Thesis for doctoral degree (Ph.D.)
2017

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# ABSTRACT

**Background and aim**: The use of hatha yogic exercises (YE) is increasing, with both healthy individuals and patients asking for alternative treatments and other means of prevention and exercise. To investigate the physical effects and experiences of practicing YE among different groups thus seem important. Specifically, this thesis aimed to investigate heart rate variability, blood pressure, cardiovascular fitness and blood parameters using different YE programs for healthy populations. Another aim was to investigate walking distance, breathlessness, lung function and health related quality of life in participants with obstructive pulmonary disease.

**Participants and methods:** *Study I* was a pilot study without a control group investigating the effects of practicing yogic inversions among 12 naïve, untrained and healthy persons (median age 51, 4 women and 8 men) while measuring cardiovascular health as heart rate variability, hand-grip strength and blood pressure. S*tudy II* used an RCT design and investigated the effects of practicing high intensity sun salutations among 44 healthy students (median age 25, 38 women and 6 men) while measuring cardiovascular fitness and blood parameters as apolipoproteins, adiponectin, leptin and glycosylated haemoglobin. *Study III* used an RCT design and investigated the effects of practicing an adapted YE program compared to a treatment as usual group (CTP) among 36 individuals with obstructive pulmonary disease (median age 64, 23 women and 13 men) while measuring six minute walk distance, dyspnea, lung function and disease specific quality of life. *Study IV* used a qualitative approach to investigate the experiences after YE (used in Study III) among 15 persons with obstructive pulmonary disease (median age 61, 10 women and 5 men).

**Results**: *Study I* showed increased heart rate variability with a significant increase in pNN50% (ES 0.45) and hand-grip strength but no effect on blood pressure. *Study II* showed no between-group effect and no effect on cardiovascular fitness. However, within the YE-group 35-40 minutes of high intensity sun salutation had an effect on the blood parameters as adiponectin and apoplipoproteinA1. *Study III* found no significant between-group effect using t-tests in any parameter after the intervention. Analysis of variance differences emerged in CRQ fatigue and emotional domains favouring the treatment as usual group (CTP). Improved six-minute walk distance in the YE-group and CTP-group emerged after 12 weeks with no between-group effects. Disease specific quality of life measuring (CRQ) showed improvement in the mastery domain in YE and in all domains in the CTP-group. The YE-group showed lower respiratory rates, the CTP-group did not. Lung function and respiratory muscle strength did not improve in YE but did in the CTP-group. Dyspnea related distress did not improve in any group. *Study IV* found that the power of practicing (learning by doing) seemed central to the facilitation of self-awareness, controlling symptoms, dyspnea and permitted discovery of new ways of breathing.

**Conclusions**: The main findings following the evaluation of different yogic programs in *Studies I-III* showed that the programs were feasible and safe with no documented adverse effects. *Study I* was a pilot study calling for caution when interpreting the results. However, there still emerged significantly increased heart rate variability and hand-grip strength. In *Study II* no significant effect emerged between the groups. However, the yogic exercise group (YE) showed increased levels of apolipoproteinA1 and adiponectin following YE intervention. *Study III* demonstrated improvement in all CRQ-domains in the CTP-group and in the mastery domain in the YE-group following a 12 week intervention. Taken together, the study resulted in significant improvements in walking distance in both groups following the 12 weeks. In the YE-group, lowered respiratory rate, improved mastery of the disease and increased oxygen saturation also emerged after the intervention. *Study IV* found that practicing YE can be a method used to empower individuals with obstructive pulmonary disorders and to help control symptoms and dyspnea. Yogic practice can serve as an efficient tool for learning new ways of breathing as well as strengthening one's self-efficacy and mastery of the disease.

To all those who want to immerse themselves in the yogic experience

*"In the end.. it's not going to matter how many breaths you took*
*But how many moments took your breath away" - Shing Xiong*

*"Do your practise and all is coming" – Patthabi Jois*

## LIST OF SCIENTIFIC PAPERS

The thesis is based on the following original papers. Each paper will be referred to by its Roman numeral (Study I-IV)

I — Marian Papp, Petra Lindfors, Niklas Storck, Per Wändell, Increased heart rate variability but no effect on blood pressure from 8 weeks of hatha yoga – a pilot study, BMC Research Notes 2013 6:59

II — Marian Papp, Petra Lindfors, Malin Nygren-Bonnier, Lennart Gullstrand, Per Wändell, Effects of High-Intensity Hatha Yoga on Cardiovascular Fitness, Adipocytokines, and Apolipoproteins in Healthy Students: A Randomized Controlled Study, The Journal of Alternative and Complementary Medicine, 2016, 22(1): 81-87

III — Marian Papp, Petra Lindfors, Per E Wändell, Malin Nygren-Bonnier, Effects of yogic exercises on functional capacity, lung function and quality of life in subjects with obstructive pulmonary disease – A Randomized Controlled Study, Eur J Phys Rehabil Med. 2016 Nov 10. [Epub ahead of print], PMID: 27830924

IV — Marian Papp; Maria Henriques; Gabriele Biguet; Per E Wändell; Malin Nygren-Bonnier, Experiences of hatha yogic exercises among patients with obstructive pulmonary disease-a qualitative study, Submitted

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Study IV. May change prior to final publication

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## List of abbreviations

| | |
|---|---|
| 6MWD | Six-minute walk distance |
| Apo B | Apolipoprotein B |
| ApoA1 | Apolipoprotein A1 |
| BP | Blood pressure |
| COPD | Chronic obstructive pulmonary disease |
| CRP | C-reactive protein |
| CRQ | Chronic Respiratory disease Questionnaire |
| CTP | Conventional training program |
| DD-index | Dyspnea related distress |
| ECG | Electro cardiogram |
| EQ-5D | EuroQoL-5D |
| f | Respiratory rate |
| FaR | Physical activity on prescription (fysisk aktivitet på recept) |
| $FEV_1$ | Forced expiratory volume in one second |
| FVC | Forced vital capacity |
| GINA | Global Initiative of Asthma |
| GOLD | Global Initiative for Chronic Obstructive Lung Disease |
| HbA1c | Glycated haemoglobin |
| HR | Heart rate |
| HRQL | Health-related quality of life |
| HRV | Heart rate variability |
| HY | Hatha Yoga |
| ITT | Intention-to-treat |
| MCID | Minimal clinical important difference |
| MET | Metabolic equivalent |
| NIH | National Centre for Complementary and Integrative health |
| $PE_{max}$ | Maximal expiratory pressure |
| PEP | Positive expiratory pressure |
| $PI_{max}$ | Maximal inspiratory pressure |
| pNN50% | NN50 count divided by the total number of all NN intervals |
| RMSSD | The square root of the mean of the sum of the squares of differences between adjacent NN intervals |
| RPE | Ratings of perceived exertion (Borg) |
| RSA | Respiratory sinus arrhythmia |
| $S_pO_2$ | Oxygen saturation (peripheral) |
| SS | Sun salutations |
| VAS | Visual analogue scale |
| $VO_{2max}$ | Maximal oxygen uptake |
| YE | Hatha yogic exercises |

# 1 Introduction
From a yogic perspective health and well-being is about self-regulation, using the yogic exercises (YE) to control and strengthen the individual. There are three main components of YE, based as it is on modern hatha yoga; namely body, breath and mind. Access to yogic tools may enable individual resources to be fully utilized in order to develop and maintain health and well-being. Optimal physical and emotional functioning suited to each person's capacity can in turn provide freedom for the individual. In yoga, it is considered a skill and a freedom to be in tune with the body and bodily changes as well as having the capacity to adapt one's needs to it, while simultaneously being able to, to some extent, forget about the body. Being in the present moment using body postures and breathing techniques to control the body is assumed to lead to strengthening self-efficacy and the ability to handle different challenges in daily life more efficiently. The yogic way of using body, breath and mind simultaneously often results in a calm and strong body as well as a stable mind empty of rumination. Together, these factors are considered to improve individuals' health in the form of physical functioning, well-being and quality of life.

## 1.1 Health
*Health* refers to function and well-being in the physical, mental and social domains [1].
This thesis' focus rests primarily on health, not disease, as well as how improving one's health empowers individuals to live an active and productive life [2]. Moreover, health remains a resource in everyday life, not the objective of living [3]. Health promotion is the process whereby you enable people to increase their control over the factors contributing to their health [4].

## 1.2 Definitions of physical function and physical activity
*Physical function* can be defined as "The capacity of an individual to carry out the physical activities of daily living" [5]. Physical function mirrors motor function and control, physical fitness, and routine physical activity [6] [7] and is an independent predictor of functional freedom[8], incapacity [9], illness, and mortality [10]. The decline of physical function could arguably differ somewhat depending on physical activity level [11]. Baseline physical functioning usually influences the rate of decline that accelerates with age [11] [12], with poor health often being associated with lower levels of the objective measures of physical function. A few such often used and valid objective physical function measures include walking speed, respiratory capacity, muscular strength, hand-grip strength, cardiovascular performance, standing balance performance and chair rise time. However, physical function can also be measured with subjective measures. Such measures include self-reports, for example the short form health survey (SF-36) [13]. Though the survey mainly assesses health, it also looks at physical function. Other commonly used self-report measures covering additional aspects of health and function include, among others, disability (incapacity), sleep, energy and mental functioning.
To maintain and prevent the decline of physical function, *physical activity* may be used [14]. Physical activity can be defined as, ''any bodily movement produced by skeletal muscles that results in energy expenditure'' [15] above resting (basal) levels [16]. Interestingly enough, physical activity and *physical fitness* are often used interchangeably, with fitness representing

a more precise measure of physical activity than self-report [17]. As such, physical fitness is a, "physiologic state of well-being that allows one to meet the demands of daily living that provides the basis for sport performance, or both" [12]. To further understand the different definitions related to physical function, others have described *fitness* as a form of physical function [14]. Additionally, *physical fitness* may be characterized by performing daily chores with vitality and without fatigue as well as with sufficient energy to enjoy recreations. "The health-related components of physical fitness is cardiorespiratory endurance, muscular endurance, muscular strength, body composition, flexibility" [15], metabolism, agility and balance [5 12]. As noted above, physical fitness may mirror the definition of physical function. Lastly, *physical exercise* is defined as, ''Physical activity that is planned, structured, and repetitive bodily movement with an objective to improve or maintain physical fitness components''[15].

## 1.3 Health benefits of physical activity for adults

Some of the proven benefits of physical activity show reduced rates of all-cause mortality, high blood pressure (BP), coronary heart disease and stroke, metabolic syndrome, type 2 diabetes, breast and colon cancer, depression and rates of falling. Moreover, additional reported health effects of physical activity include increased cardiorespiratory and muscular fitness, increased bone health, increased functional health with healthier body composition and improved cognitive function [18-21]. To provide alternative forms of exercise is important considering disease due to inactivity is the fourth leading cause of death worldwide [22]. Physical inactivity has been estimated to cause 6% of all coronary heart diseases in the world, and inactivity is considered a risk factor at the same level as smoking [21]. In 2015, the leading global causes of death from non-communicable diseases were cardiovascular disease and chronic respiratory diseases. Between 1990 and 2005, deaths due to ischemic heart disease increased by 25.8% globally while COPD decreased by 4.6%. Between 2005 and 2015, the prevalence of cardiovascular disease decreased by 10.2% and COPD by 3%, but no doubt have to decrease even further [23].

## 1.4 Using hatha yogic exercises as physical activity

Yoga derives from the Sanskrit word root Yuj, "to yoke"; to join, [24] harness and gain control over the mind's senses [25]. One of its principal aims is to increase self-realization [26 27], self-efficacy [28] and self-empowerment [29], with improved health and well-being as one of its assumed positive effects. During the practice of yogic postures, there is a great emphasis on body awareness, breath regulation and mindfulness [24 30 31 29] . Furthermore, the practice of yogic exercises during a form of physical yoga such as hatha yoga may be described as quite forceful. This style of yoga often emphasizes the body, breathing exercises and concentration in order to achieve liberation by means of perfecting a strong yogic-body [24 32] that is immune to disease [25]. Many people in the West are practicing modern hatha yoga, it being the most common style of physical yoga in the West today [33].

The number of participants worldwide exceeds 300 million, of which approximately 19% resides in Germany [31] and 36.7 million in the US (Yoga in America Study 2016) [34]. Considering its popularity, there's clearly a need to evaluate its effects on physical function.

Yogic exercises is defined by the American College of Sports Medicine as a form of multimodal (neuromotor) exercise training and can be used with the aim to increase and maintain physical function and reduce falls among the elderly [5] . The National Centre for Complementary and Integrative health (NIH) meanwhile refers to yoga as a style of mind-body practice as well as a form of meditative movement used for health purposes. Both institutions define yogic practice as a style of exercise training, though NIH adds the dimension of yogic exercises also being a meditative movement. While performing yogic exercises it's especially important to include the "paying attention" part, otherwise it becomes "gymnastics". Furthermore, hatha yoga is described as a means of balancing psychophysical energies in the body and may also be called "psychophysical yoga", emphasising the need for reflection and attention while practicing [35]. The access to modern hatha yogic exercises (YE) have become more common both in health centers, gyms but also in primary care and hospitals. In Sweden, many physiotherapists participate in shorter courses and thereafter bring YE into their physiotherapy programs. This means that hatha yoga is already today used as a complement to conventional treatments, often described as a form of physical activity and exercise. There are many similarities between physical exercise and YE, both in healthy and diseased populations [30 36], when it comes to the achieved physical and mental effects, though YE displays greater mental effects than physical exercise directly after practice. YE is considered a safe intervention; indeed as safe as usual care and exercise [37]. One could posit that some participants with low physical status are more attracted to yogic exercises considering the form is different from conventional exercise, while others use it for restorative purposes.The components of physical fitness span both health and skill [15]. The health-related components include cardiorespiratory and muscular endurance, body composition and flexibility. Yogic exercises include most of the health-related components, except possibly cardiorespiratory endurance unless one is carrying out the sun salutation sequence. Skill-related fitness components involve agility, balance, coordination, speed, power and reaction-time. These components are also often included in YE, with the possible exception of speed and power. This, however, depends greatly on style. Including yogic jumpings and rapid vinyasa (one breath per movement) in the program may improve also speed and power [15].

## 1.5 Current recommendations for multifaceted physical activity that includes YE (also called neuromotor exercise training and functional fitness training)[5].

The available recommendations for multifaceted physical activity are ≥2-3 days a week for ≥20-30 minutes per session. Though the intensity, volume, progression and pattern remain unspecified, current strength training guidelines are:

**<u>Major muscle group strength training (2-4 sets of 10-20 repetitions each) [5]</u>**

| | |
|---|---|
| Novice to intermediate | 60-70% of 1RM (repetition max) |
| Experienced | 80% of 1RM |
| Seniors | 40-50% of 1RM |
| Improvements of muscular endurance requires | 20-50% 1 RM |

**<u>Current stretching guidelines for yogic exercises (which include stretching) are:</u>**

Use stretching for the major muscle groups (best effect if warmed up)

60 seconds per exercise (seniors recommended to hold 30-60 seconds)

Repeat each exercise 2-4 times. Methods for optimal progression remain unspecified.

## 1.6 Hatha yoga - traditional view and philosophy

The below meta-analysis uses many different styles of yoga, though hatha yoga is the most common [33 38]. However, the specific effect of hatha yoga in particular requires further elucidation. Hatha yoga is a spiritual discipline to increase self-realization, self-empowerment and liberation by means of achieving a strong body and is partly based on yogic texts[29 26 27 25]. One definition of the yogic technique is, "yogah-cittavritti-nirodhah"[39], translated as, "Yoga is the cessation of movements in the consciousness". Yoga is therefore the control of the conscious mind and mental operations (Yoga sutras 1.2, yoga citta**vrtti** nirodhah= **vrtti** meaning "waves" that disturb the mind). The yogi turns his mind inward, detaching from the material world in order to realize the true nature of the self [34]. The word hatha is divided into two life force energy (prana) channels, Ha = sun/surya/right/yin and tha = moon/chandra/left/yang. Hatha yoga is the union between these two psycho-energetic principles. Hatha yoga places great emphasis on asana and breathing, the purpose being to regulate the upper (prana) and lower (apana) breaths, also called winds/vayus. One aim is to use mechanical means such as body postures (asana), breathing exercises, body seals and locks (mudras/bandhas) to cleanse the body, control and regulate the life force (prana/winds/vayus) and preserving and raising bindu (a form of liquid considered to be the essence of life (amrita) inside the brain [40]). Three different body seals/locks located in the beginning, middle and end of the spine are used to control the prana. The body utilizes these mechanical techniques to cleanse itself (shat-karmas). Common areas to cleanse include the nose, tongue, ears, eyes, mouth, stomach, heart, bladder, skull, anus and intestines [40 41]. Theos Bernard, who wrote the first dissertation on hatha yoga in the USA (in the 1950s), emphasized the importance of breath-holding [27].

Hatha yoga can be described as that of using the body, breath and mind simultaneously [30 35 40 41].

- Physical poses (asanas, mudra, bandhas) **
- Breathing exercises (pranayama, extending, controlling and maintaining one's breathing, (kumbhaka)
- Purification techniques (shat-karmas)
- Sense-withdrawal (pratyahara)
- Contemplation/mindfulness/observation/meditation (dharana, dhyana, bindu (inner essence, atman = soul)
- Samadhi, absolute light (jyotis)

**Some important yogic postures include: dhanurasana, matsyendrasana, paschimottanasana, kukkutasana, kurmasana, mayurasana, uttanakurmasana. There are also seated and lying poses.

Hatha yoga is based on a number of old texts: "Hatha yoga pradipika", authored by Svatmarama yogi in the 15th century A.D., is the first text to include asana (physical postures); Patanjali – "yoga sutras" (Raja yoga), written around 300-500 A.D., Gheranda samhita (18th century) and Shiva samhita [25-27].Yoga is often thought of as a system of awareness/consciousness of physical and psychological controls [41 42]. Merging the true self (atman=individual soul/pure consciousness) with the ultimate principle of the universal soul (Brahman)[27] is one of the philosophical goals of yoga [26]. According to Patanjali there are eight paths to freedom (liberation) [26], of which number 3, 4, 6 and 7 are the most common Western entry points to yoga practice[43]. These paths are: 1. Yama=Moral principles; 2. Niyama=Self-awareness, discipline; 3. Asana=Body postures; 4. Pranayama=Breath control; 5. Pratyahara=Sense control; 6. Dharana=Concentration; 7. Dhyana=Meditation; and 8. Samadhi= Insight.

The class of yoga styles where union is central include ; *Jnana yoga*, union by knowledge; *Bhakti yoga*, union by love and devotion; *Karma yoga*, union by action and service; *Mantra yoga*, union by voice and sound; *Yantra yoga*, union by vision and form; *Laya and kundalini yoga*, union by arousal of latent psychic nerve-force; *Tantric yoga*, general term for the physiological disciplines but also union by harnessing sexual energy; *Hatha yoga*, union by bodily mastery; and *Raja yoga*, union by mental mastery [41 44].

For more details on all aspects and description of HY, please read [29 25 30 40 41 44 45].

## 1.7 General research on yogic exercises for disease prevention and comparison with usual care

By analysing and searching through the meta-analyses of YE in pubmed (approx. 120) one may conclude that, overall, YE can be used with promising results in small to moderate effect size groups in different populations. However, larger randomized studies with active control groups of higher quality are still needed, and interpretations of the meta-analysis results have to be approached with caution. Moreover, the methodology is limited and the heterogeneity of YE studies requires further studies to be able to describe the long-term effects of yoga.
A review of the systematic reviews of the management of chronic diseases demonstrates that yoga seems most effective for reducing symptoms such as anxiety, depression, and pain [46]. A larger cross-sectional study showed that the main aims of attending yogic practise is to achieve general wellness, disease prevention, improved energy and immune function, reduced stress levels and improved overall health [47] .
Compared to usual care, yoga resulted in significant improvements in exercise capacity and health related quality of life (HRQL). Yogic exercises may be a useful addition to formal rehabilitation exercises [48]. YE programs also have similar design and component structure across chronic disease populations. Yoga is generally considered a safe therapeutic intervention that is effective when trying to diminish other health-related symptoms [49] . Yogic exercises in the West is used primarily to treat musculoskeletal and psychological symptoms [50], and seem to increase parasympathetic activity by modulating the vagal nerve [35 36 51-55] both during and after practice.
The effects of yoga intervention on fatigue, anxiety, depression and sleep disturbances were small to moderate, particularly in cancer patients (where exercise is more effective), which suggests that yoga may be used as an ancillary intervention to improve health-related quality of life when compared to psychosocial interventions [56]. Hatha yoga represents a promising method for treating anxiety [57] and could be considered an additional treatment option for patients with depressive disorders [58]. Additionally, yoga is a form of meditative movement with a moderate positive effect on the quality of sleep among older healthy people with sleep

complaints [59]. Interestingly enough, the odds of a YE study reporting positive conclusions is 25 times higher among Indian studies than elsewhere [31].

## 1.8 Physical activity for disease prevention

Regular physical activity may act both as a primary and secondary prevention method for the prevention of chronic diseases, associated as it is with a reduced risk of premature death where there is a graded linear relation between volume and health status [12], often along with the motto "more is better". Not to forget that participants with the lowest physical status will show the greatest improvement in health status [12] and is often the group that needs to improve their physical function the most.

### 1.8.1 Physical activity and rehabilitation for obstructive pulmonary disease patients

*Prevalence*: Chronic Obstructive Pulmonary Disease (COPD) and asthma have an estimated worldwide prevalence of 5-10% [60-63], with both involving chronic inflammation and airflow limitations in the lung tissue. In disease projections for the year 2020, COPD is ranked fifth worldwide in terms of burden of disease.

*Symptoms and diagnosis:* COPD causes breathlessness (dyspnea), excessive sputum production, coughing and exacerbations with a persistent airflow limitation. It is a chronic inflammation in the lung tissue with structural changes [63]. However, as COPD involves permanent structural changes [63] due to a variety of different causes [64 65], it remains largely under-diagnosed [64]. The disease progression usually covers tissue destruction with narrowing of the small airways as well as small airway fibrosis with a decreased lung elastic recoil resulting in airways that cannot remain open during expiration. These changes often lead to hyperinflation and air/gas trapping and sometimes in hypersecretion [63]. The clinical diagnosis of COPD is dyspnea, chronic cough and/or sputum production where a post-bronchodilator test below 0.70 confirms the persistent airflow limitation. In line with this, the Global Initiative for Chronic Obstructive Lung disease (GOLD)[63] has divided COPD into 4 grades (formerly called stages), of which grade 4 is the most severe. The previously used indicator forced expiratory volume in one second ($FEV_1$) is today considered an inadequate and unreliable method of measuring the disease progression, severity of breathlessness, exercise limitation and health status impairment of COPD patients. Instead a ratio of $FEV_1$/FVC (FVC=forced vital capacity) below 0.70 is currently used for all grades.

Asthma is characterized by chronic inflammation and involves episodic smooth muscle contractions due to genetic or environmental causes. Factors that trigger asthma include allergens such as pollution and strong odours, but also physical exertion [66]. Poor symptom control seem to be associated with low physical function in persons with asthma [67]. Post-bronchodilator spirometry and symptom control using an asthma control test[60] is often used for diagnosis. According to the Global Initiative of Asthma (GINA) [66], asthma can be divided into 3 grades depending on its severity. This is determined by to the number of exacerbations and includes controlled, with no exacerbations (normal lung function), partly controlled, with one or more exacerbations a year (<80% predicted $FEV_1$ (or PEF)), and uncontrolled, with one exacerbation in any given week.

*Treatment*: COPD and asthma treatments span both pharmacological and non-pharmacological methods, including smoking cessation. [63] Regular physical activity is recommended as part of a non-pharmacological treatment modality for both COPD and asthma[63 68], with the aim being to improve physical function as exercise tolerance and decreased dyspnea and tiredness. Individuals with decreased lung function often have low physical function and may avoid physical activity and rehabilitation due to fear of dyspnea [69]. Patients with obstructive pulmonary diseases tend to reduce their physical activity levels (already at GOLD II), even though rehabilitation and health maintenance through physical activity is an important factor in preventing deconditioning and slowing the disease progression [70 71]. Using physical activity can increase physical function, decrease dyspnea and prevent fear of performing physical activity in persons with asthma [72]. However, pulmonary rehabilitation and education remain important components of the non-pharmacological treatment [69 73] .

Non-pharmacological rehabilitation exercise training programmes with the goal of maintaining and improving one's health often benefit chronic obstructive pulmonary disease (COPD) patients (provided they are able to walk without difficulties). Such improvements for example include increased exercise tolerance, fewer perceived symptoms of dyspnea and reduced fatigue [74].

Current recommendations for pulmonary rehabilitation[75] state a frequency of 2-3 days/week for a duration of at least 8 weeks at Borg-RPE 12-13 with 40-50% of $VO_2$ reserve HR, as well as resistance training loads of 50-85% of maximum voluntary contraction. Others suggest that light to moderate physical activity 30 minutes per day most days of the week can improve the quality of life in individuals with COPD [76].
Physical activity may indeed improve physical endurance and strength, as well as breathing efficiency and tolerance - especially in severely impaired persons – but nevertheless cannot reverse the physiological and structural deficits in COPD patients. However, an individualized progressive exercise program might be able to increase the functional capacity (physical function) of COPD patients with 70-80% after six weeks [76]. Moreover, previous findings concur with the substantial evidence that concludes that exercise training increases exercise performance and fitness in asthmatics [77]. Physically active individuals with asthma showed less of a decline in lung function than inactive participants with asthma [78].
The pharmacological treatments often reverse obstructive symptoms more efficiently in individuals with asthma compared to patients with COPD. Thus, any pharmacological treatment is often supplemented by pulmonary rehabilitation in the form of physical activity and is equally important for both asthma and COPD to be able to optimize physical function, prevent muscle dysfunction, reduce symptoms and improve quality of life [75]. The gas trapping may and often is prevented by extended exhalations [79 80]. Yet, relatively few patients attend pulmonary hospital-based rehabilitation programs in Sweden[81] . One reason for this may involve practical barriers and worries of not being able to manage the exercises [82]. However, additional randomized controlled trials, RCT studies of breathing control and pulmonary rehabilitation exercises [79] are still needed to help patients with breathing disorders improve their physical function, symptoms and health related quality of life. Such

rehabilitation may include yogic exercises and as well as both long-term and short-term physiotherapeutic interventions [83 84]. Yogic exercises have been tested in conjunction with various diseases and report improved symptoms and physiological effects.

## 1.9 Yogic exercises for cardiovascular health

Yogic exercises show promising evidence of improving cardio-metabolic health [85], while secondary prevention methods in cardiovascular health diseases remains unproven [86]. Studies have reported significant but small effects on BP after 3-8 weeks of YE training among hypertensive individuals [87], however it would be much more efficient if all three components - body, breath and mind – were to be used. Using 8-12 week YE interventions, some studies managed to decrease BP to similar levels as those associated with usual care in participants with mild to moderate hypertension [88-91], while others only reported low-quality evidence in hypertensive patients [92]. Others still have reported that primary prevention with YE has favorable effects on diastolic blood pressure, high density lipoprotein (HDL) cholesterol and triglycerides, but uncertain effects on low density (LDL) cholesterol [93]. Moreover, systolic BP has shown to be improved after YE in persons with metabolic syndrome not adhering to conventional forms of exercise [94] . Furthermore, yogic exercises may enhance peak $VO_{2max}$ and health related quality of life in patients with chronic heart failure and could be considered for inclusion in cardiac rehabilitation programs [95]. Cardiovascular endurance training and YE seem to have an equal effect on pulse-wave velocity and stiffness in carotid arteries, with YE practitioners having a slower speed compared to sedentary individuals. This implies that YE and aerobic participants have similar elasticity in arteries [96]. Increased heart rate variability (HRV) indicates greater parasympathetic control with increased cardiac vagal modulation [97 98], and the physiological adaptation to YE are often similar [52 99] or better than conventional exercise [36 53], with a lowered resting HR indicating vagal dominance after YE [52 98 100]. Studies have reported that YE may enhance the plasticity of the autonomic nervous system and improve the ability to recover after stress [98 101]. Performing slow breathing and/or a head below the heart position (inversion) activates the baroreceptors from an altered negative pressure in the upper body [54 55 88 102].

The mechanism of inverted posture and slow breathing may involve vagal stimulation and alternating carotid sinus pressure (baroreceptors) that can restore or reactivate the baroreceptor reflex function [54 102-105]. Other smaller case studies report that the upside-down position have the potential to treat tachycardia [102 104 105] when no other methods, such as medication and manual stimulation of the vagal nerve, work. Tai [102] reported a case study where a woman with arrhythmia was able to restore normal sinus rhythm with a 20-second hand-stand after all conventional methods had failed. Yogic exercises is a safe and effective way of reducing waist circumference and systolic BP in individuals with metabolic syndrome not adhering to conventional forms of exercise [94].

## 1.10 Yogic exercises for physical/cardiorespiratory fitness

Cardiorespiratory fitness is defined as the ability to perform dynamic, moderate- to high-intensity exercise for prolonged periods of time [106]. Many movements in YE, for example the sun salutation (SS), is performed with synchronized breathing (vinyasa) involving opening and uprising exercises on inhalation and closing and downward moving exercises on

exhalation. Sun salutations is the most common sequence used in yoga classes [107], but as of yet no long term improvement in cardiovascular fitness in healthy individuals have been reported. Some studies have reported immediate responses such as increased oxygen consumption and heart rate (HR) at a satisfactory cardiovascular training level during dynamic high intensity SS, inversions and certain back bending postures [32 108 109], while others have reported no effect [110]. Interestingly, a recent larger trial showed improvements in $VO_{2max}$ after YE [111] carried out by 173 healthy
participants (mean age 52). The study found significant effects on $VO_{2max}$ (1.3-2.61 mL/kg/min) during most of the demanding hatha yogic standing postures, seated postures, inversions, back-bends and plank poses following 3 months (60 minutes per week plus 165 min. home training) without SS. Tran et. al. studied the long-term effects of hatha yoga and found a significant increase in oxygen uptake[32], 6%, when using a minimum of two hatha yoga classes per week for 8 weeks. They used a "frog" pose - a dynamic and rapid knee bending posture[32], dynamic lunges, 2-3 rounds of SS and other static postures. A "outlier" cross-sectional study from the US measured the acute effects of performing SS and reported a graded increase in oxygen consumption [108] from 7mL/kg/min at the beginning of the program to 28 ml/kg/min (80% of max HR) at the end, indicating that high intensity SS training could possibly improve and maintain cardiorespiratory fitness. Yet, one-time measures may present higher values compared to the measurement of long-term effects. Others have shown levels of 41% [112] and 40% [113] of $VO_{2max}$ with YE.

## 1.11 Yogic exercises for obstructive pulmonary diseases

Moderate-quality evidence show that YE leads to small improvements in quality of life, asthmatic symptoms [114], lung function and exercise capacity, and that it could be used as an complementary pulmonary rehabilitation program in COPD patients [115]. Yoga may be considered an ancillary intervention method or as an alternative to breathing exercises for asthma patients interested in complementary interventions [116]. Using breathing exercises for 4-15 weeks have not only shown to improve functional exercise capacity in COPD patients but also dyspnea and health-related quality of life (HRQL), however no consistent effects have so far been demonstrated. Furthermore, breathing exercises can be used to improve exercise tolerance, respiratory muscle recruitment and respiratory muscle performance as well as reduce dyspnea in those persons with COPD who are unable to undertake exercise training. A review written by Holland et. al. suggests that *only* using breathing exercises in the comprehensive management of people with COPD is not to be recommended[117] .

## 1.12 Yoga for dysfunctional breathing

Considering we do it approximately 720 times per hour or 21 000 times per day, the way we breathe can influence our health status. Consequently, small improvements in breathing technique may have significant effects on our health. Dysfunctional breathing is commonly found in patients with breathing disorders, chronic back and neck pain sufferers and in persons with cardiovascular disease, anxiety and depression[80]. It's been suggested that dysfunctional breathing can be found in as many as 30% of asthma patients and 83% of people with anxiety, while in the general population it remains around 5-11%[80].

Hyperinflated lungs, common in COPD, is suggested to increase air trapping with elevated functional residual capacity in the lungs and as a result the diaphragm can lose its doming[80]. Hyperinflation involves inflammation, spasms, hypersecretion with a reduced lung elastic recoil pressure and destruction of lung parenchyma that may decrease the diameter of the airway lumen, in turn increasing expiratory resistance and prompting airway collapse (atelectasis = airways cannot remain open) at normal functional residual capacity levels [118]. Applying resistance during breathing can be used to improve breathing. Resistance during exhalation is called positive expiratory pressure (PEP) and can be used for different purposes in order to improve lung volumes (functional residual capacity and tidal volume) and gas exchange, reduce the work of breathing and hyperinflation as well as improve airway clearance and manage dyspnea in obstructed patients. To create breathing resistance, physiotherapy often uses PEP devices, "blow bottle techniques" and pursed lip breathing[118]. A pressure of 10-25 cm $H_20$ is considered normal.

The pursed lip breathing technique and PEP devises can be used to decrease functional residual capacity in participants with hyperinflated lungs for the purposes of preventing air trapping[80 118]. Participants with breathing disorders often display inefficient expiration and partial contraction of the diaphragm[80]. Shallow and rapid breathing, that is breathing mainly using the chest and assisting breathing muscles, is usually prevented by using the diaphragm. Lateral expansion of the waist is in turn a common method used to promote diaphragm breathing[119]. Furthermore, diaphragmatic breathing creates a deeper breathing pattern, improves the breathing technique [120], prevents partial contraction of the diaphragm [80] and encourages the use of the abdominal wall [69] and greater mobility of the diaphragm, increasing functional and inspiratory capacity [121]. Breathing difficulties can also be caused by incorrect head posture[80]. Using the abdominals during exhalations assists the diaphragm doming and long, non-forceful exhalations lengthens the diaphragm and may strengthen the expiratory phase[80]. The extended exhalations result in a more efficient contraction of the diaphragm (eccentric work) and a more effective contraction during inhalation.

Some of the yogic breathing techniques (pranayama) use "internal" body resistance such as the nose and the throat. Extended exhalations are usually a common goal in pranayama, especially when a restorative effect is preferred. Ujjayi breathing (ocean sounding or victorious breath) places an internal resistance on the breathing muscles during both inspiration and expiration. The resistance is formed by constricting the throat at the same time as issuing a soft hissing sound. Yogic breathing primarily uses the nose during both inhalation and exhalation, the result being prolonged breathing phases and slower respiratory rates. Every so often a hand is used to partially block the nostrils to increase resistance further during unilateral or bilateral nostril breathing. Yogic exercises use body weight and different body positions such as strong twists to strengthen the breathing muscles. Yogic exercises also use gravity assisted body positions, for example inversions, for the purpose of assisting in airway clearance and diaphragm functioning. Moreover, a controlled and slower respiratory rate prevents hyperventilation and may improve the autonomic nervous system balance, for example through increased vagal tone. Untreated hyperventilation can lead to inspiratory muscle exhaustion [80].

## 1.13 Yogic exercises for blood parameters

Hatha yoga has been shown to have an anti-inflammatory effect[122]. Previous findings have also reported increased adiponectin and lowered leptin levels following physical exercise[123 124]. Studies done on experienced yogic practitioners have when compared to novices shown higher adiponectin levels and lower leptin levels[123 125-127]. One study [127] showed higher degrees of inflammation with higher interleukin-6 (IL-6), C-reactive protein and leptin levels in novice yogic practitioners when compared to yogic experts (2 or more years' experience), while 3 months YE have been shown to decrease IL-6, but not tumor necrosis factor (TNF-alpha)[126], in breast cancer survivors. This could be related to differences in stress response between the two groups, with different resting vagal tone varying from individual to individual. The level of the anti-inflammatory protein adiponectin was higher in yoga experts while the adiponectin to leptin ratio (ALR) was twice as high in the yoga group[125]. Study II showed an ALR increase, though not a significant one in either group. ALR is usually higher in yoga practitioners and the ratio is a sensitive and reliable marker of insulin resistance. Intense yoga participation seems to alter the leptin and adiponectin production [125] and have also been shown to increase adiponectin levels in obese postmenopausal women following yogic intervention[128]. Moreover, adiponectin levels can change relatively fast; a ten day pilot yoga intervention done on obese men resulted in increased adiponectin levels and decreased IL-6, as well as decreased BMI, BP and HR[129]. Yet, since the design involved only men this brings up the question of the difference in adiponectin between the sexes. Moreover, even though the participants in the aforementioned study were normotensive, their BP decreased. It could be posited that since stress hormone levels fluctuate with the menstrual cycle this may be one of the reasons for why men and women respond differently to stress. Other studies [130 131] have reported decreased cortisol, IL-6 and TNF-alpha levels as well as increased beta-endorphin levels following a 10 day yogic lifestyle intervention. A subgroup gender based analysis showed similar responses to cortisol and TNF-alpha levels while beta-endorphin levels increased in females only and IL-6 increased in males only[130] It's been suggested that YE may benefit adult patients with Type 2 diabetes (fasting blood glucose, HbA1c, blood lipids) [132] and may be considered as an add-on intervention for the management of Type 2 diabetes [133]. Yogic practice could be considered a complementary therapy of Type 2 diabetes due to its positive effects on short-term glycaemic control and possible effect on the lipid profile [134]. Some evidence indicates that mind-body therapies (YE included) may increase immune responses to vaccination and reduce markers of inflammation as well as influence virus-specific immune responses to vaccination [135].

## 1.14 Other benefits of yogic exercises

Yogic interventions have been reported to result in small improvements in balance and medium improvements in physical mobility in people aged 60+ years [136]. Moreover, yoga appears to offer a promising modality for arthritis [137] and may be beneficial for symptoms such as chronic neck pain and functional disability [138]. There is also strong evidence to suggest YE's short-term effectiveness, and moderate evidence for its long-term effectiveness, on chronic lower back pain, making it suitable as an additional therapy for patients with chronic lower back pain [139 140]. There have been no reported adverse effects. The strongest and most consistent evidence pertains to the short-term benefits of yoga on functional disability for lower back pain [140]. On the issue of fibromyalgia, studies on YE have reported a medium-to-high effect on pain reduction without known side effects [141]. Yoga practice has also been shown to offer moderate improvements to chronic function [142] and the induction of functional and structural brain modifications in expert meditation practitioners, especially in areas involved in self-referential processes such as self-awareness and self-regulation. It's been suggested that meditation techniques should be embraced in clinical populations for the purpose of disease prevention [143].

## 1.15 Adverse effects and injuries related to yogic exercises

No adverse effects/events connected to YE have been reported in any of the previous meta-analyses, nor has there been any proven additional adverse effects when compared to other forms of physical activity.
However, some cases have suggested that performing unusually intense sessions and/or having a medical precondition may lead to stroke, neuropathy and worsening glaucoma in conjunction with injury[31]. The risk of yoga-related injuries is estimated at 1.45 injuries per 1,000 hours of yoga practice. Moreover, a recent report points to the trunk being the area most commonly injured through sprains/strains (46.6% and 45.0% respectively). Since the largest increase in injuries (8-fold) was demonstrated among those 65 years or older, senior citizens are recommended to practise with qualified teachers for safety purposes [144].

## 1.16 The mechanisms of hatha yoga

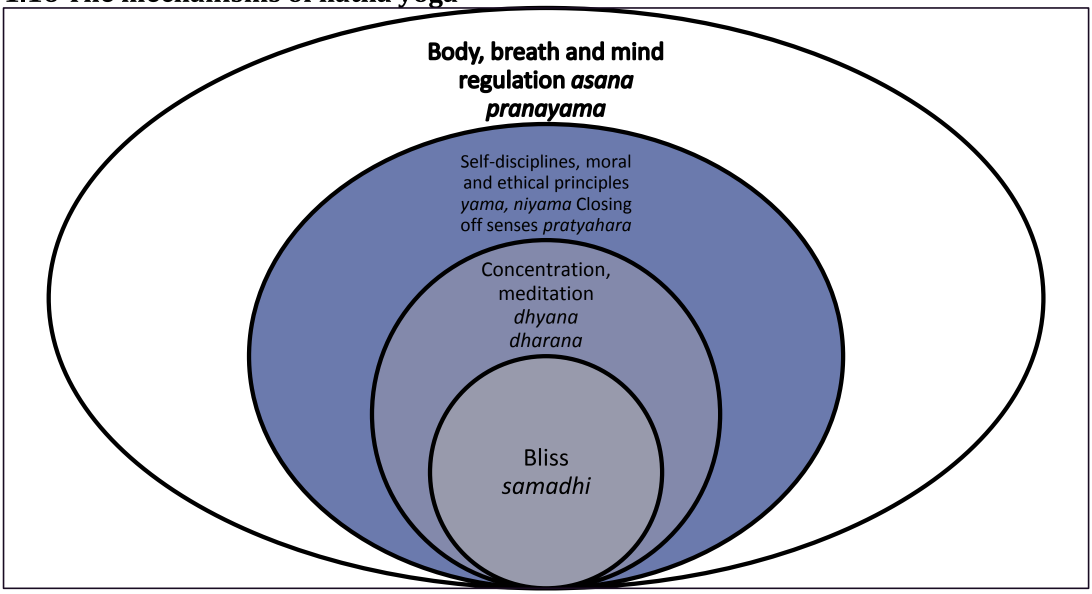


**Figure 1**. The principle of yogic practice is to work from the outside and in. Western entry points to modern hatha yoga involve body exercises, breathing exercises and concentration - represented by the outer layer in figure 1. Starting with the body is the least subtle and a common starting point for the novice yoga practitioner. The interventions in Study I-IV all focused on the component postures, breathing exercises and concentration. Based on model from Gard et al [43]. Sanskrit names in italics.

The systems network model of yoga are using [43] a top-down and bottom-up perspectives (Figure 2) and shows how practicing YE can influence self-regulation. By doing the exercises ("learning by doing") and observing with the mind the participant then feels the effects. Experiencing positive effects in body/mind in turn increases motivation and empowers the participant to continue practising. Yogic exercises are considered to increase parasympathetic activity both during (depending on style) and after practice. Parasympathetic activity decreases inflammation and may also be related to the inflammatory reflex model [51]. The nervous system can suppress an ongoing inflammation via the hypothalamic pituitary adrenal axis (HPA-axis) or via a pathway called the inflammatory reflex. The inflammatory reflex is comprised of an *afferent* arm of the vagus nerve that senses inflammation (via cytokines) and an *efferent* arm called the cholinergic anti-inflammatory pathway. The efferent arm in the inflammatory reflex modifies immune function and modulates innate immune responses while maintaining homeostasis (the alpha 7 subunit of the nicotinic acetylcholine receptor expressed on cytokine-producing cells (macrophages, mainly in tissues) that is activated via the efferent arm of the vagus nerve) [145 146].

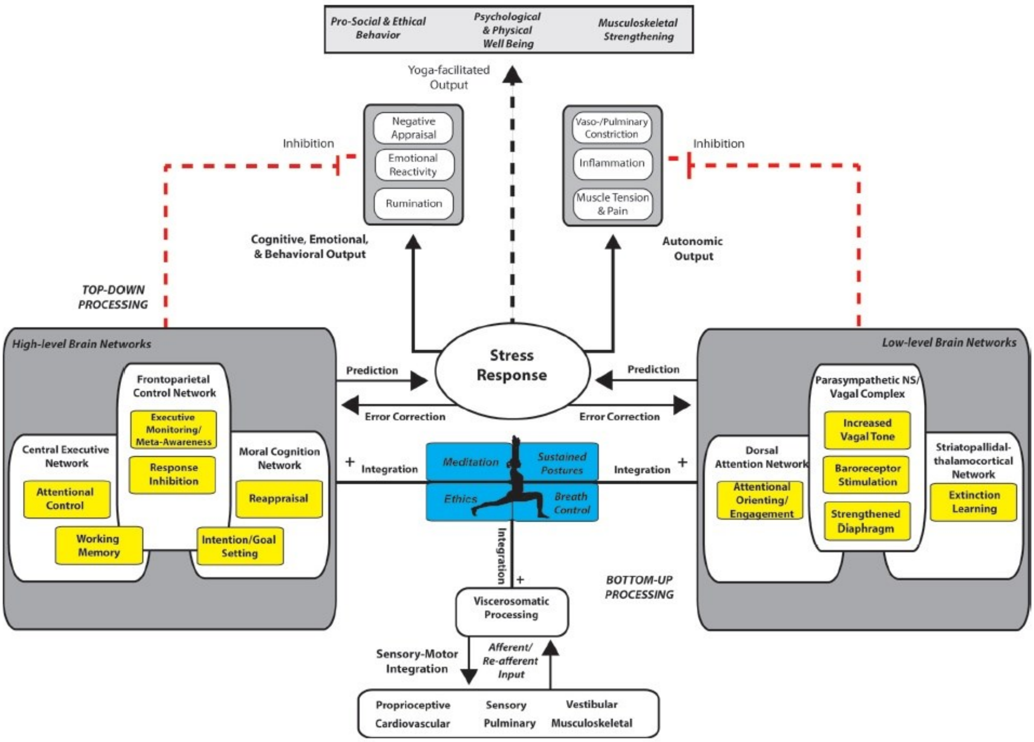


**Figure 2**. Systems network model explaining self-regulation from the bottom-up and top-down perspective used while practicing yogic exercises. Major yogic components have been included in the blue box and dotted lines signify new, adaptive pathways for reacting to stress. The regulatory processes of yoga are in yellow boxes. Used by permission of Gard et. al. [43].

## 2 Rationale for the thesis

The work included in this thesis aims to investigate the effects of newly developed hatha yogic programs (YE) among both healthy participants and in patients with obstructive pulmonary diseases. The rationale for choosing hatha yoga relates to it being the most common style of yoga practiced in the West today. Also it is easily adopted and represents the primary yoga style used in previous research [33 38], which makes it the ideal candidate for further research.

Among both healthy and diseased populations, there is a growing need and demand for alternative forms of complementary body-mind medicine and physical activity modalities that have the power to get more people involved in physical activity. Since more alternatives are likely to involve more people and allowing them to maintain activity levels, this in turn should lead to improved physical function, well-being and health in a greater percentage of the population. The following points provide the specific rationale for this thesis:

- There is a need for further evaluation of YE due to many heterogenetic studies with poor quality.
- The number of participants using YE are increasing both in the exercise arena but also in primary health care.
- Yogic exercise programs are inexpensive and can be taught in a few hour long sessions, and then continued independently and used as a form of biofeedback.
- Certain yogic programs and YE (i.e., inversions, high intensity sun salutations; certain type of YE with a certain breathing exercise sequences) remain to be investigated
- There is a lack of knowledge regarding the efficiency of YE and regarding some of the most common yogic sequences on cardiovascular fitness and health.
- Previous studies have not evaluated heart rate variability and the effects of inversions, nor the relaxation effects of using inversions during a longer time frame.
- Knowledge of yogic exercises, when using a certain sequence of breathing and postural exercises, for obstructive pulmonary diseases is limited.
- Lack of knowledge of obstructive pulmonary disease patients' experiences of YE after participation in a YE-program.
- The feasibility of the newly developed and adapted YE programs has yet to be investigated.

# 3 Aim

The overall aim of this thesis has been to investigate the objective and subjective effects of different hatha yogic exercise (YE) programs on physical function, health and health related quality of life using interventions spanning 6-12 weeks. Three different intervention programs were developed and adapted, Study I and II for healthy populations and Study III and IV for diseased.

Specific aims:

- To investigate the effects of YE focusing on inversions on heart rate variability, blood pressure and hand-grip-strength (Study I) in healthy sedentary middle aged adults.
- To investigate the effects of high intensity YE on cardiovascular fitness and metabolic biological parameters as apolipoproteins and adipocytokines (Study II) in healthy students.
- To investigate the effects of YE on physical function, mastery of the disease, quality of life, dyspnea-related distress and pulmonary function (Study III) in participants with obstructive pulmonary disease.
- To explore the experiences of participants with obstructive pulmonary disease following YE (Study IV).

# 4 Material and methods

## 4.1 Study design and analysis

Study I was an uncontrolled experimental pilot study while Studies II and III were randomized controlled experimental clinical trials (RCT). Study IV was a cross-sectional interview study with a qualitative approach. The analyses in Study I and II were performed as per protocol, Study III used an intention-to-treat model.  Study IV employed  an inductive qualitative content analysis.

## 4.2 Study population

Study I involved sedentary middle-aged working adults Study II focused on younger healthy students while Study III and IV studied middle aged COPD and asthma patients. Study I and II involved healthy populations while Study III and IV looked at participants with obstructive pulmonary diseases. All participants were residents of Stockholm, Sweden (Table C).

### 4.2.1 Inclusion and exclusion criteria

*The inclusion criteria* for Study I were: people between 25–60 years of age, of good general health with slightly elevated blood pressure (no higher than 145/95), new to YE, showcasing no regular exercise routines nor physical activity at medium to high intensity (Borg >13). *The exclusion criteria* were: people > 60 years of age, people diagnosed with high blood pressure and/or taking blood pressure medication or other medication which may affect the performance of inversions, as well as people having had surgery during the previous 6 months.

Study I and II also included the following *exclusion criteria*: people suffering from or diagnosed with a chronic disease that could potentially impede the performance of YE, such as eye disease, depression, burnout, indigestion (reflux) and heartburn, musculoskeletal injuries in the back and/or neck, or people suffering from headaches in the morning or while coughing or sneezing.

*Physical activity limits for exclusion:*

Study I: More than twice a month and/or at medium or high intensity (out of breath and sweating, Borg >13) were excluded

Study II: More than 2 hours a week at medium or high intensity (out of breath and sweating, Borg >13) were excluded.

*The inclusion criteria* for Study II were healthy students between 20–40 years of age, sedentary or performing physical exercise at medium intensity <2 hours per week or at a high intensity <1 hour per week. *The exclusion criteria* were: people <20 or >40 years of age, people diagnosed with chronic cardiovascular disease, depression and/or taking medication for heart disease, depression, anxiety or any medication that affects reactivity.

*The inclusion criteria* for studies III and IV were: people between 35-85 years of age diagnosed (according to electronic patient records) with obstructive pulmonary disease, e.g. COPD, with mild to severe obstructions with GOLD 1-3, $FEV_1/FVC < 0.70$ or people diagnosed with asthma with $FEV_1$ and a FEV% of predicted respiratory function of $30\% \leq FEV_1 \leq 90\%$. *The exclusion criteria* included people with severe neurological, orthopedic or rheumatologic injuries or diseases (each patient were examined and each case evaluated to determine if eligible to perform the exercises), people unable to walk less than 200 meters, people with decreased mobility or a chronic disease that could have had an effect on performance, people with an upcoming surgery in the next 6 months, people with a severe mental disease diagnosis (incl. those taking medication affecting attention), people who had had a heart infarction in the last 12 months or a change in medication during the last 6 weeks. The causes for exclusion covered (total n=33) high blood pressure, upcoming surgery (n=2), mental disorder (n=5), chronic illness (n=13), lack of time (n=6), language problems (n=5), scheduling problems (n=7) and no specific reason (n=3).

#### 4.2.2 Participant flow

- Study I: Of the 794 invited, 32 responded and 12 fulfilled the inclusion criteria (no drop-outs).
- Study II: 260 responders of which 54 were enrolled; 44 participants completed the study (21 yoga, 23 control). 4 drop-outs in control and 6 drop-outs in YE group.
- Study III: 127 responders of which 53 were accepted for baseline measurements, 74 failed to meet the inclusion criteria. This resulted in 40 eligible patients who were randomized for participation with 20 in each group. 3 drop-outs in YE and 1 in CTP.

For an overview of study design, participants, intervention and outcome measures using different hatha yoga programs (YE), see TABLE C (page 31)

### 4.3 Intervention, measurements and procedure

#### 4.3.1 Data collection and intervention location

In Study I, measurement took place at the participants workplace in a conference room and intervention took place at the workplace gym in Stockholm. In Study II, measurements took place in changing rooms at the sports arena and intervention took place in the exercise hall at Karolinska Institutet (Huddinge). In Study III+IV, measurements, interviews and intervention took place at the Karolinska University Hospital Huddinge.

#### 4.3.2 Instructions to participants

In each intervention the participants were instructed as a group by the instructor. The instruction covered how to achieve the best technique, biomechanics and breathing in each yogic pose and breathing exercise. The instructor also demonstrated modifications and progression of each posture. The participants were encouraged to do as much home exercising as possible during all three interventions (Study I-IV). In Study I they received a leaflet with the essential poses and in Study II-IV they received both a DVD and a leaflet containing the important poses. Study III offered encouragement to continue the training during the 6-month break.

#### 4.3.3 Interventions Study I-IV

The three different interventions used in this thesis (see Appendix) were partly based on research and individually adapted to the three different study populations. The programs were run by experienced yoga teachers individually trained by the author in the three different hatha YE programs. The programs did not include the philosophical parts of yoga and the majority of the participants were new to YE. For dose, intensity and adherence, see Table A. The YE program in Study I (Figure 3) was performed for 8 weeks in 1 hour sessions. The program focused on inverted postures and the time performing the inversions progressed from 10 min to approximately 15-20 min during the last 4-5 weeks.

**Figure 3**. Major inversion poses used in the intervention in Study I

Study II used high intensity dynamic YE postures (60 min./6 weeks) consisting of the classical sun salutation (SS) for approx. 30-40 minutes (Figure 4) and the remaining inversion poses for approx. 15 min. The SS includes 12 poses forming a dynamic sequence that is synchronized with one's breathing (vinyasa).

**Figure 4.** Vigorous sun-salutation used in Study II (note that the 3rd exercise in the top row was performed with bent knees and the 7th exercise in the top row was performed with knees on the ground, arms straight and hips high; a synthesis between the cobra pose and dog up pose.

Study III and IV yogic exercises (YE) using deep and regulated breathing performed twice a week for 60-70 min. at a time for 12 weeks. General postural and breathing instructions focused on deep breathing opened the class and each individual was then instructed to work at their own capacity. The general recommendation was to focus on extended exhalations. The program included standing, seated and back-bending poses and breathing exercises (Figure 5). Each class ended with relaxation and body scanning.

**Figure 5.** Some of the yogic exercises included in Study III. Note that many exercises were individually modified with props to suit the participants.

A conventional training program (CTP) (physiotherapeutic intervention) with the same number of sessions a week and duration as the YE group (x2/week for 60 min for 12 weeks) was used as an active control group during Study III. The program included strength and endurance training as well as stationary exercise biking (10-15 min).

### 4.3.4 Measurements and test leaders

Measurements were performed by different test leaders in each study. Study I involved only one test leader, Study II involved five different test leaders, Study III involved 8-9 different test leaders and Study IV involved one test leader (performing the interviews). No complete blinding could be achieved during any of the clinical studies. The participants were blinded to the test results during the actual intervention, though afterwards some requested and received their results. All measurements taken during Study I-III were performed within one week prior to commencing the interventions and within one week following the intervention.

### 4.3.5 Heart rate variability and heart rate

Heart rate variability (HRV) was measured usingan Aria-Delmar Holter Analyzer electrocardiogram (ECG) in Study I. Study III saw the use of a heart rate monitor device. Study I recorded heart rate variability for 24 hours, but only 2 hours (2-4 pm) were analysed using the Aria-Delmar Holter Analyzer (Spacelabs Healthcare,WA, USA). The sampling rate was 2048 Hz. The Kubios HRV analysis program, University of Kuopio, Finland, was used for the ECG analysis and performed in a lab.

Study III measured HRV with a Polar heart rate monitor (RCX5, Polar Electro Oy, Kempele, Finland) using the default settings for the Polar Pro Trainer software. Study II used the Polar HR monitor to record HR. Normal beats (RR-intervals, also called NN) in the time domain of HRV, equivalent to the difference between each R wave in milliseconds, was computed. The intervals between contiguous QRS complexes in the ECG resulting from true sinus node depolarisations were defined as NN-intervals [147]. The NN50 count equals the number of pairs of successive NN intervals differing by more than 50 ms during the 2 hour sampling period. The time domain proportion (p) pNN50% is defined as the number of all NN intervals in which the change in successive normal sinus intervals exceeds 50 milliseconds divided by the total number of NN intervals measured (pNN50 = (NN50/n-1)*100%)[147 148]. SDNN is the standard deviation of all NN intervals and RMSSD is the square root of the mean of the sum of the squares of the differences between end-to-end NN intervals. The frequency domain of the low/high frequency (LF/HF) ratio was calculated (using fast fourier transformation) to measure the balanced activity of the sympathetic and parasympathetic nervous system. High frequency refers to the power in the HF range of HRV and reflects efferent vagal activity, whereas LF reflects sympathetic activity. LF and HF were measured in normalized units (n.u) representing the relative value of each power frequency range component in relation to the total power minus the VLF (very low frequency) component [147]. Study I deleted all technical artefacts from the ECG. A text file was constructed using subsequent RR-intervals from Aria Holter and imported to Kubios software (filter setting on medium). A time series was then calculated from the RR-intervals using spline interpolation with an interpolation rate of 4 Hz. The linear trend was deleted and a Welch filter applied.

#### 4.3.6 Respiratory rate

The respiratory rate (f) in Study III was measured using a RESPeRATE ultra Omron [149] on a supine participant with a strap wound across the lower chest. Occasional manual measurements were performed to validate the results of the apparatus. Respiratory rates in Study I and II was measured approximately and visually during the YE sessions.

#### 4.3.7 Oxygen saturation

Oxygen saturation (%) ($S_pO_2$) in Study III was measure using a saturation- and pulse oximeter; (Ohmeda tuffsat) before and after the 6MWT, placed on the ring or middle finger.

#### 4.3.8 Respiratory muscle strength

Maximal inspiratory pressure ($PI_{max}$) and maximal expiratory pressure ($PE_{max}$) in Study III was taken with a MicroRPM™ (Respiratory Pressure Meter) [150] to measure respiratory muscle strength (values in cm $H_2O$).

#### 4.3.9 Lung function

Lung function in Study III was measured with Spirometry, Micro Loop, CareFusion and Micro spirometry [150 151], expressed as $FEV_1$, FVC and $FEV_1$/FVC (values in litres). Flow and strength measurements were performed with the participant seated and equipped with a nose clip and a disposable mouthpiece and included three trials.

#### 4.3.10 Cardiorespiratory fitness monitoring/oxygen uptake ($VO_{2max}$)

Study II involved providing instructions on proper technique, how to use the RPE-Borg scale and how to achieve true performance values during the Coopers test. Test leaders offered encouragement and recorded the time, perceived exertion and heart rate recovery (difference between maximal heart rate at the end of the Coopers test and after 1 minute). Systematic errors were counteracted by offering a “pre-Coopers test” before the actual test and by having the test leaders offer equal verbal encouragement to all participants.

The Coopers walk run test was used to measure cardiorespiratory performance/fitness (estimated maximal oxygen uptake, $VO_{2max}$) with a correlation of 0.92 versus 0.897 compared to the treadmill test with true $VO_{2max}$ measurements [152 153]. An additional tool ("konditionssnurran") was used to measure the time it took to run a distance of 2.000 meters at full speed [153] .

#### 4.3.11 Rating of perceived exertion, RPE

Study II and III used both the Borg CR-10 and Borg 20-RPE scales for perceived exertion while Study I only saw the use of Borg 20. The scales were also used when practicing the programs during all interventions (Study I-IV). In Study III the rating of perceived exertion was registered before and directly after the 6MWT using a Borg CR-10 for measuring fatigue in breathing and legs. The Borg 20-RPE was used to measure general tiredness in Study II before and after a completed Coopers test [154 155].

#### 4.3.12 Blood pressure

Blood pressure (BP) in Study I and III was measured [156] after approximately 5 minutes of rest in a seated position using an automatic oscillometric BP monitoring device (Omron mx3). A pillow was used to support the arm and the monitor attached to the upper arm. The measurement was standardized for all participants; in the upper arm, at the same time of the day, in the same seated position with legs on the floor, back supported and no crossed arms or legs and no talking. In Study II, BP was measured using a Welch Allyn Durashock 2-hose non-automated aneroid sphygmomanometer (AJM-8001-00l, 12 · 35 cm) with an inflatable cuff and a screw valve and the help of a stethoscope (Panascope Combination Stethoscope for auscultation).

#### 4.3.13 Hand-grip strength

An electronic hand dynamometer (Camry model EH101) was used to analyse hand-grip strength in Study I, with the participant standing upright with the monitor held in the dominant hand, arm straight in line with the chest. The grip-test was first performed at maximum strength. Then the grip was maintained for two minutes at a third of the person's maximum strength [157].

#### 4.3.14 Apolipoproteins

ApoA1/ApoB samples were analysed with DXC/LX (Beckman-Coulter).

#### 4.3.15 Adiponectin/Leptin

The blood samples were taken in laboratories and collected via a catheter. Adiponectin and leptin samples were frozen and analysed after approximately 6 months. Adiponectin levels were determined using radioimmunoassay (EMD Millipore). Leptin levels were determined using radioimmunoassay (Millipore/Linco).

#### 4.3.16 Glycosylated haemoglobin (HbA1c)

HbA1c was measured using a Variant II Turbo (Bio-Rad, Hercules,CA).

#### 4.3.17 Waist circumference

Study I-IV participants' waist circumferences were measured by placing a measuring tape horizontally midway between the lower rib margin and the hip bone. Hip measurements were taken at the widest point between the two bony prominences at the front of the hips. Waist-hip ratio was used to measure the degree of obesity [158].

#### 4.3.18 Physical capacity, six-minute walk distance test (6MWD)
A six-minute walk test done in Study III was performed to measure functional capacity [150]. The test was performed in a 50 meter long hallway with cones placed on the inside at the ends of the 50 meters in accordance with the American Thoracic Society. Cues were given every minute. The participants were told to walk as fast and as long as possible for six minutes.

#### 4.3.19 Dyspnea related distress
Study III's dyspnea related distress (DD-index) [159 160] was calculated by dividing the CR-10 Borg scores at the end of 6MWT by the total distance walked in feet during 6MWT x 1000 (meters were first converted to feet). One point was required in order to achieve minimal clinical important difference (MCID) [160].

#### 4.3.20 Chronic respiratory disease questionnaire (CRQ), health related quality of life
The Chronic Respiratory Disease Questionnaire - Self-Administrative Standardized Activities (CRQ-SAS) [161] contains 20 questions separated into 4 domains (dyspnea, fatigue, emotional and mastery). The questionnaire was completed by the participants in Study III. Each question is scored from 1-7 (with the exception of the dyspnea domain, which is scored from 1-5), with higher scores representing less severe cases. MCID required 0.5 points per domain.

#### 4.3.21 Self-reported health
Self-reported health in Study III was assessed using EuroQoL-5D (EQ-5D)[162] and included the question “how is your health today” along with a 10 cm visual analogue scale (VAS) ranging from 0-100 (100=excellent health). The participant was asked to both tick the scale and write down the number.

#### 4.3.22 Qualitative content approach
Study IV used a qualitative content analysis. It included semi-structured interviews based on inductive content analysis in accordance with Graneheim and Lundman [163].

##### 4.3.22.1 Qualitative content data collection procedures
Semi-structured interviews were conducted face to face (in Swedish) at the hospital, lasting approx. 20-45 minutes. The topics included in the interviews were: expectations, previous experience with YE and advice. The interview consisted of open-ended and broad questions concerning the participants’ experiences during and after the YE. The interviews were audio recorded with a digital Dictaphone (Olympus Digital Voice recorder VN-8500PC) and then transcribed verbatim. The interviews were numbered and the interview transcripts were anonymized.

##### 4.3.22.2 Qualitative content analysis
The first analytical step involved reading the interview transcripts to get a general idea of the content. Then came the formation of meaning units, i.e. the extraction and condensation of parts of the original text that is closely associated with the research question. The content was then read by the investigators and compared and discussed until such a time the group had reached a consensus regarding the meaning units. The analysis proceeded with the summation of the condensed meaning units and the labeling of these with a code representing a description close to the text. The text was then reread and checked against the codes several

times to ensure that no information was lost. The codes were sorted into groups representing a higher level of abstraction, and then further divided into subcategories and categories by comparing similarities and differences in codes and code groups. Both categories and sub-categories were considered expressions of the manifest content of the text and examined to be mutually exclusive. Finally, an overall theme was developed to link the underlying meaning with the emerging categories. This theme describes the latent content of the text which has to be interpreted [163]. During the analytical steps, the credibility of the preliminary findings and the process of reflexivity were addressed among the research group by carefully following up on the whole analytical process and categorization work. Divergent views concerning the categorization were discussed until such a time a consensus was reached [164 165].

<table>
<tr><th>Meaning unit</th><th>Condensed meaning unit</th><th>Code</th><th>Sub-category</th><th>Category</th></tr>
<tr><td>after a couple of times I was able to get into that mood very quickly, when you filter out all unnecessary things, you don’t bring along any thoughts about different things, instead I could easily focus on being there, in that moment and I thought that was a positive effect</td><td>after a couple of times I was able to filter out all unnecessary things, and easily focus on being there, which I thought of as something positive</td><td>Focus on the moment</td><td rowspan="2">To focus on oneself</td><td rowspan="2">A new focus and awareness</td></tr>
<tr><td>in the beginning, when we started this breathing training, then I often started coughing and sometimes I felt that I was hyperventilating and yes, but then when you have found the pace, that is your own pace and work on it, well I felt that this makes a difference, that is when the Yoga gave me something more than it did in the beginning</td><td>It was only when I found my own pace in the breathing training that I felt the difference that the yoga made and it gave something back</td><td>To focus on oneself</td></tr>
</table>

**Table A**. Example of data analysis using content analysis

## 4.4 Statistical analyses

| Study | I | II | III |
|---|---|---|---|
| **Statistics** | Student t-test<br>Mann-Whitney/<br>Wilcoxon | Mann-Whitney<br><br>/Wilcoxon<br><br>Student t-test<br><br>Analysis of differences<br>/variances<br>Spearman/Pearson | Mann-Whitney<br>/Wilcoxon<br><br>Student t-test<br><br>ANOVA<br><br>Spearman/Pearson<br><br>Chi-square test |

**Table B**. Statistical methods. Statistical significance was set to p<0.05 in Study I, II and III. Results were presented as mean and/or median with one standard deviation (SD) and/or range and a 95 % confidence interval. Statistical analysis was performed by using Stata software (Stata Corp., College Station, TX)/Version 11 and 14 and MATLAB (partly in Study I). In Study II, no significance was found between the two groups' baseline.

## 4.5 Ethical considerations

Current ethical guidelines for medical research on human participants were followed and considered before, during and after the clinical trials in order to protect the participants [166]. The programs were individually adapted for safety purposes and to prevent injury. Written and oral information was given out to all participants before the commencement of the study and all participants signed informed consent forms. The research was approved by the regional research ethics committee in Stockholm.

# 5 RESULTS

**TABLE C.** Summary of three different yoga interventions (III+IV=same intervention), ITT= intention- to-treat, PP=per-protocol. Study design, intervention, outcome measures and results after practicing different hatha yoga programs (YE).

| YOGA (YE) Intervention | I. Inversions (n=12/9*) | II. Sun salutation (SS) (n=44) | III. Yoga & breathing (n=36) | IV. Yoga & breathing (n=15) |
|---|---|---|---|---|
| **Design** | Pilot | RCT | RCT | Cross-sectional interview |
| **Length of intervention** | 8 weeks<br>1h./week | 6 weeks<br>1 h./week | 12 weeks<br>2 h./week | 12 weeks<br>2 h./week |
| **Analysis** | PP | PP | ITT | Inductive qualitative content analysis |
| **Participants**<br><br>**Women/men**<br>**Age** | Healthy inactive working adults<br>4/8<br>51 (38-59) | Healthy students<br><br>38/6<br>25 (20-39) | Asthma and/or COPD<br><br>23/13<br>64 (40-84) | Asthma and/or COPD<br><br>10/5<br>61 (44-76) |
| **Adherence to number of yoga classes** | 6 (1-8) max 8 | 4 (1-6) max 6 | 20 (3-24) max 24<br>CTP-training group;<br>19.5 (12-22) max 24 | 20 (6-24) max 24 |
| **Borg 20- RPE (general) during YE** | 13<br>(Somewhat hard) | 13-15<br>(Somewhat hard-Hard) | 10<br>(Very light/Fairly light) | 10 |
| **Primary outcomes** | Heart rate variability (HRV) | Cardiovascular fitness/endurance ($VO_{2max}$) | Walking distance (6MWD)<br>Dyspnea (breathlessness) | Experiences after yoga intervention |
| **Secondary outcomes** | Blood pressure<br>Hand-grip strength | Adiponectin<br>Blood lipids - (apolipoproteins)<br>Blood pressure | Lung function, Health-related quality of life,<br>Respiratory rate | |
| **Results of significance** | ↑pNN50 (HRV measure) (n=9)<br>↑Hand-grip strength (n=9) | ↑Adiponectin<br>↑ApolipoproteinA1 | ↑Walking distance (6MWD)<br>↑Disease specific quality of life (CRQ)<br>↓Respiratory rate<br>↑Oxygen saturation | Improved well-being and dyspnea control |

*12/9=12 total, 9 in ECG group. Note: not all participants were present during the Borg-RPE measurements. Age, adherence and Borg-RPE are presented as median and range.

**All graphs below:** Dashed lines show yogic exercise (YE) group. **All graphs presenting means and medians with profile-plots and box-plots if not otherwise stated**.

## 5.1 Heart rate variability

Study I, using an 8 week YE program, showed a medium effect (ES 0.45) on heart rate variability (HRV), with a significant increase in proportion (p) pNN50% (p=0.035) (12.7±12.5 to 18.2±13.3) at night (2h recording) after the intervention. Study III did not show any effects on HRV (5 min recording), graph not shown.

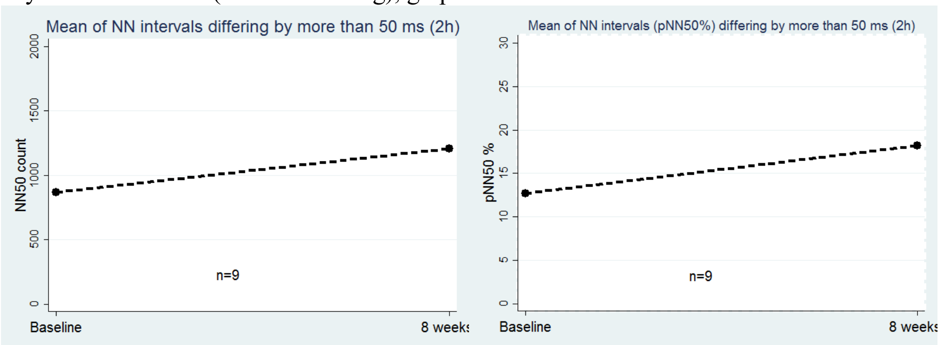


**Figure 6.** Study I HRV measures: NN-intervals and pNN50% each differing by more than 50 ms.

## 5.2 Respiratory rate and oxygen saturation

In Study III the respiratory rate (f) decreased (p=0.05) and oxygen saturation at rest increased (p=0.02) within the YE group. No significant effect emerged in the CTP group.

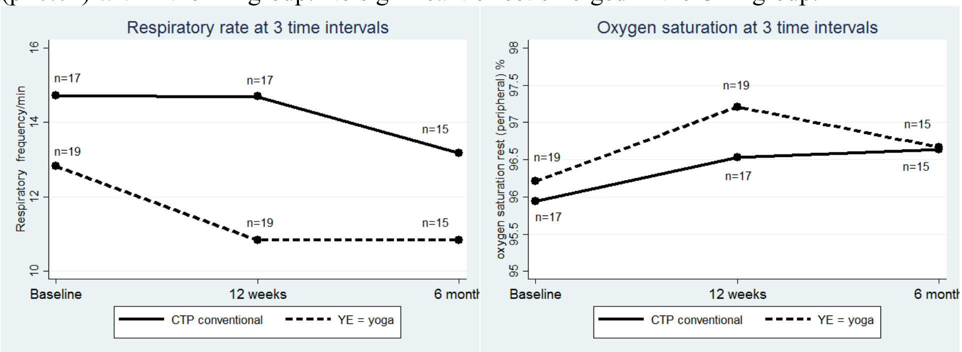


**Figure 7.** Changes in respiratory rate and oxygen saturation in Study III

## 5.3 Respiratory muscle strength

In Study III the inspiratory muscle strength (p=0.03) and expiratory muscle strength (p=0.004) increased within the CTP group. No significant effect in YE group.

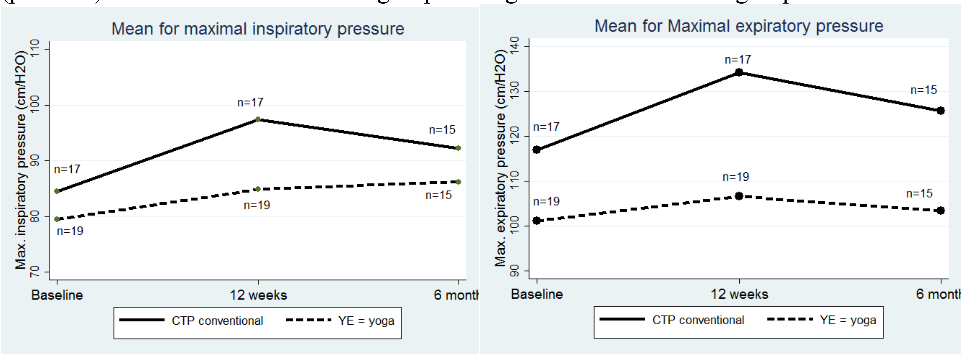


**Figure 8.** Changes in respiratory muscle strength measured across three points in the conventional and YE groups in Study III.

## 5.4 Lung function

Forced Expiratory Volume in one second ($FEV_1$) increased significantly within CTP group (p=0.01) in Study III following the intervention. No effect in YE group.

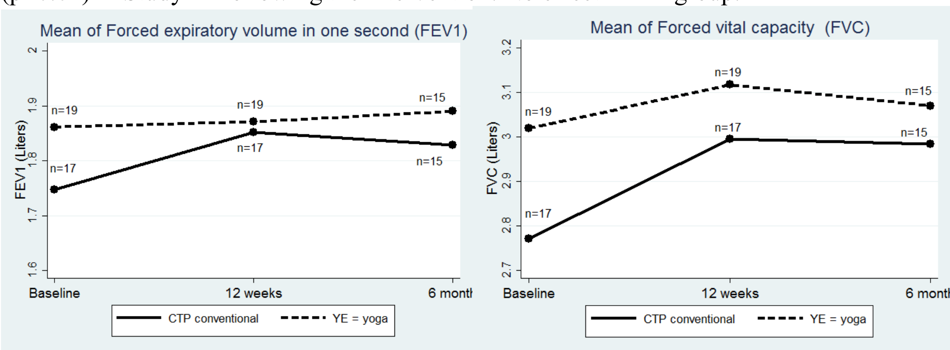


**Figure 9a.** Changes in $FEV_1$ and Forced Vital Capacity (FVC) measured across three points in Study III. See Table F for MCID.

## 5.5 $FEV_1$/FVC ratio

In Study III the $FEV_1$/FVC ratio decreased significantly in YE group (p=0.04) after 12-weeks and a trend in CTP group emerged. However no significant effects between groups.

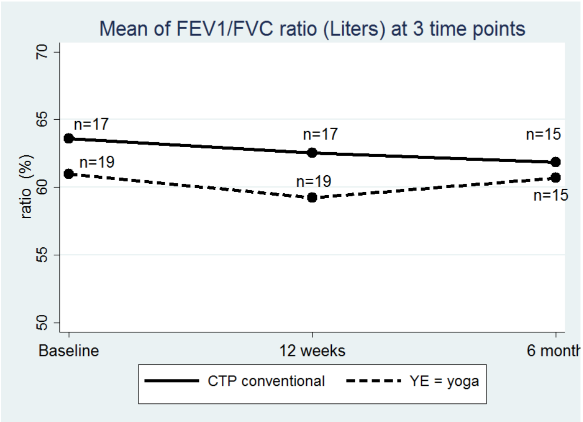


**Figure 9b**. Changes in $FEV_1$ and Forced Vital Capacity (FVC) ratio across three points in time in Study III.

## 5.6 Cardiorespiratory fitness, $VO_{2max}$

Study II showed no significant effects on cardiovascular fitness following high intensity YE (estimated using Coopers test). Mean dose: 390 minutes, ranging from 210–800 min.

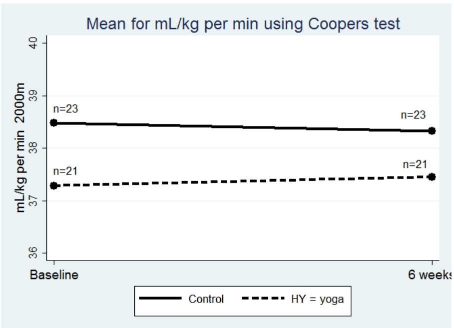


**Figure 10.** Maximal oxygen uptake measured with Coopers test before and after 6 weeks of high intensity YE during Study II, see also Table D.

**Cardiorespiratory fitness and adiponectin**

**Table D**: Study II; oxygen uptake, $VO_{2max}$ (estimated using Coopers test), time, non-responders and improvements > 2 ml $O_2$/kg/min and improvements in adiponectin using 6 weeks of high intensity hatha yogic exercises (YE) (range in parenthesis)

| N=44 | **YE (n=21)** | **Control (n=23)** |
|---|---|---|
| Minutes/seconds Coopers test (2 km) and range | 11.40 (8.18-18.31) | 11.18 (8.07-18.01) |
| Non responders to Coopers test | 5 (24%) | 4 (17%) |
| Improvement > 2 ml $O_2$/kg/min | 5 (24%) | 3 (13%) |
| Adiponectin mg/L improvement >2 units, (5-30 mg/L normal) | 7 (2-6.1) | 4 (2.4-7) |

## 5.7 Rating of perceived exertion, RPE (Borg)

No significance was detected between or within the groups on the RPE-Borg scales in any of the interventions.

**Table E.** RPE Borg-20 during YE in Study I-III

| | **RPE-Borg 20** |
|---|---|
| **Study I** | 13 |
| **Study II** | 14 (9-17), 15 (10-18) (after 25 min. and 45 min. respectively) |
| **Study III** | 10 (3.5-14) |

Note: Median and ranges. Not all participants were measured, see also Table C.

## 5.8 Blood pressure (BP)

No changes in BP were detected in Study I and II. Improved effects in diastolic blood pressure (p=0.05) emerged in CTP group in Study III after follow-up (Fig.13).

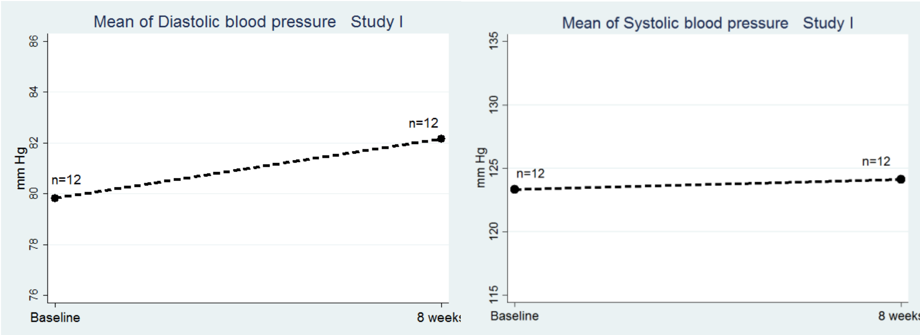


**Figure 11.** Changes in diastolic and systolic blood pressure in Study I (pilot study) after 8 weeks.

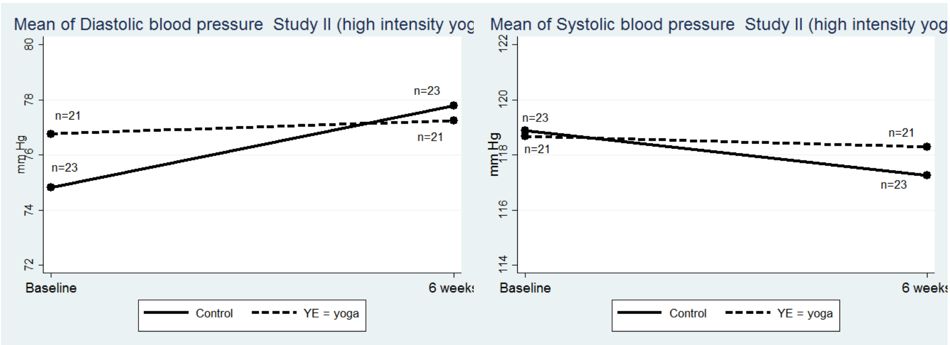


**Figure 12.** Changes in diastolic and systolic blood pressure in Study II after 6 weeks.

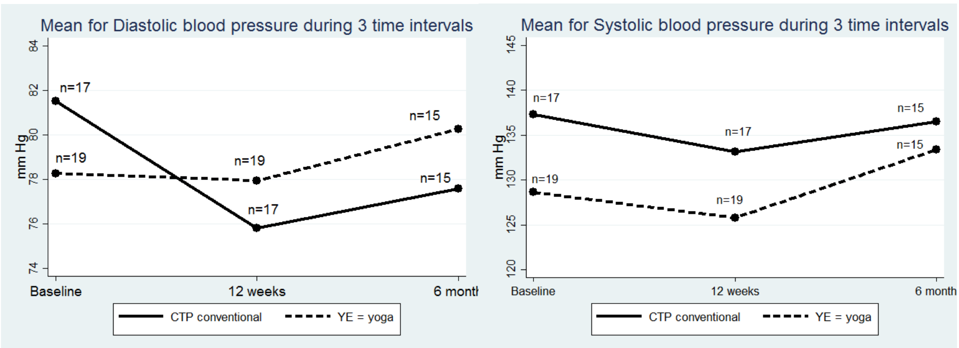


**Figure 13.** Changes in diastolic and systolic blood pressure across 3 time points in Study III

## 5.9 Hand-grip strength

Hand-grip strength improved (p=0.02) in the YE group in Study I.

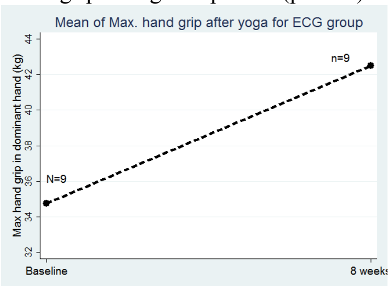


**Figure 14.** Changes in max. hand-grip strength in YE group in Study I

## 5.10 Blood parameters – adiponectin, leptin and apolipoproteins

Study II showed no significant effects on adiponectin and leptin levels between the YE and CTP group. However, adiponectin levels showed significant increases within the YE group after six weeks (8.32±3.32 to 9.68±3.83; (p=0.003)).

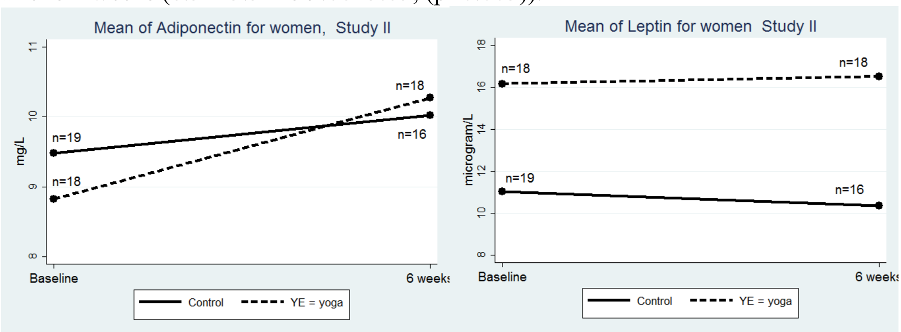


**Figure 15.** Changes after 6 weeks in adiponectin and leptin levels in Study II. Data shown applies to women as women have higher levels of adiponectin and leptin than men.

## Blood parameters

In Study II there were no significant effects on apolipoproteins levels at baseline or after the intervention between the two groups. However, ApoA1 increased within the YE group from 1.47±0.17 to 1.55±0.16; (p=0.03).

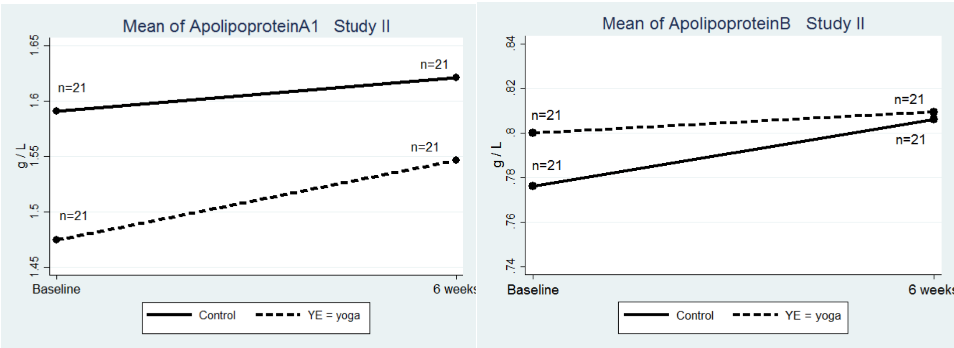


**Figure 16.** Changes after 6 weeks in ApolipoproteinA1 and Apolipoprotein B in Study II in YE and control groups

## 5.11 Glycosylated haemoglobin (HbA1c)

Study II demonstrated no significant changes to HbA1c in the control group, but in the YE group HbA1c was lowered in near significant amounts (p=0.07).

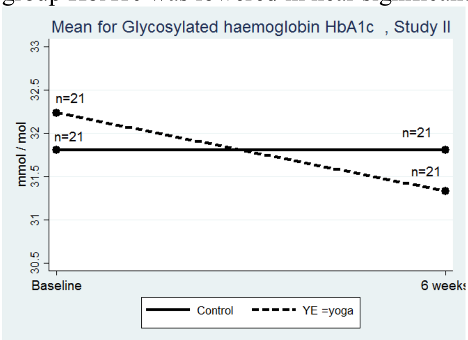


**Figure 17.** Changes after 6 weeks in glycosylated HbA1c in Study II

## 5.12 Physical capacity, six minute walk distance (6MWD)

Study III showed significant improvements in six minute walk distance results (6MWD) after 12 weeks of intervention (YE: mean difference 32.6 m; CI 10.1-55.1, (p=0.014); CTP: mean difference 42.4 m; CI 17.9-67.0, (p=0.006) for both groups. Improvements after follow-up (6 months) emerged only in the CTP group for 6MWD (p=0.04).

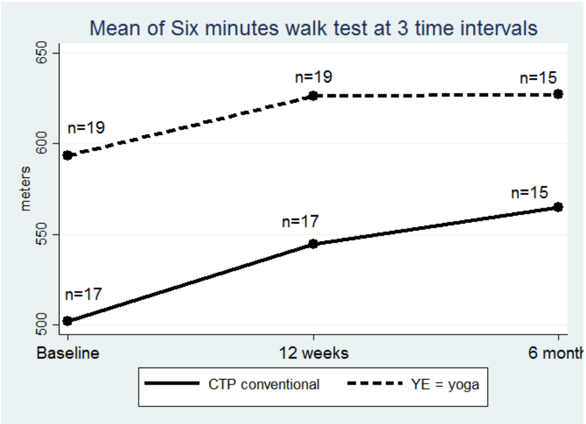


**Figure 18.** Six minute walk distance measured across three time points in Study III, see also Table F

**Table F**: Number of patients in Study III with obstructive pulmonary disease (range in parenthesis) across different points in time, with minimal clinically important difference (MCID) for six minute walk distance (6MWD) (>30, >50 meters), dyspnea related distress (DD-index) (<1 point). Forced expiratory volume in one second in litres ($FEV_1$) ≥100 ml [167].

| YE=yoga<br>CTP=conventional | **YE (n=19)**<br>**1→2** | **YE (n=15 )**<br>**2→3** | **YE (n=15)**<br>**1 →3** | **CT (n=17)**<br>**1→2** | **CT (n=15)**<br>**2→3** | **CT (n=15)**<br>**1→3** |
|---|---|---|---|---|---|---|
| **6MWD**<br>**(>30 meters)** | 7 **<br>(37-113) | 1<br>(34) | 5<br>(41-107) | 10 **<br>(31-135) | 5<br>(30-53) | 11 **<br>(49.5-123) |
| **6MWD**<br>**(>50 meters)** | 5 **<br>(82-113) | 0 | 3<br>(53-107) | 9 **<br>(57-135) | 1<br>(53) | 10 **<br>(54-123) |
| **DD-index respiration** | 3 (16%) | 0 | 1 | 7 (41%) | 4 | 5 |
| **DD-index legs** | 2 | 1 | 0 | 5 | 0 | 4 |
| **$FEV_1$/L ≥100 ml, mean/sd** | 8 (110-330) (42%)<br>220±92.6 | 4 (110-360)<br>198±111 | 5 (110-490)<br>240±152 | 9 (100-540) (53%)<br>244± 155 | 3 (230-470)<br>337±122 | 5 (140-440)<br>302±123 |

** p = <0.05; Points in time, 1=baseline; 2=after intervention; 3=six months follow up; 6MWT= Six minute walk test; DD-index=dyspnea related distress; $FEV_1$=forced expiratory volume in one second; T-test and Wilcoxon calculations used.

## 5.13 Dyspnea related distress (DD-index)

No significant effect on dyspnea-related distress appeared in any group in Study III; however MCID appeared for some participants in both groups (Table F).

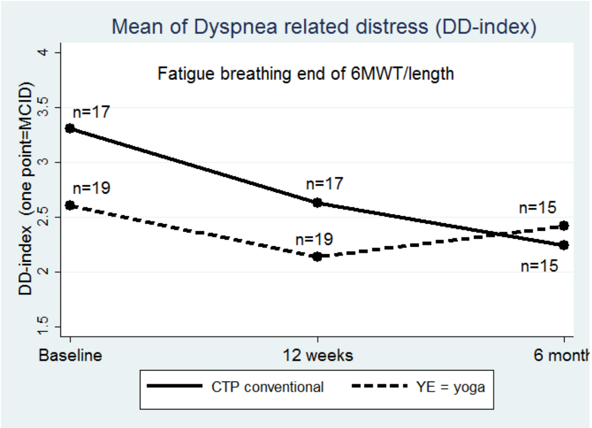


**Figure 19.** Dyspnea related distress in breathing (fatigue for legs not presented) across 3 points in time Study III.

## 5.14 Self-reported health

No between group effects emerged in self-reported health using (EQ-5D/VAS) in Study III. Eight patients in each group reported improved self-reported health after the intervention using (EQ-5D/VAS) of MCID (10 units) data not shown.

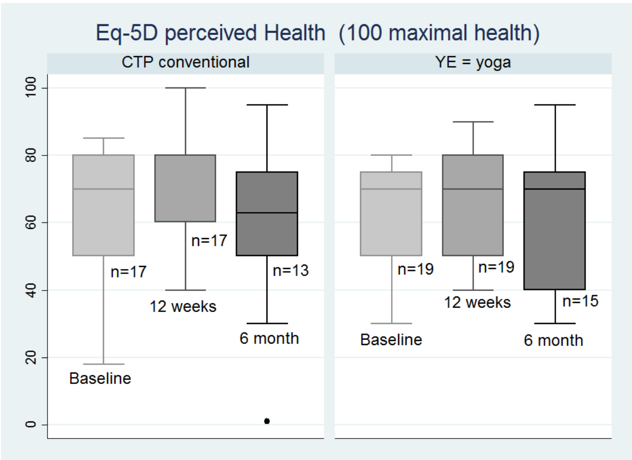


**Figure 21.** The EQ-5D decreased significantly within the CTP group (p=0.03) after 6 months.

## 5.15 Disease specific chronic respiratory disease questionnaire (CRQ) - quality of life

In Study III, while testing for interactions (group x time) with ANOVAs, there emerged significant effects on the fatigue (p=0.04) and emotional (p=0.02) domains of the CRQ, with improvements shown in the CTP group but not in the YE group after the 12 week long intervention (p=0.02 and 0.01, respectively). Improved effects after follow-up (6 months) emerged for the CTP group in the CRQ emotional domain (p=0.01). Significant effects also emerged in the YE group with regards to the CRQ mastery domain following 12 weeks.

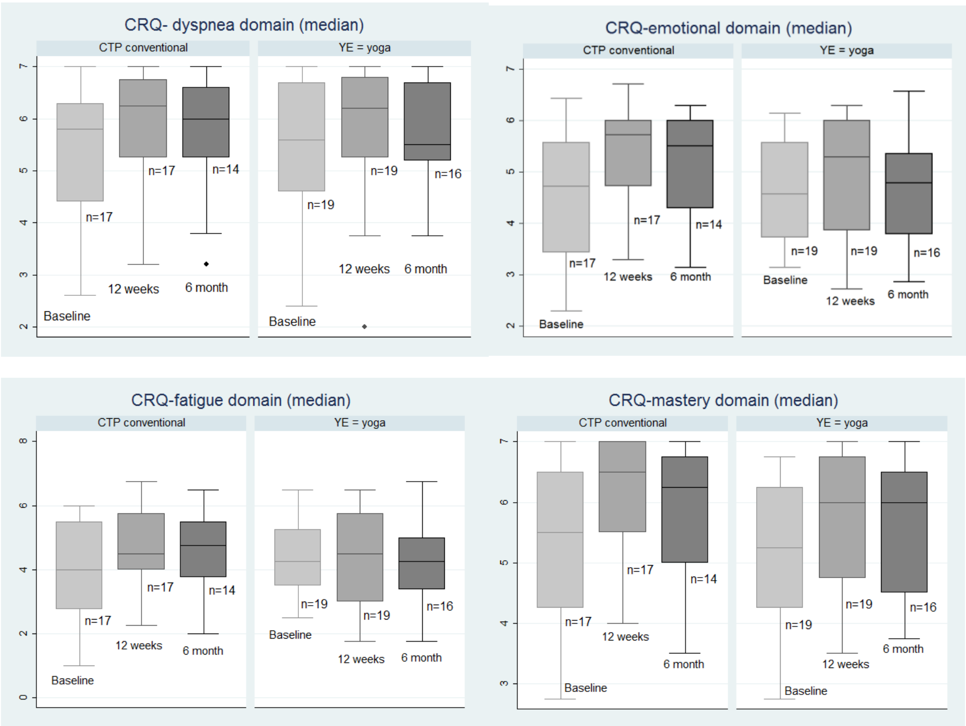


**Figure 20.** Above (four graphs): changes in all four CRQ domains across three points in time in Study III. Higher scores indicate less severity.

## 5.16 Correlation between six-minute walk test and self-reported health

Study III showed differences between 6MWD and EQ/5D VAS health at baseline and directly following intervention (12 weeks) favoring the YE group (p=0.01) (CTP group p=0.9).

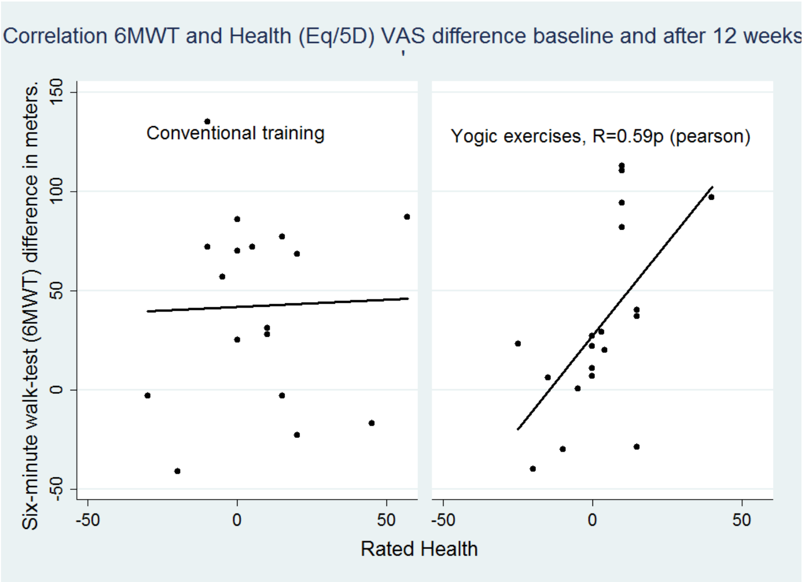


**Figure 22.** Correlation line for CTP and YE groups (R=0.59)

## 5.17 Qualitative content analysis

In Study IV three main categories emerged of the qualitative content analysis: "A new focus and awareness", "To gain new knowledge by practice" and "To experience how one can influence the own situation". The overall theme "From limitation to opportunity – to develop awareness and control over one's breathing" illustrates a learning process on different levels. Specifically, it illustrates that the participants perceived improved physical symptoms and breathing technique, greater energy/stamina and body awareness along with a new sense of control over their breathing in different situations.

In Study IV the analysis resulted in an overall theme, 3 categories and 7 sub categories (Table G).

**Table G**: Overview of the findings in Study IV using qualitative content analysis

| | | |
|---|---|---|
| **Overall theme**<br>From limitation to opportunity – to develop awareness and control over one's breathing | | |
| **Categories** | | |
| **A new focus and awareness** | **To gain new knowledge by practice** | **To experience how one can influence the own situation** |
| **Subcategories** | | |
| *To focus on oneself*<br><br>*To be aware of breathing and to discover* | *To feel safe and be guided*<br><br>*Learning by doing* | *To be able to control the breathing*<br><br>*To be able to manage stress and achieve balance*<br><br>*To have more stamina and to master challenges* |

In Study IV the three categories were (Table G):

*A new focus and awareness:* where the participants described YE as an opportunity to focus and to be aware of their breathing in a new way. Both the focus and awareness of the participants breathing was experienced in a new way and as an important part of practicing YE. Awareness and focus during practise of YE seemed necessary for developing new insights about different ways of breathing.

*To gain new knowledge by practice:* revealed that actively participating in YE involved conquering new knowledge about the body and breath by doing the exercises, that is "learning by doing". Even individuals with little previous experience of YE, mentioned that participating in YE deepened their knowledge about breathing techniques and how to use the techniques in daily life. Explicitly, the YE was experienced as an opportunity to anchor the new knowledge through the hands-on trying and practising.

*To experience how one can influence the own situation:* revealed that participating in YE created opportunities for participants themselves to control symptoms related to the lung disease but also in daily life situations. The participants reported that they were able to control the breathing and stress voluntarily, thus achieving feelings of harmony and balance. They also experienced increased energy, improved stamina, coping and feelings of safety and security while doing the YE and other physical activities.

Some selected citations of the participants' experiences in Study IV:
*I think some exercises have been really good, that is you immediately feel that they open up the airways and that you get a lot of oxygen during these exercises and so that was a great surprise, that you get that feeling in just one exercise" Interview No. 3*

*I actually think that if I feel the asthma, so instead of taking a quick Ventolin (medication), it is possible to do a breathing exercise and it works. It is not that I have stopped taking my meds but instead feel that perhaps I should but instead I do these breathing exercises and it becomes better." Interview No. 6*

*I have realized that I can cope with situations in a different way. I can do more now, can and have the strength to do more, I realize that I can walk longer without having to rest" Interview No. 13*

*I feel I learned these exercises, I will continue with these…I got this control and harmony and balance thing, and now I have it. I understand how to master it…I did, I didn't do that when I started. I will take this to my heart …" Interview No. 14*

# 6 Discussion

The main findings of this thesis involve results of evaluating different yogic exercise programs as those in *Studies I-III*. All programs were feasible and safe with no documented adverse effects. *Study I* was a pilot study calling for caution when interpreting the results. However, significant increases in heart rate variability and hand-grip strength still emerged. *Study II* showed no significant effect between the two groups. However, the yogic exercise group (YE) demonstrated increased levels of apolipoproteinA1 and adiponectin following the YE intervention. As a result of *Study II*, one might suggest that low doses of YE can improve cardiovascular and metabolic health in healthy individuals, even though cardiovascular fitness remains unaffected.

*Study III* found no significant between-group effect in any parameter after the intervention using t-tests. Analysis of variance differences emerged in CRQ fatigue and CRQ emotional domains favouring treatment as usual group (CTP).

After 12 weeks of intervention, all CRQ domains showed improvement in the CTP group whereas in the YE group only the mastery domain showed improvement. Both groups displayed significant improvements in walking distance after 12 weeks. Within the YE group showed lowered respiratory rate, improved CRQ mastery of the disease and increased oxygen saturation and a significant correlation when comparing differences in walking distance and self-reported health following the intervention. However significant effects in lung function and respiratory muscle strength emerged within CTP group but not in YE group. *Study IV* found that practicing YE may act to empower individuals with obstructive pulmonary disorders and help them control their symptoms and dyspnea. Yogic practice may serve as an efficient tool for learning new ways of breathing as well as strengthening one's self-efficacy and mastery of the disease.

## 6.1 Heart rate variability (HRV) in relation to body position and respiration

Study I, which measured HRV, included only sedentary individuals with no previous experience of YE. The rationale behind this thinking was to be able to more clearly see the effects on HRV. Study I showed improved HRV (pNN50%) after eight weeks of YE intervention with a focus on inversions, while Study III displayed no effect on HRV. Previous findings from smaller sample populations are consistent with the findings in Study I, however these do not always including inversions [98 99 101 168], while others report that YE is no better than usual care [169] or cycling [53] when it comes to HRV. Factors alternating HRV include supine [170] and inverted postures [54 170], but also slow respiratory rates (6/min) and respiratory sinus arrhythmia (RSA) has its maximal amplitude with enhanced baroreflex sensitivity [55 171]. However, while the YE group in Study III showed significantly slower respiratory rates, there was no reported effect on HRV. This could be due to the short HRV recording time (5 min.), the time of recording (daytime) and the use of a heart monitor watch. Longer monitoring time would in all likelihood have been needed in order to record any significant effect. Furthermore, previous findings have reported slower breathing frequency and resting HR following a yogic intervention [100 168]. While the recommended breathing frequency was a rate of 0.1 Hz (6 breaths/minute), Study I-III saw the majority of the participants breathing at a rate of 0.2 Hz (12 breaths/minute). However, this was not measured directly and so only represents a rough estimate of the instructor's visual inspection of breathing frequency in Study I and II. Yet, all interventions encouraged slow and deep breathing. Study I showed similar findings to those reported previously in another 12 week long yogic intervention for participants with chronic back pain. The patients participated in easy yoga with twists and light back-bending exercises and slow breathing [168] and showed significant effects on pNN50% in the YE group but no effect on HF.

Inversions were used more or less in both programs in Study I and II, though with longer duration in Study I where performance of the inversions progressed from approx. 7 min. to 20 min. during the 8 weeks of intervention. Previous research suggests that supine and inverted body postures stimulate the baroreceptor reflex (from an altered negative pressure in the upper body) and may enable parasympathetic (vagal) activity [88 102 104 172], while upright postures inhibit it [172]. The baroreceptor reflex that regulates heart rate is most likely linked to the parasympathetic nervous system [170]. However, increased vagal activity as a result of increased HRV seemed in Study I . Existing findings suggest that atrial arrhythmia can be restored through an inversion program [173] . A 40-minute program (divided into 10-minute intervals that alternates between stimulating the vagal and the sinus nerve) has been suggested as an effective form om medication for 50% of patients with atrial arrhythmia. Other smaller studies and case reports suggest that the upside-down position may have the power to treat paroxysmal supraventricular tachycardia [102 104 105] when no other methods, such as medication and manual stimulation of the vagal nerve, work. Moreover, inversions have also been known to reactivate the malfunctioning baroreflex mechanism by alternating the pressure on the baroreceptors. The mechanism may involve vagal stimulation due to increased carotid sinus pressure that in turn may restore the baroreceptor reflex function [54 102-105]. The baroreflex arc is thought to function improperly in hypertensive, ageing, stressed, inactive and depressed individuals, which in turn results in a low HRV [88 174-177]. Such was the rationale for choosing to include only inactive and healthy individuals without previous experience of practicing YE in Study I.

Measures taken after stretching typically show a rapid increase in parasympathetic activity as well as lowered HR, meaning improved HRV, and YE does indeed include a stretching component[178]. This may be one explanation for the feelings of relaxation and increased parasympathetic activity that often follows YE. The increased HRV reported after stretching may be related to the release of vasodilative agents (EDRF=endothelium-derived relaxing factor) which reduces muscle tone, but could also result from a general systemic psychic-physical relaxation [101]. Note that HRV may temporarily decrease *during* stretching.

Yoga has been recommended as a life-style modifier for pre-hypertensives and patients suffering from other diseases, including sympatho-vagal imbalances as alteration in the HRV measure of low-frequency high-frequency (LF-HF) ratio. One research group has suggested that body mass index (BMI) contributes independently to changes in LF-HF ratio and that there's a correlation between BMI and diastolic blood pressure [179]. The body mass index was somewhat high (26) in Study I, but within normal range in Study II (22) and III (25).

## 6.2 Respiratory parameters

Study III showed a significant increase in oxygen saturation ($S_pO_2$ ) and lowered respiratory rate in the YE group after 12 weeks of intervention, though no such effects were observed in the CTP group. Oxygen saturation has been reported to improve after YE [180] and the mechanism seems to primarily involve the lowered respiratory rate. Furthermore, slower and deeper breathing patterns can offer an advantage to obstructive patients [180 181] and also raise $S_pO_2$ levels. Studies I-III encouraged nasal and extended exhalations with deep breathing, which may have lowered the breathing frequency. The complete yogic three-part breath as practiced in Study III makes full use of the diaphragm and has been reported to lower the respiratory rate and improve $S_pO_2$ [180] in patients with COPD during and after yoga [115 182], as well as in elderly women [182].

Patients with COPD and asthma usually display a dysfunctional breathing pattern [183 184]. Diaphragmatic breathing as practiced in all YE interventions and particularly in Study III could have had an influence on dysfunctions already present in the participant. However, not all screening measures [184], e.g. breath holding time, $CO_2$ and mechanical function, was measured, and the detected CRQ dyspnea was not significant in the YE group in Study III. Study IV did however confirm that dyspnea improved. Moreover, others have reported that YE can strengthen the torso (e.g. through inversions, back-bends and prone poses along with strong breathing exercises) and initiate diaphragmatic breathing that in turn improves performance [183], lowers breathing frequency and increases chest expansion. To achieve optimal chest expansion, more intense yogic and breathing exercises than those included in Study III may be required. With most of the participants across all studies being new to YE, we refrained from including such high intensity exercises.

Regarding the expiratory pressure that is an advantage for patients with COPD and asthma, the yogic technique of ujjayi involving constriction of the throat to control and soften the breath was not added to a greater extent in the YE program in Study III.
Study III found no effect on either inspiratory or expiratory respiratory muscle strength in the YE group, though this did show up the CTP group after 12 weeks of intervention. Some pilot studies have reported increased strength and mobility of respiratory muscles after YE in both healthy persons and patients with COPD [62 180 185 186], while others have reported no improvements [187]. The yogic breathing techniques used in Study III used coordinated breathing movements of the upper and lower rib cage and the waist to extend the exhalation and prevent hyperinflation and "air trapping", both common in obstructive patients [80]. As reported in Study IV, where greater breathing control and less dyspnea was achieved, other factors may explain the walk-test improvement.

The forced vital capacity increased significantly in the CTP group, however, no significant between-group effect appeared. The cause for redundant effects in the YE group on lung function may relate to how lung function seldom improves in COPD, but may also be related to the YE being of an unsatisfactory dose or intensity or other unidentified factors. Deep breathing exercises was used during the YE, however, this did not improve the lung function of the participants in Study III. On the other hand, the interviews in Study IV showed improved dyspnea, control and coordination of breathing. Another reason may be that the randomization resulted in more participants with COPD ending up in the YE group and more obstructive participants with asthma ending up in the CTP group. Obviously one limitation related to the groups being imbalanced with respect to diagnoses.

As suggested in the meta-analysis [117] yogic breathing techniques constitute a safe and complementary alternative to other breathing exercises, and often seem to be more effective than usual care methods for asthma control, asthma symptoms, $FEV_1$, peak expiratory flow rate and health-related quality of life [62]. Previous data show little evidence of YE improving the $FEV_1$/FVC ratio in either healthy persons [185] or people with COPD[188], and indeed this parameter did not improve in any of the groups in Study III. Conversely, small improvements in $FEV_1$ [115 188] and the $FEV_1$/FVC-ratio after YE have been reported in both healthy and obstructive participants [160]. Improvements in $FEV_1$ with a recommended MCID of 100 ml [167] were seen in more participants in the CTP group (however non-significant) compared to the YE group, with 42% in the YE and 53% in the CTP group (Table D). The $FEV_1$/FVC ratio is however a more advantageous measure than $FEV_1$ [69 63]. However no large changes regarding the $FEV_1$/FVC ratio in any of the groups emerged in Study III. Study IV also showed improvements in dyspnea (during exertion) and quality of life even though the quantitative Study III found no such effects. One could posit that qualitative studies show more clearly the effects after YE when it comes to breathing function.

## 6.3 Heart rate (HR)

A lowered resting HR was observed with 2 beats/min. in Study II (not significant), an increase by approx. one beat in Study II and one beat in Study III following intervention. However, the changes were non-significant across all studies. Other studies have shown lowered resting HR [52 98] following YE, something which often signifies a vagal dominance [88 102 168 178]. With the measurement including another person in the room, which may create a "white coat effect", HR can differ greatly and is not an optimal measure of health or vagal dominance. While heart rate measurement wasn't performed during YE in any of the studies, RPE were. HR is not an appropriate marker for detecting the intensity of YE. When it comes to vagal dominance, measurement of HRV and breathing rate probably represents a better method for measuring YE than HR, however the time of day and recording time for measurements is important and can differ greatly between different studies.

## 6.4 Cardiorespiratory fitness, maximal oxygen consumption ($VO_{2max}$)

In Study II there were no differences in $VO_{2max}$ found either between or in groups. This may be related to low intensity YE and total performance time, but also to the fact that the participants had a good baseline for cardiovascular fitness. A recent meta-analysis [189] classified yoga as a low-intensity physical activity, but only certain exercises, such as the sun salutations (SS), met the appropriate intensity level (above three metabolic equivalents (MET)) for improvements in cardiovascular endurance in accordance with the American College of Sports Medicine and the American Heart Association guidelines[5]. This means that asana practice with MET intensities above three can be counted toward daily recommendations for moderate or vigorous physical activity [189].

No previous studies appear to have reported the effects of performing YE on cardiovascular fitness after six weeks, as was done in Study II. However, a recent larger study investigating the effects of three months of YE with a dose of 60 min./week plus home training (165 min/week) showed improvements in $VO_{2max}$. The trial covered most of the demanding hatha yogic standing postures, seated postures, inversions, back-bends and plank poses, but with no SS. Since the study included 57 postures performed over 60 minutes, the speed was in all likelihood dynamic and vigorous. The results are new and interesting and represents one of the largest studies measuring $VO_{2max}$ after YE with a gas analyzer. Naturally, the results from this study, which included a larger dose than Study II, can more easily show that improvements in $VO_{2max}$ may increase following dynamic YE in somewhat older (mean age 52) healthy participants. Furthermore, a meta-analysis has reported improved aerobic fitness in subjects favoring yoga over comparison activities, such as resistance training and cycling[190]. Yet, other investigators measuring $VO_{2max}$ found no effect from using large muscle-group movement YE three times a week at 40 min. per session [191]. It's clear that the nature of YE and speed of movement are important factors to consider if the aim is to increase cardiovascular fitness. While the nature of many of the YE seem to achieve a high HR, it's probably not enough to improve on $VO_{2max}$. Using HR as a way to measure the intensity of YE may not be appropriate (unpublished data), due to the intermittent head down position (inversion). The occasional inversion in YE increases the relaxation counts (HRV) and gives a restorative effect with alternating lowered HR and increased baroreflex. Unpublished data (by author) has shown that when measuring oxygen consumption, the intensity is not linear to the HR, and maby there is anaerobic activity. Hitherto, there seem to exist no reports of the relationship between HR and oxygen consumption during YE and, consequently, the use of HR as a measurement of YE intensity remains inappropriate [113]. However, it has been suggested [32 108 109] that the practice of SS, as included in Study II, can be used to maintain or improve cardiovascular fitness in the form of increased $VO_{2max}$ [108] with elevated HR in unfit individuals [109], providing low to moderate stress (above three MET) to the cardiovascular system. Tran et. al. have also reported getting somewhat contradictory results [32] from using a mixture of dynamic and static YE, with a 6% increase in $VO_{2max}$ in a group similar to the participants in Study II. The study discusses that the effect on the cardiorespiratory fitness could perhaps be related to the “frog pose”, dynamic lunges and a few rounds of SS [32]. Back bending YE and inversions are reported at a relative intensity of 41% of $VO_{2max}$ [112] (19 mL/kg/min). Also recommended is an intensity of 40% of $VO_{2max}$ (13 mL/kg/min) [113] after SS. High HR was noted during the yogic push-up (chatturanga) [112], and exercise which is included in the SS investigated in Study II. Interestingly enough, the above mentioned intensities nearly achieve the minimum relative intensity required to achieve cardiovascular training effects as suggested by the American College of Sports Medicine and the American

Heart Association. However, other studies have suggested that if $VO_{2max}$ falls below 40% there might be improvements achieved with low-intensity activities.

Others measuring $VO_{2max}$ [192] have noted low intensities (9.9-26.5% of $VO_{2max}$) when using YE not including dynamic poses such as SS. These lower figures are fall far below the minimum recommendations. Even though there emerged no statistical effect in Study II, 5 participants (24%) in the YE group and 3 participants (13%) in the control group improved their MCID by 2 mL/kg/min., while there also emerged a few non-responders in each group (Table D).

Additionally, the biomechanics and techniques used during the practice of YE is an important issue which suggests that longer interventions would be needed to improve one's skills. The speed of the SS has to be somewhat dynamic and fast for improvements to occur, and the aim in Study II was 2-5 seconds per movement. For an unfit individual, these types of exercises may be sufficient in order to put stress to the cardiovascular system. However, the dose was still insufficient, being only six weeks with no home training, to improve $VO_{2max}$. The rhythm of SS (12 poses) varies between different styles of yoga [44 193], with the faster performances often carried out by famous gurus (Krischnamacharya, BKS Iyengar 1968 (YouTube old films)) and the slower speeds being preferred by those looking to meditate. Reported speeds for each SS pose differs from 1-40 seconds (1.25-6.25 s. [108] 40 s. [194] 0.63-1.67 s. [195]).

## 6.5 Duration, dose and intensity

In Study I, YE participants rated the exercises “Fairly light to somewhat hard” (RPE 12–13) on the RPE-20 Borg scale. In Study II, the RPE rating was 14, indicating moderate to vigorous intensity. The primary aim of Study II was to increase cardiovascular fitness/endurance. An RPE rating of 14 is defined as “Somewhat hard to very hard” (RPE 14–17). Converting the RPE rating to the absolute intensity (by age) to MET (metabolic equivalents) is suggested to 7.2 to 10.1 MET[5] indicating sufficient intensity (i.e above 3 MET) for cardiovascular improvements to occur. While we did not measure MET specifically, the RPE ratings in Study I - 12-13 - are suggestive of a range between 4.0 to 5.9 MET (absolute intensity by age) [5]. According to this, Study I also achieved sufficient absolute intensity for cardiovascular improvements to occur, however we did not measure $VO_{2max}$ in Study I. The dose in Study II was however too low and the participants did not perform enough home training for cardiovascular endurance changes to occur. Study III was rated as a light intensity program (RPE median 10) equivalent to 2.0-3.9 MET (absolute intensity by age)[5]. Since RPE ratings were not given for all participants, considering such measurements were not carried out in every class, consequently the results have to be taken with a grain of caution. More data is needed to measure the intensities across the many diverse styles of YE. However, a recent meta-analysis did classify YE as equivalent to 3.3±1.6 MET [189], individual yogic postures averaging 2.2 METs and breathing exercises 1.3 METs. Most YE have been classified as light (under 3 METs) to moderate aerobic intensity (3-6 METs)[189]. Still, the majority of the studies proved that light intensity physical activity could be achieved with YE, and the SS has been classified as vigorous. Study II was somewhat of a brave experiment with very high intensity that required high motivation and skill from the participants. The recommendation is to perform YE at an intensity above 3 METs (sessions of at least 10 min.) for it to be used as a form of physical activity [189].

In Study II the total YE training dose during the whole intervention (both home and classes) averaged 390 min. This corresponds to a weekly average of 65 min. The RPE rating of the YE (range 14–17) was at a sufficient exertion level, but the total time spent was at the lower end of the limit and therefore unable to affect any improvements [5]. Higher RPEs (14-16) requires at least 75 min. of exertion while lower RPEs (12-13) requires 150 min. for there to be any noticeable health effects on the cardiovascular system[5 196].

In Study III the YE was of a lower intensity than the conventional training (CTP). This may relate to the YE not including any cardiovascular/endurance training nor any strength-training machines and probably results from other differences between the CTP and YE.
Thus, one could see a significant increase in walking distance in the YE group, which may have involved more efficient breathing patterns, reduced dyspnea, better coordination and improved control of breathing as well as other psychophysiological factors [192]. Study III did however include exercises for the lower limbs (movements similar to deep squats (utkatasana)), and in this respect may have been somewhat similar to conventional training. Nevertheless, with more COPD participants in the YE group, improvements in this group was limited when compared to the asthma participants who constituted the majority of the CTP group. With YE sometimes being thought of as a form of exercise training, intensity standards have yet to be determined [5]. Still, considering the dynamic intensity applied in Study II with 1–3 seconds per exercise plus the SS, a longer intervention could have generated difficulties for unfit participants with regards to motivation, and the total YE time would likely have been an issue as well.
Most studies use a time frame of 6 to 24 weeks, with 12 weeks with two or more sessions a week being the most common. Depending on expectations, hatha yogic interventions seem to have the best effect when carried out two or more times a week. However, there have been larger effects reported from engagement in more intense interventions taking place 5 days a week [197], and whenever participants have been able to continue with the training at home. Participation in a retreat may also have potential effects, but in that case maintenance is required since the effects seem to diminish in the same pattern as regular physical activity, often after 1 week. Moreover, in smaller studies seven days of intensive yoga have been shown to be able to reduce pain and improve spinal flexibility in participants with chronic lower back pain at a more satisfactory level than physical exercise [197 198]. For example, with regards to functional disability and pain outcomes in participants with back pain there were no difference detected between one or two sessions [199] a week.
Long-term follow-ups of the effects of YE are still lacking, and in Study III no significant effect could be detected past the 6-month follow-up. However, some recommendations for YE do exist, and the American College of Sports Medicine labels yoga as a form of multimodal exercise training involving motor skills that are multifaceted. The recommendation is a frequency of ≥2-3 days a week at ≥20-30 min. per session. Yet, there has been no determination of effective intensity, volume, pattern and progression of multimodal exercise [5]. To recommend an intensity for YE could possibly in the future be used to improve strength [200 201], balance [136 202], flexibility, vagal tone fitness (HRV, baroreceptor sensitivity,

HR), mental health and health related quality of life [46], though probably not cardiovascular fitness [203].

Regarding the RPE-20 Borg rating during YE, participants rated it as "Fairly light to somewhat hard" (RPE 12–13) in Study I. In Study II, the RPE rating was 14, indicating moderate to vigorous intensity. In Study II the primary aim was to increase cardiovascular fitness/endurance and the RPE rating were 14 (vigorous) and is "Somewhat hard to very hard" (RPE 14–17). Converting this to the absolute intensity by age in MET (metabolic equivalents) is suggested to 7.2 to 10.1 MET[5] indicating sufficient intensity (i.e above 3 MET) for cardiovascular improvements to occur. Unfortunately we did not measure MET but the intensity for improvement in cardiovascular endurance is proposed above 3 MET and the ratings in Study I of RPE 12-13 is suggested to range between 4.0 to 5.9 MET (absolute intensity by age)[5]. According to this, Study I also had sufficient absolute intensity for cardiovascular improvements to occur, however we did not measure $VO_{2max}$ in Study I. However in Study II the dose was too low and the participants did not perform enough home training for cardiovascular endurance changes to occur. Study III was rated as light intensity (RPE median 10) equivalent to 2.0-3.9 MET (absolute intensity by age)[5]. However RPE ratings were not measured for all participants in any of the studies since they were not measured in every class, consequently the results have to be taken with caution. Yet, more data are needed to measure intensities in different ways of diverse styles of YE. However, a recent meta-analysis classifies YE to be equivalent to 3.3±1.6 MET [189] and individual yogic postures averaged 2.2 METs and breathing exercises 1.3 METs. Though, most YE are reported as light (less than 3 METs) to moderate aerobic intensity (3-6 METs) [189]. Still, the majority of the studies showed light intensity physical activity with YE and the SS classified as vigorous. Study II was somewhat of a brave experiment with very high intensity that required high motivation and skill from the participants. The recommendation is to perform YE with the intensity being higher than 3 MET (with sessions of at least 10 min.) for it to be used as a form of physical activity [189].

In Study II the total YE training dose during the whole intervention (both home and classes) was on average 390 min. This corresponds to a weekly average of 65 min. The RPE rating in YE (range 14–17) was at a sufficient exertion but the total time was on the lower limit to show any improvements[5]. Higher RPE (14-16) requires at least 75 min of duration and lower RPE (12-13) requires 150 minutes for health effects on the cardiovascular system [5] [196].

In Study III the YE was of a lower intensity than the conventional training (CTP). This may relate to the YE not including any cardiovascular/endurance training and strength-training machines and probably results from other differences between the CTP and YE.
Thus, walk distance increased significantly in YE and may perhaps involve a more efficient breathing pattern, less dyspnea, better coordination and control of breathing and other psychophysiological factors [192]. However exercises for the lower limbs (movements similar to deep squats (utkatasana)) were included in Study III and in this aspect somewhat similar to conventional training. Nevertheless, with more COPD participants in the YE-group, improvements in this group may be limited as compared to the asthma participants who

constituted the majority in CTP-group. Nonetheless, with YE sometimes being a form of exercise training, no intensity standards have been determined [5]. Still, the dynamic intensity in Study II with 1–3 seconds per exercise using SS a longer intervention would perhaps generated difficulties with motivation for unfit participants and total YE time was likely to be an issue.

Most studies are using a time frame from 6 weeks to 24 weeks, however, 12 weeks with two or more sessions a week being the most common. Depending on expected effects of hatha yogic interventions it seems to have the best effect with 2 or more sessions a week. However there have been large effects from using intense interventions as 5 days [197] and from where participants can continue with home training. Participation in a retreat can have potential effects but maintenance is required since the effect seems to diminish in the same pattern as regular physical activity, and probably after 1 week. Moreover, in smaller studies, seven days of intensive yoga can reduced pain and improve spinal flexibility in participants with chronic lower back pain better than a physical exercise [197 198]. For example, on functional disability and pain outcomes in participants with back- pain there was no difference between one and two sessions [199] a week.

Moreover, long-term follow-ups are lacking of YE and in Study III no significant effects persisted after the 6-month follow-up. However, some recommendations for YE exist, and American College of Sports Medicine labels yoga as a form of multimodal exercise training involving motor skills that are multifaceted. The recommendation is a frequency of ≥2-3 days a week with ≥20-30 min a session. Yet, an effective intensity, volume, pattern and progression of multimodal exercise have not been determined [5]. To recommend an intensity for YE would possibly in the future be to improve strength [200 201], balance [136 202], flexibility, vagal tone fitness (HRV, baroreceptor sensitivity, HR), mental health and health related quality of life [46] but probably not for cardiovascular fitness [203].

## 6.6 Blood pressure (BP)

Despite previous studies showing significant effects on BP after 3-8 weeks of yoga in hypertensive individuals [88 90 204 205] , no such effects were observed after YE in either of the Studies I-III. In Study III, the CTP group, but not the YE group, was associated with a significant decrease in diastolic blood pressure by 5.7 units mmHg following the intervention. The clinically relevant decrease, approx. 4-5 mm Hg systolic, did not emerge in any of the groups. This is in contrast with other findings showing that yoga lowers BP. However, the participants included in Study I-III were normotensive and consequently larger BP changes could not be detected. But such findings typically emanate from studies without active comparison groups where time would likely have had an effect. This means that further studies are needed.

In addition, other studies have reported both systolic and diastolic decreases after yogic interventions [87 92-94], similar to usual care, in participants with mild to moderate hypertension [88 89 90 91] . Moreover, a systolic decrease range of 4-9.6 mm Hg and a diastolic decrease range of 3-7.2 mm Hg have been shown following YE [206] . A recent meta-analysis [207] showed the clinically important effects of YE on cardiovascular risk factors as compared to usual care. Moreover, hyperventilation is a common factor in hypertension, and inhibition of the baroreflex can represent a possible mechanism while breathing fast [208] which elevates blood pressure. A smaller study on patients with essential hypertension showed the restoration of the malfunctioning baroreflex mechanism with the lowering of blood pressure (29 units systolic and 17 units diastolic) after 3 weeks of yogic postures (including inversions)[88].

## 6.7 Hand-grip strength

Prior research suggests the presence of increased hand-grip-strength following YE [209 157 210]. Study I included hand-grip strength measurements and the results did show significant improvements, thereby aligning with previous research. Specifically, Study I showed an increase of 4 units (kg).

## 6.8 Apolipoproteins

Study II was the first study to measure apolipoproteins levels following YE. While the YE dose was small and the baseline levels were low and within normal range, there still emerged a significant effect on ApoA1 in the YE group with no between-groups effect. The mechanism behind the increased ApoA1 in the YE group seems to be similar that of physical activity, showing increased levels [124] with an improved metabolic response. Other studies have shown favorable and increased levels of HDL cholesterol (main component of ApoA)[207] with decreasing triglycerides [211] and uncertain effects on LDL cholesterol [93].

## 6.9 Adiponectin, leptin and cytokines

In Study II, the YE group showed increased adiponectin levels six weeks after the intervention. Similar effects were not found in the control group, though there was no significant between-groups effect. This indicates that the type of YE used in Study II is effective in low doses, with a potential anti-inflammatory effect and improved immunologic response in healthy individuals.

Regarding leptin, Study II saw no changes after six weeks. Still, others have reported positive effects on leptin rather than adiponectin levels 12 weeks following YE [131]. The levels may change differently. It could be that the adiponectin levels were changing faster than the leptin levels, while in other cases the opposite has been reported [131], i.e. no effect on adiponectin levels after 12 weeks. Interestingly, adiponectin and leptin levels vary between the sexes, with women having higher adiponectin and leptin levels[212] and leaner persons having higher adiponectin levels [213-215]. Studies need to remember to account for such differences. Additionally, body mass index (BMI) has a suggested connection to diastolic blood pressure [179], though participant BMI was within normal range in Study II (22).

## 6.10 Physical function: walk distance

The main findings in Study III showed that both the YE and CTP group had improved in the 6MWD after 12 weeks of intervention, with no between-group differences. Other studies and meta-analyses have reported similar findings with other yogic exercise programs [115 117 160]. In a recent study of coal miners with COPD, researchers found significant and clinically relevant effects on 6MWD after a yoga therapy intervention (including yogic counseling and lectures) [216]. Granted, this group was not fully comparable to the ones in Study III, since oxygen saturation was low and yogic exercises were performed 6 days a week at 90 minutes per session for 12 weeks. This represents a much larger dose than the one used in Study III.

Perhaps a higher dose would indeed have produced even larger effects. However, there can be a ceiling effect in the walk-test, what with the YE group having significant higher baseline levels compared to the CTP group. This means that the CTP group had a larger capacity for improvement. Yet, some MCID differences emerged in each group (Table F) for 30 meters and 50 meters. Moreover, recent findings show similar improvements in 6MWD after 12 weeks of Thai yoga (similar to hatha yoga) compared to Thai Chi and control [217]. A 3 month pilot study of COPD patients also showed improvements in 6MWD at 19 meters in the yoga group and 8.5 meters in the usual care group [160]. The YE group rated the RPE lower than the CTP group, the mechanism for which might be an increased awareness of the breathing with better coordination and control over the breathing [192]. This is confirmed in Study IV. However, with more COPD participants in the YE group, increases in this group may be limited when compared to the participants with asthma who constituted the majority of the CTP group. Improved effects on lung function and respiratory muscle strength parameters could not be found in the YE group, and there may be other psychophysiological factors that could explain the 6MWD improvement. Yet, the YE program included a few strength exercises for the upper limbs that may have helped the participants to increase their deep breathing, but not to the same degree as the CTP.

## 6.11 Dyspnea-related distress (DD-index)

Dyspnea-related distress is a new measure that shows fatigue after 6MWT. To date only one pilot study investigating YE and patients with COPD have shown significant effects on the DD-index [160]. Study III found no significant improvements in DD-index after the 6MWT, neither in the groups or between-groups. However, MCID emerged for 16% of patients in the YE and 41% of the patients in the CTP group (Table F). The DD-index is related to the RPE Borg-scale with 6MWD, meaning this measure may more adequately reflect pulmonary disease improvements.

## 6.12 Disease specific quality of life – chronic respiratory disease questionnaire (CRQ)

Both groups in Study III exhibited immediate effects after the intervention (12 weeks) on MCID (0.5 points) in CRQ, though there was a larger effect found in the CTP group. Interaction (group x time) showed significance in CRQ fatigue and CRQ emotional favouring the CTP group. This probably relates to the CTP group having had improved effects when comparing the baseline to the point in time after the follow-up. The YE group showed significance in the CRQ mastery domain, however no significant between-group effects emerged after the 12 week long intervention.

This evidence follows from earlier research [218], and the interviews conducted in Study IV qualitatively confirms the large effects shown in the YE group with regards to the mastery domain. Previously, diaphragmatic breathing and YE have had positive effects on disease-specific quality of life among patients with COPD [62 79 186], while other studies have reported no effects [160]. A pilot trial investigating patients with COPD and pulmonary arterial hypertension, which usually develops late in patients with severe COPD, found improvements in the fatigue, dyspnea and emotional domains following yoga intervention [218]. Moreover, the per-protocol analysis suggested the presence of significant additional improvements in the CRQ emotional domain in the YE group (results not shown).

## 6.13 Self-reported health

In Study III eight participants from each group reported better self-reported health after 12 weeks of intervention (data not shown) using the EQ-5D/VAS of MCID (10 units), but no significance appeared. However, the EQ-5D had decreased significantly in the CTP group at 6 months (Figure 21). Furthermore, a strong correlation emerged in the YE group when comparing differences in walking distance at baseline and after 12 weeks, indicating that an increase in walking distance resulted in improved self-reported health (Figure 22). Others have reported improved EQ-5D following the practise of adapted kundalini yoga for 12 weeks (once a week) in patients with paroxysmal atrial fibrillation[219] when compared to a control group with no intervention.

## 6.14 General effects after 6-months in Study III

In Study III, effects after 6-months were compared to baseline levels. This resulted in significant effects between CTP and YE-group in the six-minute walk test and the CRQ-emotional domain. This showed that CTP, but not YE, had longer lasting effects in 6MWT and CRQ emotional domain. This may be related to longer lasting effects in CTP group in these parameters. To achieve increased compliance after an intervention, it seems vital for patients with pulmonary diseases to maintain physical activity levels since the effects otherwise seem to diminish after 6 months. [69] This underscores the importance of researching how to help patients to maintain physical activity levels.

## 6.15 Experiences: qualitative content analysis

Study IV saw the participants in the YE group being interviewed face to face. The reported experiences included being taught new ways of controlling and using their breathing as a way to counteract symptoms, such as dyspnea and coughing, related to obstructive pulmonary disease. The participants found "learning by doing" to be helpful in becoming more focused, which in turn created a calmer and deeper breathing. Participants also reported increased body awareness, energy and stamina. Study IV represents an important complement to the traditionally measured effects on biomarkers of physical function. Patients reported increased empowerment, expressed as increased mastery of the disease. This is a valuable new finding. Improved awareness of breathing in combination with more efficient breathing techniques were experienced as an important learning opportunity as well as something that increased their perceived control over their health.

The main tools and active ingredients of YE involves working with body, breath and mind simultaneously. These three tools work together to involve the individual fully and are using both a bottom-up (doing the exercise) and top-down (observing with the mind) perspective[43]. This means that the individual is involved in the practise in a more focused way since the "listening" part is added [35 220 43]. The yogic tools fit in with the overall theme in Study IV, "From limitation to opportunity - to develop awareness and control over one's breathing". Likewise, others report that [221] self-efficacy is an important predictor of behavioural change. In general this means that the individual takes more charge of self-controlling the symptoms.

In Study IV this was reflected in the increased self-control experienced with the help of the three yogic tools. Increased self-efficacy is an important effect and goal of YE that has been reported by the participants in Study IV under the category “To experience how one can influence one's own situation”.

Increased awareness seems to be the active ingredient of YE needed for improvements to occur [222 223], especially as it pertains to patients with pain[223] and obstructive pulmonary diseases [218]. The attention part of yoga is an important instrument for these patient groups. Improved body awareness, control over one's health and pain reduction are a few of the mechanisms emerging after continuous yogic practice, i.e “learning by doing”, and is something which has also been reported in other qualitative studies [222-224].

Furthermore, the participants reported increased stamina and energy, which can be explained by the style of yoga used and that the program included vigorous poses and breathing exercises. Improved energy and stamina has been previously reported in patients with lung disorders [62 115]. One participant reported walking faster in daily life. Other studies have suggested that a better breathing technique may be a mechanism to more energy [192].

In Study IV participants reported decreased use of bronchodilators and less breathlessness as well as an increased mastery of dyspnea following YE, specified under the category “To experience how one can influence one's own situation”.

A recent Cochrane review reports that yoga to some extent improves quality of life and asthma symptoms without serious adverse events [114], and it has been suggested to serve as an alternative rehabilitation choice for patients with obstructive lung diseases [48]. Moreover, asthma symptoms, quality of life, exercise capacity and bronchial hyper reactivity have all been shown to improve in asthmatics after physical training [225] .

Using breathing exercises can improve breathing technique [79], which seems to be one of the important yogic tools to increase awareness that the patients in Study IV experienced. This has been reported under the category “To experience how one can influence one’s own situation”. Other yogic interventions [226] using only breathing exercises for 3 weeks - a total of 15 hours - showed significant improvements in sleep patterns when compared to usual care. This suggests that short interventions can have powerful and non-pharmacological effects. There were a few reported difficulties and challenges in the beginning of Study IV related to the synchronization of breathing and movements, but after 5-6 times participants reported that it became easier.

Social interactions before and after YE may have strengthened the experiences and effects of YE. However, during class, silence (no conversation) was encouraged. Being in a group setting with a common goal may have created a positive social atmosphere [218] and may have increased the participants' personal empowerment [224], as well as having added to their awareness of the self and the physical body. The importance of a positive atmosphere has been reported under the category, "To focus and be aware in a new way."

The category, “To experience how one can influence one’s own situation” and the overall theme to go from limitation to opportunity can be described as a form of improvement in quality of life, since the patients were able to master their symptoms themselves.
Other qualitative reports have reported improved quality of life (CRQ-fatigue), energy and breathing capacity with less anxiety and pain; "increased tidal volume with slowing expiration" with quotes as: "I have an overall feeling of well-being" and "excellent amount of energy" [218].
Measuring quality of life on the CRQ scale of mastery increased significantly in Study III, showing that objective and subjective data mirror each other. Rehabilitation that helps patients self-manage their symptoms and improve quality of life needs to be emphasized for this patient group.

# 7 Methodological considerations

This thesis includes both objective and subjective data in the form of questionnaires and interviews.

## 7.1 Design

Using an RCT design is considered the best method for evaluating the efficiency of different interventions and cancel out bias and the placebo effect. Moreover, in order to prevent bias, the optimal design should avoid passive comparison groups and make sure to blind both measurers and participants.

Missing outcomes and non-compliance is solved by employing the statistical concept intention-to-treat model (ITT) and there include all participants randomized to each treatment. If a participant is missing or unwilling to be re-measured, the technique of last observation carried forward should be used. Alternatively, one could also use more sophisticated statistical modeling using the available data from each individual. Study III employed an intention to treat (ITT) model and minimized the risk of bias. However, the principle of last observation carried forward was not applied to those participants who were unwilling to be measured, especially after the follow-up 6 months later. In line with ethical principles, those participants were not included in the ITT calculation if absent or sick. Factors that can occur after randomization has taken place, e.g. absence and deviations from protocol, were corrected. The Per-protocol model, which is the most common design in a majority of the published yoga studies, says to analyze only participants who've completed the full intervention [227]. Although avoided in Study III, Studies I and II did use the per-protocol model. The ITT analysis resulted in many patients with low adherence in the YE group, while the low adherence patients in the CTP group were excluded from analysis (3 classes minimum in YE and 12 minimum in CTP) due to their unwillingness to participate in additional follow-ups. This resulted in higher adherence to CTP than that of YE.

Regarding attrition bias – four participants in the YE group dropped out due to severe health issues, exacerbations and other personal reasons. Moreover, according to selection bias one cannot exclude that those participants who have a better perceived health always select themselves, i. self-selection and fulfillment of the full intervention. Perhaps those with lower health status are those who are most in need of interventions. Neither response bias can be excluded. Response bias is when the participants report their symptoms in a more optimistic way, and in a way they feel is socially acceptable or desirable. This especially applies to face-to-face interviews such as those conducted in Study IV. Additionally, the co-intervention bias is the tendency of participants to seek out and get treatment that is not part of the trial. Advice given to the participants during the intervention was to not start any new type of exercise. The participants were then asked about this at the end of the intervention, but no participants reported having done so. Being part of a trial or experiment and sign informed consent forms may also alter people's preconceptions and beliefs and create a placebo effect[228]. Seasonal variations could also have had an effect, since many people in Scandinavia are more naturally active in the spring, which is when all studies were starting.

## 7.2 Recruitment

In Study I the recruitment pool was large – based on two major corporations - however since the inclusion criteria only allowed for physical activity once a month, only 12 participants were found. The subsequent studies included a broader inclusion for feasibility purposes. In Study II, recruitment was done through a website for students (the target group), the problem with this being that the students who signed up to this website was probably interested in larger payments for participation in interventions. The recruitment process and the participants' preferences and expectations for treatment assignment and positive outcomes should therefore be considered as limitations of Studies II-IV.
Study III+IV recruited actively from a variety of channels, including websites, email, primary care general practitioners and posters pasted in hospitals and lung clinics. Seeing as there were several other research projects running simultaneously on COPD, we found it hard to get enough participants. Furthermore, the randomization process resulted in more participants with COPD ending up in the YE group while more asthma participants ended up in the CTP group. The recruitment of additional patients with COPD was also limited by the rather low prevalence of registered diagnoses in Sweden, this in turn relating to the low rate of daily smokers. Moreover, patients with severe obstructions (GOLD-4) were excluded for safety reasons, meaning that the effects of the YE program on this group remain unknown. Thus the transfer of our findings to patients with severe obstructions may not be fully realized.

Study II-III included a majority of women while Study I included a majority of men.

All the Study IV participants engaged in the YE intervention gave their permission to be interviewed. This together with the wide variety of participants, regarding gender, age and different levels of obstructive lung diseases, provided a broad view of YE experiences and thus strengthens the transfer of the findings to a wider sample. However, the information given to the participants was clear regarding the fact that the study involved two different conditions with eligible participants being randomized into either yoga or conventional treatment.

## 7.3 Hawthorne/Placebo effect

Being invited to participate in a clinical trial creates beliefs and expectations among the enrolled participants. This is one of the reasons for including a control group (especially an active control group). Specifically, a control group allows one to cancel out pure time effects and placebo effects. This means that if someone is being observed and assessed it can add to their expectations and beliefs about the treatment having positive effects. This phenomenon is called placebo and the participants receiving attention is called the Hawthorne effect. To clarify, the three components in placebo involves: "assessment and observation, a therapeutic ritual (placebo treatment), and a supportive patient-practitioner relationship", with the therapeutic ritual (patient-practitioner) being the most effective ingredient of the placebo effect [229]. Study I was a pilot-study with no controls and thus the results have to be approached with caution. Study III resulted in positive effects in both groups and they were both exposed to the Hawthorne effect. Moreover, the Hawthorne effect could have influenced the subjective measures (e.g. the CRQ scale in Study III), however the placebo effect was probably cancelled due to both groups being enrolled in an active treatment. Nevertheless, different people met the participants in the different groups 1-2 times weekly during the intervention and this could have created a placebo effect by way of the instructors [229].To avoid the therapeutic ritual part of placebo, the author did not measure or train the participants in any of the studies. It has been shown that placebo effects can produce statistically and clinically significant improvements [229], while other meta-analyses have shown no such significant effects on objective or binary outcomes of placebo. Yet, small effects can emerge in studies with subjective outcomes and for the treatment of pain [230] and mental disorders [231] .

## 7.4 Intervention program

The dose-response relationship during interventions and what duration and frequency is needed for the treatment to produce optimal effects needs to be established. Yet, for clinical trials it can be difficult to find a balance between how long people are willing to commit to participating in interventions and how long it takes to get results. Studies I and II used a once a week design, while Study III used a twice a week design. All three studies used 1-hour classes and had 1-2 instructors present during each session. In Study II the large variation in home exercises was an obvious issue. Yogic interventions can however be more cost-effective than pulmonary rehabilitation since no equipment is necessary and exercises can be partly self-taught and practiced at home.

Currently, there are no other RCTs of obstructive pulmonary disease patients using the newly developed YE program investigated in Study III. Evaluating the efficiency, safety and feasibility of this new YE program was essential to the thesis and also one of our main study objectives. The detailed program description of the interventions, as well as the follow-up 6 months after the intervention, represents its main strength.
Another strength of Study III's YE program was to include breathing exercises with prolonged exhalations and certain other specific YE. Regarding the presentation of the yoga programs the program was taught by trained yoga instructors and not the author of the thesis. Furthermore, the interaction between the instructor or measurer and the participant may have

created a therapeutic benefit. Still, the author trained the teachers in the three different programs to be able to provide a standardized quality of instruction.

The YE program design in Study III varied between CTP and YE. To achieve equal effects on lung function and respiratory muscle strength, a larger YE dose and a program with a higher dynamic intensity on the upper and lower body might have added greater benefits. Moreover, feelings of insecurity appeared when the aim of any breathing exercise was not clearly understood in Study IV. The YE program could have included more strength training exercises that are important for breathing, but one reason for there being no improvement in lung function is probably due to the nature of the YE program and most of the participants in the YE group having COPD. The follow-up of the YE group in Study III demonstrated no effects, which may be due to this group including more patients with COPD.

Experiencing an adverse effect with yogic inversions (head below heart body position) and sun salutations (including semi-inversions) could increase the risk for gastroesophageal reflux (preliminary reports), which is why these should be avoided by sensitive individuals.

To describe and keep the intervention as "clean" as possible without interfering factors is important. For example, some yogic interventions uses background music, which may affect the results. There are studies showing that listening to music can lower BP and HR [232 233]. We did not include any background music in any of the YE interventions and the room was quiet and meant exclusively for the YE connected to this thesis. People running around a room containing many assistant yoga teachers or other people should be avoided, as should disturbances from next door. Group interventions can give rise to many factors that can interfere with the results, one example being the strengthening effect that social interaction can have.

In Study II and III all measurements were taken by trained physiotherapists. In Study I, BP and hand-grip strength was measured by the author for practical reasons due to the measurements being carried out on site. Breathing frequency was measured with a device only in Study III.

## 7.5 Measurements

Study I was a small-scale longitudinal pilot study done on naive YE participants, where time spent on inversions increased from 7 minutes to 20 minutes over an eight week period, showing that YE increased HRV in the time domain (pNN50%). Yogic exercises can have a restorative effect on the autonomic nervous system. Moreover, other HRV measures, including NN50, HF and LF/HF ratio, also showed a trend towards improvement, but not a significant one. However, larger randomized controlled studies are needed to confirm the effects of different YE on the sympathetic and parasympathetic nervous system. Furthermore, in Study I the time domain HRV measures increased whereas the frequency domain HRV measures did not. Some participants were excluded due to poor ECG recording quality, therefore resulting in a smaller sample size.

Measurement of oxygen uptake in Study II was done using a Cooper field test, allowing for limited control over weather conditions (which differed slightly). However, the Golden Standard for experimental testing of $VO_{2max}$ is direct measurement using a metabolic cart with a chamber, which would have allowed for more precision. Coopers test was chosen for practical reasons, since the validity is similar to the oxygen chamber method [152 153] and since to schedule each individual for laboratory analysis with metabolic cart measurement would have been impossible.

Biomarkers used blood analysis and were performed at a certified laboratory. They were analyzed in direct relation to the intervention in Study II. The obvious strength of Study II lie in participants being gluco-metabolically healthy (very low HbA1c), and no larger effect on blood parameters could be detected after high intensity yogic exercises. Perhaps research done on individuals with lower fitness levels or on patient groups could produce such effects. Both the ApoA1 and adiponectin levels increased in the YE group, which suggests a positive metabolic effect on a somewhat active and healthy group. However, large positive effects were not expected. Yet, the increasing ApoA1 and adiponectin levels along with the lowered HbA1c in the YE group show a clear trend. The YE dose was too low to produce any cardiovascular fitness improvements, but still there emerged positive effects on ApoA1 and adiponectin levels. As regards the biomarkers, there was no correction for variations in plasma volume shifts, and further details on nutritional status would have added information. Some of the blood parameters differ between men and women, e.g. adiponectin which was only calculated for women in Study II. This was not a problem considering the majority of the participants in Study II were women.

In Study III there was a statistical imbalance in the 6MWD baseline with higher walk-distance levels in the YE group, meaning that the range for improvements (ceiling-effect) was probably smaller when compared to the CTP.

Despite variation in compliance between the groups, the overall compliance was large and allowed for testing of both YE and conventional training programs in Study III and IV. We chose to include both asthma and COPD in order to investigate the effects on both groups. Both groups showed positive effects on the validated 6MWT[234] and was performed according to guidelines [235]. The walk-test is a powerful indicator of health status impairment [236 237 238] . The walk-test was performed indoors in the same environment for all three tests. Prior research suggests that to see improvements in walk-test it should be 54 meters[239], but this has recently been changed to 26 meters for patients with severe COPD[115 240].

In Study III the YE group increased in the CRQ mastery domain, which may have increased their health and self-efficacy by teaching them new skills to master their breathlessness, thus improving their quality of life. Using self-evaluative questionnaires like CRQ represents a valid [241 242] instrument. However, there are other questionnaires that come recommended by GOLD, such as the Modified British Medical Research Council questionnaire on breathlessness or the COPD Assessment Test (CAT)[63], both of which could have been used in Study III to describe the patients' wellbeing.

The most commonly used parameter for measuring lung function is $FEV_1$ and FVC[151], both of which were used in Study III. Spirometry was performed according to guidelines [151] and is valid [243] in general practice and satisfactory in comparison with the "gold-standard spirometry test measured in certified pulmonary function laboratories . However, spirometric indices relevant to the management of COPD obtained during trained general practices showed a marginal but statistically significant increase when compared to those measured in certified pulmonary function laboratories [244]. According to GOLD, spirometry should be measured after administration of an adequate dose of short-acting inhaled bronchodilator to minimize variability, but this was not done in Study III. Instead patients were asked not to use the inhaler prior to the spirometry and respiratory strength tests to make sure that the baseline levels were similar in all the measurements in Study III. Yet, all the participants already had a diagnosis from a doctor. However, there is a certain learning process associated with spirometry, and perhaps the participants got increasingly used to the test throughout the study period. Yet, all the measurements were taken by physiotherapists and not in a laboratory. As for measurement errors, inadequate inhalation may have induced errors during the breathing tests. It's important to note that the patients varied largely both in age, disease severity (both asthma and COPD) and $FEV_1$, however $FEV_1$ is not an optimal measure. Moreover, some of the patients in the CTP group had previous experience of participating in physiotherapeutic interventions involving cycling and strength training, which made them familiar with some of the exercises, while the participants in the YE were all novices. Three participants with more severe illnesses and one younger woman dropped out from Study III, which may have been due to either the intensity of the program or personal reasons.
The number of asthma attacks and/or exacerbations as well as the strength required in large muscle groups during the interventions could have added more information about exercise interference.
Regarding oximetry, no participants in Study III fell below 92% [245], which meant arterial oxyhemoglobin saturation (%$SaO_2$) blood gas analysis were not needed and fingertip capillary gas estimation was performed. This accurately reflects the arterial pressure of $C0_2$ and arterial blood gas tension [246].

Content analysis [164 163] is suggested to report on external validity [247] practical applicability, relevance and trustworthiness [248 165] . This relates to the content analysis, as used in Study IV, involving the analysis of interview data. In Study IV credibility in data collection and analysis was assured by close cooperation within the research group with good competency in using content analyses[163], yoga teacher experiences and clinical experiences of working with obstructive pulmonary disorders as well as the interviews being performed by an independent interviewer not involved in the intervention. The interviews were performed directly after the intervention while the participants had their experiences fresh in mind. The interview guide used two test interviews in order to strengthen the interview technique. In Study IV all the participants engaged in the YE intervention accepted to be interviewed and a broad view of YE experiences emerged.

## 7.6 Statistical considerations

### 7.6.1 Power calculation

Study I was performed at a workplace with a high percentage of physically active employees. It was difficult to find sedentary individuals that fit the inclusion criteria, and this was one of the reasons for the study becoming a pilot study; initially it was planned as a RCT trial. The sample size and power for study II was sufficient at 96% power (20 was required for each group). Study III required 24 patients (calculated on DD-index) in each group and therefore a few more participants were needed to achieve 80% power. However, given the number of patients we managed to include the statistical power still reached 71%, and additional patient recruitment was deemed unfeasible. Regarding power in 6MWT in Study III we hypothesized a difference after the intervention of a MCID of 54 meters in the YE group and 30 meters in the CTP group, with the same SD (25) in each group and at 80% power. Since 18 participants were needed in each group the study was therefore powered. Calculating the power on adiponectin in Study II, we hypothesized a difference of 1 unit and 0.2 in Control group with SD (0.8) in each group and with 80% power, it required 16 participants in each group and was therefore powered.

The power for primary outcomes was calculated compared to other studies on HRV in Study I[101], oxygen uptake ($VO_{2max}$) in Study II[32] and DD-index in Study III [160]. We chose the parameters that reported clinically significant findings. In Study I the reason we choose HRV was that no other reports with similar design similar to yoga to the study planned was available at that time (2011). Study II used $VO_{2max}$ and was the only trial available with significant findings on $VO_{2max}$ (with 2 mL/kg/min) at that time, moreover the design of that study was similar to the one we planned. Study III power calculation was based on a pilot study of yoga in COPD [160], this was the only yoga trial for this patient category that was available, although DD-index is a new measure.

# 8 Future perspectives

To achieve effects on cardiovascular parameters such as oxygen uptake and health would probably require longer YE interventions with more motivated participants. Additional research is needed into the use of dynamic YE and sun salutations, with a longer duration (a suggested 12 weeks, 3 times a week for at least 40 minutes) in both trained and naïve participants.

Measuring baroreceptor sensitivity, heart rate variability (HRV) and heart rate recovery before, during and immediately after a YE program could be another interesting project.

Moreover, focusing solely on inversions to detect associated changes in the autonomic nervous system (HRV) and their effect on energy/fatigue/recovery/stress tolerance would be another very interesting approach to take.

A detailed description of the program (perhaps with film) is warranted and further interventions should introduce fewer exercises in the beginning of the intervention. Due to the heterogeneity of the available studies there exists an unequal representation of body, breath and mind exercises. To investigate which of the main components (body, breath, mind) that is the most powerful of the YE is a warranted approach for future investigations. Determining what type of YE is needed to improve walking distance and pulmonary function is another interesting perspective.

Patients requiring specific effects could possibly come to influence which intervention one would chose to use.

To determine to what extent self-efficacy is strengthened after a long/short yoga intervention [28] using self-efficacy scales.

Systematic monitoring of subjective indicators as sleep-quality, perceived stress and mental health are needed to complement qualitative data.

Future studies would be recommended to use a YE dose of 2-3 times a week to achieve optimal results and to improve breathing performance/improvements in diseased populations' probably daily practice is needed.

Regarding the effects of YE on breathing there's a lot to be investigated, such as for example breathing frequency, breath holding time, diaphragmatic mobilization, chest expansion and the use of breathing quality self-evaluations [183 184], as well as more frequent measurements of oxygen saturation.

The effects of using diaphragmatic mobilisation techniques [121] in yogic practice and the specific yogic breathing exercise bhramari (i.e humming with sound) and its long and short-term effect on health and blood pressure. Bhramari was used extensively in Study III and has been shown to increase exhaled Nitric Monoxide (NO) [249], distend capillaries and induce relaxation. Using NO as a biomarker for eosinophilic inflammation in pulmonary patients with exacerbation, pulmonary function impairments as progression of airways inflammation and pulmonary arterial hypertension might come to represent an advantageous novel biomarker.

Future clinical trials are needed for different patient groups as well as for healthy participants to further evaluate the long-term effects of yogic practice.

## 9 Practical implications

The use of yogic exercises among both healthy and diseased populations can be implemented as a complementary treatment in addition to other established methods. This pertains in particular to participants with breathing disorders, poor cardiovascular health, elevated stress levels and poor quality of life and lower-back pain. The YE can be used to empower participants as well as to improve symptoms, well-being and health.

## 10 Clinical implications

Because of the pilot design in Study I, the results have to be approached with caution. However, other studies have shown that YE increase HRV and programs such as the one used in Study I and II produce similar effects as those of physical exercise, with no reported adverse effects.

Yogic exercises may be added to other established physical training programs as a complementary treatment for healthy individuals that require higher intensities. Physical therapists may use the program for additional benefits in the treatment of patients and healthy individuals.

With the results from Study III showing similar effects in both the YE and CTP group with regards to walking distance after 12 weeks of intervention, YE seems like feasible and safe short-form version of physical exercise for patients with pulmonary disease.

While the long-term effects (after follow-up) on CRQ and walk-tests were greater in the CTP group, the YE group showed greater increases in mastery of symptoms and respiratory rates. As part of rehabilitation YE may then constitute an alternative to other physical activities or training and may be a useful addition to traditional rehabilitation programs [48], especially considering it has no reported adverse effects.

However, the randomized distribution of more patients with asthma in the CTP group and more patients with COPD in the YE group means that the results have to be interpreted cautiously. Study IV revealed the recognition of yoga as a treatment of COPD and asthma in medical practice, and its contribution to the empowerment of patients in their everyday practice is an important new finding.

# 11 Conclusions

The conclusions of this thesis were drawn from an evaluation of different yogic exercise programs on health and show that:

- Yogic inversions in naïve and untrained healthy persons increased heart rate variability but had no effect on blood pressure, however results have to be taken with caution due to the study's pilot design.
- High intensity sun salutations in healthy students showed no effect on cardiovascular fitness or any significant effect compared to control, but the yoga group showed increased levels of adiponectin and apolipoproteinA1.
- Yogic exercises (YE) for obstructive pulmonary disease patients using a customized program showed no significant effect after 12 weeks when compared to conventional treatment (CTP) in terms of improved walking distance. Both groups improved walking distance after 12 weeks. The CTP group showed improvement in all CRQ domains after 12 weeks, the YE group showed improvement in the mastery domain. In conclusion, the short term effects (after 12 weeks) of YE included improved walking distance, lowered respiratory rate, improved mastery of the disease and increased oxygen saturation.
- The detailed program description of the interventions (I-III) and the follow-up carried out 6 months after the intervention represent the main strengths of Study III. However, the long-term effects of YE were not as significant as those of CTP and more long-term follow-ups are needed for YE.
- Yogic exercises performed in Study I-III were feasible and safe with no documented adverse effects.
- The experiences of people with obstructive pulmonary disease who'd used YE revealed the importance and power of practicing (learning by doing). This appeared as a central component for facilitating self-awareness and learning new ways of breathing. The control of symptoms and breathlessness through YE practice can serve as an efficient tool for strengthening self-efficacy and mastery of the disease.

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# 14 Appendix

**PROGRAM DESCRIPTIONS**

## STUDY I Intervention (HRV-study)

The yoga program was 60 minutes and standardized. The program included general poses, inversions and semi-inversions. The postures were: cat/cow, shoulder rolls, upper body rotation in cat position, bridge pose (also on one leg), cobra, wall dog variation, wall dog moving down on the wall, down dog, half hand stand towards the wall, chest opener – lying on a roll placed under the rib cage, twisted side angle pose with the knee on the floor, shoulder stand variation to the wall, universal pose, waterfall pose and horizontal relaxation (5–8 minutes). As the intervention proceeded, the time spent on inverted poses gradually increased while the time spent on other poses decreased. The total inversion time for each participant during the last 4 weeks of the intervention was around 15-20 minutes. All participants were encouraged to practice at home between classes. If participants had little time to do so, they were encouraged to practise only the inverted poses.

## Study II – Intervention (sun salutation)

The yoga program was 60 minutes and standardized. The program included high intensity dynamic yoga postures with the classical surya namaskar (sun salutation, SS) (30-40 minutes) and other inversion poses (pincha mayurasana, half hand stand towards the wall, ardha adho mukha vrksasana, sarvangasana), parivrtta parsvakonasana, gomukasana (around 15 min.) Inversions and semi-inversions were performed at the end of the program. The SS is a collection of 12 separate poses forming a dynamic sequence. The order of the SS was the following (Figure A): tadasana, tadasana with back bend, uttanasana (with bent knees), crescent pose (right leg back), adho mukha svanasana, modified chatturanga dandasana (with buttocks up and knees on the ground), urdhva mukha svanasana (knees on the ground), adho mukha svanasana, crescent pose (right leg forward), uttanasana and standing back bend tadasana (program similar to [108]). The next round was repeated with the left leg back and forward during the crescent pose. The speed of the SS was somewhat increased during the six week period with the goal being to perform each pose for 1,5-2 seconds. Relaxation mainly involved the waterfall pose (viparita karani) or horizontal relaxation (5 minutes). Intensity: an intensity of 14-17 using the Borg RPE-scale was recommended.

## Study III – Intervention (YE and strong breathing study)

**Dose**: Two sessions per week with one session stretching 60-70 min. at a time, for 12 weeks totaling 24 sessions. Starting position: seated on a chair or meditation chair. The room was quiet without music allowing no other individuals in the room than those participating in the intervention. Props included yogic blocks and blankets. Exempting questions directed at the teacher, there was no talking during the yoga class. The majority of the subjects were yoga novices.

**Asanas**: (eyes open) Important instruction communicated during class; to rest when needed by switching into the child pose (balasana), alternatively to lean forward on the chair with the legs apart (uttanasana variation), and to work at their own capacity. General postural instructions and centering in the beginning of the class: long spine with lateral movement, widening of the waist during inhalation. Keeping hands on the waist with thumbs pointing backward.

*General breathing instructions*: Extended exhalations, all breathing done through nostrils (if possible). Complete a deep yogic breath using the diaphragm extensively during all asanas. Uddiyana bandha (pulling stomach in using first the pelvic floor muscles and then the navel—light pull in towards spine—during all exhalations) introduced after approx. 6 weeks. Performing complete yogic breaths, 3 levels on inhalation and 3 levels on exhalation. Move hands along with the breathing, inhalation starting at lower abdominal navel area, moving to the upper waist/middle chest and finishing at the upper chest below the clavicle. Exhalation starting in upper chest, moving down to middle chest and finally ending at lower abdominal movement.

Vinyasa with back bending tadasana on inhalation (initially without head back) and deep utkatasana on exhalation (with arms up and open chest, avoid leaning forward), instruction without arms and then with arms extended above the head, alternatively keeping the hands resting on the shoulders. Utkatasana progressed to sitting all the way down into the chair and later by sqatting all the way down to the floor letting the heels come up. Ardha Chandrasana (standing side stretch, one arm up while other arm down, other arm supported on thigh). Dynamic and then progressing to static holding (approx. 30 seconds on each side), alternatively while seated on chair if breathing restriction occurs. Trikonasana with chair, foot on floor under chair's seat and hand on chair's seat or on the back-rest of the chair. Press hip out to side when going down and extend arm up to ceiling. Rotation of head during the final pose. Small sun salutation, dog down and dog up, (adho mukha svanasana, urdhva mukha svanasana) dynamic sequence with the breath, 4-5 times with hands on the seat of the chair. Dog pose with wall (hands on wall at shoulder height) was also suggested if no weight on upper body is possible (approx.. 2 min). Parsvakonasana with chair, foot placed under chair's seat and hand on seat (after 4-5 weeks), emphasis on turning the chest and head if possible to get pressure change in neck. Bharadvajasana 1, using both seated and standing variations, both legs folded to the left and twist right first. Standing variation (utthita marichyasana); right side to wall with right leg up on chair and hands to wall, twist to the right (alternative given with block under heel of standing foot), then changing sides. Tiger breathing flow, Cat (marjaryasana) and cow, on all fours using extended exhalations. Strong abdominal draw-in when exhaling. Variation used by some; seated vertically on chair using simple back flexion and extension (no weight on arms). Another variation of cat pose was with flexion of wrists on floor (palms down, thumbs facing out and palms up with thumbs facing towards each other). Sphinx pose (salamba bhujangasana), walk on underarms to the right and then to the left. Bhujangasana, resting on abdomen, then arms wide with fingertips facing outwards extending up on inhalation. Setu bhandasana (bridge pose) with one leg up, progressing to feet on chair to achieve inversion. Hip resting on block with both legs up (viparita dandasana variation), then one leg lowering at a time to the floor (stretching hip flexors), then in setu bandha with block. Universal pose: supine twist to right with initial strong abdominal activity and straight spine. Rotation of head opposite to legs to improve neck mobility. Fish pose (matsyasana), supported back bend with yoga block (wood) on thoracic spine behind heart, to increase mobility in chest (chest opener); option of using rolled mat or blanket under chest. Alternative was given with either weight on elbows or baddha konasana.

Yogic breathing exercises (pranayama), seated on a chair or meditation chair, straight spine, chin slightly lowered (eyes closed), avoid leaning into back of chair (approx. 30 min). Asthma mudra was used during some of the exercises. Metronome was used during the last 5-6 weeks to get the timing and awareness of the breathing right during the breathing exercises. Kapalabhati (breath of fire), starting with 10 times working up to 30 times. Hands on lower abdominals to increase awareness of the abdominals, pull in during exhalation. Begin slowly then try to speed up. At the end of the course this involves 20 x 4. Focus on exhalation, no attention to inhalation, 2-3 minutes. Bhastrika, hands on lower abdominal, 20 times. Alternate nostril breath (nadi shodhana), using nashiki mudra, start exhalation through left nostril, inhale left, exhale right, inhale right, exhale left (=1 cycle). Begin with equal inhale and exhale (5 sec. in and 5 sec. out suggested) then try varied lengths of breathing ratios; 2-0-4-0, 6-0-12-0 no pauses, important prolonged exhalation. No pauses after inhalation. Focus on extended exhalations and if possible a short pause after each exhalation, 5-10 minutes. Sitkari (inhale through teeth, exhale through nose and closed mouth) to be used only during the first 4-5 weeks. Bharmari (mmmmm sound on exhalation), humming bee, extended outbreaths –10 minutes, powerful outbreaths with sound (sometimes with sanmukhi mudra), move sound to upper back palate and towards third eye. Viloma (Dirgha/3 part breath). Divide inhalation and exhalation into 3 parts, inhalation starting at abdomen, then same inhalation at middle ribs and final inhalation at collarbones. Exhalation starts at collarbones, middle ribs, abdomen. 2-3 minutes (sometimes with prana mudra). Hands moving to the active region of the chest. In the beginning of the course seated while supine, on back at the end of the course. Sukhasana with forward bend, hands on block or chair. Shavasana (body scanning, focus on synchronization of equal relaxation between the left and right side of the body and let the weight drop to the floor), sometimes elevated legs with feet or calves on meditation chair, once during the intervention patient tried with weight on thighs. Feet closer than arms, keep back of the shoulders pressed to the floor. Approx. 5-8 min. Home training with this program was provided on DVD (in Swedish).

**Intervention progression in HY group**

The time spent in each yoga pose was gradually increased, each pose being held from 5-40 seconds, each breathing exercise performed for a longer duration with fewer pauses towards the end of the intervention. Different variations of the poses were gradually introduced (using walls, chairs and floor). Emphasis was on the synchronisation of the breathing during the exercises. Strength was not measured in the HY group.

*BOTH GROUPS - Training maintenance and progression following intervention* (approx. 3 months after intervention): among CTP group (8 responders), 4 did not continue and 4 continued the CTP program, 8 did other exercise training. Among HY group (12 responders), 5 did not continue the HY program and 7 did, 10 did other exercise training. One patient in each group used physical activity on recipe (FaR).

## Conventional training program (CTP) (physiotherapeutic intervention)

**Dose**: Two sessions per week with one session stretching 60-70 min. at a time, for 12 weeks totaling 24 sessions. Work using strength training machines (2-4 sets each of 10-20 repetitions) was tested individually on 70 %.

Cycling 10-15 minutes at an intensity rating of 12-14 (on Borg 20-scale, approx. 50-60 rpm per minute).

CTP was performed in a gym (with gym equipment and stationary exercise bikes, adjacent to the yoga room) with background radio/music while two physiotherapists coached the subjects. Subjects were allowed to talk to each other and to the physiotherapists as well as the other subjects who were sometimes in the room.

The exercises included: Leg extensions (seated position), standing arm pull-backs with thera-band*, seated leg press, shoulder press, squats to chair with crossed arms in front of chest*, seated rowing/arm pull-backs with machine, heel lifts holding back of chair*, triceps press with machine, torso rotation with machine, standing biceps curls with free weights, seated wide on chair and torso twists with stick behind chest, hands resting at shoulder height on stick*, seated side stretches with extended arm* (lower arm resting on hip), shoulder shrugs*, seated big upward swimming arm movements with arms above head*. Calf stretch with chair*. * refers to exercises that were prescribed as home exercises.

The home exercise program for pulmonary rehabilitation was distributed on DVD and the program written out on paper. This included exercises marked with * plus walking on the spot, shoulder lifts with theraband, one arm at a time (up to shoulder level), bicep lifts seated on chair with theraband (foot on theraband), seated rows on floor with straight legs with theraband, maintaining end position. Therabands were then supplied for the home sessions.

**Intervention progression in strength in CTP group**

Load increased during the 12 week period in CTP, during the leg extension by mean 7.81 kg or by 49 % (mean start kg divided by mean kilos increased during the intervention), during straight arm pull backs by mean 2.8 kg or by 44.6 % using starting kg/kg increased during the intervention and during leg press by mean 12.3 kg, or by 29.4 % using starting kg/kg increased during the intervention. Strength was not measured in HY.