



# Physical capacity and inactivity in obstructive airway diseases: a “can do, do do” analysis

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People with bronchiectasis, severe asthma and COPD may not have the physical capacity to participate in moderate to vigorous physical activity. It is also important to consider the potential benefits of addressing other movement behaviours.

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## Abstract

**Introduction** Physical capacity is an important determinant of physical activity in people with obstructive airway disease (OAD). This study aimed to extend the “can do, do do” concept in people with OAD, to identify if people categorised into quadrants based on physical capacity and activity differ by clinical and movement behaviour characteristics.

**Methods** A total of 281 participants (bronchiectasis n=60, severe asthma n=93, COPD n=70 and control n=58) completed assessments to characterise physical capacity as “can do” versus “can’t do” (6-min walk distance < or ≥70% pred) and physical activity as “do do” versus “don’t do” (accelerometer-derived moderate to vigorous intensity physical activity (MVPA) < or ≥150 min·week<sup>-1</sup>).

**Results** The control group had a greater proportion of people in the “can do, do do” quadrant compared with the OAD groups (76% versus 10–33%). People with OAD in the “can’t do, don’t do” quadrant had worse clinical characteristics (airflow limitation, comorbidities, quality of life and functional dyspnoea) and spent less time doing light-intensity physical activity (LPA) and more time being sedentary compared with the “can do, do do” quadrant.

**Discussion** This study highlights that many people with OAD may be inactive because they do not have the physical capacity to participate in MVPA, which is further impacted by greater disease severity. It is important to consider the potential benefits of addressing LPA and sedentary behaviour due to suboptimal levels of these movement behaviours across different quadrants. Future research is needed to investigate if tailoring intervention approaches based on quadrant allocation is effective in people with OAD.

## Introduction

Physical activity is recommended for the management of obstructive airway diseases (OAD) and is associated with improved symptoms and quality of life, as well as reduced risk of hospitalisation and premature death [1–3]. However, people living with OAD engage in less physical activity than those without OAD [4]. Despite the recognised importance of addressing reduced physical activity in people with OAD, there is limited evidence around how to effectively achieve this. Low physical capacity is one of the many factors shown to be associated with reduced physical activity in OAD [5]. The “can do, do do” is a concept developed by KOOLEN *et al.* [6] to understand if a person’s *ability* (physical capacity) to perform daily life activities contributes to their *participation* (physical activity). The concept categorises people into four quadrants based on measured physical capacity (preserved physical capacity=“can do”



versus low physical capacity="can't do") and participation in physical activity (physically active="do, do" versus physically inactive="don't do"), and may help to inform strategies to optimise physical activity levels. For example, people identified as "can't do, don't do" would likely benefit from physical activity interventions that target physical capacity, whereas those in the "can do, don't do" quadrant may require a different approach.

While the "can do, do do" concept has previously been explored in OAD, little is known about potential differences between different OAD groups. The existing "can do, do do" studies have also predominantly focused on the volume of physical activity participation (steps·day<sup>-1</sup>) rather than time spent in moderate to vigorous intensity physical activity (MVPA) [6–8]. Furthermore, there is increasing evidence to support the optimisation of other movement behaviours including light-intensity physical activity (LPA) and sedentary behaviour (*i.e.* by replacing with LPA) as part of OAD management and as a stepping stone to target MVPA [9]. However, the LPA and sedentary behaviour profiles of people in each of these "can do, do do" quadrants are currently unknown. This study aims to extend the application of the "can do, do do" concept in people with and without OAD, to identify if people allocated to each quadrant, based on physical capacity and physical activity defined by MVPA, differ by clinical and sociodemographic characteristics. Furthermore, we sought to determine if time spent in LPA and sedentary behaviour differed between quadrants in people with and without OAD. Specifically, this study aims to answer the following research questions:

- 1) What proportion of people with different OAD (bronchiectasis, severe asthma and COPD) are assigned to each quadrant of the "can do, do do" concept and how does this compare with controls?
- 2) Are there differences in the clinical and movement behaviour characteristics between people with different OAD in each of the "can do, do do" concept quadrants?

We hypothesised that:

- 1) The proportion of people with different OAD assigned to each quadrant of the "can do, do do" concept is different to people without OAD and the proportion of people with COPD assigned to each quadrant of the "can do, do do" concept' is different to people with bronchiectasis and severe asthma.
- 2a) Clinical outcomes of lung function, comorbidities, functional dyspnoea, anxiety and depression symptoms, and quality of life are different between the "can do, do do" concept quadrants in people with OAD.
- 2b) Time spent in LPA and sedentary behaviour is different between the "can do, do do" concept quadrants in people with OAD.

## Methods

### Study design

This is a secondary analysis of data pooled from three studies: 1) a cross-sectional study characterising people with severe asthma, bronchiectasis and controls [10] (ethics approval: 08/08/20/3.10); 2) a cross-sectional study characterising breathlessness in people with asthma (ethics approval: 2019/ETH12515); and (3) baseline data from a randomised controlled trial in people with COPD (ethics approval: 12/12/12/3.06). Ethics approval was granted for all studies by the Hunter New England Human Research Ethics Committee. All participants completed assessments across two visits scheduled approximately 2 weeks apart. Studies were conducted according to good clinical practice guidelines and all participants provided written informed consent.

### Setting

Visits were conducted at the Hunter Medical Research Institute (Newcastle, Australia) between March 2014 and July 2022. Participants were recruited from the research databases of the John Hunter Hospital's Department of Respiratory and Sleep Medicine and the Hunter Medical Research Institute, referred by their treating clinician/physician or identified *via* community advertisement.

### Participants

Adults ( $\geq 18$  years) with either bronchiectasis, severe asthma or COPD were included in the OAD groups. The control group were adults ( $\geq 18$  years) without a known respiratory condition and without objective evidence of respiratory disease. Participants with bronchiectasis were included if they had a primary doctor diagnosis of bronchiectasis confirmed by high-resolution chest computed tomography. Participants with severe asthma were included if they had evidence of asthma (airway hyperresponsiveness or variable airflow limitation), were on monoclonal antibody therapy or were on high-dose inhaled corticosteroids with a second controller according to the American Thoracic Society (ATS)/European Respiratory Society Severe Asthma Task Force [11] and remained uncontrolled. Participants with COPD were included if they had fixed airflow

limitation (<80% pred post-bronchodilator forced expired volume in one second (FEV<sub>1</sub>) and <0.7 forced expiratory ratio or physician-confirmed COPD in people with reduced forced vital capacity (FVC)). Participants were excluded from the analysis if physical activity or physical capacity were not measured during the two visits or if physical activity data were not considered valid, as further detailed below.

### Variables and measurements

A multidimensional assessment including demographic data, medical history and smoking history was completed as previously described [10]. Spirometry was performed prior to and 15 min following 400 µg of salbutamol to assess airflow limitation (Medgraphics, CPFS/D USB Spirometer, BreezeSuite v7.1-v8.6, MGC Diagnostics, Saint Paul, MN, USA). The 2012 Global Lung Index equations were used to calculate predicted values for FEV<sub>1</sub> and FVC.

To assess physical capacity, participants completed a single 6-min walk test (6MWT), according to ATS technical standards, with the exception of using a 25 m track [12]. The total distance was recorded and expressed in relation to Australian population normative reference data to obtain percentages of predicted values [13]. Participants were considered to have preserved physical capacity if their 6-min walk distance (6MWD) was ≥70% of predicted, and low physical capacity if their 6MWD was <70% of predicted [6, – 8, 14].

Physical activity and sedentary behaviour data were obtained using a tri-axial accelerometer (ActiGraph wGT3X-BT, ActiGraph, Pensacola, FL, USA). Accelerations at 30 Hz rate in epochs of 10 s were collected from the device. Participants were instructed to wear the accelerometer around their waist on their dominant hip for 14 consecutive days. The data were managed and analysed using the ActiLife 6.11.6 Data Analysis Software (ActiGraph, Pensacola, FL, USA). Physical activity data were considered valid with ≥10 h of wear-time per day for ≥4 days [15]. Nonwear and sleep time were removed from the analysis as defined by diary logs and visual examination of the activity data. The Freedson 1998 cut-points were used to categorise sedentary time (≤99 counts·min<sup>-1</sup>), LPA (100–1952 counts·min<sup>-1</sup>) and MVPA (≥1952 counts·min<sup>-1</sup>) [16]. Participants were categorised as being physically active if they participated in ≥150 min of MVPA per week or as physically inactive if they participated <150 min of MVPA per week. A week was considered a period of 7 days, with no specific criteria for weekdays or weekends. We calculated weekly MVPA minutes by dividing the total MVPA minutes during the wearing period by the number of days worn, then multiplying by seven.

The modified Medical Research Council dyspnoea scale was researcher-administered to assess the functional impact of dyspnoea [17]. Anxiety and depression symptoms were assessed using the self-assessment hospital anxiety and depression scale (HADS) [18]. Health-related quality of life was assessed using the participant-administered St. George's Respiratory Questionnaire [19]. The Charlson comorbidity index was used to assess comorbidity levels [20].

### Statistical methods

Descriptive summary statistics were used to characterise the sample. Normality assumptions for continuous data were checked with the Shapiro–Wilk test and distributional diagnostic plots. Differences between OAD (bronchiectasis, severe asthma and COPD) and control group characteristics were evaluated using one-way analysis of variance (ANOVA) for continuous parametric variables, the Kruskal–Wallis test for nonparametric variables or the chi-squared test for dichotomous variables.

The chi-squared test was used to assess differences in the proportion of people in each of the “can do, do do” quadrants for the OAD and control groups. ANOVA evaluated clinical and movement behaviour characteristic differences between quadrants within the OAD and control groups. *Post hoc* analysis with Bonferroni corrections were conducted as appropriate. *p*-values below 0.05 were considered statistically significant. All statistical analyses were conducted using SPSS version 28 (IBM, Armonk, NY, USA).

## Results

### Participant characteristics

A total of 281 participants were included. Participant characteristics are summarised in table 1. There were 223 participants in the OAD group (bronchiectasis (n=60), severe asthma (n=93), COPD (n=70)) and 58 controls. Demographic, clinical and movement behaviour characteristics were significantly different between the OAD groups (bronchiectasis, severe asthma and COPD) and the control group, except for the proportion of current smokers and sedentary minutes per day (table 1).

Compared with each OAD group, a greater proportion of the control group had preserved physical capacity (91% *versus* 37–63%) and were active (80% *versus* 14–45%). When comparing the OAD groups, a greater

TABLE 1 Participant characteristics

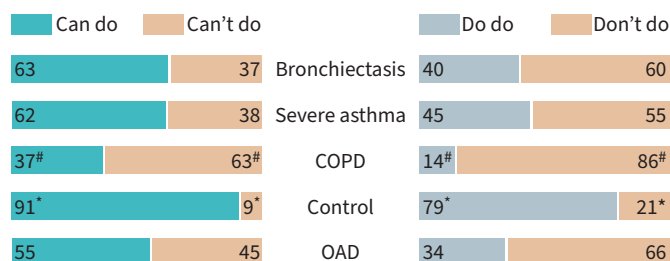
Characteristic	Bronchiectasis (n=60)	Severe asthma (n=93)	COPD (n=70)	Controls (n=58)	p-value	OAD (n=223)
<b>Demographic</b>						
Age (years)	68.5 (61.3–74.0)	63.3 (46.6–70.7)	70.7 (64.6–75.3)	56.1 (34.1–64.9)	<0.001	67.7 (59.0–72.6)
Females (n)	51 (85%)	55 (59%)	30 (43%)	32 (55%)	<0.001	136 (61%)
BMI (kg·m <sup>-2</sup> )	25.4±4.9	31.1±7.2	30.9±7.3	25.4±4.1	<0.001	29.5±7.1
CCI (score)	0 (0–3)	0 (0–3)	4 (3–5)	0 (0–0)	<0.001	0 (0–4)
Current smoker (n)	1 (2%)	5 (5%)	0 (0%)	0 (0%)	0.058	6 (3%)
Ex-smoker (n)	23 (38%)	40 (43%)	70 (100%)	14 (24%)	<0.001	133 (60%)
Pack-years (years)	2 (0–20)	3 (0–17)	45 (32–74)	0 (0–2)	<0.001	19 (1–43)
<b>Clinical</b>						
Post-BD FEV <sub>1</sub> (% pred)	79.8±23.4	76.1±20.1	58.4±16.8	97.1±13.7	<0.001	71.5±21.9
Post-BD FVC (% pred)	83.4±19.3	88.9±16.3	80.2±15.8	96.7±13.0	<0.001	84.8±17.3
Post-BD FEV <sub>1</sub> /FVC (ratio)	0.72±0.12	0.67±0.14	0.55±0.15	0.79±0.08	<0.001	0.64±0.15
6MWD (m)	458.6±111.2	466.3±104.3	376.9±123.4	613.1±79.6	<0.001	436.1±118.9
6MWD (% pred)	73.2±15.5	73.4±14.3	61.8±18.8	86.8±12.1	<0.001	69.7±16.9
mMRC (score)	1.1±0.9	1.9±1.3	1.9±1.1	0.2±0.4	<0.001	1.7±1.2
SGRQ (total score)	37.3±17.1	41.4±20.4	50.7±16.0		<0.001	43.3±18.9
HADS (total score)	9.5±6.1	11.0±6.3	11.4±7.1	5.2±4.3	<0.001	10.7±6.5
HADS anxiety (sub score)	5.8±3.8	6.4±3.9	5.9±4.1	3.8±3.0	<0.001	6.1±3.9
HADS depression (sub score)	3.7±3.1	4.6±3.2	5.6±3.7	1.3±1.7	<0.001	4.7±3.4
<b>Movement behaviours</b>						
Sedentary time (min·day <sup>-1</sup> )	702.5±110.0	720.0±225.5	734.6±118	681.8±87.3	0.255	719.9±169.6
LPA (min·day <sup>-1</sup> )	162.0 (65.1–306.3)	167.3 (134.7–208.9)	126.5 (94.2–166.3)	162.6 (127.9–191.3)	<0.001	150.1 (104.2–208.7)
MVPA (min·day <sup>-1</sup> )	15.2 (6.2–28.3)	19.5 (12.2–33.2)	7.5 (2.4–14.8)	38.8 (26.4–63.5)	<0.001	14.4 (6.4–27.4)
MVPA (min·week <sup>-1</sup> )	106.1 (43.2–198.3)	136.5 (85.1–232.4)	52.5 (17.0–103.3)	271.6 (184.6–444.7)	<0.001	100.8 (44.8–191.8)

Data are reported as mean±sd, median (interquartile range) or number (proportion). 6MWD: 6-min walk distance; BD: bronchodilator; BMI: body mass index; CCI: Charlson comorbidity index; FEV<sub>1</sub>: forced expiratory volume in 1 s; FVC: forced vital capacity; HADS: hospital anxiety and depression scale; LPA: light-intensity physical activity; mMRC: modified Medical Research Council; MVPA: moderate to vigorous physical activity OAD: obstructive airway disease; SGRQ: St George’s Respiratory Questionnaire.

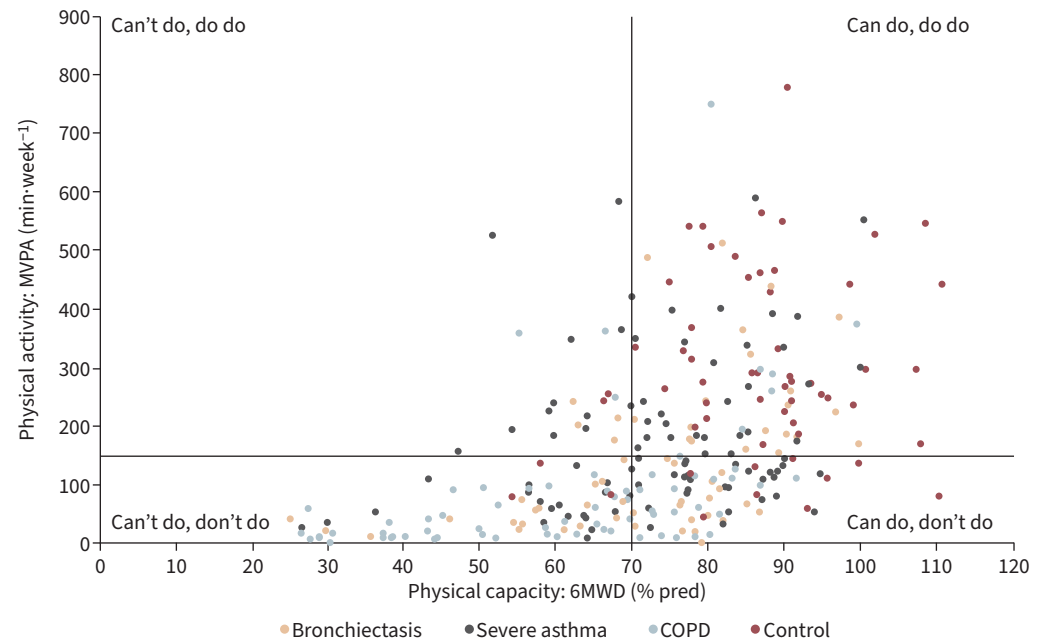
proportion of the COPD group had low physical capacity and were inactive compared with the bronchiectasis and severe asthma groups, who were similar (figure 1).

**Quadrant distribution per group**

All participants were categorised into one of the four “can do, do do” quadrants. The distribution of participants per quadrant is shown in figure 2 and table 2. The control group had a greater proportion of people in the “can do, do do” quadrant compared with the OAD groups (figure 3). The COPD group had a lower proportion of people in the “can do, do do” quadrant compared with the bronchiectasis and severe asthma groups (p<0.05) (figure 3).



**FIGURE 1** The proportion of participants with or without preserved physical capacity (“can do” versus “can’t do”) and participants that are physically active or inactive (“do do” versus “don’t do”). \*: p<0.05 compared to bronchiectasis, severe asthma and COPD; #: p<0.05 compared to bronchiectasis and severe asthma. OAD: obstructive airway disease.



**FIGURE 2** Distribution of all participants according to their physical activity levels and physical capacity. MVPA: moderate to vigorous physical activity; 6MWD: 6-min walk distance.

#### Key clinical characteristics of each quadrant, per group

Differences between the clinical characteristics per quadrant of people with OAD or controls are summarised in table 2. There were no differences in clinical characteristics between the quadrants for the control group. For the OAD groups, compared with the “can do, do do” quadrant, the “can’t do, don’t do” quadrant generally included people with more comorbidities (OAD combined and bronchiectasis), reduced FEV<sub>1</sub> % pred (OAD combined, bronchiectasis and COPD), impaired quality of life (OAD combined, bronchiectasis and severe asthma) and limitation from dyspnoea (OAD combined, bronchiectasis, severe asthma and COPD) ( $p < 0.05$ ) (figure 4). The proportion of females, body mass index and HADS total or HADS anxiety were not significantly different between the quadrants for any of the OAD groups.

#### Sedentary behaviour and LPA per quadrant for each group

Sedentary time and LPA differences in each group, and per quadrant, are summarised in table 2. For the control group, sedentary time and LPA were not different between quadrants. For the OAD combined group and the bronchiectasis and COPD groups, participants in the “can’t do, don’t do” quadrant spent significantly more time in sedentary behaviour compared with the “can do, do do” quadrant ( $p < 0.05$ ) (figure 5). People in the “can’t do, don’t do” and the “can do, don’t do” quadrants also spent less time in LPA compared with the “can do, do do” quadrant, for the OAD combined group and within each OAD group ( $p < 0.05$ ) (figure 5).

#### Discussion

We have applied the “can do, do do” quadrant concept to people with and without different OADs and explored the differences in clinical characteristics and movement behaviours according to quadrant allocation. As expected, a higher proportion of people living with different OAD had low physical capacity and reduced physical activity participation compared with people without OAD. Low physical capacity cooccurred with physical inactivity (can’t do, don’t do) for 30% of people with bronchiectasis, 25% of people with severe asthma and 59% of people with COPD. For people within this quadrant, they had more severe airflow limitation, more comorbidities, reduced health-related quality of life and greater limitations from dyspnoea, compared with people in the “can do, do do” quadrant. Movement behaviour measures were different between quadrants for the OAD groups only. Time spent participating in LPA was reduced in people in the “don’t do” compared with the “do, do” quadrants. That is, people with OAD who had reduced MVPA also had low LPA. Further, people who were categorised as “can’t do, don’t do” spent more time sedentary compared with people who were categorised as “can do, do do”.

TABLE 2 Participant characteristics per “can do, do do” quadrant and disease group

Characteristic	Can do, do do	Can do, don't do	Can't do, do do	Can't do, don't do	p-value
<b>Combined OAD</b>					
Total (n)	57 (26%)	65 (29%)	19 (9%)	82 (37%)	
Age (years)	63.0 (55.2–69.2)	69.0 (64.2–72.2)*	63.2 (51.0–70.0)	70.7 (61.9–75.4)* <sup>¶</sup>	<0.001
Female (n)	36 (63%)	48 (74%)	11 (58%)	41 (50%) <sup>#</sup>	0.031
BMI (kg·m <sup>-2</sup> )	27.6±5.1	29.6±8.0	30.8±8.2	30.4±7.3	0.146
CCI (score)	0.9±1.4	2.2±2.3*	1.4±1.7	3.3±2.4* <sup>#¶</sup>	<0.001
Post-BD FEV <sub>1</sub> (% pred)	82.5±18.8	75.2±18.1	76.5±22.0	60.1±21.4* <sup>#¶</sup>	<0.001
mMRC (score)	1.0±0.9	1.5±1.1	1.8±1.3	2.3±1.2* <sup>#</sup>	<0.001
HADS (total score)	9 (6–12)	7 (5–14)	9 (5–14)	11 (7–16)	0.443
HADS anxiety (sub score)	5.9±3.6	5.4±3.9	6.0±3.3	6.5±4.2	0.446
HADS depression (sub score)	3.3±2.3	4.5±3.4	4.4±4.1	5.8±3.7*	0.002
SGRQ (total score)	30.2±14.9	42.1±17.9*	43.3±21.6*	52.6±16.6* <sup>#</sup>	<0.001
Sedentary time (min·day <sup>-1</sup> )	692.9±167.2	713.9±153.3	665.3±205.4	762.5±166.7*	0.014
LPA (min·day <sup>-1</sup> )	250.2 (181.0–297.5)	138.3 (105.4–177.1)* <sup>¶</sup>	225.9 (172.8–277.4)	112.9 (82.7–145.0)* <sup>¶</sup>	<0.001
MVPA (min·day <sup>-1</sup> )	34.8 (26.4–51.3)	13.1 (7.7–16.9)* <sup>¶</sup>	33.8 (28.2–51.5)	6.1 (3.0–11.6)* <sup>¶</sup>	<0.001
<b>Healthy controls</b>					
Total (n)	44 (76%)	9 (16%)	2 (3%)	3 (5%)	
Age (years)	46.9±16.4	62.3±17.4	45.9±14.1	52.8±24.8	0.103
Female (n)	27 (61%)	3 (33%)	1 (50%)	1 (33%)	0.389
BMI (kg·m <sup>-2</sup> )	25.0±3.6	26.1±4.9	26.3±6.6	27.4±6.4	0.413
CCI (score)	0.2±0.7	0.7±1.9	0.0±0.0	0.0±0.0	0.472
Post-BD FEV <sub>1</sub> (% pred)	97.3±14.4	96.4±14.6	101.8±0.0	93.2±0.7	0.924
mMRC (score)	0.1±0.4	0.3±0.5	0.0±0.0	0.0±0.0	0.375
HADS (total score)	5.3±4.3	5.7±1.4	5.5±0.8	1.7±0.6	0.548
HADS anxiety (sub score)	4.0±3.1	3.9±3.3	5.0±1.4	1.0±0.0	0.391
HADS depression (sub score)	1.3±1.7	1.8±2.1	0.5±0.7	0.7±0.6	0.688
Sedentary time (min·day <sup>-1</sup> )	668.1±78.5	731.8±115.8	672.2±114.4	738.8±64.7	0.148
LPA (min·day <sup>-1</sup> )	169.4±46.9	140.6±27.2	205.9±138.9	137.7±26.2	0.168
MVPA (min·day <sup>-1</sup> )	50.6±19.7	14.7±5.1*	35.9±1.1	14.5±4.6*	<0.001
<b>Bronchiectasis</b>					
Total (n)	20 (33%)	18 (30%)	4 (7%)	18 (30%)	
Age (years)	61.6±11.9	66.8±14.4	66.3±10.3	67.6±13.9	0.503
Female (n)	16 (80%)	18 (100%)	4 (100%)	13 (72%)	0.087
BMI (kg·m <sup>-2</sup> )	25.3±4.0	25.4±6.3	26.2±8.0	25.6±4.0	0.980
CCI (score)	0.5±1.0	0.9±1.7	1.0±2.0	2.5±2.3*	0.005
Post-BD FEV <sub>1</sub> (% pred)	94.4±15.1	79.2±18.2	88.7±23.7	60.7±24.8*	<0.001
mMRC (score)	0.7±0.7	1.1±0.8	1.0±0.8	1.7±1.1*	0.011
HADS (total score)	7.9±5.6	9.2±6.6	8.5±1.3	11.9±6.5	0.232
HADS anxiety (sub score)	4.6±3.5	5.7±4.4	5.3±1.3	6.5±3.4	0.757
HADS depression (sub score)	2.3±2.0	3.4±3.0	3.3±1.8	5.2±4.1	0.053
SGRQ (total score)	27.9±15.7	33.6±16.8	38.5±9.5	50.3±14.2* <sup>#</sup>	<0.001
Sedentary time (min·day <sup>-1</sup> )	661.8±83.0	691.0±135.4	671.9±71.5	766.1±91.9*	0.022
LPA (min·day <sup>-1</sup> )	374.7±165.8	98.7±60.4* <sup>¶</sup>	411.0±58.0	90.6±67.1* <sup>¶</sup>	<0.001
MVPA (min·day <sup>-1</sup> )	38.0±16.3	9.7±5.9* <sup>¶</sup>	30.1±3.9	8.1±5.0* <sup>¶</sup>	<0.001
<b>Severe asthma</b>					
Total (n)	30 (32%)	28 (30%)	12 (13%)	23 (25%)	
Age (years)	57.6±13.4	60.4±14.5	55.4±15.8	60.0±16.1	0.732
Female (n)	18 (60%)	20 (71%)	7 (58%)	10 (44%)	0.251
BMI (kg·m <sup>-2</sup> )	29.1±6.1	32.3±8.7	32.3±7.1	31.7±6.4	0.312
CCI (score)	0.7±1.3	1.6±2.2	1.2±1.7	1.7±2.1	0.177
Post-BD FEV <sub>1</sub> (% pred)	76.7±19.0	78.3±20.6	78.0±19.5	71.7±21.7	0.675
mMRC (score)	1.4±1.2	1.8±1.1	2.3±1.4	2.7±1.2* <sup>#</sup>	<0.001
HADS (total score)	11.1±4.7	10.6±6.4	9.3±7.6	12.4±7.4	0.579
HADS anxiety (sub score)	7.0±3.3	5.8±3.9	5.4±3.7	6.9±4.6	0.480
HADS depression (sub score)	4.1±2.1	4.8±3.3	3.9±4.3	5.4±3.5	0.385
SGRQ (total score)	29.5±14.0	45.7±18.7*	40.9±25.5	52.0±19.5*	<0.001
Sedentary time (min·day <sup>-1</sup> )	710.4±222.3	728.5±198.5	645.0±251.3	761.5±250.2	0.539
LPA (min·day <sup>-1</sup> )	207.7±61.8	155.8±34.4* <sup>¶</sup>	212.7±39.7	141.3±37.1* <sup>¶</sup>	<0.001
MVPA (min·day <sup>-1</sup> )	40.8±16.6	14.7±4.7* <sup>¶</sup>	41.6±19.9	9.9±4.7* <sup>¶</sup>	<0.001

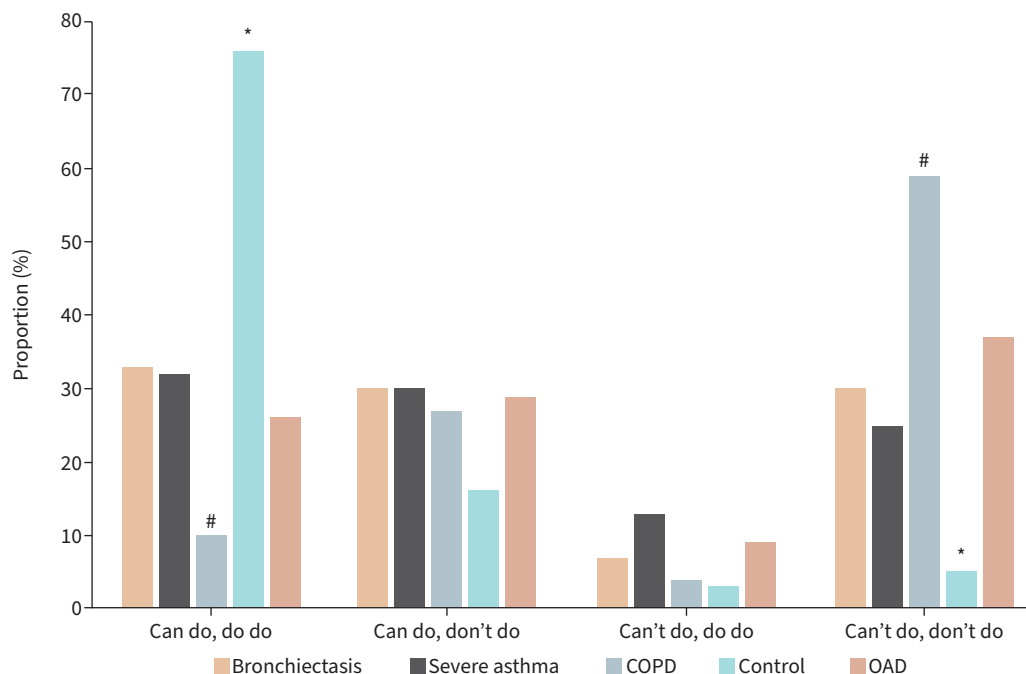
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**TABLE 2** Continued

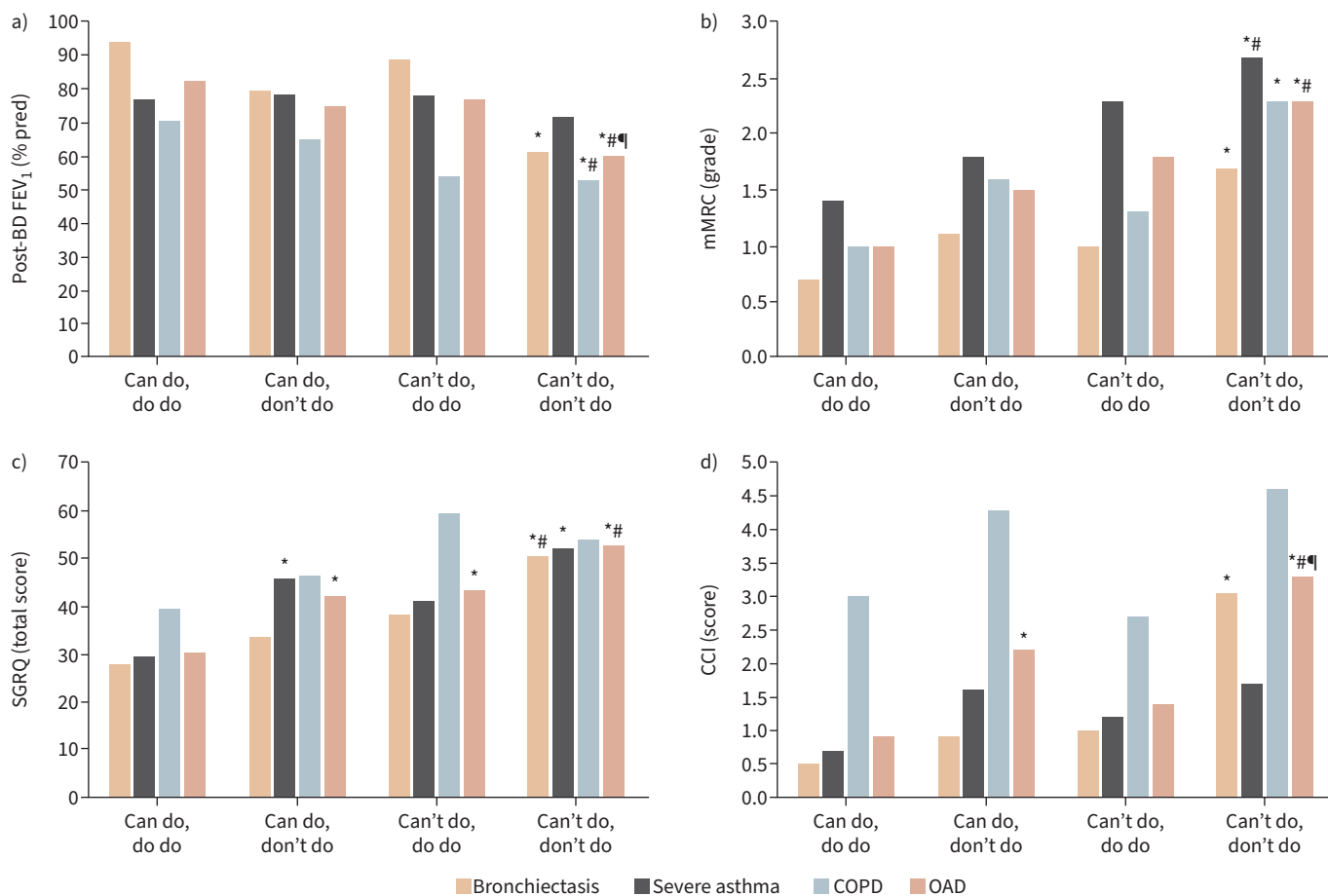
Characteristic	Can do, do do	Can do, don't do	Can't do, do do	Can't do, don't do	p-value
<b>COPD</b>					
Total (n)	7 (10%)	19 (27%)	3 (4%)	41 (59%)	
Age (years)	63.5±5.7	70.7±5.8	59.2±6.7	71.3±7.6* <sup>¶</sup>	0.003
Female (n)	2 (29%)	10 (53%)	0 (0%)	18 (44%)	0.309
BMI (kg·m <sup>-2</sup> )	29.6±2.4	29.4±6.1	30.8±13.4	31.6±8.1	0.678
CCI (score)	3.0±1.2	4.3±1.4	2.7±0.6	4.6±1.9	0.043 <sup>†</sup>
Post-BD FEV <sub>1</sub> (% pred)	70.7±16.2	65.4±12.2	53.9±18.4	53.1±16.9* <sup>¶</sup>	0.008
mMRC (score)	1.0±0.6	1.6±1.2	1.3±0.6	2.3±1.0*	0.006
HADS (total score)	8.4±7.4	10.1±6.8	17.0±5.0	12.0±7.3	0.246
HADS anxiety (sub score)	5.0±4.2	4.8±3.6	9.0±1.0	6.2±4.3	0.265
HADS depression (sub score)	3.4±3.4	5.3±3.9	8.0±4.6	6.1±3.7	0.245
SGRQ (total score)	39.3±14.9	46.4±15.9	59.3±3.2	53.9±15.9	0.051
Sedentary time (min·day <sup>-1</sup> )	638.9±77.2	700.8±71.2	737.4±120.0	766.3±130.2*	0.024
LPA (min·day <sup>-1</sup> )	204.6±64.9	147.3±41.4*	105.6±15.9*	119.6±47.9*	<0.001
MVPA (min·day <sup>-1</sup> )	47.5±28.4	10.0±6.0* <sup>¶</sup>	46.5±9.3	5.7±4.7* <sup>¶</sup>	<0.001

Data are reported as mean±SD, median (interquartile range) or number (proportion). \*: p<0.05 compared to “can do, do do”. #: p<0.05 compared to “can do, don't do”. ¶: p<0.05 compared to “can't do, do do”. \*: No longer significant *post hoc*. BD: bronchodilator; BMI: body mass index; CCI: Charlson comorbidity index; FEV<sub>1</sub>: forced expiratory volume in 1 s; HADS: hospital anxiety and depression scale; LPA: light-intensity physical activity; mMRC: modified Medical Research Council; MVPA: moderate to vigorous physical activity; OAD: obstructive airway disease; SGRQ: St George's Respiratory Questionnaire.

This study highlights the interrelationship between physical capacity and physical activity in people with OAD. Consistent with previous studies [7, 8, 14, 21], only 4–12% of the OAD population participated in the recommended amounts of physical activity when their physical capacity was impaired. That is, the “can't do, do do” quadrant was the least representative quadrant across all groups. Conversely, the “can't do, don't do” quadrant comprised approximately one third of the people with bronchiectasis or severe asthma, which is comparable to a previous study in an asthma population [8]. Alarming, more than 50%



**FIGURE 3** Proportion of participants per “can do, do do” quadrant according to participant population. \*: p<0.05 compared to bronchiectasis, severe asthma and COPD. #: p<0.05 compared to bronchiectasis and severe asthma. OAD: obstructive airway disease.

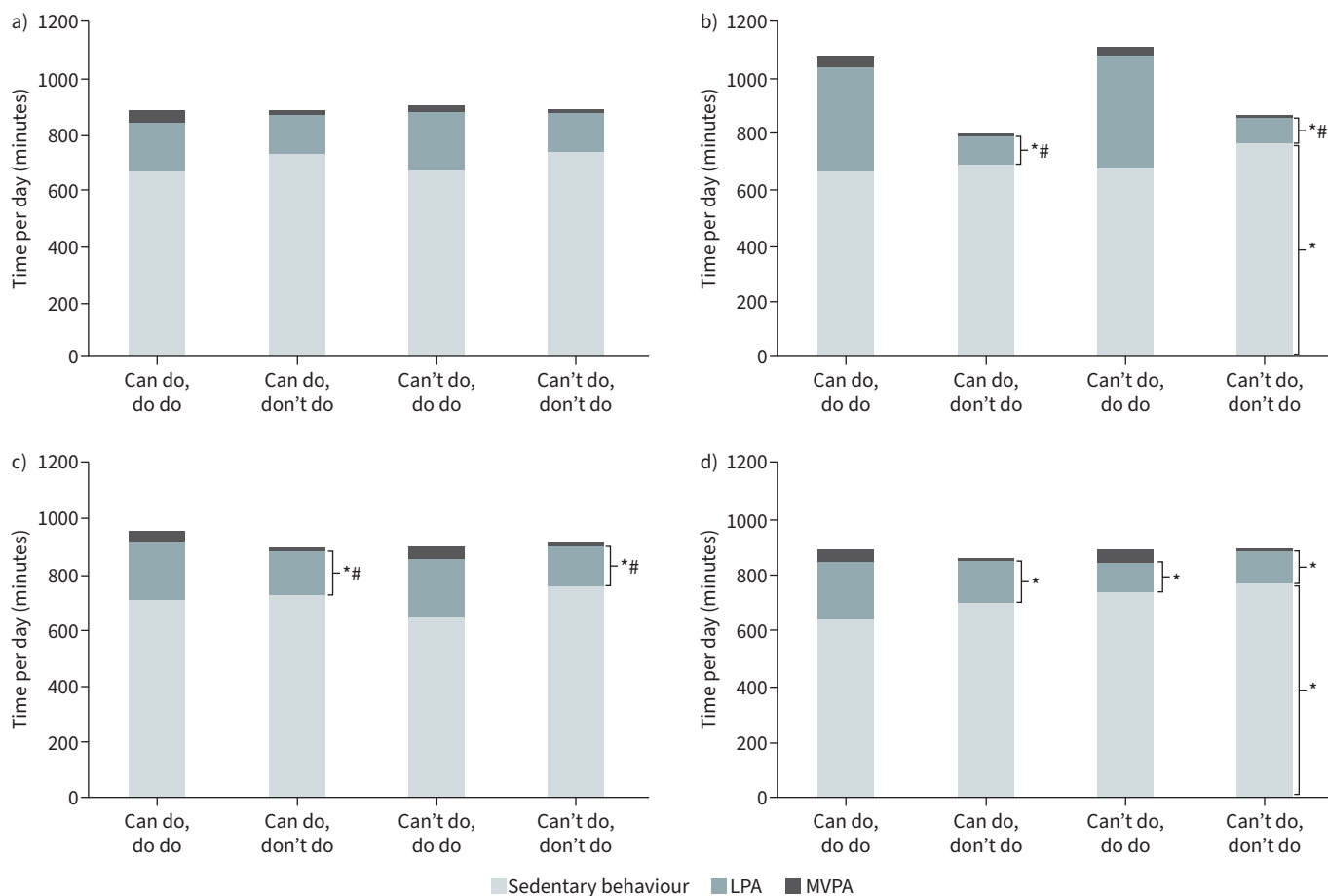


**FIGURE 4** Clinical characteristics per “can do, do do” quadrant per obstructive airway disease (OAD) group. **a)** Post-bronchodilator (BD) forced expiratory volume in 1 s (FEV<sub>1</sub>) % predicted. **b)** Modified Medical Research Council (mMRC) grade. **c)** St. George’s Respiratory Questionnaire (SGRQ) total score. **d)** Charlson comorbidity index (CCI) score. \*: p<0.05 compared to “can do, do do”. #: p<0.05 compared to “can do, don’t do”; #: p<0.05 compared to “can’t do, do do”.

of people with COPD were allocated to this quadrant, which is a higher proportion than previous studies [6, 7, 14, 21]. To assess physical activity, most previous studies have used steps per day [6–8, 14, 21]. However, using a measure of physical activity intensity (MVPA) instead of volume (steps per day) has been shown to be stronger at discriminating between quadrants in a recent “can do, do do” study in community-dwelling older adults [22]. Therefore, it is possible that the discrepancy between our COPD population and previous studies is due to the physical activity measure we used MVPA to allocate people to “do, do” versus “don’t do”. Global, international, and national guidelines recommend that people engage in a certain amount of MVPA to maintain or improve health and wellbeing outcomes [23, 24]. It is therefore important to identify people with OAD who are inactive (*i.e.* “can’t do”) in line with these guidelines. For people with OAD who are inactive and have impaired physical capacity, aerobic and resistance training has been shown to effectively increase physical capacity and, therefore, should be recommended to people who “can’t do” to build their capability to participate in MVPA [25–28]. Additionally, using absolute cut-offs, such as >3.0 metabolic equivalents of task for MVPA is also likely contributing to people with OAD not meeting physical activity guidelines recommendations. This method may not appropriately reflect the moderate effort required in this population with lung disease, as it does not take into consideration functional capacity. As such disease-specific physical activity guidelines are needed for people with OAD.

Our analysis identified that people with bronchiectasis, severe asthma and COPD who “can’t do, and don’t do” have more severe airflow limitation, more comorbidities and are limited by dyspnoea. Whilst this finding is novel for severe asthma and bronchiectasis it is consistent with previous COPD literature [6, 7, 14, 21]. It is expected that participants who have impaired physical capacity and are not physically active have worse clinical outcomes. The presence of clinical outcomes such as dyspnoea and comorbidities may





**FIGURE 5** Amount of time spent in different movement behaviours per “can do, do do” quadrant per group. a) Control. b) Bronchiectasis. c) Severe asthma. d) COPD. \*:  $p < 0.05$  compared to “can do, do do”. #:  $p < 0.05$  compared to “can't do, do do”. LPA: light-intensity physical activity; MVPA: moderate to vigorous intensity physical activity.

be contributing to inactivity as part of a vicious cycle of deconditioning [29]. People who “can't do, don't do” may require a different approach that addresses other treatable traits that are impacting their ability to be active and maintain physical capacity. Treatable traits is a precision-medicine model of care that involves identifying traits using a multidimensional assessment in an individual and creating a personalised management strategy that targets these traits [10]. This approach to patient care has been shown to be effective in people with OAD [10, 30] and treatable traits has been proposed to optimise pulmonary rehabilitation outcomes. Our study suggests that people who “can't do, don't do” may benefit from pulmonary rehabilitation most, where additional traits can be targeted to improve physical capacity and physical inactivity [31].

A novel aspect of this study is reporting and comparing LPA and sedentary time in each quadrant across each group. There is an increasing amount of evidence to support the health benefits of reducing time spent in prolonged sedentary behaviour, independent of time spent in MVPA [32]. In the general population, prolonged sedentary behaviour has shown to be associated with increased risk of all-cause mortality, cardiovascular disease and diabetes [33–35]. Emerging evidence in OAD also indicates that sedentary behaviour is associated with exacerbations, impaired health related quality of life and reduced exercise capacity [36–39]. In this study, time spent in sedentary behaviour per day was high across all quadrants in all OAD groups, the lowest amount being 10 h and 36 min (“can do, do do” in COPD). However, people in the “can't do, don't do” quadrant spent more time in sedentary behaviour compared with the other quadrants. People in the “don't do” quadrants also spent less time in LPA compared with those in the “do, do” quadrants, across the OAD groups. For people who are inactive, and particularly for those who have impaired physical capacity, re-allocation of time from sedentary to LPA may be an important strategy to improve health outcomes [9]. This is likely a more achievable step for people with

OAD who “don’t do” but perhaps specifically for people who “can’t do, don’t do”, as the amount of physical capacity needed to participate in LPA is less than MVPA.

Importantly, preserved physical capacity did not fully explain why some people with OAD do not engage in enough physical activity, replicating findings from previous studies [6–8, 14, 21]. Approximately one third of participants with bronchiectasis, severe asthma or COPD do not meet physical activity recommendations, despite having preserved physical capacity. Therefore, even if physical capacity is improved or retained, people with OAD may not participate in physical activity for other reasons. This may relate to the level of motivation, knowledge, skills and confidence that is required for people to adopt effective strategies, also known as patient activation [40]. Psychosocial barriers are also likely, including fear of symptom exacerbation, lack of self-efficacy and support to participate in physical activity [41–43]. In our study, depression symptom scores were highest in the “can’t do, don’t do” quadrant which further supports the importance of considering psychological symptoms when addressing physical inactivity in people with OAD. Implementing behaviour change strategies such as goal setting and behaviour feedback from wearable activity monitors and providing education and support may enable people who “can do, don’t do” to overcome some of these barriers and increase physical activity participation [44, 45]. For people with OAD who “can’t do, don’t do”, combining strategies that improve their physical capacity and targets behaviour change may be needed [27, 46, 47].

As a strength, our study included people with different airway diseases including bronchiectasis, severe asthma and COPD, in addition to a control group. This enabled us to compare quadrant allocations between different OAD groups. Moreover, the “can do, do do” concept has not previously been explored in people with severe asthma or bronchiectasis. This study, therefore, provides novel insights for the development of movement behaviour interventions in these patient groups. Another strength of our study was the use of a tri-axial accelerometer to measure LPA and sedentary time, in addition to MVPA. Time spent in sedentary behaviour or LPA has not been reported in previous “can do, do do” studies and our findings identify the importance of targeting different types of movement behaviour. We acknowledge that the 6MWT is not an incremental exercise test and therefore may not reflect maximal exercise capacity; however, the 6MWT was conducted according to technical standard which can elicit a peak oxygen uptake [12]. We also acknowledge that our method of calculating minutes of MVPA per week (average minutes of MVPA per day of available wear time extrapolated to estimate minutes of MVPA per day for 7 days) does not consider that some participants data were not balanced across weekdays and weekend days. Given that this method does not take into consideration that some participants may vary their time use substantially across the week (*e.g.* only active on weekend days), this may have resulted in under- or over-estimation of participants true MVPA per week. However, for participants in our study, there were no substantial differences in MVPA participation across different days of the week (*e.g.* 23 min per day on Monday *versus* 24 min·day<sup>-1</sup> on Saturday). Our data are cross-sectional and the future impact of allocation to each quadrant cannot be derived.

### Conclusion

This study highlights that many people with OAD, particularly COPD, may not be meeting physical activity recommendations because they do not have the physical capacity to participate in MVPA. Greater disease severity (airflow limitation), breathlessness and comorbidity were associated with the “can’t do, don’t do” quadrant. Targeting these treatable traits is likely important when designing physical activity interventions in people with OAD, particularly for people who have impaired physical capacity and physical activity. It is also important to consider the potential benefits of addressing LPA and sedentary behaviour as there were suboptimal levels of these movement behaviours across different quadrants. Compared with increasing time spent in MVPA, re-allocating time spent sedentary to LPA may be a more feasible approach, particularly for the 45% of people with OAD who have impaired physical capacity. Interpretation of our findings have informed the different approaches needed for people with OAD to improve their physical activity when allocated to the different quadrants of the “can do, do do” concept. Future research is needed to investigate if tailoring intervention approaches based on quadrants allocation is effective in people with OAD.

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## References

- 1 Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Prevention, Diagnosis and Management of COPD. Date last accessed: 22 May 2023. Date last updated: 2023. <https://goldcopd.org/2023-gold-report-2/>
- 2 Chang AB, Bell SC, Byrnes CA, *et al.* Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand. *Respirology* 2023; 28: 339–349.
- 3 Global Initiative for Asthma. 2023 GINA report, global strategy for asthma management and prevention. Date last accessed: 1 June 2023. Date last updated: 10 July 2023. <https://ginasthma.org/2023-gina-main-report/>
- 4 Cordova-Rivera L, Gibson PG, Gardiner PA, *et al.* Physical activity associates with disease characteristics of severe asthma, bronchiectasis and COPD. *Respirology* 2019; 24: 352–360.
- 5 Bauman AE, Reis RS, Sallis JF, *et al.* Correlates of physical activity: why are some people physically active and others not? *Lancet* 2012; 380: 258–271.
- 6 Koolen EH, van Hees HW, van Lummel RC, *et al.* “Can do” versus “do do”: a novel concept to better understand physical functioning in patients with chronic obstructive pulmonary disease. *J Clin Med* 2019; 8: 20190311.
- 7 Carl J, Schultz K, Janssens T, *et al.* The “can do, do do” concept in individuals with chronic obstructive pulmonary disease: an exploration of psychological mechanisms. *Respir Res* 2021; 22: 260.
- 8 Janssen SMJ, Spruit MA, Antons JC, *et al.* “Can do” versus “do do” in patients with asthma at first referral to a pulmonologist. *J Allergy Clin Immunol Pract* 2021; 9: 1278–1284.
- 9 Dogra S, Copeland JL, Altenburg TM, *et al.* Start with reducing sedentary behavior: a stepwise approach to physical activity counseling in clinical practice. *Patient Educ Couns* 2022; 102: 1353–1361.
- 10 McDonald VM, Clark VL, Cordova-Rivera L, *et al.* Targeting treatable traits in severe asthma: a randomised controlled trial. *Eur Respir J* 2020; 55: 1901509.
- 11 Chung KF, Wenzel SE, Brozek JL, *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–373.
- 12 Holland AE, Spruit MA, Troosters T, *et al.* An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014; 44: 1428–1446.
- 13 Jenkins S, Cecins N, Camarri B, *et al.* Regression equations to predict 6-minute walk distance in middle-aged and elderly adults. *Physiother Theory Pract* 2009; 25: 516–522.
- 14 Sievi NA, Brack T, Brutsche MH, *et al.* “Can do, don’t do” are not the lazy ones: a longitudinal study on physical functioning in patients with COPD. *Respir Res* 2020; 21: 27.
- 15 Matthews CE, Hagströmer M, Pober DM, *et al.* Best practices for using physical activity monitors in population-based research. *Med Sci Sports Exerc* 2012; 44: S68–S76.
- 16 Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc* 1998; 30: 777–781.
- 17 Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988; 93: 580–586.
- 18 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
- 19 Jones PW, Quirk FH, Baveystock CM, *et al.* A self-complete measure of health status for chronic airflow limitation. The St. George’s Respiratory Questionnaire. *Am Rev Respir Dis* 1992; 145: 1321–1327.
- 20 Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
- 21 Vaes AW, Spruit MA, Koolen EH, *et al.* “Can do, do do” quadrants and 6-year all-cause mortality in patients with COPD. *Chest* 2022; 161: 1494–1504.
- 22 Adams M, Carrascosa L, Jansen C-P, *et al.* “Can do” vs. “do do” in older adults: a cross-sectional analysis of sensor-derived physical activity patterns. *Sensors* 2023; 23: 1879.
- 23 Australian Government. Australia’s physical activity and sedentary behaviour guidelines for adults. Date last accessed: 14 January 2019. Date last updated: 10 May 2021. [www.health.gov.au/health-topics/physical-activity-and-exercise/physical-activity-and-exercise-guidelines-for-all-australians/for-adults-18-to-64-years](http://www.health.gov.au/health-topics/physical-activity-and-exercise/physical-activity-and-exercise-guidelines-for-all-australians/for-adults-18-to-64-years)

- 24 World Health Organization. WHO Guidelines on Physical Activity and Sedentary Behaviour. Geneva, World Health Organization, 2020.
- 25 Carson KV, Chandratilleke MG, Picot J, *et al.* Physical training for asthma. *Cochrane Database Syst Rev* 2013; 9: CD001116.
- 26 Lee AL, Gordon CS, Osadnik CR. Exercise training for bronchiectasis. *Cochrane Database Syst Rev* 2018; 4: CD013110.
- 27 McCarthy B, Casey D, Devane D, *et al.* Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015; 2015: Cd003793.
- 28 Ward TJC, Plumpre CD, Dolmage TE, *et al.* Change in  $V'_{O_2}$  peak in response to aerobic exercise training and the relationship with exercise prescription in people with COPD: a systematic review and meta-analysis. *Chest* 2020; 158: 131–144.
- 29 Maria AR, Gerben Ter R, Anne-Elie C, *et al.* The dyspnoea-inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur Respir J* 2018; 52: 1800079.
- 30 McDonald VM, Higgins I, Wood LG, *et al.* Multidimensional assessment and tailored interventions for COPD: respiratory utopia or common sense? *Thorax* 2013; 68: 691.
- 31 Holland AE, Wageck B, Hoffman M, *et al.* Does pulmonary rehabilitation address treatable traits? A systematic review. *Eur Respir Rev* 2022; 31: 220042.
- 32 Owen N, Healy GN, Matthews CE, *et al.* Too much sitting: the population health science of sedentary behavior. *Exerc Sport Sci Rev* 2010; 38: 105–113.
- 33 Bellettiere J, Winkler EAH, Chastin SFM, *et al.* Associations of sitting accumulation patterns with cardio-metabolic risk biomarkers in Australian adults. *PLoS One* 2017; 12: e0180119.
- 34 Biswas A, Oh PI, Faulkner GE, *et al.* Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med* 2015; 162: 123–132.
- 35 Edwardson CL, Gorely T, Davies MJ, *et al.* Association of sedentary behaviour with metabolic syndrome: a meta-analysis. *PLoS One* 2012; 7: e34916.
- 36 McNamara RJ, McKeough ZJ, McKenzie DK, *et al.* Physical comorbidities affect physical activity in chronic obstructive pulmonary disease: a prospective cohort study. *Respirology* 2014; 19: 866–872.
- 37 Cordova-Rivera L, Gardiner PA, Gibson PG, *et al.* Sedentary time in people with obstructive airway diseases. *Respir Med* 2021; 181: 106367.
- 38 Dogra S, Good J, Buman MP, *et al.* Physical activity and sedentary time are related to clinically relevant health outcomes among adults with obstructive lung disease. *BMC Pulm Med* 2018; 18: 98.
- 39 Alcaraz-Serrano V, Gimeno-Santos E, Scioscia G, *et al.* Association between physical activity and risk of hospitalisation in bronchiectasis. *Eur Respir J* 2020; 55: 1902138.
- 40 Peters JB, Antons JC, Koolen EH, *et al.* Patient activation is a treatable trait in patients with chronic airway diseases: an observational study. *Front Psychol* 2022; 13: 947402.
- 41 Mancuso CA, Sayles W, Robbins L, *et al.* Barriers and facilitators to healthy physical activity in asthma patients. *J Asthma* 2006; 43: 137–143.
- 42 Papp ME, Berg C, Lindfors P, *et al.* Experiences of physical activity and exercise among women with obstructive pulmonary disease. *Physiother Theory Pract* 2023; 39: 1681–1691.
- 43 Royle H, Kelly C. “The likes of me running and walking? No chance”: exploring the perceptions of adult patients with bronchiectasis towards exercise. *Chronic Illn* 2023; 19: 157–171.
- 44 Reilly C, Sails J, Stavropoulos-Kalinoglou A, *et al.* Physical activity promotion interventions in chronic airways disease: a systematic review and meta-analysis. *Eur Respir Rev* 2023; 32: 220109.
- 45 Tyson L, Hardeman W, Marquette M, *et al.* A systematic review of the characteristics of interventions that promote physical activity in adults with asthma. *J Health Psychol* 2022; 27: 2777–2796.
- 46 Lee AL, Hill CJ, McDonald CF, *et al.* Pulmonary rehabilitation in individuals with non-cystic fibrosis bronchiectasis: a systematic review. *Arch Phys Med Rehabil* 2017; 98: 774–782.
- 47 Osadnik CR, Gleeson C, McDonald VM, *et al.* Pulmonary rehabilitation versus usual care for adults with asthma. *Cochrane Database Syst Rev* 2022; 8: CD013485.