Blinded review of the primary endpoint results from the BEAT DB-trial

Blinded review and interpretation

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**Blinded review of the primary endpoint results from the trial:**
Breathing Exercises in Asthma Targeting Dysfunctional Breathing – the BEAT DB-trial

**Introduction**
This document presents the results of the primary outcome, mini Asthma Quality of Life Questionnaire (mini-AQLQ), of the BEAT DB-trial. Additionally, it presents results from the secondary outcomes, defined in the trial registration (registration number NCT03127059) and the published trial protocol.

**Results from the intention-to-treat analysis of the primary endpoint**

*Between-group differences*
There was a statistically significant difference of 0.34 (crude) and 0.35 (adjusted) units between groups in the mean change of the mini-AQLQ from baseline to the 6 months follow-up.

*Within-group differences*
Both groups improved significantly in mini-AQLQ from baseline to the 6 months follow-up. Group A improved 0.65 units (15%) while Group B improved 0.31 units (7%) with a number needed to treat (NNT) of 8.3 for one patient to improve at least 0.5 units in Group A compared to Group B.

**Results from the secondary intention-to-treat analysis**

*Between-group differences*
Between-groups differences in change from baseline to the 6 months follow-up in the 6-item Asthma Control Questionnaire (ACQ6), Anxiety and Depression (HADS-A, HADS-D), Nijmegen Questionnaire (NQ), 6-Minute Walk Test (6MWT), predicted Forced Expiration Volume in first second (FEV₁ % pred) and Steps per day did not differ significantly between Group A and Group B. However, there were consistent numerical trends in favour of the intervention to which Group A was allocated expect for 6MWT, which was in favour of the intervention to which Group B was allocated.

*Within-group changes*
Both groups improved significantly in ACQ6, HADS-A, and NQ from baseline to the 6 months follow-up. HADS-D improved significantly in Group A.
Interpretation 1: “Group A received breathing exercises in addition to usual care”

Our results show that breathing exercises in addition to usual care is more efficacious than usual care alone in patients with uncontrolled moderate-to-severe asthma followed by respiratory physicians in terms of improving asthma-related quality of life (mini-AQLQ).

The between group differences were substantial and considered clinically relevant, but was not accompanied by statistically significant between-group differences in asthma control (ACQ6), perceived level of breathing discomfort (NQ), physical capacity (6MWT), physical activity (steps per day) or lung function (FEV₁%pred), although all the PROMs showed a numerical trend to larger improvements in the breathing exercise group.

This is the first trial to investigate the effect of breathing exercises in addition to usual care compared with usual care alone in patients with moderate-to-severe asthma treated in a difficult asthma secondary care setting. For the first time, it provides high-quality evidence that breathing exercises in addition to usual care in patients with moderate-to-severe asthma is superior to usual care alone in improving asthma-related quality of life after 6 months. Both groups improved substantially in mini-AQLQ, ACQ6 and NQ suggesting that a usual care program is also efficacious in moderate-to-severe asthma. However, adding breathing exercises to this treatment program will improve asthma-related quality of life further.

The results support previous findings in patients with mild-to-moderate asthma followed by primary care physicians². The magnitude of improvement is slightly larger but similar to that seen in milder primary care patients², and is similar to the quality of life improvement associated with additional pharmacological interventions for patients with asthma uncontrolled on standard first-line medication (ICS)³.

Since the results are in favour of breathing exercises in addition to usual care, this confirms our primary hypothesis described in the Statistical Analyses Plan⁴ that the participants randomized to breathing exercises in addition to usual care will improve more in asthma-related QOL than participants randomized to usual care alone.

The trial supports the adjuvant use of breathing exercises in the management of patients with moderate-to-severe asthma attending a secondary care clinic.
Interpretation 2: “Group A received usual care alone”

Our results show that usual care alone is more efficacious in improving asthma-related quality of life (mini-AQLQ) than breathing exercises in addition to usual care in patients with uncontrolled moderate-to-severe asthma followed by respiratory physicians. The results indicate that patients with uncontrolled moderate-to-severe asthma on average have an inferior outcome if breathing exercises is added to usual care, suggesting that adding a physiotherapeutic treatment has a negative effect on their 6-month outcome. This is in contrast to findings in patients with milder forms of asthma.

Since usual care alone is more efficacious, and cheaper, breathing exercises seem only applicable in a sub-group of patients with moderate-to-severe asthma not able to participate in usual care. Since the results are in favour of usual care alone, this means that our primary hypothesis described in the Statistical Analyses Plan cannot be confirmed.

The trial indicates that breathing exercises should not be offered to patients with moderate-to-severe asthma attending a hospital based difficult asthma clinic.

Signatures
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Date 26.6.2020
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Date: 23/6-20
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References


