S1

Randomization

For randomization, a research randomization program was used (http://www.randomizer.org/form.htm). Randomisation was not stratified. Patients were randomly assigned in a 1:1:1 ratio using a computer-generated permuted-block scheme. Allocation took place by an independent researcher after written consent had been obtained from all subjects and baseline data were collected, ensuring concealment of allocation.

S2

Exclusion criteria

Exclusion criteria were: current smoking or a smoking history of $\geq$ 10 pack years; asthma exacerbation (need of antibiotics/oral corticosteroids) in 6 weeks before inclusion; COPD or other pulmonary pathology apart from asthma, except for adequately treated OSAS with a Apnea Hypopnea Index < 5.0; and any significant orthopaedic of neurologic problems that reduce mobility or cooperation with physical training.

S3

Exercise training program

Training was performed three times per week for twelve weeks. Each training session was divided into four parts: the warming-up, stretching, the exercises and the cooling down. Between each part, the patients had thirty seconds rest and were allowed to drink some water.

The warming up consisted of a seven-exercises routine, each exercise was thirty seconds. The routine was repeated 3 times. The intensity was progressive and patients were asked to reach a seven at the 10-grade Borg scale.

The stretching consisted of ten minutes full-body stretching exercises, and aimed to improve the range of motion of joints, to prepare the body for the training and to prevent injuries.

The number of sets completed in the exercises was increased during the first seven weeks. The patients started with three sets of four exercises. Each exercise was a bodyweight exercise and lasted 45 seconds. Between each series the patients had thirty seconds rest and they were allowed to drink some water. At the end of week seven

(training 21 sessions) patients reached six set training session of four exercises. In each training session the patients were asked to maintain the intensity during the workout close to 90% of their VO_{2max} or to reach at least a seven at the 10-grade Borg scale.
The cooling down was also five minutes at the end of the training session. It consisted of full body exercises to return vital parameters to resting rate such as heart rate and breath before leaving the facility. During the cooling down there was no intensity target.

S4

Internet based self-management program "PatientCoach"

This program offers components for goal setting, tailored information, social forum and an e-consult option with health care professionals. In addition, the PatientCoach system includes modules for self-monitoring asthma control (ACQ), weight, lung function, feedback, medication plan, reminders and alerts. Furthermore, physical activity was monitored by an automated internet-based accelerometer (Fitbit, www.fitbit.com).

S5

Assessments

Body composition

Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2). Obesity was defined as a BMI equal or greater to 30 kg/m^2. Fat mass (FM) and fat free mass (FFM) was measured with a bioelectrical impedance meter (Bodystat 1500, Bodystat Limited) and expressed as % of predicted. Metabolic syndrome was diagnosed according to the National Cholesterol Education Program's Adult treatment Panel III report (NCEP ATP-III) criteria (18).

Asthma control and asthma quality of life

Asthma control was assessed by the validated asthma control questionnaire (ACQ). It comprises 6 questions with different components of daytime symptoms and night time

symptoms (14). Asthma related quality of life was measured with the validated asthma quality of life questionnaire (AQLQ) (15). For both questionnaires, a change of > 0.5 is considered as clinically relevant (14,15). An asthma exacerbation was defined as worsening of symptoms with need for oral corticosteroids and/or antibiotics)

Lung function

Pulmonary function was measured with standard spirometry (Vmax Encore 22D, Carefusion) and bodybox (Vmax encore 62j, Carefusion) according to the American Thoracic Society (ATS) / European Respiratory Society guidelines (ERS). Post-bronchodilator values were expressed as a percentage of predicted (16) . Methacholine challenge test was used to measure bronchial hyperresponsiveness (PD20). Fractional exhaled nitric oxide (Fe_{NO}) was measured with the Niox-Flex (Aerocrine AB, Sweden) at a constant flow rate of 50 ml/s and expressed as parts per billion in accordance with the guidelines of the American Thoracic Society and European Respiratory Society (19).

Exercise capacity

Aerobic capacity (VO_{2max}) was measured with a cardiopulmonary exercise test (CPET) performed on an Ergoselect cyclometer (Ergoline, Bitz, Germany) using a maximal symptom limited cardiopulmonary incremental protocol according to the recommendations of the ATS/ACCP guidelines (17). The six-minute walking distance (6MWD) was measured by the six-minute walking test (6MWT), performed indoor using a 30 m walking course . Patient instruction and measurements were performed according to the ATS/ERS statement (25).

Daily activity

Daily activity such as daily steps and physical activity level (PAL) was measured with a portable movemonitor (DynaPort MoveMonitor, McRoberts, The Hague, The Netherlands), attached to the lower back by a belt. Participants were instructed to wear the movemonitor during 7 days at all times, except during water-related activities (20).

Blood sampling and analysis

Blood samples were obtained by venapuncture, and laboratory measurements were performed according to standard procedures by the department of Clinical Chemistry. For the analysis of serum markers of systemic inflammation, serum aliquots were frozen at -80°C and analysed in bulk. The Meso Scale Discovery Platform (Meso Scale Discovery, Gaitherburg, MD) was used to detect leptin, adiponectin and high sensitivity (hs)-CRP. Serum Pentraxin was analyzed using a commercial ELISA (Hycult Biotech (HBT)).

Sputum induction and analysis

Sputum induction with hypertonic saline (4.5%) and processing was performed by a validated method according to the guidelines (21-23). An ultrasonic nebulizer (Klava) with a two-way non-rebreathing valve (Hans Rudolph) and an output of 2 ml/min was used for induction. Before start and during the procedure, spirometry (Vmax Encore 22D, Carefusion) was performed to assess the lung function at baseline and during sputum induction. Pre-treatment with salbutamol 400 µg was given in order to prevent excessive bronchoconstriction. The expectorated sputum was kept at 4°C and processed immediately after collection to obtain cells and supernatant. For sputum processing, the whole sample was mixed with the same volume of sputolysin reagent (DTT), then placed in a shaking water bath of 37°C for 15 minutes for homogenization. After this, the sample was filtered through a 100 µm filter and centrifuged (1500 rpm;10 min). The supernatant was removed and was stored at -80°C. The cell pellet was resuspended in PBS/1% (w/v) human serum albumin (HSA). Total cell counts were determined with a Bürker Haemocytometer and cell viability was assessed using the by trypan blue exclusion method. Cytospins were made and stained with May-Grünwald-Giemsa. Differential cell counts were performed by counting at least 400 non-squamous sputum cells. Samples with more than 80% squamous cells were excluded from analysis (21-24).

Statistical analysis

Baseline variables were summarized as mean±SD for continuous variables with normal distributions, median (interquartile range) for continuous variables with skewed distributions, and n (%) for categorical variables. The 3 and 12 months differences within groups were summarized as mean±SD or median (IQR) depending on the shape of the distribution and tested with the paired Student's t-test or the nonparametric Wilcoxon matched pairs test, respectively.