STATEMENT OF INTENT

Clinical guidelines are produced to help health professionals and consumers make decisions about health care in specific clinical circumstances. Research has shown that if properly developed, communicated and implemented, guidelines can improve care. While guidelines represent a statement of best practice based on the latest available evidence (at the time of publishing), they are not intended to replace the health professional’s judgment in each individual case.
## CONTENTS

1. *Purpose*  
   Page 3
2. *About the Guideline*  
   Page 5
3. *Introduction*  
   Page 13
4. *Summary*  
   Page 15
5. *Diagnosis of Asthma*  
   Page 21
6. *General Principles of Pharmaceutical Therapy in Asthma*  
   Page 29
   - Relievers  
     Page 29
   - Preventers  
     Page 29
   - Aims of Drug Therapy  
     Page 29
   - Treatment of Acute Severe Asthma  
     Page 30
   - Pharmaceutical Principles in Acute Asthma  
     Page 31
   - Pharmaceutical Principles in Chronic Asthma  
     Page 32
   - Management of Chronic Asthma  
     Page 42
7. *Management of Asthma in the Māori Community*  
   Page 45
8. *Non-Pharmaceutical and Complementary Therapies*  
   Page 47
9. *Secondary Prevention of Asthma in Adults*  
   Page 49
10. *Education, Self-Management and Routine Clinical Care*  
    Page 51
11. *Implementation Strategy*  
    Page 55
12. *Audit and Performance Indicators*  
    Page 57
13. *Appendices*  
    Page 59
    - Glossary  
      Page 89
    - Methodology Terms  
      Page 91
    - References  
      Page 97
The purpose of the guideline is to provide an evidence-based summary of the diagnostic management and treatment options available for asthma in the adult population of New Zealand.

This guideline seeks to assist adults with asthma and their health care advisors evaluate the latest evidence and make informed decisions to improve health outcomes.
ABOUT THE GUIDELINE

FOREWORD

The New Zealand Guidelines Group Incorporated (NZGG) is a not-for-profit organisation established to promote effective health and disability services. Guidelines make a contribution to this aim by sharing the latest international studies and interpreting these in a practical way for adoption in the New Zealand setting.

Asthma is a chronic condition that affects a significant proportion of New Zealanders, with the overall incidence rising [1]. It is a significant cost to the New Zealand health care system.

This guideline addresses the best practice for the treatment of asthma in the adult population—that is, people 16 years of age and over. This guideline does not address special subgroups that may require different treatment such as children, pregnant and/or lactating women or the elderly. Nor does it seek to thoroughly address the use of complementary treatments for asthma. The NZGG hopes to publish a series of supplements addressing these populations and areas in the future.

Fortunately, there is a large body of robust evidence that demonstrates that the symptoms and adverse consequences of asthma can be effectively mitigated by modern treatment strategies.

GUIDELINE DEVELOPMENT PROCESS

In 2000 the Asthma Working Group, a committee convened under the auspices of the New Zealand Guidelines Group to advise the Ministry of Health on issues and strategies relating to asthma, commissioned a project to develop an evidence-based best practice guideline on the diagnosis, treatment and management of asthma in adults. A multidisciplinary group of professionals and consumers was convened as the guideline development team. The New Zealand Health Technology Assessment group (NZHTA) was engaged to provide technical support in the search and critical appraisal of the literature.

As there are a number of published international guidelines that have systematically reviewed the evidence relating to asthma, the asthma guideline development team elected not to repeat a review of all the literature but to use existing guidelines as a base or “seed” resource.

A systematic search was therefore made for published guidelines on adult asthma. These were evaluated using the AGREE assessment tool. Those developed in a systematic way, so that their recommendations were reliably and explicitly evidence-based, were selected as “seed” guidelines.

These included the:

• Canadian Asthma Consensus Report 1999 [2]
• The Australian Asthma Management Handbook [3]

These selected guidelines have reviewed literature published up to 1999.

The asthma guideline development team then identified questions and strategies for a systematic search and inclusion criteria for studies relating to the following:
1. Diagnosis of asthma
2. Non-pharmaceutical strategies for secondary prevention
3. Education and patient self-management
4. Pharmaceutical therapies

Studies that expressed outcomes in terms of commonly assessed POEM (Patient Oriented Evidence that Matters) endpoints only were included.
(Refer to Appendix 7).

Only therapies available or licensed for use within New Zealand were included for review. NZGG now has a policy of evaluating all internationally available treatments and therapies when a new guideline is developed. However, this policy was approved at a stage when most of the research for the adult asthma guideline had already been conducted. After reviewing international practice to ensure no potentially important therapy would be excluded, it was decided, to proceed with the current NZ focused review, rather than delay the release of the guideline. An assessment of all therapies will be included in a review of the guidelines, in three years.

A systematic critical review of the selected literature published from 1 January 1997 to December 2000 was undertaken by the NZHTA in Christchurch (Refer to Appendix 7) and by the member(s) of the working group responsible for drafting the particular section of the guideline. Attempts were also made to identify and include unpublished work and conference abstracts. Where evidence was available from RCTs and systematic reviews, recommendations were based on these. Where there was a lack of evidence from high quality studies, recommendations were based on the best available evidence or expert opinion. This search was subsequently updated in March 2002 prior to completion of the guideline.

The NZHTA also performed a search (2002) for pertinent qualitative literature, which was critically reviewed by Dr Isobel Martin and her staff of the Dunedin School of Medicine (Refer Appendix 7).

EVIDENCE AND GUIDELINE RECOMMENDATION GRADING SYSTEM USED FOR THIS GUIDELINE

The asthma guideline development team agreed to rank the evidence according to the revised system of the Scottish Intercollegiate Guidelines Network (SIGN). The SIGN Grading System for Recommendations in Evidence-Based Clinical Guidelines is a revised version of the system developed by the US Agency for Health Care Policy and Research (AHCPR). More information on this grading system can be found at www.sign.ac.uk

### LEVELS OF EVIDENCE

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.</td>
</tr>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.</td>
</tr>
<tr>
<td>1-</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal.</td>
</tr>
<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.</td>
</tr>
<tr>
<td>2-</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytic studies, eg, case reports, case series.</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion.</td>
</tr>
</tbody>
</table>

Studies that were graded 1- or 2- were considered similar to level 3 or 4 evidence because of methodological flaws. Qualitative material was systematically appraised for quality, but was not ascribed a level of evidence.
GRADES OF RECOMMENDATION

A
At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; OR
A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.

B
A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; OR
Extrapolated evidence from studies rated as 1++ or 1+.

C
A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; OR
Extrapolated evidence from studies rated as 2++.

D
Evidence level 3 or 4; OR
Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINT

Recommended best practice based on the clinical experience of the guideline development group

In general the authors responsible for drafting each section of the guideline graded the evidence for each individual section. The whole group carefully reviewed the summary of conclusions and recommendations and any disagreements were resolved by consensus. The guideline was collated and edited by the project manager.

It is intended that this guideline should be reviewed in 2005. Interim modifications will be made to the on-line version of the guideline when needed. The process for review will be the standard NZGG process: a guideline review group will be convened to conduct a brief literature review to evaluate the validity of the content. Following the review, a recommendation will be made which will be either:

• to set a further review date, if the contents are found to be still current; or
• to update the guideline – that is, to modify some details (such as medication details) to bring the contents up to date with minor changes in practice; or
• to fully revise the guideline – if major changes in practice or guideline structure are identified that need to be incorporated or improved.

The process for updating or revision will be in accordance with NZGG policy and practice at that time, as detailed on the web site at www.nzgg.org.nz

The guideline development team has included the level of evidence alongside the references. This is formatted as [reference (level of evidence)].
GAPS BETWEEN CURRENT PRACTICE AND EVIDENCE

How big is the gap between current and optimum care?

<table>
<thead>
<tr>
<th>GAPS</th>
<th>Current Practice</th>
<th>Guideline-identified Best Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single PEFR recordings, which have little diagnostic value [5 (2+)]</td>
<td>Diagnosis requires careful history taking and can be confirmed by multiple PEFR testing and/or spirometry with reversibility testing</td>
<td></td>
</tr>
<tr>
<td>Data from PreMeC [6, 7 (1)] suggested that there is considerable variation throughout New Zealand in the prescribed doses of inhaled corticosteroids (ICS)</td>
<td>ICS have a relatively flat dose response curve and most adults with asthma may be managed on lower doses [8 (2)]</td>
<td></td>
</tr>
<tr>
<td>The current average daily dose of fluticasone in New Zealand is currently 70-80% of beclomethasone [6, 7 (1)], a disproportionate ratio not explained by the selective prescription of fluticasone to the individual with more severe asthma</td>
<td>Fluticasone propionate has twice the potency of beclomethasone [9 (1++)] and should be prescribed accordingly</td>
<td></td>
</tr>
<tr>
<td>Use of long-acting β₂-agonists (LABAs) only after extended trial of ICS at 750 µg/day BDP (See Pharmac access criteria, Appendix 3)</td>
<td>Recent evidence supports the value of LABAs introduced at lower doses of ICS for improved symptom control and reduction in exacerbation rates [10 (1+)]</td>
<td></td>
</tr>
<tr>
<td>Variable education materials provided to adults with asthma</td>
<td>Evidence shows that providing educational materials alone to adults with asthma is not effective, and supports a more structured programme of self-management [11 (1+)] including regular medical review</td>
<td></td>
</tr>
<tr>
<td>Advocating benefits of allergen avoidance that appeared promising on the basis of patho-physiological modelling</td>
<td>Most strategies for allergen avoidance have failed to show effectiveness in terms of patient related outcomes such as symptom control or exacerbations [12 (1++)], except in those patients known to be allergic to specific allergens after testing</td>
<td></td>
</tr>
<tr>
<td>Use of complementary and alternative therapies such as acupuncture; manual therapies, homeopathy, Alexander technique, or speleo-therapeutic interventions, and breathing exercises</td>
<td>There is insufficient evidence to support the use of such therapies [13-17 (1+)] in clinical practice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>There is limited evidence only for the effectiveness of certain types of breathing exercises [18] for asthma in clinical practice (1+)</td>
<td></td>
</tr>
</tbody>
</table>

Thus some aspects of current practice are not supported by our review of the evidence. Changes in prescribing patterns after the publication of this guideline can be measured and provide a partial basis for the evaluation of implementation of this guideline.

How much effort will it take to close the gap?

In order to change practitioner behaviour and increase consumer awareness, a multi-dimensional educational programme for health professionals to encourage appropriate, evidence-based treatment and management of asthma will be required, along with a campaign targeted at informing consumers.

Is there a reasonable likelihood that the recommended changes could be implemented?

The guideline development team believes that the recommendations in this guideline can make a significant improvement in the care and treatment of adults with asthma over a reasonably short timeframe, and this confidence is supported by the planned, evidence-based implementation programme.

1 See education resources in Appendix 5 for more details.
CONSULTATION

An early draft of this guideline was widely distributed to consumer, primary health care organisations, provider organisations, expert reviewers, asthma nurses, and other clinicians for comment. It has been extensively modified to address the feedback received. The previous draft of the guideline has been piloted amongst primary health care practitioners and modified as a result of their feedback.

The guideline was sent to the following organisations as part of the peer review process:

- Aotearoa (NZ) College of Nurses Inc.
- Asthma and Respiratory Foundation of New Zealand (Inc.)
- Asthma New Zealand - The Lung Association (Inc.)
- Pharmac
- Researched Medicines Industry Association of New Zealand Inc (RMI)
- Royal New Zealand College of General Practitioners
- Royal New Zealand College of Physicians
- The Thoracic Society of Australia and New Zealand (NZ Branch)
- Toi Te Ora Public Health
- Barbara Scott, Wellington Independent Practitioner’s Association
- Dr Christine Jenkins, Thoracic Physician, Institute of Respiratory Medicine, Sydney, Australia
- Karen Lombard, Manawatu Independent Practitioner’s Association.

Asthma societies:

- Ashburton Asthma Society
- Auckland Asthma Society
- Canterbury Asthma Society
- Gisborne & East Coast Asthma Society
- Hawkes Bay Asthma Society
- Manawatu Asthma Society
- Nelson Asthma Society
- North Otago Asthma Society
- Northland Asthma Society
- Otago Asthma Society
- Rotorua Asthma Society
- South Canterbury Asthma Society
- Southland Asthma Society
- Taranaki Asthma Society
- Tauranga Asthma Society
- Tu Kotahi Māori Asthma Society
- Waikato Asthma & Respiratory Society
- Waimate Asthma Support Group
- Wairarapa Asthma Society
- Wanganui Asthma Society
- Wellington Asthma Society
- West Coast Asthma Society & Buller Support Group
- Whakatane Asthma and CORD Support Group.

The guideline development team are appreciative of the time and effort from the respondents to our request for feedback.
ENDORSEMENTS

Endorsement of this guideline has been received from:

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Larry Skiba
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Rowena Cave  
Asthma Guideline Project Manager, New Zealand Guidelines Group Inc.

Funding  
This guideline was developed by the New Zealand Guidelines Group Inc., and funded by the Ministry of Health.

Declarations of competing interests  
Peter Black has received research funding, travel support or has acted as a consultant for the New Zealand or international offices of the following companies:
- GlaxoSmithKline NZ Ltd
- AstraZeneca NZ Ltd
- Aventis
- Pfizer.

Julian Crane has received research funding, travel support or has acted as a consultant for the New Zealand or international offices of the following companies:
- GlaxoSmithKline NZ Ltd
- Air Flow Products (Asthma Foundation)
- AAAAI.

Ian Town has received research funding, travel support or has acted as a consultant for the New Zealand or international offices of the following companies:
- GlaxoSmithKline NZ Ltd
- AstraZeneca NZ Ltd
- Boehringer Ingelheim (NZ) Ltd
- Merck Sharp & Dohme (NZ) Ltd.

Stephen Child has received funding from the following companies for the presentation of talks to General Practitioners:
- AstraZeneca NZ Ltd
- GlaxoSmithKline NZ Ltd
- Boehringer Ingelheim (NZ) Ltd.

Errol Raumati has received funding for travel and accommodation from the following company:
- GlaxoSmithKline NZ Ltd.

Peter Moodie has received honorariums for his membership of the Glaxo Foundation from:
- GlaxoSmithKline NZ Ltd.

Acknowledgements  
The guideline team would like to thank Ray Kirk, Peter Day and Robert Weir of the NZHTA for their dedication, work and sound advice proffered. Thanks are also due to Isobel Martin for her assistance in reviewing the qualitative material; to Adrian Slack and the Health Services Research Council for preparation of the balance sheet, and to Dr Christine Jenkins and the other reviewers of the first draft of this guideline. Thanks also to Catherine Marshall and Leonie Brunt for coordinating production of the guideline.
INTRODUCTION

Asthma is a chronic condition that may cause uncomfortable respiratory symptoms such as wheezing, shortness of breath, coughing or a ‘tight’ chest on a daily basis. During exacerbations of the illness, increasingly severe symptoms can develop, requiring more intensive therapy. In a proportion of such cases, hospital admission is required and in some a fatal outcome occurs despite best treatment. Asthma may occur in response to any of a number of triggers, such as allergens, infection, exercise and other non-specific irritants.

Over 15% of adult New Zealanders are affected by asthma and the overall incidence of asthma in New Zealand is rising [1]. Internationally, the rate of increase has been estimated to be as much as 50% every 10 to 15 years.

The incidence of asthma is slightly higher amongst Māori than non-Māori, and slightly lower in Pacific Island adults, but morbidity, including the rate of hospitalisation, is twice as high for Māori as non-Māori. Females report more severe and higher rates of symptoms, which decline with age in non-Māori whereas they are the same or higher in Māori, consistent with decreased access to health care and inadequate management for Māori with asthma [19]. Many lifestyle, socio-economic, educational, cultural, healthcare and genetic factors influence asthma in any ethnic group, and often untangling them is impossible [20].

Asthma is a significant cost to both the New Zealand health care system, the individual with asthma and their family. The cost to New Zealand has been variously estimated to be from at least $375 million [1] to as much as $800 million [21] each year. Around 77% of the cost is due to uncontrolled asthma, indicating that there are significant gains to be made both in terms of improving the well-being of adults with asthma and reducing the costs. It was estimated in 1996 that the cost to the individual with asthma was NZ$1039 per year, and asthma often affects more than one member of a family [22].

The causes of asthma remain uncertain. It is not yet understood why symptoms develop or disappear. The central feature of asthma is that the lining of the air passages in the lungs is persistently inflamed and sensitive - even if there are no symptoms at the time. The treatment of asthma concentrates on trying to suppress this inflammation by use of inhaled corticosteroids.

Asthma is a condition that usually responds to appropriate medication and in the majority, symptoms are easily controlled allowing the person with asthma to live a normal life. Newer classes of drugs such as the long-acting β2-agonists offer a significant new dimension to control of symptoms.

An important aspect of care is that the person with asthma can be in control of their own management – essential to achieving this goal is the use of a self-management plan developed by the primary health care team in partnership with the patient.

There are many support groups available for adults with asthma in New Zealand. These include Asthma Societies affiliated with the Asthma and Respiratory Foundation of New Zealand and Asthma New Zealand along with iwi and Pacific Groups, listed in Appendix 5.
SUMMARY

**Diagnosis**
- The key diagnostic indicators are a history of cough, wheeze and shortness of breath and evidence of reversible airflow obstruction, either spontaneously over time or in response to treatment.
- Asthma attacks with acute wheezing and reduced peak expiratory flow rate are highly specific for asthma.
- Single peak expiratory flow rate (PEFR) recordings have little diagnostic value, but PEFR variability of greater than 15% is highly specific for asthma.

**Pharmacotherapy**
- There are no clinically significant differences between devices for inhaled medication.
- Inhaled corticosteroids have a key role in reducing symptoms, improving lung function, slowing the rate of decline, and reducing hospital admissions and mortality.
- Most adults with asthma can be managed on low to moderate doses of inhaled corticosteroids. Inhaled corticosteroids should be started in low doses and increased where necessary to achieve control, then back-titrated to the lowest effective dose.
- Long-acting β₂-agonists in moderate to severe asthma improve day and night symptom control, improve lung function and reduce exacerbation rate.
- Theophylline is an effective third line therapy.
- Ipratropium, used in combination with salbutamol, improves clinical outcomes when used early in acute asthma.
- Spacers plus metered dose inhalers are an effective alternative to nebulised therapy in mild to moderate exacerbations.

**Non-pharmacological treatments**
- In adults with allergic asthma, in whom there is evidence of house dust mite sensitivity, barrier methods to control exposure to the allergen can be beneficial.
- Use of environmental approaches such as miticidal agents, air filtration devices, special vacuuming, conventional or steam cleaning of carpet and household furnishings, or domestic mechanical ventilation and heat recovery is only of benefit when there is an adult with asthma known to be atopic in the household.
- Immunotherapy reduces asthma symptoms and use of medication in adults with allergic asthma, but its efficacy relative to other therapies is unknown, and there are serious risks associated with its use.

**Education**
- Asthma initiatives by Māori providers for Māori must, to sustain the benefits, be ongoing programmes, rather than short-term interventions.
- A structured programme of education, self-management and self-monitoring strategies, written information and a written self-management plan improves outcomes for adults with asthma.
- Adequate education in and regular review of use of inhaler devices to check competency (to ensure effective delivery) should be provided for adults with asthma.
RECOMMENDATIONS

DIAGNOSIS OF ASTHMA

- In adults presenting for a first non-acute assessment, physical examination is usually non-contributory unless an audible wheeze is present or detected on auscultation of the chest.
- Doctors should investigate the possibility of an occupational cause in all adult onset asthma.
- Adults with asthma allergic rhinitis and/or eczema should have their atopic status assessed with skin prick testing to common allergens such as house dust mites, cats, grasses and moulds.

GENERAL PRINCIPLES OF PHARMACEUTICAL THERAPY IN ACUTE ASTHMA

- The addition of inhaled anticholinergic medication at the first presentation of acute asthma over a period of 90 minutes improves peak flow and symptoms and reduces hospital admissions.
- Systemic corticosteroids should be given early in acute severe asthma.
- β₂-agonists should be administered as required by inhalation and titrated using objective and clinical measures of airflow obstruction.
- Supplemental oxygen should be used in acute severe asthma to maintain a SaO₂ > 94%.

GENERAL PRINCIPLES OF PHARMACEUTICAL THERAPY IN CHRONIC ASTHMA

- Short-acting β₂-agonists should be used on an as required basis to relieve symptoms. They should not be used in a regular and fixed regimen eg, QID, as a maintenance treatment agent.
- Anticholinergic agents are not recommended first line but can be used in those unable to tolerate β₂-agonists or in combination with β₂-agonists.
- Use a delivery device that the patient prefers and can use effectively.
- The use of 2 or more canisters of β₂-agonists/ month or > 12 puffs a day is a marker of poor control for asthma.

KEY

- A Well designed meta-analysis (MA) of RCT, or a body or evidence which are consistently applicable
- B Very well designed observational studies or extrapolated evidence from RCTs or MAs
- C Lower quality observational studies or extrapolated evidence from B
- D Non analytical studies or expert opinion
- ✔️ Good Practice Point
### INHALED CORTICOSTEROIDS (ICS)

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>Treatment with inhaled corticosteroids is recommended in those who have daily symptoms of asthma or patients requiring SABAs daily.</th>
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<tbody>
<tr>
<td>B</td>
<td>Most adults with asthma should be initiated on treatment with low dose inhaled corticosteroids (beclomethasone dipropionate equivalent 400 µg/ day).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Fluticasone propionate is at least twice as potent as beclomethasone dipropionate.</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Once-daily treatment with budesonide is as effective as twice-daily in mild asthma, once control has been achieved.</td>
</tr>
<tr>
<td>B</td>
<td>ICS have a relatively flat dose response curve. Little additional benefit is gained from doses above 500 µg/ day of fluticasone propionate or 800 µg/ day of beclomethasone dipropionate/budesonide.</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>There is evidence of an increased risk of cataracts, reduced bone mineral density, glaucoma and bruising of the skin with long-term treatment with high dose ICS (eg, more than 800 µg/ day beclomethasone dipropionate).</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Early treatment with ICS in people with persistent symptoms and impaired lung function leads to better lung function in the medium term, and may help prevent the development of irreversible airflow limitation.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓</td>
<td>High doses of ICS should be avoided where possible for adults with asthma who have pre-existing conditions or vulnerability to conditions such as osteoporosis or cataracts.</td>
</tr>
<tr>
<td></td>
<td>✓</td>
<td>The guideline team recommends that LABAs should always be considered in individuals who continue to experience symptoms despite taking moderate (800 µg BDP/day) doses of ICS as this is at the top end of the dose response curve of ICS and higher doses are associated with increased risk of adverse effects (opinion).</td>
</tr>
</tbody>
</table>

### LONG-ACTING B₂-AGONISTS (LABAs)

|   | A | In people who continue to experience symptoms despite taking inhaled corticosteroids (greater than 400 µg BDP/BUD), the addition of long-acting B₂-agonists is more effective than doubling the dose of ICS in improving symptoms, reducing exacerbations and reducing adverse effects. |
|   | A | In people taking inhaled corticosteroids, long-acting B₂-agonists are more effective in controlling symptoms than regular use of regular short-acting B₂-agonists. |
|   | A | Long-acting B₂-agonists are more effective than theophylline in control of nocturnal asthma including night waking and need for rescue medication, symptom scores, symptom free days and have fewer adverse effects. |
| B | Long-acting B₂-agonists should not be used for the treatment of acute (or chronic) symptoms of asthma in the absence of inhaled anti-inflammatory therapy. |
| C | There is insufficient evidence to establish whether oral long-acting B2-agonists confer the same benefits in controlling exacerbations as inhaled long-acting B2-agonists. |
### LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRAs)

| A | Inhaled corticosteroids (in the dose equivalent of 250-400 µg/day beclomethasone dipropionate) are more effective than LTRAs in reducing symptoms including night waking, and the need for rescue β2-agonists. |
| A | Inhaled corticosteroids produce better lung function and quality of life and reduced symptoms and reduced need for rescue β2-agonists than LTRAs. |
| A | LTRAs are associated with increased adverse withdrawal effects compared with ICS. |
| A | Adding LTRAs to inhaled corticosteroids has shown small additional improvement in symptom control but not to the extent of that of adding LABAs. |
| ✓ | LTRAs may have a preventative role in aspirin and exercise induced asthma and in those who cannot take inhaled therapy. |

### CROMONES

| A | Sodium cromoglycate can be used as alternative to or in addition to short-acting β2-agonists for the prevention of exercise induced asthma. |
| A | Sodium cromoglycate requires more frequent administration than inhaled corticosteroids and the onset of benefit may be delayed. |
| A | There is no additional benefit in adding sodium cromoglycate to an established regimen of inhaled or systemic corticosteroid. |

### THEOPHYLLINE

| A | Theophylline should not be used as first line therapy. |
| A | Theophylline is associated with more frequent adverse effects and is less effective than salmeterol in improving lung function, relieving both night and day symptoms and reducing the need for rescue therapy. |
| A | Theophylline has a narrow therapeutic index and variable metabolism. |
| B | Adding theophylline to low dose ICS (400 µg beclomethasone dipropionate/day) may be an effective alternative to doubling the dose of ICS. |
| ✓ | Serum monitoring of theophylline is recommended. A clinical effect has been demonstrated at serum levels of 29 – 55 µmol/L. Where necessary the dose can be titrated up to a serum level of 82 µmol/L. |
DEVICES

**A** Inhaled drug delivery is superior to oral (or parenteral) delivery for short-acting β₂-agonists, anticholinergics, long-acting β₂-agonists and inhaled corticosteroids.

**A** There is no significant difference between delivery devices when used correctly.

**A** MDIs plus spacers are at least as effective as wet nebulisers in mild to moderate acute asthmatic episodes.

**A** Adults with asthma should receive adequate training in their inhaler technique to ensure competence.

**B** People’s technique in using their devices should be reassessed and reinforced frequently at appropriate opportunities.

✓ Choice of device should be made on the basis of ease of use, patient preference and overall cost.

✓ There is no evidence that any particular device reduces the risk of systemic adverse effects.

✓ Dry powder devices and MDI plus spacers may reduce oropharyngeal adverse effects.

MANAGEMENT OF ASTHMA IN THE MĀORI COMMUNITY

**D** Management of Māori asthma by Māori providers must, to sustain the benefits, be an ongoing programme, rather than a short-term intervention.

✓ Health professionals providing care for Māori adults with asthma should be sensitive to the particular needs of Māori, and encourage the use of a support person or advocate.

NON-PHARMACEUTICAL AND COMPLEMENTARY THERAPIES

**A** Immunotherapy reduces asthma symptoms and use of medication but its long-term effects and efficacy relative to other therapies is unknown and there are serious risks associated with its use.

**A** Various breathing exercises have shown no overall beneficial outcomes in the clinical treatment of asthma.

**B** Buteyko Breathing Techniques may be helpful in reducing reliever use and improving quality of life, but this will involve a considerable cost to the patient. There is no benefit to other aspects of management of asthma.

✓ Health professionals should be open to the possibility of the use of complementary therapies by people they are caring for. It could be suggested that use of such therapies be considered a trial to achieve better control, and methods for self assessment and monitoring could be discussed.

✓ Careful monitoring after immunotherapy is essential due to the risk of anaphylaxis. Close supervision is required for 1 – 2 hours.
## Secondary Prevention of Asthma in Adults

**B**
In adults with house dust mite allergic asthma, dust mite-impermeable covers applied to the mattress, duvet, and pillows reduces exposure to the allergen and decreases symptoms.

- Adults with house dust mite allergic asthma should consider minimising dust exposure by:
  - regular vacuuming with a cleaner which has a HEPA filter,
  - removing soft furnishings and carpet from bedrooms, in addition to using the barrier methods.

## Education, Self-Management and Routine Clinical Care

**A**
Primary health care teams should use a checklist of patient information and instruction, as part of their practice structure for adults with asthma.

**A**
Primary health care teams should make arrangements to review all adults with asthma on their register at least once a year.

**A**
All adults with asthma should be offered a customised self-management plan.

**A**
A structured educational programme should be provided for adults with asthma.

**C**
The use of peak expiratory flow monitoring in self-management plans may be beneficial.

**C**
Adults with asthma in primary health care should be reviewed regularly by a nurse with training in management of people with more severe asthma.

**D**
Practices should frequently conduct audit or quality improvement activities linking the management of adults with asthma to guidelines for best practice.

- Health professionals providing care for adults with asthma should be aware of the needs of adults with asthma from socially disadvantaged populations.
- Where there is a failure to control asthma symptoms, practitioners should consider the possibility of non-adherence to treatment.
- A request for a repeat inhaler, and/or a visit to the pharmacist should be used as an opportunity for a brief review of pattern of medication use and inhaler technique.

## Audit and Performance Indicators

- Comprehensive details about each adult with asthma should be recorded as part of routine clinical practice.
- Audit of asthma performance indicators is necessary to monitor quality of adult with asthma’s care, and to ensure best practice services are provided. Audit should take place every twelve months.

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5 See Appendix 4 for a suggested checklist for consultations.
DIAGNOSIS OF ASTHMA

Asthma is a very common condition in New Zealand with a high level of awareness in the community. Asthma is the most common cause of chronic respiratory symptoms in young adults. The key diagnostic indicators are a history of cough, wheeze and shortness of breath and evidence of reversible airflow obstruction, either spontaneously over time or in response to treatment [23, 53 (4)].

**Indicative symptoms**
- 25-30% of adults with a cough lasting more than 3 – 4 weeks, at night time or with exercise, will have asthma [54 (2+)]
- In non smoking adults, wheeze as a diagnostic factor for asthma has a sensitivity of 69% and specificity of 91% [23 (2)]
- Shortness of breath and chest tightness as isolated symptoms are not sensitive indicators of asthma, except in the presence of wheeze [23 (2)].

**Family and personal history**
- Adults with a history of wheezing as a child, or a background of atopy, who later present with respiratory symptoms, should be investigated for asthma in the first instance [28 (4)]
- Factors which suggest a diagnosis of asthma include a family history of asthma, hay fever, eczema or specific allergy to house dust mite, cats, pollens, food or medication [28 (4)].

**Exacerbations**
- Exacerbations of symptoms may occur in response to infection, exercise, allergen exposure, occupational exposure, medication (eg, NSAID)\(^2\), smoking, stress, and spontaneously (for no apparent reason).
- Asthma attacks with acute wheezing and reduced peak expiratory flow rate are highly specific for asthma [55 (2+)].

**GOOD PRACTICE POINT**

In adults presenting for a first non-acute assessment, physical examination is usually non-contributory unless an audible wheeze is present or detected on auscultation of the chest.

**Peak Expiratory Flow Rate (PEFR)**
- Single PEFR recordings have little diagnostic value for asthma [5 (3)]
- Day to day PEFR variability of greater than 15% is highly specific for asthma [24-31 (2-)].

**Response to therapy**
- The diagnosis should be made positively, using bronchodilator response testing (see below); or through demonstrating a greater than 15% improvement with anti-inflammatory treatment (2 weeks oral corticosteroids [40 mg prednisone/ day] or 4 weeks inhaled corticosteroids [400 µg beclomethasone or equivalent twice daily]) [56 (3)].

\(^{2}\) For details of medications known to produce asthma symptoms, see Appendix 1.
**Diagnostic tests**

- The most sensitive test for airways obstruction is spirometry. A low (< 70%) FEV₁/FVC ratio is diagnostic of obstruction. If possible this should be used to confirm the diagnosis of asthma [57, 58 (3)]. Spirometry in general practice must be subject to appropriate quality assurance procedures [58 (3)].
- Standardisation of peak flow should be ensured (eg, using the same peak flow meter both before and after therapy).
- Specialist assessment for occupational asthma is recommended in any adults whose symptoms appear to be aggravated at work and/or improve at weekends or holidays [57 (3)].
- Measuring of bronchial hyper-responsiveness (BHR) with a methacholine, histamine or saline challenge test or exercise provocation should be considered when the diagnosis is unclear [57 (3)], or for excluding asthma in intending SCUBA divers with a previous history of asthma.

**GOOD PRACTICE POINTS**

- **Doctors should investigate the possibility of an occupational cause in all adult onset asthma.**
- **Adults with asthma allergic rhinitis and/or eczema should have their atopic status assessed with skin prick testing to common allergens such as house dust mites, cats, grasses and moulds.**

**Exercise induced asthma**

Exercise induced asthma (EIA) may be the only symptom of asthma in some people, but may also be an indication of under-treated asthma. The diagnosis of EIA can be confirmed when the patient has a fall in PEFR of more than 15% after exercise by a formal exercise challenge test, but is not excluded by a negative test. A formal hyperventilation challenge is more sensitive and specific for EIA. See Appendix 2 for EIA details and legal controls on medications for sports competitors.

**Differential diagnoses**

There are many conditions that can cause respiratory symptoms similar to those of asthma. These include (in approximate order of frequency of occurrence, although the age of the person being assessed and the clinical context will impact on this order):

1. Upper Respiratory Tract (URT) disease (eg, sinusitis) causing post nasal drip and coughing
2. Post infective bronchial hyperresponsiveness, including whooping cough *(can only be definitively diagnosed if tested for with a bronchial challenge)*
3. Chronic Obstructive Pulmonary Disease (COPD) including age of onset, gradual progression, past history of cigarette smoking. See Table 1
4. Left ventricular failure
5. Central airways obstruction/foreign body
6. Vocal cord dysfunction
7. Hyperventilation
8. Bronchiectasis

In smokers, it is important to distinguish COPD from asthma in order to avoid inappropriate use of inhaled corticosteroids, which has been shown not to alter the natural history [59(1++)].
Table 1: Differences between asthma and chronic obstructive pulmonary disease

<table>
<thead>
<tr>
<th>Feature</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Often younger (childhood)</td>
<td>Usually older</td>
</tr>
<tr>
<td>Rapid onset</td>
<td>Often</td>
<td>Rare</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Sometimes</td>
<td>Almost Always</td>
</tr>
<tr>
<td>Allergic background</td>
<td>Often</td>
<td>Seldom</td>
</tr>
<tr>
<td>Cough and sputum</td>
<td>Sometimes</td>
<td>Often</td>
</tr>
<tr>
<td>Wheeze</td>
<td>Often</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Diurnal peak flow variability</td>
<td>Usual</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Bronchial hyperresponsiveness*</td>
<td>Usual</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Reversible airflow obstruction†</td>
<td>Usual</td>
<td>Sometimes</td>
</tr>
</tbody>
</table>

(Adapted from *Clinical Management of Asthma: Diagnosis of Adults, in Asthma and Rhinitis* [60].)

* Defined as a PC20 ≤ 8 mg/ml methacholine or histamine.
† Defined as a 15% or greater improvement in FEV₁ 15 minutes after 400 µg inhaled salbutamol.)
DIAGNOSIS ALGORITHM

Asthma Symptoms

Symptom and peak flow diary for 14 days OR spirometry with bronchodilator

Spirometry shows reversibility

PEFR and/or spirometry shows airflow obstruction?

Diary shows symptoms and PEFR variability

YES

NO

YES

NO

YES

Other diagnosis

Review by respiratory physician

COPD

Do not use inhaled corticosteroids routinely

YES

NO

YES

NO

NO

NO

NO

Methacholine, saline OR histamine OR exercise challenge

Smoker?

YES

NO

+ve

-ve

15%/200mls or greater improvement in FEV₁ or PEFR?

Oral prednisone x 2 weeks OR Inhaled corticosteroid x 4 weeks

ASTHMA CONFIRMED

Start appropriate treatment

ABBREVIATIONS

COPD Chronic obstructive pulmonary disease

PEFR Peak expiratory flow rate
**Severity of asthma**

Asthma severity is judged by the attending doctor on the basis of symptoms, pulmonary function and impact on activity. Over time, the number of exacerbations and the response to treatment can also inform the assessment of severity.

The successful clinical management of adult asthma is subject to numerous factors. One factor is the accurate assessment of the asthma’s severity by the individual with asthma and physician. It has been found that only 54% of moderate to severe adults with asthma accurately rate their severity, while ~20% underestimate and ~27% overestimate.

**Table 2: Severity criteria in asthma – as applied before therapy is initiated**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Clinical features</th>
<th>Lung function</th>
<th>Challenge test</th>
</tr>
</thead>
</table>
| Mild     | • Intermittent, brief symptoms less than 1 – 2 times/week  
• Minimal nocturnal symptoms  
• Few exacerbations and asymptomatic in between  
• No emergency medical requirements | • PEFR > 80% predicted  
• PEFR variability < 20%  
• Normal spirometry | • PC_{10} methacholine > 2 mg/ml < 8 mg/ml  
• PC_{15} hypertonic saline > 6ml [62]  
• Exercise: > 15% fall in FEV1 after exercise. |
| Moderate | • Daily symptoms  
• Nocturnal symptoms > 2 times/month  
• Occasional acute episodes | • PEFR 60 – 80% predicted  
• PEFR variability 20-30%  
• Spirometry abnormal with obstructive pattern but > 60% predicted | • PC_{20} methacholine 0.25-2 mg/ml  
• PC_{15} hypertonic saline = 2.1ml – 6ml |
| Severe   | • Daily persistent symptoms  
• Frequent nocturnal symptoms  
• Physical activities limited  
• School or work absenteeism  
• Acute severe episode requiring emergency treatment or admission to hospital | • PEFR < 60% predicted  
• PEFR variability > 30%  
• FEV1 < 60% predicted  
• Poor reversibility to inhaled bronchodilator | • PC_{20} methacholine < 0.25 mg/ml  
• PC_{15} hypertonic saline < 2ml |

(Adapted from *Annals of Allergy, Asthma and Immunology* and the US International consensus report on the Diagnosis and Treatment of Asthma [61, 63].)

Notes: Methacholine/histamine challenges have poor sensitivity and specificity. PEFR variability has poor sensitivity.

All challenges to be performed in an accredited pulmonary function laboratory. Challenge testing is not considered routine practice in the assessment of asthma severity, but may be helpful in providing disability assessment and in selected cases for clinical research purposes. An exercise challenge is considered to be positive if there is a ≥ 15% drop from the baseline measure. Larger drops would be expected in more severe asthma [64].
Figure 1: Peak expiratory flow rate nomogram in males

(Reference, Leinter et al, 1963 Amer. Rev. Dis. 88 644-651.)

Figure 2: Peak expiratory flow rate nomogram in females

(Reference, Pelzer & Thompson, 1964 Med J 2 123)
Figure 3. Example of Spirometry in Asthma

Spirometry from a computerised spirometer (expiratory flow volume/time) demonstrating airflow obstruction (lower/yellow trace) as seen in asthma and a significant reversible component demonstrated after the administration of nebulised bronchodilator (middle/dark blue trace). Both compared to predicted values (top/light blue trace). (Courtesy Ms M Swanney, Christchurch Hospital.)
GENERAL PRINCIPLES OF PHARMACEUTICAL THERAPY IN ASTHMA

The effectiveness of drug therapy in asthma has been established for many years. It remains the mainstay of asthma management, and almost all adults with asthma will benefit from some form of drug therapy.

The pharmaceutical agents used for asthma can be classified into two main groups, relievers and preventers. One important issue in asthma management is the over-use of relievers and the under-use of long-term preventer medication [65].

RELIEVERS

Relievers are drugs that have a direct bronchodilator effect and relieve the symptoms of asthma. The short-acting β2-agonists such as salbutamol and terbutaline treat the immediate symptoms of asthma, and are taken on an as required or demand basis.

Ipratropium is an anticholinergic bronchodilator. It has a slower onset of action and has a useful role in treatment of acute asthma when combined with a β2-agonist.

The long-acting β2-agonists cause prolonged bronchodilation (for up to 12 hours). These are usually taken twice daily on a regular basis. When used in combination with inhaled corticosteroids (ICS) they have been shown to improve control of symptoms and allow a reduction of the dose of ICS.

Theophyllines are orally active compounds that also control symptoms and may have some anti-inflammatory properties.

PREVENTERS

Preventer agents possess anti-inflammatory properties and are generally taken regularly to reduce symptoms and exacerbations. These include the ICS such as beclomethasone dipropionate, budesonide and fluticasone propionate, and the cromones: cromoglycate and nedocromil.

There are also the leukotriene receptor antagonists, which are oral medications with anti-inflammatory properties.

Oral or parenteral corticosteroid agents are potent anti-inflammatory agents reserved for use in acute or very severe chronic asthma.

AIMS OF DRUG THERAPY

The aim of drug therapy is to gain and maintain control of asthma with the lowest effective doses of medication.

The goal in all asthma treatment is to minimise symptoms with the fewest possible adverse effects. But, as the severity of asthma increases, adults with asthma and their health professionals may need to consider carefully the trade-off between symptom control, patient safety (especially the prevention of life threatening asthma) and the adverse effects and risks of medication.

Except for those with mild asthma, most individuals will require ongoing and regular daily management with preventer therapy. Strategies that support individuals to maintain a regular treatment regimen will be associated with improved outcomes [11 (1+)].
Adults with asthma should be involved in selecting a delivery device that they can use effectively and that is suitable for them [2, 67 (1++)]. The person’s technique using reliever devices and other barriers to following the treatment regimen should be reviewed regularly [2 (2-)].

TREATMENT OF ACUTE SEVERE ASTHMA

ACUTE SEVERE ASTHMA TREATMENT ALGORITHM

**Acute Mild to Moderate Asthma**
- PEFR > 50%
- Speech normal
- Respiration rate < 25 breaths/minute
- Pulse < 110 beats/minute

**Acute Severe Asthma**
- PEFR < 50% predicted or best
- Cannot complete sentences
- Respiratory rate > 25 breaths/minute
- Pulse > 110 beats/minute

**Immediate Action**
- Give Oxygen 6 – 8 litres/minute
- Document severity of airflow obstruction (peak flow or FEV₁)
- No sedatives of any kind

**Life-Threatening Features**
- PEFR < 33% predicted or best
- SaO₂ < 92%
- Silent chest, cyanosis or feeble respiratory effort
- Bradycardia or hypotension
- Exhaustion confusion or coma

**TRANSFER TO NEAREST HOSPITAL**

**Transfer to hospital**
- Continue high flow oxygen
- Repeat salbutamol 5 mg plus ipratropium 0.5 mg via wet nebuliser
- Continue IV hydrocortisone 100 – 200 mg 6 hourly

**Improving?**

- Salbutamol 800 µg plus ipratropium 80 µg via MDI + spacer
  Repeat at 10 – 15 minute intervals as needed
- Oral prednisone 30 – 60 mg

- Salbutamol 5 mg plus ipratropium 0.5 mg via wet nebuliser
  Repeat at 10 – 15 minute intervals
- Oral prednisone 30 – 60 mg or IV hydrocortisone 100 – 200 mg

**YES**

- Continue oxygen until lung function improved and SaO₂ > 96% on air
- Continue inhaled β₂-agonist 1 – 4 hourly or more frequently as required
- Continue prednisone 30 – 60 mg daily

**NO**

- Continue oxygen until lung function improved and SaO₂ > 96% on air
- Continue inhaled β₂-agonist 1 – 4 hourly or more frequently as required
- Continue prednisone 30 – 60 mg daily

**ABBREVIATIONS**
- FEV₁: Forced expiratory volume
- MDI: Metered dose inhaler
- PEFR: Peak expiratory flow rate
Criteria for admission to hospital

Individuals with any of these features should be immediately admitted to hospital [68 (4)]:

- Patients with any feature of a life-threatening or near-fatal attack
- Patients with any feature of a severe attack persisting after initial treatment.

Patients whose peak flow is greater than 75% best or predicted 2 hours after initial treatment, may be discharged unless they have one of the following risk factors for poorer outcomes, when admission may be appropriate:

- Living alone/socially isolated
- Psychological problems
- Physical handicap or learning difficulties
- Previous near fatal or brittle asthma
- Exacerbation despite adequate dose oral steroids prior to presentation
- Presentation at night
- Pregnancy.

PHARMACEUTICAL PRINCIPLES IN ACUTE ASTHMA

Oxygen

Supplemental oxygen should be used in treating people with acute severe asthma to maintain a SaO₂ > 94% [2 (4)].

Short-acting β₂-agonists (SABAs)

Short-acting β₂-agonists are a mainstay of therapy and should be administered as required by inhalation (MDI + spacer in mild asthma, or by wet nebulisation in more severe), and titrated using objective and clinical measures of airflow obstruction [2 (2)].

Anticholinergics

The addition of inhaled anticholinergic medication (ipratroprium 0.5 mg via nebuliser or 80 µg via MDI) at the first presentation of acute asthma improves peak flow rate and symptoms over 90 minutes and reduces hospital admissions (NNT=18) [45-52 (1)]. There is insufficient evidence to say whether continuing ipratropium after the first dose confers additional benefit.

Delivery Devices

The use of an MDI plus holding chamber spacer produce outcomes in adults that are at least equivalent to nebuliser delivery [39 (1++)], except in very severe episodes.

Systemic Corticosteroids

Systemic corticosteroids should be given early in acute severe asthma [69 (1++)].

A short course of corticosteroids according to response (eg, 40 mg prednisone for 4–10 days) following an acute exacerbation of asthma reduces the number of relapses requiring additional medical care (OR 0.35, NNT=13) and decreases β₂-agonist use without any apparent increase in adverse effects [66 (1++)].

There is no evidence of benefit in using a dose of more than 100 mg of prednisone or prednisolone [70 (1++)].

Inhaled corticosteroids reduce admission rates in people with acute asthma who are not receiving concomitant systemic corticosteroids [71 (1++)]. However, there is insufficient evidence to determine whether ICS provide additional benefit when used in combination with standard systemic oral corticosteroid therapy. There is some evidence that high dose ICS alone may be as effective as oral corticosteroid therapy when used in mild asthmatics but further research is required to clarify this [69 (2)]. Oral prednisone is recommended for all acute severe episodes (4).

Theophylline

In acute asthma, intravenous aminophylline does not result in any additional bronchodilation or reduction in length of hospital stay compared with β₂-agonists. Aminophylline is associated with three times the rate of arrhythmia and four times the rate of vomiting as intravenous salbutamol [72 (1++)].
### PHARMACEUTICAL PRINCIPLES IN CHRONIC ASTHMA

#### Short-acting β₂-agonists

Short-acting inhaled β₂-agonists (SABAs) are the medication of choice for relief of acute symptoms of asthma [2 (2+)]. They are also useful for the prevention of exercise induced asthma [73 (1++)].

SABAs should be delivered by a device that is both easy to use effectively and portable.

There is no advantage in using SABAs regularly, and potentially a small clinical risk of bronchial hyperreactivity [2 (2+)].

#### Anticholinergic agents and combination agents

Anticholinergic agents have a slower onset of bronchodilator action than β₂-agonists, but provide some additional bronchodilation when used in combination. While there is evidence for the beneficial role of the combination in acute asthma, there is no evidence to indicate clinical benefit in its use in the day-to-day control of symptoms [2 (3)]. Anticholinergic agents can be delivered independently or in combination devices also containing SABAs.

Anticholinergic agents alone are not recommended as a first line treatment but can be used in those unable to tolerate β₂-agonists [2 (3)].

### RECOMMENDATIONS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>The addition of inhaled anticholinergic medication at the first presentation of acute asthma over a period of 90 minutes improves peak flow and symptoms and reduces hospital admissions.</td>
</tr>
<tr>
<td>B</td>
<td>Systemic corticosteroids should be given early in acute severe asthma.</td>
</tr>
<tr>
<td>B</td>
<td>β₂-agonists should be administered as required by inhalation and titrated using objective and clinical measures of airflow obstruction.</td>
</tr>
<tr>
<td>D</td>
<td>Supplemental oxygen should be used in acute severe asthma to maintain a SaO₂ &gt; 94%.</td>
</tr>
</tbody>
</table>

### GOOD PRACTICE POINTS

- All patients with symptomatic asthma should be prescribed an inhaled short-acting β₂-agonist.
- Use a delivery device that the patient prefers and can use effectively.
- The use of 2 or more canisters of β₂-agonists/ month or > 12 puffs a day is a marker of poor control for asthma.

---

**KEY**

- A Well designed meta-analysis (MA) of RCT, or a body or evidence which are consistently applicable
- B Very well designed observational studies or extrapolated evidence from RCTs or MAs
- C Lower quality observational studies or extrapolated evidence from B
- D Non analytical studies or expert opinion
- ✔ Good Practice Point

---

**RECOMMENDATIONS**

- **A** Short-acting β₂-agonists should be used on an as required basis to relieve symptoms. They should not be used in a regular and fixed regimen eg, QID, as a maintenance treatment agent.
- **C** Anticholinergic agents are not recommended first line but can be used in those unable to tolerate β₂-agonists or in combination with β₂-agonists.
Inhaled corticosteroids

Efficacy of inhaled corticosteroids

Treatment with inhaled corticosteroids is recommended in individuals who have daily symptoms of asthma [41, 74 (1++)].

In individuals with persistent symptoms of asthma, treatment with inhaled corticosteroids [41, 74, 42 (1++)] leads to:

- decreased symptoms
- reduced use of rescue medication
- improved lung function
- decreased exacerbations
- reduced hospital admissions
- reduced mortality.

Treatment with inhaled corticosteroids is more effective than:

- regular short-acting inhaled β₂-agonists (ie, salbutamol, terbutaline)
- long-acting inhaled β₂-agonists alone
- cromones ie, sodium cromoglycate, nedocromil
- theophylline
- anti-leukotrienes [76 (1+)].

Early versus late introduction of inhaled corticosteroids

Treatment with inhaled corticosteroids should not be delayed in people with persistent symptoms and impaired lung function [77 (1-)]. In an observational study, a delay of several years between the onset of symptoms and the initiation of treatment was more likely to be associated with a degree of irreversibility (ie, impaired baseline lung function) [77 (1-)].

There is currently insufficient high quality evidence to say whether there is any benefit of initiating treatment early if adults with asthma have only mild and infrequent symptoms.

Dose response

With conventional doses of inhaled corticosteroids there is a relatively flat dose-response for the effect on lung functions and symptoms [8 (2)].

Most of the effect of inhaled fluticasone propionate on symptoms and lung function is achieved with doses of 500 µg/ day or less. Very little additional benefit is seen with increasing doses. Similarly doses of budesonide or beclomethasone propionate of more than 800 µg/ day confer little additional benefit [8 (2)].

While most of the benefits of inhaled steroids on lung function and symptoms is seen with low doses of inhaled steroids (200 – 400 µg/ day of beclomethasone or budesonide) there is evidence from some studies that moderate doses of inhaled steroids (eg, 800 µg/ day budesonide) are associated with fewer exacerbations than low dose inhaled steroids. Not all studies are consistent with this [79]. In a meta-analysis of studies on inhaled fluticasone propionate (Holt), 90% of the benefit in preventing exacerbations was seen with a dose of only 155 µg/ day [21].

Table 3: Doses of fluticasone (µg/ day) at which 80% and 90% of the maximum effect is achieved

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>80% of maximum effect achieved</th>
<th>90% of maximum effect achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>146</td>
<td>209</td>
</tr>
<tr>
<td>Morning PEFR</td>
<td>172</td>
<td>247</td>
</tr>
<tr>
<td>Evening peak flow</td>
<td>175</td>
<td>251</td>
</tr>
<tr>
<td>Use of rescue medication</td>
<td>71</td>
<td>102</td>
</tr>
<tr>
<td>Major exacerbation</td>
<td>108</td>
<td>155</td>
</tr>
<tr>
<td>Night awakenings</td>
<td>135</td>
<td>193</td>
</tr>
</tbody>
</table>

The effect obtained by 100 µg/ day of fluticasone propionate was considered to be the maximum effect for the purposes of this analysis [129].
### Initiating treatment with low dose as opposed to high dose inhaled corticosteroids

Most people with mild to moderate asthma should be initiated on treatment with a dose of inhaled corticosteroids appropriate to the severity of their symptoms [41 (1++)].

It has been argued that initiation of treatment with high dose inhaled corticosteroids followed by back-titration once control has been achieved leads to more rapid control of asthma.

In mild to moderate asthma this strategy is not supported by the available evidence. Initiating treatment with low doses of ICS (eg, budesonide equivalent 400 µg/ day) achieves asthma control as rapidly as starting treatment with higher doses (eg, budesonide ≥ 800 µg/ day) [41 (1++)]. There may be a place for starting with high dose inhaled steroids followed by back-titration in patients with severe asthma although this approach has not been formally tested in randomised controlled trials (3).

In those newly-diagnosed adults with asthma who have moderate to severe symptoms, or a FEV₁ < 60% predicted, a short course of oral corticosteroids should be considered to quickly establish control of the asthma (D).

### Adverse effects of inhaled corticosteroids

Adults with asthma should be maintained on the lowest dose of inhaled steroid that controls their asthma.

Moderate and low dose (less than 800 µg/ day beclomethasone dipropionate equivalent) ICS are well tolerated with little in the way of systemic adverse effects. Systemic absorption increases with higher doses. In cross sectional observational studies there is evidence of an increased risk of cataracts, reduced bone mineral density, glaucoma and bruising of the skin with long term treatment with high dose inhaled corticosteroids [81 (1-)].

### Additional treatment

It is more effective to add a long-acting inhaled β₂-agonist than to double the dose of inhaled corticosteroids [82 (1++)].

In most people whose asthma is not controlled despite treatment with a moderate dose of inhaled corticosteroids (400 µg/ day of beclomethasone dipropionate or equivalent), it is more effective to add in treatment with a long-acting inhaled β₂-agonist than it is to double the dose of inhaled steroid. At doses of ICS above 800 µg/ day, a few patients may respond further, but adverse effects become more frequent [82, 83 (1++)].

### Potency

Fluticasone propionate is twice as potent as budesonide and beclomethasone dipropionate [9 (1++)]. Despite this, in New Zealand the average prescribed dose of fluticasone propionate is more than twice that for beclomethasone dipropionate. Similarly, the average prescribed dose of budesonide is greater than that of beclomethasone dipropionate [7 (1+)].

It seems unlikely that these differences result solely from the selection of people with more severe asthma to treatment with fluticasone propionate and budesonide. We suspect it may reflect both the availability of high dose preparations of fluticasone propionate and budesonide, and a lack of awareness of the relatively flat dose response seen with inhaled corticosteroids.

### Once daily treatment versus twice daily treatment

In mild, stable asthma, once daily treatment with budesonide is as effective as twice daily treatment if the same total daily dose is used [84 (1-)]. Once daily fluticasone propionate and beclomethasone dipropionate may also be effective in mild asthma, although with these medicines there is insufficient evidence to determine whether once daily treatment is as effective as twice daily treatment.

### ICS verses oral corticosteroids

ICS in a dose over 300 µg/ day is as effective as an oral daily dose of prednisolone 7.5 to 10 mg, and is associated with fewer adverse effects [85 (1++)].

### ICS use in exacerbations

In patients on treatment with low dose inhaled steroids (eg, 200 µg/ day budesonide) increasing the dose of inhaled steroids during exacerbations led to better long term asthma control [128]. This strategy has yet to be demonstrated to be effective in patients on long term treatment with moderate or high doses of inhaled steroids.
## RECOMMENDATIONS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Treatment with inhaled corticosteroids is recommended in those who have daily symptoms of asthma or patients requiring SABAs daily.</td>
</tr>
<tr>
<td>B</td>
<td>Most adults with asthma should be initiated on treatment with low dose inhaled corticosteroids (beclomethasone dipropionate equivalent 400 µg/day).</td>
</tr>
<tr>
<td>A</td>
<td>Fluticasone propionate is at least twice as potent as beclomethasone dipropionate.</td>
</tr>
<tr>
<td>A</td>
<td>Once-daily treatment with budesonide is as effective as twice-daily in mild asthma, once control has been achieved.</td>
</tr>
<tr>
<td>B</td>
<td>ICS have a relatively flat dose response curve. Little additional benefit is gained from doses above 500 µg/day of fluticasone propionate or 800 µg/day of beclomethasone dipropionate/budesonide.</td>
</tr>
<tr>
<td>B</td>
<td>There is evidence of an increased risk of cataracts, reduced bone mineral density, glaucoma and bruising of the skin with long-term treatment with high dose ICS (e.g., more than 800 µg/day beclomethasone dipropionate).</td>
</tr>
<tr>
<td>C</td>
<td>Early treatment with ICS in people with persistent symptoms and impaired lung function leads to better lung function in the medium term, and may help prevent the development of irreversible airflow limitation.</td>
</tr>
</tbody>
</table>

### GOOD PRACTICE POINT

- High doses of ICS should be avoided where possible for adults with asthma who have pre-existing conditions or vulnerability to conditions such as osteoporosis or cataracts.

### Long-acting β₂-agonists

The long-acting β₂-agonists (LABAs) formoterol and salmeterol provide sustained bronchodilation, and protect the airways from bronchoconstriction secondary to exposure to allergens, non-specific stimuli or exercise. They should normally be used in a twice-daily regular dose regimen [82 (1-)].

LABAs are not recommended for the treatment of acute (or chronic) symptoms of asthma in the absence of inhaled anti-inflammatory therapy. The dose of LABAs should not be increased during exacerbations [80 (1+)]. Instead, short-acting β₂-agonists (SABAs) should be used for exacerbations.

### LABAs versus SABAs

In people taking inhaled corticosteroids, long-acting β₂-agonists are more effective than the regular use of short-acting β₂-agonists in controlling symptoms [10, 42, 83 (1+)].

### LABAs and ICS

In people who continue to experience symptoms despite taking inhaled corticosteroids, the addition of long-acting β₂-agonists improves symptoms (night time waking and the need for rescue medication), reduces exacerbations and reduces adverse effects. The effect is equivalent to at least doubling the dose of the ICS (at a beclomethasone dipropionate equivalent dose of 400 µg/day) [42 (1+)] and therefore LABAs can allow a reduction in the ICS dose. However, because the incidence of adverse effects from ICS is minimal up to a dose of 800 µg/day BDP equivalent, and some people will respond to these doses of ICS alone, it is recommended that titration of ICS to this level is trialled before initiating LABAs.

### GOOD PRACTICE POINT

- The guideline team recommends that LABAs should always be considered in individuals who continue to experience symptoms despite taking moderate (800 µg BDP/day) doses of ICS as this is at the top end of the dose response curve of ICS and higher doses are associated with increased risk of adverse effects (opinion).
Table 4: LABAs compared with doubled dose ICS

<table>
<thead>
<tr>
<th>Effect</th>
<th>NNT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days without symptoms</td>
<td>9</td>
</tr>
<tr>
<td>Nights without symptoms</td>
<td>20</td>
</tr>
<tr>
<td>Days without rescue treatment</td>
<td>7</td>
</tr>
<tr>
<td>Nights without rescue treatment</td>
<td>11</td>
</tr>
<tr>
<td>Any exacerbation over 3 months</td>
<td>36</td>
</tr>
<tr>
<td>Severe exacerbation over 3 months</td>
<td>41</td>
</tr>
</tbody>
</table>

(Derived from MIASMA study [81].)

* Numbers Needed to Treat: see glossary for a definition of NNT

**Oral long-acting \( \beta_2 \)-agonists**

The oral LABA, bambuterol (20 mg/day) is as effective as inhaled salmeterol (50 µg bd) in improving symptoms and lung function and reducing the need for rescue medication. The oral drug is associated with more adverse effects [89 (1–)]. There is insufficient evidence to establish whether oral long-acting \( \beta_2 \)-agonists confer the same benefits in controlling exacerbations as inhaled long-acting \( \beta_2 \)-agonists.

**Long-acting \( \beta_2 \)-agonists compared with theophylline**

LABAs are more effective than theophylline in control of nocturnal asthma, including night waking and need for rescue medication, symptom scores, and symptom free days. They also produce fewer adverse effects (RR 0.38, NNH 2.6) [90 (1++)].

<table>
<thead>
<tr>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> In people who continue to experience symptoms despite taking inhaled corticosteroids (greater than 400 µg BDP/BUD), the addition of long-acting ( \beta_2 )-agonists is more effective than doubling the dose of ICS in improving symptoms, reducing exacerbations and reducing adverse effects.</td>
</tr>
<tr>
<td><strong>A</strong> In people taking inhaled corticosteroids, long-acting ( \beta_2 )-agonists are more effective in controlling symptoms than regular use of regular short-acting ( \beta_2 )-agonists.</td>
</tr>
<tr>
<td><strong>A</strong> Long-acting ( \beta_2 )-agonists are more effective than theophylline in control of nocturnal asthma including night waking and need for rescue medication, symptom scores, symptom free days and have fewer adverse effects.</td>
</tr>
<tr>
<td><strong>B</strong> Long-acting ( \beta_2 )-agonists should not be used for the treatment of acute (or chronic) symptoms of asthma in the absence of inhaled anti-inflammatory therapy.</td>
</tr>
<tr>
<td><strong>C</strong> There is insufficient evidence to establish whether oral long-acting ( \beta_2 )-agonists confer the same benefits in controlling exacerbations as inhaled long-acting ( \beta_2 )-agonists.</td>
</tr>
</tbody>
</table>

**Leukotriene receptor antagonists (LTRAs)**

Leukotriene receptor antagonists (eg, montelukast) are orally active compounds that bind to cysteinyll leukotriene receptors and improve parameters of asthmatic inflammation. These properties help to control asthma, in particular aspirin and exercise induced asthma [91 (2)].

**LTRAs as monotherapy**

LTRAs used alone are effective in improving symptoms, reducing EIA and protecting against exacerbations, but they are less effective than inhaled corticosteroids [40 (1+)].
**LTRAs and ICS**

Inhaled corticosteroids (in the dose equivalent of 250-400 µg/day beclomethasone dipropionate) are more effective than LTRAs in reducing symptoms including night waking, and the need for rescue β₂-agonists. They also produce better lung function [40 (1+)]. There is a relatively flat dose response curve for doses higher than 10 mg montelukast [76 (1+)].

The reported rate of adverse effects is similar, but LTRAs are associated with a greater risk of discontinuation (RR=1.4) compared with inhaled corticosteroids [40 (1+)].

**Adding LTRAs to inhaled corticosteroids**

Addition of LTRAs to ICS provides a small improvement in lung function, small decrease in exacerbations, and a small improvement in symptoms [40 (1++)]. Addition of LTRAs to ICS leads to smaller improvements in lung function than LABAs.

**LTRAs and long-acting β₂-agonists**

Two studies have found montelukast superior to salmeterol in preventing exercise induced asthma [127, 128 (1+)]. Alternatively salmeterol was superior to oral zafirlukast in maintaining lung function symptom free days and need for rescue medication [96 (1+)].

**LTRAs compared with Theophylline**

No evidence was found to identify the relative efficacy of leukotriene receptor antagonists and theophylline.

### RECOMMENDATIONS

| A | Inhaled corticosteroids (in the dose equivalent of 250-400 µg/day beclomethasone dipropionate) are more effective than LTRAs in reducing symptoms including night waking, and the need for rescue β₂-agonists. |
| A | Inhaled corticosteroids produce better lung function and quality of life and reduce symptoms and reduce need for rescue β₂-agonists than LTRAs. |
| A | LTRAs are associated with increased adverse withdrawal effects compared with ICS. |
| A | Adding LTRAs to inhaled corticosteroids has shown small additional improvement in symptom control but not to the extent of that of adding LABAs. |

### GOOD PRACTICE POINT

** ✔️ LTRAs may have a preventative role in aspirin and exercise induced asthma and in those who cannot take inhaled therapy.**

**Cromones**

Sodium cromoglycate and nedocromil are less effective than ICS in preventing asthma, and have been used less frequently in the treatment of adult asthma since other agents have become available. They can help to reduce allergen-induced responses following short term exposure, but they are a less effective alternative than short-acting β₂-agonists in the prevention of exercise induced asthma, and:

- there is no additional benefit from adding sodium cromoglycate to an established regimen of inhaled or systemic corticosteroid [2 (2+)];
- sodium cromoglycate QID and nedocromil BID can be used as less effective alternatives to short-acting β₂-agonists for the prevention of exercise induced asthma [2, 95 (1++)];
- sodium cromoglycate requires more frequent administration than ICS [4 (3)];
- benefits from cromones may take six weeks or more to become detectable [4 (3)].

Most adults with asthma will be maintained on 8 – 10 mg/ day. 5 mg for frail elderly patients and those with heart failure or inconsistent treatment with medicines. That inhibits the clearance of theophylline and 7 – 8 mg in most others.
RECOMMENDATIONS

A  Sodium cromoglycate can be used as alternative to or in addition to short-acting B₂-agonists for the prevention of exercise induced asthma.

A  Sodium cromoglycate requires more frequent administration than inhaled corticosteroids and the onset of benefit may be delayed.

A  There is no additional benefit in adding sodium cromoglycate to an established regimen of inhaled or systemic corticosteroid.

Theophylline

There has in recent years been renewed interest in the value of theophylline with recognition that it possesses some anti-inflammatory and immunoregulatory properties in addition to its bronchodilator actions [44 (1+)].

Adding theophylline to moderate dose (budesonide 800 µg/day) ICS has been shown to be as effective as using high dose ICS (1600 µg/day) alone and can therefore be considered as a third line agent for those not well controlled on ICS and LABAs [43, 44 (1+)].

Further it has been recognised that theophylline provides useful effects at lower serum concentrations than previously recommended (29 – 55 µmol/L rather than 55 – 110 µmol/L) and that at this level adverse effects are significantly reduced [43, 44 (1+)].

Theophylline has a narrow therapeutic to toxicity ratio and, as its bioavailability varies between individuals and within individuals according to their clinical status, measuring serum concentrations is still recommended [92].

Theophylline clearance is subject to several drug interactions: cimetidine, β-blockers, and quinolone antibiotics (eg, ciprofloxacin, enoxacin, norfloxacin, erythromycin, triacetyloleandomycin) and oral contraceptives inhibit clearance. Other xanthine medications and heavy caffeine consumption also decrease clearance. Hepatic enzyme inducers (eg, phenytoin, barbiturates, rifampicin and smoking) increase theophylline clearance. Theophylline also increases the clearance of lithium [92].

Dose: for adults with no risk factors (the elderly, those with cardiac failure, liver disease or on medication known to interact with theophylline), theophylline should be initiated at 5 – 8 mg/ kg/ day and titrate according to clinical response and serum concentration. Serum concentrations should be measured 3 or more days after the dose is changed. Benefit is seen with concentrations of 29 – 55 µmol/ L but some individuals may benefit from having higher serum concentrations (up to 82 µmol/ L). Use higher doses for younger smokers, moderate doses for well non-smokers and low doses for those on enzyme inhibitors (macrolide, rifamycin, ciprofloxacin, SSRI) and those with hepatic insufficiency, cor pulmonale and cardiac failure.

Common adverse effects include headache, nausea, vomiting, abdominal discomfort, restlessness and insomnia. There can be also increased acid secretion, gastro-oesophageal reflux and diuresis. High serum concentrations cause agitation, convulsions, tachyarythmias, coma and death.

Theophylline: summary

Theophylline should not be used as first line therapy in adults with asthma [2 (2+)]. Theophylline is associated with more frequent adverse effects and it less effective than salmeterol in improving lung function; relieving both night and day symptoms and reducing the need for rescue therapy [90 (1+)].

In people taking low dose inhaled corticosteroids (400 µg beclometasone dipropionate/ day), the addition of theophylline is as effective as using high (doubled) dose (800 µg/ day) ICS in maintaining symptoms score and need for rescue medication both day and night and improves lung function [2 (2+)].
### Table 5: Adverse effects of theophylline and salmeterol

<table>
<thead>
<tr>
<th>Theophylline</th>
<th>Salmeterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Nausea</td>
<td>Tremor</td>
</tr>
<tr>
<td>Headaches</td>
<td>Headaches</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>Muscle cramps</td>
</tr>
<tr>
<td>Gastro-oesophageal reflux</td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td></td>
</tr>
<tr>
<td>Muscle cramps</td>
<td></td>
</tr>
</tbody>
</table>

### RECOMMENDATIONS

A Theophylline should not be used as first line therapy.

A Theophylline is associated with more frequent adverse effects and is less effective than salmeterol in improving lung function, relieving both night and day symptoms and reducing the need for rescue therapy.

A Theophylline has a narrow therapeutic index and variable metabolism.

B Adding theophylline to low dose ICS (400 µg beclomethasone dipropionate/day) may be an effective alternative to doubling the dose of ICS.

### GOOD PRACTICE POINT

Serum monitoring of theophylline is recommended. A clinical effect has been demonstrated at serum levels of 29 – 55 µmol/L. Where necessary the dose can be titrated up to a serum level of 82 µmol/L.

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**Exercise induced asthma**

SABAs are effective in preventing exercise induced asthma (EIA) [2 (2+)].

LABAs and LTRAs are both effective in preventing exercise induced asthma [2 (2+)]. LABA protection against EIA lasts longest with the first few doses, after which the duration of effect reduces, so repeat doses may be necessary [93 (1++)].

Nedocromil and sodium cromoglycate are equally effective in reducing and preventing exercise induced bronchoconstriction for up to 2 hours after inhalation [95 (1++)].

4 mg inhaled nedocromil used before exercise reduces the severity (ie, it decreases the fall in peak flow) and duration (ie, it reduces the time to recover pre-exercise peak flow from 30 to 10 minutes) of exercise induced bronchoconstriction. This effect appears to be more pronounced in people with severe exercise induced bronchoconstriction [67 (1++)].

Nedocromil is less effective than SABAs for the prevention of exercise induced asthma [2 (2+)].

The effects of ICS on exercise induced asthma were initially thought to be minimal. However, a number of studies have shown a clear reduction in the extent of exercise induced bronchospasm after prolonged (> 4 weeks) ICS use. The effect on EIA is dose dependent [94 (2+)].

**Devices**

Inhaled drug delivery is superior (in terms of benefit/harm ratio) to oral or parenteral delivery (although this method is rarely used) for short-acting β₂-agonists, anticholinergics, long-acting β₂-agonists and inhaled corticosteroids [2 (1-)].
The commonly available delivery systems are the metered dose inhaler (MDI), metered dose inhaler with or without the use of a spacer, and dry powder devices.

Provided the devices are used correctly there is no evidence of long-term clinical advantage of one device over another [81 (1-)].

Dry powder devices and MDI + spacers may reduce the oropharyngeal disposition of medication and may reduce the local effects of inhaled corticosteroids [2 (2+)]. However, there is no evidence that these devices reduce the systemic adverse effects of such agents, possibly because the systemic absorption of such agents occurs as much through the bronchial circulation as it does through oral or gastrointestinal absorption [2 (2+)].

Dry powder devices compared with MDI

There is no evidence of superiority of any particular one of the MDIs and dry powder devices for SABAs, ICS and LABAs in terms of lung function and symptom relief [96 (1+)].

Propellants

Numerous studies have failed to demonstrate any significant difference in symptom control, lung function or adverse events between HFA verses CFC propelled inhalers (for SABAs, ICS or cromones) [96, 97 (1++)], other than HFA beclomethasone dipropionate (QVAR) [98 (1+)].

Device Selection and Training

It is essential that adults with asthma are competently trained in the correct technique of inhaler use. With good instruction most adults are able to effectively use any of the commercially available devices [2 (2-)]. The device that best fits the needs of the patient should be chosen [2 (3)].

Before consideration of an increase of therapy, people’s technique in using their devices should be reassessed. Patient’s inhaler technique should be reinforced regularly [2 (3)], especially if the asthma is poorly controlled. Health professionals should teach and/or check correct inhaler technique whenever devices are prescribed or dispensed [2 (2+)].

MDI and spacers compared with wet nebulisation in acute asthma

A Cochrane review of 16 trials included an analysis of 375 adults with mild to moderate acute asthma and found that metered-dose inhalers with holding chambers produced outcomes that were at least equivalent to nebuliser delivery. The odds ratio of hospital admission for a holding chamber versus nebuliser was 1.12, (95% C.I. 0.45 to 2.76). Length of stay in the emergency department was similar for the two delivery methods. Peak flow and forced expiratory volume were also similar for the two delivery methods [39 (1++)].

Devices and long-acting ß2-agonists

Dry powder devices of LABAs all provide similar clinical effectiveness [38 (1+)]. The preferences of the adults with asthma and their capability to use the device effectively should inform the choice of delivery device.

Dry powder devices that combine both LABA and ICS in one unit are now available. Such combination dry powder devices have similar but not improved clinical effectiveness as giving the same medication via separate devices [99 (1+)]. Although, combination dry powder devices may appear more convenient, the fixed dosing of such devices makes titration of the ICS portion of the dose more difficult.

3 Note: This study did not include patients with very severe episodes.

KEY - see page 7 for details
A Well designed meta-analysis (MA) of RCT, or a body or evidence which are consistently applicable
B Very well designed observational studies or extrapolated evidence from RCTs or MAs
C Lower quality observational studies or extrapolated evidence from B
D Non analytical studies or expert opinion
✓ Good Practice Point
RECOMMENDATIONS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Inhaled drug delivery is superior to oral (or parenteral) delivery for short-acting β₂-agonists, anticholinergics, long-acting β₂-agonists and inhaled corticosteroids.</td>
</tr>
<tr>
<td><strong>A</strong></td>
<td>There is no significant difference between delivery devices when used correctly.</td>
</tr>
<tr>
<td><strong>A</strong></td>
<td>MDIs plus spacers are at least as effective as wet nebulisers in mild to moderate acute asthmatic episodes.</td>
</tr>
<tr>
<td><strong>A</strong></td>
<td>Adults with asthma should receive adequate training in their inhaler technique to ensure competence.</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>People’s technique in using their devices should be reassessed and reinforced frequently at appropriate opportunities.</td>
</tr>
</tbody>
</table>

GOOD PRACTICE POINTS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>Choice of device should be made on the basis of ease of use, patient preference and overall cost.</td>
</tr>
<tr>
<td>✓</td>
<td>There is no evidence that any particular device reduces the risk of systemic adverse effects.</td>
</tr>
<tr>
<td>✓</td>
<td>Dry powder devices and MDI plus spacers may reduce oropharyngeal adverse effects.</td>
</tr>
</tbody>
</table>

**Antihistamines and ketotifen**

Antihistamines and ketotifen are ineffective for treating asthma [87 (1++)].
MANAGEMENT OF CHRONIC ASTHMA

Drug management of chronic asthma

When initiating or considering an increase in medical management of acute asthma, the process of review below should be followed. This process applies to each step.

Adequate control of symptoms achieved?

YES

Continue treatment and consider back-titration of medication to lowest effective dose

YES

Progress to next step of therapy

NO

Review environmental factors, compliance and inhaler technique. Correct if necessary.

There are a significant number of adults with asthma inadequately controlled despite combination therapy of inhaled steroids and an additional drug (eg, a LABA). There are few studies in this patient group to guide management for this group. The recommendations for treatment are based on extrapolations from trials of add-on therapy to ICS and previous guidelines.
**MANAGEMENT OF CHRONIC ASTHMA ALGORITHM**

This is a stepwise approach to asthma, although individuals newly diagnosed with asthma may begin treatment at differing points in this algorithm depending on the severity of their asthma.

### β2-agonists
- PRN use of a portable device, used correctly.

### Inhaled corticosteroids
- Reduce symptoms, exacerbations, hospital admissions and mortality
- Consider introduction of ICS if daily symptoms of asthma
- Have a relatively flat dose response curve so that most benefit is obtained from lower doses
- In mild to moderate asthma initiate at 400 µg BDP/ day as higher doses do not lead to more rapid control
- Higher doses may be considered in more severe asthma
- There are no clinically significant differences between agents in effectiveness or risk of adverse effects
- Fluticasone is twice as potent as BDP/BUD.

### LABAs
- Reduce symptoms, exacerbations and hospital admissions
- Use a fixed dose regimen
- Do not increase dose in acute asthma
- Adding LABAs is more effective than doubling dose of ICS (at dose of 400 µg/ day) and should always be considered if doses of ICS greater than 800 µg/ day are required.

### High dose ICS
- Titrate dose up to BDP/BUD equivalent of 1600 µg/ day
- Use a spacer if using MDI
- Adverse effects include reduced bone mineral density, cataract formation, oropharyngeal candididasis, dysphonia and HPA axis suppression.

### Theophyllines
- Should not be used first line but improve symptoms when added to ICS and may reduce steroid requirements
- Are less effective than LABAs as third line therapy
- Start with 5-8mg/ kg/ day and titrate according to clinical response and serum concentration. Serum concentrations should be measured 3 or more days after the dose is changed. Benefit is seen with concentrations of 29 – 55 µmol/L but some individuals may benefit from having higher serum concentrations (up to 82 µmol/L). Use higher doses for younger smokers, moderate doses for well non-smokers and low doses for those on enzyme inhibitors (macrolide, rifampicin, ciprofloxacin, SSRI) and those with hepatic insufficiency, cor pulmonale and cardiac failure.

### Leukotriene receptor antagonists
- Less effective and more adverse effects than low dose ICS
- Can improve symptoms and reduce exacerbations when added to ICS particularly in aspirin and exercise induced asthma
- Less effective than adding LABAs to ICS.

### Oral Steroids
- Specialist review recommended
- Use lowest dose possible.

---

**ABBREVIATIONS**
- BDP: beclomethasome dipropionate
- BUD: budesonide
- ICS: Inhaled corticosteroids
- LABAs: Long-acting β2-agonists
- MDI: Metered dose inhaler

* Pharmac Access Criteria, see Appendix 3.

** Not currently on the pharmaceutical schedule in New Zealand.
**KEY** - see page 7 for details

A. Well designed meta-analysis (MA) of RCT, or a body or evidence which are consistently applicable
B. Very well designed observational studies or extrapolated evidence from RCTs or MAs
C. Lower quality observational studies or extrapolated evidence from B
D. Non analytical studies or expert opinion

✓ Good Practice Point
While this guideline for the treatment and management of asthma applies equally across all groups within the New Zealand population, there are some issues specific to Māori with asthma.

Many Māori adults with asthma find the costs and location of care difficult, while many also hold a sense of self-blame (Whakama). Medical practitioners may interpret Māori as passive, when in fact they are being protective when using treatments or accessing services and this may contribute to poor utilisation of services [105]. Use of a Māori support person or advocate may be of benefit to Māori with asthma when consulting a practitioner.

A trial of a Māori self-management asthma plan found that although there was evidence for continued improved outcomes two years after the program, by six years the benefits were lost [106]. Despite the unsustained trends, examining the cultural appropriateness of the plan found four key benefits: cultural affirmation, increased access to other health services, increased sense of control over health and positive impacts on the extended family [35, 36].

**RECOMMENDATION**

Management of Māori asthma by Māori providers must, to sustain the benefits, be an ongoing programme, rather than a short-term intervention.

**GOOD PRACTICE POINT**

Health professionals providing care for Māori adults with asthma should be sensitive to the particular needs of Māori, and encourage the use of a support person or advocate.
KEY - see page 7 for details
A Well designed meta-analysis (MA) of RCT, or a body of evidence which are consistently applicable
B Very well designed observational studies or extrapolated evidence from RCTs or MAs
C Lower quality observational studies or extrapolated evidence from B
D Non analytical studies or expert opinion
✓ Good Practice Point
Complementary therapies are widely used by adults with asthma. One study showed that only 41% of adults with asthma had never tried any complementary therapy, of those, 67% were willing to. Further, the major sources of information were not health professionals, but friends, family and the media [107]. Some complementary medicines and approaches may interact with prescribed medications and medical management. It is important that clinicians be alert to the possibility that people may be using complementary approaches [108].

GOOD PRACTICE POINT

Health professionals should be open to the possibility of the use of complementary therapies by people they are caring for. It could be suggested that use of such therapies be considered a trial to achieve better control, and methods for self assessment and monitoring could be discussed.

Immunotherapy

Allergen-specific immunotherapy involves injecting an extract of the allergen under the skin. It is also known as hyposensitisation or desensitisation, and carries a risk of potentially fatal anaphylaxis.

A systematic review of allergen immunotherapy by the Cochrane collaboration included fifty-four trials. There were 25 trials of immunotherapy for house mite allergy; 13 for pollen allergy; eight for animal dander allergy; two for cladosporium mould allergy; and six looking at multiple allergens. However, concealment of allocation was only adequate in 11 of these trials [12 [1++]].

Overall, there was a significant reduction in asthma symptoms and requirement for medication following immunotherapy. There was also a significant improvement in asthma symptom scores (standardised mean difference -0.52, 95% CI: -0.70 to -0.35). People receiving immunotherapy were less likely to report a worsening of asthma symptoms than those receiving placebo treatment were (OR 0.27, 95% CI: 0.21 to 0.35). People randomised to immunotherapy were less likely to require medication than those randomised to placebo (OR 0.28, 95% CI: 0.19 to 0.42). Allergen immunotherapy reduced allergen-specific bronchial hyper-reactivity, with also some reduction in non-specific bronchial hyper-reactivity. There was no consistent effect on lung function.

RECOMMENDATION

Immunotherapy reduces asthma symptoms and use of medication but its long-term effects and efficacy relative to other therapies is unknown and there are serious risks associated with its use.
Breathing exercises

A Cochrane systematic review failed to find any benefit of breathing exercises generally [18 (1++)]. However, a randomised controlled trial was conducted of Buteyko Breathing Techniques (BBT) in Asthma. BBTs are based on the premise that the pathophysiology in asthma is due to hypocapnia as a result of hyperventilation. Adults with asthma are taught a series of exercises purporting to correct this. The trial found no benefit of BBT on measures of FEV₁, PEFR or exacerbations, nor did it affect CO₂ levels. However, there were significant improvements in other measures, such as a reduction in the use of bronchodilators and inhaled corticosteroids, and improved quality of life [109 (1-)]. There was a probability of bias in the findings, as the experimental group were followed up more assiduously than the control group. BBT is taught in the community through seminars at a significant cost to the participant.

RECOMMENDATIONS

A Various breathing exercises have shown no overall beneficial outcomes in the clinical treatment of asthma.

B Buteyko Breathing Techniques may be helpful in reducing reliever use and improving quality of life, but this will involve a considerable cost to the patient. There is no benefit to other aspects of management of asthma.

Other therapies

There is insufficient evidence of adequate quality to determine benefit from:

- relaxation techniques including hypnotherapy for asthma [110 (1+)]
- acupuncture in chronic asthma [13 (1+)]
- manual therapies (including physical therapy, massage, chiropractic and osteopathy) for adults with asthma [14 (1+)]
- homeopathy in asthma [15 (1+)]
- the “Alexander technique” physical therapy on the symptoms of chronic asthma [16 (1+)]
- the efficacy of speleo-therapeutic interventions in the treatment of chronic asthma [17 (1+)].
SECONDARY PREVENTION OF ASTHMA IN ADULTS

A review of the literature by New Zealand Health Technology Assessment showed that the secondary prevention of asthma has been limited to barrier methods for reducing exposure to house dust mite allergen (HDM). Firstly, there is now considerable evidence that very high levels of major allergen Der P1 exist in New Zealand [112 (2-)]; secondly, HDM is the major indoor allergen to which the population of New Zealand is sensitised [113 (2-)]; and thirdly, allergen avoidance studies have concentrated on house dust mites [114 (2-)].

In adults with allergic asthma, in whom there is evidence of house dust mite sensitivity (through either a positive skin-prick test or specific serum IgE on radioallergosorbent testing (RAST)), dust mite-impermeable covers should be applied to the mattress, duvet, and pillows [32-34 (2-)].

RECOMMENDATION

B In adults with house dust mite allergic asthma, dust mite-impermeable covers applied to the mattress, duvet, and pillows reduces exposure to the allergen and decreases symptoms.

GOOD PRACTICE POINT

Adults with house dust mite allergic asthma should consider minimising dust exposure by:
- regular vacuuming with a cleaner which has a HEPA filter,
- removing soft furnishings and carpet from bedrooms, in addition to using the barrier methods.

In other adults with asthma, there is no evidence of sufficient quality to support any of the following secondary prevention measures:
- Miticidal agents applied to household furnishing, bedding or carpets
- Air filtration devices
- Vacuuming
- Conventional carpet cleaning
- Steam cleaning of carpet and household furnishings
- Domestic mechanical ventilation and heat recovery in a temperate climate.
KEY - see page 7 for details
A  Well designed meta-analysis (MA) of RCT, or a body of evidence which are consistently applicable
B  Very well designed observational studies or extrapolated evidence from RCTs or MAs
C  Lower quality observational studies or extrapolated evidence from B
D  Non-analytical studies or expert opinion
✓  Good Practice Point
EDUCATION, SELF-MANAGEMENT AND ROUTINE CLINICAL CARE

General principles
Effective management of asthma requires not only pharmaceutical management, but also patient education and a well-managed patient–doctor relationship. The key aspect to adults with asthma of the patient–doctor relationship is continuity of care [100]. Health care delivery that allows continuity of care leads to positive outcomes in managing asthma.

The under-utilisation of preventer medication can result in over-use of relievers. Research into the beliefs of adults with asthma about inhaler use found that underestimation of reliever use, asthma severity and overestimation of preventer use was common. Higher preventer use also correlated with satisfaction with the doctor, positive attitudes to using inhalers and knowing the benefits of preventer medication [101]. Clinicians should be aware that there is an established link between socio-economic status and adverse asthma outcomes [102].

Furthermore, many ethnic subgroups have poorer clinical outcomes, including higher hospital admission and exacerbation rates. These population groups can also be disadvantaged by perceived lack of access to medical facilities, linguistic difficulties and cultural isolation [103].

GOOD PRACTICE POINT
Health professionals providing care for adults with asthma should be aware of the needs of adults with asthma from socially disadvantaged populations.

Adherence
Patient adherence with all aspects of asthma management is very variable and the degree of compliance with prescribed treatment should be considered where there is a failure to control asthma symptoms. Patients are more likely to under-use than over-use medications, and adults under 60 years of age are less likely to take medications as prescribed [104 (1+)]. There is no clear evidence to say how adherence may be improved.

GOOD PRACTICE POINT
Where there is a failure to control asthma symptoms, practitioners should consider the possibility of non-adherence to treatment.

Education
Increased patient dissatisfaction is correlated with poor asthma control, perceived inadequate patient–provider communication and medication issues [115]. Education programs are one way of addressing this problem. Individualising education and self-management programs can be aided by defining patient preferences in respect to decision making. However, a study of autonomy preference in people with moderate
to severe asthma showed a tendency to prefer physician decision-making, especially in regard to medication changes, though the patient would prefer to decide when to consult [116].

Asthma has the potential to adversely affect an individual’s employment. A study conducted in South Auckland showed that over half of those surveyed and who were currently working had experienced occupational constraints as a result of their asthma [117]. Many (77%) were reluctant to disclose their diagnosis to the employer. Therefore strategies are needed to aid adults with asthma in managing the disease and their employment as the added stresses of trying to conceal/self-manage their condition may worsen it.

**Self-management**

The use of individualised self-management plans (SMP) results in fewer days lost from work, fewer hospital admissions and emergency episodes in general practice, less use of rescue medication and improved lung function [11, 118 (1++)]. They are equally effective when used with or without peak flow monitoring or symptom diaries, and whether using a “credit card” or paper format.

In adults with asthma, optimum self-management and education consists of a structured programme, which teaches adults with asthma how to detect and manage worsening symptoms and encourages the optimal use of medications including good adherence [3, 4 (2+)]. Essential components of such a programme would include:

- Written information about asthma
- Self-monitoring of symptoms and/or peak flow [119, 120 (2+)]
- Regular review by a doctor or nurse, which involves assessment of medications and assessment of current asthma severity
- Acknowledgement that lung function alone is not an adequate measure of the overall patient status and that quality of life considerations must be incorporated when assessing the impact of disease
- An individualised written self-management plan [3, 4 (2+)]
- Maintaining open dialogue between health professionals and adults with asthma with a view to greater involvement of the adults with asthma in decision-making but not total abdication of responsibility to the adults with asthma.

Although it is not usually necessary to include the use of peak expiratory flow monitoring in self-management plans, this may be beneficial for people with more severe or brittle asthma [119, 120 (2+)].

In adults with asthma, providing information as the only educational input does not result in any clinically important improvements in health care utilisation or lung function [11(1++)].

**Routine clinical care**

Regular clinical review of adults with asthma reduces work absenteeism, exacerbation rate and improves symptom control [118 (1+)]. Primary health care teams should keep a patient register with information and instruction for adults with asthma as part of their practice structure [3 (2+)].

Primary health care teams should make arrangements to review all adults with asthma on their register at least once a year. This review may be undertaken by a practice nurse or trained educator [11 (1++)]. Specially trained asthma nurses may achieve better outcomes for the people they work with [121, 122 (4)]. Practice audit or quality improvement activities which link the management of adults with asthma to guidelines for best practice and provide feedback on individual patients appear to produce the best outcomes [123, 124 (1+)]. A checklist for adult asthma consultations is suggested in appendix 4.

[4 See Appendix 5 for details of where to obtain examples of Asthma management plans.]
### RECOMMENDATIONS

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
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</table>
| A     | Primary health care teams should use a checklist of patient information and instruction, as part of their practice structure for adults with asthma.  

See Appendix 4 for a suggested checklist for consultations. |
| A     | Primary health care teams should make arrangements to review all adults with asthma on their register at least once a year. |
| A     | All adults with asthma should be offered a customised self-management plan. |
| A     | A structured educational programme should be provided for adults with asthma. |
| C     | The use of peak expiratory flow monitoring in self-management plans may be beneficial. |
| C     | Adults with asthma in primary health care should be reviewed regularly by a nurse with training in management of people with more severe asthma. |
| D     | Practices should frequently conduct audit or quality improvement activities linking the management of adults with asthma to guidelines for best practice. |

### GOOD PRACTICE POINT

- A request for a repeat inhaler, and/or a visit to the pharmacist should be used as an opportunity for a brief review of pattern of medication use and inhaler technique.
IMPLEMENTATION STRATEGY

Education programmes
Even if the most appropriate asthma management plans are formulated, patient and provider attitudes can be major barriers to implementing them in clinical practice. One study showed that both groups were unenthusiastic about management plans, health professionals doubting people’s ability to assimilate information and people denying that the plans would be of use to them [125].

Furthermore, GPs feel past guidelines for asthma control have been impractical and confusing due to differing originating bodies and that there was little incentive to educate. The two main concerns have been inconsistency in recommendations for both treatment and patient behaviour issues [126].

Education of both adults with asthma and practitioners about this guideline should address these issues specifically. It is intended that this guideline will result in the following opportunities:

Education
• A facilitator’s pack for regional continuing medical education (CME, CNE) and others (e.g., small group education sessions for provider and support organisations) targeted at specific groups (such as GPs, pharmacists, asthma nurses, practice nurses or other primary health care nurses and asthma associations) will be developed
• On-line and downloadable self-audit CME will be developed
• The NZGG will work with relevant organisations to promote and facilitate educational programmes
• A practice audit programme linking to the treatment of adults with asthma to promote best outcomes will be developed.

Summaries
Summaries of this guideline will be produced for:
• Primary health care clinicians
• Consumers
• Māori and Pacific Island populations.

Tools
Various tools to facilitate the use of this guideline will be developed, including:
• pop-up diagnostic and treatment algorithms for practitioner software systems
• interactive guidelines available from the NZGG web site and on disk
• wallet cards for adults with asthma.

Identification of barriers to best practice
During production of this guideline, a number of barriers to the care recommended by the guideline have been identified such as the cost to the consumer of regular consultation and review, and the gap between the Pharmac access criteria for LABAs at the outset of the guideline development and the identified best practice. On national issues such as these, the dissemination and implementation of the guideline will include the NZGG and the guideline development group developing proposals for processes by which the barriers can be addressed.

There is likely to be considerable regional variation in the particular barriers that will apply. The NZGG is also developing a handbook for the local adaptation of national guidelines, which addresses the issue of how regional service providers may identify regional barriers to best practice and formulate strategies to overcome them.
Quality
Adults with asthma, service providers and funders of asthma services all have an interest in the quality of the care and management of adults with asthma. This places a responsibility on service providers to collect information relevant to different perspectives. This chapter suggests:
• A minimum data set for collection relating to each individual with asthma; and
• Additional data for periodic audit (by an internal or external agency).

Suggested data for routine collection
• Basic demographics of adults with asthma in each practice (age, gender and ethnicity)
• Current medications, and devices prescribed and dose levels
• Peak flow levels recorded at each asthma related visit
• Details of allergen testing results where appropriate
• Information about the dates of discussions about device and spacer use/ inhaler technique and information about use of a self-management plan (this can be provided by the primary health care nurse or respiratory educator)
• Spirometry results, if available
• Risk factors eg, smoking
• Ongoing recording and monitoring of:
  - ICS use and doses
  - SABA use
  - Night waking
  - Limitation of daily activity
• Details of emergency department treatments and/ or admissions to hospital
• Details of adverse events or effects eg, thrush
• Number of days of work/daily activities
• Psychosocial issues associated with asthma addressed
• Any barriers to concordance to treatment plan.

Audit
Audit is a systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which a service, such as a primary health care practice, is meeting best practice standards. In order to assess whether adult asthma services are being provided effectively, a register of patients with asthma may be established and a system alert for repeat prescriptions. In addition, the following performance indicators may be assessed.
Suggested performance indicators

- Percentage of adults on asthma register as a proportion of adults enrolled in the practice.
- Number of:
  - individuals with suboptimal control taking ICS at more than 800 µg and who are not taking LABAs
  - preventers prescribed proportional to relievers prescribed
  - systematic steroid treatments per year
  - adults with asthma offered a self-management plan
  - adults with asthma who had inhaler technique checked and self-management plans reviewed within the last twelve months.
- Number and frequency of emergency nebuliser treatments attendance and hospital admissions.

In addition to these indicators, primary health care organisations and District Health Boards will want to review prescribing patterns. This information is available from hospital and pharmaceutical datawarehouses. Further work on indicators will be undertaken over the next 12 months. This information will be available on the NZGG website www.nzgg.org.nz

GOOD PRACTICE POINTS

- Comprehensive details about each adult with asthma should be recorded as part of routine clinical practice.
- Audit of asthma performance indicators is necessary to monitor quality of adult with asthma’s care, and to ensure best practice services are provided. Audit should take place every twelve months.
APPENDICES

1 Medications Known to Cause Asthma Symptoms
2 Asthma and Sports: Banned & Allowed Medication
3 Pharmac Access Criteria
4 Suggested Checklist for Adult Asthma Consultations
5 Examples of Asthma Management Plans and Educational Resources, Asthma Organisations
6 Research Gaps
7 Search Strategy for the Systematic Review of Asthma
APPENDIX 1: MEDICATIONS KNOWN TO CAUSE ASTHMA SYMPTOMS

Note: this list is an indication only.

- Beta-blockers
- Cholinergic agents
- Cholinesterase inhibitors
- Beta-blockers applied as eye-drops may also cause problems
- Aspirin and NSAIDs – usually characterised by flushing and rhinorrhoea. May produce a life threatening asthma attack
- Carbamazepine
- Some parenteral drugs (such as penicillin, iron dextran complex, hydrocortisone, ipratropium bromide, aminophylline, N-acetyl cysteine)
- Tartrazine (yellow food dye)
- Preservatives (such as bisulphates, metabisulphates and benzalkonium chloride)
- Echinacea (frequently recommended for colds, flu and respiratory infections, but triggers asthma in some people)
- Royal Jelly (has caused fatal exacerbations in some people).

All may lead to bronchoconstriction

Source: Asthma Management Handbook 2002 [3].
APPENDIX 2: ASTHMA AND SPORTS - BANNED & ALLOWED MEDICATION

Asthma medications banned and allowed by the NZ Sports Drug Agency are listed below

Valid in New Zealand from 1 September 2001 to 31 December 2002.

The position regarding asthma drugs has changed. (E)Formoterol (eg, Foradil, Oxis) has been added to the list of inhaled β₂-agonists permitted with a prior medical declaration. What is described below applies to the programme operated by the NZSDA only.

Asthma is usually treated by using inhaled drugs or oral drugs or a combination of both. Drugs in the various categories are listed below.

### Table 6: Inhalers and bronchodilators

<table>
<thead>
<tr>
<th>ALLOWED</th>
<th>ALLOWED</th>
<th>ALLOWED* with declaration (see below)</th>
<th>BANNED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids (inhaled) Permitted in NZSDA programme. May require notification overseas.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ß₂-agonists (inhaled) May be used only for asthma treatment - requires advance medical declaration.</td>
<td></td>
<td>Berotec</td>
<td></td>
</tr>
<tr>
<td>Intal</td>
<td>Becoforte</td>
<td>Aironir</td>
<td>Medihaler Epi</td>
</tr>
<tr>
<td>Tilade</td>
<td>Becodisk (Inc. 200, Junior &amp; Forte)</td>
<td>Asmol (Inc. Uni-Dose)</td>
<td>Medihaler Iso</td>
</tr>
<tr>
<td>Vicrom</td>
<td>Becotide (Inc. 100 &amp; Junior)</td>
<td>Bricanyl</td>
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<tr>
<td></td>
<td>Flixotide</td>
<td>Foradil</td>
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<tr>
<td></td>
<td>Pulmicort</td>
<td>Oxis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respocort (Inc.100,100S, 250, 250S)</td>
<td>Respolin</td>
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<tr>
<td></td>
<td></td>
<td>Serevent</td>
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<tr>
<td></td>
<td></td>
<td>Ventodisk</td>
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<tr>
<td></td>
<td></td>
<td>Ventolin (Inc. Forte –inhaled only)</td>
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</tr>
</tbody>
</table>

1. Any athlete competing at national level or above who is subject to drug testing must notify their national sporting organisation of the use of ß₂-agonists, inhaled corticosteroids. Use of Prednisone is allowable in New Zealand only (see NZSDA Information Sheet).

2. Any athlete competing at Olympic level requires a positive hypertonic saline challenge or equivalent test before they will be allowed to use ß₂-agonists.

* NOTE:
* Competitors using these medications must obtain a form specifying that they suffer from asthma or exercise induced asthma, the date of diagnosis, and signed by the diagnosing doctor. This form must be lodged with the national sporting organisation of the competitor and the NZSDA prior to testing (ie, as soon as such diagnosis is made).
* Competitors competing overseas should clarify requirements with respect to use and notification of both ß₂-agonists and corticosteroids through the National Sporting Organisation or by ringing the Drug Free Sport Hotline. You are advised to always have copies of a medical declaration for inhaled ß₂-agonists and (if necessary) corticosteroids available to lodge with the medical authority appointed by the event organisers or International Federation prior to competition.
* Justification for diagnosis including respiratory function test results will be required at Olympic Games and possibly elsewhere.

### Table 7: Oral (ie, Tablet or Syrup)

<table>
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<tr>
<th>ALLOWED</th>
<th>ALLOWED* (subject to note below)</th>
<th>BANNED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuelin (Inc. 24,SR, SR Sprinkle)</td>
<td>Apo-Prednisone</td>
<td>Ventolin (syrup)</td>
</tr>
<tr>
<td>Theo-Dur</td>
<td>Prednisolone</td>
<td>Volmax</td>
</tr>
<tr>
<td></td>
<td>Prednisone</td>
<td></td>
</tr>
</tbody>
</table>

* In recognition of the medical necessity for use of systemic corticosteroids where symptoms are acute, the New Zealand Sports Drug Agency, within its programme only, permits their use, for a recognised medical condition. Competitors who receive this treatment should obtain a note from their doctor, verifying this. In the event of a positive test report this note will be required by the New Zealand Sports Drug Agency.

ANTIHISTAMINES: All antihistamines are allowed including Eye Drops, Nasal Drops, Topical Creams and Oral Medications, eg, Avil, Claratyne, Hismanol, Polaramine, Teldane, Zyrtec.

You are advised to declare all medication at the time of a drug test, including asthma medication, even if they are listed above as “allowed”.

**If in doubt talk to your doctor, chemist or use**

DRUG FREE SPORT HOTLINE; 0800-DRUGFREE (0800-378437).
You can also visit the NZ Sports Drug Agency website: www.nzsda.co.nz
APPENDIX 3: PHARMAC ACCESS CRITERIA

The Pharmaceutical Management Agency lists the following access criteria in its August 2002 update of the Pharmaceutical Schedule. Pharmaceutical Schedule updates are available at www.pharmac.govt.nz

**Inhaled corticosteroids - nebuliser solution**

BUDESONIDE

Note: The cost of nebuliser therapy greatly exceeds other inhaled forms. Steroid nebulising solution can cause cataract formation.

Nebuliser soln, 500 µg/ml, 2 ml - Special Authority

PULMICORT

Special Authority - Hospital pharmacy

a) Only for children under 2 years of age or children with major physical or intellectual disabilities who lack the necessary coordination to use aerosols with a spacer device.

b) Specialist must make application – paediatrician/respiratory physician.

**Inhaled beta-adrenoceptor agonists - metered dose inhalers**

**Low dose**

SALBUTAMOL

Available on a PSO

Aerosol inhaler, 100 µg/dose CFC-free

Aerosol inhaler, 100 µg/dose CFC-free

**High dose**

SALBUTAMOL

Available on a PSO

Aerosol inhaler, 200 µg/dose

FENOTEROL HYDROBROMIDE

Aerosol inhaler, 100 µg/dose

Aerosol inhaler, 200 µg/dose

Special Authority - Retail pharmacy:

a) Approval for subsidy will be granted if:

   - the patient has been on the product prior to 1 August 1990 (when it was removed from the Pharmaceutical Schedule)
   - alternatives (salbutamol & terbutaline) have been tried
   - the patient has asthma or chronic obstructive airways disease (COAD).

b) The dose must be provided on the application.

**Inhaled beta-adrenoceptor agonists - breath activated devices**

**Medium dose**

SALBUTAMOL - Available on a PSO

Aerosol inhaler, 100 µg/dose, breath activated

Powder for inhalation, 50 µg/dose, breath activated
### Inhaled beta-adrenoceptor agonists - long-acting

#### Metered dose inhalers

**SALMETEROL - Special Authority**

Aerosol inhaler, 25 µg/ dose

**Breath activated devices**

**EFORMOTEROL FUMARATE**

- Powder for inhalation, 6 µg/ dose, breath activated – Subsidy by endorsement

Subsidy is available for patients with poorly controlled asthma where:

a) at least three months of 750 µg or more daily of inhaled beclomethasone or budesonide (or 400 µg of fluticasone) for adults has been used; or

b) at least three months of 400 µg or more daily of inhaled beclomethasone or budesonide (or 200 µg of fluticasone) for children 12 years or older has been used.

The prescription must be endorsed accordingly. We recommend that the words used to indicate eligibility are “poor control with ICS” or “certified condition”.

**BUDESONIDE WITH EFORMOTEROL - Special Authority**

- Powder for inhalation 100 µg with eformoterol fumarate 6 µg
- Powder for inhalation 200 µg with eformoterol fumarate 6 µg

**EFORMOTEROL FUMARATE - Special Authority**

- Powder for inhalation, 12 µg/ dose, and monodose device
- Powder for inhalation, 12 µg/ dose, breath activated

**SALMETEROL - Special Authority**

- Powder for inhalation, 50 µg/ dose, 4 doses/ disk
- Powder for inhalation, 50 µg/ dose, breath activated

Special Authority - Retail pharmacy for eformoterol fumarate (12 µg/ dose), eformoterol fumarate with budesonide and salmeterol.

a) Special Authority criteria either under point I (in its entirety), or point II (in its entirety), or point III (in its entirety) must apply before patients have access to subsidy.

b) Special Authority approvals (CHEM numbers) are interchangeable among all presentations of inhaled long-acting β₂-agonists and eformoterol fumarate with budesonide.

c) Applications for Special Authority to be made by general practitioners or an appropriate specialist.

d) Approvals valid for two years.

e) Patients are to be reviewed at least at six months to assess compliance and effectiveness of therapy.

f) Applications to be made on a PHARMAC approved form.

g) The re-application criteria under each point below (I, II or III) are:

   1) compliance (prescriber determined) with medication; and
   2) improved asthma symptom control.
h) Children who turn 12, and are stabilised on an inhaled LABA, are not required to try Oxis Turbuhaler 6 µg in order to have continued access to their original inhaled LABA.

I) Serevent MDI, Serevent Diskhaler, Serevent Accuhaler, Foradil, Oxis Turbuhaler 12 µg, Symbicort Turbuhaler Subsidy is available for:
- children with poorly controlled asthma under the age of 12 who required at least three months of 400 µg or more daily inhaled beclomethasone or budesonide (or 200 µg or more of fluticasone); or
- adults with poorly controlled asthma who required at least three months of 1500 µg or more daily of inhaled beclomethasone or budesonide (or 750 µg or more of fluticasone).

II. Serevent MDI, Serevent Diskhaler, Serevent Accuhaler Subsidy is available for patients with poorly controlled asthma aged 12 years and over, under the following criteria:
- at least three months of 750 µg or more daily of inhaled beclomethasone or budesonide (or 400 µg of fluticasone) for adults, or 400 µg or more daily inhaled beclomethasone or budesonide (or 200 µg of fluticasone) for children 12 years or older has been used; and
- patients either:
  - are hypersensitive to eformoterol; or
  - have developed a product related adverse event that resolved on cessation and recurred on re-challenge with Oxis Turbuhaler 6 µg; or
  - after a six week trial of Oxis Turbuhaler 6 µg (with doses of 12–24 µg/ day) failed to show evidence of improved asthma control.

III. Serevent MDI and spacer (with or without mask)
Subsidy is available in rare circumstances for patients with poorly controlled asthma aged 12 years and over, under the following criteria:
- have documented serious mental or physical* disability who are incapable of being taught to use the appropriate breath activated device; and
- at least three months of 750 µg or more daily of inhaled beclomethasone or budesonide (or 400 µg of fluticasone) for adults, or 400 µg or more daily inhaled beclomethasone or budesonide (or 200 µg of fluticasone) for children 12 years or older has been used.

Applications must be made on a PHARMAC approved form, which contains a free text box for “Turbuhaler failures” where the nature of the documented serious mental or physical disability is to be recorded.

*Hand grips for the Turbuhaler are available free of charge from AstraZeneca for patients with problems with manual dexterity.

### Inhaled beta-adrenoceptor agonists - nebuliser solutions

#### Low dose

- SALBUTAMOL - Available on a PSO
  - Nebuliser soln, 1 mg/ ml, 2.5ml

#### High dose

- SALBUTAMOL - Available on a PSO
  - Nebuliser soln, 2 mg/ ml, 2.5ml

### Inhaled anticholinergic agents - nebuliser solutions

#### Low dose

- IPRATROPIUM BROMIDE - Available on a PSO
  - Nebuliser soln, 250 µg/ ml, 1ml

#### High dose

- IPRATROPIUM BROMIDE - Available on a PSO
  - Nebuliser soln, 500 µg/ 2ml, 2ml

Inhaled beta-adrenoceptor agonist and anticholinergic agents - metered dose inhalers
FENOTEROL HYDROBROMIDE WITH IPRATROPIUM BROMIDE - Special Authority
Aerosol inhaler, 100 µg with ipratropium bromide, 40 µg/ dose
Special Authority - Retail pharmacy:
a) Approval for subsidy will be granted if:
   • the patient has been on the product prior to 1 August 1990 (when it was removed from the Pharmaceutical Schedule)
   • alternatives (salbutamol & terbutaline) have been tried
   • the patient has asthma or chronic obstructive airways disease (COAD).
b) The dose must be provided on the application.

Inhaled beta-adrenoceptor agonist and anticholinergic agents - nebuliser solution
SALBUTAMOL WITH IPRATROPIUM BROMIDE - Available on a PSO
Nebuliser soln, 2.5 mg with ipratropium bromide 0.5 mg/ 2.5 mlvial, 2.5ml

Beta-adrenoceptor agonists - injection
SALBUTAMOL
Inj 500 µg/ ml, 1ml - Available on a PSO

Theophylline derivatives
AMINOPHYLLINE
† Oral liq 25 mg/ ml - Retail pharmacy-specialist
Oral liquid is:
a) Retail pharmacy-specialist; and
b) Prescriptions must be written by a paediatrician or paediatric cardiologist; or
c) On the recommendation of a paediatrician or paediatric cardiologist.
Inj 25 mg/ ml, 10 ml - Available on a PSO.
APPENDIX 4: SUGGESTED CHECKLIST FOR ADULT ASTHMA CONSULTATIONS

The following three questions should be asked at every consultation and the response documented in the individual’s record:

1. How many doses of your reliever have you taken each day over the last week? (Record the mean/average number of doses per day).

2. Over the last 2 weeks, how many times have you been woken from sleep because of asthma symptoms such as wheezing or coughing, or needed to take your reliever medication? (Record the number of nights).

3. Over the last 2 weeks on how many days has your physical activity been limited by asthma? (Record the number of days).

Other useful screening questions

How many days have you had off from work or other daily activities due to asthma or chest problems in the last year?

Have you been admitted to hospital within the last 12 months for asthma?

Have you required any emergency nebuliser treatments in the last 12 months?

Have you required a course of corticosteroid tablets (prednisone) in the last 12 months?

Do you smoke at present?

What were your highest and lowest peak flow rates in the last year?
RECOMMENDED ADULT ASTHMA DATA FORM

Name: ___________________________  DOB: _____________  Sex: M / F

Ask the individual with which ethnic group they identify: __________________________

Current asthma status

PEFR:____________________________________

☐ Number of doses of reliever per day (average over the last 4 weeks)
☐ Number of courses of prednisone in last year
☐ Number of emergency nebuliser admissions in the last year
☐ Number of days off work/ limits on daily activity in the last year

Y/N Night waking?

Y/N Smoker? Number of attempts at quitting: ______________

Highest: _______________ and lowest: _______________ peak flows

Results of Spirometry (including date of test): __________________________

Exacerbations in previous 12 months: __________________________

Current medications and dose levels

SABA: ___________________________  LABA: ___________________________

ICS: ___________________________  Other (ALTA or theophylline): __________________________

Y/N Taking prescribed medication? Compliance/adherence: ☐ 80-100%  ☐ 50-80%  ☐ <50%

Y/N Inhaler technique adequate?

Y/N Understands what asthma is?

Asthma self-management plan

Y/N Has self-management plan?

Y/N Understands self-management plan?

Y/N Understands how to use devices?

Y/N Triggers identified (including sensitivity to house dust mites)?

Y/N Control of relevant environmental factors, eg, smoke or house dust mite exposure in sensitive individuals?

Y/N Understands use of medication?

Y/N Annual Influenza vaccine?

Y/N Skin testing indicated?

Y/N Understands how to recognise deterioration?

Y/N Goals of treatment discussed?

Y/N Individual’s concerns discussed?

Y/N Knows how to contact health services?

Y/N Knows how to manage exercise induced asthma?

Y/N Has other materials and resources?

Y/N Has other sources of information, eg, asthma societies?

Side effects of medication: ______________________________________

If adult with asthma is well – consider back-titrating ICS medication.

Date of next Plan review: ______________________________________

Signature: ______________________________________  Date: _____________

Copies of this checklist can be downloaded from NZGG’s website www.nzgg.org.nz
APPENDIX 5: EXAMPLES OF ASTHMA MANAGEMENT PLANS AND EDUCATIONAL RESOURCES, ASTHMA ORGANISATIONS

An asthma self-management plan should include the information shown in this example:

**ASTHMA MANAGEMENT PLAN OUTLINE**

Name: _______________________________ Date: ____________

**Peak Flow:**

- [ ] Okay
- [ ] Consider reviewing your treatment with your GP
- [ ] Get help now

Primary Health Care Nurse/ Doctor: ___________________________ Phone: _______________

Asthma Specialist: ___________________________ Phone: _______________

Nearest Medical Facility: ___________________________

Address: ___________________________________________

Phone: (Emergency) ______________ (Business) ______________

1. **Maintenance plan**
The following medications need to be taken every day:

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2a. **Episode treatment plan – chronic**
When the following early warning signs worsen over a period of _________ (time interval):

__________________________________________________________________________

__________________________________________________________________________

I should add the following medication and/or additional dosages:

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

if this does not relieve symptoms within _________ (time interval)
or if I need more than _________ treatments of _________ in 24 hours
or if I need a treatment of _________ within 2 hours of a previous treatment, then I should call my doctor.
2b. Episode treatment plan - acute

When the following symptoms appear suddenly:

I should add the following medication and/or additional dosages:

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If this does not relieve symptoms within ___________ (time interval)
or if I need more than ___________ treatments in 24 hours or if I need treatment within 2 hours of a previous treatment,

**I should call my doctor**

2c. Episode treatment plan - emergency

If my doctor is unavailable, I should take the following medication until help is obtained:

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If I have severe symptoms
(eg, not being able to talk, blue color of fingernails, lips or other parts of my body),
or if I am getting worse very fast,

**I need immediate medical help.**

*Call 111.*
A number of adult asthma self-management plans are available on-line. The following web sites have asthma plans freely downloadable:

- The Asthma and Respiratory Foundation of New Zealand have their Asthma Management Plans at: www.asthmanz.co.nz/
- The British National Asthma Campaign have the UK action plans available at www.actionasthma.co.uk/actionasthma/home/community.asp
- The American Asthma Education & Resource Council, based in California, have Asthma plans available at: home.earthlink.net/~claudiarn/asthma/plan.html

In addition, asthma self-management plans can be obtained from asthma support organisations in New Zealand such as the following:

<table>
<thead>
<tr>
<th>Society</th>
<th>Address</th>
<th>Tel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auckland Asthma Society</td>
<td>581 Mt Eden Road, Mt Eden, Auckland</td>
<td>(09) 630 2293</td>
</tr>
<tr>
<td>Canterbury Asthma Society</td>
<td>P O Box 13-091, Christchurch</td>
<td>(03) 366 5235</td>
</tr>
<tr>
<td>Gisborne &amp; East Coast Asthma Society</td>
<td>P O Box 797, Gisborne</td>
<td>(06) 868 5041</td>
</tr>
<tr>
<td>Hawkes Bay Asthma Society</td>
<td>P O Box 4043, Napier</td>
<td>(06) 835 0018</td>
</tr>
<tr>
<td>Kapiti Asthma Society</td>
<td>35 Martin Road, Paraparumu Beach</td>
<td>(04) 902 6855</td>
</tr>
<tr>
<td>Manawatu Asthma Society</td>
<td>P O Box 5164, Palmerston North</td>
<td>(06) 358 7491</td>
</tr>
<tr>
<td>Marlborough Asthma Society</td>
<td>P O Box 374, Blenheim</td>
<td>(03) 578 2387</td>
</tr>
<tr>
<td>Matamata Asthma Society</td>
<td>P O Box 8, Matamata</td>
<td>(07) 888 6233</td>
</tr>
<tr>
<td>Nelson Asthma Society</td>
<td>P O Box 450, Nelson</td>
<td>(03) 546 7675</td>
</tr>
<tr>
<td>Northland Asthma Society</td>
<td>1/15 Central Avenue, Whangarei</td>
<td>(09) 438 5205</td>
</tr>
<tr>
<td>North Otago Asthma Society</td>
<td>P O Box 16, Oamaru</td>
<td>(03) 434 7111</td>
</tr>
<tr>
<td>Otago Asthma Society</td>
<td>P O Box 5494, Dunedin</td>
<td>(03) 471 6167</td>
</tr>
<tr>
<td>Rotorua Asthma Society</td>
<td>P O Box 472, Rotorua</td>
<td>(07) 347 1012</td>
</tr>
<tr>
<td>Southland Asthma Society</td>
<td>480 Dee Street, Invercargill</td>
<td>(03) 214 2356</td>
</tr>
<tr>
<td>South Canterbury Asthma Society</td>
<td>P O Box 267, Timaru</td>
<td>(03) 688 5571</td>
</tr>
<tr>
<td>Taranaki Asthma Society</td>
<td>P O Box 186, New Plymouth</td>
<td>(06) 753 5105</td>
</tr>
<tr>
<td>Taupo Asthma Society</td>
<td>P O Box 595, Taupo</td>
<td>(07) 377 6015</td>
</tr>
<tr>
<td>Tauranga Asthma Society</td>
<td>P O Box 217, Tauranga</td>
<td>(07) 578 4602</td>
</tr>
<tr>
<td>Tu Kotahi Māori Asthma Society</td>
<td>22 Barnes Street, Seaview, Lower Hutt</td>
<td>(04) 939 4629</td>
</tr>
<tr>
<td>Waikato Asthma &amp; Respiratory Society</td>
<td>P O Box 7013, Hamilton East</td>
<td>(07) 839 6222</td>
</tr>
<tr>
<td>Waimate Asthma Support Group</td>
<td>24 Naylors Street, Waimate</td>
<td>(03) 689 8524</td>
</tr>
<tr>
<td>Waipara Asthma Society</td>
<td>P O Box 2097, Kurupuni, Masterton</td>
<td>(06) 377 1175</td>
</tr>
<tr>
<td>Wanganui Asthma Society</td>
<td>P O Box 790, Wanganui</td>
<td>(06) 345 2703</td>
</tr>
<tr>
<td>Wellington Regional Asthma Society</td>
<td>Pember House, 16 Hagley Street, Porirua</td>
<td>(04) 237 4520</td>
</tr>
<tr>
<td>Whakatane Asthma &amp; COPD Support Group</td>
<td>105 Woodlands Road, Opotu</td>
<td>(07) 315 6151</td>
</tr>
</tbody>
</table>
APPENDIX 6: RESEARCH GAPS

In the process of development of this guideline, the team found that there was insufficient evidence of adequate quality on a number of issues. These are listed below.

Non-pharmaceutical management of chronic asthma
There is a need for well operationalised research to determine how to effectively improve adherence to treatment and management regimes.

Management of asthma in the Māori community
More rigorously controlled studies are needed to determine the best approaches to improving the care and treatment of asthma in the Māori community.

Non-pharmaceutical and complementary therapies
- The extent and impact of the use in New Zealand of alternative and complementary therapies for asthma has yet to be determined
- There is a need for well operationalised research to determine the comparative and long term effects of immunotherapy
- Studies of particular complementary therapies (acupuncture; herbal remedies; homeopathy; hypnotism in susceptible subjects; and some breathing exercises) showed indications that more carefully controlled and targeted research on their use in asthma may be justified.

Secondary prevention of asthma in adults
Well operationalised research is needed to:
- determine the degree of benefit of barrier methods in adults with house dust mite allergic asthma
- identify any potential benefit of other secondary prevention measures in all adults with asthma.
APPENDIX 7: SEARCH STRATEGY FOR THE SYSTEMATIC REVIEW OF ASTHMA

Search methodology

Search strategy
Searches have been restricted to information from 1997 onwards, in all languages. Original searches were carried out in December 2000. An update of Premedline, Current Contents and the Science Citation Index is planned for the end of March 2001.

A very broad combined search of the Premedline, Medline, Embase, Current Contents, and Cinahl databases for papers on any aspect of asthma in New Zealand will be completed by the end of January 2001.

Principal sources of information
The following databases were searched using the search strategies outlined below:

Bibliographic databases
- Medline
- Embase
- Current Contents
- Science Citation Index
- Cinahl
- Cochrane Library Controlled Trials Register
- Index New Zealand.

Review databases
- Cochrane Library Systematic Reviews & Protocols
- Database of Abstracts of Reviews of Effectiveness
- NHS Economic Evaluation Database
- Best Evidence.

Library catalogues
- New Zealand Ministry of Health library
- New Zealand Bibliographic database - Te Puna
- US National Library of Medicine
- World Health Organisation.

Websites
- Health Canada
- US Centers for Disease Control
- British Thoracic Society
- EGuidelines (UK)
- University of Dundee Asthma Research Unit (UK General Practice Airways Group)
- UK Department of Health publications
- Meta-register of Controlled Trials
- TRIP - Turning Research into Practice
- Health Evidence Bulletins Wales
- OMNI - Organised Medical Networked Information
- European Federation of Asthma and Allergy Associations
- GINA - Global Information Network on Asthma
- Canadian Office for Health Technology Assessment
- Canadian Network for Asthma Care
- Canadian Lung Association
• Canadian Thoracic Society
• Asthma Society of Canada
• ClinicalTrials.gov
• American Academy of Allergy Asthma and Immunology
• JAMA Asthma Information Center - Physicians Section
• US National Heart, Lung, and Blood Institute
• US Asthma Clinical Research Network
• US National Institute of Allergy and Infectious Diseases
• Thoracic Society of New Zealand and Australia
• Australian Department of Health & Aged Care
• Ministerial Asthma Working Party.

Other
• Citation searching retrospective: reference sections of key papers will be scanned for relevant publications
• Citation searching prospective: key papers will be searched via the Science Citation Index to locate subsequent publications which have cited them.

Note that hand searching of journals, contacting of manufacturers, or contacting of authors for unpublished research will not be undertaken during the search process.

Major search terms used
• Index terms from Medline (MeSH headings): asthma, asthma-drug therapy, anti-asthmatic agents, bronchodilator agents, randomized controlled trials, controlled clinical trials, meta-analysis, guidelines, practice guidelines, double-blind method, single-blind method, comparative study, treatment outcome
• Index terms from Embase: asthma, asthma-drug therapy, randomized controlled trial, drug comparison, double-blind procedure, single-blind procedure, meta-analysis
• Additional keywords used (not standard index terms): systematic review, systematic overview, effectiv*, efficacy
• Keywords used for exclusions: child*, infant*, pediatric*, paediatric* as title words when adult* was not also in the title; copd, chronic obstructive, rhinitis, as title words when asthma was not also in the title.

Search filters used to identify randomized controlled trials, meta-analysis, and guidelines in the literature were adapted from those produced by the Center for Reviews and Dissemination at the University of York.

Inclusion criteria
Studies published in English, French and German language from 1997 onwards (final search completed 30 March 2001) are included. The population of interest is defined as adults with acute or chronic asthma, including aspirin and exercise induced asthma. A strict definition of adult based on age inclusion criteria has been avoided. Where both children and adults make up the study population these studies have been included.

Studies conducted in hospital, emergency department, A & M clinic, general practitioner and pharmaceutical usage settings are included. Only Randomized Controlled Trials and Systematic Reviews and Meta-Analysis (as a subset of Systematic reviews) of Randomized Controlled Trials are included. Only studies conducted using double blinding or single blinding if no double blinding studies in a particular class comparison or open if no double blinding or single blinding studies in a particular class comparison are included.

Only studies with an enrollment sample size of 30 patients or more have been included. This criteria was applied to ensure a higher degree of statistical power and to account for patient attrition during the study duration.

(In using the evidence the team decided to take a cascade approach relating to the level of available evidence for each question (intervention)). In essence the NZHTA would need to critically appraise only the higher level studies and scan the abstracts for lower level studies to see if there was discordance. If so, these lower level studies would also need to be appraised and summarised

1. Level One: use recommendations from Cochrane reviews where available. Trials of larger than 100 subjects published after the review would be scanned to see if there was any discordance with the Cochrane review and critically appraised only if so
2. Level Two: In the absence of a Cochrane review if there are 3 or more trials with n > 100, these would be critically reviewed. The group would scan trials with n > 50 to see if there was any significant discordance
3. Level Three: in absence of above and if 3 or more trials with n > 50 these would be critically reviewed with a scan of level four
4. Level four in absence of above critical review of trials \( n > 30 \).

Drug class interventions that Pharmac have or propose to license in New Zealand will be included:

- Anticholinergic/including oxitropium
- \( \beta_2 \)-agonist short/long-acting oral/inhaled
  - Salbutamol
  - Salmeterol
  - Formoterol
  - Albuterol
  + others
- Steroid
- Leukotriene antagonist
- Theophylline
- Nedocromil
- Acupuncture
- Immunotherapy
- Device
- CFC/HFA propellant (we considered that there are patient-related outcomes (around issues of relative deposition in lung and its consequences).

Several relevant interventions have been subjected to Cochrane Reviews. Topics covered include immunotherapy, acupuncture, leukotriene receptor antagonists compared to inhaled corticosteroids, corticosteroids in acute and post-acute asthma, holding chambers versus nebulisers in acute asthma, long-acting \( \beta_2 \)-agonists versus theophylline and nedocromil for preventing exercise-induced bronchoconstriction.

The studies covered in these reviews have been excluded from individual appraisal. Only the Cochrane systematic reviews themselves have been appraised.

Studies with all or some of the following study outcome endpoints have been included. These relate to commonly assessed POEMs.

Endpoints:
- Relapse
- Rescue medicine use
- Symptom ratings
- Quality of life
- Spirometric outcomes (eg. FEV\(_1\), PEFR)
- Methacholine challenge
- Exercise challenge
- Time to onset of effect and maximal effect
- Cost
- Safety endpoints – cortisol, pulse, BP, tremor
- Health care usage – hospital admission, ED attendance, length of stay.

Exclusion Criteria

Studies including:
- Any patients with COPD
- Only children (classified as 12 years or younger or article using the term child or children or paediatric)
- A focus on asthma in pregnancy.

Search strategies for asthma therapeutics

Medline One
1. exp asthma/dt (2876)
2. randomized controlled trials/ or randomized controlled trial.pt. (44090)
3. controlled clinical trials/ or controlled clinical trial.pt. (9382)
Medline Two
1 exp ASTHMA/ci, nu, dh, dt, px, rt, rh, su, th [Chemically Induced, Nursing, Diet Therapy, Drug Therapy, Psychology, Radiotherapy, Rehabilitation, Surgery, Therapy] (4549)
2 limit 1 to (clinical trial or clinical trial, phase iv or controlled clinical trial or meta analysis or multicenter study or randomized controlled trial) (1051)
3 child:.ti. (36346)
4 2 not 3 (856)
animal/ (437966)
human/ (1090130)
5 and 6 (137484)
4 and (6 or 7) (855)
research/ (7508)
Clinical Protocols/ (1880)
feasibility studies/ (3750)
reproducibility of results/ (27183)
research design/ (5737)
double-blind method/ (13842)
patient selection/ (5489)
random allocation/ (5354)
sample size/ (703)
or/9-17 (68066)
epidemiologic research design/ (185)
crossover studies/ (4948)
matched pair analysis/ (540)
sample size/ (703)
sensitivity.mp. and ‘specificity’/ [mp=title, abstract, registry number word, mesh subject heading] (12423)
Single-Blind Method/ (2297)
or/19-24 (20555)
clinical trials/ (9996)
Clinical Trials, Phase IV/ (20)
controlled clinical trials/ (855)
multicenter trials/ (1496)
randomized controlled trials/ (7360)
or/26-30 (18323)
placebos/ (2285)
comparative study/ (148426)
“Outcome Assessment (Health Care)”/ (5040)
treatment outcome/ (55175)
medical futility/ (300)
treatment failure/ (3137)
or/32-37 (201054)
random:.mp. (67238)
single-blind:.mp. (2622)
double-blind:.mp. (15487)
three-blind:.mp. (17)
double-dummy:.mp. (217)
mask:.mp. (5078)
sham.mp. (5564)
placebo:.mp. (15900)
control: trial:.mp. (7404)
efficacy.mp. (40563)
effectiveness.mp. (19336)
or/39-49 (129476)
8 and 25 and 38 (110)
8 and (25 or 31 or 38 or 50) (748)
52 not 51 (638)
8 and 18 (450)
8 and 25 (218)
8 and 31 (14)
57 8 and 38 (420)
58 8 and 50 (685)
59 55 not 54 (52)
60 56 not 55 (14)
85 61 from 54 keep (SELECTED REFERENCES)

Embase
1 exp ASTHMA/pc, rt, dm, rh, dt, su, th [Prevention, Radiotherapy, Disease Management, Rehabilitation, Drug Therapy, Surgery, Therapy] (15382)
2 Major Clinical Study/ (503543)
3 Clinical Study/ (1085)
4 Clinical Article/ (546908)
5 Controlled Study/ (1080347)
6 PREVENTION/ (9035)
7 THERAPY/ (9171)
8 or/2-7 (1794449)
9 1 and 8 (6810)
10 limit 9 to yr=1997-2001 (2459)
11 (child: or pediatric: or infant:).ti. (141191)
12 10 not 11 (1985)
13 animal/ (6599)
14 human/ (2803280)
15 13 and 14 (11153)
16 12 and (14 or 15) (1897)
17 Controlled Study/ (1080347)
18 Case Control Study/ (5166)
19 randomized controlled trial/ (49059)
20 or/17-19 (1085585)
21 drug comparison/ (1788)
22 Clinical Trial/ (184432)
23 multicenter study/ (17496)
24 Phase 4 Clinical Trial/ (251)
25 or/21-24 (186669)
26 Major Clinical Study/ (503543)
27 medical research/ (20276)
28 clinical research/ (6842)
29 drug research/ (6605)
30 or/27-29 (32559)
31 Evidence Based Medicine/ (3327)
32 meta-analysis/ (10677)
33 outcomes research/ (7617)
34 or/31-33 (20997)
35 RANDOMIZATION/ (2624)
36 crossover procedure/ (10029)
37 double blind procedure/ (32575)
38 single blind procedure/ (2880)
39 placebo/ (24698)
40 or/35-39 (55833)
41 triple-blind.mp. (42)
42 double-dummy.mp. (646)
43 mask:.mp. (14340)
44 sham.mp. (15088)
45 placebo:.mp. (56007)
control: trial:.mp. (59723)
efficacy.mp. (186786)
effectiveness.mp. (62386)
or/41-48 (324858)
16 and (20 or 21 or 25 or 26 or 30 or 34 or 40 or 49) (1723)
limit 50 to yr=1997-2001 (1723)
16 and (20 or 21 or 25 or 26 or 30 or 34 or 40) (1669)
limit 52 to yr=1997-2001 (1669)
16 and 20 (1229)
16 and 21 (0)
16 and 25 (986)
16 and 26 (881)
16 and 30 (4)
16 and 34 (69)
16 and 40 (669)
16 and 49 (1010)
or/54-61 (1723)
exp asthma/dt (13531)
63 and 8 (6057)
64 not 11 (4972)
66 and (14 or 15) (4807)
66 and (20 or 21 or 25 of 26.mp. or 30 or 34 or 40 or 49) [mp=title, abstract, heading word, trade name, manufacturer name] (3437)
limit 67 to yr=1997-2001 (1313)
from 51 keep (SELECTED REFERENCES)

Embase Two
1 exp ASTHM A/pc, rt, dm, rh, dt, su, th [Prevention, Radiotherapy, Disease Management, Rehabilitation, Drug Therapy, Surgery, Therapy] (15382)
2 randomized controlled trial/ (49059)
3 Evidence Based Medicine/ (3327)
4 meta-analysis/ (10677)
5 RANDOMIZATION/ (2624)
6 double blind procedure/ (32575)
7 single blind procedure/ (2880)
8 placebo/(24698)
9 triple-blind.mp. (42)
10 double-dummy.mp. (646)
11 mask:.mp. (14340)
12 sham.mp. (15088)
13 placebo:.mp. (56007)
14 control: trial:.mp. (59723)
15 controlled clinical trial.mp. (1824)
16 (systematic: adj review:.mp. (1701)
17 (systematic: adj overview).mp. (106)
18 practice guideline/. (21230)
19 or/2-18 (161913)
20 1 and 19 (3232)
21 limit 20 to yr=1997-2000 (1661)
22 (child: or toddler or infant:.ti. (127485)
23 adult:.ti. (43216)
24 22 and 23 (3236)
25 22 not 24 (124249)
(rhinitis or eczema) not asthma).ti. (2997)
26 21 not 25 (1421)
27 (healthy volunteer: or healthy subject: or human volunteer:).ti. (5584)
28 26 not 27 (1418)
29 from 30 keep (SELECTED REFERENCES)
30 28 not 29 (1415)
31 (paediatric: or pediatric: or rhinitis or chronic obstructive or copd or child:).ti,ab. (221742)
32 31 or 33 or 35 (306)
33 (child: or paediatric: or pediatric:).jw. (105360)
34 38 and (39 or 40) (45)
35 from 31 keep (SELECTED REFERENCES)
36 38 not 42 (430)
37 from 43 keep (SELECTED REFERENCES)
38 Embase Three
39 randomized controlled trial/ (49243)
40 meta-analysis/ (10712)
41 RANDOMIZATION/ (2628)
42 double blind procedure/ (32653)
43 single blind procedure/ (2890)
44 placebo/ (24762)
45 triple-blind.mp. (42)
46 double-dummy.mp. (647)
47 mask:.mp. (14369)
48 sham.mp. (15119)
49 placebo:.mp. (56121)
50 control: trial:.mp. (59936)
51 controlled clinical trial.mp. (1827)
52 (systematic: adj review:).mp. (1712)
53 (systematic: adj overview).mp. (106)
54 practice guideline/ (21364)
55 or/1-16 (160253)
56 asthma/dt (12762)
57 limit 19 to yr=1997-2000 (1443)
58 letter:.ti. (26037)
59 case report/ (430369)
60 or/21-23 (590898)
61 20 not 24 (1395)
62 (paediatric: or pediatric: or child:).jw. (105679)
63 26 not 25 (1288)
64 (paediatric: or pediatric: or child:) and adult:.ti. (3231)
65 (paediatric: or pediatric: or child:).ti. (119959)
66 29 not 28 (116728)
67 27 not 30 (1133)
68 (rhinitis or copd or chronic obstructive) and asthma:.ti. (526)
(chronic obstructive or copd or rhinitis).ti. (6131)
33 33 not 32 (5605)
34 31 not 34 (1116)
35 limit 35 to yr=2000 (221)
36 limit 35 to yr=1999 (318)
37 limit 35 to yr=1998 (300)
38 limit 35 to yr=1997 (278)
39 from 36 keep (SELECTED REFERENCES)
40 from 37 keep (SELECTED REFERENCES)
41 from 38 keep (SELECTED REFERENCES)
42 from 39 keep (SELECTED REFERENCES)
43 Cinahl

1 exp ASTHMA/dt, th [Drug Therapy, Therapy] (1561)
2 Double-Blind Studies/ (1712)
3 Random Assignment/ (3234)
4 placebos/ (968)
5 random sample/ (4022)
6 simple random sample/ (151)
7 Stratified Random Sample/ (704)
8 systematic random sample/ (53)
9 random:.mp. (14963)
10 single-blind:.mp. (510)
11 double-blind:.mp. (2059)
12 triple-blind:.mp. (2)
13 double-dummy:.mp. (27)
14 mask:.mp. (737)
15 sham.mp. (203)
16 placebo:.mp. (2168)
17 (control: adj2 trial:).mp. [mp=title, cinahl subject heading, abstract, instrumentation] (2586)
18 or/2-17 (17997)
19 1 and 18 (201)
20 limit 19 to yr=1997-2000 (145)
21 (child: or infant: or pediatric).ti. (28390)
22 20 not 21 (120)
23 from 22 keep (SELECTED REFERENCES)

Current Contents

asthma.mp. [mp=abstract, title, author keywords, keywords plus]
double blind:.ti,ab.
meta-analy:.ti,ab.
(systematic: adj (review or overview)).ti,ab.
randomized controlled trial:.ti,ab.
controlled clinical trial:.ti,ab.
or/2-6
1 and 7
limit 8 to yr=1997-2000
(child: or paediatric or pediatric).ti.
9 not 10
from 11 keep (SELECTED REFERENCES)
from 11 keep (SELECTED REFERENCES)
12 or 13
from 11 keep (SELECTED REFERENCES)
from 11 keep (SELECTED REFERENCES)
14 or 15 or 16
11 not 17
(child: or infant: or pediatric: or paediatric:).ti,ab.
18 and 19
from 20 keep (SELECTED REFERENCES)
18 not 21

Combined Premedline/Medline/Embase/Current Contents Cinahl – broad New Zealand search – planned
1 exp asthma/ (52742)
2 asthma.mp. (82944)
3 1 or 2 (83257)
4 new zealand/ or new zealand.mp. (30727)
5 new zealand.in. (57602)
6 4 or 5 (77006)
7 3 and 6 (1343)
8 limit 7 to yr=1997-2000 (691)
9 remove duplicates from 8 (355)
10 (letter or news).pt. (652061)
11 9 not 10 (330)
12 case report/ or case report.mp. (647075)
13 11 not 12 (325)
14 (child: or infant: or pediatric: or paediatric:).ti. (365724)
15 13 not 14 (265)

Cochrane Library Controlled Trials Register
ASTHMA:ME
ASTHMA:TI
#1 OR #2
CHILD OR PEDIATRIC* OR PAEDIATRIC*:TI
#3 NOT #4
LIMIT TO YR 1997-2000

Review databases: Cochrane Library Systematic Reviews & Protocols, DARE, HTA, NHS EED, Best Evidence
Because these databases are small and of such high quality they were searched simply using the word asthma then sifted manually for relevant references

Other databases and sources
Other databases and sources without indexing were searched using combinations of the headings and textwords from the above strategies in simple, iterative searches such as:
Asthma AND guideline*
Asthma NOT (pediatric OR paediatric OR child* OR infant* OR copd OR chronic obstructive OR rhinitis)
Scope of Systematic Review of Asthma – self-management and education
The development of this systematic review protocol involved consultation between the NZHTA and the asthma education and self-management sub-committee of the Asthma Working Group.

Search methodology
Search strategy
Searches were restricted to information published from 1st January 1998 onwards, in all languages. Original searches were carried out in May 2001.

Principal sources of information
The following databases were searched using the search strategies outlined:
Bibliographic databases
- Medline
- Embase
- Current Contents
- Science Citation Index
- Cinahl
- Cochrane Library Controlled Trials Register
- Index New Zealand
- Psychinfo
- Eric.

Review databases
- Cochrane Library Systematic Reviews & Protocols
- Database of Abstracts of Reviews of Effectiveness
- NHS Economic Evaluation Database
- Best Evidence.

Library catalogues
- New Zealand Ministry of Health library
- New Zealand Bibliographic database - Te Puna
- US National Library of Medicine
- World Health Organisation.

Websites
- Health Canada
- US Centers for Disease Control
- British Thoracic Society
- EGuidelines (UK)
- University of Dundee Asthma Research Unit
- UK General Practice Airways Group
- UK Department of Health publications
- Meta-register of Controlled Trials
- TRIP - Turning Research into Practice
- Health Evidence Bulletins Wales
- OMNI - Organised Medical Networked Information
- European Federation of Asthma and Allergy Associations
- GINA - Global Information Network on Asthma
- Canadian Office for Health Technology Assessment
- Canadian Network for Asthma Care
- Canadian Lung Association
- Canadian Thoracic Society
- Asthma Society of Canada
- ClinicalTrials.gov
- American Academy of Allergy Asthma and Immunology
- JAMA Asthma Information Center - Physicians Section
- US National Heart, Lung, and Blood Institute
- US Asthma Clinical Research Network
- US National Institute of Allergy and Infections Diseases
- Thoracic Society of New Zealand and Australia
- Australian Department of Health & Aged Care
- Ministerial Asthma Working Party.
Note: hand searching of journals, contacting of manufacturers, or contacting of authors for unpublished research was not undertaken during the search process.

**Major search terms used**
- Publication types searched on Medline (additional to above index terms) were randomized controlled trial, controlled clinical trial, meta-analysis, guideline
- Index terms from Embase: asthma, self care, patient education, health education, randomized controlled trial, clinical trial, randomization, meta-analysis, practice guideline
- Additional keywords used (not standard index terms): systematic review, systematic overview, self care, self manage*, cluster, random*, action plan, action plans
- Keywords used for exclusions: child*, pediatr*, paediatr* as title words when adult* was not also in the title

Search filters used to identify randomized controlled trials, meta-analyses, and guidelines in the literature were adapted from those produced by the Center for Reviews and Dissemination at the University of York.

**Study inclusion criteria**
Studies published in English, French and German language from 1998 onwards are included. The population of interest is defined as adults with acute or chronic asthma. A strict definition of adult based on age inclusion criteria has been avoided. Where both children and adults make up the study population these studies have been included.

Studies conducted in hospital, emergency department, outpatient clinic, general practitioner and community settings are included. Only randomised controlled trials are included. Systematic reviews and meta-analyses (as a subset of systematic reviews) of randomised controlled trials were to be included if the researchers searched Medline and at least one other database. No relevant reviews or meta-analyses were found.

The interventions of interest were:
- asthma education of all types
- patient self-management with written action plans using self-monitoring, regular review or optimal self-management
- patient self-management by PEFR monitoring compared with symptom monitoring.

Asthma education intervention studies were not conducted using double blinding. Such blinding is difficult to achieve in educational settings. Instead single blinding was considered appropriate where outcome assessment was done blind to group allocation. True placebo comparison is also difficult to achieve in educational intervention study settings because of ethical considerations. In most studies usual care from a medical practitioner involving some limited level of education was used in the control group.

**Study exclusion criteria**
Studies were excluded if they included:
- only patients with Chronic obstructive pulmonary disease (COPD)
- only patient compliance (medication, device use) outcomes
- only children (classified as 12 years or younger or an article using the term ‘child’ or ‘children’ or ‘paediatric’ or ‘pediatric’)
- an economic evaluation/cost-benefit analysis alone
- small patient numbers (n < 30), major methodological problems, non-RCT, significant absence of study methodology
- letters, non-systematic reviews, editorials and comments were also excluded.

**Interventions**
Following is a list of the main systematic review comparisons between different asthma education and self-management interventions:
- Asthma education with patient self-management (information only) compared with usual care
- Asthma education with patient self-management (self-monitoring and regular review) compared with usual care
- Asthma education with patient self-management (optimal self-management) compared with usual care
- Asthma education with patient self-management (self-monitoring only) compared with usual care
- Asthma education with patient self-management using PEFR monitoring compared with symptom monitoring

These interventions have been subjected to Cochrane Reviews. Topics covered include written action plans, self-management using PEFR or symptoms, regular medical review, asthma education including information only interventions.

The studies covered in these reviews have been excluded from individual appraisal, being pre 1998. The Cochrane systematic reviews themselves should be regarded as high quality appraised literature.
Patient outcomes

Studies with all or some of the following outcome measures have been included:

- hospital admissions
- rescue medicine use
- symptom ratings/peak flow diary
- quality of life
- spirometric outcomes (eg, FEV1, PEFR)
- ED visits
- days lost from school/work
- unscheduled doctors visits.

Study selection

Studies were selected for appraisal using a two-stage process. Initially the titles and abstracts (where available) identified from the search strategy were scanned and excluded as appropriate. The full text articles were retrieved for the remaining studies and these were appraised if they fulfilled the study selection criteria outlined above.

There were 281 studies identified by the search strategy. Thirty-nine full text articles were obtained after excluding studies based on examination of the search titles and abstracts. A further 21 of these full text articles did not fulfil the inclusion criteria. Therefore 18 articles were fully appraised and are included in this report.

Scope of systematic review of asthma diagnosis

The development of this systematic review protocol involved extensive consultation between NZHTA and the Diagnosis Subcommittee of the Asthma Working Group of the New Zealand Guidelines Group.

Search methodology

Search strategy

Searches were restricted to information published from 1st January 1997 onwards, in English. Original searches were carried out in January 2001. Infants and children were excluded. Chronic obstructive respiratory disease was also excluded.

An additional very broad combined search of the Pre-Medline, Medline, Embase, Current Contents, and Cinahl databases for papers on any aspect of asthma in New Zealand was also completed in March 2001.

Principal sources of information

The following databases were searched using the search strategies outlined:

Bibliographic databases

- Medline
- Embase
- Cinahl
- Current Contents
- Science Citation Index

Review databases

- Cochrane Library
- Best Evidence
- Centre for Reviews & Dissemination databases.

Library catalogues

- New Zealand Ministry of Health library
- New Zealand Bibliographic database - Te Puna
- US National Library of Medicine
- World Health Organisation.

Websites

- Health Canada
- US Centers for Disease Control
Major search terms used

- Index terms from Medline (MeSH headings): asthma, diagnosis, asthma-diagnosis-differential, sensitivity and specificity, forced expiratory volume, peak expiratory flow rate, hay fever, rhinitis, cough, dyspnea, eczema
- Index terms from Embase: asthma, diagnosis, asthma-diagnosis, differential diagnosis, forced expiratory volume, peak expiratory flow rate, cough, dyspnea, eczema, hay fever, rhinitis
- Additional keywords used: (not standard index terms): short* near breath*, dyspnoea, wheeze, tight* near chest, allerg*, atop*
- Keywords used for exclusions: child*, infant*, paediatric* or pediatric* [as title words or words in journal titles], chronic obstructive, coad, copd [as title words], asthma-chemically induced.

Study inclusion criteria

Studies published in English language from 1997 onwards are included. The population of interest is defined as adults with acute or chronic asthma, including aspirin, exercise and occupational induced asthma. A strict definition of adult based on age inclusion criteria has been avoided. Where both children and adults make up the study population these studies have been included.

Studies appraised were restricted to systematic reviews or original research appearing in the published literature.

Studies were included if they compared the validity of various symptoms, signs and investigations (henceforth referred to in aggregate as “screening tests”) between people with and without asthma. The screening tests of interest were:

- cough
- wheeze
- dyspnoea
- past history of asthma
- family history of asthma
• allergen induced symptoms
• peak expiratory flow rate (PEFR)
• spirometry
• challenge testing
• sputum eosinophils
• sputum eosinophil cationic protein (ECP)
• serum ECP
• blood eosinophils
• serum IgE

Models that included the above screening tests were also included in this review.

Study exclusion criteria
Studies were excluded if they only included children (classified as 12 years or younger or an article using the term ‘child’ or ‘children’ or ‘paediatric’ or ‘pediatric’). Letters, non-systematic reviews, editorials and comments were also excluded.

Patient outcomes
When possible, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were presented in the results. Other measures of effect were used as necessary.

Study selection
Studies were selected for appraisal using a two-stage process. Initially the titles and abstracts (where available) identified from the search strategy were scanned and excluded as appropriate. The full text articles were retrieved for the remaining studies and these were appraised if they fulfilled the study selection criteria outlined above.

There were 1402 studies identified by the search strategy. Ninety-six full text articles were obtained after excluding studies from the search titles and abstracts. A further 62 of these full text articles did not fulfil the inclusion criteria. Therefore, 34 articles were fully appraised and are included in this report.

Qualitative research in adult asthma management
SCOPE All aspects of patient management in primary and outpatient care, particularly where it impacts on compliance, improved quality of life, and patient satisfaction.

Information on methodologies was excluded
Information in English from 1990 onwards is included

This work is an NZHTA Information Package ie, a comprehensive search of the published literature and selected grey literature sources on the topic described above according to the NZHTA search protocol.

Sources searched

Bibliographic databases
• Medline
• Embase
• Current Contents
• Cinahl
• Web of Science
• Psychinfo
• Index New Zealand.

Library catalogues
• New Zealand bibliographic database – Te Puna
• NZHTA In-house Collection.

Websites
New Zealand
• Te Puna web directory
• Ministry of Health
• The Thoracic Society of Australia and New Zealand
• The Asthma and Respiratory Foundation of New Zealand

Great Britain
• Organised Networked Medical Information (OMNI)
• Department of Health
• National Asthma Campaign
• British Lung Foundation

Australia
• Asthma Australia
• Australia Lung Foundation
• Cooperative Research Centre for Asthma
• Institute of Respiratory Medicine
• National Asthma Campaign

United States
• American Lung Association
• Agency for Healthcare Research and Quality
• American Academy of Allergy Asthma and Immunology
• American Thoracic Society
• Asthma and Allergy Foundation of America

Canada
• Health Canada
• Asthma Society of Canada
• Canadian Lung Association
• Canadian Medical Association
• Canadian Network of Asthma Care.

Search engines
• Google
• SearchNZ.

Combined references from bibliographic database searches
• Medline
• Embase
• Current Contents
• Cinahl
• Psychinfo
• Web of Science
• Combined file of references from bibliographic databases.

References with abstracts where available from the searches of Medline, Embase, Cinahl, Psychinfo, Web of Science, and Current Contents databases. The references have been downloaded into a bibliographic package (Endnote) so that duplicates can be identified and deleted. Please note that occasional corruption of references occurs during this process which is difficult to identify. If any such instances prevent locating a particular reference, please contact Margaret Paterson at NZHTA (email: margaret.paterson@chmeds.ac.nz)

• References from Index New Zealand

References from the Index New Zealand database. This database provides coverage of some sources not included in the international databases.

Section three: Internet search
Information taken from the internet search. Documents are arranged by country of origin: New Zealand, Australia, Canada, Great Britain, and the USA.

Not in electronic file.
Please note particularly that in searching “grey” literature within the timeframe for a Level One search it is not possible to state that full coverage has been made.

Section four: Full text articles supplied

Full text articles, chosen from the studies mentioned in the evidence-based reviews. The articles are limited to those which were easily available from local resources. They do not necessarily represent the best or only useful references from the search.
GLOSSARY

Acupuncture: The Chinese therapeutic process where needles are inserted to specific bodily locations to alleviate symptoms.


Alexander technique: A CAM therapy: a method purporting to improve ease and freedom of movement, balance and co-ordination; and to teach constructive self-awareness. Also used for rehabilitation, pain management and stress relief.

Aminophylline: A theophylline-related bronchodilator.

Anticholinergics: Agents that inhibit the cholinergic (parasympathetic) system.

Antileukotriene agents: Selective leukotriene receptor antagonists.

Atopy: A tendency to respond to allergic stimuli, probably familial (ie. with a genetic basis). This response can be localised to one bodily area or generalised and may include: rash, itching, hives, swelling, difficulty breathing, and/or low blood pressure.

Back-titrate: To determine the optimum dose of medication following introduction of a high dose by means of a gradual, stepwise reduction and observation of effect.

BiD: (Latin - *bis in die*) Twice a day.

Bradycardia: A slowness of the heart beat, as evidenced by slowing of the pulse rate to less than 60 beats per minute.

Breathing exercises: Any therapy based on regulation of breathing, such as yogic breathing, Buteyko, etc.

Bronchial hyperresponsiveness (also termed bronchial hyperreactivity): Tendency of the smooth muscle of the tracheobronchial tree to contract more intensely in response to a given stimulus than it does in normal individuals. This condition is present in virtually all symptomatic patients with asthma. The most prominent manifestation of this smooth muscle contraction is a decrease in airway calibre that can be readily measured in the pulmonary function laboratory.

Bronchiectasis: Chronic dilation of the bronchi (the larger air passages in the lungs), marked by daily cough and sputum production.

Bronchodilator: A medication that acts to dilate (enlarge) the lumen of the airway to allow the unrestricted passage of air. These medications are commonly given to those with asthma who manifest wheezing.

Corticosteroids: A group of synthetic hormones including prednisone, prednisolone, methylprednisolone and used in the treatment of asthma.

Cromones: Medications that can help to reduce allergen-induced responses following short term exposure.

Cysteinyl leukotrienes: A family of hydroxyeicosatrienoic (HETE) acid derivatives in which the lipid moiety is conjugated to cysteine. Members of the group are potent pharmacological mediators of inflammation.

Eicosanoids: A class of endogenous, unsaturated fatty acids derived from arachidonic acid. They include prostaglandins, leukotrienes, thromboxanes, and hydroxyeicosatetraenoic acid compounds (HETE).
**Eosinophil:** Polymorphonuclear leucocyte (granulocyte) of the myeloid series, of which the granules stain red with eosin. Typically seen in the airways of adults with asthma.

**Fluticasone:** Fluticasone propionate: an inhaled corticosteroid.

**Homeopathy:** The art of curing, founded on resemblances; the theory and its practice that disease is cured (tuto, cito, et jucunde) by remedies which produce on a healthy person effects similar to the symptoms of the complaint under which the patient suffers, the remedies being usually administered in minute doses. This system was founded by Dr. Samuel Hahnemann, and is opposed to allopathy, or heteropathy.

**Hypotension:** Abnormally low blood pressure.

**ICS:** Inhaled corticosteroid medication.

**Immunotherapy:** Immunotherapy is any form of treatment that uses the body’s natural abilities that constitute the immune system to fight infection and disease or to protect the body from some of the adverse effects of treatment. In this guideline, the specific immunotherapy referred to is desensitisation, which is stimulation of the immune system with gradually increasing doses of the substances to which a person is allergic, the aim being to modify or stop the allergy “war” (by reducing the strength of the IgE and its effect on the mast cells). This form of treatment is very effective for allergies to pollen, house dust mites, cats, and especially stinging insects (e.g., bees, hornets, wasps, ants). Allergy immunotherapy usually takes 6 months to a year to become effective and injections (“shots”) are usually required for 3-5 years.

**Ipratropium:** Ipratropium Bromide: anticholinergic bronchodilator.

**Long-acting beta-agonists:** These bronchodilators stimulate beta-adrenergic receptors to widen the airways. Bronchodilators that act on all beta-adrenergic receptors, such as adrenaline, cause side effects such as rapid heartbeat, restlessness, headache, and muscle tremors. Bronchodilators that act mainly on ß₂-adrenergic receptors, which are found primarily on cells in the lungs, have little effect on other organs.

Longer-acting bronchodilators are used for prevention rather than for acute attacks of asthma.

**Manual therapies:** Includes physiotherapy, respiratory therapy, chiropractic and osteopathy.

**MDI:** Metered dose inhaler.

**Medsafe:** The New Zealand Medicines and Medical Devices Safety Authority. It is a business unit of the Ministry of Health and is the authority responsible for the regulation of therapeutic products in New Zealand [www.medsafe.govt.nz](http://www.medsafe.govt.nz)

**Methacholine:** Methacholine bromide: A cholinergic agonist with predominantly muscarinic effects.

**Montelukast:** Montelukast sodium: selective leukotriene receptor antagonist.

**Nebulisation:** Conversion to a spray/mist by compressed air through a jet nebuliser.

**NSAID:** Non steroidal anti-inflammatory drug.

**PEFR:** Peak expiratory flow rate.

**Prednisone:** An oral corticosteroid.

**PreMeC:** The National Preferred Medicines Centre Incorporated. [www.premec.org.nz](http://www.premec.org.nz)

**PRN:** (Latin - pro re na’ta) According to need.

**RAST testing:** Radioallergosorbent testing: to measure specific IgE antibodies in serum. Used as an alternative to skin tests to determine sensitivity to specific allergens.

**Reversible airflow obstruction:** Where a 15% or greater improvement in FEV₁ 15 minutes after 400 µg Salbutamol is achieved.

**Salbutamol:** A short-acting ß₂-adrenergic bronchodilator.
Speleo-therapy: A CAM approach to asthma therapy based on the ionisation of air in mountain caves and salt mines. ‘Speleo-hospitals’ which are sited in these caves and mines claim effective treatment of asthma and other respiratory disorders.

Spirometry: Measuring the air entering and leaving the lungs by means of a spirometer.

Theophylline: A bronchodilator.

Wheezing: breathing with difficulty, usually with a whistling sound.

### METHODOLOGY TERMS

**Absolute risk reduction:** The effect of a treatment can be expressed as the difference between relevant outcomes in the treatment and control groups by subtracting one rate (given by the proportion who experienced the event of interest) from the other. The reciprocal is the number needed to treat (NNT).

**Accuracy** (see also validity): The degree to which a measurement represents the true value of the variable that is being measured.

**Adverse event:** A non-beneficial outcome measured in a study of an intervention that may or may not have been caused by the intervention.

**Adverse reaction:** Any undesirable or unwanted consequence of a preventive, diagnostic or therapeutic procedure.

**AGREE assessment tool:** A questionnaire to aid in the quality appraisal/assessment of evidence-based clinical practice guidelines.

**Allocation (or assignment to groups in a study):** The way that subjects are assigned to the different groups in a study (e.g., drug treatment/placebo; usual treatment/no treatment). This may be by a random method (see RCT) or a nonrandom method (see pseudo-randomized controlled study).

**Applicability** (see also external validity, generalisability): Encompasses the application of results to both individual women and groups of women. This is the preferred term as it includes the idea of particularising or individualising treatment and is closest to the general aim of clinical practice. It addresses whether a particular treatment that showed an overall benefit in a study can be expected to convey the same benefit to an individual woman.

**Baseline risk:** An estimate of an individual woman’s (untreated) risk of an outcome.

**Bias:** Bias is a systematic deviation of a measurement from the ‘true’ value leading to either an over- or underestimation of the treatment effect. Bias can originate from many different sources, such as allocation of participants, measurement, interpretation, publication and review of data.

**Blinding** (see Concealing):
- **single-blind** studies: only the subjects are blind to their allocations;
- **double-blind** studies: both observers and subjects are ignorant of the treatment allocations.

**Case-control study:** Participants with a certain outcome or disease and an appropriate group of controls without the outcome or disease are selected (usually with careful consideration of appropriate choice of controls, matching, etc) and then information is obtained on whether the subjects have been exposed to the factor under investigation.

**Case series:** The intervention has been used in a series of participants (may or may not be consecutive series) and the results reported. There is no separate control group for comparison.

**Clinical outcome:** An outcome for a study that is defined on the basis of the clinical outcome being studied (e.g., fracture in osteoporosis, peptic ulcer healing and relapse rates).

**Clinically important effect** (see also statistically significant effect): An outcome that improves the clinical outlook for the participant. The recommendations made in clinical practice guidelines should be both highly statistically significant and clinically important (so that the 95% CI includes clinically important effects).

**Cochrane Collaboration:** The Cochrane Collaboration is an international network that aims to prepare, maintain and disseminate high quality systematic reviews based on RCTs and when RCTs are not available, the best available evidence from other sources. It promotes the use of explicit methods to minimise bias, and rigorous peer review.
**Cohort study:** Data are obtained from groups who have been exposed, or not exposed, to the new technology or factor of interest (eg. from databases). Careful consideration is usually given to participant selection, choice of outcomes, appropriate controls, matching, etc. However, data on outcomes may be limited.

**Comparative study:** A study including a comparison or control group.

**Concealing:** Now the preferred way of referring to the Blinding process used in epidemiological studies and clinical trials in which the observers and the subjects have no knowledge as to which treatment groups subjects are assigned. It is undertaken in order to minimise bias occurring in participant’s response and outcome measurement. There are four levels of concealment:

1) the allocation to treatment groups is concealed from the subjects/participants;
2) the allocation to treatment groups is concealed from both the subjects and the clinicians involved;
3) the allocation to treatment groups is concealed from the subjects, the clinicians involved and the experimenter;
4) the allocation to treatment groups is concealed from the subjects, the clinicians involved, the experimenter and the statistician analysing the results.

**Confidence interval (CI):** An interval within which the population parameter (the ‘true’ value) is expected to lie with a given degree of certainty (eg, 95%).

**Confounding:** The measure of a treatment effect is distorted because of differences in variables between the treatment and control groups that are also related to the outcome. For example, if the treatment (or new intervention) is trailed in younger participants then it may appear to be more effective than the comparator, not because it is better, but because the younger participants had better outcomes.

**Cross-sectional study:** A study that examines the relationship between diseases (or other health-related characteristics) and other variables of interest as they exist in a defined population at one particular time (ie, exposure and outcomes are both measured at the same time).

**Double-blind study** (see blinding)

**Effectiveness:** The extent to which an intervention produces favourable outcomes under usual or everyday conditions.

**Efficacy:** The extent to which an intervention produces favourable outcomes under ideally controlled conditions such as in a RCT.

**Evidence:** Data about the effectiveness of a new treatment or intervention derived from studies comparing it with an appropriate alternative. Preferably the evidence is derived from a good quality RCT, but it may not be.

**Evidence-based medicine/health care:** The process of finding relevant information in the medical literature to address a specific clinical problem. Patient care based on evidence derived from the best available studies.

**External validity** (see also generalisability, applicability): Also called generalisability, is the degree to which the results of a study can be applied to situations other than those under consideration by the study eg, for routine clinical practice.

**Extrapolation:** Refers to the application of results to a wider population and means to infer, predict, extend, or project the results beyond that which was recorded, observed or experienced.

**Generalisability** (see also external validity, applicability): Refers to the extent to which a study’s results provide a correct basis for generalisation beyond the setting of the study and the particular people studied. It implies the application of the results of a study to a group or population.

**Gold standard:** A method, procedure or measurement that is widely regarded or accepted as being the best available. Often used to compare with new methods.

**Heterogeneity:** Refers to the differences in treatment effect between studies contributing to a meta-analysis. If there is significant heterogeneity, this suggests that the trials are not estimating a single common treatment effect.

**Historical controls:** Data from either a previously published series or previously treated patients at an institution that are used for comparison with a prospectively collected group of patients exposed to the technology or intervention of interest at the same institution.

**Incidence:** The number of new events (new cases of a disease) in a defined population, within a specified period of time.
Intention to treat (ITT): An analysis of a clinical trial where participants are analysed according to the group to which they were initially randomly allocated, regardless of whether or not they dropped out, fully complied with the treatment, or crossed over and received the other treatment. By preserving the original groups one can be more confident that they are comparable.

Interaction: The relationship between a single variable (or covariate) and the treatment effect.

Intermediate outcomes: A true clinical endpoint that is not the ultimate endpoint of the disease but occurs quite late in the causal chain and represents manifestation of disease.

Intervention: An intervention will generally be a therapeutic procedure such as treatment with a pharmaceutical agent, surgery, a dietary supplement, a dietary change or psychotherapy. Some other interventions are less obvious, such as early detection (screening), educational materials for participants, or legislation. The key characteristic is that a person or their environment is manipulated in order to benefit that person.

Level of evidence: A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.

Meta-analysis: Results from several studies, identified in a systematic review, are combined and summarized quantitatively.

Nonrandomized cross-over design: Participants in a trial are measured before and after introduction or withdrawal of the intervention and the order of introduction and withdrawal is not randomised.

Null hypothesis: The hypothesis that states that there is no difference between two or more interventions or two or more groups, eg, males and females. The null hypothesis states that the results observed in a study (eg, the apparent beneficial effects of the intervention) are no different from what might have occurred as a result of the operation of chance alone.

Number needed to harm (NNH) (see also number needed to treat): When the treatment increases the risk of the outcome, then the inverse of the absolute risk reduction is called the number needed to harm.

Number needed to treat (NNT) (see also number needed to harm): When the treatment reduces the risk of specified adverse outcomes of a condition, NNT is the number of participants with a particular condition who must receive a treatment for a prescribed period in order to prevent the occurrence of the adverse outcomes. This number is the inverse of the absolute risk reduction.

Observational studies: Also known as epidemiological studies. These are usually undertaken by investigators who are not involved in the clinical care of the participants being studied, and who are not using the technology under investigation in this group of participants.

Odds ratio (OR): Ratio of the odds of the outcome in the treatment group to the corresponding odds in the control group.

Patient expected event rate (PEER): The probability that a patient will experience a particular event (eg, a stroke or myocardial infarction) if left untreated. Also known as baseline risk.

Patient-relevant outcome: Any health outcome that is meaningful to the patient. It can be the best surrogate outcome, resources provided as part of treatment, impact on productivity (indirect) or one that cannot be measured (eg, pain, suffering). Common examples include: primary clinical outcomes, quality of life and economic outcomes.

Precision: A measure of how close the estimate is to the true value. It is defined as the inverse of the variance of a measurement or estimate. It is related to the P-value (the smaller the P-value, the greater the precision). (Also called statistical precision.)

Prevalence: Prevalence is a measure of the proportion of people in a population who have some attribute or disease at a given point in time or during some time period.

Primary prevention: Strategies undertaken to limit the incidence of disease by controlling causes and risk factors.

Pseudo-randomized controlled study: An experimental comparison study in which subjects are allocated to treatment/intervention or control/placebo groups in a nonrandom way (such as alternate allocation, allocation by day of week, odd–even study numbers, etc.). These groups may therefore differ from each other in ways other than the presence of the intervention being tested. This contrasts to ‘true’ experiments (RCTs) where the outcomes are compared for groups formed by random assignment (and are therefore equivalent to each other in all respects except for the intervention).
Publication bias: Bias caused by the results of a trial being more likely to be published if a statistically significant benefit of treatment is found.

P-value (see also confidence interval, precision, statistically significant effect): The probability (obtained from a statistical test) that the null hypothesis (that there is no treatment effect) is incorrectly rejected.

NOTE: The p-value is often misunderstood. It does not, as commonly believed, represent the probability that the null hypothesis (that there is no treatment effect) is true (a small P-value therefore being desirable). The P-value obtained from a statistical test corresponds to the probability of claiming that there is a treatment effect when in fact there is no real effect.

Quality of evidence (see also strength of evidence): Degree to which bias has been prevented through the design and conduct of research from which evidence is derived.

Quality of life: The degree to which persons perceive themselves able to function physically, emotionally and socially. In a more ‘quantitative’ sense, an estimate of remaining life free of impairment, disability, or handicap as captured by the concept of quality-adjusted life-years (QALYs).

Random error: The portion of variation in a measurement that has no apparent connection to any other measurement or variable, generally regarded as due to chance.

Randomization: A process of allocating participants to treatment or control groups within a controlled trial by using a random mechanism, such as coin toss, random number table, or computer-generated random numbers. Study subjects have an equal chance of being allocated to an intervention or control group thus the two groups are comparable.

Randomized controlled trial: An experimental comparison study in which participants are allocated to treatment/intervention or control/placebo groups using a random mechanism, such as coin toss, random number table, or computer-generated random numbers. Participants have an equal chance of being allocated to an intervention or control group and therefore allocation bias is eliminated.

Randomised cross-over trial: Participants are measured before and after exposure to different technologies (or placebo) which are administered in a random order (and usually blinded).

Relative risk or risk ratio (RR): Ratio of the proportions in the treatment and control groups with the outcome. This expresses the risk of the outcome in the treatment group relative to that in the control group.

Relative risk reduction (RRR): The relative reduction in risk associated with an intervention. This measure is used when the outcome of interest is an adverse event and the intervention reduces the risk. It is calculated as one minus the relative risk, or:

\[ RRR = 1 - \frac{\text{event rate in treatment group}}{\text{event rate in control group}} \]

Relevance: The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

Reliability: Also called consistency or reproducibility. The degree of stability that exists when a measurement is repeatedly made under different conditions or by different observers.

Risk difference (RD): The difference (absolute) in the proportions with the outcome between the treatment and control groups. If the outcome represents an adverse event (such as death) and the risk difference is negative (below 0) this suggests that the treatment reduces the risk – referred to as the absolute risk reduction.

Secondary prevention: Strategies undertaken to cure patients and reduce the more serious consequences of disease through early diagnosis and treatment.

Selection bias: Error due to systematic differences in characteristics between those who are selected for study and those who are not. It invalidates conclusions and generalisations that might otherwise be drawn from such studies.

Size of effect: Refers to the size (or the distance from the null value indicating no treatment effect) of the summary measure (or point estimate) of the treatment effect and the inclusion of only clinically important effects in the 95% confidence interval.

Statistically significant effect (see also clinically important effect): An outcome for which the difference between the intervention and control groups is statistically significant (ie, the P-value is ~ 0.05). A statistically significant effect is not necessarily clinically important.

Statistical precision (see precision)

Strength of evidence: The strength of evidence for an intervention effect includes the level (type of studies), quality (how well the studies were designed and performed to eliminate bias) and statistical precision (P-value and confidence interval).
**Surrogate outcome:** Physiological or biochemical markers that can be relatively quickly and easily measured and that are taken as predictive of important clinical outcomes. They are often used when observation of clinical outcomes requires longer follow-up. Also called intermediate outcome.

**Systematic review:** The process of systematically locating, appraising and synthesizing evidence from scientific studies in order to obtain a reliable overview.

**Type I error:** When the null hypothesis (that there is no treatment effect) is incorrectly rejected.

**Type II error:** When the null hypothesis (that there is no treatment effect) is not rejected, but is actually false.

**Validity:** Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.

Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).

**Variance:** A measure of the variation shown by a set of observations, defined by the sum of the squares of deviation from the mean, divided by the number of degrees of freedom in the set of observations.
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