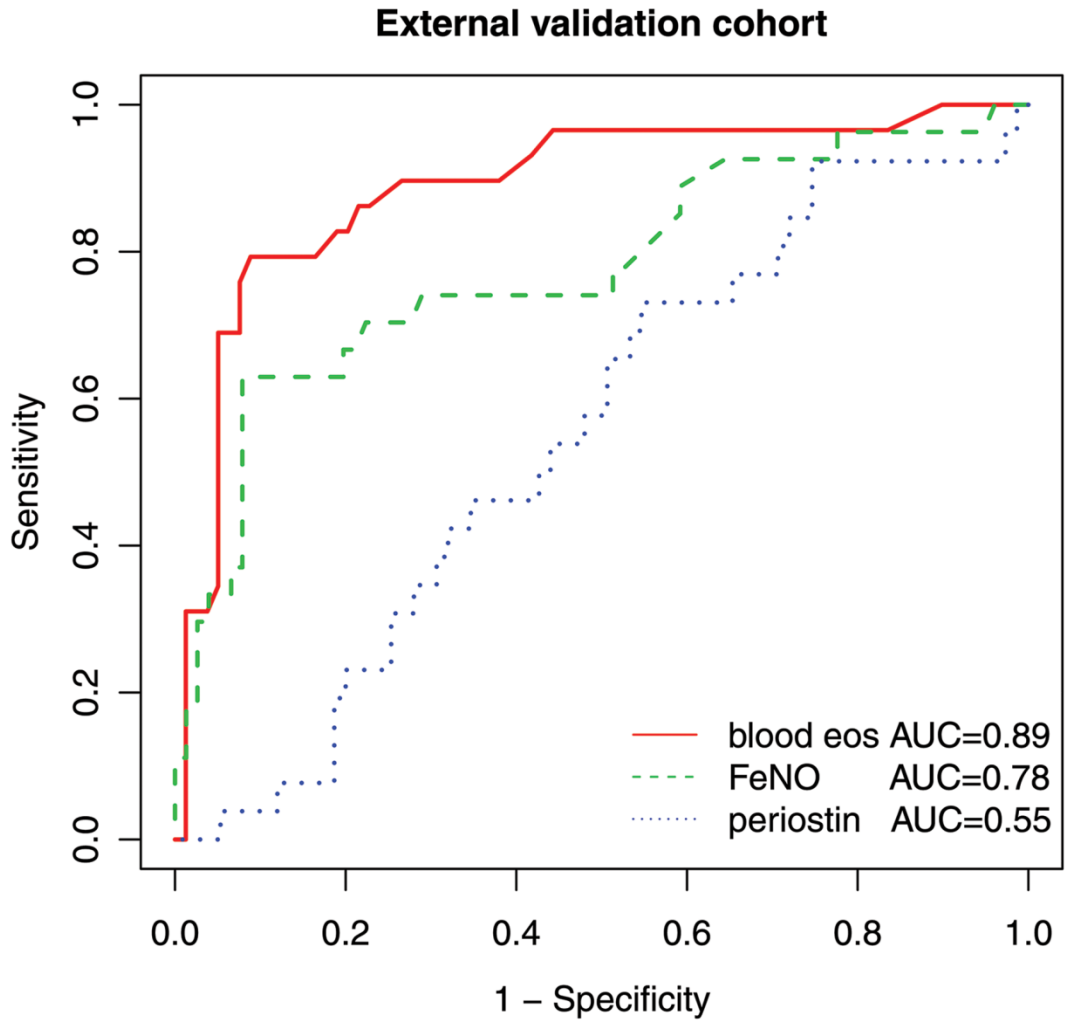


Receiver operating characteristics curve analyses of the sensitivity and the specificity of blood eosinophils, FENO and serum periostin for the diagnosis of eosinophilic inflammation. AUC, area under the curve.



Wagener AH, et al. Thorax 2014;

Do available biomarkers meet the ideal characteristics for asthma?

	Ideal characteristics of biomarker					
Biomarker	Easily measurable	Ability to distinguish a mechanism causally linked to important clinical outcome	Reliable and reproducible in the clinical setting	Ability to provide information about disease prognosis and clinical outcomes	Mechanistically linked to the therapeutic target	Cost-effective
Bronchial biopsy	–	++	–	–	++	–
Bronchoalveolar lavage	–	++	–	–	++	–
Sputum induction	+	++	–	+++	+	+
FeNO	++	++	+++	++	++	++
VOCs	++	+++	+	–	++	?
Exhaled breath condensate	+++	+	–	++	++	?
Exhaled breath temperature	+++	–	–	+	+	+++
Blood eosinophil counts	+++	+++	+++	++	+++	+++
Activation profile of eosinophils	+	++	–	–	+++	?
Serum periostin	+++	+++	+++	+++	+++	+++
Chitinase-like protein YKL-40	+	–	–	–	+	?
Blood ILC2s	–	+++	–	++	++	?
Serum IgE	+++	–	–	+	+	?

FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; ILC2s, type 2 innate lymphoid cells; VOCs, volatile organic compounds.

Pavord ID et al, Clin Exp Allergy 2017; 47 : 148–160

Results of Bacci Study: 1000mcg beclomethasone/day for 4 weeks

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N = 67	High Sputum Eosinophils (n=50 or 74% of sample)		Low Sputum Eosinophils (n= 17 or 26% of sample)	
Variable	Baseline	After 4 wks	Baseline	After 4 wks
Eosinophils (%)	18.2 (3.1-80.1)	1.8 * (0 – 14.5)	1 (0 – 2.7)	0.6 (0 – 11.9)
Neutrophils (%)	41 (8.2 – 86.2)	51.5 (5.6 – 92.2)	60.6 (26.4 – 94.7)	62.5 (0 – 82.8)
ECP (μg/L)	420 (1 – 1,920)	122 * (4 – 1,010)	24 (2 – 380)	68 (4 – 1,432)

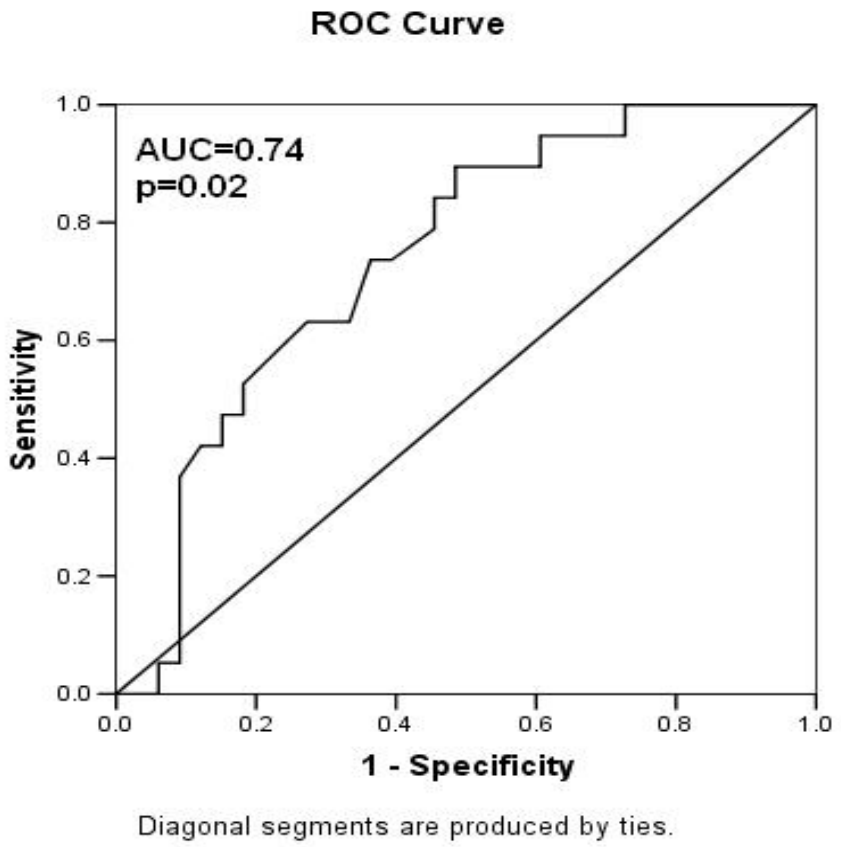
Data presented as median (range)
ECP = Eosinophil Cationic Protein
***Significant difference between groups for eosinophils & ECP at baseline p< 0.01**

Lung function before and after corticosteroid treatment

	High Sputum Eosinophils			Low Sputum Eosinophils		
Variables	**Baseline**	**After 2 wk**	**After 4 wk**	**Baseline**	**After 2 wk**	**After 4 wk**
FEV1, % predicted	87.9 ± 15.4	97.3 ± 14.5§	96.9 ± 14.5§	90.2 ± 17.3	91.7± 17.7	91.2± 20.0

Bacci Chest 2006;129(3):565-72

ROC curve of serum *eosinophils* at predicting +ve sputum *neutrophils* (>76%)



Cut point of 0.23 has sensitivity 65%, specificity 53% (p=0.03, n=508) Schleich et al. Personal communication

Blood eosinophils stable particularly at low levels – benefit of Web Eclair

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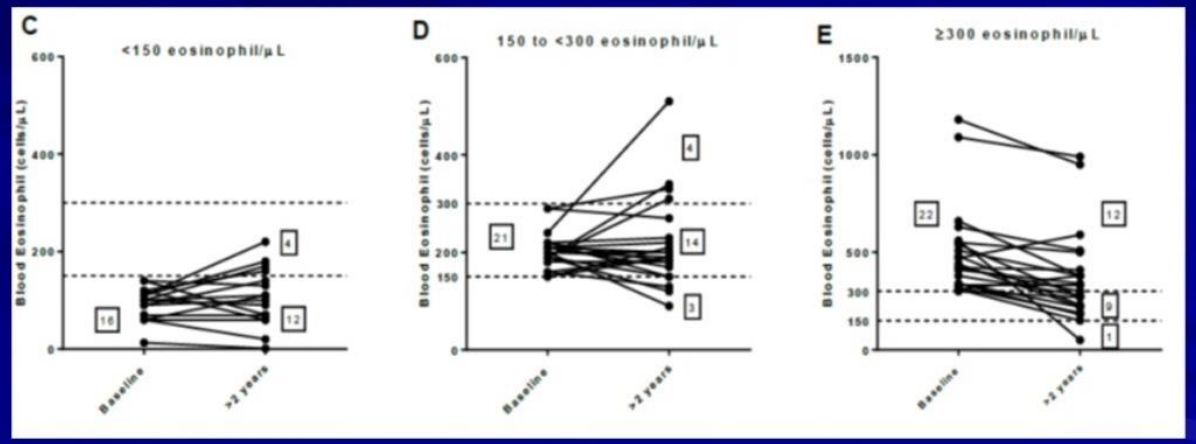
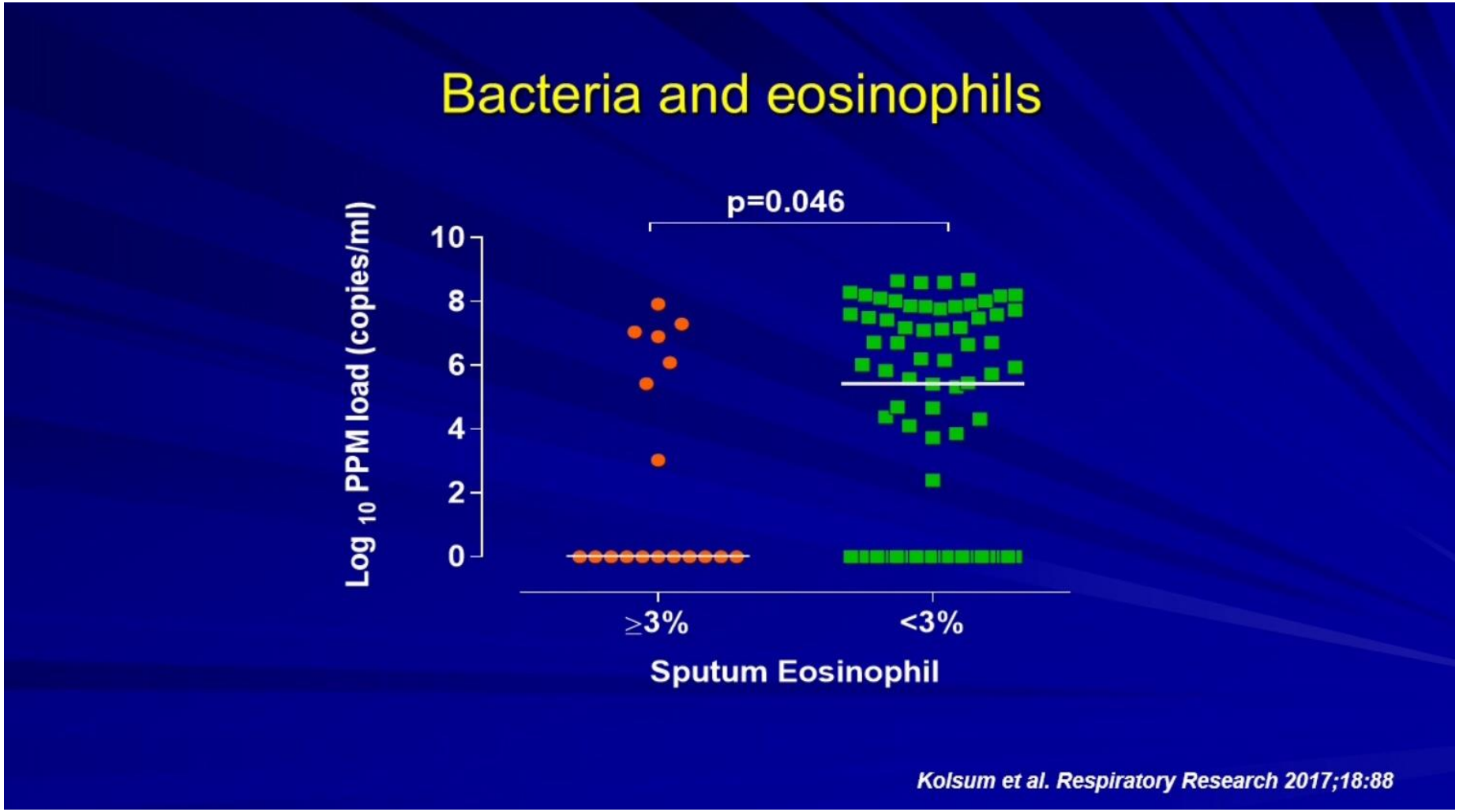
Stability of blood eosinophils



Southworth et al ERJ 2018

Pathogenic bacterial load highest in those with low eosinophil counts



We can control asthma with existing medications in 80-90%

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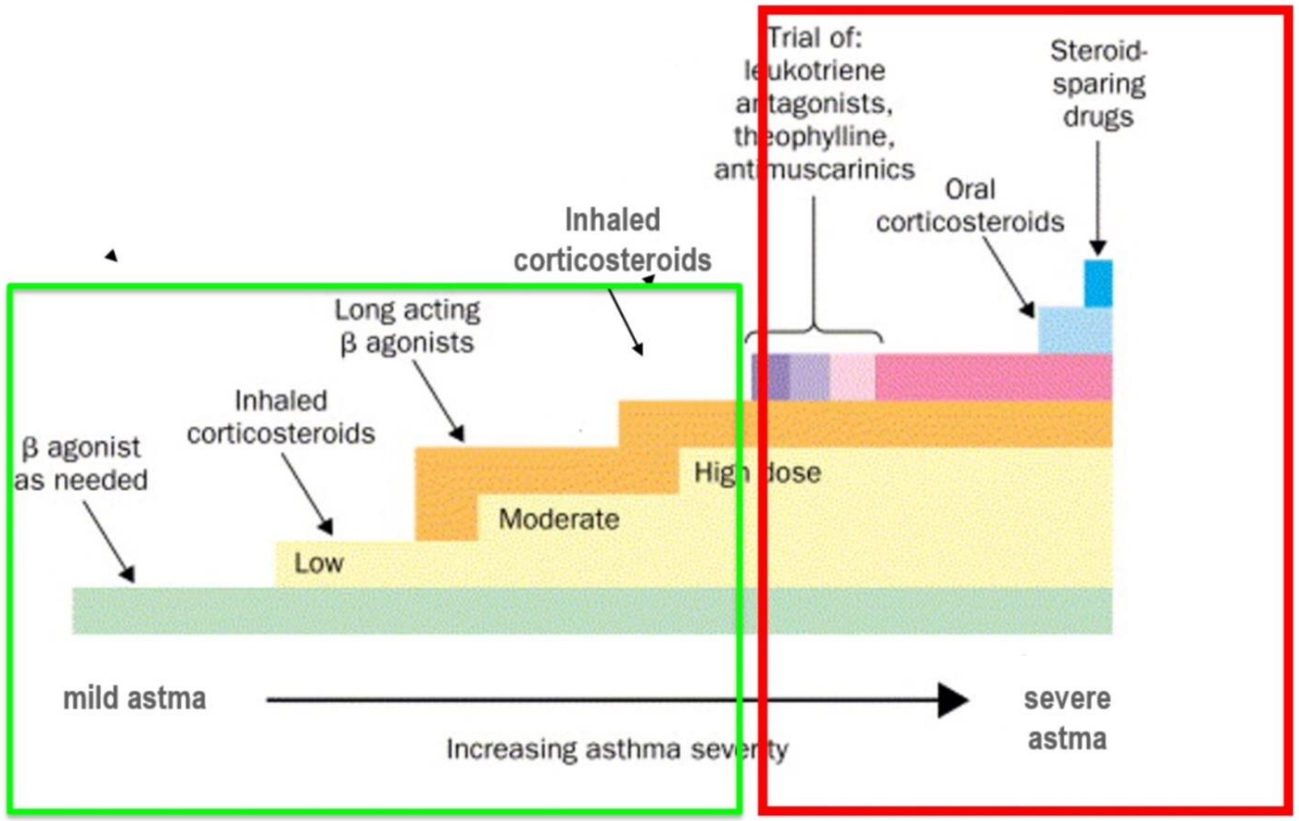
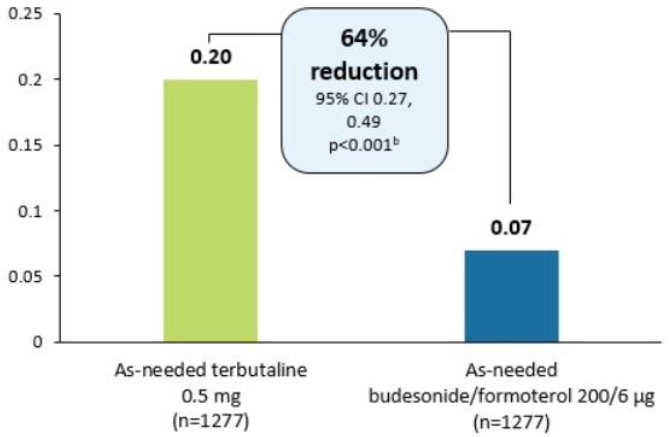
Control of eosinophilic asthma in >80% of patients



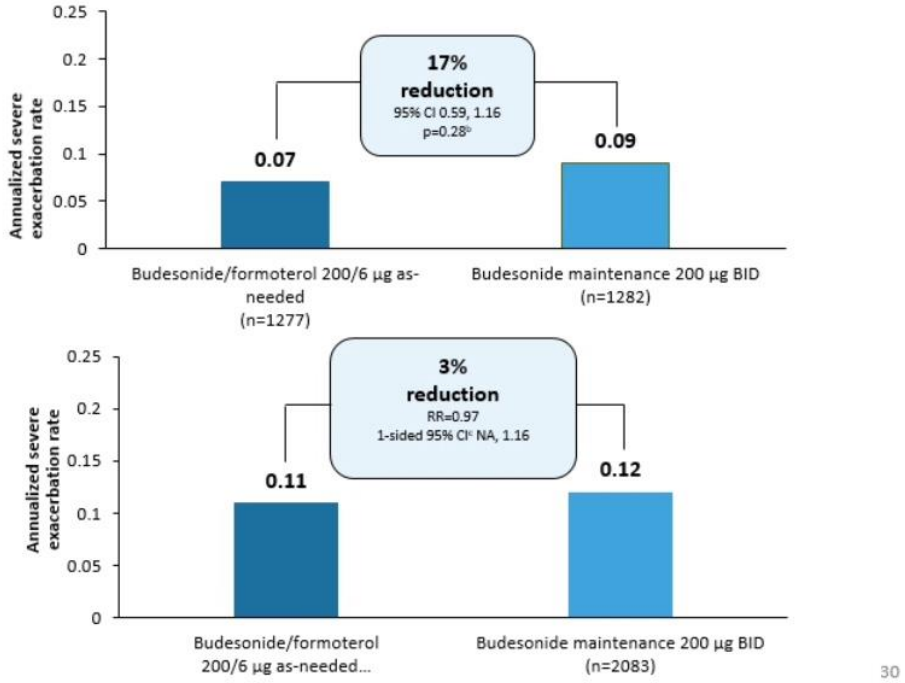
PRN vs fixed dose regimens in mild asthma

As-needed Combination Therapy as a Solution

Patients on budesonide/formoterol as-needed had a 64% lower severe exacerbation rate compared to terbutaline as-needed only



Budesonide/formoterol as-needed was equivalent to budesonide maintenance BID in both SYGMA 1 & 2 at preventing severe exacerbations[1,2]



1. O'Byrne PM et al. *N Engl J Med*. 2018;378:1865-1876; 2. Bateman ED et al. *N Engl J Med*. 2018;378:1877-1887.

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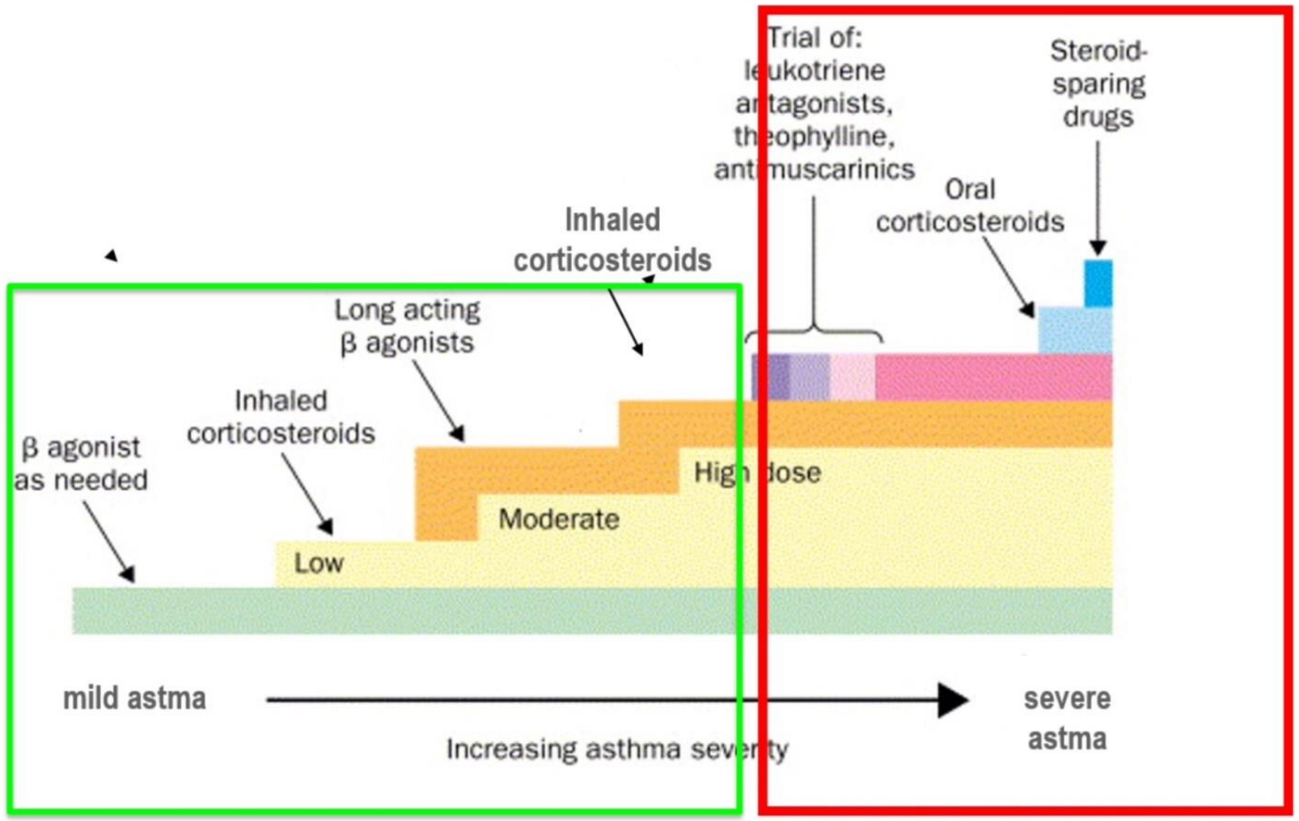
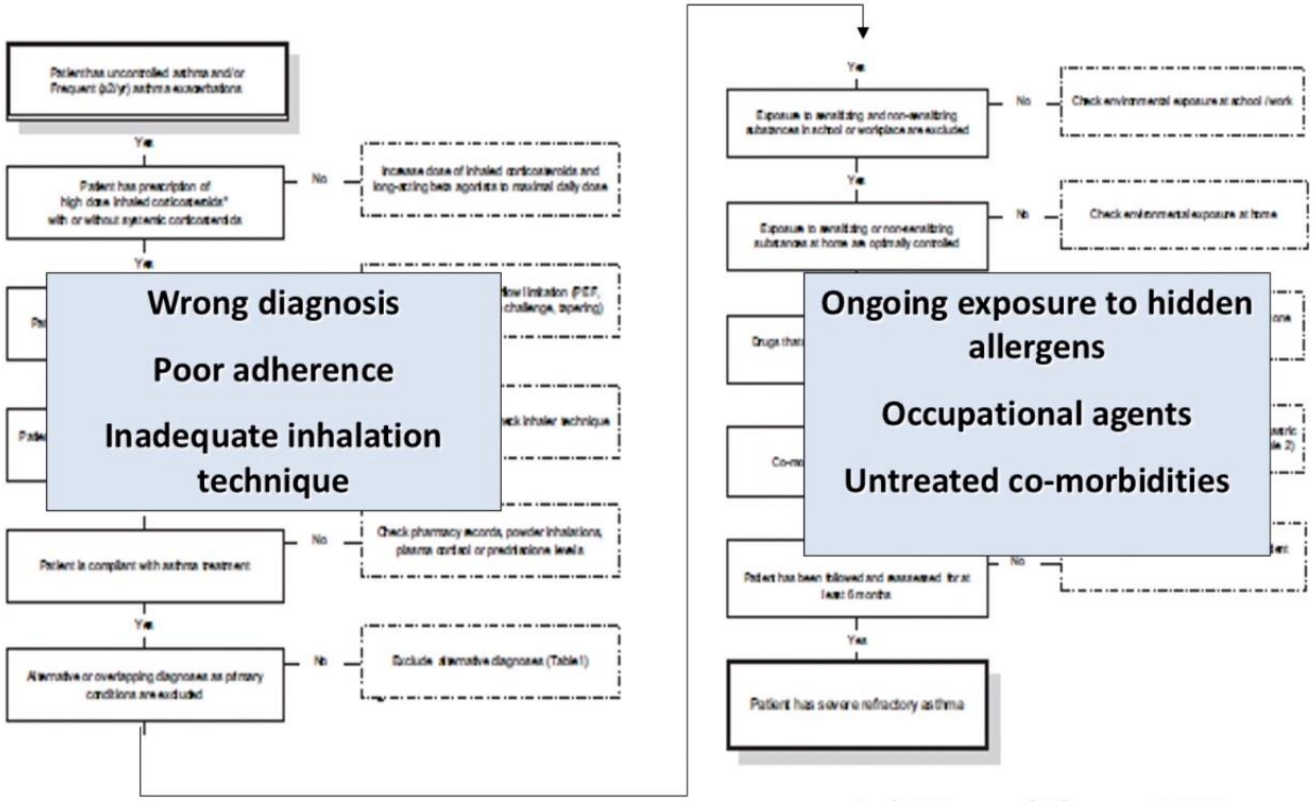


Check List for Severe Asthma

Checklist for evaluating patients with difficult-to-control asthma

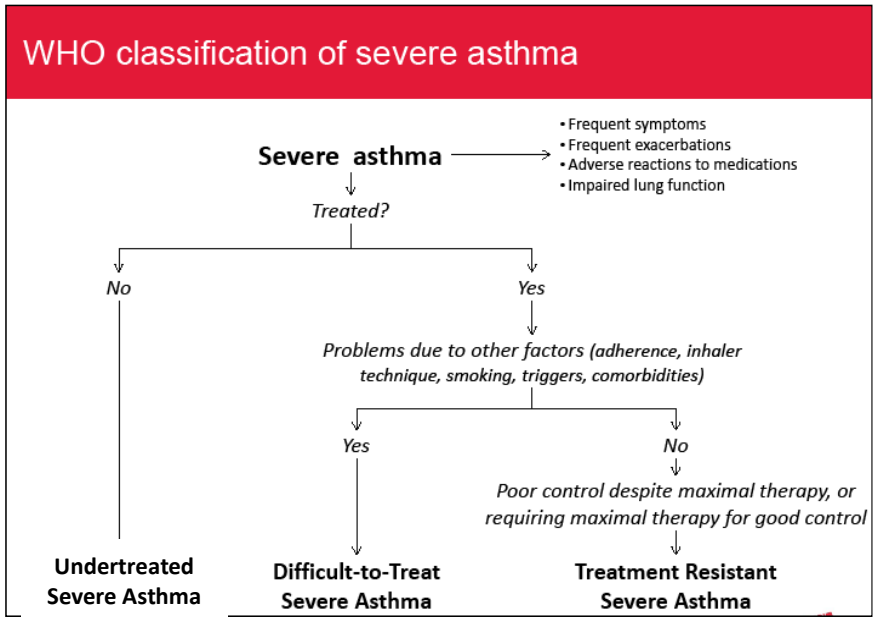


Bel EH. *et al* Thorax 2011

Outcome Measures

Maximum treatment:

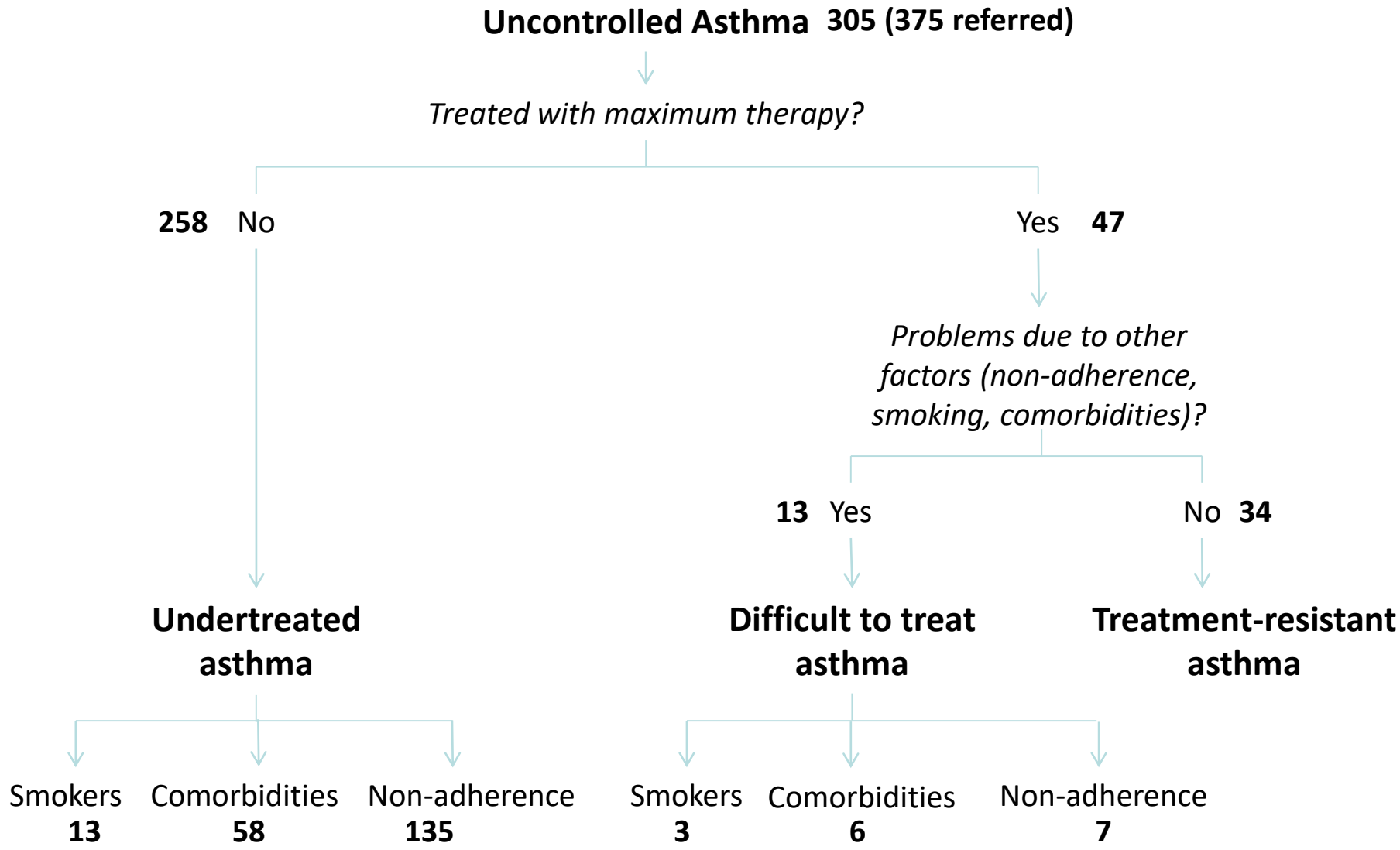
1. Inhaled corticosteroids >1200 ugBDP equiv/day
2. Use of 2nd controller e.g. LABA, Spiriva



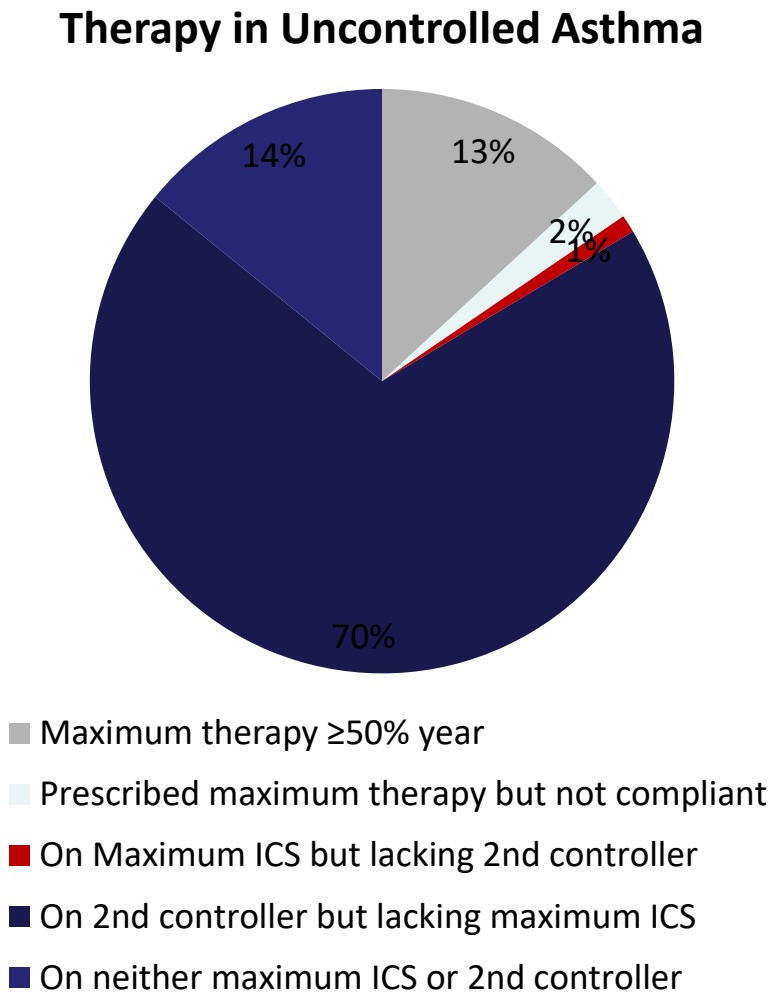
1. "Poor symptom control" in Clinic letter
2. ≥2 courses of oral prednisone in the last 12 months
3. Any hospitalisation for asthma
4. Persistent airflow limitation

Adherence: patients dispensed ≥7 prescriptions in the previous 12 months

Middlemore Hospital
Asthma OP Clinic -GP referral



Is there a gap in management?



- Only 15% of those with Severe Asthma are prescribed maximal therapy
- 84% are on suboptimal inhaled corticosteroid therapy

Potential reasons?

- Clinically appropriate
- Eosinophilic inflammation adequately controlled or Neutrophilic inflammation -24% on macrolide therapy
- Unable to prescribe maximum dose on combination LABA/ICS therapy
- Hesitancy to prescribe

Potential reasons for lack of use of maximum doses of inhaled steroids in severe asthma

1. Maximum effect achieved with doses of Fluticasone at 500mcg/day.
   Holt S et al BMJ; 323: 1-8

2. Concern regarding systemic side effects of inhaled steroids.
   Martin RJ. Am J. Resp Crit Care Med 2002.

3. High percentage with COPD (ACOS syndrome)
   – fear of increased risk of pneumonia
   Suissa S, Thorax 2013; 68:3 1029

4. Poor adherence with treatment (+/- 50%)

5. Lack of ability to adjust inhaled steroid dose in fixed combination therapies.

Inhaler Chart- SABA,SAMA,ICS,ICS/LABA

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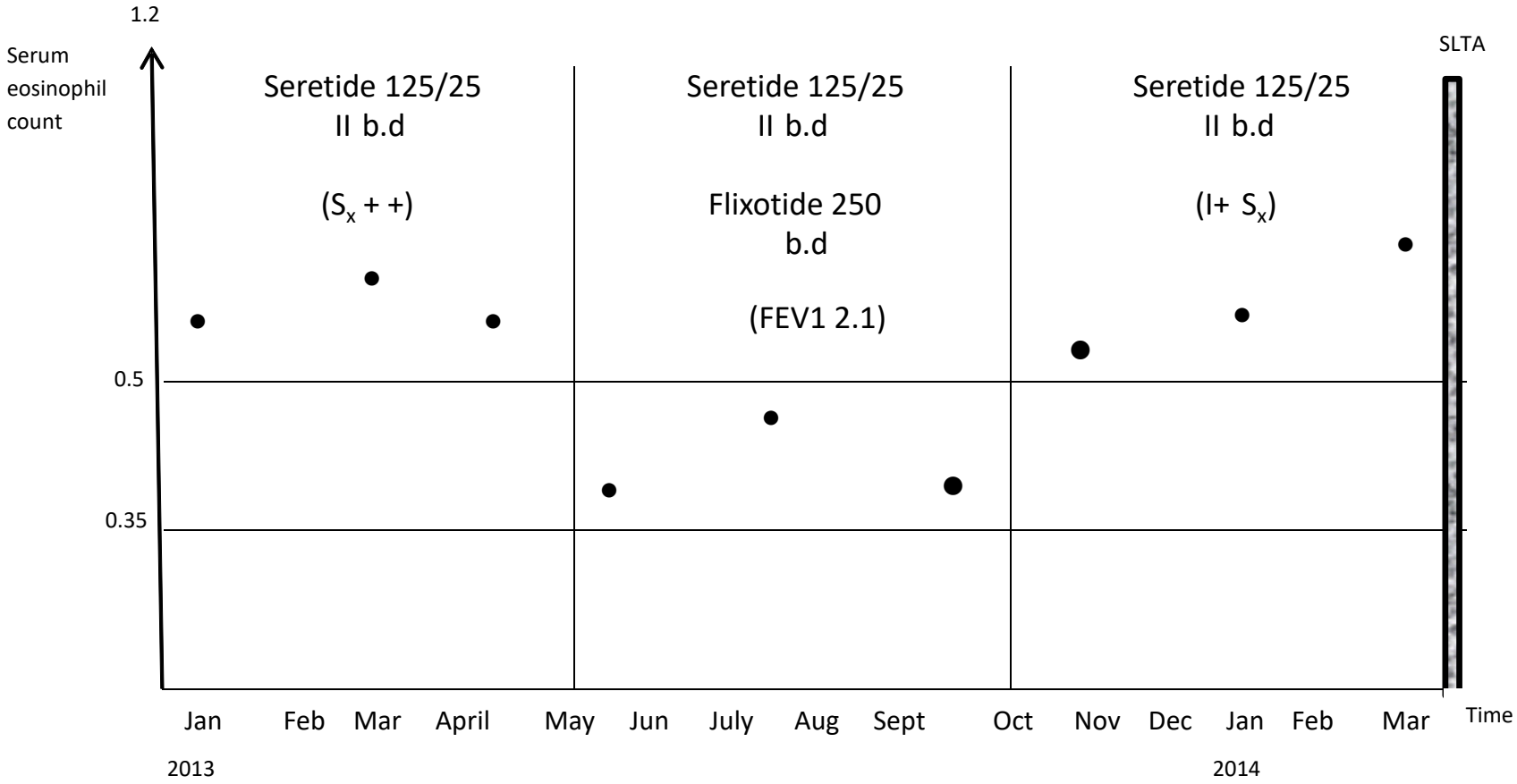
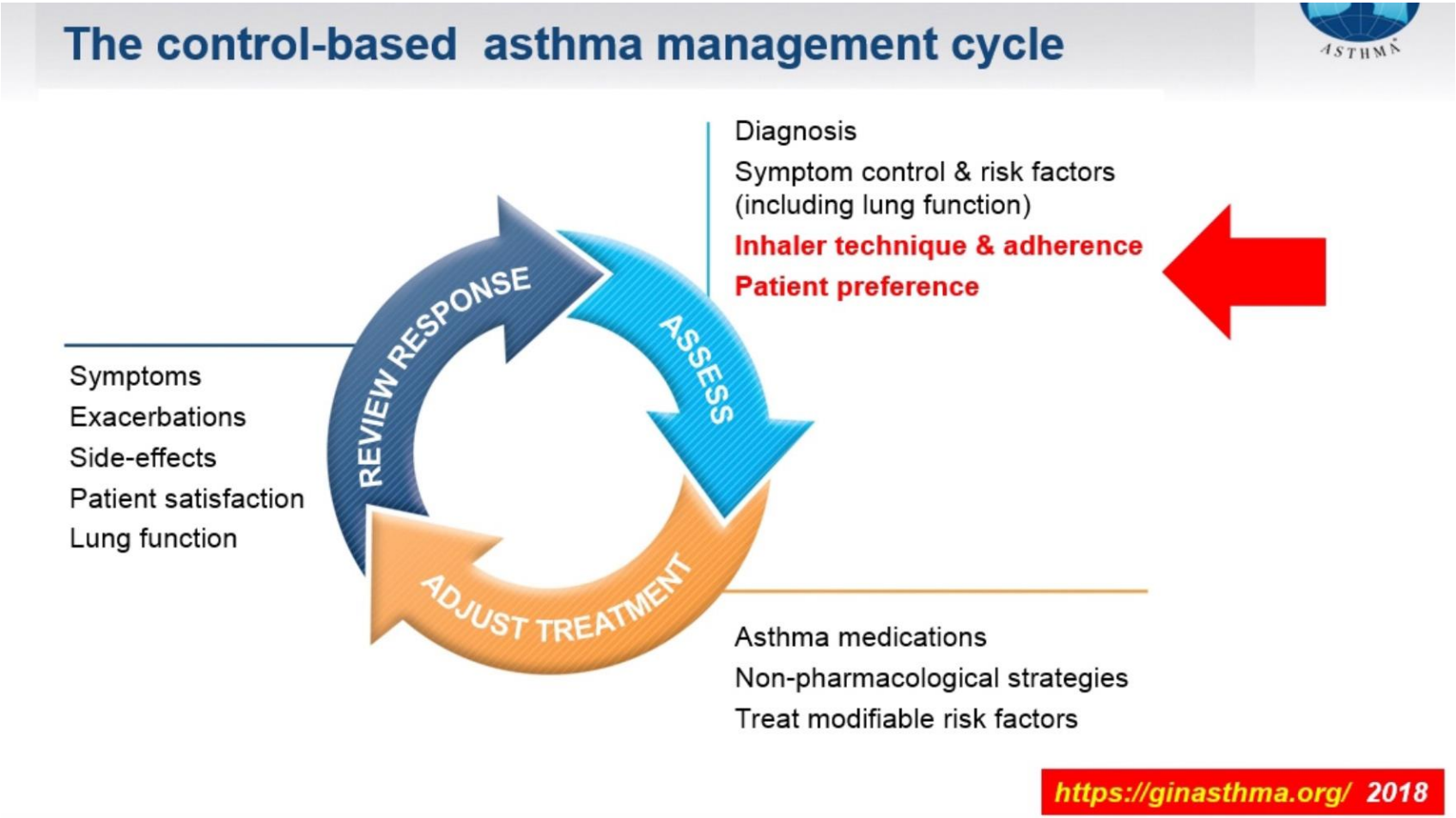
Short Acting Beta2 Agonists (SABA)					Short Acting Muscarinic Antagonists (SAMA)	Combination SABA + SAMA	
SALBUTAMOL				TERBUTALINE	IPRATROPIUM	SALBUTAMOL – IPRATROPIUM	RELIEVERS
							
100mcg	100mcg	100mcg	100mcg	250mcg	20mcg	100/20	
Respigen	SalAir	Ventolin	Salamol	Bricanyl Turbuhaler	Atrovent	Duolin HFA	
Inhaled Corticosteroids (ICS)							PREVENTERS
FLUTICASONE propionate Aerosol inhaler and Accuhaler				BUDESONIDE	BECLOMETHASONE dipropionate	BECLOMETHASONE dipropionate (ultra fine particle)	
							
50mcg 125mcg 250mcg	50mcg 125mcg 250mcg	50mcg 100mcg 250mcg		100mcg 200mcg 400mcg	50mcg 100mcg 250mcg	50mcg 100mcg	
Floair	Flixotide	Flixotide Accuhaler		Pulmicort Turbuhaler	Beclazone	Qvar	
Combination Inhaled Corticosteroids (ICS) + Long Acting Beta2 Agonists (LABA)							
FLUTICASONE propionate + SALMETEROL Aerosol inhaler and Accuhaler				FLUTICASONE furoate + VILANTEROL	BUDESONIDE + FORMOTEROL Turbuhaler and Aerosol inhaler		
							
50/25 125/25 250/25	50/25 125/25 250/25	100/50 250/50		100/25 200/25	100/6 200/6 400/12	100/6 200/6	
RexAir	Seretide	Seretide Accuhaler		Breo Ellipta	Symbicort Turbuhaler	Vannair	

Use of regular FBC to monitor patients with severe asthma

Mr A.N – 48yr old Maori. $^{FEV1}/_{FVC}$ – $^{1.7}/_{3.5}$ (FEV_1 70% predicted)



Personalised control based asthma management



Spirometry in General Practice

- 50% GPs own spirometer *(25% Piko6, 25% Flow/Volume)*
- Upskill GP/practice nurses with 2 hour workshop

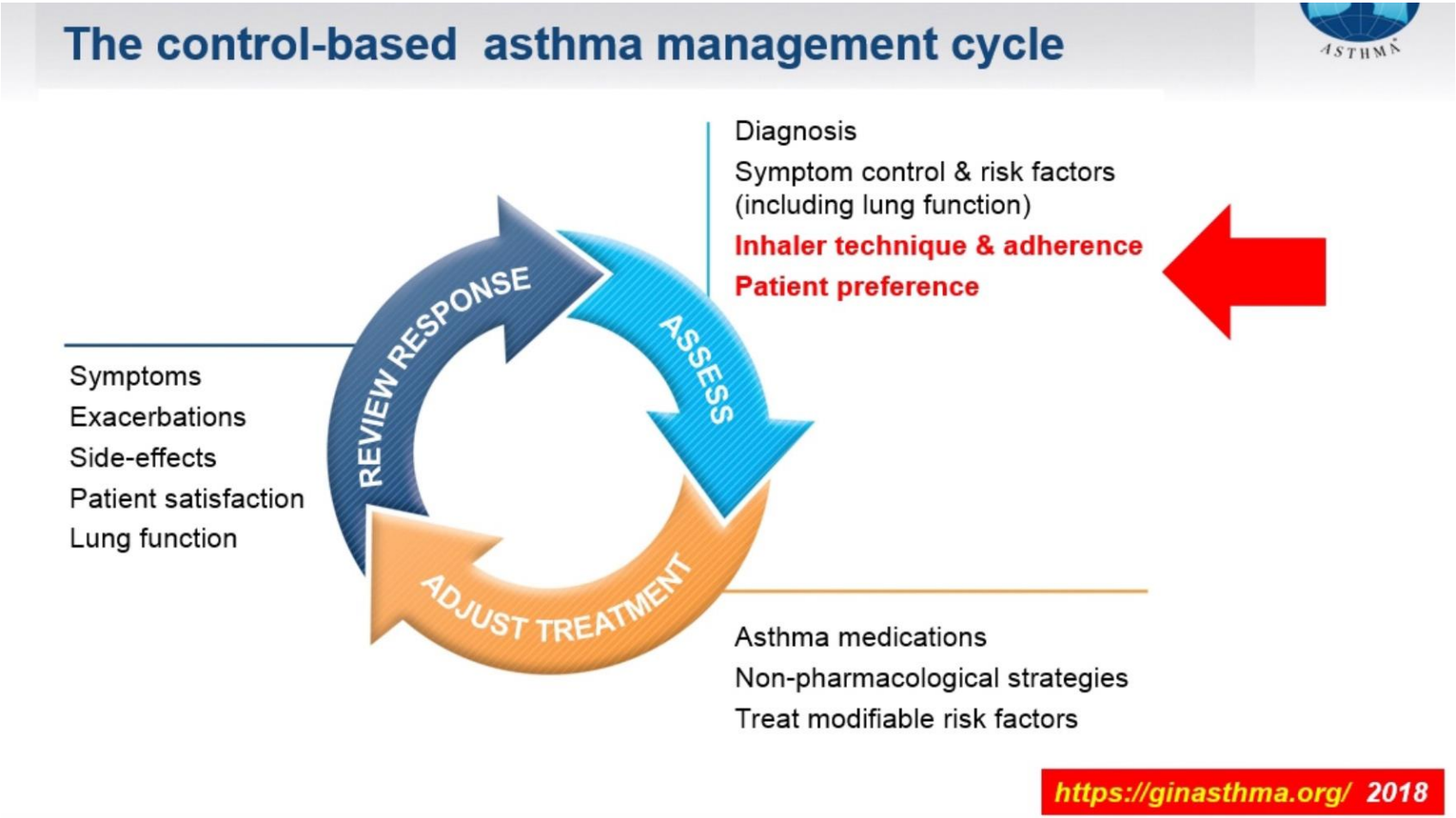
  40% ATS standards (DVD)

  60% ATS standards (2 hr workshop)

  80% ATS Standards (primary care service/resp physicians)

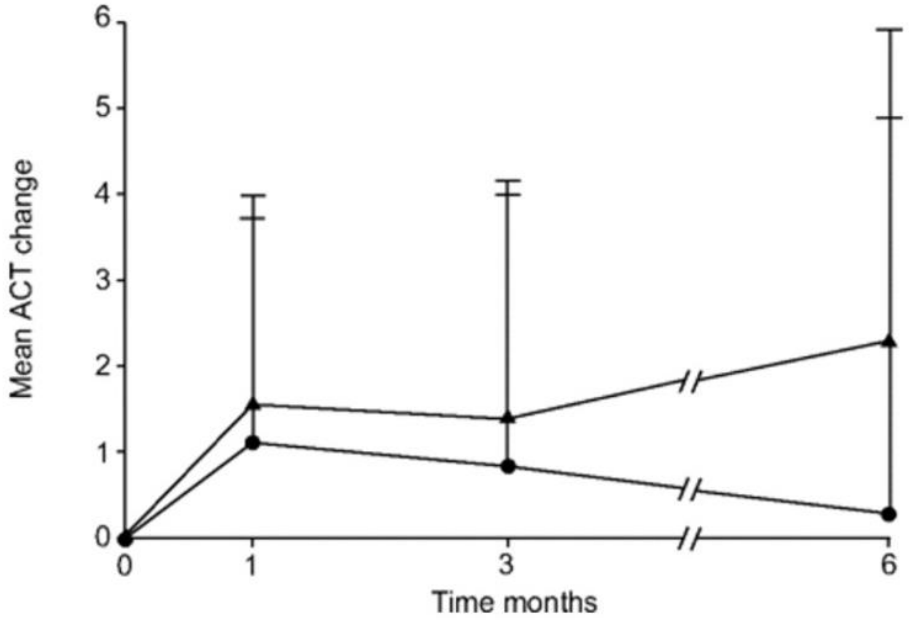
  88% ATS Standards (Lung Fn lab)
- QI overseen by physiologist

Personalised control based asthma management



Poor inhaler technique-cause of “Severe Asthma” in 30-50%

Poor inhaler technique in patients with difficult-to-control asthma



Mehuys E, et al. Eur Respir J. 2008

All physicians should be familiar with the inhalers they prescribe

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Only 14.2% of physicians (*n>1500*) have adequate knowledge of inhaled therapy

- Of those using a DPI ***less than 50%*** identified ***"inhale deeply and forcefully"*** as the most important step during inhalation
- **Only 28%** checked inhalation technique when prescribing a new inhaler

Plaza V et al, JAMPDD 2012

Who does the training?

No training in Undergraduate, Postgraduate or Specialisation

➡ **Mandatory Assessment during Training – Theory & Inhaler 'station'**

UK Inhaler Group

- **Inhaler Standards and Competency Document**

Framework for assessing HCP inhaler competency

https://ukiginhalerstandards.educationforhealth.org/

Choice of inhaler and drug are of equal importance

Drug vs. Device

*Federico Lavorini[1], Omar S Usmani[2]
Prim Care Respir J 2013; 22(4): 383-392
Primary Care RESPIRATORY JOURNAL
www.thepcrj.org

"…the **choice of a new compound *will be secondary*** to the need to choose the **appropriate inhaler device** for the patient…"

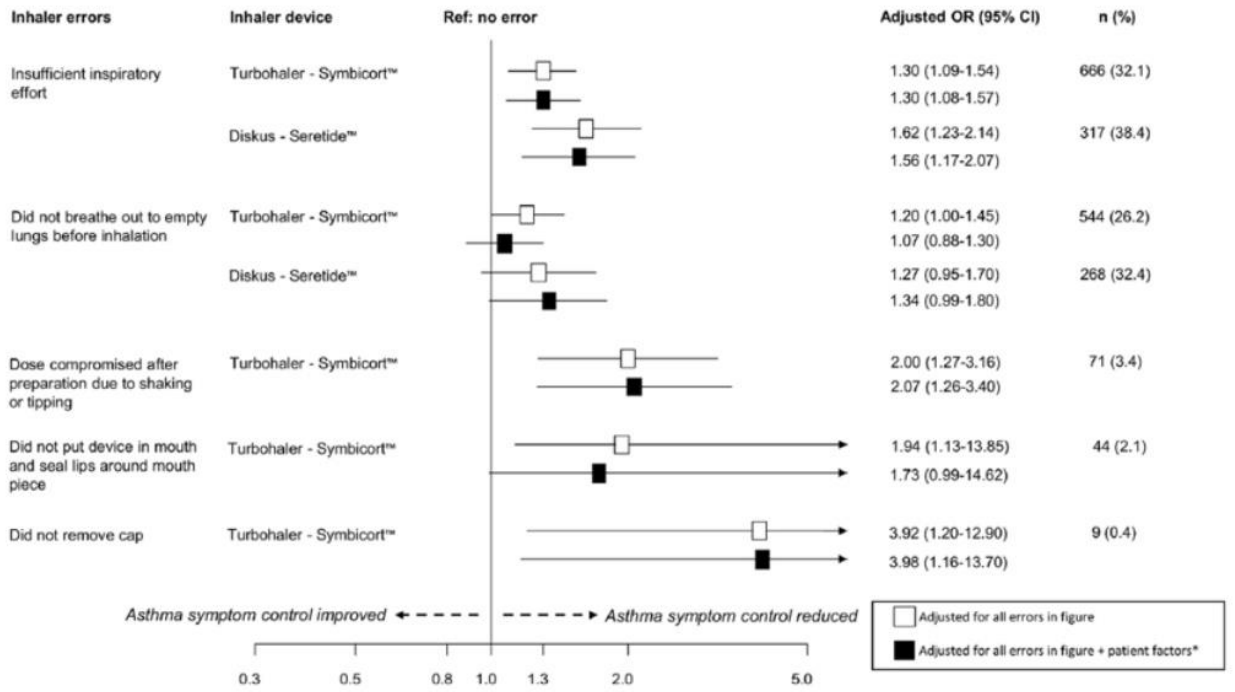
Lavorini F, Usmani OS, Prim Care Respir J 2013

"Inhaler Phenotyping"
: Personalising the device to patient

Usmani OS et al, Guidelines.co.uk [March 2017]

Association between Inhaler error and Asthma Control

Association Between Inhaler Errors for DPIs and Uncontrolled Asthma



Errors omitted despite a significant univariable association were omitted because they were correlated with another error.
*Patient factors used to adjust were age, sex, smoking status, BMI, rhinitis, and paracetamol use.
BMI: body mass index; Ref: reference group in logistic regression

Price DB, et al. J Allergy Clin Immunol Pract 2017;5(4):1071-1081.e9

Speed of inhalation most critical factor wrt MDIs

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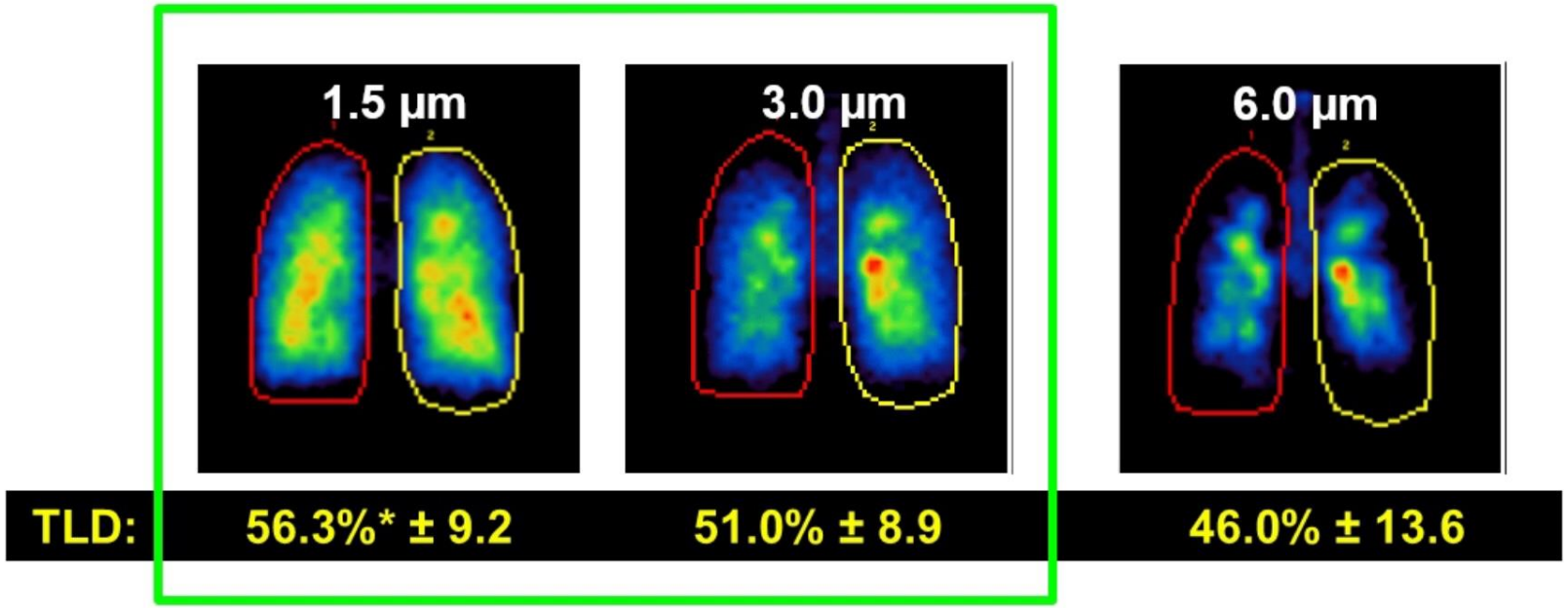
on Lung Deposition in Asthma



- **SLOW inhalation better than fast**

Gamma camera images of ^{99m}Tc-labelled salbutamol 30 µg monodisperse aerosols in the same patient with asthma

Lung deposition data are shown as mean ± standard deviation, as a percentage of the delivered radionuclide dose
*p < 0.01 vs 6.0 µm particle size; TLD: total lung deposition.

Usmani OS et al, AJRCCM 2005;172:1497–504

Summary: Critically important to defining inhaler type (DPI vs MDI)

- Ability to inhale deeply and forcefully after full expiration (DPI)
- Slow long inspiration (well co-ordinated) with 6 second breath hold (MDI)

Be consistent ie prescribe all MDIs or Respimat vs prescribe all DPIs (increase adherence)

Note: 90% asthmatics prefer MDIs to manage acute attack (potential for spacer)

Inhaled steroids and devices are not all equal

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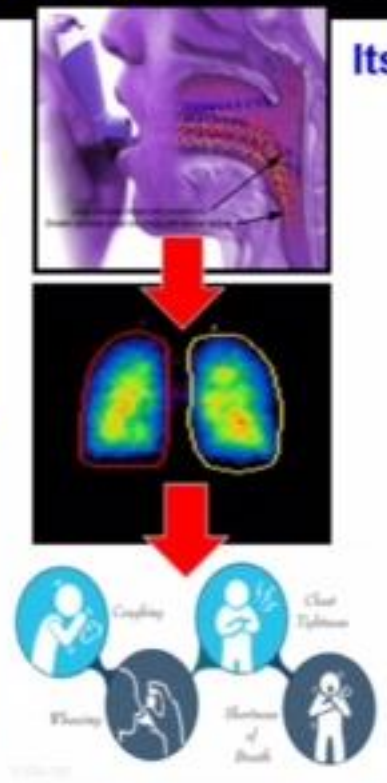
Determines Drug's Clinical Effectiveness

Device Characteristics

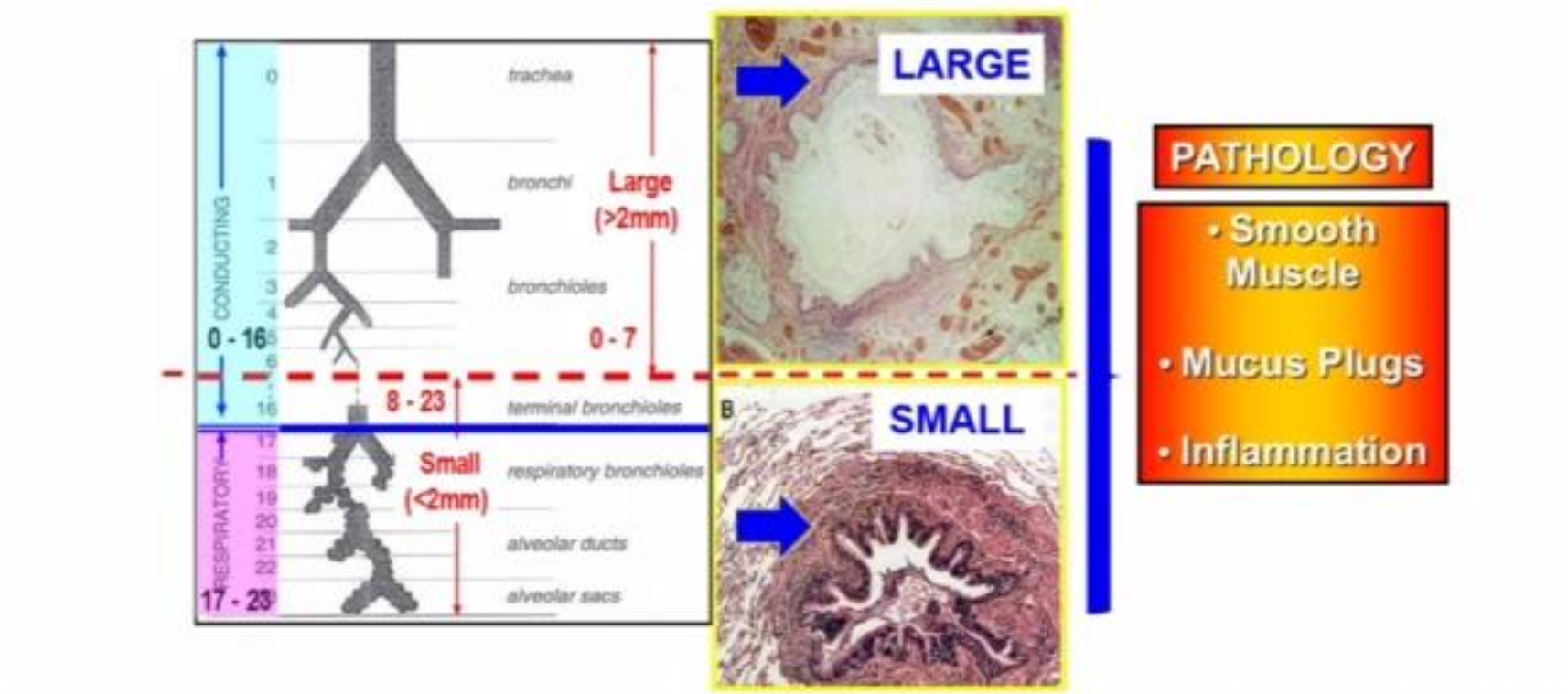
- Particle size
- Fine particle fraction
- Aerosol velocity
- Aerosol plume speed & duration
- Particle density
- Particle charge
- Lipophilicity
- Hygroscopicity



Its not just about dose equivalence

	Low dose	Moderate dose	High dose
Beclometasone dipropionate[1]			
Standard particle CFC-free inhalers	200–500 micrograms per day in 2 divided doses	600–1,000 micrograms per day in 2 divided doses	1,200–2,000 micrograms per day in 2 divided doses
Extra-fine particle CFC-free inhalers[1]	100–200 micrograms per day in 2 divided doses	300–400 micrograms per day in 2 divided doses	500–800 micrograms per day in 2 divided doses
Budesonide			
Dry powder inhalers	200–400 micrograms per day as a single dose or in 2 divided doses	600–800 micrograms per day as a single dose or in 2 divided doses	1,000–1,600 micrograms per day in 2 divided doses
Ciclesonide			
Metered dose inhaler	80–160 micrograms per day as a single dose	240–320 micrograms per day as a single dose or in 2 divided doses	400–640 micrograms per day in 2 divided doses
Fluticasone propionate			
Metered dose and dry powder inhalers[1]	100–250 micrograms per day in 2 divided doses	500–1,000 micrograms per day in 2 divided doses	1,000–2,000 micrograms per day in 2 divided doses
Fluticasone furoate[1]			
Dry powder inhaler	-	100 micrograms as a single daily dose	200 micrograms as a single daily dose
Mometasone furoate			
Dry powder inhaler	200 micrograms per day as a single dose a day	400 micrograms per day in 2 divided doses	Up to 800 micrograms per day in 2 divided doses

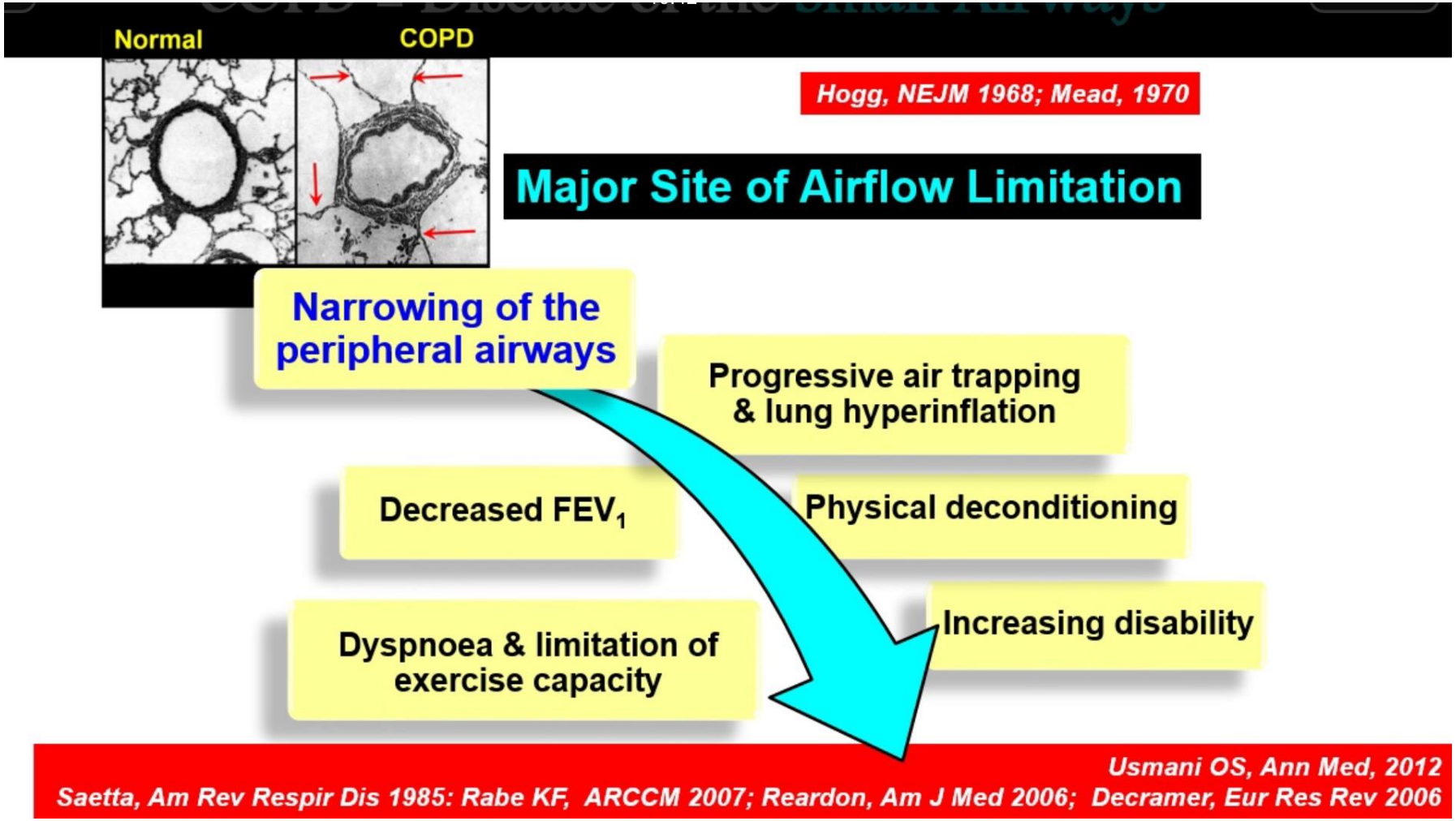
Asthma =eosinophilic inflammation of ***all airways***

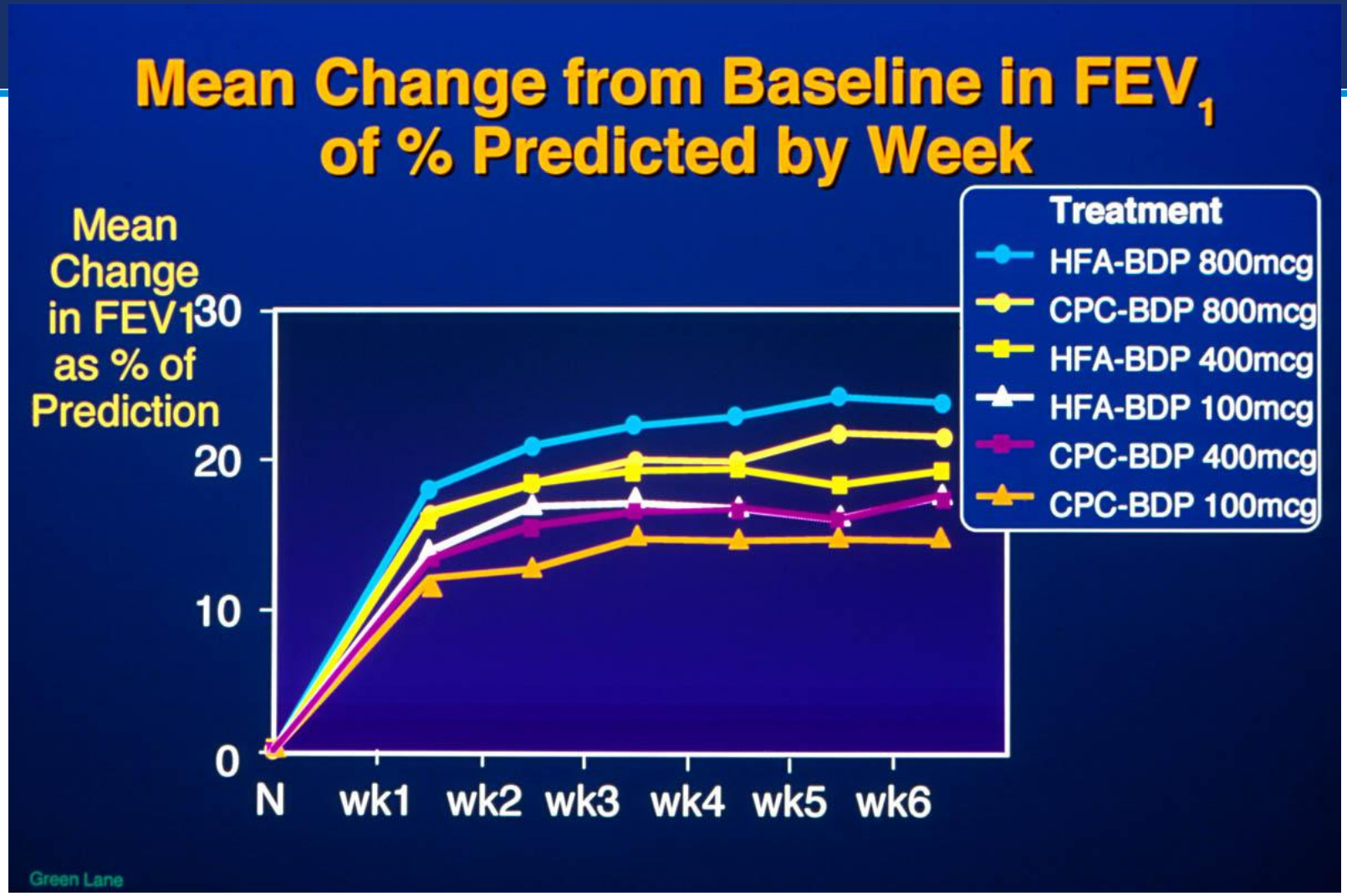


Usmani OS, Ann Med, 2012

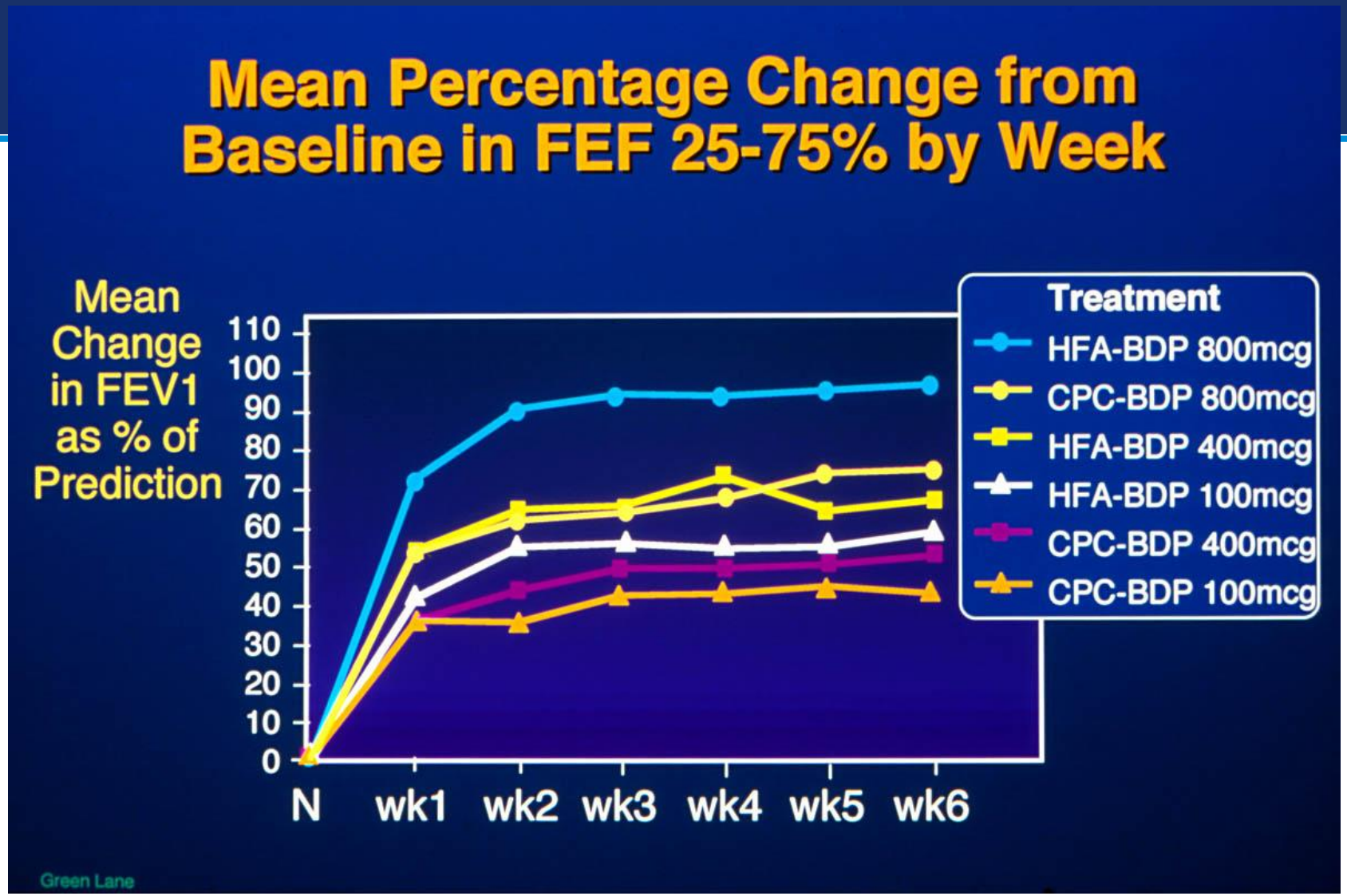
Mauad, AJRCCM 2006; Hamid, JACI 1997; Carroll, ERJ 1997; Simoes, Clin Exp Allergy 2005; Dohlnikoff, JACI 2009

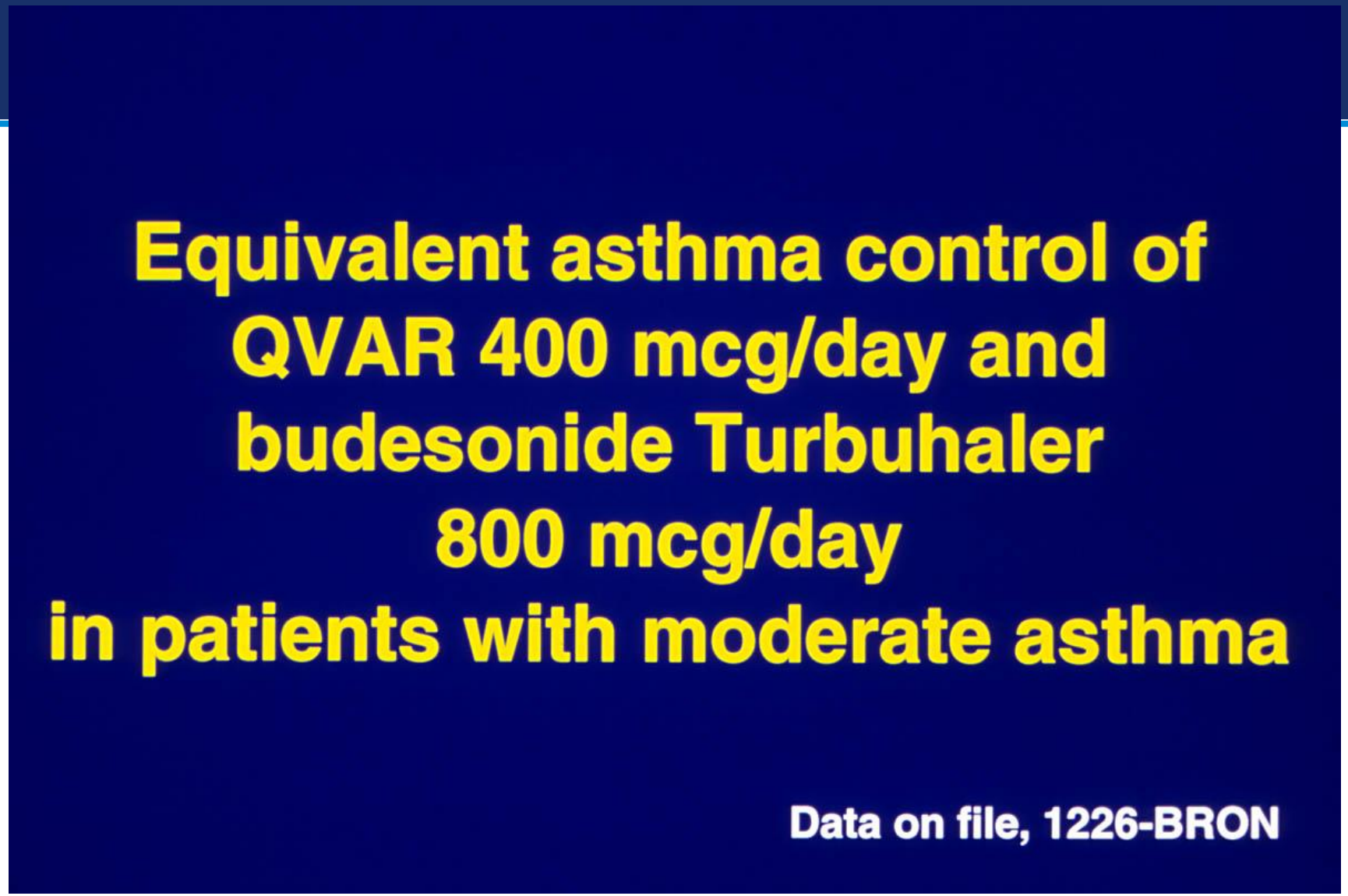
Earliest and most substantial site of airflow limitation= small airways

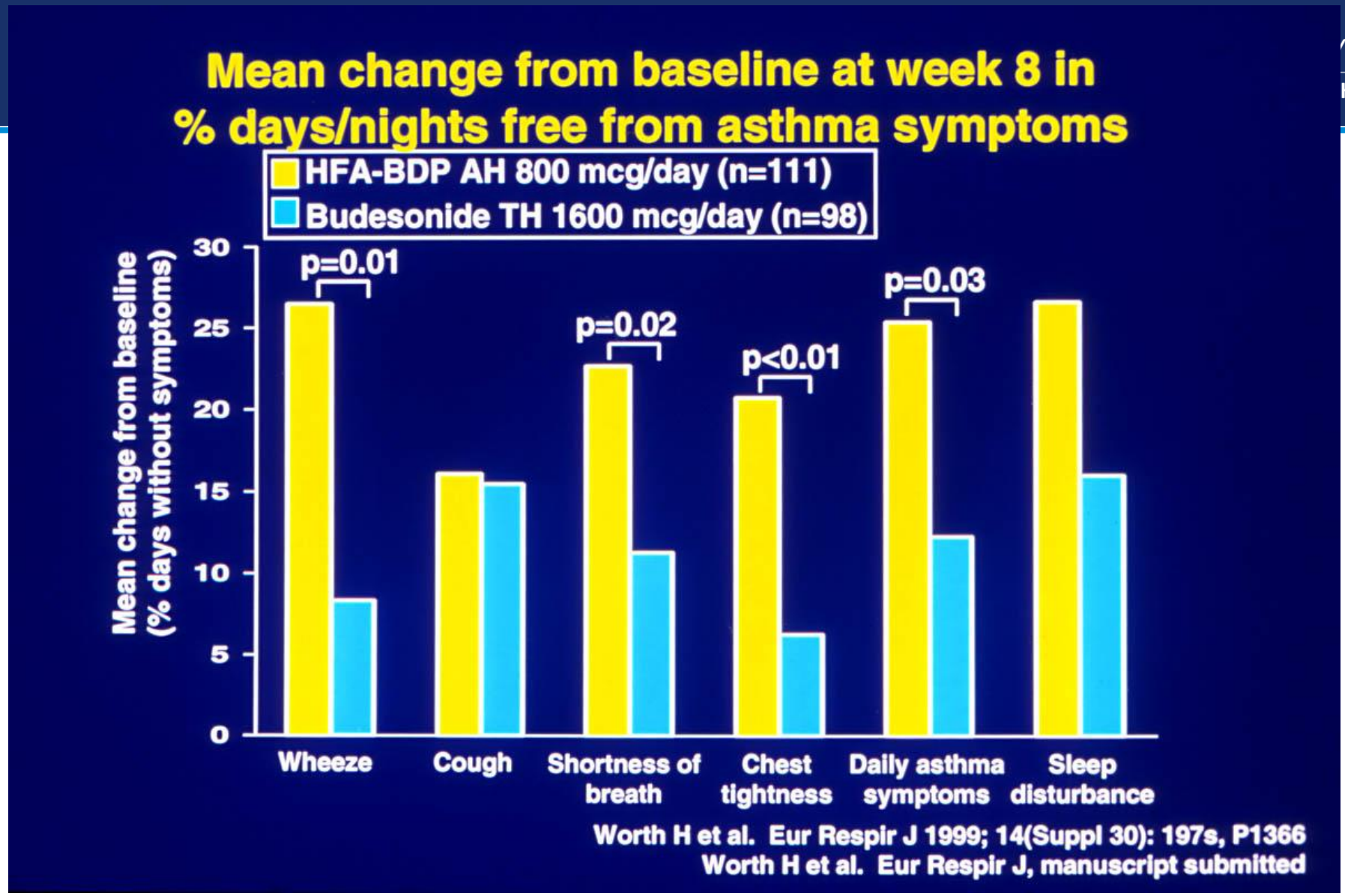



Mean Change from Baseline in FEV1 of % Predicted by Week
Mean Change in FEV1 as % of Prediction
30
20
10
0
N
wk1
wk2
wk3
wk4
wk5
wk6
Treatment
HFA-BDP 800mcg
CPC-BDP 800mcg
HFA-BDP 400mcg
HFA-BDP 100mcg
CPC-BDP 400mcg
CPC-BDP 100mcg
Green Lane

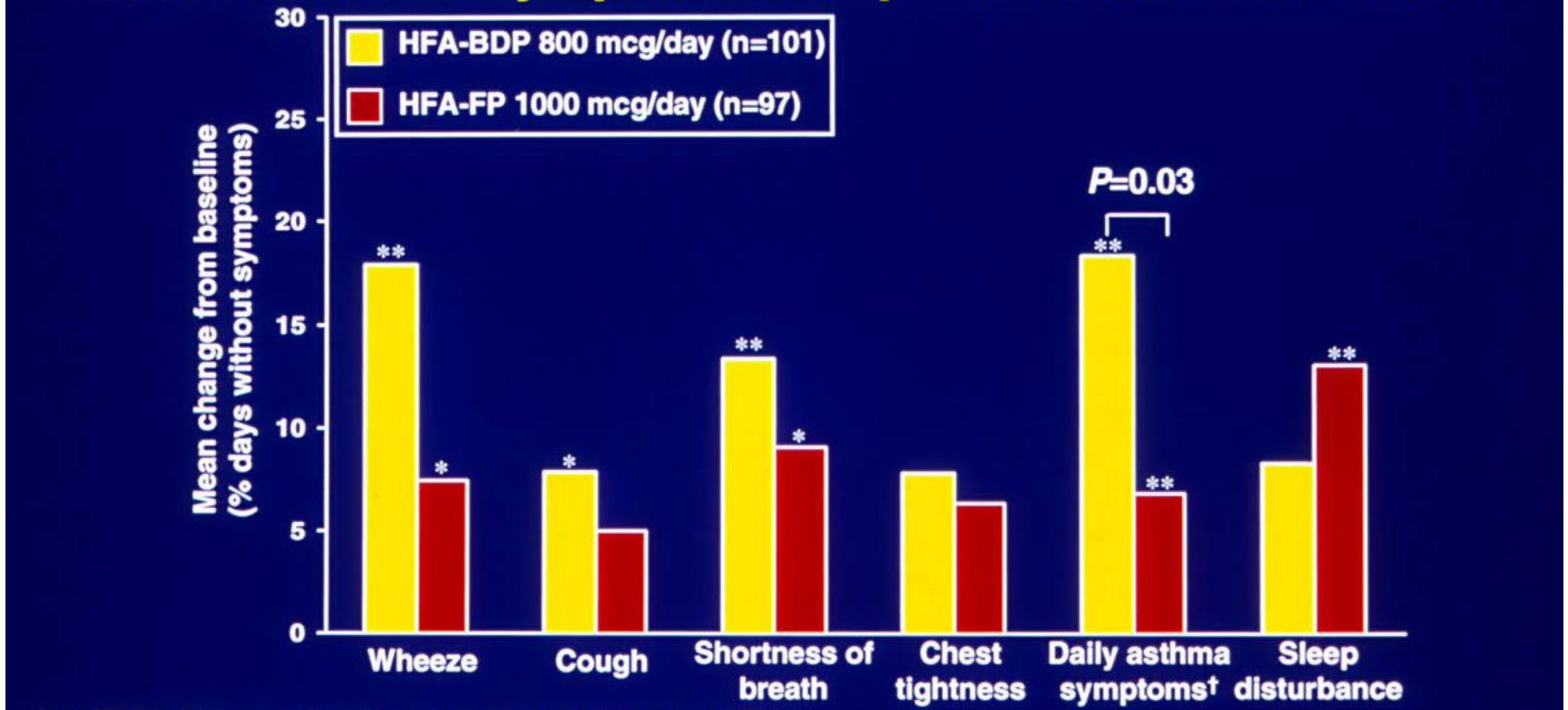
Mean Percentage Change from Baseline in FEF 25-75% by Week




Equivalent asthma control of
QVAR 400 mcg/day and
budesonide Turbuhaler
800 mcg/day
in patients with moderate asthma
Data on file, 1226-BRON


Mean change from baseline at week 8 in
% days/nights free from asthma symptoms
HFA-BDP AH 800 mcg/day (n=111)
Budesonide TH 1600 mcg/day (n=98)
Mean change from baseline
(% days without symptoms)
30
25
20
15
10
5
0
p=0.01
p=0.02
p<0.01
p=0.03
Wheeze
Cough
Shortness of breath
Chest tightness
Daily asthma symptoms
Sleep disturbance
Worth H et al. Eur Respir J 1999; 14(Suppl 30): 197s, P1366
Worth H et al. Eur Respir J, manuscript submitted

Mean change from baseline in percentage of days/nights without asthma symptoms/sleep disturbance at week 3



* p<0.05 within treatment group change from baseline
** p<0.01 within treatment group change from baseline
† Number of days without any daytime asthma symptom (no wheeze, no cough, no shortness of breath, no chest tightness)

Aubier M et al. Allergy, manuscript submitted

Real-World Effectiveness of Extrafine Hydrofluoroalkane Beclomethasone and Fluticasone: UK and US data compared

by G Colice et al

ATS - 2011

Outcome Summary

	UK		US	
INITIATING ICS				
ICS	**FP** n=1,319	**EF HFA-BDP** n=1,319	**FP** n=12,672	**EF HFA-BDP** n=4,224
Asthma control (adjusted odds ratio, 95% CI)	1.00	***1.30 (1.02, 1.64)****	1.00	1.05 (0.98, 1.14)
Adjusted exacerbation rate ratio (95% CI)	1.00	0.96 (0.85, 1.09)	1.00	0.98 (0.92, 1.05)
Median (IQR) ICS prescribed at the index date, mcg	***220*** (176, 440)	***160*** (80-160)	***440*** (176-440)	***160*** (160-320)
Percentage of patients using ≥200mcg SABA daily (%)	31.1%	28.0%	24.8%	17.6%

Extrafine inhaled medication achieves significantly better control

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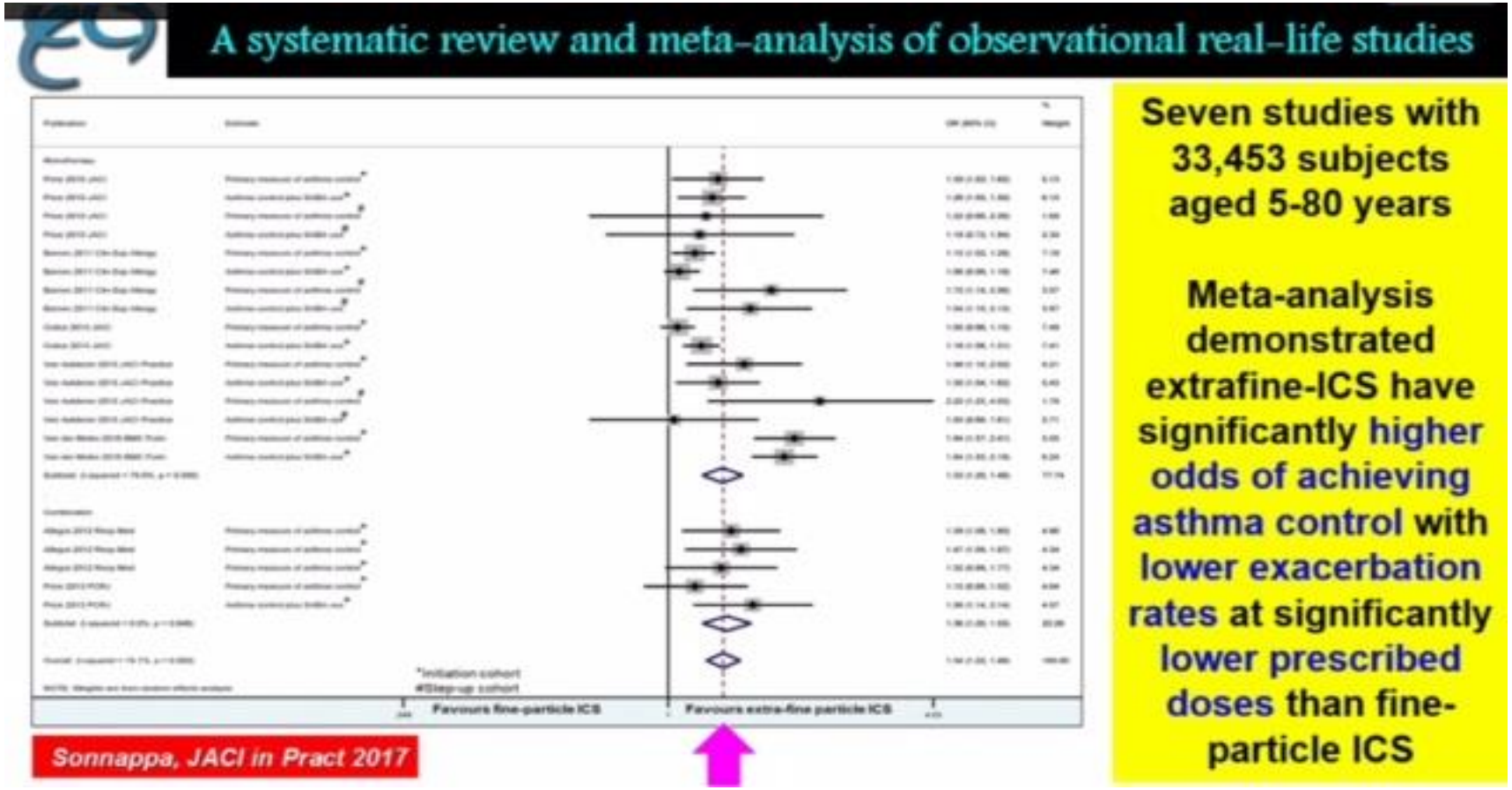
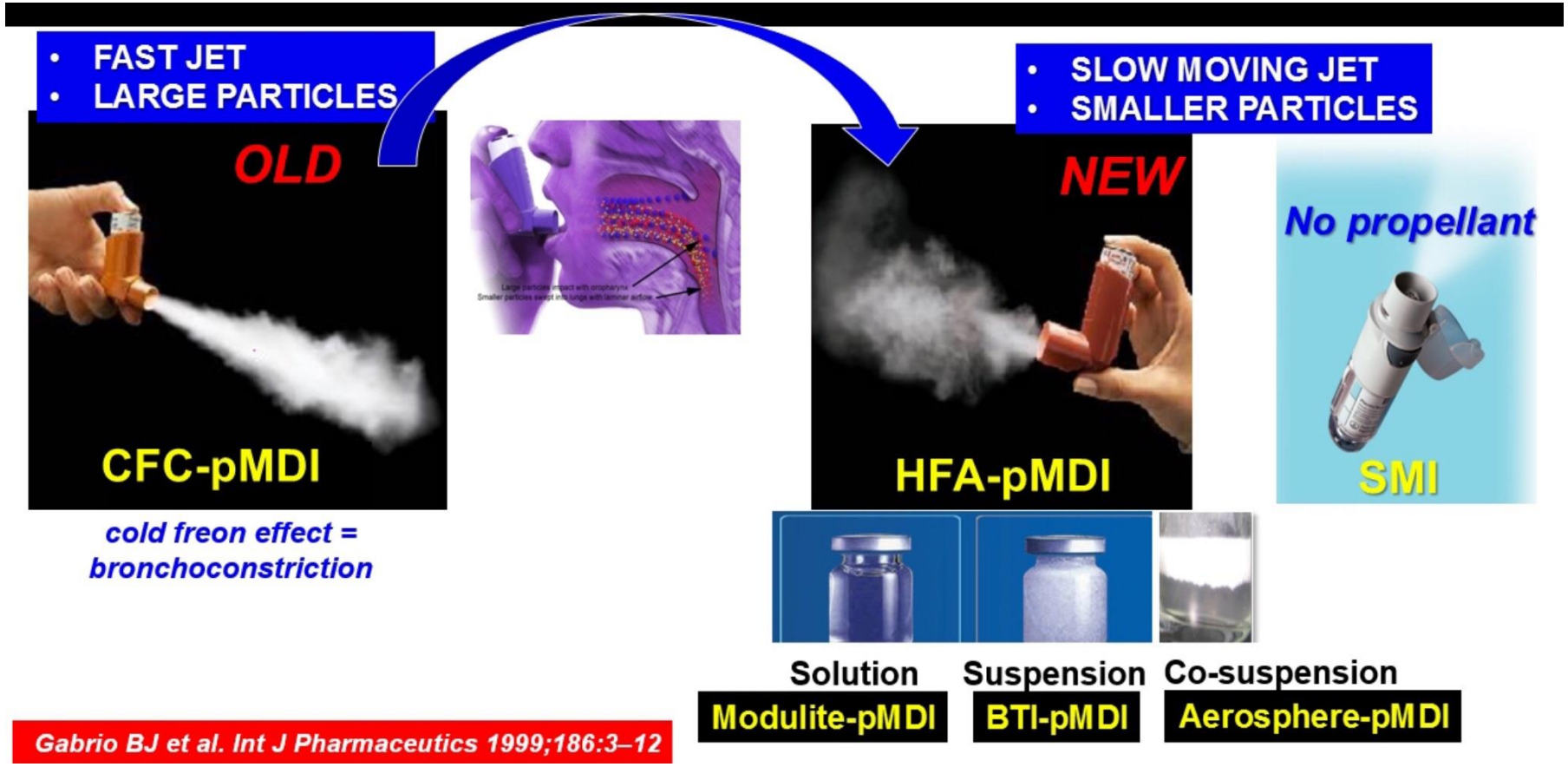


Seven studies with 33,453 subjects aged 5-80 years

Meta-analysis demonstrated extrafine-ICS have significantly higher odds of achieving asthma control with lower exacerbation rates at significantly lower prescribed doses than fine-particle ICS

Respimat and Qvar MDI slowest moving jet with smaller particles



50% of “severe” asthmatics in Middlemore Clinic poorly adherent-dispensing data

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When Treatment Isn’t Working… Think Non-Adherence!

Time for one-person trials

Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy, says **Nicholas J. Schork**.

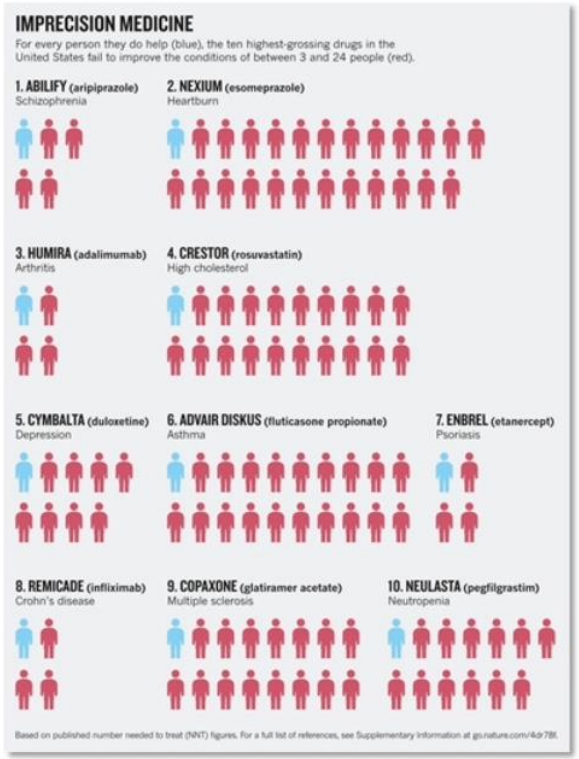
Every day, millions of people are taking medications that will not help them. The top ten highest-grossing drugs in the United States help between 1 in 25 and 1 in 4 of the people who take them (see ‘Imprecision medicine’). For some drugs, such as statins — routinely used to lower cholesterol — as few as 1 in 50 may benefit[1]. There are even drugs that are harmful to certain ethnic groups because of the bias towards white Western participants in classical clinical trials[2].

Recognition that physicians need to take individual variability into account is driving huge interest in ‘precision’ medicine. In January, US President Barack Obama announced a US$215-million national Precision Medicine Initiative. This includes, among other things, the establishment of a national database of the genetic and other data of one million people in the United States.

Classical clinical trials harvest a handful of measurements from thousands of people. Precision medicine requires different ways of testing interventions. Researchers need to probe the myriad factors — genetic and environmental, among others — that shape a person’s response to a particular treatment.

Studies that focus on a single person — known as *N*-of-1 trials — will be a crucial part of the mix. Physicians have long done these in an ad hoc way. For instance, a doctor may prescribe one drug for hypertension and monitor its effect on a person’s blood pressure before trying a different one. But few clinicians or researchers have formalized this approach into well-designed trials — usually just a handful of measurements are taken, and only during treatment.

If enough data are collected over a sufficiently long time, and appropriate control interventions are used, the trial participant can be confidently identified as a responder or non-responder to a treatment. Aggregated results of many *N*-of-1 trials (all carried out in the same way) will offer information about how to better treat subsets of the population or even the population at large.



Nature, 30 April 2015

>50% OPs and >82% IPs poorly adherent

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Poor adherence in difficult-to-control asthma

Prescriptions Filled in 6 Mo	Number of Patients
0–25%	16 (9%)
26–50%	47 (26%)
51–75%	34 (19%)
76–100%	47 (26%)
>100%	38 (21%)

Gamble *et al* AJRCCM 2009

Difference between Research Studies and Real Life

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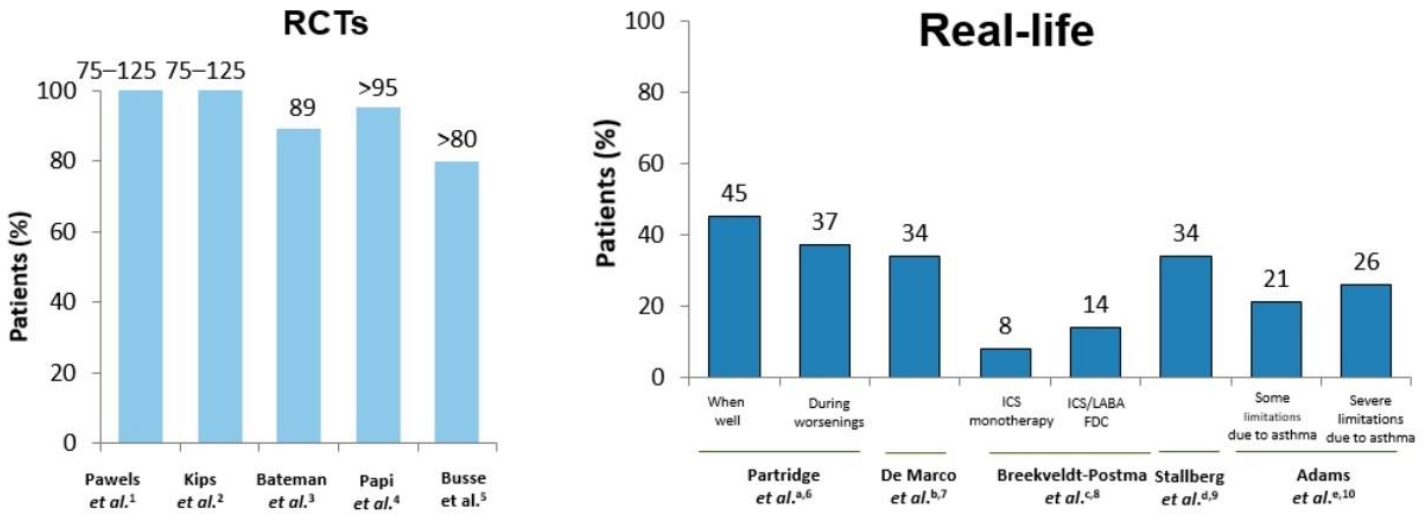
Adherence in RCTs and Real-Life

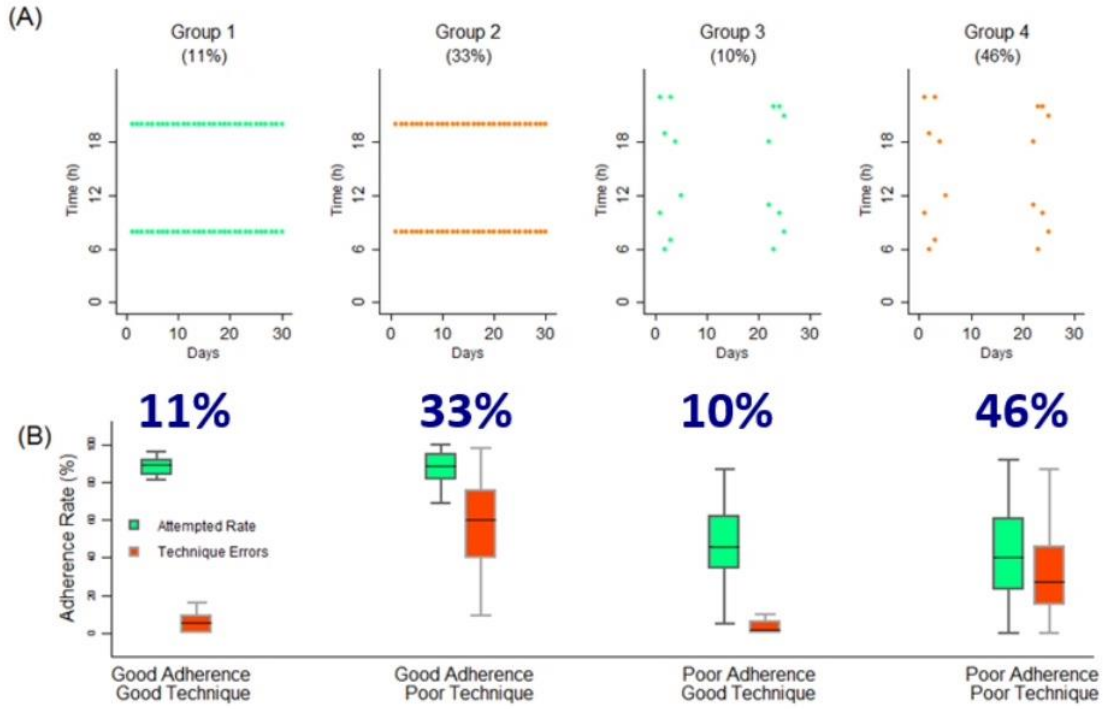


[a]Used regular maintenance medication prescribed. [b]Used medication daily over the previous 3 months. [c]Persistence over 1 year (renewal of initial ICS prescription. [d]Regularly followed the prescription most days a week all year round. [e]Reports current use of ICS therapy.

1. Pawels R *et al. N Engl J Med* 1997;337:1405–11; 2. Kips J *et al. Am J Respir Crit Care Med* 2000;161:996–1001; 3. Bateman E. *et al. Am J Respir Crit Care* 2004;170:836–44; 4. Papi A *et al. Eur Respir J* 2007;29:682–9; 5. Busse W *et al. J Allergy Clin Immunol* 2008;121:1407–14; 6. Partridge MR *et al. BMC Pulm Med* 2006;6:13; 7. De Marco R *et al. Int Arch Allergy Immunol* 2005;138:225–34; 8. Breekveldt-Postma NS *et al. Pharmacoepidemiol Drug Saf* 2008;17:411–22; 9. Stallberg B *et al. Respir Med* 2003;97:835–43; 10. Adams RJ *et al. J Allergy Clin Immunol* 2002;110:58–64

Adherence and inhaler technique groups

Adherence Rates for Different User Groups



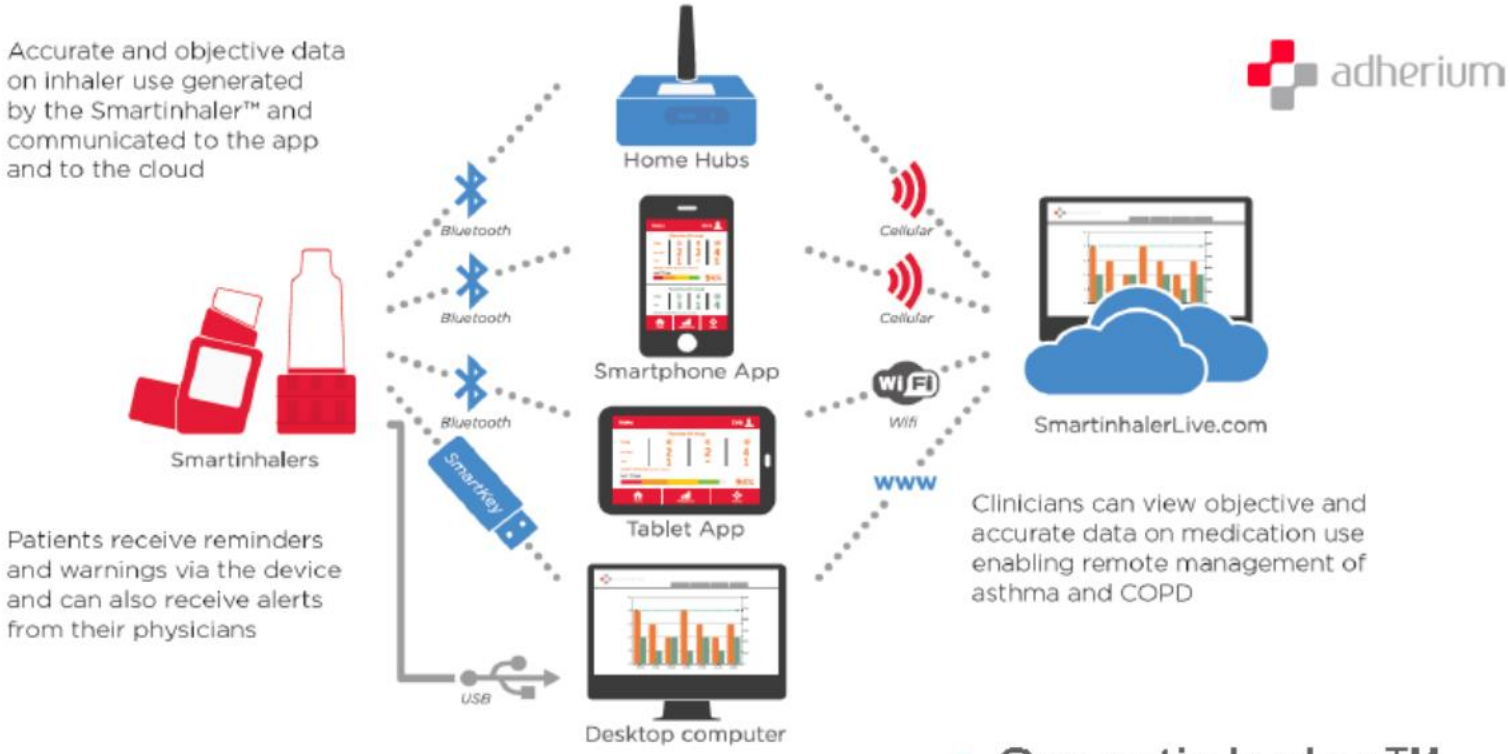
Sulaiman I, et al. Am J Respir Crit Care Med 2017;195(10):1333-1343

Smartinhalers Devices

- Models for many medications e.g. Seretide, Flixotide, Ventolin, Vannair, Symbicort
- Records date & time of pMDI actuation *
- NZ and TGA registered,
- Reminder (Beeper)
- Rechargeable Battery and cable or disposable
- Automatic Bluetooth communications to Smartphone/Tablet
- Quick Start Guide and Product Manual
- ** Note: does not detect inhalation*

Smartinhalers are available for many inhalers in NZ

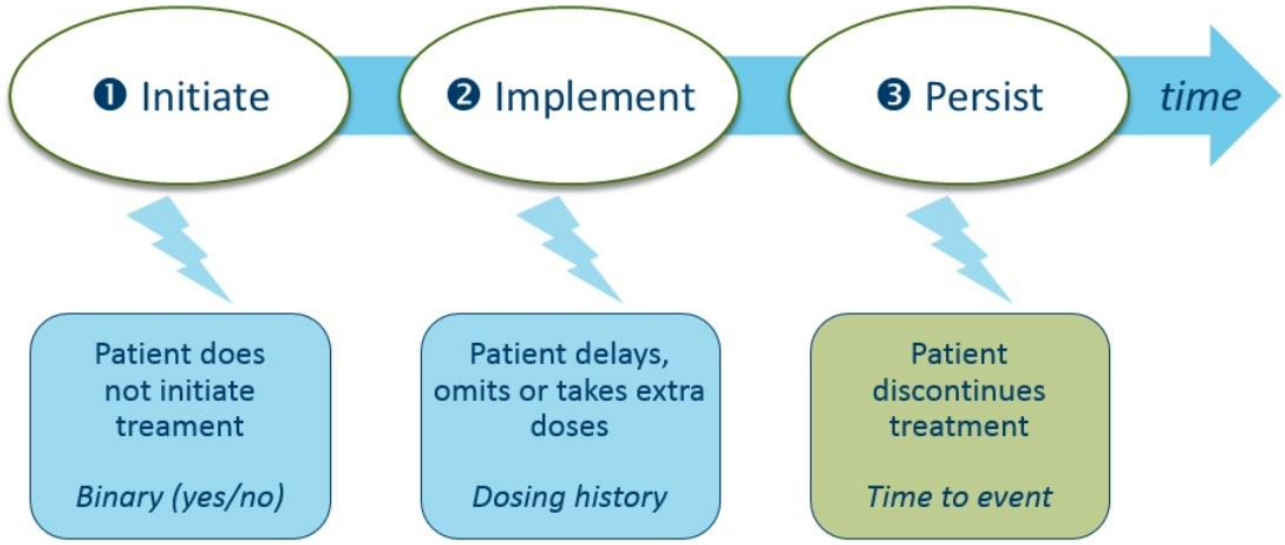
Smartinhaler Platform



Differing patterns of non adherence

How Do We Define Adherence?

The process by which patients take their medications as prescribed



Vrijens et al. Br J Clin Pharmacol 2012;73:691-705

Patterns of non adherence differ

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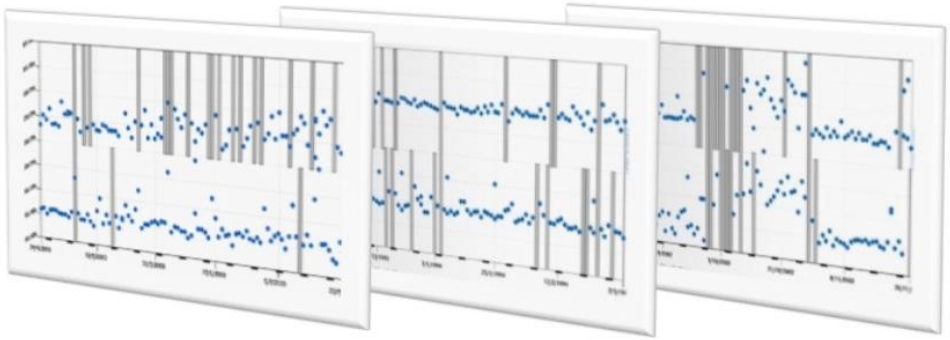
Percentage Adherence Does Not Always Tell the Whole Story

Each of the 4 patients took 75% of prescribed doses during a 3-month period



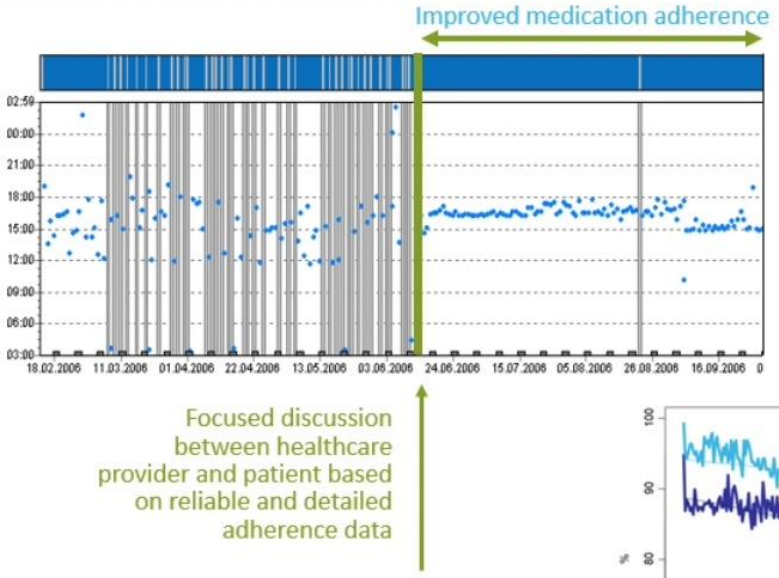
Problem with evening dose | Sporadic dosing | Drug holiday

Vrijens B, et al. Expert Rev Clin Pharmacol 2014;7(5):633-44

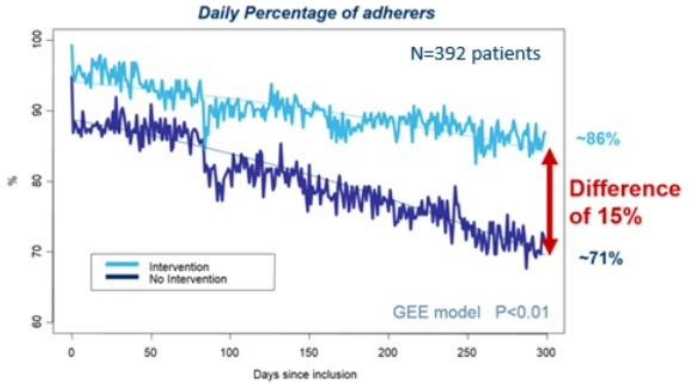
Focussed discussion on adherence

"What Can Be Measured Can Be Managed"

–Deming, WE



Example of a successful intervention



Vrijens B, et al. Pharmacoepidemiol Drug Saf 2006;15(2):115-21

Adherium WiFi based Smartinhaler – Partial soln

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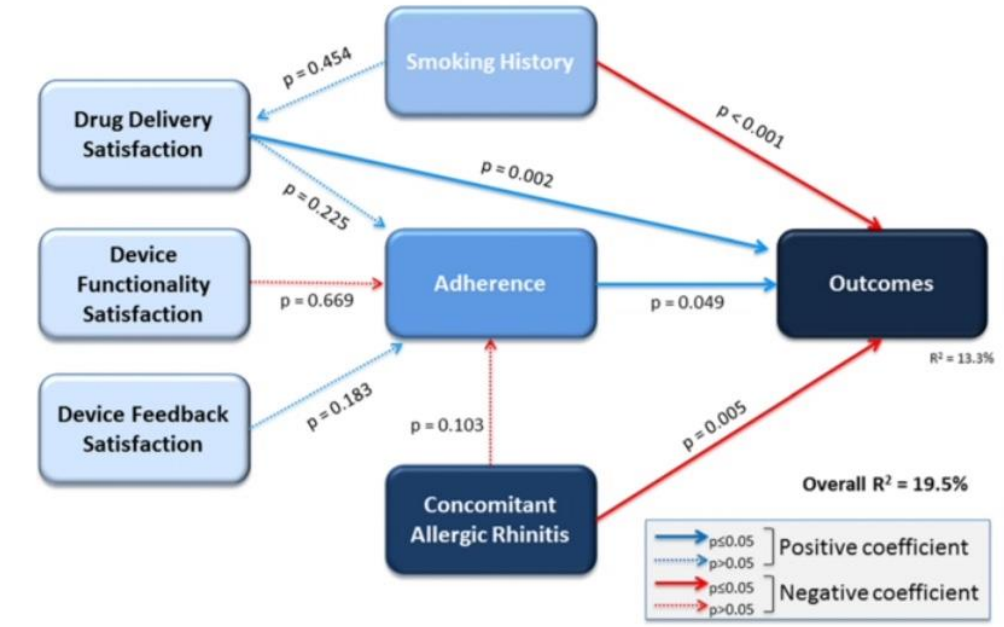
Electronic Monitors

Advantages	Disadvantages
• Can provide detailed information on patterns of use • Can identify dose-response relationship • Can identify medication "dumping" • Under some circumstances may enhance adherence	• Often cannot confirm ingestion • Can be 'expensive' • Potential for reactivity • May interfere with established routines • Requires trained staff and quality control procedures • Vulnerable to mechanical problems • Not currently available for all types of meds

Finding right inhaler important

Inhaler Satisfaction Improves Treatment Adherence



Partial least squares path modeling analysis examining the relationship between inhaler device satisfaction, medication adherence, smoking history, allergic rhinitis, and patient outcomes

Price D, et al. World Allergy Organ J 2015;8(1):26

Non-Adherence-a major clinical and health economic problem

Non-adherence is a critical clinical and economic problem.[4]

- Poor medication adherence costs the healthcare industry in excess of $317 billion in related costs annually.

Annual costs of medication non-adherence:

- range from US$100 to US$290 billion[6] in the USA
- €125 billion[7] in Europe
- A$7 billion[8 9] in Australia
- NZ$1 billion in New Zealand
- 10% of hospitalisations in older adults are attributed to medication non-adherence[10 11]
- typical non-adherent patient requiring three extra medical visits per year.[12]

30% patients do not get their prescription filled

Primary reasons for poor adherence

Random analysis of 4 million member database - adjusted for PAB

- Two key factors inadequate access and financial concerns

- Inability to visit pharmacy
- Patient schedule
- Forgetfulness
- Procrastination

- Patients who had medicines delivered were more adherent
- Mail order a preferred option because Rx is delivered and total out of pocket expenses less

Random analysis of 4 million member database - adjusted for PAB

AM J Manag Care. 2013;19(10):798-804

Courier Service improves adherence

Delivering medicines vs traditional model – impact on Adherence

- 14 out of the 15 studies reviewed, showed that patients who use mail-order pharmacies are more adherent than those who use retail pharmacies.
  - Examination of the Link Between Medication Adherence and Use of Mail-Order Pharmacies in Chronic Disease States
    - Elena V. Fernandez, Jennifer A. McDaniel, and Norman V. Carroll, Journal of Managed Care & Specialty Pharmacy 2016 22:11, 1247-1259
- 84.7% of patients where diabetes medications were delivered achieved good adherence compared to 76.9% who used local pharmacies.
  - Am J Manag Care. 2010 Jan; 16(1): 33–40.
- 85.0% of patients who had their statin delivered achieved target LDL-C levels compared with 74.2% of patients who used local pharmacies ($p < 0.001$).
  - Schmittdiel, J.A., Karter, A.J., Dyer, W. et al. J GEN INTERN MED (2011) 26: 1396.

82% of asthmatics discharged from hospital poorly adherent and 40% do not pick up script

Significant clinical gains when medicines delivered

Express Scripts' Research Report. 'Evaluating the Impact of ScreenRx® on Prescription Costs.' 2015

- Pulmonary arterial hypertension:
  - 17% higher adherence when filling prescriptions through home delivery
  - 32% fewer hospitalizations
  - 35% fewer emergency room visits
  - Significantly less in medical expenses per patient per year
- Multiple sclerosis:
  - 32% higher adherence
  - 39% fewer hospitalizations
  - 39% fewer ER visits
  - saving 31% annually on medical expenses
- Rheumatoid arthritis:
  - 16% higher adherence
  - 9% fewer hospitalizations
  - 13% fewer ER visits
  - saving 16% annually on medical expenses

MMH to trial in asthma, COPD, Diabetes, Gout

Medication adherence as a predictor of 30-day hospital readmissions

Patient preference and adherence 2017:11 801-810

- 4-item Morisky Medication adherence scale administered by a pharmacist at admission

Findings

- Patients with low and intermediate adherence were 2.45-fold higher odds of readmission compared to patients with high adherence p=0.005

Conclusion

- Medication adherence assessed at hospital admission independently identified 30 day readmission risk

Solutions to adherence/technique issues

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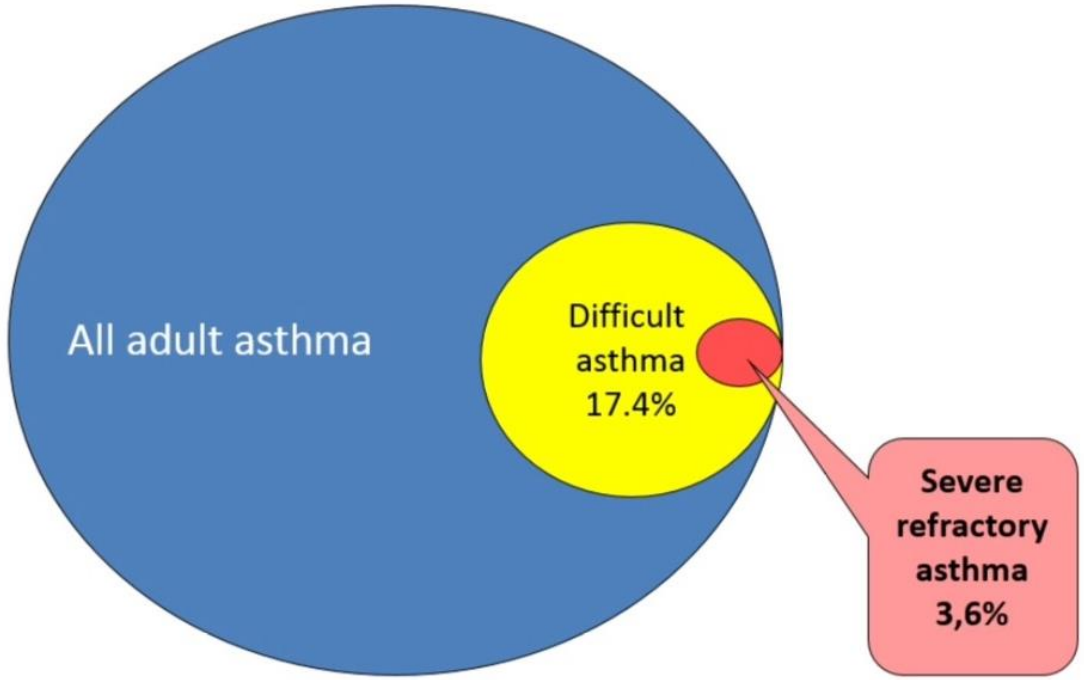
What Can We Do?

- Be aware
- Set common goals
- Solve inhaler technique issues
- Simpler regimes
- Use electronic monitoring methods

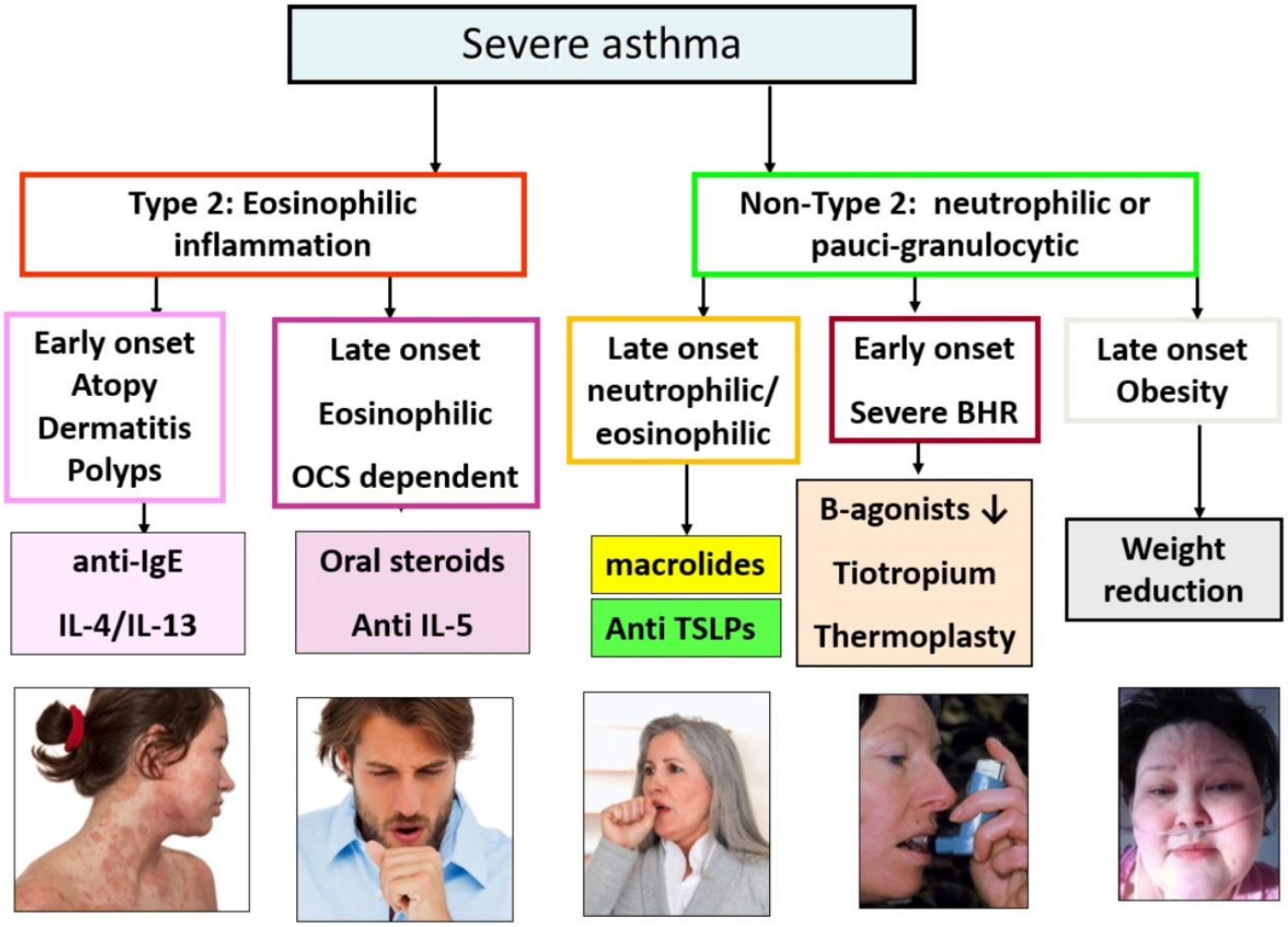
Severe Asthma small minority

Severe eosinophilic asthma: small minority of asthma patients



Hekking PP et al J Allergy Clin Immunol 2015

Updated Treatment by Phenotypes



Models of Care and Referral Pathways for Severe Asthma
Australasian Severe Asthma Network 2019

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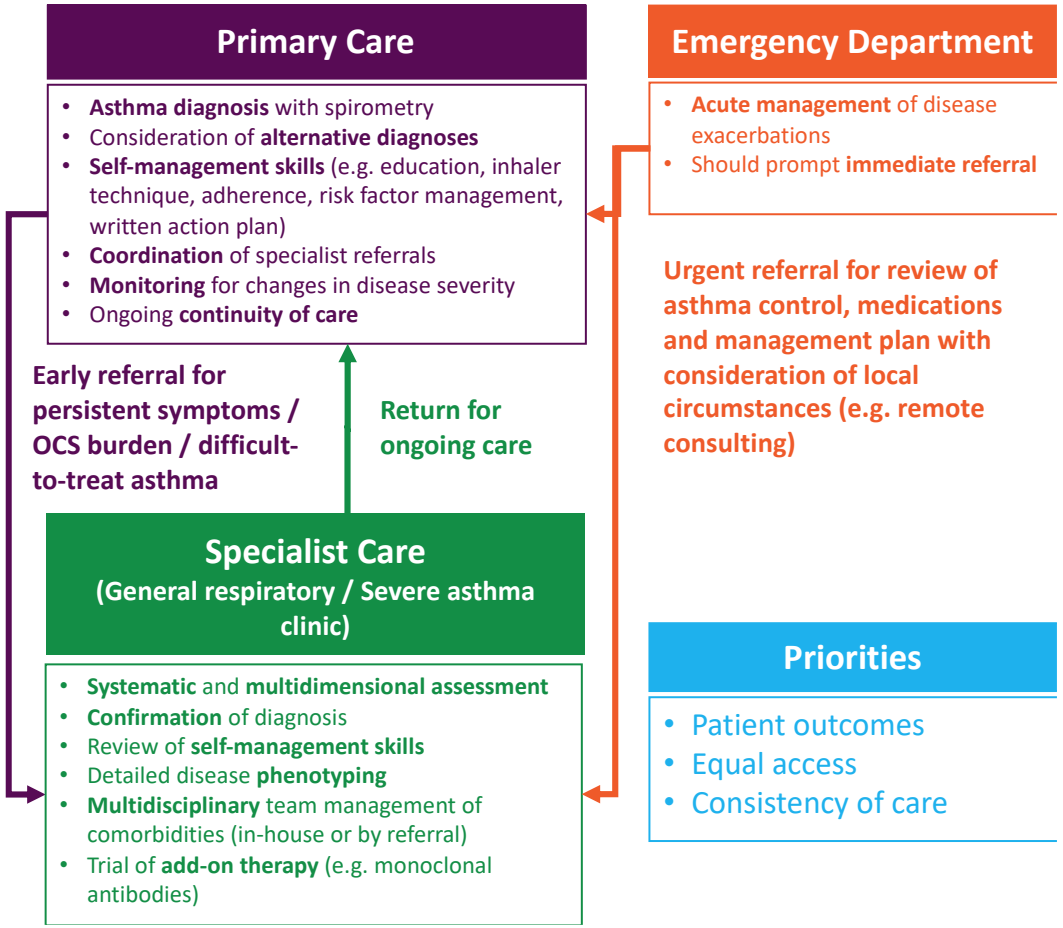
A model of care for severe asthma management, including clinical settings, assessment and management considerations and referral pathways.



Summary Asthma

- Use Symptoms (ACT), exacerbation frequency, SABA use, FEV1 , Eosinophil level to assess control
- We are overusing LABAs and underutilising ICSs (dose)
- Poor at back titration of ICS/LABA
- 50% are poorly adherent (80% admitted pts)
- 50% have poor inhaler technique
- Many patients prescribed wrong inhaler (DPI vs MDI, SABA vs SABA/ICS, LABA/ICS or ICS alone, Type of ICS, Combination therapies vs ICS +LABA/LAMA in overlap syndrome)

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