

## Evaluation of the differences in the clinical manifestations of chronic obstructive pulmonary disease between men and women: a cross-sectional analytical study

### *Avaliação das diferenças nas manifestações clínicas da doença pulmonar obstrutiva crônica entre homens e mulheres: um estudo transversal analítico*

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**ABSTRACT:** *Introduction:* In the latter, there was a predominance of men among COPD patients; however, the prevalence of COPD among women has been increasing. Thus, knowing the presentation of the disease in this group is of great importance for planning the therapeutic approach. *Objective:* To evaluate the differences in COPD symptoms in men and women, as well as their impact and the associated risk factors in both sexes. *Methodology:* This was an analytical, observational and cross-sectional study in which 203 patients with COPD were evaluated, with spirometric diagnosis being the main inclusion criterion. The descriptive analysis was stratified between sexes, and nonparametric tests were performed. The COPD Assessment Test (CAT), Charlson Comorbidity Index and FRAIL-BR questionnaires were applied, and these were the variables studied between genders. *Results:* the impact of the symptoms measured with CAT was greater in women ( $p = 0.04$ ) and clinically significant. *Conclusion:* Women with COPD are more symptomatic.

**Keywords:** Chronic obstructive pulmonary disease; Gender; Women.

**RESUMO:** *Introdução:* Apesar de ser uma doença tipicamente masculina, a prevalência da DPOC entre as mulheres vem crescendo. Assim, conhecer a apresentação da doença neste grupo é de grande importância para o planejamento da abordagem terapêutica. *Objetivo:* Avaliar as diferenças de sintomas da DPOC em homens e mulheres, bem como seu impacto e os fatores de risco associados em ambos os sexos. *Metodologia:* Estudo analítico, observacional e transversal em que foram avaliados 203 pacientes com DPOC, sendo o diagnóstico espirométrico o principal critério de inclusão. A análise descritiva foi estratificada entre gêneros e foram realizados testes não paramétricos. Foram aplicados os questionários COPD Assessment Test (CAT), Charlson Comorbidity Index e FRAIL-BR, sendo estas as variáveis estudadas entre os gêneros. *Resultados:* O impacto dos sintomas medidos com o CAT foi maior nas mulheres ( $p=0,04$ ) e clinicamente significativo. *Conclusão:* Mulheres com DPOC são mais sintomáticas.

**Palavras-chaves:** Doença pulmonar obstrutiva crônica; Gênero; Mulheres.

Study conducted at the Juarez Barbosa High-Cost Medicines Center. A poster was presented at the VIII Brazilian Congress of COPD and Smoking with the partial results of this study in João Pessoa-PB on August 16, 2019.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and pulmonary airflow limitation<sup>1</sup>. It is a heterogeneous, progressive disease and is associated with systemic repercussions that compromise the health status of the patient<sup>2-5</sup>. It is a major public health problem and is the most prevalent chronic respiratory disease in the world, reaching more than 10% of the adult population worldwide<sup>4,6,7</sup>. Currently, it is the third leading cause of death worldwide. In Brazil, deaths from COPD represent more than 40,000 cases annually, and the expenditure on the Unified Health System reached 103 million reais in 2011, referring to 142,635 hospitalizations<sup>8</sup>. Unfortunately, these values tend to worsen in the coming decades due to the continuous exposure of the population to risk factors, and a large part of this increase will be among women<sup>1,6,9</sup>.

The influence of sex on the heterogeneity of COPD has been widely studied in the last two decades. Studies conducted in research centers in different countries have reported that, for the same smoking load, women report more intense symptoms, have a greater impact on quality of life, have more frequent and early exacerbations, lower tolerance to physical exercise, and worse perception of the disease itself. Another important point of this discussion is the numerous consequences of anxiety and depression related to lung disease, which can be expressed by greater difficulty in smoking cessation, impaired quality of life and more frequent sleep disorders<sup>11,12,14-17</sup>.

Studies increasingly point to a possible susceptibility and sex-specific morbidity<sup>5</sup>. It is known that smoking is the most important risk factor for the onset of COPD, and it is possible that women are more vulnerable to its toxicity, presenting more intense symptoms and a greater decline in lung function<sup>14</sup>. In addition, it is likely that, for this reason, females seem to experience a lower quality of life than males with a similar history and smoking load<sup>12</sup>.

Despite the recent interest in the differences in COPD between sexes, the amount of information found in the literature is still scarce. Few studies and reports have been found, especially comparing the impact of the disease in both sexes, from the point of view of clinical and symptomatic presentation. Once the impact and importance of COPD on the Brazilian and global population is considered, a detailed investigation on the subject becomes necessary, even so that it is possible, in the future, for a gender-specific adaptation of patient management and follow-up. Thus, the present study aims to evaluate the differences in symptoms and their impact on men and women with COPD.

## METHODOLOGY

This is an analytical, observational and cross-sectional study conducted in Goiânia - GO at the Central State Medicines of High Cost (CMAC) between January 2018 and January 2020. The individuals who composed the sample were included sequentially by a convenience sampling technique. The recruited patients were among those registered in the Program for Public Access to High-Cost Medication for the treatment of COPD maintenance of SES-GO and were invited to participate in the study when they attended the CMAC-GO for medication withdrawal.

Patients who met the following inclusion criteria were studied: patients with dyspnea, chronic cough or sputum producers and exposed to COPD risk factors, confirmed by spirometric evaluation (FEV<sub>1</sub>/FVC after bronchodilator <0.7) or clinical diagnosis by a pulmonologist or general practitioner; user of medication provided by CMAC-GO for treatment of COPD and exclusively registered in the medication supply program; clinical stability (last exacerbation for more than 4 weeks and/or last hospitalization for more than 6 weeks); and individuals able to provide consent via informed consent form. The risk factors considered were exposure to smoke, smoking, asthma and other risk factors for obstruction. The following definitions of COPD exacerbation were considered: worsening of symptoms, baseline respiratory symptoms: dyspnea, cough, sputum production, and change in sputum color. The definitions of COPD diagnosis and exacerbation were considered according to GOLD 2018<sup>1</sup>. Patients with interstitial lung disease, collagen disease, use of anti-IGE, alpha-1-antitrypsin deficiency, and cystic fibrosis were excluded. Patients registered in the CMAC system as having COPD and asthma were not excluded; only those who reported COPD during the interview were included in the system as only asthmatic.

The variables were collected using a pretested data collection instrument<sup>18</sup>: sociodemographic data, FEV<sub>1</sub> (through spirometry delivered by users to the unit during registration), dispensed medication, dyspnea (mMRC), adherence to medication (through verification in the CMAC-GO system if there was a lack of patient in the dispensing of medications), occurrence of exacerbations in the last 12 months, current smoking and another risk factor for fixed obstruction of COPD. COPD symptoms questionnaires were applied: COPD Assessment Test (CAT)<sup>19</sup>, comorbidity questionnaire (Charlson Comorbidity Index)<sup>20</sup> and FRAIL-BR (questionnaire for assessment of frailty syndrome)<sup>21</sup>.

This study was approved by the Ethics Committee of the Clinics Hospital of the Federal University of Goiás and then passed on to the Leide das Neves Ferreira Ethics Committee of the State Health Department of the State of Goiás. It was also approved by the Institutional Review Committee of the Federal University of Goiás (CAAE 79462917.9.0000.5078). The informed consent form was

signed by all patients in accordance with the principles of the Declaration of Good Clinical Practice of Helsinki.

### Analysis and statistical modeling

The data were analyzed using SPSS software, version 24.0. Initially, the descriptive analysis was performed for the total sample and stratified for men and women. The quantitative variables were expressed as medians and interquartile ranges (IQRs) due to lack of normality, and the qualitative variables were expressed as absolute (n) and relative (%) frequencies. To analyze the differences between men and women, nonparametric tests were performed. The qualitative variables were compared between groups using Pearson's chi-square or Fisher's exact test, and the quantitative variables were compared using the Mann-Whitney test for independent samples. Variables with  $p < 0.05$  were considered statistically significant.

## RESULTS

A total of 847 people were invited to participate. Of these, 162 refused to participate in the study, 192 were not the patients themselves at the time of withdrawal, being relatives or other persons authorized to perform the study, 127 did not have spirometry and 163 did not meet the inclusion criteria. Finally, data from 203 patients were analyzed (Figure 1), of which 94 were female (46.3%) and 109 were male (53.7%).

Men and women were similar in age, with a median of 68 years, but there was a higher proportion of elderly

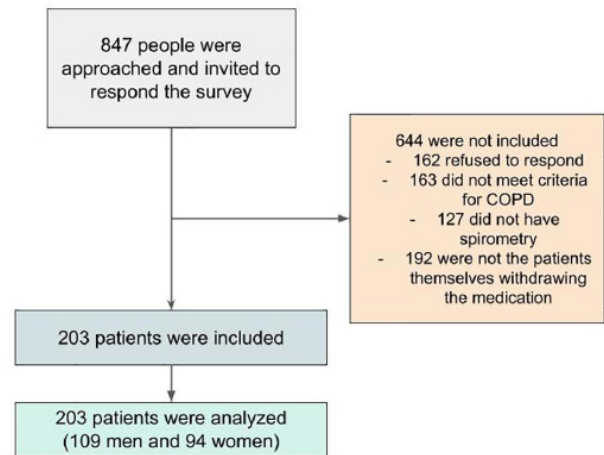


Figure 1: Patient capture system

women (Table 1). Regarding the other clinical variables, men and women were similar regarding the following variables: presence of exacerbation in the last 12 months, hospitalization in the last 12 months and FEV1%. The prevalence of current smoking was higher in women than in men. The presence of asthma was similar between sexes (Table 1).

There was no significant difference between the sexes regarding the results of the FRAIL-BR and CCI questionnaires, which quantify frailty and the burden of comorbidities, respectively. Of the total, 86.2% of patients were classified as adherent to the medication.

Table 1. Descriptive and comparative analysis of clinical characteristics between men and women.

Variables	Total (n=203)		Masculino (n=109)		Feminino (n=94)		p
Age (years), median (IQR)	68	(62-73)	68	(64-73)	67	(59-72)	0,014♦
Age group (years), n (%)							
< 60 anos	67	82,3	97	89	70	74,5	<b>0,007*</b>
≥ 60 anos	36	17,7	12	11	24	25,5	
Exacerbation in the last 12 months, n (%)	115	56,7	61	56	54	57,4	0,832♦
Hospitalization in the last 12 months, n (%)	43	21,2	21	19,3	22	23,4	0,472*
VEF1(%), mediana (IIQ)	52	(39-64)	52	(37,5-62,7)	54,5	(41-65)	0,264♦
Current smoking, n (%)	27	13,30	9	8,30	18	19,10	<b>0,023*</b>
Asthma, n (%)	45	22,20	21	19,30	24	25,50	0,284*

IIQ: Intervalo interquartil; \*Teste de qui-quadrado de Pearson; ♦ Teste de Mann-Whitney para amostras independentes. VEF1: Volume expiratório forçado no primeiro segundo

**Table 2.** Descriptive and comparative analysis of the questionnaires applied and use of COPD medications between genders

Variables	Total (n=203)		Male (n=109)		Female (n=94)		p
Charlson Comorbidity Index (CCI), median (IQR)	3	(3-4)	4	(3-5)	3	(3-4)	0,095♦
FRAIL scale, median (IQR)	2,0	(1,0-3,0)	2,5	(1,0-3,0)	2	(1-3)	0,343*
Patient compliance to medication, n (%)	170	83,7	93	85,3	77	81,9	0,515*
Using formoterol alone	34	16,7	19	17,4	15	16	0,779*
Using formoterol/budesonide	86	42,5	42	38,5	44	36,8	0,234*
Using budesonide alone	1	0,5	1	0,9	--	--	1,000□
Using salmeterol/fluticasone	65	32	40	36,7	25	26	0,124*
Using tiotropium	121	59,6	70	64,2	51	54,3	0,149*
Using other medication	17	8,4	11	10,1	6	6,4	0,324*

IQR: Interquartile range; \*Pearson’s chi-square test; □ Fisher’s exact test; □ Mann–Whitney test for independent samples

The medians of mMRC (dyspnea) and CAT (impact of symptoms) were 3 and 15, respectively. Dyspnea was

similar between men and women, but the median CAT was higher in women than in men (Table 3).

**Table 3.** Descriptive and comparative analysis of symptomatology between men and women

Variables	Total (n=203)		Male (n=109)		Female (n=94)		p
mMRC, median (IQR)	3	(2-4)	3	(2-4)	3	(2-4)	0,404♦
CAT, median (IQR)	15	(7-21)	13	(6-20)	16	(8,8-23)	0,041♦

IIQ: Intervalo intercuartil; ♦Teste de Mann–Whitney para amostras independentes.

## DISCUSSION

In this study, there was a significant difference in the median (of values) CAT between women and men (16 versus 13; p = 0.04). As demonstrated in the study conducted in London in 2014 by Kon<sup>24</sup>, values above 2 points are considered clinically significant; therefore, we can affirm that the difference found here between men and women is truly relevant in medical practice. The women obtained higher scores on a questionnaire that evaluated both physical symptoms and aspects related to the impact of the disease on quality of life. Therefore, we can see that the disease affects women in a different way, which should be taken into account in decision-making. decisions regarding these patients.

Our results are consistent with other studies conducted in different research centers<sup>2-6,10,12,15,16,25</sup>, which

have shown that, for the same degree of airflow obstruction, patients with COPD exhibit heterogeneous clinical features. In addition, COPD surveillance studies suggest greater intolerance to exercise, greater impairment of health status, worse quality of life and higher levels of depression and anxiety in women<sup>2</sup>. All these findings agree with ours, and therefore, we can see the difference in the impact of COPD in relation to gender.

There are data that relate the divergence in clinical manifestations between sexes to the difference in the susceptibility of women to smoke<sup>3,10</sup>. There is also some evidence of a difference in the perception of care received between men and women, which could interfere with the perception of their health status<sup>11</sup>. In addition, anxiety, depression, greater susceptibility of women to smoking and hormonal and anatomical differences are factors of great importance when considering the explanation for such

evidence<sup>15,16</sup>. Regarding anatomy, women have lower lung volume and relatively smaller airways than men, so there may be a higher concentration of tobacco per unit area on the surface of the small airways, leading to greater damage to them<sup>1,12,13,15,25</sup>.

The inflammatory response to cigarette smoke may be different between sexes due to the diversity of expression and activity of cytochrome P450 enzymes<sup>14,17</sup>. Estradiol stimulates the hyperfunctioning of such smoke-metabolizing enzymes, increasing oxidative stress in the airway epithelium and making the female lungs more susceptible to damage in response to smoking. The possible role of hormonal fluctuation in perimenopause in the decline of lung function is also suggested. All these events are related to a greater deterioration of the female respiratory system, generating a greater propensity of women to develop COPD, greater risk of hospitalizations and higher mortality from respiratory failure in those who have severe disease, even with a similar smoking burden<sup>4,10,12,14,17</sup>.

Therefore, the large number of clinical studies conducted in recent years addressing the greater risk of women developing more severe COPD, presenting more intense symptoms, with significant worsening of the quality of life and other negative outcomes<sup>13</sup> is observed.

Despite the significant difference relative to the CAT, there was no difference in the mMRC values for the two sexes. As the mMRC scale specifically evaluates the presence and degrees of dyspnea, it is possible to state that there was no symptomatic difference in dyspnea between sexes. It is assumed, therefore, that the difference observed in the CAT values can be explained by other aspects of the symptoms, such as cough, sputum, chest pain, activities at home, energy and sleep. This may indicate that our results point not only to a more significant symptomatology in females but also to a greater impairment of quality of life among women. This result would also result in social and family consequences, as women are usually responsible for activities related to the domestic environment.

Some studies differ from our findings regarding dyspnea. A cohort of 4484 patients with COPD, for example, showed that women report severe dyspnea more frequently than men, suggesting that women may be significantly more symptomatic regarding the dyspnea factor<sup>15</sup>. This difference is possibly related to the large disparity between sample sizes.

The comparison between sexes in this study could be safely performed due to the median FEV1 found in our study (53%), which showed equivalent lung function between the sexes. In addition, both genders had the same level of frailty and the same load of comorbidities, as demonstrated by the FRAIL-BR and CCI questionnaires, respectively. Thus, it was found that, for the same lung function, frailty and similar comorbidities, women with COPD reported greater impacts on their health status.

There was a higher proportion of elderly women than men (25.5% versus 11.0%;  $p = 0.007$ ), which can be explained by the greater longevity of women in the general population. Men have a higher mortality rate, mainly due to involvement in deaths from external causes, higher consumption of licit and illicit drugs and lower demand for health services<sup>22</sup>.

The prevalence of current smoking was significantly higher in women (19.1% versus 8.3%;  $p = 0.023$ ), which interferes with the interpretation of clinical manifestations presented by patients<sup>26</sup>. The maintenance of smoking is one of the main aggravating factors of COPD. Patients who continue to smoke have a progressive decrease in lung function and symptoms produced directly by tobacco<sup>26,27</sup>. There is suggestive evidence that smoking cessation is more difficult among women. A study conducted in Canada suggested that women with a history of smoking and COPD have higher rates of nicotine dependence than men<sup>11</sup>. Other studies have shown that female smokers are more influenced by negative mood, faster nicotine metabolism and a higher prevalence of depression<sup>23</sup>. Therefore, it is clear that women face greater physiological, social and psychological difficulties when they stop smoking.

A possible confounding factor for the greater symptomatology in women could be a higher prevalence, among the female sample, of Asthma Overlap Syndrome and COPD. The presence of this syndrome would result in more severe clinical manifestations than COPD itself, with worsening of the patient's health status<sup>28</sup>. However, the prevalence of asthma in this study was not significantly different between sexes.

The present study has limitations. The inclusion of patients occurred sequentially, generating a nonhomogeneous sample. Thus, it is possible that it does not reliably translate the population into its varieties and demographic characteristics. In addition, it should be considered that only patients able to go to CMAC-GO were included; thus, there was no evaluation of patients with more severe and disabling disease, which may generate a sample not corresponding to the symptomatic reality of all patients with COPD.

Even with such weaknesses of the study, our results highlight what has become a topic of interest in the study of COPD: the evidence that the disease presents different behavior in females. For the same pulmonary impairment, women with COPD are more symptomatic. Due to the small amount of information on the subject in the literature, this study provides relevant information on COPD in Brazilian women.

Despite the growing discoveries, there is still a need for more studies investigating the differences in the mechanisms of oxidative stress and airway fibrosis between sexes so that, in the future, together with the knowledge of the differences in symptoms, the treatment of COPD can be more specific and personalized in each of the genera<sup>14</sup>.

We conclude, therefore, that there is an important difference regarding the symptoms of COPD between the sexes. Our results showed that although there was no

significant difference in pulmonary air function, women had higher CAT values than men, a difference that can be considered clinically relevant.

**Authors participations:** *MFR*: Compliance with being responsible for the accuracy or integrity of any part of the study, participation in the review and approval of the final version. *ACGF*: Substantial contribution to the study design or data interpretation, participation in the review and approval of the final version. *GGB*: Substantial contribution to the study design or data interpretation and participation in the drafting of the preliminary version. *IRSC*: Substantial contribution to the study design or data interpretation and participation in the drafting of the preliminary version. *MASA*: Substantial contribution to the study design or data interpretation and participation in the drafting of the preliminary version.

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The authors deny other conflicts of interest in this study.

## REFERENCES

- Global Initiative for Chronic Obstructive Lung Disease. Fontana, WI, USA; 2020. Available from: [www.goldcopd.org](http://www.goldcopd.org).
- Ferrari R, Tanni SE, Lucheta PA, Faganello MM, Antonialli R, Godoy I. Preditores do estado de saúde em pacientes com DPOC de acordo com o gênero. *J Bras Pneumol*. 2010;36(1):37-43. doi: 10.1590/S1806-37132010000100008.
- Gu SY, Deng XJ, Li QY, Sun XW, Xu JF, Li HP. Gender differences of chronic obstructive pulmonary disease associated with manifestations on HRCT. *Clin Respir J*. 2017;11(1):28-35. doi: 10.1111/crj.12297.
- Jia G, Lu M, Wu R, Chen Y, Yao W. Gender difference on the knowledge, attitude, and practice of COPD diagnosis and treatment: A national, multicenter, cross-sectional survey in China. *Int J COPD*. 2018;13:3269-80. doi: 10.2147/COPD.S176173.
- Lisspers K, Larsson K, Janson C, Ställberg B, Tsiligianni I, Gutzwiller FS, et al. Gender differences among Swedish COPD patients: results from the ARCTIC, a real-world retrospective cohort study. *NPJ Prim Care Respir Med*. 2019;29(1):1-8. <http://dx.doi.org/10.1038/s41533-019-0157-3>.
- Almagro P, López García F, Cabrera F, Montero L, Morchón D, Díez J, et al. Comorbidity and gender-related differences in patients hospitalized for COPD. The ECCO study. *Respir Med*. 2010;104(2):253-9. doi: 10.1016/j.rmed.2009.09.019.
- Soriano JB, Kendrick PJ, Paulson KR, Gupta V, Abrams EM, Adedoyin RA, et al. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med*. 2020;8(6):585-96. doi: 10.1016/S2213-2600(20)30105-3.
- Rabahi MF. Epidemiologia da DPOC: enfrentando desafios. *Pulmão RJ*. 2013;4-8. <http://repositorio.bc.ufg.br/handle/ri/17374>.
- Ntritsos G, Franek J, Belbasis L, Christou MA, Markozannes G, Altman P, et al. Gender-specific estimates of COPD prevalence: A systematic review and meta-analysis. *Int J COPD*. 2018;13:1507-14. doi: 10.2147/COPD.S146390.
- Raghavan D, Varkey A, Bartter T. Chronic obstructive pulmonary disease: the impact of gender. *Curr Opin Pulm Med*. 2017;23(2):117-23. doi: 10.1097/MCP.0000000000000353.
- Jenkins CR, Chapman KR, Donohue JF, Roche N, Tsiligianni I, Han MLK. Improving the management of COPD in women. *Chest*. 2017;151(3):686-96. doi: 10.1016/j.chest.2016.10.031.
- Gut-Gobert C, Cavaillès A, Dixmier A, Guillot S, Jouneau S, Leroyer C, et al. Women and COPD: do we need more evidence? *Eur Respir Rev*. 2019;28(151). <http://dx.doi.org/10.1183/16000617.0055-2018>.
- Sørheim IC, Johannessen A, Gulsvik A, Bakke PS, Silverman EK, DeMeo DL. Gender differences in COPD: Are women more susceptible to smoking effects than men? *Thorax*. 2010;65(6):480-5. doi: 10.1136/thx.2009.122002.
- Barnes PJ. Sex differences in chronic obstructive pulmonary disease mechanisms. *Am J Respir Crit Care Med*. 2016;193(8):813-24. doi: 10.1164/rccm.201512-2379ED.
- DeMeo DL, Ramagopalan S, Kavati A, Vegesna A, Han MK, Yadao A, et al. Women manifest more severe COPD symptoms across the life course. *Int J COPD*. 2018;13:3021-9. doi: 10.2147/COPD.S160270.
- Martinez CH, Rappala S, Plauschinat CA, Giardino ND, Rogers B, Beresford J, et al. Gender differences in symptoms and care delivery for chronic obstructive pulmonary disease. *J Womens Health (Larchmt)*. 2012;21(12):1267-74. doi: 10.1089/jwh.2012.3650.
- Martinez FJ, Curtis JL, Sciruba F, Mumford J, Giardino ND, Weinmann G, et al. Sex differences in severe pulmonary emphysema. *Am J Respir Crit Care Med*. 2007;176(3):243-52. doi: 10.1164/rccm.200606-828OC.
- Dias LS. Avaliação da fragilidade em pacientes com doença pulmonar obstrutiva crônica [dissertação]. Goiânia, GO: Universidade Federal de Goiás; 2020. p.14-5. Disponível

em <http://repositorio.bc.ufg.br/tede/handle/tede/10832>.

19. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J*. 2009;34(3):648-54. doi: 10.1183/09031936.00102509.
20. 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;40:373-83. doi: 10.1016/0021-9681(87)90171-8.
21. Fabricio-Wehbe SCC, Cruz IR, Haas VJ, Diniz MA, Dantas RAS, Rodrigues RAP. Reprodutibilidade da versão Brasileira adaptada da Edmonton Frail Scale para idosos residentes na comunidade. *Rev Latino-Am Enfermagem*. 2013;21(6):1330-6. doi: 10.1590/0104-1169.2933.2371.
22. Veras RP, Ramos LR, Kalache A. Crescimento da população idosa no Brasil: transformações e consequências na sociedade. *Rev Saúde Pública*. 1987;21(3):225-33. doi: 10.1590/S0034-89101987000300007.
23. Lombardi EMS, Prado GF, Santos U de P, Fernandes FLA. O tabagismo e a mulher: riscos, impactos e desafios. *J Bras Pneumol*. 2011;37(1):118-28. doi: 10.1590/S1806-37132011000100017.
24. Kon SSC, Canavan JL, Jones SE, Nolan CM, Clark AL, Dickson MJ, et al. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *Lancet Respir Med*. 2014;2(3):195-203. doi: 10.1016/S2213-2600(14)70001-3
25. Prescott E, Bjerg AM, Andersen PK, Lange P, Vestbo J. Gender difference in smoking effects on lung function and risk of hospitalization for COPD: Results from a Danish Longitudinal Population Study. *Eur Respir J*. 1997;10(4):822-7. doi: 10.1183/09031936.97.10040822.
26. Nunes E. Consumo de tabaco. Efeitos na saúde. *Rev Port Med Geral Fam*. 2006;22:225-44. doi: 10.32385/rpmgf.v22i2.10231.
27. Araújo AJ. Tratamento do tabagismo pode impactar a DPOC. *Pulmão RJ*. 2009;1(1):20-33.
28. Reis AP, Stirbulov R. Síndrome de sobreposição asma e DPOC. *Arq Asma Alerg Imunol*. 2017;1(2):189-94. doi: 10.5935/2526-5393.20170022.

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