

Final Report for CRC for Asthma 2006

Enhanced Evidence Based Guidelines for Asthma Management

Introduction and Aims

Asthma guidelines form a key part of asthma management. When based upon best evidence, they can provide the clinician with an invaluable aid to best practice.

The aims of Project 10 were:

- to provide best evidence to support and enhance the current Australian Asthma Management Plan (AAMP) by conducting a series of systematic reviews of randomised controlled trials (RCTs) of asthma self management and inhaled corticosteroid (ICS) use,
- to summarise and present the results of systematic reviews in clinically meaningful terms.

Asthma Self-Management

Asthma self-management education plays an important role in the management of asthma, and is described in Step 6 of the AAMP. Education about asthma and self-management of asthma are now key recommendations of asthma management guidelines. A series of asthma education reviews were updated to include the results of 55 RCTs in three separate reviews comparing limited education (information only), self-management education versus usual care and a comparison of different options for self-management education. They clarify the type and intensity of education that is needed to reduce asthma morbidity.

Limited Education (Information only) Review

A Cochrane systematic review of 12 RCTs found that limited education programmes that offer information about asthma but not self-management skills did not reduce hospitalisation rates or visits to the doctor for asthma. The positive outcomes from limited asthma education were a reduction in symptoms.

Asthma Self-Management Education

Four main components of asthma education programmes can be identified, and are described below. This review examined the effects of education programmes, classified in terms of these 4 components. Interventions that provide 2 or more components are termed self-management education. Interventions using all 4 components are termed optimal self-management education.

- Information: this is the transfer of information about asthma and its management.
- Self-monitoring: This involves regular assessment of either symptoms or peak expiratory flow by the participant.
- Regular medical review: The assessment of asthma control, severity and medications by a medical practitioner forms the basis of the regular medical review component.
- A written action plan: This is an individualised written plan produced for the purpose of patient self-management of asthma exacerbations. The action plan is characterised by being individualised to the patient's underlying asthma severity and treatment. The action plan also informs the patient when and how to modify medications and when and how to access the medical system in response to worsening asthma.

The effects of an asthma self-management intervention on asthma outcomes were evaluated in 36 RCTs involving 6090 participants. Interventions using all 4 components were considered to provide an optimal self-management programme. There were 15 studies that compared an optimal self-management programme, or its components, to usual care. The studies showed that with a self-management programme, there was a reduction in the proportion of subjects reporting hospitalisations and ER visits for asthma, unscheduled doctors visits for asthma, days lost from work due to asthma, and episodes of nocturnal asthma. The effects were large enough to be of both clinical and statistical significance. There was also a gradation of effect. Those interventions which included a written action plan, consistently showed an effect, whereas less intense interventions were not always of obvious benefit. There was an overall positive effect of asthma self-management which led to an improvement in PEF ($p < 0.05$), significant reduction in indirect costs and reductions in total costs.

Options for Asthma Self-Management

There are several different modalities available for asthma education. This review evaluated programmes that: 1. Optimized asthma control through ICS use by regular medical review or by individualized written action plans, 2. Used written self-management plans based on PEF or symptoms self-monitoring and 3. Compared different options for the delivery of optimal self-management programmes.

Overall there was no difference in asthma outcomes for the six studies comparing optimised asthma control by regular medical review or individualised written action plans. These results indicate that regular medical review is an acceptable alternative to an asthma education programme, provided that the medical review includes assessment of severity, optimisation of medication and instruction on management of exacerbation.

In reviewing the six trials that compared PEF and symptom self-monitoring no significant differences in health outcomes were found suggesting that the use of either method is effective. This is a clinically important observation as self-monitoring can be tailored to patient preference, patient characteristics and the resources available.

Reducing the intensity of self-management education or level of clinical review may reduce its effectiveness.

These reviews provide level 1 evidence to support Step 6 of the AAMP to 'educate and review regularly'. We extended this work in a systematic review of step 5 of the AAMP defining the effective components of a written action plan, and addressing the efficacy of doubling inhaled steroid doses.

Written Action Plans

Written action plans for asthma facilitate the early detection and treatment of an asthma exacerbation. A systematic review was conducted to determine the impact of individual components of written action plans on asthma health outcomes.

This review included 26 randomised controlled trials that compared written action plans as part of their self-management intervention to usual care. Action plans were classified as being individualised and complete if they specified when and how to increase treatment ($n=17$), and as incomplete ($n=4$) or non-specific ($n=5$), if they did not include these instructions.

Individualised written action plans based on personal best PEF, using two to four action points, and recommending both ICS and OCS for treatment of exacerbations consistently improve asthma health outcomes. Other variations appear less beneficial or require further study. The observations of this review provide a guide to the types of variations possible with written action plans, and strongly support the use of individualised, complete, written action plans.

Achieve Best Lung Function

In asthma, ICS substantially improves morbidity and mortality, and is the basis of pharmacotherapy for disease control. Step 2 of the AAMP recommends that the initial type and dose of corticosteroid therapy for asthma be initiated according to the degree of airflow obstruction.

Steroid Efficacy

We sought to evaluate the balance between the efficacy and safety of different doses of ICS for asthma, and to communicate this to prescribers in an efficient way using the evidence based measures of number-needed-to-treat (NNT) and number-needed-to-harm (NNH). A review of corticosteroid steroid efficacy at different doses for asthma, relating to Step 2 of the AAMP, provided level 1 evidence to support the dose response effect of corticosteroid use and highlighted the benefit and harm at different doses of inhaled corticosteroids. ICS were highly efficacious, with a relatively flat dose-response curve (Figure 1). Only 3 patients needed to be treated with fluticasone (FP) 100mcg daily to prevent worsening asthma (NNT 3), and the NNT for FP 1000mcg was 2.1 patients. The dose response curve for side effects was steep. For a dose of FP 100mcg, oral candidiasis developed in only 1 out of every 90 subjects treated (NNH 90). In contrast the NNH for FP 1000 and 2000mcg daily were 23 and 6 respectively.

Level 1 evidence supports the use of low dose ICS in asthma.

Initial ICS Dose

Asthma guidelines vary in their recommendations for initial inhaled corticosteroid (ICS) dose in asthma. A systematic literature review was conducted to establish the optimal starting dose of ICS for asthma in adults. This review included the results of 26 randomised controlled trials that compared high initial ICS to moderate or low initial ICS. The results provided level 1 evidence for optimal starting ICS dose.

14 publications describing 13 trials were included in the review. For studies that compared a step down approach to constant moderate/low dose ICS there was no difference in lung function, symptoms, or rescue medications between the two treatment approaches. Change in morning peak flow was similar for high compared to moderate dose ICS. When compared to low dose ICS, moderate dose ICS significantly improved morning peak flow l/min (change from baseline WMD 11.14, 95%CI 1.34 to 20.93) and nocturnal symptoms (SMD -0.29, 95%CI -0.53 to -0.06).

For patients with asthma who require ICS, commencing with a moderate dose is equivalent to commencing with a high dose and stepping-down. The small non-significant benefits of commencing with a high ICS dose are not of sufficient clinical benefit to warrant its use. Initial moderate ICS doses appear to be more effective than initial low ICS dose.

ICS-Sparing effects of addition of LABA

The addition of LABA to ICS therapy can improve asthma symptoms and reduce exacerbations. The addition of LABA may also have an ICS-sparing effect and permit a reduction in ICS maintenance dose. This review was conducted to determine the magnitude of maintenance ICS dose reduction possible with the addition of long acting beta agonists while maintaining asthma control. 10 trials were included in the review. There was no difference in exacerbations requiring oral corticosteroids (OCS) (RR1.0, 95%CI 0.07 to 1.32) or airway inflammation for studies that compared a reduced dose (mean 60% reduction) ICS/LABA combination to a fixed moderate/high dose ICS. There were also significant improvements in lung function (FEV1, PEF and rescue free days) with the addition of LABA. In conclusion the addition of LABA has an ICS-sparing effect for subjects with asthma using moderate maintenance dose ICS. This review provides level 1 evidence for the magnitude of dose reduction in maintenance ICS that is possible with the addition of long acting beta agonists while maintaining asthma control.

LABA and ICS combination therapy

A review of LABA and ICS combination therapy compared to ICS alone compared and contrast the efficacy and safety of long-acting beta-agonists and inhaled corticosteroid therapy against different maintenance inhaled corticosteroid strategies in adults with asthma. Cochrane systematic reviews of RCTs were identified that compared the addition of LABA to ICS against 3 ICS strategies: 1. a similar ICS dose (n=4312 subjects) 2. a higher ICS dose (n=4951) 3. a similar ICS dose in steroid naïve subjects (n=968). The addition of LABA to ICS significantly reduced the risk of exacerbations when compared to a similar ICS dose (NNT=18) (Figure 2). The effects of LABA/ICS therapy on exacerbations compared to the other maintenance ICS strategies were not statistically significant. LABA added to ICS therapy led to significant improvements in asthma control when compared to all 3 maintenance ICS strategies (Figure 2). There was an increased risk of tremor with LABA/ICS combination therapy that reached significance for initial therapy (NNH =21), and when compared to a higher ICS dose (NNH =74). Maintenance asthma therapy with LABA/ICS therapy has differential effects on asthma control and asthma exacerbations. The greatest benefit and least harm of long-acting beta-agonists therapy comes when they are added to a similar ICS dose in adults with symptomatic asthma.

These data complement our previous review of efficacy and harm for ICS.

Predictors of Loss of Asthma Control

A systematic review of predictors of loss of asthma control was conducted. This review included the results of ten prospective trials conducted to establish the predictive value of non-invasive markers of airway inflammation for monitoring deterioration in asthma control following back titration of inhaled corticosteroid therapy. Ten trials that assessed the value of non-invasive markers (airway hyperresponsiveness, exhaled nitric oxide, and sputum and blood eosinophils) to predict a loss of asthma control were included in the review. There was insufficient evidence to establish the predictive value of any individual marker but a positive result to more than one marker at baseline may be predictive of loss of control. The results of this review were used to inform design of Project 7 trials.

Summary

Project 10 has completed a series of systematic reviews that provide best evidence to support and enhance the current Australian Asthma Management Plan (AAMP). These reviews provide level 1 evidence for self-management education and written action plan use, corticosteroid efficacy at different doses, optimal starting ICS doses, the corticosteroid-sparing effects of the addition of LABA and LABA/ICS combination therapy. An economic analysis of this data demonstrated significant savings achievable once implemented: (\$3 million/yr).

Publications

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Figure 1: Number Needed to Treat or Harm for Increasing Fluticasone Doses.

* Statistical heterogeneity present.

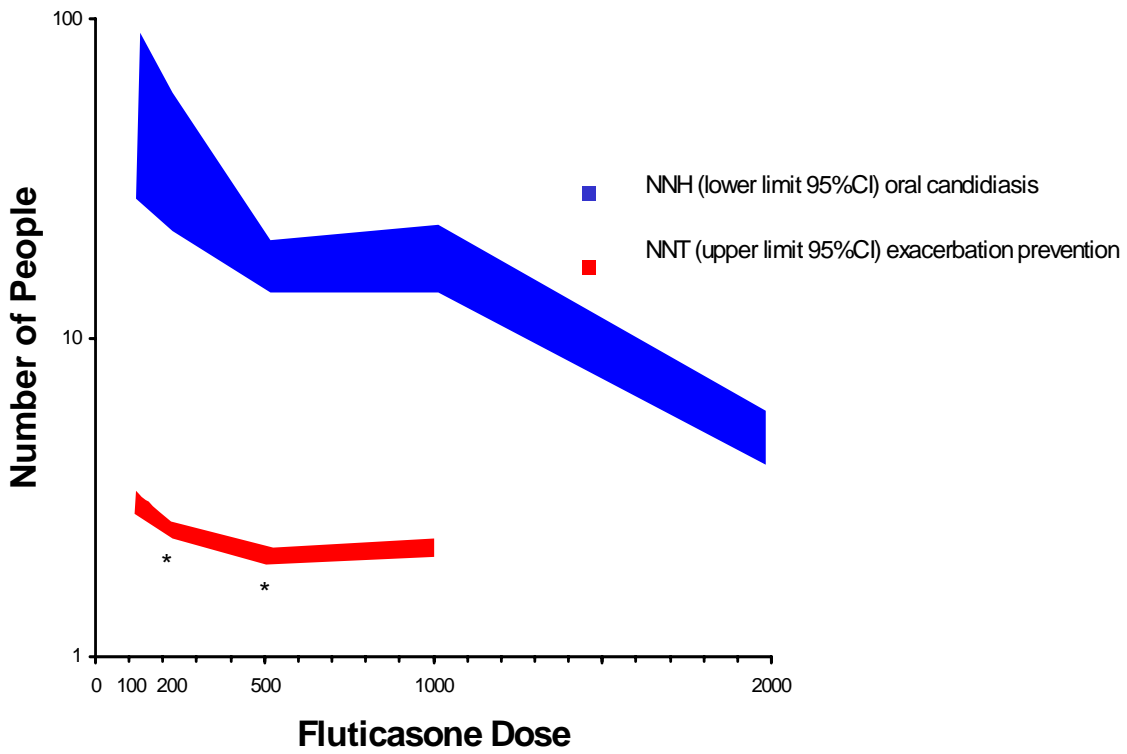


Figure 2: Efficacy of LABA/ICS on asthma control and exacerbations

