ASTHMA

DR ANDY POWELL

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The great asthma myth: A third of those diagnosed DON'T have the condition, study finds

- Breathing tests were conducte
- Researchers found that 33% di
- While 90% were able to stop us
- Experts say many doctors are n

By BEN SPENCER MEDICAL CORRESPO
PUBLISHED: 16:47, 17 January 2017 | U

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A third of adults diagnosed with a research suggests.

Experts think many people are mis recover to the extent the asthma i

They say doctors are too often dia the proper tests.

'Doctors wouldn't diagnose diabet broken bone without ordering an night.

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How asthma inhalers may be USELESS for thousands of sufferers - because they actually h

- Pauline Saunders, 52, from O
- 'The GP thought it was asthm
- She was, in fact, suffering fro

By LUCY ELKINS FOR DAILY MAIL
PUBLISHED: 23:19, 7 March 2016 | U

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Told by her GP that she had asth surprise.

The 52-year-old human resource for weeks.

It was so severe that she could t minutes she would start hacking

'It was really getting me down,' asthmatics are. It was a throaty

'But the GP thought it was asthn every day for a fortnight to dam

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More than 1m people with asthma may NOT have the condition and could be taking medic

- NICE says there is no evic
- Watchdog is concerned t
- Now advises doctors to c
- This includes a spirometr
- However asthma charitie

By MADLEN DAVIES FOR MAILO
PUBLISHED: 07:09, 28 January

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More than a million people r misdiagnosed, experts warn

Almost a third of the 4.1m pe 'clear evidence' of the incur Health and Care Excellence

This means they may be rec

However, asthma charities v patients 'do not receive ade

And experts cautioned that prescribed medication unle

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Up to half of children diagnosed with asthma might NOT have the condition

- Asthma could be mis-diagnosed in up to 50% of children with the condition
- Research claims doctors are failing to carry out appropriate lung tests
- Drugs used to manage asthma can cause cramps and throat infections

By TAMMY HUGHES FOR THE DAILY MAIL
PUBLISHED: 08:14, 26 February 2016 | UPDATED: 04:38, 29 February 2016

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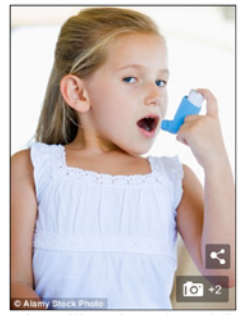
Asthma could be mis-diagnosed in up to half of children found to have the condition, according to a study.

The research has been conducted in the Netherlands but is being published in the British Journal of General Practice.

It is also being taken into account by officials at National Institute for Health and Care Excellence (NICE) as they reconsider procedures for diagnosis.

The study - published in the Daily Telegraph - follows claims by the NHS watchdog last year that a third of 'asthmatic' adults showed no clinical signs and had probably been misdiagnosed.

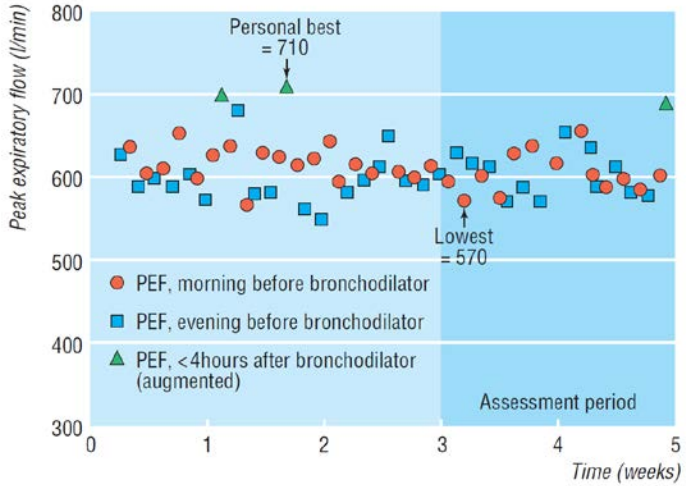


WHY ASTHMA STILL KILLS (THE NRAD)

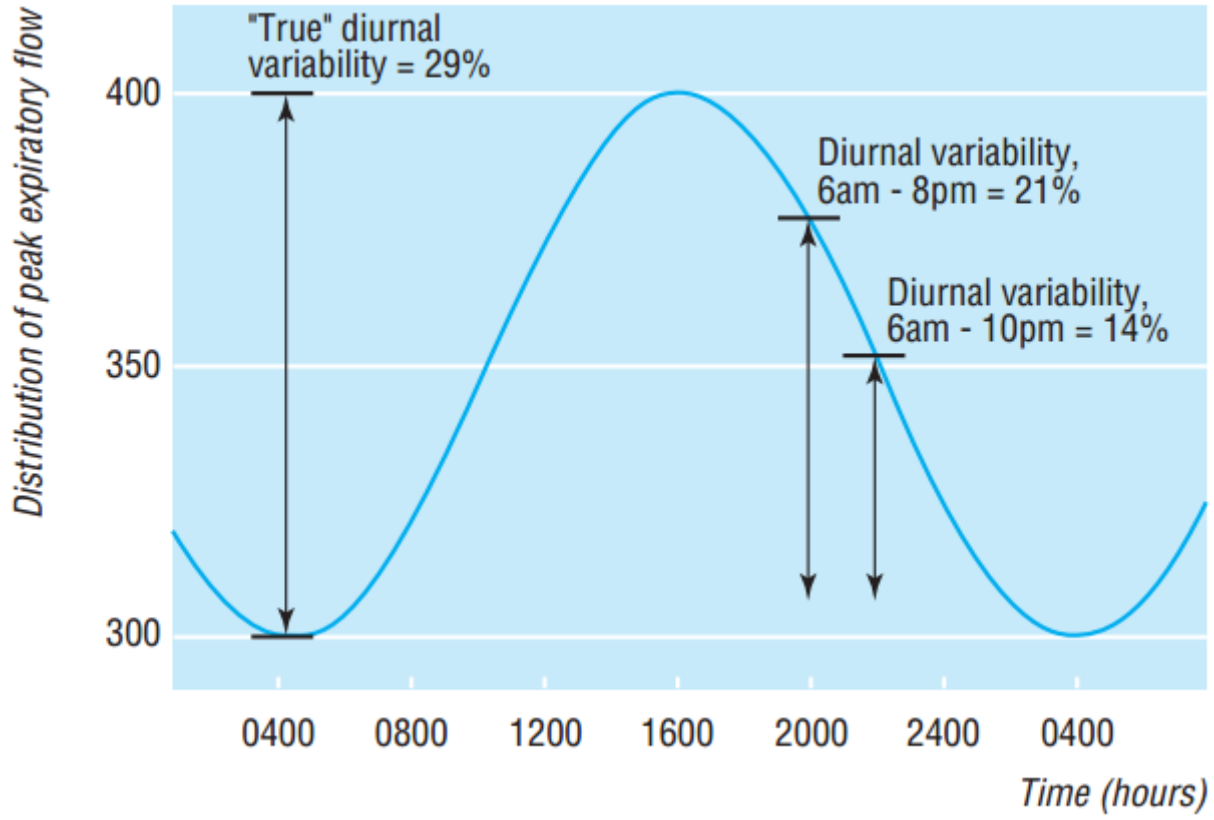
- 45% died without seeking medical assistance
- 21% had ED attendance at least once in the previous year
- Only 23% had action plans
- 58% being treated for ‘mild’ or ‘moderate’ asthma
- Median age diagnosis 37
- Avoidable - Implementation of asthma guidelines (46%)
- 39% had more than 12 short acting inhalers in the year before
- 80% had fewer than 12 preventer inhalers in the year before

DIAGNOSIS

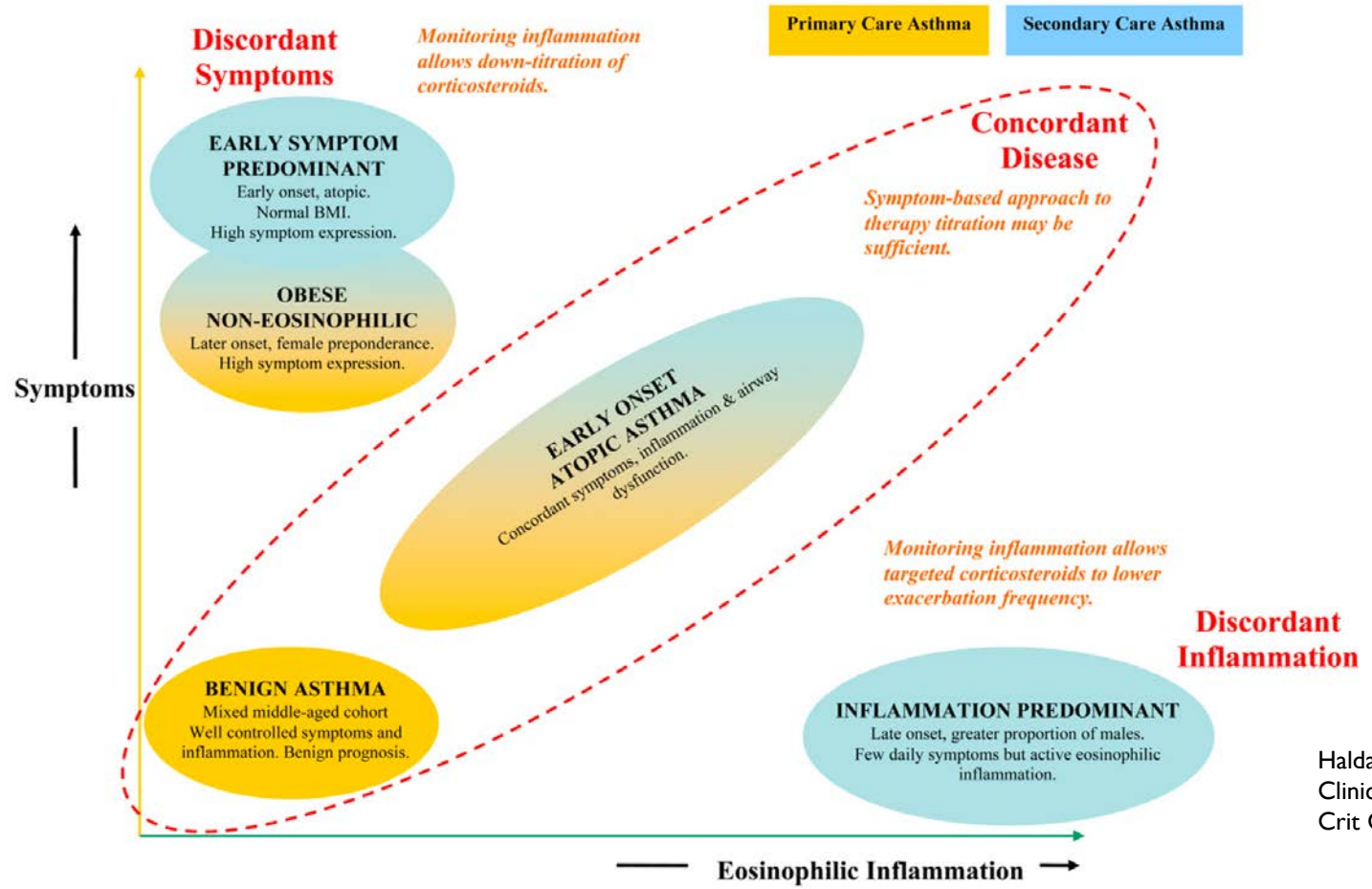
- Spirometry
  - Evidence of obstruction (when symptomatic) eg. FEV1% < 0.7 (PPV 45-100%, NPV 18-73%)
  - Postbronchodilation improvement in FEV1 of 12% (and at least 200ml in adults). (PPV 53-82%, NPV 22-68%)
- Peak flow diaries
  - Variability = $\frac{(Highest\ PEF - Lowest\ PEF)}{Mean\ PEF} \times 100$
  - Mean variability > 20% (PPV 97%, NPV 10%)
  - Mean variability > 15% (PPV 60-67%, NPV 60%)
  - Diurnal variation > 15% on >3 days/week (PPV 82%, NPV 64%)
    - DV = $\frac{(Highest\ PEF - Lowest\ PEF)}{Highest\ PEF} \times 100$
    - DV > 15% for >4 days (probability 83%), DV > 20% for >3 days (probability 88%) (Thiadens HA et al. Eur Respir J 1998;12:842-7)



VARIATION


"True" diurnal
variability = 29%
Diurnal variability,
6am - 8pm = 21%
Diurnal variability,
6am - 10pm = 14%
400
350
300
0400
0800
1200
1600
2000
2400
0400
Distribution of peak expiratory flow
Time (hours)

PHENOTYPES/ENDOTYPES



Haldar P et al. Cluster Analysis and Clinical Asthma Phenotype. Am J Respir Crit Care Med 2008;178:218-24.

ACCURACY OF DIAGNOSIS

- Looked at 613 patients age > 18 with physician diagnosed asthma in last 5 years (only 45% daily medication = mild disease) (JAMA 2017;317(3):269-79)
  - Serial diagnostic tests – spirometry with reversibility (≥12% and ≥200ml), metacholine challenge
  - If both negative then ICS and LABA halved and repeat metacholine challenge in 3 weeks (along with PEF diary)
  - If still negative, no worsening of symptoms, normal PEF diary, then stopped and repeated
  - If negative (as above) then alternative diagnoises considered and challenge at 6 and 12 months
- 410 asthma confirmed (86 reversibility at first visit, 287 hyperresponsiveness, 9 worsening of symptoms, 28 pulmonologist diagnosed)
  - 203 (33%) current asthma ruled out (only 43.8% had initial diagnostic spirometry)
  - 22 had hyperresponsiveness subsequently (but 16 asymptomatic) – only 1 needed oral steroids
- What does this mean?? – remission v. misdiagnosis (what about airway inflammation….)

THE THIRD STEP…

- LABA+ICS (Am J Respir Crit Care Med 2004;170:836-44)
  - GOAL suggested better and quicker control with LABA+ICS
  - (But high reversibility ≈ 26%, no markers of airway inflammation)
- Increase dose ICS alone (An Am Thorac Soc 2015;12(6):796-806)
  - 'Real world' observational study in UK
  - Asthma control ICS v. ICS/LABA (small particle) OR 0.99 (0.88-1.12) and (large particle) OR 0.85 (0.67-1.07)
- Add LRTA (J Allergy Clin Immunol 2013;132(1):63-9)
  - 'Real world' observational study in Canada
  - Poorer adherence and more OP visits and reliever medications dispensed

DRAFT NICE GUIDANCE 2016

- ‘The clinical review highlighted that the main benefit of choosing ICS + LABA over ICS + LTRA was a reduction in the number of exacerbations. There was no evidence that it impacted hospitalised exacerbations, though due to the small number of hospitalisations a study would need thousands of participants to be adequately powered. Finally, there was some evidence that LABAs improved quality of life…’
- BUT ICS+LRTA at step 3 would save £700 over lifetime therefore ICS+LABA -> ‘not considered cost effective …’

LABA SAFETY

- Long-acting beta-agonists (LABAs) have been shown to increase the risk of asthma-related death among adults and the risk of asthma-related hospitalization among children.
- Children – 6208 children (4-11) needing daily Rx and exacerbation(s) in last year randomised to FP or S/FP for 26 weeks. Non inferiority HR 1.28 (0.73 – 2.27) p=0.006 (N Engl J Med 2016; 375:840-849)
- Adults – 11693 (12+) needing daily Rx and 1-4 exacerbations in last year randomised to BUD or F/BUD. Non-inferiority HR 1.07 (0.70 – 1.65). Fewer exacerbations HR 0.84 (0.74 – 0.94) p=0.002 (N Engl J Med 2016; 375:850-860)
- MHRA
  - Always prescribe LABA with concomitant ICS and only when ICS alone are not sufficient to control asthma symptoms
  - LABA should not be initiated in patients with rapidly deteriorating asthma

OPTIONS AT STEP 4…

- LAMA (NEJM 2012;367:1198-1207)
  - 2 RCTs with Spiriva Respimat. Patients where symptomatic at step 3/4 and some post-bronchodilator airflow obstruction (FEV1<80% and FVC<70%). Non-smokers or light smokers (<10 pack/years)
  - Increased time to first severe exacerbation (by 56 days), 21% reduction in risk of severe exacerbation (HR 0.79, p=0.03)
  - Note recent TIOSPIR trial – Respimat non-inferior to Handihaler – risk of death HR 0.96 (0.84-1.09)
- SMART Regime (Lancet Resp Med 2013;1(1):23-31)
  - Patients with recent exacerbation randomised to Symbicort MDI 200/6 2 puffs bd with extra puff when needed v. salbutamol MDI 2 puffs when needed.
  - Fewer high use (>8 Symbicort v. >16 salbutamol) days 5.1 v. 8.9 days (p=0.01). Fewer exacerbations 0.53 v. 0.97 weighted mean rate per year (p=0.004)
  - Greater ICS usage but less oral steroid use

OPTIONS AT STEP 4…

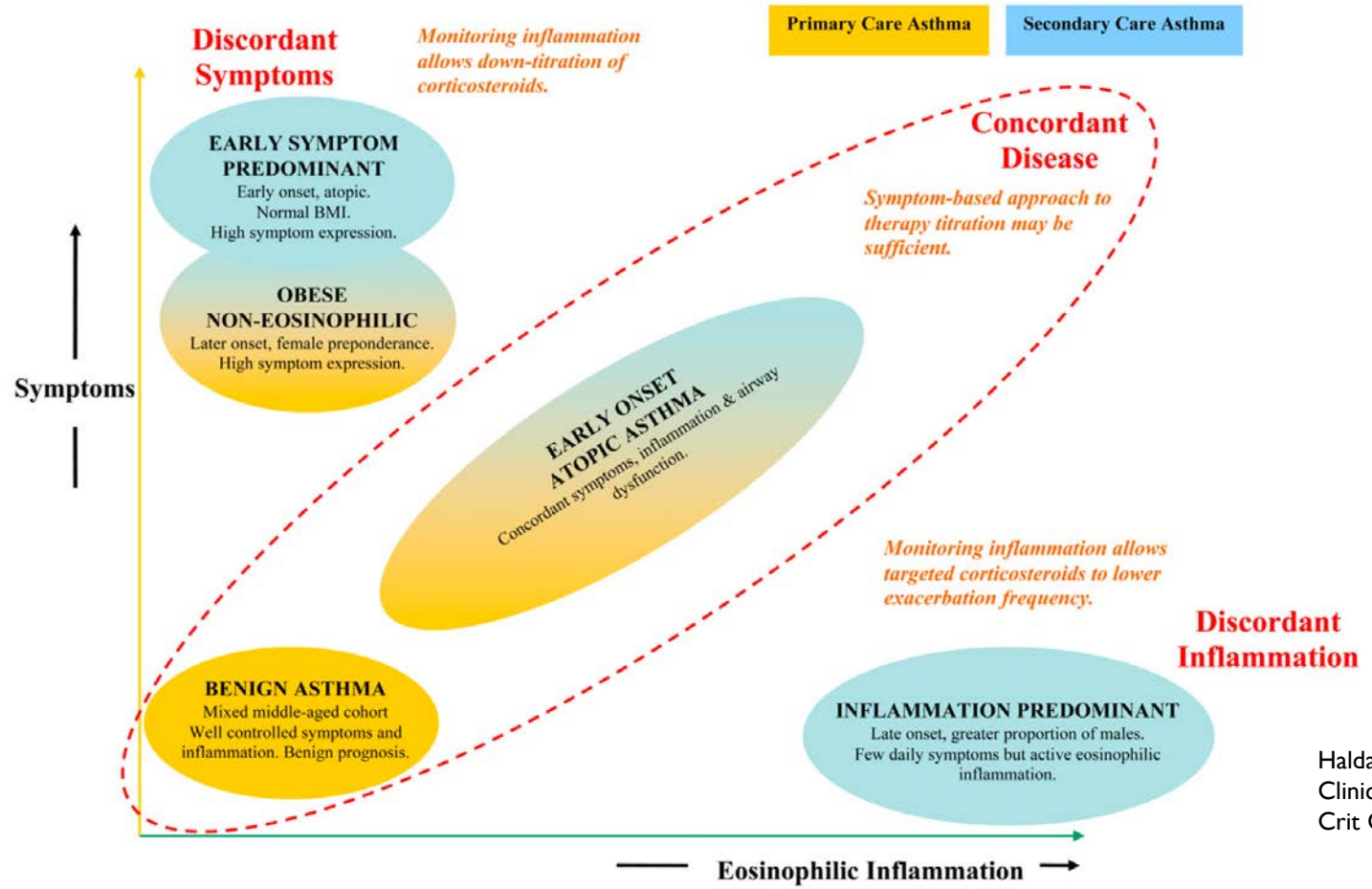
- Extrafine particle (Respiratory Research 2012;13:112-122)
  - 1017 patients with uncontrolled/partially controlled (ACT<20) asthma. Real life study.
  - Total control (ACS=25) 77/301 (extrafine) v. 31/268 (non-extrafine) $p<0.001$ (eBDP/F v. BUD/F)
  - Exacerbations (last 3/12) 40/301 (13.3%) (eBDP/F) v. 19/145 (13.1%) (BUD/F) v. 25/123 (20.3%) (FP/S)
  - One exacerbation in 67% poor/uncontrolled group v. 6% controlled/total controlled group $p<0.001$
  - Better quality of life scores
  - BUT recent systematic review and meta-analysis – 'Based on the available literature, no clinically significant differences in efficacy or safety were observed comparing small and standard particle size ICS medications for the treatment of asthma.' (BMC Pulmonary Medicine 2017;17:31)

STEP 1…. OR NOT

- Post-hoc analysis of START study – mild asthma diagnosed objectively in past 2 years and symptoms at least once week but not daily in last 3 months and less than 30 days ICS/year.
- Randomised to budesonide 400mcg once daily (n=3577) or placebo (n=3561). Seen every 3 months for 3 years. Symptom questions
- Outcome – SARE (Significant Asthma Related Event) – admission or emergency treatment, death, change in postbronchodilator FEV1. Stratified by symptoms in 2 weeks prior to randomisation.
- Time to first SARE longer
  - 0 - 1 symptom days/week – HR 0.54 (0.34 – 0.86)
  - >1 - ≤2 symptom days/week – HR 0.60 (0.39 – 0.93)
  - >2 symptoms days/week – HR 0.57 (0.41 – 0.79)
- Reality – reduction of 9 SAREs/year/1000 patients, 90 courses steroids/year/1000 patients (<1 per patient/10 years)

Reddel HK et al. Lancet 2017;389:157-66.

PHENOTYPES/ENDOTYPES



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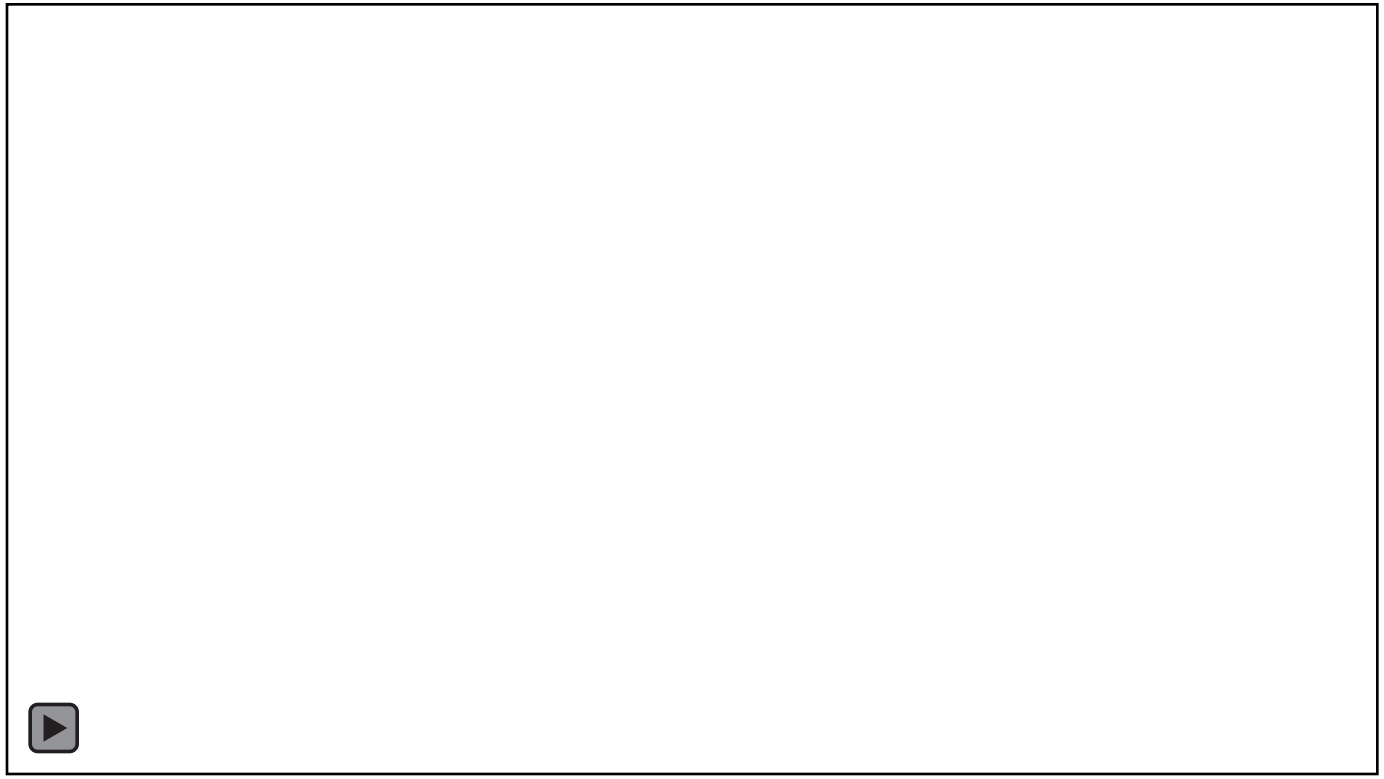
OTHER CONSIDERATIONS

- Rhinitis
  - Poor asthma control associated with self reported arthritis (OR 4.62)
- Inhalers MDI (pMDI v. Respimat), DPI (integral drug v. tablets)
- Inhaler technique (PCRJ 2011;20(1):92-6)
  - Review of MDI technique. 85.6% pMDI users failed first assessment. Trained again and 74.8% failed second assessment. Trained again and 65.7% still failed.
- ICS Bioavailability
  - 10% inhaled. 90% swallowed.
  - Beclomethasone 26%. Fluticasone/Ciclesonide <1%

INHALER TECHNIQUE



ANOTHER CONSIDERATION….

STEPPING DOWN

- 1000mcg daily of inhaled fluticasone = 10mg prednisolone daily (Lipworth BJ. Arch Intern Med 1999;159:941-55)
- Reduce dose of ICS (and treatment burden) whilst maintaining asthma control
- Stable with good control for at least 3 months
- Seek advice if:
  - Previous near-fatal asthma, or ICU admissions
  - Steroid requiring exacerbation in the last 6 months
  - Adverse behavioural or psychosocial features
- Reduce dose 25-50% every 3-6 months

DIFFICULT TO CONTROL ASTHMA

- Is the diagnosis secure??
- Is the patient on the appropriate conventional step for their symptoms??
- Are there any specific treatments/considerations for their asthma endotype??
- Compliance and inhaler technique??
- Fine particle steroid / LAMA??
- (S)MART regimes??
- Are smoking cessation or weight loss appropriate??
- Is there rhinitis, GORD, dysfunctional breathing, vitamin D deficiency??
- Psychology??
- Action plan and review (and step down)??

EXACERBATIONS

- Should we double preventer inhalers?? (Lancet 2004;363:271-5)
  - 390 asthmatics on step 2+ with 1+ exacerbations in previous year
  - Monitoring PEF for 1 year. Whenever dipped > 15% or symptoms worse given either additional placebo inhaler or steroid inhaler to double usual ICS dose. Backup oral prednisolone
  - No difference in prednisolone usage 11% (active) v. 12% (placebo) group (p=0.8)
- Should we quadruple preventer inhalers?? (Am J Respir Crit Care Med 2009;180:598-602)
  - 403 asthmatics. Very similar to above. Extra inhaler given to quadruple ICS dose.
  - 12/56 (active) v. 19/38 (placebo) starting ICS required prednisolone (p=0.004)
- What about high dose ICS?? (Thorax 1996;51:1087-92)
  - 413 asthmatics with acute exacerbation. Randomised to inhaled fluticasone 1000mcg bd, or tapering prednisolone.
  - Treatment failure defined as PEF < 60% best/predicted, persistent symptoms, occurred in 23% prednisolone v. 27% ICS (p=0.31)

WHCCG ASTHMA GUIDELINES

Adult Asthma Inhaler Guide

NHS West Hampshire Clinical Commissioning Group

Inhaler Choice

SELECTING AN INHALER THE PATIENT CAN AND WILL USE IS CRITICAL
Check ability to generate appropriate inspiratory flow using an In-Check device (on Turbohaler and pMDI settings)

DPI – DEEP, FORCEFUL, LONG technique. Consider ability to generate inspiratory flow for reliever medication during an exacerbation. Ideally breath hold 10s after inhalation.
pMDI – GENTLE, SLOW, LONG technique. Use a spacer unless technique consistently excellent. If cannot inspire for 5 sec and hold then use tidal breathing technique (5 normal 'tidal' breaths per actuation into spacer v. one larger breath). Always actuate one puff at a time into the spacer and minimise delay between actuation and inhalation.

pMDI – requires hand strength to depress, some have dose counter (Flutiform), may need re-priming after non-use.
Turbohaler – minimal grip needed (can get additional base gripper), lactose taste, dose counter.
Ellipta – minimal dexterity, no taste, dose counter, actuated every time opened (wasted), 6/52 shelf life, don't block vents.

	(Step 1 SABA only)	Step 2 Low ICS	Step 3 LABA/Low ICS	Step 3/4 LABA/Moderate ICS	Step 4 LABA/High ICS		Step 4 Alternative
MDI	**Ventolin 100 Evohaler Aerochamber plus 2 puffs prn (*)**	**Clenil Modulite 100 Volumatic 2 puffs bd (*)**	**Flutiform 50/5 Aerochamber plus 2 puffs bd (*)**	**Flutiform 125/5 Aerochamber plus 2 puffs bd (*)**	Flutiform 250/10 Aerochamber plus 2 puffs bd	OR	**LABA/Moderate ICS AND** either Montelukast 10mg nocte (LRTA) **OR** Spiriva Respimat 2 puffs om (LAMA)
Extrafine Particle MDI	**Ventolin 100 Evohaler Aerochamber plus 2 puffs prn (*)**	**Qvar 50 MDI Aerochamber plus 2 puffs bd**	**Fostair 100/6 MDI Aerochamber plus 1 puff bd**	**Fostair 100/6 MDI Aerochamber plus 2 puffs bd**	**Fostair 200/6 MDI Aerochamber plus 2 puffs bd**	OR	
Turbohaler DPI	**Bricanyl 1 puff prn (*)**	**Pulmicort 100 2 puffs bd (*)**	Symbicort 100/6 2 puffs bd (*)	Symbicort 200/6 2 puffs bd (*)	Symbicort 400/12 2 puffs bd (*)	OR	
Extrafine Particle DPI	Ventolin 200 Accuhaler 1 puff prn (*) (Not extrafine particle)	**Flixotide 50 Accuhaler 2 puffs bd (*) (Not extrafine particle)**	**Fostair 100/6 NEXThaler 1 puff bd**	**Fostair 100/6 NEXThaler 2 puffs bd**	**Fostair 200/6 NEXThaler 2 puffs bd**	OR	
Once Daily DPI	Ventolin 200 Accuhaler 1 puff prn (*)		**Relvar 92/22 Ellipta 1 puff om (*)**		**Relvar 184/22 Ellipta 1 puff om (*)**	OR	

Notes

Spacers

Spacers should be washed with hot soapy water monthly (not just with water) and NOT wiped dry. They should be replaced every year.

After use of ICS

Patients should be encouraged to wash their mouth out with water after using a steroid containing inhaler.

Flo-Tone

Consider using a Flo-Tone with a pMDI to ensure correct inspiratory flow rate.

* - Licenced age > 12

Other treatment considerations

- Refer all uncontrolled step 4 patients to secondary care
- Consider referral for weight loss and smoking cessation
- Consider (S)MART regimes – using Fostair 100/6 or Symbicort 100/6 or 200/6 – using one inhaler as a preventer and reliever at step 4
- Step down after 6 months of stability
- Only patients with very mild and intermittent symptoms should be step 1
- Treat any associated rhinitis or reflux (use Hull Cough Hypersensitivity Questionnaire > 13/70)
- Screen for dysfunctional breathing (use Nijmegen Questionnaire > 23/60)
- Treat vitamin D deficiency
- **All need a written personal action plan**
- **All inhalers should be prescribed by BRAND**

DPI V. MDI

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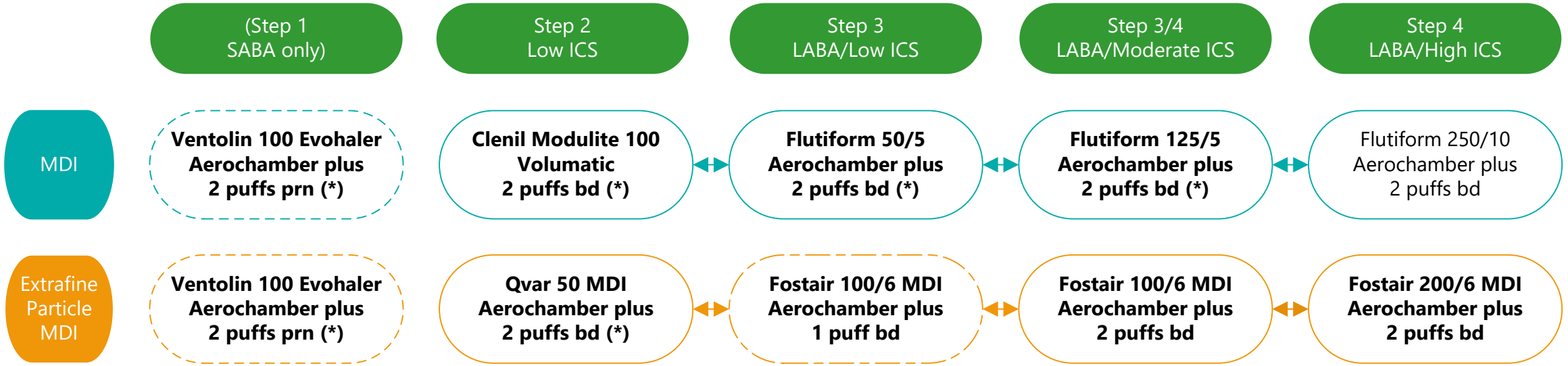
MDI


(Step 1
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Step 2
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Clenil Modulite 100
Volumatic
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Flutiform 50/5
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Aerochamber plus
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Flutiform 250/10
Aerochamber plus
2 puffs bd
Extrafine
Particle
MDI
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Aerochamber plus
2 puffs prn (*)
Qvar 50 MDI
Aerochamber plus
2 puffs bd (*)
Fostair 100/6 MDI
Aerochamber plus
1 puff bd
Fostair 100/6 MDI
Aerochamber plus
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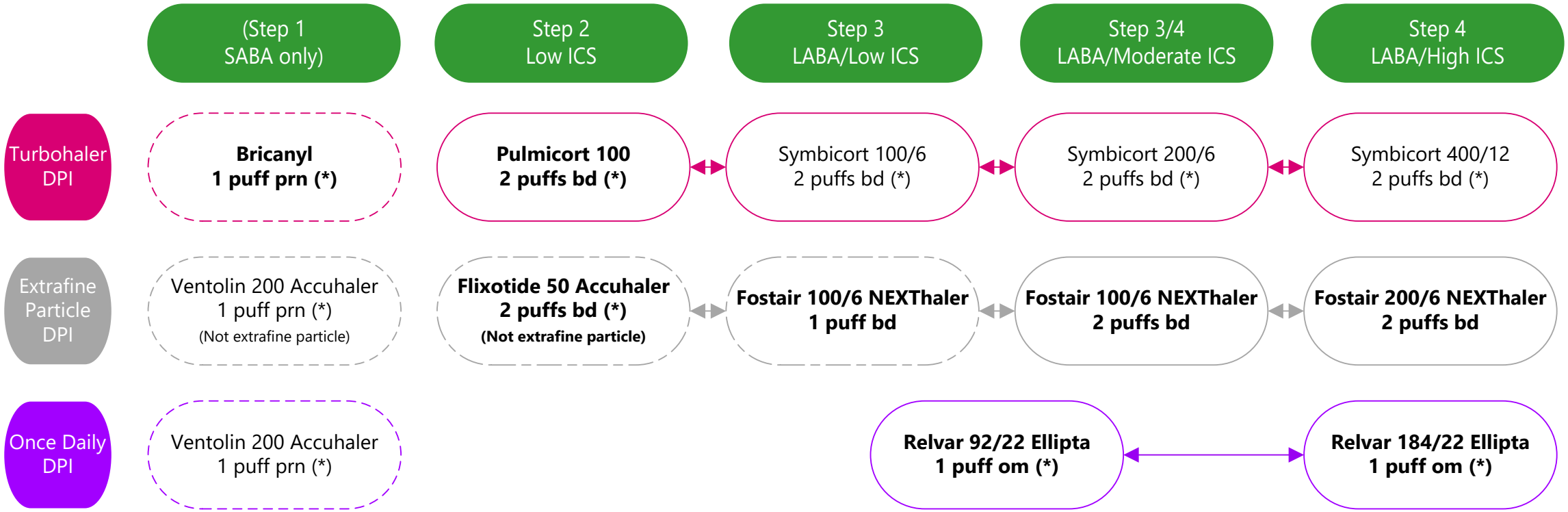
Fostair 200/6 MDI
Aerochamber plus
2 puffs bd

DPI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LABA/High ICS
Turbohaler DPI
Bricanyl
1 puff prn (*)
Pulmicort 100
2 puffs bd (*)
Symbicort 100/6
2 puffs bd (*)
Symbicort 200/6
2 puffs bd (*)
Symbicort 400/12
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2 puffs bd
Once Daily DPI
Ventolin 200 Accuhaler
1 puff prn (*)
Relvar 92/22 Ellipta
1 puff om (*)
Relvar 184/22 Ellipta
1 puff om (*)

OTHER TREATMENT OPTIONS

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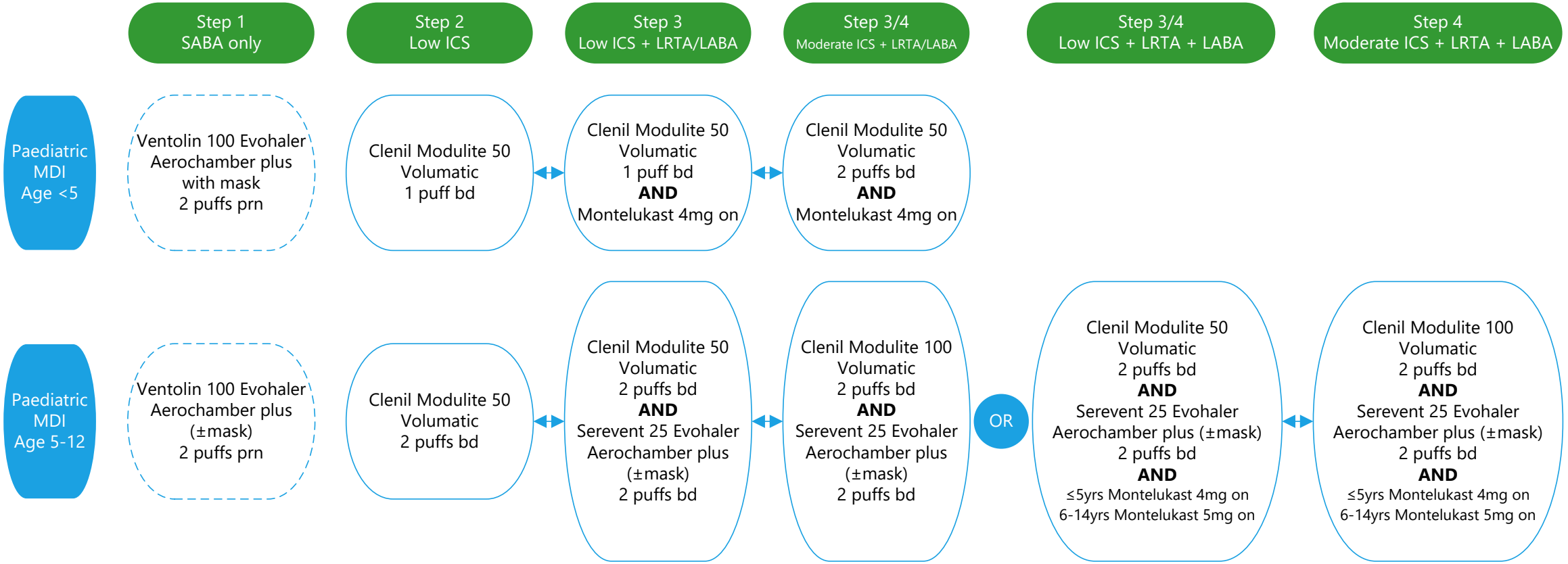
ICS IN CHILDREN

- Childhood Asthma Management Program (CAMP) (Curr Respir Care Rep 2012;1:243-50)
  - 1041 children aged 5-12 with mild-moderate asthma randomised to budesonide, nedocromil or placebo for 4-6 years and followed for a total of 9.1 years.
  - At this time the budesonide group had a height reduction of 0.9cm (p=0.01)
  - Small decrease (not leading to osteopenia or fractures) in boys
  - Budesonide was associated with 43% fewer hospitalisations, 45% fewer urgent care visits and 43% fewer prednisolone courses

DRAFT WHCCG ASTHMA GUIDELINES FOR CHILDREN



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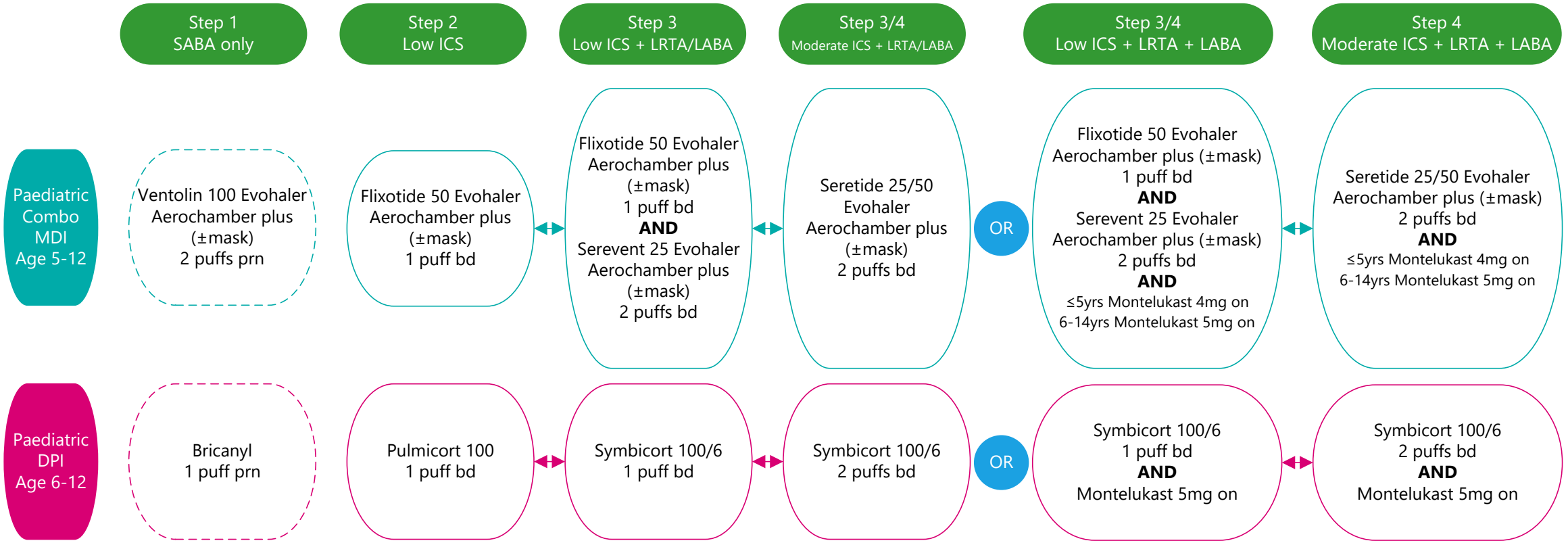

SUMMARY

- Uncontrolled asthma is associated with morbidity and mortality
- Diagnosis can be tricky, is an overall assessment of multiple evidence sources and should be revisited if not clear
- Clear evidence for stepping up and stepping down
- LABA/ICS is preferred at step 3 (adults)
- Options at step 4 include LAMA and extrafine particle ICS. LRTA is less preferable (adults)
- Written Personalised Action Plans should always be used and be simple
- Doubling ICS for exacerbations has little value
- Don’t be afraid of ICS in children