Research activity following Asthma Treatment Uncertainty Priority Setting Exercise in 2007 – paper updated January 2010

This paper captures relevant research activity following the completion of JLA priority setting exercise. The activity may range from uncertainties being submitted to commissioning research programmes, to partner organisation's own research and strategy development.

Priorities for research

1 (a) What are the adverse effects associated with long-term use of *short and long-acting bronchodilators; inhaled and oral steroids; and combination and additive* therapies in adults?
(N.B this includes children aged 12 years old and over)

1 (b) What are the adverse effects associated with long-term use of *short and long-acting bronchodilators; inhaled and oral steroids; and combination and additive* therapies in children?

2. What is the most effective way of managing asthma with other health problems?

3. What are the key components of successful "Self- Management" for a person with asthma?

4. What is the most effective strategy to educate people with asthma and health professionals about managing the adverse effects of drug therapies?

5. What is the most effective way of managing asthma triggers?

6. What is the role of complementary therapies in asthma management?

7. What are the benefits of breathing exercises as a form of physical therapy for asthma?

8. What type of patient (children and adults) and health professional education is most effective in gaining asthma control?

9. What is the most effective way to manage consultations and asthma control in adolescence and young people?

10. Psychological interventions for adults with asthma?

Asthma UK (Partner)

Priorities 1a and 1 b

Asthma UK is interested in the concerns that people with asthma have about steroid treatments for asthma (corticosteroids) and the effect that these concerns have on how they take their medicine. We are also intrigued to understand the perspectives of healthcare professionals on both the concerns and use of steroid treatments for asthma, and how their perspectives compare to what people affected by asthma tell us.

Therefore in a joint project with Professor Rob Horne (based at the Centre for Behavioral Medicine within the School of Pharmacy in London) and Education for Health, we developed some questionnaire surveys to enable us to understand more about this subject, and asked people affected by asthma and healthcare professionals for their perspectives on it.

We have received over 3,000 completed questionnaires from people with asthma or carers of children with asthma. In addition, we received completed questionnaires from more than 200 healthcare professionals. We are currently in the process of analysing all of the data arising from these questionnaires.

The questionnaires intended for people with asthma and parents or carers of children with asthma aimed to establish:

- their experiences of side effects
- the level of information they have received about side effects
- their use or their child's use of steroid treatments
- their approach to dealing with concerns about side effects
- how they respond to their concerns
- future needs they may have to help overcome concerns about steroids.

There were two separate questionnaires for:

- People with asthma who are currently receiving a steroid treatment (by inhaler or tablet) for their asthma or have done within the last three years.
- Parents or carers of children with asthma who are currently receiving a steroid treatment (by inhaler or tablet) for their child's asthma or have done within the last three years.

The questionnaires intended for healthcare professionals aimed to establish how healthcare professionals perceived that people with asthma, and parents or carers of children with asthma, would respond to the questions asked of them in their own questionnaires, based on the interactions that they have with people affected by asthma in their work. For example this included their perception of the most commonly reported side effects and concerns from people affected by asthma, and the associated effects on how they then take their steroid medicines.

Next steps are to analyse results and clarify understanding these treatment concerns and identifying an appropriate intervention (December 2009).

Priority 3

"Boosting asthma expectations to improve quality of life".
A vital study to boost people's expectations about the level of control over asthma they can achieve. (Oct 2009)

Priority 10

"Can dealing with depression improve severe asthma control?"
Belfast-based researchers are collecting preliminary evidence on the benefits of prescribing anti-depressants for people with severe asthma, who are also depressed, (October 2009)

Priority 7

Breathing exercises and self-management question submitted to the HTA.

Strategy Development

Asthma UK currently has two research strategies, one for basic research and another for clinical research, each with their own priority areas. *"In our new strategic plan beginning October 08, we will be moving towards developing a single research strategy and obviously the JLA priorities will feed into discussions*". (Quote from J Versnel, Director of R & D)

Cochrane Airways Group (member of partnership)

Priorities 1a and 1 b

Cates CJ, Lasserson TJ. Regular fixed-dose treatment with formoterol and inhaled corticosteroids versus regular treatment with salmeterol and inhaled corticosteroids for chronic asthma: serious adverse events (Protocol). Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD007694. DOI: 10.1002/14651858.CD007694.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with formoterol and inhaled steroids for chronic asthma: serious adverse events. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD006924. DOI: 10.1002/14651858.CD006924.pub2.

Authors' conclusions
It is not possible, from the data in this review, to reassure people with asthma that inhaled corticosteroids with regular formoterol carries no risk of increasing mortality in comparison to inhaled corticosteroids alone as all four deaths occurred among 6,594 people using inhaled corticosteroids with formoterol. On the other hand, we have found no conclusive evidence of harm and there was only one asthma related death registered during over 3,000 patient year observation on formoterol. In adults, the decrease in asthma-related serious adverse events on regular formoterol with inhaled corticosteroids was not accompanied by a decrease in all cause serious adverse events. In children the number of events was too small, and consequently the results too imprecise, to determine whether the increase in all cause non-fatal serious adverse events found in the previous meta-analysis on regular formoterol alone is abolished by the additional use of inhaled corticosteroids. Clinical decisions and information for patients regarding regular use of formoterol have to take into account the balance between known symptomatic benefits of formoterol and the degree of uncertainty and concern associated with its potential harmful effects.

Implications for research
Future research should clearly specify the number of patients with fatal and non-fatal serious adverse events by treatment group and cause. Any new surveillance study to investigate the impact of regular formoterol and inhaled corticosteroids on all-cause mortality would need to be very large.

Cates CJ, Cates MJ, Lasserson TJ. Regular treatment with formoterol for chronic asthma: serious adverse events. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD006923. DOI: 10.1002/14651858.CD006923.pub2.

Authors' conclusions
In comparison with placebo, we have found an increased risk of serious adverse events with regular formoterol, and this does not appear to be abolished in patients taking inhaled corticosteroids. The effect on serious adverse events of regular formoterol in children was greater than the effect in adults, but the difference between age-groups was not significant.

Implications for research
Data on all-cause serious adverse events should be more fully reported in medical journals, and not combined with all adverse events or limited to those events that are thought by the investigator to be drug-related.

Regular treatment with formoterol versus regular treatment with salmeterol for chronic asthma: serious adverse events (Protocol). Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD007695. DOI: 10.1002/14651858.CD007695.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with salmeterol and inhaled steroids for chronic asthma: serious adverse events. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD006922. DOI: 10.1002/14651858.CD006922.pub2.

Authors' conclusions
No significant differences have been found in fatal or non-fatal serious adverse events in trials in which regular salmeterol has been randomly allocated with inhaled corticosteroids, in comparison to inhaled corticosteroids at the same dose. Although 10,873 adults and 1,173 children have been included in trials, the number of patients suffering adverse events is too small, and the results are too imprecise to confidently rule out a relative increase in all-cause mortality or non-fatal adverse events. It is therefore not possible to determine whether the increase in all-cause non-fatal serious adverse events reported in the previous meta-analysis on regular salmeterol alone is abolished by the additional use of regular inhaled corticosteroids. The absolute difference between groups in the risk of serious adverse events was small. There were no asthma-related deaths and few asthma-related serious adverse events. Clinical decisions and information for patients regarding regular use of salmeterol have to take into account the balance between known symptomatic benefits of salmeterol and the degree of uncertainty and concern associated with its potential harmful effects.

Implications for research
Studies on children are currently lacking in this area. In order to further quantify the risks of regular salmeterol with inhaled corticosteroids a large-scale surveillance study is required. Future research should clearly specify the number of patients with

fatal and non-fatal serious adverse events by treatment group and cause, and outcomes should be verified by an independent outcome panel.

Cates CJ, Cates MJ. Regular treatment with salmeterol for chronic asthma: serious adverse events. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD006363. DOI: 10.1002/14651858.CD006363.pub2.

Authors' conclusions
In comparison with placebo, we have found an increased risk of serious adverse events with regular salmeterol. There is also a clear increase in risk of asthma-related mortality in patients not using inhaled corticosteroids in the two large surveillance studies. Although the increase in asthma-related mortality was smaller in patients taking inhaled corticosteroids at baseline, the confidence interval is wide, so it cannot be concluded that the inhaled corticosteroids abolish the risks of regular salmeterol. The adverse effects of regular salmeterol in children remain uncertain due to the small number of children studied.

Implications for research
Data on serious adverse events should be more fully reported in medical journals. In view of the increasing use of salmeterol in combination with inhaled corticosteroids, further studies investigating the impact of salmeterol alone on serious adverse events in adults may not be feasible, but studies using a combination of salmeterol and inhaled steroids should collect and fully report data on fatal and non-fatal serious adverse events. The evidence base for assessing the risks and benefits of salmeterol in children is currently weak.

Priority 1a

Dissertation by Njeri Kigundu.

Short-acting beta 2-agonists (SABAs) are the mainstay of treatment for acute symptoms of asthma. Research into the long term effects of SABAs has been identified as a priority by patients. The dissertation assesses the incidence, prevalence and risk of long-term adverse events associated with SABA use. (Unpublished at present)