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Author: Honkoop, Persijn

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Chapter 8

Summary

This thesis aimed to contribute to the improvement of several components of the management of asthma in primary care. The main part of this thesis consists of the AC-CURATE trial. In this trial we compared three different management strategies for adult patients with asthma in primary care. In the first management strategy, we targeted 'Controlled asthma', which is the currently recommended aim in clinical guidelines. 'Controlled asthma' means patients should experience hardly any symptoms of their asthma. A downside of this strategy is that it usually requires relatively high doses of medication. The second management strategy, targeted 'Partly Controlled asthma' and in this strategy some symptoms were allowed. This should lead to a lower requirement to step-up treatment in response to symptoms, which would lead to less medication usage and thus less side-effects. The third management strategy evaluated the use of adding a measurement of Fractional exhaled Nitric Oxide (FeNO), a possible indicator of airways inflammation. In the other two strategies, assessment of current control on asthma, was based on the conventional markers lung function and symptoms. Adding FeNO could aid in assessing current control and help guide therapy choices. In order to establish the best management treatment strategy, we assessed as many relevant indicators as possible. Therefore we not only assessed clinical parameters, such as asthma control and exacerbations, but we also assessed the societal perspective, by performing a cost-effectiveness analysis and the patient's perspective by measuring relevant issues such as quality of life and adherence. The conclusions from our trial can be summarized as follows:

- From a societal perspective, as well as a patient's and a clinical perspective, a symptom- plus FeNO-driven strategy is the preferred management strategy for adult asthma patients in primary care.
- Treatment aimed at 'FeNO guided Controlled asthma' improves asthma control with a high probability of cost-effectiveness and without increasing medication use and costs compared to aiming at 'Partly Controlled asthma'.
- Treatment aiming at 'Controlled asthma' leads to increased asthma medication use and costs, without a significant improvement in asthma control, quality of life or exacerbation rate, compared to aiming at 'Partly Controlled asthma' or to aiming at 'FeNO guided Controlled asthma'.
- FeNO shows a weak correlation with respiratory symptoms and lung function
- If FeNO is incorporated as a marker of asthma control in primary care, it enables 'fine-tuning' when categorizing asthma control in almost half of the patients

Additionally we performed two other studies. In the first study, we aimed to improve the usefulness of asthma action plans. In an asthma action plan a certain threshold level of symptoms or peak flow is defined, called an Action Point. If a patient's symptoms or peak flow exceed that threshold level, the patient is advised to take immediate action. Usually

there are several different Action Points within one asthma action plan, each with their own threshold levels and with different actions to be taken. The most important Action Point is the one that indicates a severe exacerbation is imminent and advises to start oral corticosteroids or immediately visit a physician/hospital. In our study we aimed to identify the best threshold-levels for this Action Point. In order to decide the best threshold levels it is important that they provide a good sensitivity and specificity with regard to detecting exacerbations. Furthermore, it is also important that an exacerbation is detected well in advance to allow appropriate treatment. Finally, it is also important that an Action Point has a low Number Needed to Treat, since false positive predictions will result in over treatment. Our results show that the optimal action point for the early detection of asthma exacerbations consists of two components:

- A ≥ 2 standard deviations increase in a composite symptom score from a mean symptom score acquired during a baseline, combined with a fall in PEF to $< 70\%$ of personal best, both occurring within a one week window.

This Action Point detected exacerbations 4.1 days before occurrence, with a sensitivity of 85.1%, specificity of 97.2% and a number needed to treat (NNT) of 6.

Finally we explored the potential hazards of using a questionnaire in a different setting than it was originally validated for. To this purpose we compared the results of an assessment of the Asthma Control Questionnaire online, with the results of that same questionnaire assessed by a practice nurse together with the patient. Both questionnaires were completed within one week of each other. We concluded that:

- Assessment of asthma control by the Asthma Control Questionnaire is influenced by the type of administration. Control over asthma symptoms is perceived as higher when interacting with a caregiver than in an online self-assessment

