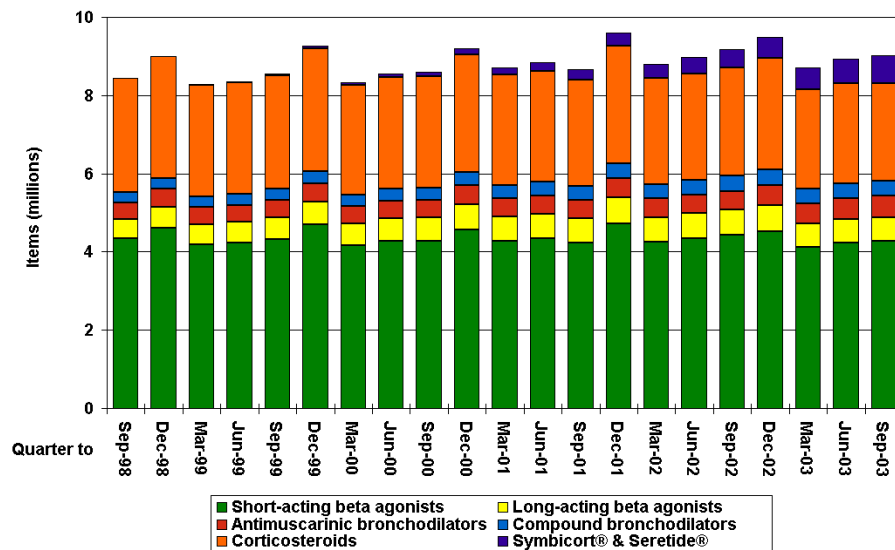


## PACT Centre Pages - *PRESCRIBING OF DRUGS FOR ASTHMA AND COPD*

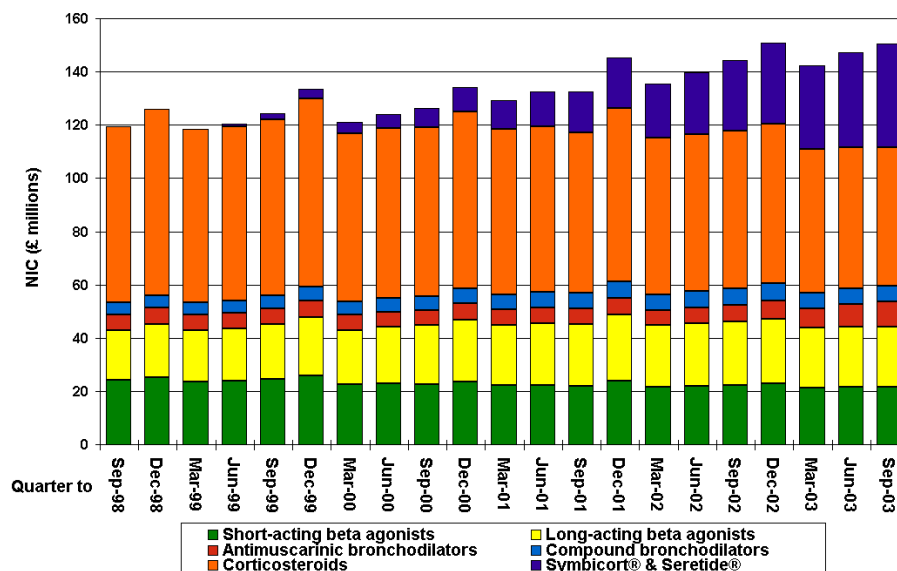
It is estimated that over 5.1 million people in the UK have asthma and 1.4 million of these are children. Although mortality from asthma has declined there are still around 1,500 deaths from asthma each year, most are in the elderly. Diagnosed asthma accounts for 1 in 20 of all GP consultations in children.<sup>1</sup> Chronic obstructive pulmonary disease (COPD) has been diagnosed in nearly 900,000 people in the UK. Half as many again are thought to be living with COPD without the disease being diagnosed.<sup>2</sup> COPD is a major cause of mortality and increasing morbidity with a sharp increase in the number of hospital admissions due to COPD from 1995 onwards.<sup>3</sup> The new General Medical Services contract contains quality indicators for asthma and COPD. For new COPD patients the initial diagnosis must be confirmed by spirometry including reversibility testing. In both domains, points are awarded for patients receiving the influenza vaccine.

Prescribing of drugs to treat asthma and COPD (chart 1) has remained steady with a seasonal variation; there is higher prescribing in the quarter to December each year. Spending on these drugs (chart 2) has increased by just over £30 million per quarter in the last 5 years; much of this increase is from prescribing of Seretide<sup>®</sup> and Symbicort<sup>®</sup>.

Trends in Prescribing of Drugs for Asthma and COPD in General Practice in England



Trends in Spending on Drugs for Asthma and COPD in General Practice in England



## Asthma

The British Thoracic Society and Scottish Intercollegiate Guidelines Network recently produced a joint guideline on management of asthma across patients of all ages.<sup>4</sup> A stepwise approach is used for managing chronic asthma with treatment initiated on the most appropriate step according to initial severity to achieve early symptom control. Stepping up or down is then used to maintain control. The guidelines now contain three stepped pathways for different age groups: adults, children aged 5-12 years and children under 5 years. All steroid doses in the pathway are based on beclometasone or equivalent via a metered dose inhaler, adjustment may be necessary for fluticasone and/or other devices. Before initiating a new therapy, compliance with existing therapies should be checked, e.g. inhaler technique and trigger factors should be investigated.<sup>4</sup>

Summary of stepwise management in adults:

- Step 1: Inhaled short-acting  $\beta_2$  agonist as required
  - Step 2: Step 1 plus inhaled steroid 200-800micrograms/day
  - Step 3: Step 2 plus inhaled long-acting  $\beta_2$  agonist (LABA)
- Assess control of asthma:
- good response to LABA – continue LABA
  - benefit from LABA but control still inadequate – continue LABA and increase inhaled steroid dose to 800micrograms/day
  - no response to LABA – stop LABA and increase inhaled steroid to 800micrograms/day
- If control still inadequate, institute trial of other therapies, e.g. leukotriene receptor antagonists or SR theophylline
- Step 4: Consider trials of: increasing inhaled steroid up to 2000micrograms/day, addition of fourth drug e.g. leukotriene receptor antagonist, sustained release (SR) theophylline or  $\beta_2$  agonist tablet.

- Step 5: Use daily steroid tablet in lowest dose providing adequate control. Maintain high dose inhaled steroid at 2000micrograms/day.

Addition of a regular inhaled steroid (step 2) is the recommended preventative therapy for adults and children to achieve overall treatment goals. Inhaled steroids have been shown to be more effective when given twice daily, the initial starting dose should be appropriate to disease severity then titrated to the lowest dose to maintain effective control (400micrograms reasonable for adults).<sup>4</sup> A recent randomised controlled trial investigated stepping down of inhaled steroids, patients received either no alteration to their usual dose (control group, at least 800micrograms/day beclometasone or equivalent) or a 50% reduction in dose.<sup>5</sup> The main limitation to this study was its small size (259 patients). The primary outcome measure compared exacerbation rates: no significant difference was found between the two groups. A step down approach might therefore reduce the risk of adverse effects without compromising asthma control. Adrenal crises have been observed more frequently following the use of fluticasone, possibly because higher than licensed doses of fluticasone are prescribed more widely in children than for other inhaled corticosteroids.<sup>6</sup> Step 3 involves add-on therapy for those whose asthma is poorly controlled. Adding a LABA has been found to be more effective at improving symptoms and lung function than adding either placebo, leukotriene antagonists or increasing the dose of inhaled steroids.<sup>7</sup> There is no difference in efficacy between giving inhaled steroids and LABAs in combination or in separate inhalers.<sup>4</sup> Step 4 offers the addition of a fourth drug, clinical trial evidence is limited in this situation therefore treatment choice depends mainly on patient response. Patients may need to be considered for referral before progressing to step 5.

Management of children aged 5-12 years follows the same steps but with a lower dose of inhaled steroid (suggested starting dose 200micrograms/day). At step 2 if an inhaled steroid is unsuitable another preventer drug could be used instead (e.g. leukotriene receptor antagonist or SR theophylline). Sodium cromoglicate is now considered to be ineffective in children, nedocromil sodium is still of benefit in 5-12 year olds.<sup>4</sup> In children under 5 years a low dose inhaled steroid (200-400micrograms/day) or leukotriene receptor antagonist should be initiated at step 2 if a steroid is unsuitable. Recommended add-on therapy is a trial of a leukotriene receptor antagonist in 2-5 year olds. If the child is under 2 years they should be referred to a respiratory paediatrician.

Pressurised metered dose inhalers (MDIs) are the most frequently prescribed device (see table 1) and the most cost effective. Current evidence suggests that alternative inhaler devices or nebulisers are no more effective than standard MDIs with or without a spacer device.<sup>8</sup> Teaching patients how to use an inhaler device is crucial to its effectiveness. A Cochrane review comparing nebulisers to MDIs plus spacer in exacerbations of asthma found that clinical outcomes for the MDIs were equivalent to nebulisers.<sup>9</sup> NICE guidance recommends that for children under 5 years with chronic asthma, treatment should be via a MDI and spacer system. Nebulised therapy may be considered if this combination is ineffective. For children aged 3 to 5 years a dry powder inhaler may also be considered.<sup>10</sup>

**Table 1: Changes in Prescribing of Short-acting  $\beta_2$  Agonists by Device in the Last 5 years**

	Items (millions)			Net Ingredient Cost (£ millions)		
	Quarter to		% change	Quarter to		% change
	Sep 98	Sep 03		Sep 98	Sep 03	
Plain MDI	2.98	3.09	4%	9.35	9.53	2%
Breath actuated MDI	0.34	0.48	42%	3.18	4.54	43%
Dry powder device	0.61	0.44	-27%	6.58	4.25	-35%

### **Chronic obstructive pulmonary disease**

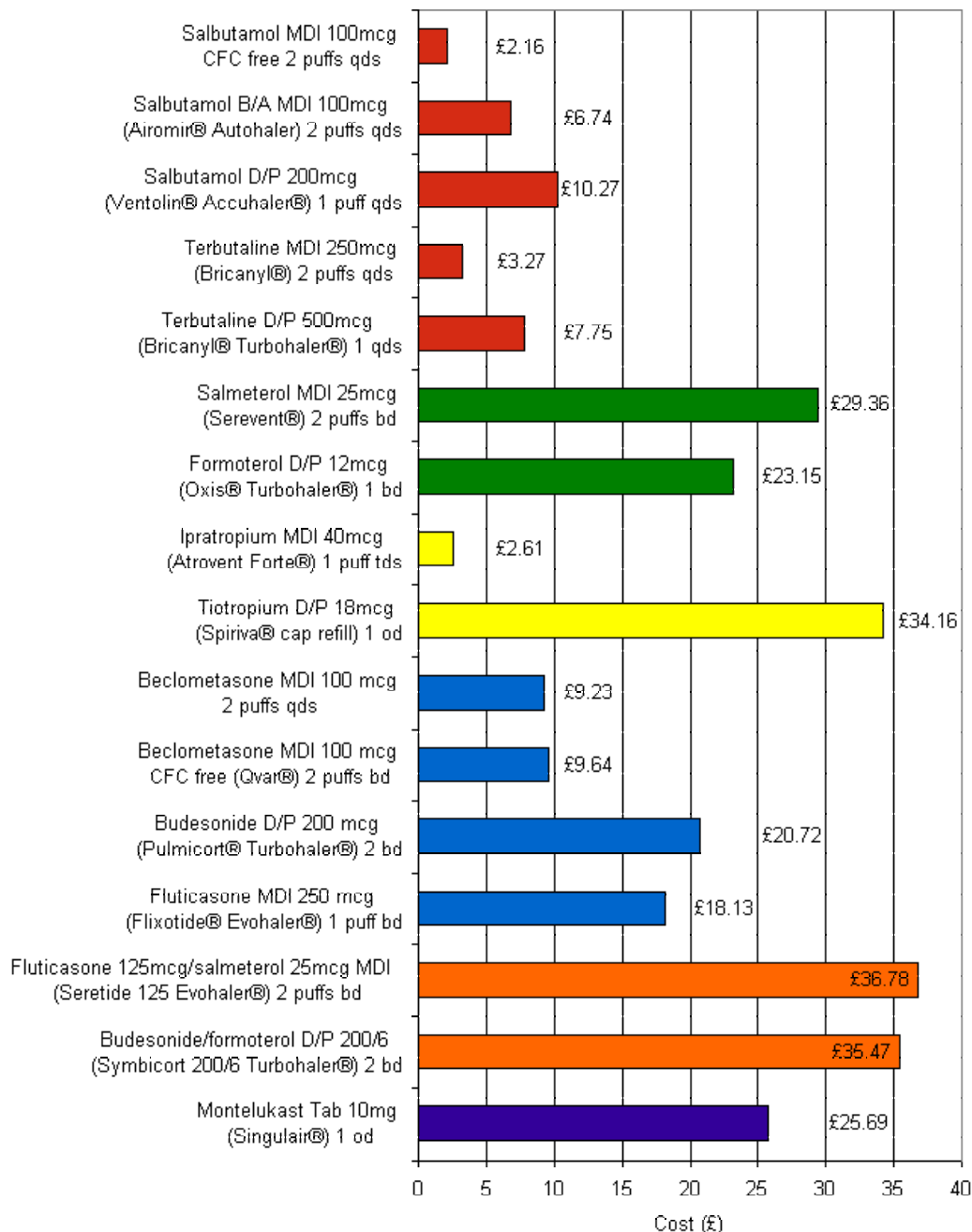
COPD is characterised by airflow obstruction which is usually progressive, not fully reversible and does not change markedly over several months. The disease is predominantly caused by smoking.<sup>2</sup> The BTS guidelines for COPD have a stepped management plan known as the COPD escalator. NICE draft guidelines are due for publication in February 2004.

Stopping smoking is one of the most important interventions that should be encouraged at all stages of patient management. It can prevent the accelerated decline seen in many COPD patients and reduces cough and sputum production, but it cannot restore lung function. NICE draft guidelines recommend considering diagnosis of COPD in patients over 35 years who have a high risk factor (generally smoking) and who present with exertional breathlessness, chronic cough, regular sputum production, frequent winter 'bronchitis' or wheeze.<sup>2</sup> Spirometry should be used to confirm airflow obstruction. Short acting  $\beta_2$  agonists should be the initial treatment for the relief of breathlessness and exercise limitation. LABAs are used if patients remain symptomatic and inhaled corticosteroids can be added if either the forced expiratory volume in one second (FEV<sub>1</sub>) is less than or equal to 50% predicted or where two or more exacerbations require treatment in a 12 month period. The balance of evidence currently suggests that inhaled steroids in COPD do not modify the rate of decline of lung function but do reduce the number of exacerbations and decline in health status in patients with more severe disease.<sup>3</sup> Inhaled anticholinergics have been found to significantly improve FEV<sub>1</sub>, exercise capacity and symptoms over placebo.<sup>11</sup> One trial found that tiotropium significantly improved FEV<sub>1</sub> and quality of life compared with a LABA.<sup>11</sup>

The need for oxygen therapy should be assessed in all patients with a severe airflow obstruction (FEV<sub>1</sub> less than 30% predicted) and considered in patients with FEV<sub>1</sub> 30-50% predicted.<sup>2</sup> Patients should breathe oxygen for 15 or more hours a day to gain the benefits. Limited evidence suggests improved survival over 2 years for domiciliary

oxygen versus no oxygen in people with COPD and hypoxaemia.<sup>3,11</sup> Prescribing of oxygen cylinders has increased by 36% in the last 5 years to 183,000 items costing £3.8 million for the quarter ending September 2003.

### Cost for 28 Days Treatment



Prices based on Drug Tariff January 2004 or Chemist & Druggist January 2004. Dose based on WHO DDDs where appropriate, otherwise BNF stated dose. The WHO DDD is a unit of measurement based on the assumed average maintenance dose in adults. It may not necessarily reflect the actual dose used.

## Prescribing data

Prescribing of short-acting  $\beta_2$  agonists has remained steady over the last 5 years (4.3 million items per quarter) whilst cost has decreased by 11%. Salbutamol use has risen slightly to 4.0 million items at a cost of £19.0 million, quarter to September 2003. Terbutaline items have decreased by 28% to 299,000 items costing £2.6 million per quarter. Prescriptions for LABAs have increased by 24% in the last 5 years to 609,000 items at a cost of £22.6 million (quarter to September 2003) and now cost more than the short-acting  $\beta_2$  agonists (£21.7 million). Salmeterol accounts for 542,000 items and eformoterol 66,000 items, quarter to September 2003.

The cost of antimuscarinic bronchodilators prescribed as single preparations has doubled in the last 5 years, mainly due to the introduction of tiotropium which accounts for 16% of prescribing (89,000 items) and 39% of cost (£3.6 million). Ipratropium accounts for 433,000 items at a cost of £5.4 million, quarter to September 2003. Prescribing of the combination product ipratropium with salbutamol has almost doubled over the last 5 years to 362,000 items per quarter, costing £5.8 million.

Inhaled corticosteroid prescription items have increased by 10% in the last 5 years to 3.2 million items. Beclometasone is still the most commonly prescribed with 1.9 million items, costing £29.7 million, quarter to September 2003. Fluticasone accounts for 452,000 items at a cost of £19.2 million. Compound corticosteroid preparations make up one fifth of all inhaled corticosteroid prescribing but 43% of cost. Over three-quarters of this prescribing is for fluticasone with salmeterol (557,000 items, £32.8 million, quarter to September 2003).

Prescribing of aminophylline has decreased to 129,000 items at a cost of £599,000 and theophylline has fallen to 146,000 items at a cost of £776,000, quarter to September 2003. Prescribing of leukotriene receptor antagonists has now reached 130,000 items (£2.9 million), quarter to September 2003. Cromoglicic acid, nedocromil and ketotifen only account for 23,000 items between them at a cost of £0.6 million.

## References

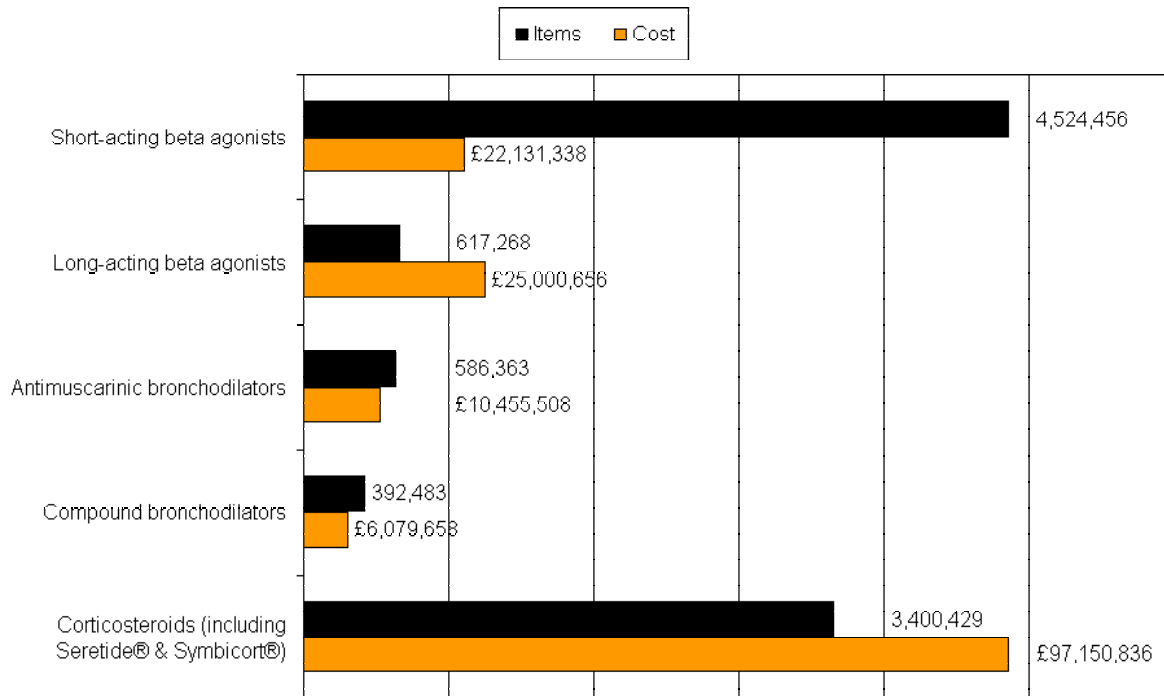
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## Summary

- Introduction of a long-acting  $\beta_2$  agonist is now preferred to increasing the dose of inhaled steroid in chronic asthma management
- Use the lowest dose of inhaled steroid that will maintain effective control.
- In children aged 5-12 years a leukotriene receptor antagonist or SR theophylline are suitable if a steroid cannot be used
- Nebulisers or alternative inhaler devices have not been found to be anymore effective than standard metered dose inhalers
- Smoking cessation is beneficial at any stage of COPD management
- Long-acting  $\beta_2$  agonists should be used in COPD patients who remain symptomatic on short-acting  $\beta_2$  agonists

## Prescribing and Spending on Drugs for Asthma and COPD in England for Quarter to December 03



	Quarter to December 03	
	National	
	ITEMS/1000 PUs	NIC/1000 PUs
Short-acting beta agonists	65.15	£318.69
Corticosteroids (excluding Seretide® & Symbicort®)	37.60	£773.98
Long-acting beta agonists	8.88	£360.01
Seretide® & Symbicort®	11.36	£624.99
Leukotriene receptor antagonists	1.96	£63.21