EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Original article

Association between physical activity and risk of hospitalisation in bronchiectasis

V. Alcaraz-Serrano, E. Gimeno-Santos, G. Scioscia, A. Gabarrús, A. Navarro, B. Herrero-Cortina, R. Amaro, L. Fernández-Barat, A. Torres

Please cite this article as: Alcaraz-Serrano V, Gimeno-Santos E, Scioscia G, *et al*. Association between physical activity and risk of hospitalisation in bronchiectasis. *Eur Respir J* 2020; in press (https://doi.org/10.1183/13993003.02138-2019).

ORIGINAL ARTICLE:

TITLE: Association between physical activity and risk of hospitalisation in bronchiectasis

Alcaraz-Serrano V[1*], Gimeno-Santos E[2,3*], Scioscia G[4], Gabarrús A[1], Navarro A[5], Herrero-Cortina B[6,7], Amaro R[8] , Fernández-Barat L[1], Torres A[1,8]

* Both authors contributed equally to this work

Authors' full names:

Alcaraz-Serrano, Victoria (victoriaalcarazserrano@gmail.com)

Gimeno-Santos, Elena (elenagimeno@gmail.com)

Scioscia, Giulia (giuliascioscia84@gmail.com)

Gabarrús, Albert (gabarrus@clinic.cat)

Navarro, Adrià (adrianp@blanquerna.url.edu)

Herrero-Cortina, Beatriz (beafisiorespi@gmail.com)

Amaro, Rosanel (ramaro@clinic.cat)

Fernández-Barat, Laia (lfernan1@clinic.cat)

Torres, Antoni (atorres@clinic.cat)

Authors' affiliation(s):

[1] Fundació Clínic per la Recerca Biomèdica (FCRB), CIBERES. Hospital Clinic de Barcelona (Spain)

[2] Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). Hospital Clinic de Barcelona (Spain)

[3] Barcelona Institute for Global Health (ISGlobal), Barcelona (Spain)

[4] Institute of Respiratory Diseases, Department of Medical and Surgical Sciences, University of Foggia (Italy)

[5] Vitruvi Centre de Biosalut, Barcelona (Spain)

[6] Universidad San Jorge, Zaragoza (Spain)

[7] Centre for Inflammation Research, Queen´s Medical Research Institute, University of Edinburgh, (UK)

[8] Institut Clínic Respiratori, Hospital Clínic de Barcelona (Spain)

Conflict of interest: None declared

Correspondence author

Dr. Elena Gimeno-Santos,

Respiratory Clinic Institute, Hospital Clinic de Barcelona, Institut d'Investigacions

Biomèdiques August Pi i Sunyer (IDIBAPS),

Carrer Villarroel, 170, 08036 Barcelona, Spain

E-mail: elenagimeno@gmail.com

Take-home message:

Adult patients with bronchiectasis and reduced physical activity (<6,290 steps per day) or high sedentary behaviour (≥7.8 hours per day) have a higher than average risk of hospital admission due to exacerbation after 1-year follow-up.

Word count: 3172/3000

Abstract: 248/250

Abstract

Background: Patients with bronchiectasis have a less active lifestyle than healthy peers, but the association with hospital admission has not been explored. The aim of this study was to investigate the association between (i) any physical activity (PA) variable and (ii) sedentary time with hospitalisation due to exacerbation in adults with bronchiectasis.

Methods: In this prospective observational study, baseline lung function, quality of life, exercise tolerance, severity of bronchiectasis and PA were recorded. PA was objectively assessed over a week using a SenseWear armband, and the results were expressed in steps per day and sedentary time. Number of hospitalisations due to a bronchiectasis exacerbation and time to first event were recorded after 1-year follow-up.

Results: Sixty-four patients with bronchiectasis were analysed, of whom 15 (23%) were hospitalised during the follow-up. Hospitalised patients showed poor baseline clinical and severity outcomes, fewer steps walked per day and more sedentary behaviour than the non-hospitalised group. Patients who walked ≤6,290 steps per day or spent ≥7.8 hours per day in sedentary behaviour had an increased risk of hospital admission due to bronchiectasis exacerbation at 1-year follow-up. Specifically, ≥7.8 hours of sedentary behaviour was associated with a 5.9-fold higher risk of hospital admission in the following year.

Conclusions: Low levels of PA and high sedentary time at baseline were associated with a risk of hospitalisation due to bronchiectasis exacerbation. If these findings are validated in future studies, it might be appropriate to include PA and sedentary behaviour as an item in severity scores.

Keywords: Bronchiectasis, Hospitalisations, Physical activity, Steps per day, Sedentary time, Exacerbation.

Background

In adults with non-cystic fibrosis (CF) bronchiectasis, the pathogenic vicious circle of persistent infection, neutrophilic inflammation and impaired mucociliary clearance leads to an increase of bacterial load and recurrent exacerbations and in turn raises healthcare costs [1],[2]. Moreover, the presence of comorbidities and a history of hospitalisations increase the risk of further hospital admission due to bronchiectasis exacerbation [3],[4]. In Spain [5], the annual incidence of hospitalisations due to bronchiectasis exacerbations was reported to be around 15.5 per 100,000 population; while in Germany [4] and the United States [6] it was 9.4 and 16.5 respectively. These hospitalisations are associated with a higher mortality and a decline in respiratory function and poor quality of life [7],[8]. The current disease burden and hospitalisation trends due to bronchiectasis exacerbation are steadily increasing; and appear to be related to age and disease severity [3].

Longitudinal studies in patients with chronic obstructive pulmonary disease (COPD) have consistently demonstrated the association between low levels of physical activity (PA) and a higher risk of both mortality and hospitalisations due to exacerbations [9],[10],[11],[12]. Similarly, patients with CF who participate regularly in PA programs show better prognostic outcomes, increased respiratory function, elevated quality of life and enhanced clearance of sputum [13],[14].

PA can be defined as “any bodily movement produced by the contraction of a skeletal muscle that increases energy expenditure above a basal level”; which includes exercise and activities as part of work, leisure or movement [15]. PA is often classified as being of light, moderate or vigorous, according to the level of energy expenditure required [16]. For its part, sedentary behaviour is defined by low energy expenditure (<1.5

metabolic equivalent of tasks; MET) in a sitting or reclining posture during waking hours [17].

Although it has been demonstrated that only 11% of the bronchiectasis population met the recommended PA guidelines of ≥150 min of at least moderate activity per week [18], the current evidence on PA and sedentary behaviour and their association with bronchiectasis hospitalisations is scarce. We hypothesised that steps per day and sedentary time would be strongly associated with the presence of hospital admission due to a bronchiectasis exacerbation.

Therefore, the principal aim of this longitudinal study was to investigate the association between: (i) any PA variable (steps per day, moderate PA and moderate-to-vigorous PA (MVPA)) and (ii) sedentary time; and hospital admission due to exacerbation in adults with bronchiectasis. The second aim was to estimate cut-off points for steps per day and sedentary time that might indicate the risk of hospital admission.

Methods

Study design and subjects

This was a prospective observational study conducted at the pulmonology service of a tertiary care hospital in Barcelona (Spain). Subjects who met the selection criteria were included consecutively in the study between March 2016 and August 2017. Inclusion criteria were as follows: (i) adults (≥18 years old) diagnosed with bronchiectasis, confirmed by computed tomography (CT) scan and with symptoms of the disease; (ii) clinical stability (no exacerbations and no significant change in symptoms and/or medication in the last four weeks); (iii) the ability to perform all the clinical tests and understand the process and the purposes of the study; (iv) giving informed consent. Exclusion criteria were: (i) any physical and psychological disorder that might interfere with protocol compliance; (ii) diagnosis of CF, sarcoidosis, pulmonary fibrosis, active tuberculosis or non-tuberculosis mycobacterial infection in treatment; (iii) participation in a pulmonary rehabilitation (PR) programme in the last year; (iv) respiratory insufficiency and/or oxygen therapy.

The study was approved by the Clinical Research Ethics Committee of the Hospital Clinic (Ethics Approval Reference: HCB/2016/0012).

Measurements

Baseline clinical and physical activity measurements

Socio-demographic and clinical data were collected at baseline, including the etiologic diagnosis of bronchiectasis, current treatment, comorbidities (Charlson Comorbidity Index [19]) and the presence and number of exacerbations (that not require hospitalisation) and hospitalisations due to bronchiectasis in the 12 months prior to the study. Exacerbations were defined according to the international consensus

statement [7]. Disease severity was calculated using the Bronchiectasis Severity Index (BSI) [20] score. Dyspnoea was measured using the Medical Research Council (MRC) scale [21]. Lung function was assessed with EasyOne^{TM}WorldSpirometer (ndd Medical Technologies, Zurich, Switzerland) and was classified according to the American Thoracic Society/European Respiratory Society Guidelines [22]. Exercise capacity was measured using the 6-minute walking test (6MWT) [23]. Quality of life was assessed using the Quality of Life Bronchiectasis questionnaire (QoL-B) [24] and the impact of coughing on the quality of life using the Leicester Cough Questionnaire (LCQ) [25].

PA was the independent variable and was measured using the tri-axial accelerometer SenseWear Armband (SWA) (BodyMedia Inc., Pittsburgh, PA, USA). Participants were asked to wear the SWA for the maximum period of time over seven days, except during water-based activities. It was worn in the triceps area, at the back of the dominant arm.

Intensity of PA was reported as the MET and classified as sedentary (≤1.5 MET), light (1.6 - <3.0 MET), moderate (3.0 - <6.0 MET) and vigorous (≥6.0 MET) [27]. The mean time (in minutes) spent at each level of intensity was recorded. MVPA was calculated with the mean of minutes spent in moderate and vigorous PA on the valid days. Sedentary time was analysed considering the number of minutes that the patient spent at ≤1.5 MET intensity.

Follow-up data collection

The follow-up period lasted 12 months. The number of patients hospitalised at least once in the past year due to a bronchiectasis exacerbation and the time to first hospitalisation were prospectively recorded through the revision of the medical

dataset. The dependent variable was the presence of hospitalisation due to an exacerbation of bronchiectasis during 12 months follow-up.

The need for hospitalisation and discharge were defined by an independent medical doctor who was not involved in the study. The authors checked that all exacerbations met the consensus definition [7]. Patients were classified into hospitalised vs. non-hospitalised groups depending on presence or absence of hospitalisation due to a bronchiectasis exacerbation during the follow-up.

Patients who participated in a PR and/or PA programme during the follow-up were excluded from the final analysis.

Statistical analysis

Prior to any analysis we calculated whether the number of patients included would allow the identification of significant differences in PA and sedentary time between hospitalised vs. non-hospitalised groups. Calculations were performed with the program GRANMO 7.10 [28] and accepting an alpha risk of 0.05 in a two-sided test with 15 subjects in the hospitalised group and 49 in the non-hospitalised group. The statistical power needed to recognise a statistically significant difference was 94% in PA and 96% in sedentary time.

Data are presented as numbers and percentages of patients for categorical variables, as means and standard deviations (SD) for normally distributed data, and as medians, and 1^{st} and 3^{rd} percentiles (P_{25};P_{75}) for non-normally distributed data. The assumption of normality was checked by means of Shapiro-Wilk tests.

In accordance with previous research for reducing the noise in PA analyses [26], the data were considered valid if patients presented ≥8 hours of waking hours (08 am to

10 pm) per day for ≥4 weekdays during the assessment period. A sensitivity analysis was performed including weekend data.

A receiver operating characteristic (ROC) curve was constructed to determine the best cut-off point for steps per day for presence of bronchiectasis hospitalisation (hospitalisation yes or no), and also for sedentary time, moderate PA and MVPA. Youden's index [29] was defined for all points along the ROC curves, and the maximum value of the index was used as a criterion for selecting the optimum cut-off points. Kaplan-Meier analysis was used to compare the association of steps per day and sedentary time with time to first hospitalisation due to an exacerbation of bronchiectasis; the probabilities of hospitalisation in the two groups were analysed using the log-rank test. Univariate and multivariable logistic regression analyses were performed to identify variables associated with bronchiectasis hospitalisations. Due to the limited number of patients in the hospitalised and non-hospitalised groups, and in order to exclude bias related to overestimation or underestimation of the regression coefficient variance, the only variables analysed in the univariate analysis were age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Factors showing an association in the univariate analyses ($p<0.10$) were entered into two multivariable regression models, the first adjusted for steps per day and the second for sedentary time. The final variable selection was performed using the backward stepwise selection method (likelihood ratio) ($p_{in}<0.05$, $p_{out}>0.10$), except for age and gender which had to appear in both models. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the overall fit of the final model. The areas under the ROC

curve (AUCs) of the multivariable models for hospitalisations due to bronchiectasis were then calculated.

The internal validity of the final models was assessed using ordinary nonparametric bootstrapping with 1,000 bootstrap samples and bias-corrected, accelerated 95% CIs.

We used the multiple imputation method [30] for missing data in the multivariable analyses.

The level of significance was set at 0.05 (two-tailed). All analyses were performed using IBM SPSS Statistics version 25.0 (Armonk, New York, USA).

Results

Baseline clinical and PA data

Of the 72 patients with bronchiectasis recruited at baseline, 64 were included in the follow-up analysis (**Figure 1**). The study population was classified into two groups according to the presence of hospitalisation due to an exacerbation during the 1-year follow-up: a) hospitalised patients, N=15 (23%); and b) non-hospitalised patients, N=49 (77%). Baseline clinical and PA characteristics are shown in **Table 1**. Hospitalised patients were more likely to have chronic colonisation by *Pseudomonas aeruginosa*, more hospitalisations in the 12 months prior to the study, poor dyspnoea, worse lung function and quality of life, a higher comorbidity index and a more severe BSI score.

The number of patients with COPD and bronchiectasis overlap was low. Four patients (6%), two per group, had a smoking history of >10 packs/year and a FEV_1/FVC <70%. The distribution between the groups did not differ significantly (13% vs. 4%; p=0.455).

In terms of PA, hospitalised patients took fewer of steps per day, spent more time sedentary and had lower levels of MVPA than non-hospitalised ones. Light PA and exercise capacity did not differ between groups.

Steps per day and sedentary time cut-off points and hospitalisation risk

Table 2 presents the best cut-off points for steps per day, sedentary time, moderate PA and MVPA for predicting hospital admission during follow-up. Light and vigorous PA had very low sensitivity and specificity without presenting statistically significant differences. Kaplan–Meier curves evaluating the time to first hospitalisation due bronchiectasis exacerbation according to steps per day and sedentary time are represented in **Figure 2**. Patients with ≤6,290 steps per day or ≥7.8 hours per day of sedentary behaviour had a higher risk of hospital admission due to bronchiectasis exacerbation at 1-year follow-up than patients with more steps per day or less sedentary time ($p<0.001$).

Association between PA outcomes and hospitalisation due to an exacerbation of bronchiectasis

In accordance with the proposed cut-off values, the logistic regression model showed a higher risk of hospitalisation for bronchiectasis patients with low levels of PA (<6,290 steps/day) and sedentary behaviour (≥7.8 hours). After adjusting for all relevant confounders (age, gender, chronic colonisation by *Pseudomonas aeruginosa*, and hospitalisations 12 months prior to the study), sedentary behaviour raised the risk of hospitalisation 5.91 times (**Table 3** and **Online Table1** of the Supplementary material). When the final model was adjusted for the factors gender and BSI, sedentary behaviour also raised the risk of hospitalisation 5.34 times (**Online Table1**).

After excluding patients with a smoking history of ≥10 packs/year and after adjusting for all relevant confounders, low physical activity (<6,290 steps/day) raised the risk of hospitalisation by 8.7 times (**Online Table2**).

The sensitivity analyses including weekend data showed reductions in the cut-off points and the size of the associations, although the significance of the effect remained unchanged with regard to the analyses including only weekdays (**Online Table 3-4-5** and **Figures 1 A-B**).

Internal validation of the final models was conducted using bootstrapping with 1,000 samples. All variables remained significant after a bootstrapping procedure, with small 95% CIs around the original coefficients.

Discussion

To our knowledge, this is the first study to investigate the association between PA, sedentary time and risk of hospitalisation in patients with bronchiectasis. We confirmed that patients hospitalised for an exacerbation of bronchiectasis during the 1-year follow-up presented poor clinical characteristics, higher severity, and lower levels of PA at baseline compared than those not hospitalised. This study is the first to propose cut-off points for steps per day (<6290) and number of hours spent in sedentary behaviour (≥7.8) in order to objectively identify patients with bronchiectasis who are at a higher risk for hospital admission in the next year. Finally, the risk for hospitalisation in patients with bronchiectasis exacerbation was significantly higher (5.91 times) in those who spent ≥7.8 hours/day in sedentary behaviour.

Little is known about PA behaviour in the bronchiectasis populations. In a recent study, José et al. [31] measured PA with a pedometer and demonstrated that patients with

bronchiectasis showed lower PA levels than healthy controls. They also concluded that patients affected by bronchiectasis who appeared to be more active in daily life were the ones with better pulmonary function, functional capacity and lower dyspnoea. In fact this Brazilian bronchiectasis population was surprisingly active: mean of 8,007 steps/day vs. 10,994 in healthy peers.

Bradley et al. in 2015 [18] analysed PA in 63 patients with bronchiectasis measured by an ActiGraph GT3X+ accelerometer. The mean number of steps per day was 6,001 vs. 6,880 in our population and the mean daily time spent in sedentary behaviour in those subjects was 10.5h compared to 7.2h in our study. We stress that this finding is unlikely to be related to disease severity, as Bradley and co-authors' population presented lower severity levels (BSI score: 49% mild, 33% moderate and 18% severe) than ours (BSI: 36% mild, 35% moderate and 29% severe). A point to be considered is that the patients with lower PA levels were the ones with greater severity. Consequently, the lower PA may be due to physical impairment in the more severe patients, who in turn have more exacerbations.

Regarding BSI [20], the item "hospitalisations in the previous 2 years" had the highest score of all, and is a recognized predictor of 4-year mortality, further hospital admissions, exacerbations and worse quality of life. The history of hospitalisation due to a bronchiectasis exacerbation is an important clinical outcome because of its negative consequences for the prognosis of the disease. In a recent cohort of 651 patients, 23.2% were defined as "frequent exacerbators" and presented poorer severity scores, more systemic inflammation and a greater use of antibiotic and anti-inflammatory therapies. Those authors concluded that a history of at least two exacerbations or one hospitalisation/year was the variable with the best prognostic

value of 5-year all-cause mortality, with an AUC of 0.75 (CI 95% 0.69 to 0.81) p<0.001 [32]. No information was available about PA levels in that population.

In view of our results, the groups did not differ in terms of exercise capacity or light PA, while time spent in sedentary behaviour was the only factor that raised the risk of hospitalisation, by 5.91 times. Although the differences in exercise capacity were not statistically significant, they were greater than the minimal important difference defined for patients with bronchiectasis [33]. We believe that breaking the sedentary habit in the population with bronchiectasis might have a significant clinical impact on reducing the number of hospitalisations and on improving quality of life.

Previous studies have sought to find cut-off points of time spent in sedentary behaviour and steps per day in chronic respiratory diseases. Furlanetto et al. in 2017 [12] were the first to propose an objectively cut-off point for sedentarism in subjects affected by COPD and to investigate the association of this variable with long-term mortality. They demonstrated that the mortality risk was 4.09 times higher in patients who spent ≥8.5 h/day seated, with an AUC 0.76 (sensitivity 84% and specificity 65%). It has also been shown that the longer the time spent in sedentary behaviour per day, the higher the number of COPD exacerbations, although this was not analysed in terms of hospitalisation [34]. Our results are in line with previous studies in patients with COPD, perhaps due to similarities in PA behaviour in patients with these two chronic respiratory diseases. In the same line, the risk of hospitalisation during follow-up in our population remained in the same direction after excluding patients who had a smoking history of >10 packs/year. However, these findings should be interpreted carefully because after excluding these patients the sample size fell by 25%.

It is well known that increased sedentary behaviour is associated with worsened health effects, which may differ from those caused by reduced PA in daily life [35], in both healthy subjects and patients with chronic respiratory diseases [10]. Strategies for reducing sedentary behaviour and for increasing PA will be key components of future bronchiectasis management in order to improve outcomes such as quality of life and to reduce the risk of hospitalisation.

The main strengths of our study were the fact that PA was measured with an objective and validated tool such as an accelerometer, and the reduction of the bias due to seasonality thanks to the inclusion and follow-up of patients over a whole year. One limitation of our study might be the analyses of the PA parameters on weekdays. However since the significance of the effect remained unchanged, with regard to the analyses including weekend, we are confident that the magnitude of the association was not overestimated. Another possible limitation is the fact that the number of hospitalisations was calculated using only medical history data and we might have missed some patients hospitalised at different centres.

Future studies should consider the inclusion of patients with bronchiectasis from other countries and other ethnicities in order to compare and contrast the results reported here. It will also be important to determine whether reducing the time spent in sedentary behaviour can significantly lower the percentage of hospitalised patients.

Conclusions

For the first time, we demonstrate an association between hospitalisation due to bronchiectasis exacerbation and PA behaviour. Hospitalised bronchiectasis patients had lower PA and higher sedentary behaviour than their non-hospitalised ones.

Patients who walked 6290 steps per day or less or spent 7.8 hours per day or more in sedentary behaviour increased the risk of hospitalisation during 1-year follow-up. Moreover, sedentary behaviour alone increased the risk of hospital admission 5.91 times. Objectively measured sedentary behaviour could be an independent predictor of hospitalisation due to exacerbation in patients with bronchiectasis. If this finding is validated in future studies, it may be appropriate to include PA and sedentary behaviour as an item in severity scores.

Acknowledgements

The authors would like to thank the patients for taking part in the study.

Funding

This work was supported by the *Sociedad Española de Neumología y Cirugía Torácica* (SEPAR 052/2014), and the *Col·legi Fisioterapeutes Catalunya* (047913/2016). Elena Gimeno-Santos received personal funding from the *Instituto de Salud Carlos III*, via a Sara Borrell contract (Acción Estratégica en Salud 2016).

Contributions

VAS had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. VAS designed and developed the study protocol. VAS and AN collected the data from patients. VAS, EGS and AG participated in the statistical analysis and data interpretation. VAS, EGS and GS participated in the writing of the manuscript. All the authors have read and approved the final version of the manuscript, fully approve it, and qualify for authorship.

References

1. Flume PA, Chalmers JD, Olivier KN. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. *Lancet* 2018; 392: 880–890.
2. Watt AP, Brown V, Courtney J, Kelly M, Garske L, Elborn JS, Ennis M. Neutrophil apoptosis, proinflammatory mediators and cell counts in bronchiectasis. *Thorax* 2004; 59: 231–236.
3. Menéndez R, Méndez R, Polverino E, Rosales-Mayor E, Amara-Elori I, Reyes S, Posadas T, Fernández-Barat L, Torres A. Factors associated with hospitalization in bronchiectasis exacerbations: A one-year follow-up study. *Respir. Res.*2017; 18: 1–8.
4. Ringshausen FC, de Roux A, Pletz MW, Hämäläinen N, Welte T, Rademacher J. Bronchiectasis-Associated Hospitalizations in Germany, 2005-2011: A Population-Based Study of Disease Burden and Trends. *PLoS One* 2013; 8: (8): e71109.
5. Sánchez-Muñoz G, López de Andrés A, Jiménez-García R, Carrasco-Garrido P, Hernández-Barrera V, Pedraza-Serrano F, Puente-Maestu L, de Miguel-Díez J. Time Trends in Hospital Admissions for Bronchiectasis: Analysis of the Spanish National Hospital Discharge Data (2004 to 2013). *PLoS One* 2016; 11: e0162282.
6. Seitz AE, Olivier KN, Steiner CA, De Oca RM, Holland SM, Prevots DR. Trends and burden of bronchiectasis-associated hospitalizations in the United States, 1993-2006. *Chest* 2010; 138: 944–949.
7. Hill AT, Haworth CS, Aliberti S, Barker A, Blasi F, Boersma W, Chalmers JD, De Soyza A, Dimakou K, Elborn JS, Feldman C, Flume P, Goeminne PC, Loebinger

MR, Menendez R, Morgan L, Murris M, Polverino E, Quittner A, Ringshausen FC, Tino G, Torres A, Vendrell M, Welte T, Wilson R, Wong C, O'Donnell A, Aksamit T, EMBARC/BRR definitions working group. Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research. *Eur. Respir. J.* 2017; 49: 1700051.

8. Cantón R, Máiz L, Escribano A, Olveira C, Oliver A, Asensio O, Gartner S, Roma E, Quintana-Gallego E, Salcedo A, Girón R, Barrio MI, Pastor MD, Prados C, Martínez-Martínez MT, Barberán J, Castón JJ, Martínez-Martínez L, Poveda JL, Vázquez C, de Gracia J, Solé A, en representación del Grupo Español de Consenso del Tratamiento Antimicrobiano en el Paciente con Fibrosis Quística. Consenso español para la prevención y el tratamiento de la infección bronquial por *Pseudomonas aeruginosa* en el paciente con fibrosis quística. *Arch. Bronconeumol.* 2015; 51: 140–150.
9. Gimeno-Santos E, Frei A, Steurer-Stey C, de Batlle J, Rabinovich RA, Raste Y, Hopkinson NS, Polkey MI, van Remoortel H, Troosters T, Kulich K, Karlsson N, Puhan MA, Garcia-Aymerich J. Determinants and outcomes of physical activity in patients with COPD: a systematic review. *Thorax* 2014; 69: 731–739.
10. Lewthwaite H, Effing TW, Olds T, Williams MT. Physical activity, sedentary behaviour and sleep in COPD guidelines: A systematic review. *Chron. Respir. Dis.*2017; 14: 231–244
11. Demeyer H, Donaire-Gonzalez D, Gimeno-Santos E, Ramon MA, de Batlle J, Benet M, Serra I, Guerra S, Farrero E, Rodriguez E, Ferrer J, Sauleda J, Monso E, Gea J, Rodriguez-Roisin R, Agusti A, Antó JM, Garcia-Aymerich J. Physical Activity Is Associated with Attenuated Disease Progression in COPD. *Med. Sci. Sport.*

Exerc. 2019; 51(5):833-840.

12. Furlanetto KC, Donária L, Schneider LP, Lopes JR, Ribeiro M, Fernandes KB, Hernandes NA, Pitta F. Sedentary Behavior Is an Independent Predictor of Mortality in Subjects With COPD. *Respir. Care* 2017; 62: 579–587.

13. Flume PA, Robinson KA, O'Sullivan BP, Finder JD, Vender RL, Willey-Courand DB, White TB, Marshall BC. Cystic fibrosis pulmonary guidelines: airway clearance therapies. *Respir. Care* 2009; 54: 522–537.

14. Spruit MA, Singh SJ, Garvey C, Zu Wallack R, Nici L, Rochester C, Hill K, Holland AE, Lareau SC, Man WDC, Pitta F, Sewell L, Raskin J, Bourbeau J, Crouch R, Franssen FME, Casaburi R, Vercoulen JH, Vogiatzis I, Gosselink R, Clini EM, Effing TW, Maltais F, Van Der Palen J, Troosters T, Janssen DJA, Collins E, Garcia-Aymerich J, Brooks D, Fahy BF, et al. An official American thoracic society/European respiratory society statement: Key concepts and advances in pulmonary rehabilitation. *Am. J. Respir. Crit. Care Med.* 2013; 188(8):e13-64.

15. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.*1985; 100: 126–131.

16. Hill K, Gardiner PA, Cavalheri V, Jenkins SC, Healy GN. Physical activity and sedentary behaviour: Applying lessons to chronic obstructive pulmonary disease. *Intern. Med. J.* 2015; 45: 474–482.

17. Sedentary Behaviour Research Network. Letter to the Editor: "standardized use of the terms "sedentary" and "sedentary behaviours." *Appl Physiol Nutr Metab. Act.* 2012; 37(3): 540–2.

18. Bradley JM, Wilson JJ, Hayes K, Kent L, Mcdonough S, Tully MA, Bradbury I, Kirk

A, Cosgrove D, Convery R, Kelly M, Elborn JS, Neill BO. Sedentary behaviour and physical activity in bronchiectasis : a cross-sectional study. BMC Pulmonary Medicine; 2015; 15:61.

19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J. Chronic Dis.* 1987; 40: 373–383.

20. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, Poppelwell L, Salih W, Pesci A, Dupont LJ, Fardon TC, De Soyza A, Hill AT. The bronchiectasis severity index an international derivation and validation study. *Am. J. Respir. Crit. Care Med.* 2014; 189: 576–585.

21. Hester KLM, Macfarlane JG, Tedd H, Jary H, McAlinden P, Rostron L, Small T, Newton JL, De Soyza A. Fatigue in bronchiectasis. *QJM* 2012; 105: 235–240.

22. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates a, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. *Eur. Respir. J.* 2005; 26: 319–338.

23. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin BW, Sciurba FC, Pitta F, Wanger J, MacIntyre N, Kaminsky DA, Culver BH, Revill SM, Hernandes NA, Andrianopoulos V, Camillo CA, Mitchell KE, Lee AL, Hill CJ, Singh SJ. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur. Respir. J.* 2014; 44: 1428–1446.

24. Olveira C, Olveira G, Espildora F, Giron R-M, Muñoz G, Quittner AL, Martinez-Garcia M-A. Validation of a Quality of Life Questionnaire for Bronchiectasis:

psychometric analyses of the Spanish QOL-B-V3.0. *Qual. Life Res.* 2014; 23(4):1279-92.

25. Muñoz G, Buxó M, De Gracia J, Olveira C, Martinez-Garcia MA, Giron R, Polverino E, Alvarez A, Birring SS, Vendrell M. Validation of a Spanish version of the Leicester Cough Questionnaire in non-cystic fibrosis bronchiectasis. *Chron. Respir. Dis.* 2016; 13: 128–136.
26. Demeyer H, Burtin C, Van Remoortel H, Hornikx M, Langer D, Decramer M, Gosselink R, Janssens W, Troosters T. Standardizing the Analysis of Physical Activity in Patients With COPD Following a Pulmonary Rehabilitation Program. *Chest* 2014; 146(2): 318–327.
27. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR, Schmitz KH, Emplaincourt PO, Jacobs DR, Leon AS. Compendium of physical activities: an update of activity codes and MET intensities. *Med. Sci. Sports Exerc* 2000; 32 (9 Suppl): S498-504.
28. Marrugat J, Vila J, Pavesi M, Sanz F. Estimation of the sample size in clinical and epidemiological investigations. *Med. Clin. (Barc).*1998; 111: 267–276.
29. Youden WJ. Index for rating diagnostic tests. *Cancer* 1950; 3: 32–35.
30. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM, Carpenter JR. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009; 338:b2393.
31. José A, Ramos TM, de Castro RAS, de Oliveira CS, de Camargo AA, Athanazio RA, Rached SZ, Stelmach R, Dal Corso S. Reduced Physical Activity With Bronchiectasis. *Respir. Care* 2018; 63: 1498–1505.
32. Martinez-Garcia MÁ, Athanazio R, Gramblicka G, Corso M, Cavalcanti Lundgren

F, Fernandes de Figueiredo M, Arancibia F, Rached S, Girón R, Máiz Carro L, de la Rosa Carrillo D, Prados C, Olveira C. Prognostic Value of Frequent Exacerbations in Bronchiectasis: The Relationship With Disease Severity. *Arch. Bronconeumol.*; 2019; 55: 81–87.

33. Lee AL, Hill CJ, Cecins N, Jenkins S, Mcdonald CF, Burge AT, Rautela L, Stirling RG, Thompson PJ, Holland AE. ScienceDirect Minimal important difference in field walking tests in non-cystic fibrosis bronchiectasis following exercise training. *Respir. Med.*2014; 108: 1303–1309.

34. Hartman JE, Marike Boezen H, De Greef MH, Hacken NHT. Physical and psychosocial factors associated with physical activity in patients with chronic obstructive pulmonary disease. *Arch. Phys. Med. Rehabil.* 2013; 94(12): 2396-2402.e7

35. Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. *Appl. Physiol. Nutr. Metab.* 2010; 35(6): 725–740.

Table1. *Baseline characteristics of hospitalised vs. non-hospitalised bronchiectasis patients*

	All patients	Hospitalised	Non-hospitalised	p value
	N=64	N=15 (23%)	N=49 (77%)	
Demographics				
Male	21 (33)	6 (40)	15 (31)	0.501
Age, years	62.9 (14.9)	64.3 (17.4)	62.2 (14.5)	0.510
BMI, kg/m^2	24.6 (4.3)	24.3 (4.1)	24.6 (4.5)	0.924
Retired	41 (64)	11 (73)	30 (61)	0.550
Former smokers	20 (31)	5 (33)	15 (31)	0.923
Smoking habit, packs/year	30 [8.5; 60]	40 [25.5; 86.5]	19.2 [7; 60]	0.119
Chronic colonisation	23 (36)	11 (73)	12 (24)	**0.001**
Pseudomonas aeruginosa	19 (29)	10 (66)	9 (18)	**0.000**
Haemophilus influenza	2 (3)	0 (0)	2 (4)	0.430
Staphylococcus aureus	2 (3)	1 (6)	1 (2)	0.371
Dyspnoea (MRC Scale, 1-5)	2 [2; 2]	2 [2; 3]	2 [2; 2]	**0.004**
Exacerbations and hospitalisations 12 months prior to the study				
Exacerbated patients	45 (70)	11 (73)	34 (70)	0.772
Nº exacerbations	1 [0; 2]	2 [0; 4]	1 [0; 2]	0.171
Hospitalised patients	13 (20)	7 (47)	6 (12)	**0.004**
Nº hospitalisations	0 [0; 0]	0 [0; 1]	0 [0; 0]	**0.004**
Aetiology				
Post-infectious	29 (45)	6 (40)	23 (47)	0.639
Idiopathic	14 (22)	5 (33)	9 (18)	0.224
Associated with COPD	4 (6)	2 (13)	2 (4)	0.455
Others	17 (26)	2 (13)	15 (30)	-
Severity				
Charlson Comorbidities Index				**0.031**
Mild	51 (79)	9 (60)	42 (86)	
Moderate	9 (14)	4 (26)	5 (10)	
High	4 (6)	2 (13)	2 (4)	
BSI stage				**0.001**
Mild	23 (36)	2 (13)	21 (43)	
Moderate	22 (34)	3 (20)	19 (39)	
Severe	19 (29)	10 (66)	9 (18)	
Pulmonary function				
FEV_1, % predicted	72 (19.8)	62.1 (18.7)	75.2 (19.9)	**0.020**
FEV_1, L	1.94 (0.81)	1.82 (0.94)	1.99 (0.78)	0.366
FVC, % predicted	80.6 (17.1)	72.7 (15.3)	83.1 (17.7)	**0.026**
FVC, L	2.82 (0.83)	2.6 (0.75)	2.89 (0.86)	0.342
FEV_1/FVC, %	86 (18.6)	82 (22.1)	86.92 (17.7)	0.495
6MWT, meters	512.7 (93.5)	467.7 (116)	522.7 (83)	0.063
Respiratory medication[a]				
Inhaled steroids	45 (70)	11 (73)	34 (69)	0.772

Long acting beta agonist	48 (75)	12 (80)	36 (73)	0.612
Long acting antimuscarinics	28 (44)	12 (80)	16 (32)	**0.001**
Antibiotic	11 (17)	3 (20)	8 (16)	0.743
Quality of Life				
Quality of Life Bronchiectasis Questionnaire*				
Physical Function	57.3 (33.8), 0-100	53.3 (35.2), 0-100	58.5 (33.7), 0-100	0.588
Role Function	75.5 (28), 0-100	53.3 (32.9), 0-100	82.3 (22.7), 33.3-100	**0.001**
Vitality	58.6 (25.5), 0-100	45.6 (33.6), 0-100	62.6 (21.4), 16.7-100	**0.033**
Emotional Function	73.7 (28.6), 0-100	64.4 (30.1), 0-100	76.5 (27.8), 0-100	0.140
Social Function	68.2 (31.7), 0-100	54.4 (35.9), 0-100	72.4 (29.4), 0-100	0.072
Treatment Burden	69.8 (40.6), 0-100	75.5 (36.6), 0-100	68.0 (41.9), 0-100	0.670
Health Perceptions	52.9 (26.5), 0-100	35.5 (30.8), 0-100	58.2 (22.8), 0-100	**0.007**
Respiratory Symptoms	76.3 (22.6), 33.3-100	67.8 (22.4), 33.3-100	78.9 (22.5), 33.3-100	0.052
Leicester Cough Questionnaire	15.8 [11.8; 19.4]	15 [10.4; 18.7]	16.6 [12.4; 19.5]	0.292
Physical	15.3 [12; 18.4]	14.2 [11.2; 16.9]	15.7 [12; 18.4]	0.115
Psychological	15.6 [11.1; 19.3]	14.6 [9.4; 18.4]	16.7 [12; 19.9]	0.243
Social	18 [13; 21]	18 [11.2; 19.5]	18.7 [13.1; 21]	0.582
Physical Activity				
Light PA, 1.6 - <3.0 MET-min/day	211.4 (79)	186 (42.5)	222.3 (87.5)	0.178
Moderate PA, 3.0 - <6.0 MET-min/day	117 (82)	81.9 (63)	127.3 (83.4)	**0.015**
Vigorous PA, 6.0 - <8.7 MET-min/day	0.78 (1.86)	0.55 (1.6)	0.9 (2)	0.546
MVPA, min/day	115.5 (78.5)	82.4 (64.2)	125.3 (78.6)	**0.015**
Steps per day	6,880 (3,447)	4,740 (3,196)	7,563 (3,382)	**0.003**
Sedentary time, hours per day	7.17 (1.8)	8.22 (1.48)	6.83 (1.74)	**0.005**

Data are presented as n (%), mean (SD) or median (P_{25};P_{75}). *Data presented as mean (SD), and range.

Abbreviations. BMI: body mass index; MRC: medical research council; Nº: number; COPD: chronic obstructive pulmonary disease; BSI: bronchiectasis severity index; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; 6MWT: 6 minutes walking test; PA: physical activity; MET: metabolic equivalent tasks; MVPA: moderate-to-vigorous physical activity.

[a] Patients may have had more than one medication.

Table2. S*teps per day, sedentary time, moderate PA and MVPA cut-off points for hospitalisation*

Hospitalisation variable	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Best Cut-off	p value
Steps per day	0.75 (0.60 to 0.89)	61	73	6,290	0.003
Sedentary time (hours)	0.74 (0.59 to 0.88)	73	74	7.8	0.005
Moderate PA (min)	0.71 (0.55 to 0.87)	67	73	84.4	0.015
MVPA (min)	0.71 (0.55 to 0.87)	85	53	66.3	0.015

Abbreviations. AUC: area under the curve; CI: confidence interval; PA: physical activity; min: minutes; MVPA: moderate-to-vigorous physical activity.

Table3. *Crude and adjusted associations between level of physical activity in steps per day and sedentary time and bronchiectasis hospitalisations.*

	N	Crude OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Steps per day [a]					
High physical activity (≥6,290 steps/day)	43	1.00		1.00	
Low physical activity (<6,290 steps/day)	21	4.62 (1.36 to 15.68)	0.014	4.20 (0.82 to 21.47)	0.085
Sedentary time [b]					
Sedentary (≥7.8h)	24	7.62 (2.06 to 28.18)	0.002	5.91 (1.26 to 27.81)	0.024
No sedentary (<7.8h)	40	1.00		1.00	

Abbreviations. OR: odds-ratio; CI: confidence interval; h: hours

Data are shown as estimated ORs (95% CIs) of the explanatory variables in the low f physical activity group. The OR represents the odds that low physical activity will occur given exposure to the explanatory variable, compared to the odds of the outcome occurring in the absence of that exposure. The P-values are based on the null hypothesis that all ORs relating to an explanatory variable are equal to unity (no effect).

[a] Multivariable model adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.85. Area under the ROC curve for the multivariable model, AUC = 0.86 (0.76 to 0.97).

[b] Multivariable model adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.78. Area under the ROC curve for the multivariable model, AUC = 0.87 (0.76 to 0.97).

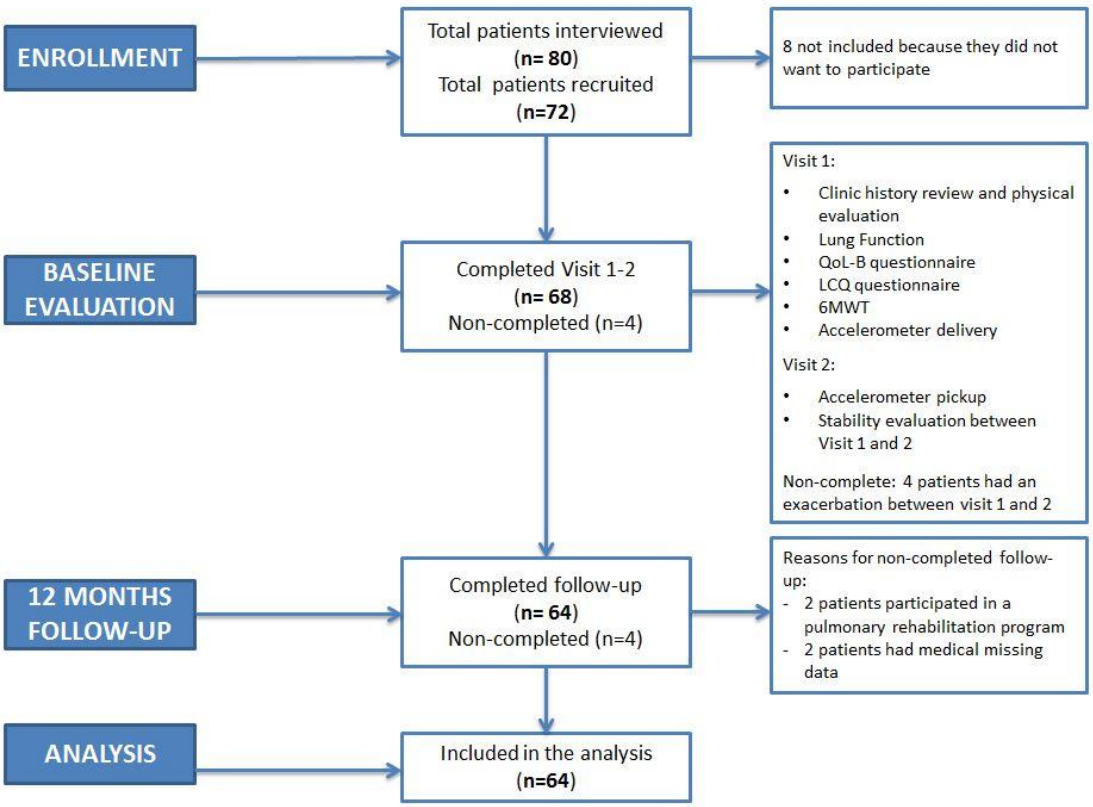
Figures legend

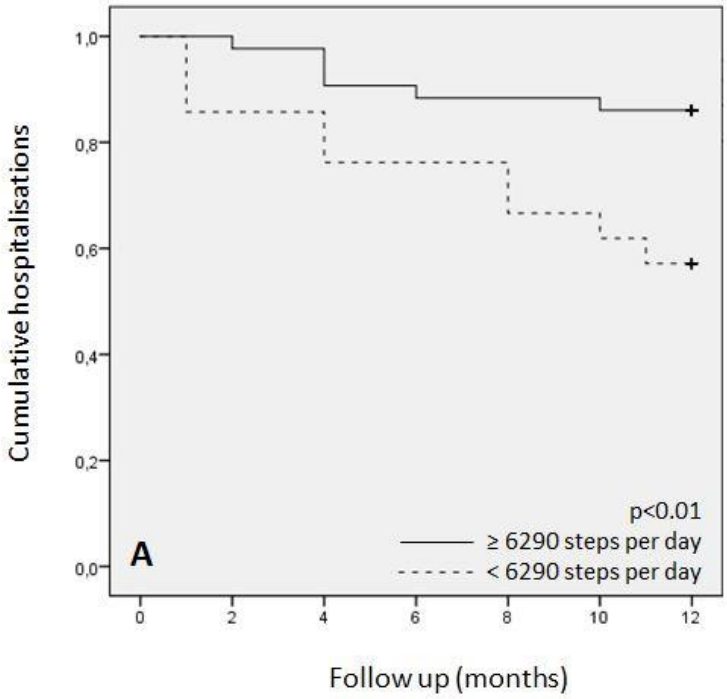
Figure 1. Enrolment flow chart.

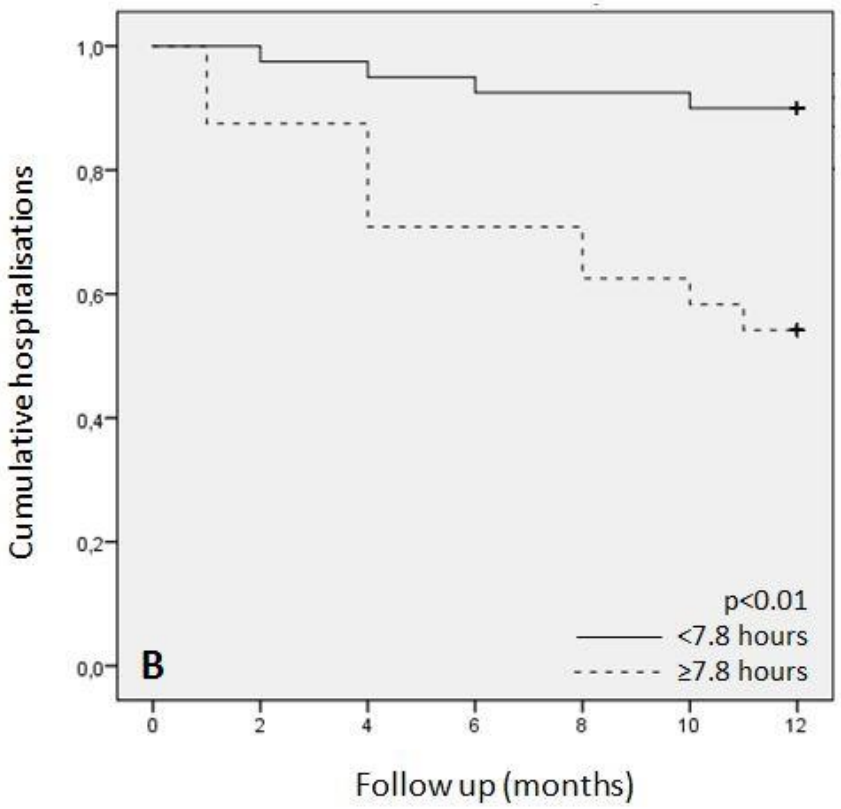
Abbreviations. QoL-B: Quality of Life Bronchiectasis questionnaire; LCQ: Leicester cough questionnaire; 6MWT: 6 minute walking test.

Figures 2. Kaplan-Meier graphics according to ROC curve cut-off points.

2A. <6290 steps per day; 2B. ≥7.8 hours of sedentary behaviour.


ENROLLMENT
Total patients interviewed
(n= 80)
Total patients recruited
(n=72)
8 not included because they did not want to participate
BASELINE EVALUATION
Completed Visit 1-2
(n= 68)
Non-completed (n=4)
Visit 1:
Clinic history review and physical evaluation
Lung Function
QoL-B questionnaire
LCQ questionnaire
6MWT
Accelerometer delivery
Visit 2:
Accelerometer pickup
Stability evaluation between Visit 1 and 2
Non-complete: 4 patients had an exacerbation between visit 1 and 2
12 MONTHS FOLLOW-UP
Completed follow-up
(n= 64)
Non-completed (n=4)
Reasons for non-completed follow-up:
- 2 patients participated in a pulmonary rehabilitation program
- 2 patients had medical missing data
ANALYSIS
Included in the analysis
(n=64)


1,0
0,8
0,6
0,4
0,2
0,0
Cumulative hospitalisations
A
p<0.01
≥ 6290 steps per day
< 6290 steps per day
0
2
4
6
8
10
12
Follow up (months)


Cumulative hospitalisations
1,0
0,8
0,6
0,4
0,2
0,0
B
p<0.01
<7.8 hours
≥7.8 hours
0
2
4
6
8
10
12
Follow up (months)

ONLINE MATERIAL

Manuscript: Association between physical activity and risk of hospitalisation in bronchiectasis

Alcaraz-Serrano V[1*], Gimeno-Santos E[2,3*], Scioscia G[4], Gabarrús A[1], Navarro A[5], Herrero-Cortina B[6,7], Amaro R[8] , Fernández-Barat L[1], Torres A[1,8]

* Both authors contributed equally to this study

Conflict of interest: None declared

Correspondence author

Dr. Elena Gimeno-Santos,

Respiratory Clinic Institute, Hospital Clinic de Barcelona, Institut d'Investigacions

Biomèdiques August Pi i Sunyer (IDIBAPS),

Carrer Villarroel, 170, 08036 Barcelona, Spain

E-mail: elenagimeno@gmail.com

Index

Online Table1. Crude and adjusted associations between level of physical activity in steps per day and sedentary time with bronchiectasis hospitalisations.

	N	Crude OR (95% CI)	p value	Adjusted OR (95% CI) [a]	p value	Adjusted OR (95% CI) [b]	p value	Adjusted OR (95% CI) [c]	p value	Adjusted OR (95% CI) [d]	p value
Steps per day						-	-			-	-
High physical activity (≥6,290 steps per day)	43	1.00		1.00		-	-	1.00		-	-
Low physical activity (<6,290 steps per day)	21	4.62 (1.36 to 15.68)	0.014	4.20 (0.82 to 21.47)	0.085	-	-	3.37 (0.85 to 13.39)	0.085	-	-
Sedentary time				-	-			-	-		
Sedentary (≥7.8h)	24	7.62 (2.06 to 28.18)	0.002	-	-	5.91 (1.26 to 27.81)	0.024	-	-	5.34 (1.29 to 22.46)	0.020
No sedentary (<7.8h)	40	1.00		-	-	1.00		-	-	1.00	
Age (+1 year)	64	1.01 (0.97 to 1.05)	0.646	0.99 (0.94 to 1.04)	0.681	0.99 (0.94 to 1.05)	0.804	-	-	-	-
Gender											
Male	21	1.00		1.00		1.00		1.00		1.00	
Female	43	0.66 (0.20 to 2.19)	0.500	0.55 (0.13 to 2.42)	0.432	0.83 (0.19 to 3.68)	0.802	0.76 (0.18 to 3.37)	0.715	1.14 (0.27 to 4.77)	0.861
Pseudomonas aeruginosa								-	-	-	-
No	45	1.00		1.00		1.00		-	-	-	-
Yes	19	8.89 (2.44 to 32.43)	0.001	5.83 (1.35 to 25.16)	0.018	6.82 (1.56 to 29.94)	0.011	-	-	-	-
Hospitalisations 12 months prior to the study								-	-	-	-
No	51	1.00		1.00		1.00		-	-	-	-
Yes	13	6.27 (1.66 to 23.62)	0.007	6.70 (1.38 to 32.65)	0.018	5.65 (1.12 to 28.44)	0.036	-	-	-	-
MRC Dyspnoea Scale			0.347	-	-	-	-	-	-	-	-
1	12	1.00		-	-	-	-	-	-	-	-
2	39	2.41 (0.27 to 21.81)	0.435	-	-	-	-	-	-	-	-
3	10	7.33 (0.66 to 81.36)	0.105	-	-	-	-	-	-	-	-

4	3	-	-	-	-	-	-	-	-	-	-
FEV_1 (+1 %)	64	0.97 (0.94 to 1.00)	0.034	-	-	-	-	-	-	-	-
BSI stage			0.004	-	-	-	-		0.022		0.035
Mild	23	1.00		-	-	-	-	1.00		1.00	
Moderate	22	1.66 (0.25 to 11.02)	0.601	-	-	-	-	1.46 (0.20 to 10.43)	0.707	1.99 (0.27 to 14.5)	0.495
Severe	19	11.67 (2.12 to 64.33)	0.005	-	-	-	-	8.35 (1.43 to 48.71)	0.018	8.79 (1.47 to 52.5)	0.017
6MWT (+1 meter)	64	0.99 (0.99 to 1.00)	0.056	-	-	-	-	-	-	-	-

Abbreviations. OR: odds-ratio; CI: confidence interval; h: hours; MRC: medical research council; FEV_1: forced expiratory volume in one second; BSI: bronchiectasis severity index; 6MWT: 6 minutes walking test.

Data are shown as estimated ORs (95% CIs) of the explanatory variables in the low level of physical activity group. The OR represents the odds that low level of physical activity will occur given exposure to the explanatory variable, compared to the odds of the outcome occurring in the absence of that exposure. The P-values are based on the null hypothesis that all ORs relating to an explanatory variable are equal to unity (no effect).

[a] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.85. Area under the ROC curve for the multivariable model, AUC = 0.86 (0.76 to 0.97).

[b] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.78. Area under the ROC curve for the multivariable model, AUC = 0.87 (0.76 to 0.97).

[c] Initial multivariable model comprised gender and BSI stage. Final multivariable model was adjusted for gender and BSI. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.986. Area under the ROC curve for the multivariable model, AUC = 0.80 (0.67 to 0.94).

[d] Initial multivariable model comprised gender and BSI stage. Final multivariable model was adjusted for gender and BSI. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.606. Area under the ROC curve for the multivariable model, AUC = 0.81 (0.67 to 0.95).

Online Table2. Crude and adjusted associations between level of physical activity in steps per day and sedentary time excluding patients with ≥10 pack/year of tobacco.

	N	Crude OR (95% CI)	p value	Adjusted OR (95% CI) [a]	p value	Adjusted OR (95% CI) [b]	p value
Steps per day						-	-
High physical activity (≥6,290 steps per day)	36	1.00		1.00		-	-
Low physical activity(<6,290 steps per day)	12	4.43 (1.00 to 19.58)	0.050	8.7 (1.16 to 65.01)	0.035	-	-
Sedentary time				-	-		
Sedentary (≥7.8h)	14	5.62 (1.27 to 24.86)	0.023	-	-	5.54 (0.77 to 40.01)	0.089
No sedentary (<7.8h)	34	1.00		-	-	1.00	
Age (+1 year)	48	0.983 (0.94 to 1.03)	0.450	0.94 (0.88 to 1.00)	0.056	0.95 (0.88 to 1.02)	0.169
Gender							
Male	15	1.00		1.00		1.00	
Female	33	1.07 (0.24 to 4.90)	0.924	1.34 (0.17 to 10.46)	0.778	1.19 (0.15 to 9.65)	0.870
Pseudomonas aeruginosa				-	-		
No	34	1.00		-	-	1.00	
Yes	14	10.3 (2.13 to 50.26)	0.004	-	-	8.50 (1.14 to 63.39)	0.037
Hospitalisations 12 months prior to the study							
No	37	1.00		1.00		1.00	
Yes	11	9.90 (2.05 to 47.89)	0.004	19.3 (2.39 to 155.6)	0.005	15.93 (1.60 to 158.3)	0.018
FEV_1 (+1 %)	48	0.97 (0.94 to 1.00)	0.217	-	-	-	-
BSI stage			0.071	-	-	-	-
Mild	15	1.00		-	-	-	-
Moderate	19	2.62 (0.24 to 28.19)	0.426	-	-	-	-

Severe	14	10.5 (1.06 to 103.5)	0.044	-	-	-	-
6MWT (+1 meter)	48	0.99 (0.98 to 1.00)	0.336	-	-	-	-

Abbreviations. OR: odds-ratio; CI: confidence interval; h: hours; MRC: medical research council; FEV_1: forced expiratory volume in one second; BSI: bronchiectasis severity index; 6MWT: 6 minutes walking test.

Data are shown as estimated ORs (95% CIs) of the explanatory variables in the low level of physical activity group. The OR represents the odds that low level of physical activity will occur given exposure to the explanatory variable, compared to the odds of the outcome occurring in the absence of that exposure. The P-values are based on the null hypothesis that all ORs relating to an explanatory variable are equal to unity (no effect).

[a] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.76. Area under the ROC curve for the multivariable model, AUC = 0.87 (0.75 to 0.98).

[b] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.35. Area under the ROC curve for the multivariable model, AUC = 0.89 (0.78 to 1.00).

Online Table3. Physical activity baseline characteristics of hospitalised vs. non-hospitalised bronchiectasis patients including weekend data.

	All patients	Hospitalised	Non-hospitalised	p value
	N=64	N=15 (23%)	N=49 (77%)	
Physical Activity				
Light PA, 1.6 - <3.0 MET-min/day	211.4 (75.9)	184.3 (37.0)	220.2 (82.8)	0.110
Moderate PA, 3.0 - <6.0 MET-min/day	112.9 (80	84.4 (64)	121.6 (82.8)	0.050
Vigorous PA, 6.0 - <8.7 MET-min/day	0.81 (2.17)	0.4 (1.1)	0.9 (2.4)	0.486
MVPA, min/day	113.9 (80.6)	85.1 (64.5)	122.7 (83.5)	**0.047**
Steps per day	6,933 (3,345)	5,156.11 (3464)	7,477.4 (3,146)	**0.019**
Sedentary time, hours per day	7.51 (1.77)	8.53 (1.52)	7.21 (1.74)	**0.018**

Data are presented as n (%), mean (SD) or median (P_{25};P_{75}). *Data presented as mean (SD), and range.

Abbreviations. BMI: body mass index; MRC: medical research council; COPD: chronic obstructive pulmonary disease; BSI: bronchiectasis severity index; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; 6MWT: 6 minutes walking test; PA: physical activity; MET: metabolic equivalent tasks; MVPA: moderate-to-vigorous physical activity.

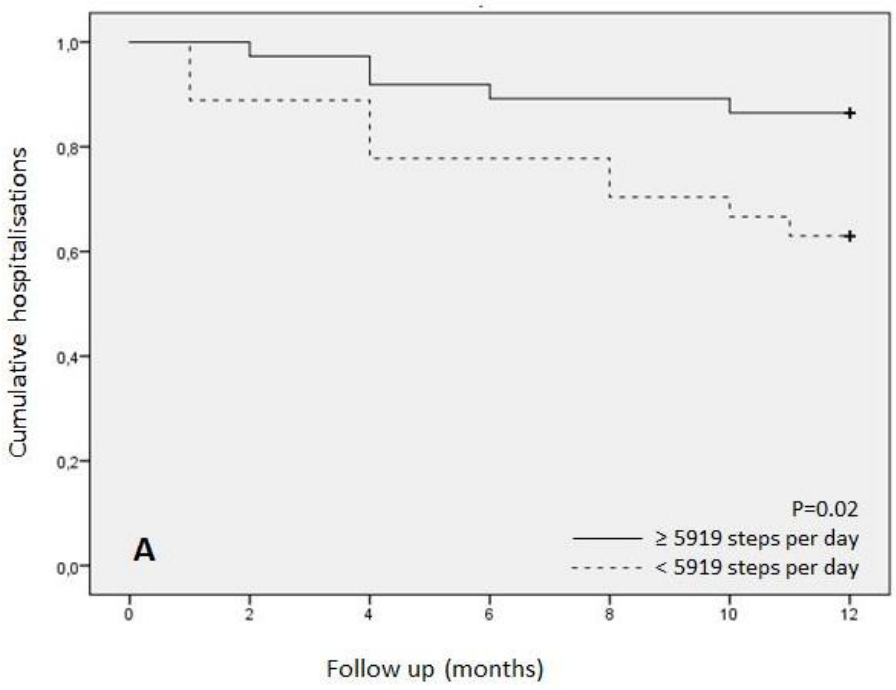
[a] Could have more than one medication.

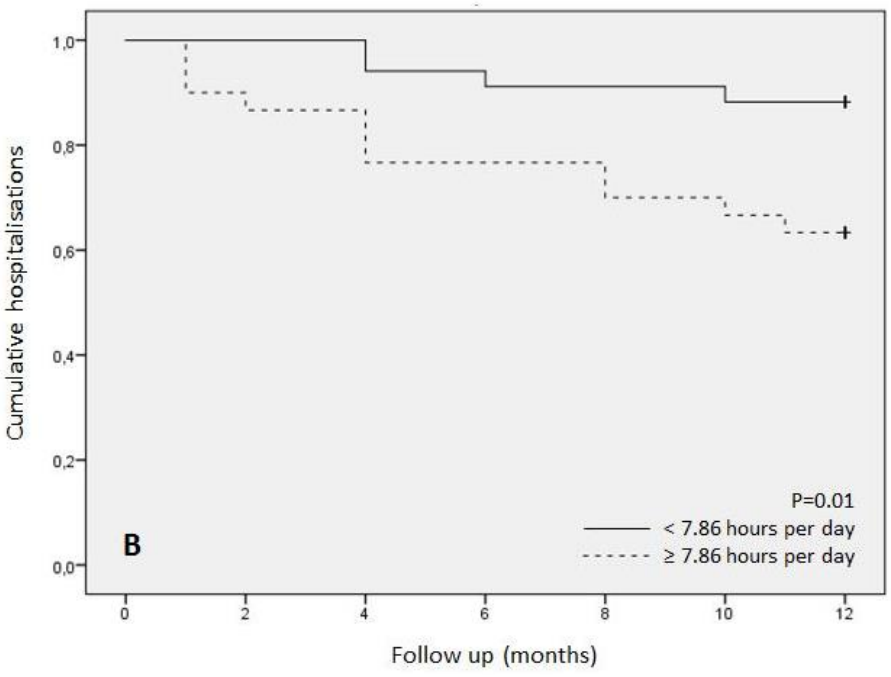
Online Table4. Steps per day, sedentary time, moderate PA and MVPA cut-off points for hospitalisation including weekend data.

Hospitalisation variable	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Best Cut-off	p value
Steps per day	0.71 (0.54 to 0.87)	65	67	5,919	0.017
Sedentary time (hours)	0.72 (0.57 to 0.87)	73	63	7.86	0.009
Moderate PA (min)	0.67 (0.50 to 0.84)	61	60	89.6	0.050
MVPA (min)	0.67 (0.50 to 0.84)	61	60	89.9	0.047

Abbreviations. AUC: area under the curve; CI: confidence interval; PA: physical activity; min: minutes; MVPA: moderate-to-vigorous physical activity.

Figure1. Kaplan-Meier graphics according to ROC curve cut-off points including weekend data.
1A. <5919 steps per day; 1B. ≥7.86 hours of sedentary behaviour.





Online Table5. Crude and adjusted associations between level of physical activity in steps per day and sedentary time and bronchiectasis hospitalisations including weekend data.

	N	Crude OR (95% CI)	p value	Adjusted OR (95% CI) [a]	p value	Adjusted OR (95% CI) [b]	p value
Steps per day						-	-
High physical activity (≥5,919 steps per day)	37	1.00		1.00		-	-
Low physical activity (<5,919 steps per day)	27	3.76 (1.11 to 12.80)	0.034	4.75 (0.89 to 25.48)	0.069	-	-
Sedentary time				-	-		
Sedentary (≥7.8h)	34	4.34 (1.21 to 15.63)	0.025	-	-	2.96 (0.66 to 13.30)	0.158
Non-sedentary (<7.8h)	30	1.00		-	-	1.00	
Age (+1 year)	64	1.01 (0.97 to 1.05)	0.646	0.99 (0.94 to 1.04)	0.717	1.00 (0.95 to 1.05)	0.977
Gender			0.500		0.429		0.592
Male	21	1.00		1.00		1.00	
Female	43	0.66 (0.20 to 2.19)		0.55 (0.12 to 2.44)		0.68 (0.16 to 2.84)	
Pseudomonas aeruginosa			0.001		0.014		0.007
No	45	1.00		1.00		1.00	
Yes	19	8.89 (2.44 to 32.43)		6.12 (1.44 to 26.04)		7.17 (1.72 to 29.79)	
Hospitalisations 12 months prior to the study			0.007		0.013		0.028
No	51	1.00		1.00		1.00	
Yes	13	6.27 (1.66 to 23.62)		8.22 (1.55 to 43.62)		5.57 (1.21 to 25.75)	
MRC Dyspnoea Scale			0.347	-	-	-	-
1	12	1.00		-	-	-	-
2	39	2.41 (0.27 to 21.81)	0.435	-	-	-	-

3	10	7.33 (0.66 to 81.36)	0.105	-	-	-	-
4	3	-	-	-	-	-	-
FEV_1 (+1 %)	64	0.97 (0.94 to 1.00)	0.034	-	-	-	-
BSI stage			0.004	-	-	-	-
Mild	23	1.00		-	-	-	-
Moderate	22	1.66 (0.25 to 11.02)	0.601	-	-	-	-
Severe	19	11.67 (2.12 to 64.33)	0.005	-	-	-	-
6MWT (+1 meter)	64	0.99 (0.99 to 1.00)	0.050	-	-	-	-

Abbreviations. OR: odds-ratio; CI: confidence interval; h: hours; MRC: medical research council; FEV_1: forced expiratory volume in one second; BSI: bronchiectasis severity index; 6MWT: 6 minutes walking test.

Data are shown as estimated ORs (95% CIs) of the explanatory variables in the low level of physical activity group. The OR represents the odds that low level of physical activity will occur given exposure to the explanatory variable, compared to the odds of the outcome occurring in the absence of that exposure. The P-values are based on the null hypothesis that all ORs relating to an explanatory variable are equal to unity (no effect).

[a] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.27. Area under the ROC curve for the multivariable model, AUC = 0.86 (0.75 to 0.97).

[b] Initial multivariable model comprised age, gender, chronic colonisation by *Pseudomonas aeruginosa*, hospitalisations 12 months prior to the study, MRC Dyspnoea Scale, FEV_1 %predicted, BSI stage and 6MWT. Final multivariable model was adjusted for age, gender, chronic colonisation by *Pseudomonas aeruginosa* and hospitalisations 12 months prior to the study. Hosmer–Lemeshow goodness-of-fit test for the multivariable model, p = 0.14. Area under the ROC curve for the multivariable model, AUC = 0.84 (0.72 to 0.96).