Dysfunctional breathing

clinical characteristics and treatment

CARINA HAGMAN
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Abstract

Background: Dysfunctional breathing (DB) is a respiratory disorder involving an upper chest breathing pattern and respiratory symptoms that cannot be attributed to a medical diagnosis.

Aim: The overall aim of this thesis was to describe patients with DB and investigate clinical outcomes after physiotherapy treatment.

Methods: Study I was descriptive and comparative, that included 25 patients with DB and 25 age- and sex-matched patients with asthma. Health-related quality of life (HRQoL), anxiety, depression, sense of coherence, influence on daily life due to breathing problems, respiratory symptoms, emergency room visits and asthma medication were investigated. Study II, a 5-year follow-up study based on the same sample as study I (22 patients with DB, 23 patients with asthma), studied treatment outcomes after information and breathing retraining. Study III was descriptive and correlational (20 healthy subjects), investigating whether the Respiratory Movement Measuring Instrument (RMMI) can discriminate between different breathing patterns in varying body positions. Study III also studied correlations between respiratory movements and breathing volumes (12 healthy subjects). Study IV was a single-subject AB design with follow-ups. Self-registered patient-specific respiratory symptoms and respiratory-related activity limitations and breathing pattern (measured with the RMMI) were evaluated after an intervention consisting of information and breathing retraining in five patients with DB.

Results: Patients with DB had lower HRQoL (SF-36): vitality (mean 47 vs. 62), social functioning (70 vs. 94) and role emotional (64 vs. 94) (p<0.05) than patients with asthma. The DB group had a higher prevalence of anxiety (56% vs. 24%) and experienced more breathing problems than the asthma group. Patients with DB had made several emergency room visits and had been treated with asthma medication. At the 5-year follow-up, patients with DB showed improved HRQoL (SF-36): physical function 77 to 87 (p=0.04), decreased breathing problems and emergency room visits, and they were not treated with asthma medication. The RMMI can differentiate between different breathing patterns in different body positions. Strong correlations between respiratory movements and breathing volumes were observed (rs 0.86-1.00). The results in study IV indicate that patients with DB benefit from information and breathing retraining regarding decreased respiratory symptoms and activity limitations and improved breathing pattern.

Keywords: dysfunctional breathing, breathing pattern, breathing retraining, respiratory movement measuring instrument, respiratory symptoms, respiratory-related activity limitations

Carina Hagman, Department of Neuroscience, Physiotherapy, Box 593, Uppsala University, SE-751 24 UPPSALA, Sweden.

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To my family
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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## Abbreviations

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<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>DA</td>
<td>Dysfunktionell andning</td>
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<tr>
<td>DB</td>
<td>Dysfunctional breathing</td>
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<tr>
<td>CGI-I</td>
<td>Clinical Global Impression Scale - Improvement</td>
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<tr>
<td>CO₂</td>
<td>Carbon dioxide</td>
</tr>
<tr>
<td>EQ VAS</td>
<td>EuroQol Visual Analogue Scale</td>
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<tr>
<td>FEV₁</td>
<td>Forced expiratory volume in one second</td>
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<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
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<tr>
<td>HADS</td>
<td>Hospital Anxiety and Depression Scale</td>
</tr>
<tr>
<td>HADS-A</td>
<td>Hospital Anxiety and Depression Scale - Anxiety subscale</td>
</tr>
<tr>
<td>HADS-D</td>
<td>Hospital Anxiety and Depression Scale - Depression subscale</td>
</tr>
<tr>
<td>HRQoL</td>
<td>Health-related quality of life</td>
</tr>
<tr>
<td>NQ</td>
<td>Nijmegen Questionnaire</td>
</tr>
<tr>
<td>NRS</td>
<td>Numeric rating scale</td>
</tr>
<tr>
<td>PND</td>
<td>Percentage of nonoverlapping data</td>
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<tr>
<td>RMMI</td>
<td>Respiratory Movement Measuring Instrument</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
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<tr>
<td>SF-36</td>
<td>Medical Outcome Survey Short Form 36 Questionnaire</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
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<td>VC</td>
<td>Vital capacity</td>
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Background

Respiratory function

All human life is dependent on respiration and it is one of our most vital functions. Respiration can be divided into three phases: cellular, internal and external respiration. Cellular respiration refers to the utilisation of oxygen by the mitochondria; internal respiration refers to the biochemistry of oxygen and carbon dioxide (CO₂) distribution to and from tissues; and external respiration refers to the mechanics of breathing, i.e. the flow of air in and out of the lungs.

Historically, the purpose of breathing was an enigma for a long time. Hippocrates (460-370 BC) did not associate breathing with the lungs but described breathing patterns. Later, Aristotle (384-322 BC) believed that the purpose of breathing was to cool the heart. It was thought that the movements of the thorax were due to lung movements and that the diaphragm played no role in breathing (1). Today, it is evident that the act of breathing serves the purpose of respiration, i.e. the exchange of oxygen and CO₂, and that breathing is dependent on muscles working together in a coordinated manner (2).

The act of breathing is unique in that it is considered as the only vital function that can be under both automatic and voluntary control (3-5). It is regulated by automatic centres in the brainstem and by voluntary signals initiated in the cerebral cortex (4). The dual nature of breathing is advantageous (e.g., complex and precise voluntary changes in breathing can be made when speaking, eating or holding one’s breath underwater) (4). The dual control, however, can create problems in the sense that breathing can affect our physiological and psychological well-being (3, 6). Most of the time we are unaware of our breathing, but as soon as something physical or psychological causes the breathing to change, it immediately affects our sense of well-being (3). Breathlessness and dyspnoea are examples of symptoms that can be defined as an unpleasant or uncomfortable awareness of breathing (7).

Breathing can be considered as an independent variable that affects emotion, cognition and behaviour but also as a dependent variable that reflects changes in emotion, cognition and behaviour (8). Conscious or unconscious changes in breathing can affect both our feelings and thoughts, and breathing increases when an increased metabolic demand occurs (as in exercise) or by emotions or thoughts (as anger, fear, anxiety) (8). For instance, excessive breathing with an upper chest breathing pattern can be triggered by a stressful
event associated with e.g. anxiety. This breathing pattern can generate unpleasant sensations such as dyspnoea, pain or tightness in the chest (3).

There are many factors that cause normal breathing to become negatively affected, including neuromuscular (9), psychological, biochemical or biomechanical factors (10) (Figure 1). It is important to have these different factors in mind when screening for respiratory diseases or disorders. Biomechanical aspects influence the functionality of breathing and patients with unexplained breathing symptoms (such as dyspnoea) often show abnormalities in their breathing pattern (11, 12).

**Figure 1.** Factors associated with breathing.

### Respiratory muscles and breathing pattern

**Respiratory muscles**
The respiratory muscles serve as a biomechanical mechanism of the breathing system (9, 13) acting in concert to transport air in and out of the lungs. Alterations in the performance of the respiratory muscles may reduce the effectiveness of ventilation (14). The respiratory muscles can be divided into three groups: the inspiratory, expiratory and accessory muscles. Breathing is dependent upon the coordinated efforts of these muscle groups (9). During normal, quiet breathing, inspiration is active while expiration is largely passive (3, 9). Normal, quiet inspiration is predominantly generated by the diaphragm but external intercostal muscles and scalene muscles also act to inflate the thorax (9, 15). If the diaphragm is dysfunctional, the other respiratory muscles change their function, often becoming overloaded (13). The respiratory muscles work to overcome the elastic recoil of the lungs and the chest wall as well as the airway resistance. The work performed by the respiratory muscles in a
resting, healthy person is very small, with an oxygen consumption of about 2% of the metabolic rate (16).

**Breathing pattern**

Respiratory movements are divided into abdominal and rib cage movements (17). These two styles of breathing are endpoints on a continuum rather than discrete categories. Thus, one can breathe with any combination of rib cage and abdominal breathing. Breathing patterns can be described and calculated from respiratory movements: (rib cage movements)/(rib cage movements + abdominal movements), indicating the proportion of respiratory movements that can be attributed to the expansion of the rib cage.

When discussing respiratory movements and breathing patterns, body posture must be taken into account (18). The major function of the respiratory muscles is to produce ventilation, although they are also activated during postural tasks of the trunk and the head (4). For instance, the diaphragm acts in conjunction with other muscles as a postural muscle in sitting and standing positions, which is not the case in supine position (19). An upright posture, sitting or standing position, is associated with greater respiratory movements in the rib cage, whereas in supine position the abdominal movements are dominant (20). In addition, in supine position the weight of the abdominal contents pushes the diaphragm cranially so that its fibres are extended and therefore can contract more effectively (20).

There are no standardised reference values of respiratory movements available for clinical use (21) and the variation in values of percentages of rib cage movement in healthy individuals is quite large in different studies (22). Studies have reported rib cage movement values of 20-45%, 40-70 and 50-70% in supine, sitting and standing positions, respectively (20, 23-25). A limitation in several studies is that it is not specified whether the subjects are sitting and standing with or without support at the time the breathing pattern is measured. When sitting or standing with support, the diaphragm can focus more on the breathing than on the postural function.

Whether the breathing pattern is affected by age and sex remains unclear. Kaneko et al. have suggested that percentages of rib cage movements decrease with age (21), whereas other studies have shown that age has no influence on breathing pattern (22, 24, 26). Some studies indicate that males have lower percentages of rib cage movement than females (21, 26, 27). Some studies, however, indicate that the breathing pattern is not affected by sex (22, 24). The discrepancies that pertain to the effects of body position, age and sex might be related to the type of measuring instrument used in different studies (21). Not only body position, age and sex might affect the breathing pattern. A general and important problem with measuring breathing pattern is that the measurement procedure itself can modify the spontaneous breathing pattern, just because the subject brings attention to it (28).
Measurements of breathing pattern

Assessing the breathing pattern is an important part of the investigation of patients with breathing problems. Furthermore, it is a component of the evaluation of interventions that aim to improve breathing pattern. Assessment of breathing pattern can be performed in different ways, from visual observations to measurements with technical equipment. An instrument that has been developed for both research and clinical use is the Respiratory Movement Measuring Instrument (RMMI) (Figure 2). The RMMI is a non-invasive instrument that measures bilateral anteroposterior movements of the abdomen and upper and lower thorax with six laser distance sensors (29). Signals from the laser distance sensors are digitalised and relayed in a computer program for data analysis. It has been shown that the RMMI is able to differentiate the distribution of motion between the rib cage and abdomen in supine position (natural, abdominal and upper chest breathing) and in a sitting position (natural breathing) in adult healthy subjects (30). Whether this also applies to abdominal and upper chest breathing in a sitting position and for different breathing patterns in standing position has not yet been confirmed. Nor has it been investigated to what extent respiratory movements, measured with the RMMI, correlate with breathing volumes.

![Figure 2. Measurement with the Respiratory Movement Measuring Instrument (RMMI).](image)

Dysfunctional breathing

Description and definition

There is still no gold standard definition of dysfunctional breathing (DB) or for the diagnosis of DB (31). A clinical definition has been suggested as
“breathing which is unable to perform its various functions efficiently and is inappropriate for the needs of the individual at that time” (13). Another suggested definition is “an alternation in the normal biomechanical patterns of breathing that result in intermittent or chronic symptoms which may be respiratory and/or non-respiratory” (32). DB is considered a respiratory disorder in which an upper chest breathing pattern at rest is a main characteristic (10). The changes in breathing pattern can be chronic or recurrent (33), causing respiratory, respiratory-related and non-respiratory symptoms that cannot be attributed to a specific medical diagnosis (31, 34). The aetiology of DB is essentially unknown. It has been suggested that both physiological and psychological factors can cause prolonged changes in breathing pattern (35). The initial response with an upper chest breathing pattern due to, e.g., psychological states or various disease states may be an appropriate response. However, if the upper chest breathing pattern is retained after the conditions that initiated their occurrence have passed, it is considered a dysfunctional breathing pattern (13). DB can manifest alone or in association with other diseases such as asthma (33). DB is implicated in both physical and psychological health (10), and the presence of different symptoms such as breathlessness, dyspnoea and chest tightness can result in anxiety, which can provoke further breathing irregularity (8).

Patients with DB often undergo several investigations with negative results and remain undiagnosed, because the diversity of symptoms and clinical signs make diagnosis difficult (36). A diagnosis of DB should be considered when other causes have been excluded (37, 38). When screening for DB, it is recommended to include biochemical measures (e.g., end tidal CO2), biomechanical measures (e.g., the assessment of breathing pattern) and psychological features (e.g., anxiety) as DB is proposed to have dimensions related to those functions of breathing (10, 39). Respiratory symptoms and tests of respiratory function (e.g., spirometry) should also be investigated (10). However, it is important to recognise DB whether it occurs alone or in conjunction with other respiratory disorders or diseases so the patients can be provided with appropriate information and treatment.

In this thesis DB was defined as the presence of a dominant upper chest breathing pattern during quiet breathing at rest in a sitting position (with support), without underlying medical causes and accompanied by respiratory symptoms.

Prevalence

Because of the lack of established diagnostic criteria of DB, statements of prevalence are difficult to interpret. Thomas et al. have suggested that DB affects up to 10% of the general adult population (with or without asthma) and about 30% of adults with asthma (40). Large sex differences have been reported, with one study showing that 14% of women without asthma have
symptoms suggestive of DB compared with 2% in men without asthma (38). In patients with asthma 35% of women and 20% of men were suggested to have DB (38). The surveys by Thomas et al., investigating the prevalence of DB, were undertaken in a general practice in the United Kingdom and were based on a self-completed questionnaire, the Nijmegen Questionnaire (NQ), which was originally developed to detect hyperventilation syndrome (41, 42). The NQ is not validated in an asthma population and several questions are related to symptoms such as shortness of breath, pain and constriction in the chest – symptoms common both in asthma and DB (43). Thus, this poses a risk of DB being overestimated in patients with asthma (44). It is important to reach a consensus of the diagnosis of DB if its prevalence is to be established.

Breathing pattern and respiratory symptoms
Alteration in the breathing pattern is reported in patients with DB (45, 46). An upper chest dominant breathing pattern has been observed, and the extent of upper chest dominant breathing seems to be an important cause of symptoms such as breathlessness and dyspnoea (45). The abnormal afferent proprioceptive input associated with such a breathing pattern can directly result in the perception of respiratory symptoms (46). One hypothesis is that sensations of breathlessness and dyspnoea arise from dissociations between what the brain expects and what it receives from receptors in the respiratory muscles, i.e. a mismatch between motor output and sensory input (16, 47). In addition, an upper chest breathing pattern is generally associated with dynamic hyperinflation (32, 48). Hyperinflation leads to larger respiratory work because the elastic recoil of the lungs and chest increases and the respiratory rate is often increased. Hyperinflation causes biomechanical changes that affect the respiratory muscles negatively, making them work less effectively (16). The increased respiratory work and effect on respiratory muscles can also cause such symptoms as breathlessness, dyspnoea, chest tightness and chest pressure (3, 49).

Differential diagnoses
The symptoms of DB have similarities with other disorders and diseases such as panic disorder, hyperventilation syndrome, vocal cord dysfunction, sensory hyperreactivity and asthma. DB can also coexist with other diseases or disorders (50).

Panic disorder
Panic disorder is characterised by recurrent unexpected attacks of severe anxiety or fear (panic). There is a sudden onset of symptoms including palpitations, sweating, trembling or shaking, sensations of shortness of breath or
smothering, a feeling of choking, chest pain or discomfort, nausea or abdominal distress, a feeling of dizziness, unsteady, lightheaded or faint, derealisation (feeling of unreality) or depersonalisation (being detached from oneself), fear of losing control or going crazy, fear of dying, chills or flushes and paraesthesia (numbness or tingling sensations) (51). Several of the symptoms (e.g., shortness of breath, dizziness, paraesthesia) described in panic disorder are due to hyperventilation (decreased levels of CO₂). In Sweden, the prevalence in adults has been estimated to be about 2% (52). Treatment of panic disorder can include cognitive behavioural therapy and medication. (53, 54). Treatment with controlled diaphragmatic breathing can be recommended for patients that hyperventilate with the purpose of achieving respiratory control and restoring normal levels of CO₂ (53).

**Hyperventilation syndrome**

Hyperventilation is defined as breathing in excess of metabolic requirements (i.e. CO₂ production) and is associated with hypocapnia (55). Hyperventilation is associated with a wide range of symptoms and an abnormality in respiratory control. Examples of symptoms are breathlessness, frequent sighing, dizziness, paraesthesia and palpitations (56). The term “hyperventilation syndrome” was first used by Kerr et al. in 1938 to describe patients with somatic symptoms of both hypocapnia and anxiety (56). As in DB, the prevalence is difficult to assess because of varying diagnostic criteria (55, 57). The prevalence has previously been estimated to 6-10% (58). However, the term hyperventilation syndrome has been used in so many different contexts that its usefulness is questioned (55). Some symptoms associated with hyperventilation syndrome have been shown to be unrelated to hypocapnia and may be due to other mechanisms (10, 46, 59). Recommended treatment for hyperventilation syndrome, without any underlying somatic disease, is information and breathing retraining (60-62).

**Vocal cord dysfunction**

Vocal cord dysfunction is included in the consensus term “inducible laryngeal obstruction” (63). The term refers to conditions in the larynx (the glottic or supraglottic structures) that cause breathing problems (63). Vocal cord dysfunction is a respiratory disorder that can overlap with DB and asthma, and just like DB, vocal cord dysfunction can be misdiagnosed as asthma (64). Vocal cord dysfunction is characterised by an intermittent paradoxical adduction of the vocal cords, mainly during the inspiratory phase, leading to airflow obstruction (64, 65). Symptoms such as stridor, wheezing, cough and breathlessness during exercise are common. These symptoms can masquerade as bronchoconstriction (65). The diagnosis is based on laryngoscopy, and an abnormal inspiratory flow volume loops at spirometry can also be seen when patients are symptomatic (64, 65). The prevalence of vocal cord dysfunction varies widely in the literature with a seemingly female predominance (66).
Treatment of vocal cord dysfunction usually involves a combination of information, breathing techniques and sometimes psychological counselling (64, 65).

**Sensory hyperreactivity**

DB has also been suggested to coexist with sensory hyperreactivity (31, 67). The term sensory hyperreactivity was introduced in the 1990s. The diagnosis is based on increased cough sensitivity to inhaled capsaicin and a high score on the Chemical Sensitivity Scale for Sensory Hyperreactivity questionnaire (68). Symptoms such as irritation of the eyes, nose and throat, heavy breathing, difficulties in breathing, chest pressure, cough and phlegm are induced by chemicals and scents (69). The prevalence is estimated to be 6% in the adult Swedish population, being more common in females than in males (68). Studies have suggested that patients with sensory hyperreactivity might have impaired chest mobility and abdominal breathing movements (70) and that they benefit from physiotherapeutic intervention containing movement and breathing instructions and relaxation (67). Improvements after treatment have been seen for chest mobility, feeling of chest pressure and capsaicin cough sensitivity.

**Asthma**

In the Global Initiative for Asthma report asthma is defined as “a heterogeneous disease, usually characterised by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation” (71). Asthma is a common chronic respiratory disease with an estimated prevalence of about 9% in adults in Sweden (72). The prevalence of asthma still seems to increase in most parts of the world (72). Because there is no current cure, primary treatment is pharmacological therapy that aims to control or relieve symptoms.

DB can be related to symptoms that may be wrongly attributed to asthma (73). Thus, it is not uncommon that patients with DB are misdiagnosed and prescribed asthma medication unnecessarily (34, 74, 75). Some studies indicate that as many as a third of individuals with diagnosed asthma in developed countries do not actually have asthma (75, 76), and that about 10% of patients diagnosed as having asthma actually suffer from a “functional breathing disorder” (75). A dysfunctional breathing pattern such as dynamic hyperinflation without any bronchoconstriction has been proposed to be an important contributor to exaggerated dyspnoea in patients with asthma (77). In the latest Global Initiative for Asthma report (71) DB has been reported as a differential diagnosis of asthma and that DB may occur in association with asthma. Because individuals with DB are often misdiagnosed as having asthma, it would
be important to investigate whether there are differences and similarities between patients with DB and patients with asthma in order to facilitate early, correct diagnosis and to avoid delay of effective treatment.

Treatment

Different kinds of breathing retraining methods are available. These methods were mainly developed to control symptoms of suggested hyperventilation in patients with asthma (78). Examples of different breathing techniques are the Buteyko method, yoga and the Papworth method. They are based on different underlying philosophies, but all include some form of breathing modification as the primary component. The theory underlying the Buteyko breathing technique, which was developed in the 1950s, is that hypocapnia is a major contributor to symptoms related to asthma (79). The technique focuses on increasing CO₂ levels by reducing the depth and frequency of respiration and by breath-holding exercises. Advice and training on nasal breathing are also included. Yoga is an ancient technique from India that consists of controlling breathing with deep breathing exercises and mental concentration to produce a reduction in breathing frequency (78, 80). The Papworth technique focuses on the use of an appropriate breathing pattern to reduce symptoms due to dysfunctional breathing, including hyperventilation and hyperinflation (78, 81). Breathing retraining (with diaphragmatic breathing), education, relaxation, integration of breathing and relaxing techniques into daily life are included in the Papworth method (81). The Papworth method has been implemented by physiotherapists since the 1960s (81). Another recently developed technique is the Lotorp method (82), with focus on breathing exercises in combination with massage of the thoracic muscles. The method has been tested in patients with asthma. A reduction of symptoms and exercise-induced breathing problems and increased chest expansion have been demonstrated (82).

Dysfunctional breathing

At present, there is no standard treatment for DB (37) and studies concerning interventions for DB are scarce. Information and breathing retraining have been recommended as the primary treatment for patients with “disordered breathing” (e.g., DB and hyperventilation syndrome), with or without asthma (60). The intervention targets normalisation of the breathing pattern, with relaxed diaphragmatic breathing as a major component (36). The aims are to encourage patients to gradually alter their upper chest breathing pattern, as well as to restore and maintain a normal breathing pattern (36). When evaluating the effects of treatment in patients with DB, biochemical, biomechanical and psychological features are recommended to be included (10, 39) (Figure 1). Respiratory symptoms should also be evaluated. One study on patients with DB found a reduction in respiratory symptoms and an improved breathing pattern after breathing retraining and relaxation (45).
There is a lack of studies on respiratory-related activity limitations in patients with DB, and it is not known whether activity limitations are affected by breathing retraining. Further, there is a lack of research that includes objective measurements of breathing pattern (i.e. respiratory movements in the rib cage and abdomen) in patients with DB. In addition, investigations of long-term clinical outcomes after information and breathing retraining interventions are needed to increase knowledge of treatment in patients with DB.

**Dysfunctional breathing in association with asthma**

The role of information and breathing retraining has been investigated in a randomised controlled trial on patients with DB in association with asthma (83). The study showed improved HRQoL and decreased respiratory symptoms (83).

**Asthma**

The purpose of breathing retraining for patients with asthma is based on the assumption that people with asthma have abnormal or dysfunctional breathing patterns (84-86). Breathing retraining that contains information and breathing retraining in patients with asthma has been shown to be effective in improving respiratory symptoms, HRQoL and psychological well-being (81, 87). Moreover, it may reduce the use of rescue bronchodilator medication (81, 87). There is no evidence that breathing retraining has an effect on objective measures of respiratory function (e.g., airway physiology, inflammation or hyper-responsiveness) (86, 87). The Global Initiative for Asthma report states that “breathing exercises may be a useful supplement to medications” in patients with asthma (71). The British guideline in management of asthma suggest “Breathing exercise programs (including physiotherapist-taught methods) can be offered to people with asthma as an adjuvant to pharmacological treatment to improve health-related quality of life (HRQoL) and reduce symptoms” (88).

**Rationale for this thesis**

Experiencing breathing problems caused by DB without being diagnosed and not knowing how to cope with the symptoms can be stressful with negative effects on daily life (89, 90). Knowledge of DB is limited, although the disorder seems to be common and there is still no consensus about a definition or diagnostic criteria. Symptoms due to DB can be misinterpreted and DB is often misdiagnosed as asthma, leading to unnecessary asthma medication and a lost opportunity for appropriate treatment. More knowledge about DB and similarities and differences in DB and asthma are required to facilitate the diagnosis of DB. Studies indicate that patients with DB benefit from interventions including information and breathing retraining but more studies are
needed. Studies on respiratory-related activity limitations in patients with DB and objective evaluations of breathing pattern after breathing retraining are scarce. Investigations with long-term follow-ups after breathing retraining are needed to establish the persistence of effects and confirm the use of breathing retraining methods.
Aims

The overall aim of this thesis was to describe patients with dysfunctional breathing (DB), and to investigate clinical outcomes after treatment with information and breathing retraining.

Specific aims

To describe patients with DB and investigate differences and similarities between patients with DB and patients with asthma for health-related quality of life, anxiety, depression, sense of coherence, influence on daily life due to breathing problems, respiratory symptoms, emergency room visits and asthma medication (Study I).

To investigate changes at a 5-year follow-up for health-related quality of life, anxiety, depression, sense of coherence, influence on daily life due to breathing problems, respiratory symptoms, emergency room visits and asthma medication in patients with DB who had received information and breathing retraining (Study II).

To investigate whether the Respiratory Movement Measuring Instrument can discriminate between normal, abdominal and upper chest breathing patterns and to study correlations between respiratory movements and breathing volumes in different body positions (Study III).

To investigate patient-specific respiratory symptoms, respiratory-related activity limitations and breathing pattern in patients with DB who were followed for 12 months after an intervention with information and breathing retraining. (Study IV).
Methods

Design and ethics
This thesis consists of four studies based on three samples. In study I, 50 patients participated, 25 with DB and 25 with asthma. Study II was a 5-year follow-up of patients included in study I (22 patients with DB and 23 patients with asthma). In study III, 20 healthy subjects took part and study IV included five patients with DB.

Ethical approval was obtained by the Ethics Committee of Uppsala University, Sweden for studies I and II (Ups 03-666) and The Regional Ethical Review Board in Uppsala, Sweden for study III (Dnr 2009/407) and study IV (Dnr 2013/285). Participants were given oral and written information about the studies and informed consent was obtained from each participant. The study designs, sample sizes and data collection process are presented in Table 1.

Table 1. Overview of study designs, sample sizes and the data collection process in the four studies included in the thesis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample size</th>
<th>Collection of data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study I</td>
<td>Descriptive, cross-sectional, comparative</td>
<td>50 (25 DB, 25 asthma)</td>
<td>Patient journal, Self-reported questionnaires</td>
</tr>
<tr>
<td>Study II</td>
<td>Follow-up, comparative</td>
<td>45 (22 DB, 23 asthma)</td>
<td>Self-reported questionnaires</td>
</tr>
<tr>
<td>Study III</td>
<td>Descriptive, correlational</td>
<td>20 (healthy subjects)</td>
<td>RMMI, Spirometry</td>
</tr>
<tr>
<td>Study IV</td>
<td>A series of five single-subject AB designs with long-term follow-up</td>
<td>5 (DB)</td>
<td>Continuous self-registrations RMMI Self-reported questionnaires Capnography Measurement of chest expansion</td>
</tr>
</tbody>
</table>

DB= dysfunctional breathing, RMMI= Respiratory Movement Measuring Instrument
Participants and procedures

Study I

Fifty patients were recruited from a lung and allergy outpatient department in Sweden. Twenty-five newly referred patients identified as having DB were consecutively invited to take part in the study (19 females and 6 males, aged 20-73 years) and 25 age- and sex-matched patients with asthma were included. The patients with asthma were selected from a list of patients at the lung and allergy outpatient department and those who fulfilled the inclusion criteria were contacted by mail and informed about the purpose of the study. Within 2 weeks, they were contacted by phone for further information and invited to participate in the study. The 50 patients fulfilled the following criteria: aged 16-80 years, forced expiratory volume in 1 s (FEV₁) and vital capacity (VC) ≥80% of the predicted value, resting oxygen saturation ≥95% and no concomitant disease. Patients with DB did not have asthma and patients with asthma did not have DB. Data were collected by questionnaires for HRQoL, anxiety, depression, sense of coherence, influence on daily life due to breathing problems, emergency room visits, medications and respiratory symptoms. Data on emergency room visits and medication were also collected from patient journals. In addition, data on spirometry, oxygen saturation, weight and height for patients with asthma were collected from the journals. The questionnaires were sent to the patients with asthma by mail while the patients with DB answered the questionnaires at the clinic. Data were collected from January to December 2004.

Study II

Study II was based on the same sample of patients as in study I. Forty-five patients from study I participated. Two patients, one in each group, had died and two in the DB group and one in the asthma group did not return the questionnaires. At the 5-year follow-up, the same questionnaires as in study I, plus a DB criterion list (see the DB criterion list in the paragraph Data collection, Symptoms associated with dysfunctional breathing), were sent to the patients by mail. To increase the response rate one or two postal reminders were sent if necessary. After inclusion and data collection in study I, the patients with DB received 1-4 individual physiotherapy sessions of information and breathing retraining. The number of visits was determined based on each patient’s individual needs. The patients with asthma did not receive physiotherapy intervention. Data were collected from January to December 2009.

Study III

Twenty healthy subjects (10 females and 10 males, 26-55 years of age) comprised the study population. They were mainly recruited from the hospital
staff. To be eligible for participation they had to be 20-60 years of age, have a body mass index (BMI) of <30 kg/m², FEV₁ and forced vital capacity (FVC) ≥80% of predicted values, resting oxygen saturation ≥95%, normal values for chest expansion, non-smoker for the past year and <10 pack-years smoking history, no ongoing pregnancy, no concomitant disease and no current respiratory symptoms. All 20 subjects participated in the part of the study that compared different breathing patterns in different body positions. Breathing patterns were measured with the RMMI (Figure 2). Twelve of the subjects also participated in the investigation looking at correlations between respiratory movements and breathing volumes in different body positions. Respiratory movements (measured with the RMMI) were measured simultaneously at different breathing volumes (measured with the Cardio Perfect dynamic spirometer). Data were collected from February to October 2011.

Study IV
Five female patients (ages 19-51 years) with DB participated in the study. They were recruited from a lung and allergy outpatient department in Sweden and were consecutively invited to take part in the study. Inclusion criteria were 18-70 years old, BMI <30 kg/m², FEV₁ and FVC ≥80% of predicted values, resting oxygen ≥95%, normal values for chest expansion, non-smoker for the past year and <10 pack-years smoking history, no ongoing pregnancy or breastfeeding, no asthma or other concomitant diseases that can affect respiratory function, self-rated level of patient-specific respiratory symptoms and respiratory-related activity limitations ≥3 on a numeric rating scale (NRS) 0-10 (low scores indicate a low degree of respiratory symptoms and activity limitations), no previous diagnosis or treatment of DB and no ongoing physical or psychological treatment such as yoga, meditation and psychotherapy. The baseline (A phase) lasted for 3-6 weeks, depending on when stability of respiratory symptoms and activity limitations was achieved. The intervention phase (B phase) included four individual treatment sessions (one session every second week) and two booster sessions 1 and 3 months after the treatment sessions. Primary outcomes were patient-specific respiratory symptoms, respiratory-related activity limitations and breathing pattern. Daily self-registrations of patient-specific respiratory symptoms and activity limitations continued during the first 8 weeks of the intervention phase and were resumed for 2 weeks in conjunction with the booster sessions. Follow-ups were carried out 3, 6 and 12 months after the end of the intervention phase. Daily self-registrations of patient-specific respiratory symptoms and activity limitations were again resumed in periods of 2 weeks in conjunction with each follow-up. Measurements of breathing pattern and secondary outcomes were performed in conjunction with every visits with the physiotherapist, except for HRQoL, anxiety, depression and chest expansion that were performed at baseline (A phase), at the last booster session (B phase) and at the three follow-ups. There
were 10 physiotherapy visits, including the baseline visit. Table 2 provides an overview of the study procedure.

The intervention consisted of information and breathing retraining. Data on patient-specific respiratory symptoms and respiratory-related activity limitations were collected by continuous self-registrations via a website. Breathing pattern was measured with the RMMI. Data on chest expansion, end tidal CO₂, HRQoL, ratings of change of respiratory symptoms and activity limitations, symptoms associated with DB, anxiety, depression and the amount of time/day spent on breathing retraining were also collected. Data were collected from December 2013 to March 2016.
Table 2. **Overview of the study procedure in study IV.** The follow-ups were carried out 3, 6 and 12 months after the end of the intervention phase.

<table>
<thead>
<tr>
<th>Time after baseline (weeks)</th>
<th>Inclusion (A phase) (3-6 weeks)</th>
<th>Baseline (A phase) (3-6 weeks)</th>
<th>Intervention (B phase) (19 weeks)</th>
<th>Follow-ups</th>
<th>3-month</th>
<th>6-month</th>
<th>12-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy visits (n)</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>18</td>
<td>31</td>
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<tr>
<td>Physiotherapy treatment</td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>booster</td>
<td>booster</td>
</tr>
<tr>
<td>Daily self-registered respiratory symptoms and respiratory-related activity limitations</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Daily self-registered time spent on breathing retraining</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Breathing pattern (RMMI)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Chest expansion</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>End tidal CO₂</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Symptoms (DB criterion list and NQ)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Anxiety and depression (HADS)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Health-related quality of life (EQ VAS)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Patients’ self-rated change of respiratory symptoms and respiratory-related activity limitations (CGI-I)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

RMMI=Respiratory Movement Measuring Instrument, CO₂=carbon dioxide, DB=dysfunctional breathing, NQ=Nijmegen Questionnaire, HADS=Hospital Anxiety and Depression Scale, EQ VAS=EuroQol Visual Analogue Scale, CGI-I=Clinical Global Impression Scale – Improvement.
Identification of patients with dysfunctional breathing

In this thesis the diagnosis of DB was based on examinations by a physician and the presence of a dominant upper chest breathing pattern during quiet breathing at rest in a sitting position (with support). The breathing pattern was observed and assessed visually by a physician and a physiotherapist. The patients should also have at least 5 out of 10 symptoms on a DB criterion list (see DB criterion list in the paragraph Data collection, Symptoms associated with dysfunctional breathing). The DB criterion list was specifically developed for study I. It was assembled by asking four specialists in allergology and one physiotherapist, all with experience of patients with DB, to independently identify the 10 most common symptoms in patients with DB. These symptoms were compiled and provided the basis for the criterion list. The list was retrospectively compared with 51 medical records in patients with a dominant upper chest breathing pattern and breathing problems of a dysfunctional nature. The review of the medical records showed that the 51 patients had a median of 5 (minimum 3 – maximum 8) symptoms according to the DB criterion list. There was clinical consensus in the group that 5 of 10 criteria gave a reasonable diagnostic level.

Intervention

Studies II and IV

Studies II and IV involved the same treatment conditions but with a different number of visits. Study II had a pragmatic approach, whereas the treatment was more standardised in study IV. In study II, the patients had received from 1-4 individual treatment sessions. The first session lasted 90 minutes and the following sessions about 60 minutes with 1-3 months in between. In study IV, the patients received four individual treatment sessions and two booster sessions. The first treatment session lasted about 90 minutes, the following three sessions 45-60 minutes and the two booster sessions about 40 minutes (measurements included in all sessions).

The physiotherapy-based treatment sessions in studies II and IV had similarities with the Papworth method (78, 81) consisting of information and breathing pattern modification with abdominal breathing as a central component. Home exercises were also included. The information package contained information about anatomy and physiology in order to explain how normal respiration works, possible symptoms and effects of an upper chest breathing pattern (“dysfunctional breathing”) and how breathing retraining can reduce respiratory symptoms and respiratory-related activity limitations. The breathing retraining program aimed to encourage the patients to gradually alter their breathing pattern from thoracic breathing to abdominal breathing, with the
goal to restore and maintain a normal breathing pattern. The first step was to make the patients aware of their current breathing pattern by asking them to pay particular attention to which part of the chest or abdomen that moved during breathing. They were taught an abdominal breathing pattern in different body positions (supine, sitting and standing) and in different situations to optimise their breathing pattern. The breathing retraining intervention started with the patients in supine position, so the postural reflexes were switched off and the diaphragm could focus on breathing. The patients were encouraged to be aware of their breathing pattern and apply an abdominal breathing pattern that could be carried over into daily living activities in different body positions and situations. The breathing retraining exercise was recommended to take place several times each day for about 10-30 minutes/day and could be carried out for example while sitting on the bus, watching television and lying in bed before going to sleep. The two additional booster sessions contained repetition of information, breathing retraining and encouragement to practice abdominal breathing.

Data collection

An overview of variables in relation to questionnaires and instruments used in studies I-IV is presented in Table 3.

Table 3. Overview of variables in relation to the questionnaires and instruments used in the four studies included in the thesis.

<table>
<thead>
<tr>
<th>Variables and instruments</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of disorder/disease</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Asthma medication</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>DB criterion list</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Nijmegen Questionnaire</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Medical Outcome Survey Short Form 36</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EuroQol Visual Analogue Scale</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Sense of Coherence Scale</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influence on daily life</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Movement Measuring Instrument</td>
<td></td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Cardio Perfect dynamic spirometer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest expansion</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End tidal carbon dioxide</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-specific respiratory symptoms and respiratory-related activity limitations</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Global Impression Scale - Improvement</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Adherence to breathing retraining</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>

DB=dysfunctional breathing
Symptoms associated with dysfunctional breathing (studies I, II and IV)
A DB criterion list containing 10 symptoms typical for DB was used: (i) difficulties in inspiratory breathing, (ii) sensation of being unable to take deep breaths, (iii) increased breathing frequency (>16/minutes), (iv) frequent sighing/yawning, (v) frequent need to clear the throat, (vi) muscle and joint tenderness in the upper part of the chest (sternocostal joints and/or intercostal muscles), (vii) hacking cough, (viii) chest tightness, (ix) sensation of a lump in the throat and (x) previous or current effects of stress (0=no symptoms, 10=10 symptoms). A score of ≥5 was one of the inclusion criteria in studies I and IV. In study II, the item “increased breathing frequency” was omitted because the DB criterion list was sent by mail to the patients.

The Nijmegen Questionnaire (NQ) assesses 16 symptoms associated with abnormal breathing on a 5-point Likert scale (0-4). The total score can range from 0-64, with higher scores indicating more complaints (41, 42). The score is related to breathing pattern disorders and can be used to reflect subjective aspects of dysfunctional breathing and evaluate whether patients with high scores benefit from interventions such as breathing retraining (39).

Health-related quality of life (studies I, II and IV)
In studies I and II, the Swedish version I of the Medical Outcome Survey Short Form 36 (SF-36) (91) was used. The SF-36 comprises 36 items across eight domains: physical function, role physical, bodily pain, general health, vitality, social function, role emotional and mental health. For each domain, the score ranges from 0 to 100, with higher scores representing better self-reported health. Based on these eight scales, two summary scales have been constructed: the Physical Component Summary scale and the Mental Component Summary scale. The Swedish version of the SF-36 has good reliability and construct validity across general populations (92).

In study IV, the EuroQol Visual Analogue Scale (EQ VAS) (93) was used to measure HRQoL. The EQ VAS is a vertical scale with values between 100 (best imaginable health) and 0 (worst imaginable health). The instrument has good validity and reliability (93).

Anxiety and depression (studies I, II and IV)
The Hospital Anxiety and Depression Scale (HADS) is a screening instrument used to measure anxiety and depression. The HADS consists of a 7-item anxiety subscale (HADS-A) and a 7-item depression subscale (HADS-D) (94). Each item is rated on a 4-point Likert scale (0-3), with higher scores indicating more severe signs of anxiety or depression. Scores for each subscale range from 0 to 21, with scores categorised as follows: non-cases 0-7, doubtful cases 8-10 and definite cases 11-21. The reliability and validity of the Swedish version has been shown to be good (95).
**Sense of Coherence Scale (studies I and II)**

The *Sense of Coherence Scale* measures a person’s ability to cope with stressful situations. The scale consists of 29 items (11 items on comprehensibility, 10 on manageability and 8 on meaningfulness) with a 7-point Likert scale (1-7). Possible sum scores can range from 29 to 203, with higher scores indicating a stronger sense of coherence (96). The scale has been judged as having satisfactory reliability and validity (97, 98).

**Influence on daily life (studies I and II)**

A questionnaire was constructed for studies I and II. It consisted of items regarding influence on daily life due to breathing problems. Most of the items were rated on a visual analogue scale (VAS) (0-10 cm, where 0 indicates the best value and 10 the worst).

**Breathing pattern and respiratory movements (studies III and IV)**

Breathing pattern and respiratory movements were measured with the *Respiratory Movement Measuring Instrument (RMMI)* (ReMo Inc., Keldnaholt, Reykavik, Iceland). It is a reliable instrument (99), being sensitive to changes in breathing pattern (29, 30).

**Breathing volume (study III)**

Breathing volumes were measured by the *Cardio Perfect dynamic spirometer* (Welch Allyn, New York, USA).

**Chest expansion (studies III and IV)**

Chest expansion was measured circumferentially at the level of the xiphoid process using a centimetre tape. Expansion was defined as the difference between maximum inspiration and maximum expiration (100, 101). The method has been shown to be reliable in healthy subjects (102).

**End tidal carbon dioxide (study IV)**

End tidal CO₂ was measured in kPa with a capnograph (LifeSense capnography/pulse oximeter LS1-9R, Nonin Medical, Inc., Plymouth, MN, USA) using a nasal sample line.

**Patient-specific respiratory symptoms and respiratory-related activity limitations (study IV)**

Data on patient-specific respiratory symptoms and respiratory-related activity limitations were continuously collected and registered via a website. The Patient-Specific Functional Scale (103) was used to list the respiratory symptoms and activity-limitations at inclusion. The patient-specific respiratory symptoms and respiratory-related activity limitations were scored on an 11-point
(0-10) numeric rating scale (NRS) (104), where low values indicate a low degree of respiratory symptoms and activity limitations. The two interrelated questions, “Has something special happened today? If yes, what has happened” were included in the data collection.

Patients’ self-rated changes of patient-specific respiratory symptoms and respiratory-related activity limitations (study IV)
The Clinical Global Impression Scale – Improvements (CGI-I) (105, 106) was used to obtain the patients’ rating of change for patient-specific respiratory symptoms and respiratory-related activity limitations. The CGI-I is a 7-point rating scale (1=very much improved to 7=very much worse) assessing to what degree the patient rates the improvement or deterioration of illness relative to the baseline level before the intervention. The instrument was developed for use in clinical trials to provide a brief assessment of the clinician’s view of the patients’ improvement or deterioration (106).

Adherence to breathing retraining (study IV)
Time spent on breathing retraining (minutes/day) was collected and registered in a diary parallel to the registration of respiratory symptoms and respiratory-related activity limitations.

Data analyses
Statistical analyses were performed using the Statistical Package for Social Science (SPSS) software version 17, 18 (SPSS Inc., Chicago, IL, USA), 19 and 21 (IBM Corp., Armonk, NY, USA). Data analyses used in studies I-IV are presented in Table 4.

Table 4. Data analyses used in studies I-IV.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean and standard deviation</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Standard error of the mean (SEM)</td>
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<tr>
<td>Mann-Whitney U test</td>
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<tr>
<td>Chi-squared test</td>
<td>x</td>
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<tr>
<td>Fisher’s exact test</td>
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<tr>
<td>Unpaired t-test</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Paired t-test</td>
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<td>McNemar test</td>
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<td>Wilcoxon signed-rank test</td>
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<tr>
<td>Friedman’s test</td>
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<td>Bonferroni correction</td>
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<td>Visual analysis of trend (celeration lines)</td>
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<td>x</td>
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<td>Percentages of nonoverlapping data</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two standard deviation band method</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Studies I and II
Data were analysed for statistically significant differences between the groups using the unpaired $t$-test, Mann-Whitney U test, Chi-squared test and Fisher’s exact test. For differences within groups over time the paired $t$-test, McNemar test and Wilcoxon signed-rank tests were performed. A p-value of <0.05 was considered as statistically significant.

Study III
The range of respiratory movements was calculated as the mean of the values obtained from the left and right sensors of the RMMI at the level of the axillae (upper thorax) and the umbilicus (abdomen). Breathing patterns were calculated as percentage of upper thoracic contribution to respiratory movements, i.e. (upper thoracic respiratory movements)/(upper thoracic movements + abdominal respiratory movements). Friedman’s test was used to analyse differences between the different breathing patterns in each body position; Wilcoxon signed-rank test was performed as a post hoc test; Bonferroni adjustment was used post hoc, adjusting the p-value with a factor of three, as three tests were used; and Spearman’s rho was applied to test the relationship between respiratory movements and breathing volumes. Correlations were classified as weak ($rs$<0.45), moderate ($rs$ 0.45-0.70) or strong ($rs$>0.70) according to Cohens proposal (107). Statistically significant differences were assumed when p<0.05.

Study IV
Continuous data on respiratory symptoms and respiratory-related activity limitations were graphically displayed for each patient. Celeration lines were developed using the split-middle technique for visual analysis of trends (108). Changes of means and percentage of nonoverlapping data (PND) between phases were calculated (109, 110). PND refers to the proportion of data points in the intervention phase and follow-up phases that do not overlap with the baseline data points. Higher PND scores reflect a more effective intervention and it is assumed to be the most common and simplest effect size metric (110). PND ranges from 0 to 100%, with interpretation guidelines: >70% for effective interventions, 50-70% for questionable effectiveness and <50 for no observed effect (111). A semi-statistical analysis was performed with the 2 standard deviation (SD) band method (112), where means and SD are calculated from the baseline data (A phase). A general rule is that a significant difference (p<0.05) is obtained if at least two consecutive data points in the intervention (B phase) or follow-up phase fall outside of the 2 SD band (112).

The range of respiratory movements was calculated as the mean of the values obtained from the left and right sensors at the level of the axillae (upper thorax) and the umbilicus (abdomen). Breathing patterns were calculated as the percentage of upper thoracic contribution to respiratory movements, i.e.
(upper thoracic respiratory movements)/(upper thoracic movements + abdominal respiratory movements).
Results

Study I

Patient characteristics at inclusion are presented in Table 5.

Patients with DB had poorer HRQoL (as measured with the SF-36) compared with patients with asthma: vitality (mean 47 vs. 62), social function (mean 70 vs. 94) and role emotional (mean 64 vs. 94) (p<0.05). The DB group had a higher prevalence of anxiety (≥8 on HADS-A) (56% vs. 24%), a lower sense of coherence (mean 134 vs. 156) (p<0.05) and a higher degree of symptoms associated with abnormal breathing (mean score on NQ 26 vs. 15) (p<0.001). The DB group experienced greater impact on their daily life due to breathing problems than patients with asthma (p<0.001). Breathing problems had a negative impact on physical activity in both groups. Scores ≥8 (HADS-D), which indicates depression, were seen in a third of the patients with DB. The DB group had had breathing problems for in mean 7 years before being diagnosed as having DB and 10 of 25 (40%) had made emergency room visits in the past 12 months due to breathing problems. Fifteen (60%) of the patients with DB had previously been treated with asthma medication, although they did not have asthma. (Figure 3).

Table 5. Patient characteristics at inclusion in study I. Number of patients (n) and mean (SD).

<table>
<thead>
<tr>
<th></th>
<th>DB (n=25)</th>
<th>Asthma (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females/males (n)</td>
<td>19/6</td>
<td>19/6</td>
<td>-</td>
</tr>
<tr>
<td>Age</td>
<td>47 (15)</td>
<td>47 (15)</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26 (3)</td>
<td>26 (3)</td>
<td>-</td>
</tr>
<tr>
<td>Smokers (n)</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Ex-smokers (n)</td>
<td>5</td>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>Duration of disorder/disease (years)</td>
<td>7 (8)</td>
<td>23 (13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ER visits in the past 12 months (n)</td>
<td>10</td>
<td>4</td>
<td>0.11</td>
</tr>
<tr>
<td>Score on DB criterion list</td>
<td>7.6 (1.5)</td>
<td>1.3 (0.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asthma medication</td>
<td>15*</td>
<td>25</td>
<td>0.001</td>
</tr>
</tbody>
</table>

DB=dysfunctional breathing, BMI=body mass index, ER=emergency room, *=before inclusion. DB criterion list contains 10 symptoms, 0=no symptoms, 10=10 symptoms.
Figure 3. Asthma medication before inclusion in patients with dysfunctional breathing (n=25). Fifteen patients had been treated with asthma medication, some of them with more than one medicine. ICS=inhaled corticosteroids, LABA= long-acting beta2-agonist, SABA=short-acting beta2-agonist.

Study II

Study II included only patients who were available both at baseline (study I) and at the 5-year follow-up (22 patients with DB and 23 patients with asthma). HRQoL (SF-36), physical function, had improved in patients with DB from a mean score of 77 to a mean of 87 (p=0.04). Emergency room visits had decreased both regarding number of patients and number of visits, with number of visits decreasing from 18 to 2 (p=0.02). None of the patients with DB were treated with asthma medication at the 5-year follow-up. Symptoms associated with DB (DB criterion list) had decreased from a mean score of 6.9 to 2.7 (p<0.001), and 19 patients of 22 (86%) had a score of <5 at the 5-year follow-up (Figure 4). The NQ score had decreased from a mean of 27 to a mean of 22 (p=0.03). Their breathing problems had less impact on both daily life (p<0.001) and physical activities (p<0.05). Further, the breathing problems were less affected by stress (p=0.03). No changes in anxiety or depression scores as measured with HADS were found.
Figure 4. Results of the dysfunctional breathing (DB) criterion list (with 9 items) for the DB group (n=22) at baseline (study I) and at the 5-year follow-up (study II). In study II, the DB criterion list contained 9 symptoms instead of 10; the item “increased breathing frequency” was omitted because the list was sent to the patients by mail. 0=no symptoms, 9=9 symptoms.

Study III

The RMMI was able to discriminate between different breathing patterns in different body positions (supine, sitting and standing with support) (p<0.001) (Figure 5). Strong correlations were observed between respiratory movements and breathing volumes in different body positions (Spearman’s rho 0.86-1.00).
Study IV

Five female patients participated in the study. The two patient-specific respiratory symptoms and two respiratory-related activity limitations rated by the patients as most important to deal with were analysed and reported. Example of a graph of a patient’s self-rated symptom is shown in Figure 6. In most patients improvements were especially observed at the end of the intervention phase and maintained at all follow-ups. At the 12-month follow-up, two patients showed considerable improvement in respiratory symptoms and activity limitations and three showed partial improvement. Based on the 2 SD method band, three patients had improved in their two symptoms and two activity limitations, one patient showed improvement in two symptoms and one activity limitation and one patient showed improvement in one symptom (Table 6). Table 6 also summarises the patients’ ratings of change in respiratory symptoms and activity limitations (CGI-I). Breathing pattern had improved, i.e. it had become more abdominal in four patients (Table 7). Results of changes in symptoms associated with DB, HRQoL, anxiety and depression are presented in Table 7. The score on the DB criterion list had decreased and was below the inclusion level of ≥5 in four of the patients (Figure 7). All patients had
normal values of end tidal CO₂ and chest expansion at baseline and throughout the study.

Figure 6. Example of a graph of a patient’s self-rated symptom “chest pressure” during baseline (B), intervention (I), 3-month (3-m), 6-month (6-m) and 12-month (12-m) follow-up. The follow-ups were performed 3, 6 and 12 months after the end of the intervention phase. Y-axis shows the numeric rating scale from 0-10 (low scores indicate a low degree of the symptom). X-axis shows the possible number of measurement occasions.
Table 6. Calculations of mean values on a numeric rating scale from 0-10 (low scores indicate a low degree of respiratory symptoms/activity limitations) for each patient (P) and each phase. Percentage of nonoverlapping data, 2 standard deviation (SD) band method with two consecutive points outside the 2 SD band corresponding to significant differences and patients’ self-rated change in respiratory symptoms and activity limitations (rated on Clinical Global Impression – Improvement scale over time from the baseline visit).

<table>
<thead>
<tr>
<th>P</th>
<th>Patient-specific respiratory symptoms and respiratory-related activity limitations</th>
<th>Mean values (0-10)</th>
<th>Percentage of nonoverlapping data (%)</th>
<th>2 SD band method</th>
<th>Clinical Global Impression – Improvement (1-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>I</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>1</td>
<td>Difficult to breath in</td>
<td>5.5</td>
<td>2.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Chest pressure</td>
<td>4.4</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Walk briskly</td>
<td>5.0</td>
<td>2.5</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Climb the stairs</td>
<td>5.2</td>
<td>2.0</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Difficult to breathe in</td>
<td>6.5</td>
<td>4.1</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>Unable to breathe deeply</td>
<td>6.2</td>
<td>4.0</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Walk uphill</td>
<td>5.2</td>
<td>3.3</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Climb the stairs</td>
<td>5.2</td>
<td>3.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Difficult to breathe in</td>
<td>6.2</td>
<td>1.9</td>
<td>1.7</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>Chest pressure</td>
<td>6.5</td>
<td>3.0</td>
<td>2.2</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Walk briskly</td>
<td>4.8</td>
<td>1.3</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Gymnastics</td>
<td>10</td>
<td>2.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Problem getting air</td>
<td>4.6</td>
<td>2.6</td>
<td>1.2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Unable to breathe deeply</td>
<td>4.8</td>
<td>2.7</td>
<td>0.8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Talk loud</td>
<td>5.6</td>
<td>4.8</td>
<td>4.2</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>Sing</td>
<td>8.1</td>
<td>6.7</td>
<td>5.0</td>
<td>3.0</td>
</tr>
<tr>
<td>5</td>
<td>Difficult to breathe in</td>
<td>4.0</td>
<td>2.5</td>
<td>2.9</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>Chest pressure</td>
<td>4.0</td>
<td>1.7</td>
<td>2.2</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>Kissing</td>
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<td>2.7</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>Talk loud</td>
<td>4.2</td>
<td>2.2</td>
<td>1.8</td>
<td>2.0</td>
</tr>
</tbody>
</table>

B = baseline, I = intervention, 3 = 3-month follow-up, 6 = 6-month follow-up, 12 = 12-month follow-up, x = corresponding to a significant difference, - = not corresponding to a significant difference, * = end of the intervention phase. Clinical Global Impression – Improvement scale: 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, 7 = very much worse.
Table 7. Changes in breathing pattern, symptoms (DB criterion list and NQ), health-related quality of life (EQ VAS), anxiety (HADS-A) and depression (HADS-D) during the course of study IV.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Phases</th>
<th>Breathing pattern (upper thoracic contribution to respiratory movements, %)</th>
<th>DB criterion list (0-10)</th>
<th>NQ (0-64)</th>
<th>EQ VAS (0-100)</th>
<th>HADS-A (0-21)</th>
<th>HADS-D (0-21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Baseline</td>
<td>28</td>
<td>6</td>
<td>27</td>
<td>50</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>End of intervention</td>
<td>18</td>
<td>4</td>
<td>8</td>
<td>80</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3-month follow-up</td>
<td>19</td>
<td>1</td>
<td>8</td>
<td>80</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6-month follow-up</td>
<td>24</td>
<td>0</td>
<td>9</td>
<td>85</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>12-month follow-up</td>
<td>24</td>
<td>0</td>
<td>2</td>
<td>85</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Baseline</td>
<td>67</td>
<td>5</td>
<td>24</td>
<td>95</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>End of intervention</td>
<td>47</td>
<td>0</td>
<td>4</td>
<td>96</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3-month follow-up</td>
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<td>0</td>
<td>3</td>
<td>96</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6-month follow-up</td>
<td>34</td>
<td>0</td>
<td>1</td>
<td>95</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>12-month follow-up</td>
<td>35</td>
<td>0</td>
<td>2</td>
<td>95</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Baseline</td>
<td>49</td>
<td>7</td>
<td>34</td>
<td>15</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>End of intervention</td>
<td>39</td>
<td>0</td>
<td>14</td>
<td>80</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3-month follow-up</td>
<td>46</td>
<td>5</td>
<td>22</td>
<td>90</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6-month follow-up</td>
<td>39</td>
<td>1</td>
<td>19</td>
<td>80</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>12-month follow-up</td>
<td>50</td>
<td>5</td>
<td>30</td>
<td>90</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Baseline</td>
<td>50</td>
<td>10</td>
<td>30</td>
<td>25</td>
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<td>End of intervention</td>
<td>30</td>
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<td>9</td>
<td>60</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
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<td>3-month follow-up</td>
<td>28</td>
<td>4</td>
<td>17</td>
<td>50</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>6-month follow-up</td>
<td>32</td>
<td>3</td>
<td>9</td>
<td>85</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>12-month follow-up</td>
<td>35</td>
<td>0</td>
<td>10</td>
<td>80</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>Baseline</td>
<td>51</td>
<td>6</td>
<td>25</td>
<td>80</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>End of intervention</td>
<td>37</td>
<td>2</td>
<td>15</td>
<td>80</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3-month follow-up</td>
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<td>2</td>
<td>19</td>
<td>83</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6-month follow-up</td>
<td>43</td>
<td>2</td>
<td>13</td>
<td>85</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>12-month follow-up</td>
<td>50</td>
<td>2</td>
<td>16</td>
<td>80</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

DB=dysfunctional breathing, NQ=Nijmegen Questionnaire, EQ VAS=EuroQol Visual Analogue Scale, HADS-A=Hospital Anxiety and Depression Scale – Anxiety, HADS-D=Hospital Anxiety and Depression Scale – Depression. DB criterion list contains 10 symptoms, 0=no symptoms, 10=10 symptoms. NQ; the higher score the more distress is present because of symptoms associated with abnormal breathing. EQ VAS; 0=worst imaginable health, 100=best imaginable health. HADS; 0-7=non cases, 8-10=doubtful cases, 11-21=definite cases.
Figure 7. Patients’ (P) score on the dysfunctional breathing (DB) criterion list at baseline (B), at the end of the intervention (I) and at the 3-month (3-m), 6-month (6-m) and 12-month follow-up (12-m). The follow-ups were performed 3, 6 and 12 months after the end of the intervention. A score of ≥5 was one of the inclusion criteria. 0=no symptoms, 10=10 symptoms.
Discussion

Summary of results
Patients with DB had experienced breathing problems over a long period of time before being diagnosed, had been treated with asthma medication and visited the emergency room because of their breathing problems. A third of the patients with DB had scores on the HADS-D indicating depression. Compared with patients with asthma, patients with DB had poorer HRQoL, more anxiety, poorer sense of coherence, more respiratory symptoms and experienced greater influence on daily life due to breathing problems. Both patients with DB and asthma had impact on physical activity because of their breathing problems. The majority of patients with DB were females.

At the 5-year follow-up, after patients with DB had received information and breathing retraining, patients with DB were no longer taking asthma medication, the number of emergency room visits had decreased, respiratory symptoms and influence on daily life due to breathing problems had decreased and HRQoL was enhanced.

The RMMI was found to measure different breathing patterns in different body positions. In addition, there were strong correlations between respiratory movements and breathing volumes.

Patients with DB seem to benefit from information and breathing retraining as measured by a decrease in patient-specific respiratory symptoms and respiratory-related activity limitations and improved breathing patterns.

Impact of dysfunctional breathing
Many of the patients with DB had experienced breathing problems for a long time without receiving a correct diagnosis (studies I and IV). Moreover, several patients with DB had made emergency room visits because of breathing problems (study I). These findings are in accordance with those reported in other studies showing that patients with DB often remain undiagnosed or are misdiagnosed owing to a diversity of clinical signs and symptoms (36). Having breathing problems without being diagnosed and obtaining optimal treatment can increase health care consumption (89, 113). An underlying cause of increased health care consumption can be related to the patients not knowing
the cause of their breathing problems. When symptoms remain unexplained, fear of illness may arise and lead to increased emergency room visits (114).

A majority of the patients with DB had their breathing problems misdiagnosed as asthma and were on asthma medication prior to the studies (studies I and IV). These findings are in line with other studies showing that DB can be misdiagnosed as asthma with the probable risk of prescription of unnecessary asthma medication (74-76). The consequences of a misdiagnosis of asthma include the patient’s potential exposure to the adverse effects of asthma medication, the cost of asthma medication and social and psychological consequences for the patient stamped with a chronic respiratory disease. There is also a lost opportunity to appropriately treat the true cause of the patient’s respiratory symptoms (76). Finally, because DB can occur in association with genuine asthma, there is a risk that these patients are prescribed excessive doses of asthma medication (74, 75).

In study I, the patients with DB, in comparison with patients with asthma, reported lower HRQoL for psychological health (measured with the SF-36). HRQoL has been shown to correlate poorly with pulmonary function in patients with asthma, but patients with more symptoms have a lower HRQoL (115-117). In study I patients with asthma had a lower degree of breathing symptoms than patients with DB, which might explain the difference between the two groups in HRQoL. In addition, the fact that the asthma and DB group differed in the length of time that they had their disorder (23 years for the patients with asthma vs. 7 for the patients with DB) may also have contributed to the differences in HRQoL. Another possible explanation for the impaired HRQoL in the patients with DB is that experiencing breathing problems without being diagnosed and not knowing how to cope with them can be stressful (90) and hence have a detrimental effect on HRQoL. An explanation could also be that DB is a consequence of impaired HRQoL.

Many patients with DB had scores ≥8 on the HADS-A, which would indicate anxiety. In study I, II and IV 14 of 25 patients (56%), 11 of 22 (50%) and 3 of 5, respectively, presented symptoms of anxiety at baseline. A certain degree of anxiety due to distressing symptoms such as breathing problems is natural, but the relationship between anxiety and DB is still unclear. Scores of ≥8 on the HADS-D, which indicate depression, were seen in 8 of 25 patients (32%) with DB in study I, in 3 of 22 (14%) in study II and in 2 of 5 at baseline in study IV. Consistent associations have been found between anxiety/depression (measured with the HADS) and respiratory symptoms in patients with asthma, but not between anxiety/depression and pulmonary function (118). These results may be explained by the presence of DB, and it is suggested that psychological status should be assessed in patients with respiratory symptoms (118).

Patients with DB experienced breathing problems and reported that these problems negatively affected their daily life (study I). In study IV, patients with DB experienced respiratory-related activity limitations both in physical
activities and in other activities (e.g., when talking loudly). Previous studies on patients with DB and patients with DB associated with asthma have mainly focused on symptoms (45, 83, 119) and not on the impact of the symptoms on everyday life and on activity limitations. However, it is important to include those aspects in the investigation and treatment in order to help the patients function better in every day settings.

Assessment of dysfunctional breathing

The assessment of DB is not yet standardised, but it is recommended that the assessment should include measurements of biomechanical, biochemical and psychological factors, respiratory symptoms and tests of respiratory functions (10). A careful history and examination is important (113) and it is especially pertinent to exclude other causes of the breathing problems (37, 38).

Assessment of the breathing pattern is an important part of the investigation of patients with breathing problems. Such an assessment can be done both visually and with technical equipment, such as the RMMI. A problem is that the large variations in reference values found in the normal breathing pattern in different body positions (21) can make it difficult to determine to what degree the breathing pattern is disturbed. In addition, the natural breathing pattern can be modified just because the person brings attention to it (28). However, objective measurements can be advantageous in evaluating the breathing pattern over time. In studies I and IV, the breathing pattern was visually assessed at the time of inclusion. It was assessed while the patients were dressed and they were not aware that their breathing pattern was being analysed. An advantage of this assessment procedure is that it does not affect a person’s spontaneous breathing pattern. This is important in that persons often change their breathing pattern when they know they are being observed (28, 35). A disadvantage with visual analysis of the breathing pattern is that it is a subjective assessment and thus it can be difficult to evaluate changes over time. In addition, the validity and reliability of visual analysis have not been studied.

In study III, it was shown that the RMMI can discriminate between different breathing patterns in varying body positions. Study III also demonstrated strong correlations between respiratory movements and breathing volumes. The ability to measure breathing patterns in different body positions is important as breathing patterns change in relation to body position (20). An advantage with the RMMI is that the use of a mouthpiece, mask or nose clip is not required. The application of these devices can alter a person’s breathing pattern by increasing tidal volume and decreasing breathing frequency (17, 18, 120, 121). Another advantage is that RMMI does not require a laboratory setting. It is documented that observations in a laboratory may induce anxiety that leads to an altered breathing pattern (120). The fact that the measurements with the RMMI can be shown not only in curves but also in millimeters is an
important advantage because it makes it easy to monitor a person’s breathing pattern over time and because treatment that aims to affect the breathing pattern can be evaluated. A disadvantage of the RMMI is that the upper part of the subject’s body must be partially undressed because the laser sensors cannot measure through clothing. Some persons may find it uncomfortable to have their upper body exposed and this awkward feeling may inadvertently change their breathing pattern. Other disadvantages with the RMMI are that the measurements have to be performed with the subject at rest in stable body positions and measures can only be made for a maximum of two consecutive minutes.

In study IV, all participants had normal end tidal CO₂ values throughout the study, indicating that they did not have hyperventilation syndrome. Nor did the CO₂ levels correspond to the scores on the NQ. The weak and variable relationship between the CO₂ levels and NQ scores has been discussed previously (10, 39).

The assessment of HRQoL in patients with DB is important because it has been suggested that HRQoL can be impaired in patients who experience breathing problems without being diagnosed and not knowing how to cope with them (89, 113).

As shown in studies I, II and IV, anxiety and depression (measured with the HADS) seem to be common in patients with DB and therefore these symptoms should be included in the assessment.

For measurements of respiratory symptoms, the NQ and DB criterion list were used in this thesis. It has previously been shown that high scores on the NQ are related to patients with a thoracic dominant breathing pattern (45). The NQ can be used to evaluate whether patients with high scores benefit from breathing retraining (39). Thomas et al. claim that the NQ score may be used as a continuous variable instead of as a dichotomous variable to measure the level of unpleasantness that is due to respiratory symptoms (122). Because there was no existing questionnaire to assess DB, except the NQ, the DB criterion list was constructed and used in studies I, II and IV. A cutoff score of ≥5 (out of 10) was chosen to identify patients with DB and as an inclusion criterion. After the intervention, the score of the DB criterion list was <5 in a majority of the patients with DB. This result indicates that the DB criterion list could be useful in the assessment of DB, as well as in evaluating the effects of breathing retraining. However, the DB criterion list has to be further developed and evaluated for psychometric properties in patients with DB.

In study IV, patients with DB experienced respiratory-related activity limitations for physical activities and other activities, such as “to sing”. It is important to assess the presence of possible activity limitations in order to help the patient overcome them and to reduce their impact on the individual’s daily life.

A vast majority of the patients with DB in this thesis were females which is in accord with other studies (38, 40, 45), but it has not yet been looked into
why there is this relative dominance of females over males. An explanation may be that symptoms in men and women are interpreted differently (e.g., that men who complain of chest symptoms are more often referred to a cardiac department and women more often to a pulmonary department). The reason can also be that the prevalence of DB is in fact higher in women. In patients with asthma women have a greater perception of dyspnoea and have poorer HRQoL than men with matched severity of the asthma disease (123). It has also been shown in patients with asthma that women have a higher degree of health care utilisation, including emergency room visits, than men (124, 125). Whether these sex differences also exist in patients with DB remain unknown.

Treatment outcomes of information and breathing retraining in dysfunctional breathing

Study II was a 5-year follow-up of patients with DB who had received information and breathing retraining. However, because of the design, it cannot be determine when the improvements occurred. In study IV, the improvements were mainly observed at the end of the intervention phase and at the follow-ups. This pattern is in line with a study by Thomas et al. (83). The study included patients with DB in association with asthma and it was shown that improvements in symptoms were not observed 1 month after the intervention but after 6 months. A late onset of improvements after information and breathing retraining is also in agreement with clinical experience. A possible explanation of the late treatment effects may be that to obtain an improvement, a change in behaviour is required and it takes time to restore and maintain patterns of movements, such as a breathing pattern.

In study IV, changes towards a more abdominal breathing pattern were observed in 4 of the 5 patients with persistent results at the 12-month follow-up. Courtney et al. have shown that breathing pattern and respiratory symptoms were improved in patients with DB after a breathing and relaxing therapy (45). In Courtney et al.’s study the breathing pattern was evaluated by manual assessment of respiratory movements. A novel method in this thesis was that the breathing pattern was objectively evaluated (measured with the RMMI) before and after treatment in patients with DB. However, the relationship between treatment and breathing pattern need further investigation as does the relationship between breathing pattern, respiratory symptoms and activity limitations.

HRQoL (measured with the SF-36) improved with respect to physical health but not with respect to mental health (study II). In study IV, HRQoL (measured with the EQ VAS) improved in 3 of the 5 patients, with 2 having high, stable values throughout the study. Because of the study designs (in studies II and IV), it cannot be determined whether the improvement in HRQoL was because of information about DB, decreased breathing problems or other
causes. A randomised controlled trial has shown improved HRQoL after information and breathing retraining in patients with DB in association with asthma (83). The Asthma Quality of Life Questionnaire (126) was used in the study and activities, symptoms and environmental domains showed improvements 1 month after the intervention, with persistent improvement in the domain of activities after 6 months (83). In addition, symptoms associated with DB (measured with the NQ) had also decreased after 6 month.

In study II, no changes in the anxiety or depression scores (measured with the HADS) were noted after treatment. In study IV, 2 of the 5 patients showed improvements in anxiety while one showed deterioration. Concerning signs of depression, 2 of the 5 patients had improved at the 12-month follow-up. Further studies are needed to elucidate the relationship between anxiety, depression and DB.

Respiratory symptoms (measured with the DB criterion list and NQ) decreased after the intervention (studies II and IV). Reduction of respiratory symptoms (measured with the NQ) after breathing retraining has also been shown previously (45). These results strengthen the assumption that DB is related to the NQ score and that the NQ can be used to evaluate whether patients with DB benefit from breathing retraining (45, 127).

A new approach in this thesis was that respiratory-related activity limitations were investigated and evaluated. Improvements were found after treatment. This finding is important because activity limitations affect the patients’ ability to function in their social, family and work environment. In addition, to have a physical activity limitation can involve health risks as physical activity is an important factor in reducing the risk of acquiring a disability disease (128).

Another important finding in this thesis was that patients with DB who were treated with asthma medications before diagnosis and treatment were not prescribed asthma medications at the long-term follow-ups in studies II and IV. Incorrect treatment with asthma medication can have consequences both for the patients and for the health economic, i.e., adverse events due to the medication and the cost of medication. Further, emergency room visits due to breathing problems in patients with DB had decreased at the 5-year follow-up in study II. An explanation could be that the patients had received an explanation of their breathing problems, had a reduction in symptoms and had strategies to handle symptoms if they appeared.

Methodological considerations

A strength of this thesis was that very few of the subjects declined to participate and that only a small number dropped out. In study I, two patients (one with DB and one with asthma) declined to participate because of time constraints. In study II, five patients had dropped out at the 5-year follow-up (3/25
with DB and 2/25 with asthma). The response rate in the questionnaires was good in all studies.

Because there is as yet no consensus regarding a definition of DB, the questionnaires used were not tested for their validity or reliability for patients with DB. Nevertheless, one of the questionnaires (the NQ) has previously been used in studies in patients with DB and some are generic (HADS, SF-36, EQ VAS, Sense of Coherence Scale) and can be used for patients with DB. The DB criterion list and the questionnaire investigating influence daily life due to breathing problems were constructed for the studies. Before the questionnaires were used in study I, they were all tested on five patients with DB and five with asthma. Before study IV was conducted, the questionnaires were tested on one patient with DB. All individuals agreed that the questions were relevant and easy to understand and to answer.

An advantage of the intervention used was that patients were encouraged to work on improving attention to their breathing pattern and correct it when necessary. The intention was to make them independent of the therapist. Such independence was further strengthened because there was no need for technical support. The intervention was well tolerated by the patients. For instance, in study IV, the participants reported performing their breathing retraining 5-7 days a week during the first 10 weeks of the intervention phase.

Because of the study designs (in studies II and IV), it cannot be determined whether one of the components in the intervention is more important than the other. The informational part of the intervention may be as effective as the breathing retraining part. In addition, it cannot be determined to what extent professional attention and the interactions between the patients and the therapist affected the results, especially as the therapist also evaluated the results. The continuous self-rating of patient-specific respiratory symptoms and activity limitations in study IV may also have affected the outcomes.

A strength of study IV was that domains known to be important for the individual patient to function in everyday life were investigated. Additionally, the long-term follow-up was essential because improvements in respiratory symptoms and activity limitations seem to have a late onset.

An attempt to control for response shift bias in the continuous registration of patient-specific respiratory symptoms and respiratory-related activity limitations was made by having the patients rate the change in their respiratory symptoms and activity-limitations on the CGI–I.

Another strength of study IV was that the daily self-registered patient-specific respiratory symptoms and respiratory-related activity limitations were performed at a web page, which made it possible to ensure that the patients registered on a daily bases and not retrospectively.

In study III, the RMMI was investigated before implementing it in study IV to see whether it could discriminate between different breathing patterns and whether the measurements correlate with breathing volumes. A strength of study IV is the measure of the breathing pattern with the RMMI because
breathing pattern in patients with DB has not been objectively evaluated before.

The single-subject design used in study IV provides the possibility to obtain detailed information about how treatment is implemented, the feasibility of measures and individual effects (129). The design can be used as a first step to evaluate diagnosis and treatment that are relatively unexplored before attempts are made to establish evidence using larger studies (129). The AB design is considered analogous to a quasi-experimental design, including threats to history (129). An attempt to control for threats to history was made by adding the questions “Has something special happened today? If yes, what has happened?” in the continuous self-registrations of respiratory symptoms and activity limitations. The increased number of single-subject AB cases due to direct replication and that all patients showed improvement also strengthened internal validity and mitigated the possibility that extraneous factors caused the effects (130). In addition, because most of the baselines consisted of many data points, this ruled out several threats to internal validity, such as instrumentation, testing and regression towards the mean (131).

One limitation in studies I and II was that no power analysis was performed, which poses a risk of a type II error, i.e. failing to detect an effect or difference that is really present.

Another limitation was a potential bias in the sampling procedure of patients with asthma in study I. The patients with asthma were matched for age and sex but not for the duration of their disease. The fact that the group with asthma had had their disease for a mean of 23 years (vs. 7 years for the DB group) can have affected the results. For example, the differences in HRQoL can have been affected by a response shift because some patients with long-term disability might experience their HRQoL as better compared with the first years of the disease (132).

The findings after the intervention in studies II and IV need to be considered in relation to the limitations of the study designs and methods used, especially with respect to threats to internal validity. However, the degree of improvement shown and that the patients had experienced their breathing problem for a long time prior to the intervention may indicate that the intervention was the main contributor to the observed improvements.

**External validity**

The patients with DB were only recruited from one lung and allergy outpatient department in Sweden, which limits the external validity of the studies and the ability to generalise the findings to the entire DB population. Replications in other samples and with other types of designs are needed to increase the external validity of the findings.
The majority of the patients with DB were women. This lack of a uniform distribution between the sexes is consistent with previous reports on the prevalence of DB (38, 40). Still, future studies that include more men are needed to improve external validity.

Another threat to external validity concerns the reactivity of experimental arrangements, i.e. the participants’ behaviour may have altered because they were aware of the fact that they were participating in a study.

In single-subject designs restricted external validity is a well-known limitation. In study IV, direct replication with five patients was used to improve generalisability (129).
Conclusions

Patients with DB often made emergency room visits because of their breathing problems, were treated with asthma medication and showed signs of depression. Compared with patients with asthma they were more disabled in terms of health-related quality of life, anxiety, sense of coherence, influence on daily life and respiratory symptoms. Breathing problems had a negative impact on physical activity in both DB and asthma groups.

Patients with DB had improved in health-related quality of life, influence on daily life, respiratory symptoms, decreased number of emergency room visits and they were not treated with asthma medication five years after the intervention.

The Respiratory Movement Measuring Instrument (RMMI) was found to discriminate different breathing patterns in different body positions. Strong correlations were observed between respiratory movements and breathing volumes.

Patients with DB showed improvements in patient-specific respiratory symptoms, respiratory-related activity limitations and breathing pattern after the intervention. These improvements persisted at the 12-month follow-up.

Clinical implications and future research

Clinicians should be aware that DB problems seems to be common among adults and that they can occur alone or in association with other diseases or disorders. A correct assessment provides opportunity for appropriate treatment. In addition, it is also important to avoid unnecessary treatment. The findings in the thesis indicate that patients with DB benefit from information and breathing retraining. When evaluating changes in breathing pattern, it is valuable to measure the breathing pattern in an objective way as a complement to visual analysis. The RMMI is an instrument that is easy to use in a clinical setting to measure breathing pattern.

The present findings contribute to the knowledge about DB but many questions remain, suggesting the need for further research.
Consensus about diagnostic criteria are needed to be able to study the prevalence of DB and to develop guidelines for assessment and treatment.

There is a need for larger studies with experimental design to further evaluate the effects of information and breathing retraining in patients with DB.

Because breathing retraining should be considered as a multicomponent behaviour change intervention (86), it would be worthwhile to investigate whether patients with DB benefit from inclusion of clearly defined behaviour change techniques.

In the clinical environment breathing pattern is often not evaluated systematically. It is not always possible to use an instrument to objectively measure an individual’s breathing pattern. In addition, such an instrument could affect a person’s natural breathing pattern. Therefore, it would be of value to study the reliability and validity of visual inspection of breathing patterns and compare this approach with objective measurements.

More long-term follow-up studies are needed to investigate whether the improvements reported here are maintained over time. However, if they cannot be maintained over time, research should be done on developing techniques to maintain the improvements.

Finally, studies are needed to investigate and explain the presence of female dominance in patients with DB.
Svensk sammanfattning (Swedish summary)

Termen dysfunktionell andning (DA) beskriver personer med ett andningsmönster som är förlagt högt upp i bröstkorgen. Personer med DA har andningsbesvär som inte kan tillskrivas en medicinsk diagnos såsom t.ex. astma eller kroniskt obstruktiv lungsjukdom. Det råder ännu ingen konsensus angående definition/diagnostisering eller behandling av DA och det finns ett stort behov av mera kunskap om andningsbesvär av dysfunktionell karaktär för att kunna identifiera och behandla dessa patienter på ett adekvat sätt. Prevalensen uppskattas till ca 10 % i den vuxna populationen (hos personer med och utan astma) och till ca 30 % hos de med astma. DA förkommer oftare hos kvinnor än hos män. Det är vanligt att personer med DA inte blir diagnostiserade eller får en astmadiagnos. DA kan förkomma som enskilt tillstånd men även tillsammans med andra tillstånd och sjukdomar. I det dagliga arbetet med personer med andningsbesvär är det av vikt för kliniker att ha DA i åtanke i samband med bedömning och behandling av patienter med oklara andningsbesvär. Definitionen av DA i denna avhandling baseras på att personen har ett dominerande högt andningsmönster i vila, sittande med stöd utan att det föreligger några medicinska orsaker samt att de har andningssymtom.

Det övergripande syftet med denna avhandling var att beskriva vuxna patienter med DA samt att utvärdera behandlingsresultat efter information och andningsträning.


Det andra delarbetet är en 5-års uppföljning av de patienter som deltog i delarbetet ett. Patienterna med DA hade erhållit individuell behandling bestående av information och andningsträning. Enkätsvar inhämtades från 22 patienter med DA och 23 patienter med astma, då det fanns ett bortfall på fem patienter. Vid 5-års uppföljning hade patienterna med DA minskat antalet ak-
utbesök och ingen använde astmamediciner. De hade en förbättrad hälsorelaterad livskvalitet inom den fysiska domänen, hade färre andningssymtom och var mindre påverkade i dagligt liv och i samband med fysisk aktivitet.

I det tredje delarbetet undersöktes om Respiratory Movement Measuring Instrument (RMMI) kan mäta olika typer av andningsmönster (spontan naturlig andning, basal andning och andning högt upp i bröstkorgen) i olika kroppspositioner (liggande, sittande med stöd och stående med stöd). Tjugo friska försökspersoner deltog. Det undersöktes även om andningsrörelser korrelerar till andetagsvolymer i de olika kroppspositionerna. En subgrupp på 12 friska försökspersoner deltog i underökningen. Resultaten visade att RMMI kan särskilja olika andningsmönster i olika kroppspositioner samt att det föreligger starka korrelationer mellan andningsrörelser mätta med RMMI och andetagsvolymer.

I det fjärde delarbetet deltog fem patienter med DA. De fick en individuell intervention bestående av information och andningsträning. De följdes sedan upp 3, 6 och 12 månader efter interventionens slut. Data om två patientspecifika andningssymtom och två andningsrelaterade aktivitetsbegränsningar samlades kontinuerligt in med hjälp av självskattningsformulär. Andningsmönster mättes (med RMMI) före, under och efter interventionen. Förbättringar i symtom, aktivitetsbegränsningar och andningsmönster sågs framför allt i slutet av interventionen. Vid 12-månaders uppföljning upptäcktes två av de fem patienterna en stor förbättring i sina andningssymtom och aktivitetsbegränsningar. De resterande tre patienterna upptäckte förbättringar i några av sina andningssymtom och aktivitetsbegränsningar. Fyra patienter hade förbättrat sitt andningsmönster till en mera basal andning.

Sammanfattningsvis har denna avhandling visat att patienter med DA hade upplevt besvär under lång tid innan de identifierats med DA, många hade sökt sjukvård akut på grund av sina andningsbesvär och en majoritet hade blivit behandlade med astmamediciner. En tredjedel upptäckte tecken på förekomst av depression. Jämfört med patienter med astma upptäckte de lägre livskvalitet, mera förekomst av oro, svagare känsla av sammanhang och andningsbesvär påverkade det dagliga livet negativt i större omfattning.

RMMI kan användas för att objektivt mäta och utvärdera andningsmönster då den kan särskilja olika andningsmönster i olika kroppspositioner och då korrelationerna mellan uppmätta andningsrörelser och andetagsvolymer är starka.

Efter behandling bestående av information och andningsträning upptäckte patienter med DA en förbättrad hälsorelaterad livskvalitet, minskade andningssymtom och aktivitetsbegränsningar, minskat påverkan i dagligt liv, förbättrat andningsmönster och konsumtionen av akut sjukvård hade minskat. Dessa resultat indikerar att patienter med DA har nytta av information och andningsträning.
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A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)