Original Article
Cross-sectional study of pain-related variables before and during the COVID-19 pandemic in patients with COPD

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ABSTRACT
Background: The impact of the COVID-19 pandemic influences of COPD patients. The worsening of their health status may contribute to a higher pain prevalence.

Aim: The aim of this study was to analyze the pain-related variables before and during the COVID-19 pandemic in patients with chronic obstructive pulmonary disease.

Methods: In this cross-sectional case-control study, stable patients with chronic obstructive pulmonary disease without a COVID-19 diagnosis were evaluated before and during the pandemic. The main outcomes were the pronociceptive pain profile (general pain sensitivity, pain intensity, pain interference, and pressure pain sensitivity) and the psychological vulnerability (perceived health status, anxiety, and depression).

Results: Our results showed that patients with chronic obstructive pulmonary disease during COVID-19 pandemic experienced higher general pain sensitivity and intensity with statistical differences in pain interference (p < .001), being the overall perceived health status lower than before the pandemic (p < .05).

Conclusions: We concluded that patients with chronic obstructive pulmonary disease during the COVID-19 pandemic showed a rise the pronociceptive pain profile accompanied by increased psychological vulnerability.

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Since the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported, health care systems have been affected by the worldwide spread of cases and the increasing difficulty of managing population needs (Ohannesian et al., 2020). The effect of the COVID-19 pandemic has been particularly strong on subjects suffering from single or multiple chronic illnesses, the disabled, and those with unstable health status (Giansanti et al., 2020). As such, all chronic respiratory patients are particularly affected by this outbreak.

In the case of patients with chronic obstructive pulmonary disease (COPD), while the COVID-19 pandemic continues, health systems have experienced many difficulties with their diagnosis and routine management. Additionally, patients with COPD show increased anxiety in the presence of COVID-19 infection, denial of care, associated symptoms, and death (Philip et al., 2020).

The COVID-19 pandemic influences the general health status of patients with COPD and other comorbidities, affecting all health-related outcomes because of their previous vulnerability (Leung et al., 2020).

Well-known symptoms of COPD include dyspnea, cough, and wheezing, and other symptoms such as nausea, fatigue, and insomnia are also regularly reported (Janssen et al., 2011), but recent literature indicates that pain is also a significant COPD symptom, with an estimated prevalence of 32%-60% (van Dam et al., 2014). There are multiple factors related to COPD that may contribute to a higher pain prevalence in patients with COPD, highlighting the systemic inflammatory process, musculoskeletal disorders, comorbidities (Roberts et al., 2013), sedentary lifestyle, and worse clinical symptoms such as quality of life, breathlessness, insomnia, fatigue, anxiety, depression (Borge et al., 2010), and malnutrition risk (Borge et al., 2011).

However, the actual situation has exposed a variety of chronic pathologies with a worsening of their clinical outcomes due to the restriction of physical activity, social isolation, the difficulty of follow-ups, and general management of the pathologies. In this...
line, more research on this topic is needed, specifically pain-related variables which can be affected during the COVID-19 pandemic in patients with COPD worsening all health-related outcomes.

Therefore, the purpose of this study was to analyze the pain-related variables before and during the COVID-19 pandemic in COPD patients.

Methods

Study Design and Setting

This cross-sectional case-control study was performed between November 2018 and February 2021. Ethical approval for this study was obtained from the ethics committee of the San Cecilio and Virgen de las Nieves University Hospital (Granada, Spain) in accordance with the Declaration of Helsinki review in 2013. The study was registered in ClinicalTrials.org (NCT04319523).

Participants

Patients with COPD were recruited during their routine clinical visits from the Pneumology Service. The inclusion criteria of was: (1) stable COPD patients with a grade III and IV of Global Initiative for Chronic Obstructive Lung Disease (GOLD) (Vestbo et al., 2013); (2) 60 years of age or older without COVID-19 diagnosis during the study; and (3) provided informed consent for research participation. Exclusion criteria included: (1) the presence of psychiatric or cognitive disorders, progressive neurological disorders, cancer, or chronic pain; (2) cognitive impairment or inability to understand the tests; (3) diagnosis of widespread chronic pain or other causes of acute pain; and (4) incapacity to provide informed consent. Patients who suffered any health problem and experienced an exacerbation of COPD in the previous month were also excluded to ensure the patient’s symptoms were stable.

Patients who agreed to participate and met the eligibility criteria were provided with an explanation of the study protocol and invited to give written informed consent. All participants in this study signed informed consent before their inclusion in the study.

Measurements

After signing informed consent, all participants were evaluated before and during the COVID-19 pandemic, being the COVID-19 lockdown on 14 March 2020. Descriptive data of participants (age, sex, comorbidities, employment status, and marital status), body mass index, and handgrip strength were collected. The comorbidities were assessed by the Charlson Comorbidity index (Charlson et al., 1994).

Cognitive impairment was measured with the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005). Functionality was evaluated with the Functional Independence Measure (FIM) (Hamilton et al., 1994). Sleep quality was assessed by the Pittsburgh sleep quality index (PSQI) (Buysse et al., 1989).

Respiratory function outcomes measured included forced expiratory volume in the first second (FEV1%), dyspnea, and fatigue perceptions. FEV1% was assessed with a spirometer (CareFusion, Micro Spirometer, Basingstoke, UK) following the criteria of the American Thoracic Society (ATS) (Watz et al., 2009). Additionally, dyspnea perception was recorded using the modified Borg Scale (Borg et al., 1982), functional impairment related to dyspnea was measured with the London Chest Activity of Daily Living Scale (LCADL) (Garrod et al., 2000), and fatigue perception with the Fatigue Severity Scale (FSS) (Fisk et al., 1994).

The health impairment in patients with COPD was evaluated using the St George’s Respiratory Questionnaire (Jones et al., 1991).

This questionnaire is divided into the following domains: respiratory symptoms, activities limited by dyspnea, and psychosocial effects.

The pain-related variables comprise the pronociceptive pain profile defined as patients with facilitated pain processing and/or reduced pain-modulatory capabilities (Cheng et al., 2015) (general pain sensitivity, pain intensity, pain interference, and pressure pain sensitivity) and the coexistence of psychological vulnerability (perceived health status, anxiety, and depression) among patients with COPD.

The Pain Sensitivity Questionnaire (PSQ) evaluated general pain sensitivity. It is composed of 17 items, each describing an activity of daily life and asking the patients to rate how painful this activity would be for them on a numeric rating scale ranging from 0 (not painful) to 10 (worst pain imaginable). A higher score in the questionnaire indicated a greater pain sensitivity (Ruscheweyh et al., 2012).

The Brief Pain Inventory (BPI) assessed pain intensity and pain interference. Patients rate the intensity of their pain during the previous week, on average, and “right now.” Patients also rate their level of pain interference in seven backgrounds: (1) work; (2) activity; (3) mood; (4) enjoyment; (5) sleep; (6) walking; and (7) relationships. The intensity subscale is scored between 0 and 40, and the interference subscale is between 0 and 70. Higher scores reflect worse pain intensity or interference (Cleeland et al., 1994).

Pressure pain thresholds (PPT) was used to measure pressure pain sensitivity in muscles with the algometer (Somedic AB, Horby, Sweden). With the patient in a seated position, the pressure was applied three times at five bilateral points of the body: the distal thumb phalangeal, the gracilis muscle tendon at the inside of the knee, the distal of the middle part of the clavicle, the supraspinous muscle, and the trapezius muscle’s second portion. When the participant reported that pressure changed to pain, the pressure was stopped, and the mean value was registered (Johansson et al., 2012).

The perceived health status was measured with the EuroQol-5D (EQ-5D) tool. This measure contains two parts, a descriptive questionnaire about health impairment and a numerical scale about health status perception. The descriptive questionnaire includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The numerical scale ranges from 0 (defined as the worst imaginable health state) to 100 (defined as the best imaginable health state) (Rabin et al., 2001).

The Hospital Anxiety and Depression Scale (HAD) measured the anxiety and depression symptoms. It consists of 14 items, depression (seven items) and anxiety (seven times), each with four answer options. Each of the subscale scores ranges from 0 to 21, corresponding to total scores of 0 to 42, with higher scores indicating major anxiety and depression symptoms (Herrero et al., 2003).

Sample Size

The sample size calculation was guided by estimates of the minimal clinically important difference in the BPI (Tanaka et al., 2002). Our analysis indicated that a sample size of 24 participants is needed to ensure at least 21 participants and to find significant differences between groups, assuming a loss rate of 10% with a significance level of 0.05.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 23.0 software for Windows (SPSS Inc. and IBM Company). Results are expressed as mean and statistical deviation (SD). Differences in characteristics between COPD patients before and after the
COVID-19 pandemic were tested using the independent sample t test for numeric variables with normal distribution, the Wilcoxon test for numeric variables with no normal distribution, and the χ² test for nominal variables. The statistical analysis was conducted at a 95% confidence level. A p value < .05 was considered statistically significant.

**Results**

The recruitment and selection of patients with COPD across the study appeared in Fig. 1. The final study sample was composed of 24 patients with COPD.

The characteristics of patients with COPD evaluated at before and during the COVID-19 pandemic are shown in Table 1.

The mean age of patients with COPD was 67.60 ± 6.13 years with a male predominance (79%), and the incidence of comorbidities was 3.75 ± 0.89. All patients were retired and the 87.3% living accompanied. When patients with COPD were compared before and during COVID-19, the descriptive data of participants showed no significant differences between groups. The body mass index, cognitive impairment, handgrip strength, functionality, and sleep quality were similar before and during COVID-19 (p < .05). However, regarding respiratory function, patients with COPD have shown statistical differences in dyspnea and fatigue perception, and respiratory symptoms over time (p < .001).

The pronociceptive pain profile and psychological vulnerability of patients with COPD are shown in the Table 2.

Investigating the pronociceptive pain profile and the psychological vulnerability of patients with COPD before and during the COVID-19 pandemic revealed all symptoms increased over time. As shown in Table 2, patients with COPD during the COVID-19 pandemic experienced higher general pain sensitivity and intensity with statistical differences in pain interference (p < .001). Furthermore, the pressure pain sensitivity in the five bilateral points of the body have shown a higher sensitivity during COVID-19, highlighted the bilateral thumbs, gracilis, and supraspinous muscles (p < .001).

The overall perceived health status was much lower during COVID-19 than before the COVID-19 period (p < .05). However, anxiety and depression were not statistically different before and during the COVID-19 pandemic.

### Table 1: Characteristic Descriptive of COPD Patients Before and During COVID-19 Pandemic

|                           | Pre-COVID-19 (n = 24) | During COVID-19 (n = 24) | p       |
|---------------------------|-----------------------|--------------------------|---------|
| BMI (kg/m²)               | 28.41 ± 4.44          | 29.65 ± 7.51             | .497    |
| Cognitive impairment      | 17.75 ± 3.89          | 15.40 ± 3.28             | .9      |
| Hand grip strength (kg)   | 31.22 ± 9.54          | 24.06 ± 8.65             | .931    |
| Functionality             | 114.89 ± 14.29        | 119.75 ± 10.75           | .23     |
| Sleep quality             | 9 ± 4.28              | 9.92 ± 3.45              | .092    |
| Respiratory function      |                       |                          |         |
| FEV₁%                     | 33.55 ± 11.41         | 36.25 ± 12.20            | .93     |
| Dyspnoea perception       | 3.25 ± 2.83           | 7.25 ± 3.49              | <.001*  |
| Functional impairment related to dyspnoea | 22.42 ± 14.12  | 30.38 ± 9.86            | .205    |
| Fatigue perception        | 40.25 ± 20.89         | 55.11 ± 11.12            | <.001*  |
| Health impairment in COPD patient |                |                          |         |
| Respiratory symptoms      | 58.2 ± 19.43          | 65.1 ± 37.31             | <.001*  |
| Activities limited by dyspnoea | 71.11 ± 22.17  | 80.19 ± 21.18           | .895    |
| Psychosocial impact       | 60 ± 18.33            | 69 ± 14.97               | .964    |
| Total                     | 63.09 ± 17.69         | 72 ± 20.31               | .217    |

* p < .001.

Data expressed as mean ± SD. BMI = body mass index; COPD = chronic obstructive pulmonary disease; FEV₁% = forced expiratory volume in the first second; SD = standard deviation.
Discussion

We have shown that during the COVID-19 pandemic, there was an increase in the pronociceptive pain profile and psychological vulnerability was enhanced in patients with COPD. Patients presenting with COPD during the COVID-19 pandemic had intensified the dyspnea and fatigue perfection compared with before the pandemic but had similar FEV-1 obstructive degree. Thus, these findings highlight the effect of respiratory symptoms as the most affected of health characteristics of COPD.

The COVID-19 pandemic produced for some people the suspension of commuting, changes to education and work, and increased time with family, highlighting decreased stress and increased psychological general wellbeing (Andrew et al., 2020; Greenberg et al., 2020). However, other people developed more anxiety, anger, stress, or agitation during the lockdown mainly due to the fear of infection, loneliness, socioeconomic problems, and loss of employment (WHO, 2020; Townsend et al., 2020; Bu et al., 2020). Evidence from around the world on psychological change potentially attributable to the COVID-19 pandemic is being studied. McGinty et al. (2020) showed increased rates of psychological distress among adults during the COVID-19 pandemic, compared with before the pandemic.

Depression and anxiety are associated with increased pain perception, whereas prolonged duration of pain leads to increased psychological vulnerability (Zis et al., 2017). In addition, Vardar-Yagli et al. (2019) observed that pain perception, severity, and sensitivity are increased in patients with COPD compared with the general population (Vardar-Yagli et al., 2019). Recently, studies similar to ours also observed a change in the clinical profile of acute (Silva et al., 2020) and chronic (Tilliridou et al., 2021) respiratory diseases before and during the COVID-19 pandemic.

Limitations

Several limitations of this study should be considered. First, the sample size was relatively small but sufficient to detect statistical differences in pain assessments. Second, the use of questionnaires may have underestimated or overestimated some of the information. In addition, the course of COPD is clinically characterized by a worsening of dyspnea, cough, and spumt production, which were not analyzed in this study. Moreover, the population included in the study had a moderate to severe profile of COPD. Our initial purpose here was to investigate the association between the pain-related variables and the presence of psychological vulnerability among stable patients with COPD, although, given these special circumstances, our methods required some modifications. Participants may have been less motivated to engage in the study during the COVID-19 pandemic. Likewise, our evaluation was modified from what we initially planned; for instance the Semmes-Weinstein monofilaments were excluded in the evaluation of sensitivity to pressure/touch. A further limitation of this study is that it focused on examining the pain-related variables before and during the COVID-19 pandemic in patients with COPD, but a healthy control group for comparison is recommended. Further studies are needed to determine other aspects of COPD symptomatology that can be influenced during COVID-19 pandemic.

Further Research

These findings highlight the patient’s psychological distress likely due to the pandemic and their COPD symptoms and report them as pain. Developing and implementing education programs that allow COPD patients to achieve and enhance the control of their illness is recommended. Moreover, early diagnostic surveys should be recommended to prevent and recognize pain in these patients. Future studies evaluating pain and its characteristics to determine health status effect are recommended. The illness knowledge, psychological, physical, and social aspects should be encouraged to prevent pronociceptive pain in COPD patients.

Conclusion

During the COVID-19 pandemic, patients with COPD showed an increase in the pronociceptive pain profile accompanied by a worse psychological vulnerability compared with patients with COPD before the COVID-19 pandemic.

Table 2

| Pronociceptive Pain Profile and Psychological Vulnerability of COPD Patients | Pre-COVID-19 (n = 24) | During COVID-19 (n = 24) | p |
|---|---|---|---|
| General pain sensitivity | 96.13 ± 19.18 | 116.67 ± 6.2 | .011b |
| Pain intensity | 0 | 2.16 ± 6.17 | .010b |
| Pain interference | 0 | 1.92 ± 3.74 | <.001b |
| Pressure pain sensitivity | 2.86 ± 0.86 | 1 ± 0.73 | <.001b |
| R thumb | 2.43 ± 0.76 | 0.75 ± 0.86 | <.001b |
| R gracilis muscle | 2.29 ± 0.91 | 0.50 ± 0.52 | <.001b |
| L gracies muscle | 2 ± 0.92 | 1 ± 0.73 | <.001b |
| R subclavian muscle | 1.57 ± 0.94 | 1 ± 0.23 | <.001b |
| L subclavian muscle | 1.86 ± 1.02 | 0.75 ± 0.45 | <.001b |
| R supraspinous muscle | 1.86 ± 1.03 | 0.5 ± 0.52 | <.001b |
| L supraspinous muscle | 2 ± 1.11 | 1 ± 0.73 | <.001b |
| R trapezius muscle | 2.14 ± 1.03 | 1.5 ± 1.16 | .033b |
| L trapezius muscle | 2.14 ± 1.18 | 1.25 ± 1.13 | .011b |
| Psychological vulnerability | | | |
| Perceived health status | | | |
| Overall health status | 51.67 ± 16.59 | 40 ± 8.10 | .049a |
| Anxiety and depression | | | |
| Anxiety | 6.33 ± 4.63 | 9.78 ± 4.05 | .745 |
| Depression | 5 ± 3.84 | 8.33 ± 3.91 | .785 |
| Total | 11.33 ± 7.29 | 18.11 ± 6.63 | .569 |

* p < .05.  
* b p < .001.

Data expressed as mean ± SD. R = right; L = left; SD = standard deviation.
Declaration of Competing Interest

The authors declare that they have no conflict of interest.

References

Andrew, A., Cattan, S., Dias, M. C., Farquharson, C., Kraftman, L., Krutikova, S., ... & Sevilla, A. (2020). How are mothers and fathers balancing work and family under lockdown? Institute for Fiscal Studies (IFS) Briefing Note B2N290. Retrieved Month XX, XXXX, from https://ifs.org.uk/uploads/B2N290-Mothers-and-fathers-balancing-work-and-life-under-lockdown.pdf

Borg, G. A. (1982). Psychophysical bases of perceived exertion. Medicine & Science in Sports & Exercise, 14(5), 377–381.

Borge, C. R., Wahl, A. K., & Moun, T. (2010). Association of breathlessness with multiple symptoms in chronic obstructive pulmonary disease. Journal of Advanced Nursing, 66(12), 2688–2700.

Borge, C. R., Wahl, A. K., & Moun, T. (2011). Pain and quality of life with chronic obstructive pulmonary disease. Heart & Lung, 40(3), e90–e101.

Bu, F., Sceptoe, A., & Fancourt, D. (2020). Who is lonely in lockdown? Cross-cohort analyses of predictors of loneliness before and during the COVID-19 pandemic. Public Health, 186, 31–34.

Buyse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Research, 28(2), 193–213.

Charlson, M., Szatrowski, T. P., Peterson, J., & Gold, J. (1994). Validation of a combined comorbidity index. Journal of Clinical Epidemiology, 47(11), 1245–1251.

Cheng, J. C., Erpelding, N., Kucyi, A., DeSouza, D. D., & Davis, K. D. (2015). Individual differences in temporal summation of pain reflect pronociceptive and antinociceptive brain structure and function. Journal of Neuroscience, 35(26), 9689–9700.

Cleeland, C. S., & Ryan, K. (1994). Pain assessment: Global use of the Brief Pain Inventory. Annals of the Academy of Medicine, Singapore, 23(2), 129–138.

Fisk, J. D., Rito, P. G., Ross, L., Haase, D. A., Marrie, T. J., & Schleich, W. F. (1994). Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. Clinical Infectious Diseases, 18(Supplement 1), S79–S83.

Garrod, R., Bestall, J. C., Paul, E. A., Wedzicha, J. A., & Jones, P. W. (2000). Development and validation of a standardized measure of activity of daily living in patients with severe COPD: The London Chest Activity of Daily Living scale (LCADL). Respiratory Medicine, 94(6), 589–596.

Giansanti, D. (2020). The Italian fight against the COVID-19 pandemic in the second phase: The renewed opportunity of telemedicine. Telemedicine Journal and e-Health, 26(11), 1328–1331.

Greenberg, N., Docherty, M., Gaanapragasam, S., & Wessely, S. (2020). Managing mental health challenges faced by healthcare workers during covid-19 pandemic. BMJ, 368,m1211.

Hamilton, B. B., Laughlin, J. A., Fiedler, R. C., & Granger, C. V. (1994). Interrelater reliability of the 7-level functional independence measure (FIM). Scandinavian Journal of Rehabilitation Medicine, 26(3), 115–119.

Herrero, M. J., Blanch, J., Peri, J. M., De Pablo, J., Pintos, L., & Bulbena, A. (2003). A validation study of the hospital anxiety and depression scale (HADS) in a Spanish populati. General Hospital Psychiatry, 25(4), 277–283.

Janssen, D. J., Spruit, M. A., Uszko-Lencer, N. H., Schols, J. M. G. A., & Wouters, E. F. M. (2011). Symptoms, comorbidities, and health care in advanced chronic obstructive pulmonary disease or chronic heart failure. Journal of palliative medicine, 14(6), 735–743.

Johansson, E.-L., Ternestedt-Hassel, E., Olelen, M. F., & Millqvist, E. (2012). Respiratory movement and pain thresholds in airway environmental sensitivity, asthma and COPD. Respiratory Medicine, 106(7), 1006–1013.

Jones, P. W., Quirk, F. H., & Baveystock, C. M. (1991). The St George’s Respiratory Questionnaire. Respiratory Medicine, 85(Suppl B), 25–31.

Leung, J. M., Niikura, M., Yang, C. W. T., & Sin, D. D. (2020). Covid-19 and COPD. European Respiratory Journal, 56(2), Article 2002108.

McIntyre, E. E., Presskreischer, R., Han, H., & Barry, C. L. (2020). Psychological distress and loneliness reported by US adults in 2018 and April 2020. JAMA, 324(1), 93–94.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, L., ... Cheitkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society, 53(4), 695–699.

Ohannessian, R., Duong, T. A., & O’done, A. (2020). Global telemedicine implementation and integration within health systems to fight the COVID-19 pandemic: A call to action. JMIR Public Health and Surveillance, 6(2), e18810.

Philip, K. E., Lonergan, B., Cumella, A., Farrington-Douglas, J., Laffan, M., & Hopkins, N. S. (2020). COVID-19 related concerns of people with long-term respiratory conditions: A qualitative study. BMC Pulmonary Medicine, 20(1), 319.

Rabin, R., & Charro, F. D. (2001). EQ-SD: A measure of health status from the Euro-Qol Group. Annals of Medicine, 33(3), 337–341.

Roberts, M. H., Mapel, D. W., Hartry, A., Von Worye, A., & Thomson, H. (2013). Chronic pain and pain medication use in chronic obstructive pulmonary disease. A cross-sectional study. Annals of the American Thoracic Society, 10(4), 290–298.

Rucheweyh, R., Verneuer, B., Dany, K., Marziniak, M., Wołowski, A., Chołak-Eckri, R., ... Knecht, S. (2012). Validation of the pain sensitivity questionnaire in chronic pain patients. Pain, 153(6), 1210–1218.

Silva, A. P. D. S. C., Maia, L. T. S., & Souza, W. V. (2020). Severe acute respiratory syndrome in Pernambuco: Comparison of patterns before and during the COVID-19 pandemic. Ciência & Saúde Coletiva, 25, 4141–4150.

Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2002). Impact of dyspneic pain, and fatigue on daily life activities in ambulatory patients with advanced lung cancer. Journal of Pain and Symptom Management, 23(5), 417–423.

Tilliridou, V., Kirkbride, R., Dickinson, R.,Tierman, J., Yong, G. L., van Beek, E. J., ... Williams, M. C. (2021). Pulmonary embolism severity before and during the COVID-19 pandemic. British Journal of Radiology, 94(1123), Article 20210264.

Townsend, E., Nielsen, E., Allister, R., & Cassidy, S. A. (2020). Key ethical questions for research during the COVID-19 pandemic. Lancet Psychiatry, 7(5), 381–383.

van Dam van Isselt, E., Croneenwegen-Spikema, K. H., Spruit-van Eijk, M., Chava- nnes, N. H., de Waal, M. W. M., Janssen, D. J. A., & Achterberg, W. P. (2014). Pain in patients with COPD: A systematic review and meta-analysis. BMJ Open, 4(9), Article e009398.

Vardar-Yildiz, N., Saglam, M., Calik-Kutucu, E., Inal-Ince, D., Aritkan, H., & Copolu, L. (2019). Increased pain sensitivity, postural abnormalities, and functional balance impairment in obstructive lung disease compared to healthy sub- jects. Heart & Lung, 48(4), 351–355.

Vestbo, J., Hurd, S. S., Agustí, A. G., Jones, P. W., Vogelmeier, C., Anzueto, A., ... Rodríguez-Roisín, R. (2013). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. American Journal of Respiratory and Critical Care Medicine, 187(4), 347–365.

Watz, H., Waschki, B., Meyer, T., & Magnusson, H. (2009). Physical activity in pa- tients with COPD. European Respiratory Journal, 33(2), 262–272.

World Health Organization (WHO) (2020). Mental health and psychosocial consider- ations during COVID-19 outbreak, 18 March 2020. Retrieved June 30, 2021, from https://apps.who.int/iris/handle/10665/331490

Zis, P., Daskalaki, A., Bountouri, I., Sykioti, P., Varrasi, G., & Paladini, A. (2017). Depression and chronic pain in the elderly: Links and management challenges. Clinical Interventions in Aging, 12, 709.