

# Correlates and Predictors of Health-Related Quality of Life among Patients with COPD: An Integrative Review

Nazih Abu Tabar<sup>1,2\*</sup> , Jafar Alasad Alshraideh<sup>1</sup>

<sup>1</sup>School of Nursing, The University of Jordan, Amman, Jordan

<sup>2</sup>Nursing Department, Ministry of Health, Amman, Jordan

Email: \*n-tabar@hotmail.com, jalasad@ju.edu.jo

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## Abstract

**Background:** Health-related quality of life is an important outcome variable with COPD patients. Impaired health-related quality of life among COPD patients is closely related to various factors. There are many factors that predict the HRQoL and the correlation with other important variables. Predictors of health-related quality of life were debatable in the literature. **Aim:** This review aimed to describe the correlation with HRQoL and to explore the predictors of HRQoL among patients with COPD. **Methods:** An integrative review method was conducted. A search protocol was conducted using EBSCO, Pubmed, CINAHL, Ovid, ProQuest, Cochrane, and Google Scholar databases up to October 1, 2019. **Results:** The review results out of 30 articles that discuss the predictors of HRQoL and 22 articles that discuss the HRQoL correlations with other important variables. The HRQoL predictors are classified according to sociodemographic factors and clinical factors, and also, the correlation and prediction of HRQoL with anxiety, fatigue, and uncertainty. The results of this review showed controversies in predictors between the studies. The most retrieved predictors were age, educational level, comorbidities, socioeconomic status, FEV1% predicted, GOLD stages, and the number of hospitalizations. The variables of anxiety and fatigue were strongly correlated and predicted HRQoL. While uncertainty was not reported as a significant HRQoL predictor. **Conclusion:** This review provides support about reliable predictors than unreliable one although some predictors still need further research in different races and cultures. Future research is needed to explore whether uncertainty can predict HRQoL among patients with COPD.

## Keywords

HRQoL, COPD Integrative Review, Uncertainty, Anxiety, Fatigue

## 1. Introduction

Health-related quality of life (HRQoL) is an important outcome variable in many chronic diseases that have an impact on different aspects of a person's life. Chronic Obstructive Pulmonary Disease (COPD) is one of those diseases in which HRQoL is affected and becoming a major environmental and public health issue [1]. Globally, COPD is considered a significant cause of mortality and morbidity across the modern world [2] [3]. COPD is likely to increase in the coming years due to higher smoking prevalence, aging populations in many countries, and the spreading of environmental pollutants [4]. This made COPD the fourth leading cause of death and expected to become the third major cause of death by 2030 worldwide [5].

Chronic Obstructive Pulmonary Disease continues to be an important health burden [6]. COPD is a complex, multifaceted disease. It affects patients in many ways and results in significant impairment in their quality of life (QoL) [7]. It has a major impact on personal health status at large and HRQoL in specific. HRQoL was defined as a very broad concept referring to the quality of life that is directly related to health or illness [8]. HRQoL and QoL are used interchangeably [9]. HRQoL is composed of various aspects that involve physical, mental, emotional, and social wellbeing, which is completely different for each patient [10]. Impaired quality of life among COPD patients is closely related to the symptoms of shortness of breath, dyspnea, and impaired physical activities, like fatigue, and mental problems, like anxiety [1] [11] [12]. Therefore, the evaluation of HRQoL is an important outcome measure in assessing patients with COPD which informs about the causes of the burden of this disease and leads to improve patient management and develops policy decisions [13].

Furthermore, COPD is a distressing, difficult, and progressive condition that makes life miserable for many patients [14]. Thereby, COPD leads to a progressive worsening in HRQoL aspects among those patients who are having this disease [15]. Many studies reported an impairment of HRQoL among COPD patients which measured through using generic or specific HRQoL tools [8] [16] [17] [18]. COPD is a complicated and comorbid disease that has many associated risk factors that can contribute to a significant impairment in functional, psychosocial, emotional and economic costs on the individual, community, and health services [1]. The associated factors lead to a gradual deterioration in the HRQoL, such as: severity of disease symptoms, the impact of symptoms on the subsequent reduction in daily activities, non-adherence management, and therapeutic noncompliance and psychosocial effect [6]. The interest in the associated factors contributing to HRQoL among patients with COPD is increasing [10] [19]. The associated factors were classified in to sociodemographic and clinical variables, functional, psychological, and emotional among patients with COPD. Also, these factors are significant in discovering the main factors that predict the worsening in HRQoL level and explaining the correlation of HRQoL with other variables, specifically the level of anxiety, fatigue, uncertainty among those patients.

The integrative review aimed to identify and summarize relevant kinds of literature which are described HRQoL predictors and correlation of HRQoL with other variables specifically limited to perceived anxiety, level of fatigue and perceived uncertainty in patients with COPD. The findings of this review will contribute in adopting these predictors for updating clinical practice guidelines, institutional policy regarding the routine assessment and clinical intervention options with COPD patients, and improve knowledge among healthcare providers about the potential impact of psychosocial and physiological wellness on the health status of COPD patients. In addition to providing healthcare researchers with needed information that will help them in appraising and discussing the study results according to their study purpose.

## 2. Methods

### 2.1. Data Sources and Search Strategies

The integrative review was conducted to identify studies describe the predictors of HRQoL and correlate HRQoL with other specific variables among COPD patients. The online databases used in the literature review were PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), ProQuest, Medline, Google Scholar, SAGE Journals, Wiley online Library, Science Direct and EBSCOhost, Ovid journals, and Cochrane for systematic review articles. Literature searches were conducted for articles published up to October 1, 2019. The keywords used for searching in the online databases were COPD, pulmonary disease, anxiety, fatigue, uncertainty, HRQoL, QoL, and systematic review, and a combination thereof. The possible combinations of words were used using Boolean operators like AND or OR. Search in PubMed was conducted by utilizing a highly sensitive search filter technique. All the founded articles were screened for inclusion criteria. Each article retrieved in the search was independently assessed by the researcher in double methods. Researchers reviewed the titles and abstracts of each article. If the article indicated potential inclusion, the full-text of the article was assessed using the inclusion criteria. Any disagreement over the eligibility of particular articles was resolved through reviewing the article again in full or consulting another researcher.

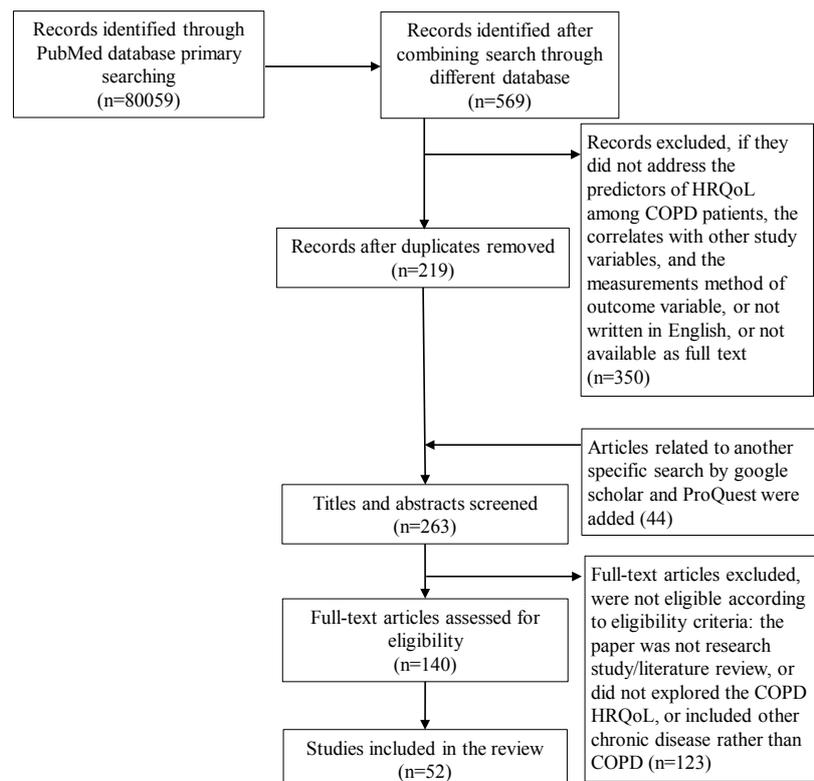
### 2.2. Inclusion and Exclusion Criteria

The articles met the following inclusion criteria were considered for full review: 1) discussed and reported at least two predictors of HRQoL or at least the correlations with one of following variables (*i.e.* anxiety, fatigue, uncertainty); 2) include HRQoL as outcome variable 3) the measurement of HRQoL was reported with valid and reliable tool; and 4) articles were provided in full text and published in English. Although excluding the publications written in another language than English will introduce a language bias, the English language is still generally perceived to be the universal language of science. The papers include overlapping pulmonary diseases like asthma, obstructive sleep apnea (OSA) or

didn't meet the inclusion criteria were excluded.

### 2.3. Process of Identifying the Relevant Studies and Data Extraction

The potential articles were first screened for their titles and abstracts. Then, the relevant articles were reviewed in full for consideration of inclusion in the current review. The selection was according to fixed inclusion and exclusion criteria. The primary search in PubMed databases retrieved (80059) articles including research articles and systematic reviews and (44) articles through other resources. After combing three specific variables (anxiety, fatigue, and uncertainty) in the same search engine, (569) articles were identified. After removing duplicates (219) articles were identified. (350) records were excluded because they did not meet the inclusion criteria. From the reviewed titles and abstracts, (140) articles met our search criteria and were reviewed in full. Afterward, the selected articles were assessed for eligibility based on their full text. Of these, (52) final articles were selected. The relatively low number of articles was reflected in the scarcity of evidence around the study variables. After an in-depth review of the included articles, results were summarized according to the following two headings: predictors of HRQoL among COPD patients and the correlation between HRQoL and other specific variables. **Figure 1** demonstrates a flow chart for the selection of studies included in the literature review.



**Figure 1.** Prisma flow chart for the selection of studies included in the literature review.

### 3. Results

Health-related quality of life (HRQoL) was recognized as an important outcome when evaluating patients with COPD [20]. The fact that HRQoL is the result of the interaction of physical, psychological, and social factors can justify several predictors of HRQoL among COPD patients which were reported in the literature. These predictive factors were reported into five groups: demographic factors, comorbidity, factors related to the disease, psychological factors, and other related factors. HRQoL was comprised of several domains that involve physical, mental, and social wellbeing which significantly differs for each patient [10]. Impaired quality of life is closely related to shortness of breath, impaired physical activities, and mental problems such as; anxiety [17]. COPD was found clearly correlated with fatigue, anxiety and reduced HRQoL. Therefore, HRQoL should be measured in tools that assess physical, social, and psychological domains. Currently, many HRQoL tools are available. Although there are generic HRQoL tools, which can be used to evaluate HRQoL in general for any population, there are disease-specific tools that can be used in patients with a certain disease experience [21]. So, the recommendation of using a disease-specific tool is needed to cover specific HRQoL aspects and patient-related experiences [22].

In this review, the predictive factors were described into two Tables; **Table 1** presents the characteristics of the (30) studies analyzing factors predicting the HRQoL among patients with COPD and **Table 2** presents characteristics of (22) studies describing the correlations and predictive factors between HRQoL and other variables limited to (anxiety, fatigue, and uncertainty). So, to address the purpose of this integrative review, the findings were categorized under the following headings; predictors related to sociodemographic and clinical variables and correlate and predictors between HRQoL and other variables.

**Table 1.** Characteristics of the studies analyzing factors predicting the HRQoL of patients with COPD (N = 30).

Author/Date	Study Sample	Study design	Data Collection Period	The instrument used to measure HRQoL	Predicting factor of HRQoL	Non predicting factor of HRQoL
(Wu <i>et al.</i> , 2019)	154 patients	A cross-sectional design	Between December 2016 and November 2017	CCQ	Age, Smoking status, Disease duration	Gender, marital status, employment status, BMI
(Shah, Shah, & Kachoria, 2019)	60 patients	A prospective, cross-sectional study	From April to September 2017	SGRQ-C	Age, Nutrition, Smoking status, Alcohol intake, Socioeconomic status, Duration and severity of the disease, Presence of comorbidities, Type of COPD medication used, BMI	Sex, Education level, Employment status, Dietary habits
(Wytrychiewicz <i>et al.</i> , 2019)	105 patients	Descriptive correlational study	NA	Newley developed a tool which assesses eight aspects of potentially affecting QoL	Smoking status, BMI	Sex, Age, Marital status, Place of residence, Education, professional activity, Years since COPD diagnosis, Number of hospitalizations due to COPD

## Continued

(Ghilley, Bhadoria, & Pandit, 2018)	120 patients	Descriptive correlational	NA	SGRQ-C	FEV1/FVC (%) ratio	Age, BMI, Smoke pack/year, GOLD stage
(Pati <i>et al.</i> , 2018)	110 patients	The parallel mixed-method study design was	Between June and July 2014	SGRQ	Advanced age, Sex/female, More than two comorbidities, Low income, Family support	Occupation, Place of living
(Gaude & Desai, 2018)	44 patients	Cross-sectional study	Between October 2016-November 2016	SGRQ	NA	Age, Sex, Smoking, BMI, Socioeconomic status, Occupation type
(Farg, Sobh, Elsayy, & Fahmy, 2018)	200 patients	A cross-sectional observational multicenter study	2 years	Arabic version of SGRQ.	FEV1 % Predicted, New, GOLD stage (ABCD), Comorbidity, particularly IHD, mMRC, Frequency of exacerbations per year, 6MWD	Age, BMI, GOLD Spirometrics staging, BODE index, FEV1/FVC (%), Smoking pack/year
(Brandl <i>et al.</i> , 2018)	206 patients	A prospective patient cohort study	1 year and 4 months	Short-Form (SF-12) Health Survey Questionnaire	CAT, Number of, exacerbations (years), FEV1 % Predicted, Living alone	Age, Female gender, High educational level, Smoking, Number of medications, Disease duration
(Lee <i>et al.</i> , 2017)	1264 patients	Prospective cohort	Between December 2011 and November 2015	SGRQ-C	Age, Education, No of comorbidities, 6MWD, Depression level, mMRC	Sex, BMI, Smoking status, FEV1% predicted
(Das, Bam, & Ghimire, 2017)	81 patients	Descriptive observational cross-sectional	5 months	SGRQ-C	Smoking status	Age, Sex, Occupation, Education, Medications
(Cheruvu, Odhiambo, Mowls, Zullo, & Gudina, 2016)	16602 patients	Telephone survey designed	From the 2011 and 2012	A newly developed tool which contains four HRQOL indicators	Sex, Age, Current smoker	Activity limitation, Unmarried, Level of education less than a college degree
(Kwon & Kim, 2016)	2734 patients	Cross-sectional survey study	Between 2007-2012	EQ-5D	Age, Sex, Severity of COPD, Diabetes and hypertension comorbidities, Smoking status	Educational level, Income level
(Martinez <i>et al.</i> , 2016)	4097 participants in the COPD Gene study and 1522 participants in SPIROMICS	a cross-sectional analysis of data from participants with COPD in two cohorts	NA	SGRQ	Race, Smoking status, Moderate to severe dyspnea, exacerbation frequency, Presence of chronic bronchitis symptoms	Comorbidities, Activity level, Anxiety, and depression
(Sharma & Joshi, 2015)	40 patients	A cross-sectional hospital-based study	From August 6, 2014, to August 7, 2014	a 56-item QOL questionnaire developed by the researcher	Age, Current smoker, Education level, Comorbidities, Hospital no of admission last three months, Need of drugs regularly	Sex, Marital status, Place of residence, Family type, Work status, Economic status, Duration of COPD, Smoking status
(Hong <i>et al.</i> , 2015)	1178 patients	A cross-sectional survey analysis	Between the year of 2007 and 2010	EQ-5D	Old age, female gender, lower education level, many comorbid diseases, severe airflow obstruction (Gold stage)	BMI, ever-smoking
(Ekici, Bulcun, Karakoc, Senturk, & Ekici, 2015)	62 patients	Descriptive correlational	NA	SGRQ	FEV1 % Predicted, mMRC, Anxiety scores	Age, BMI, Total number of hospitalizations, Depression score
(Xiang <i>et al.</i> , 2015)	142 COPD outpatients and 218 controlled COPD	Case-control study	May 1, 2004, to April 30, 2005.	MOS-SF-12 SGRQ	Marital status, Education, Religious belief, Life event in the past year	COPD severity, Living with others, Age/year, Sex/male, No of comorbidities, No of hospitalization last year ADLs

## Continued

(Bentsen, Miaskowski, & Rustøen, 2014)	100 patients	Cross-sectional study	NA	SGRQ	Age, Anxiety score	Number of comorbidities, Pain intensity, Depression score, Physical functions, GOLD Spirometrics staging, FEV1 % Predicted
(Bonsaksen, Haukeland-Parker, Lerdal, & Fagermoen, 2014)	127 patients	Prospective longitudinal design	12 months after course completion	Short Form 12, version 2 (SF-12v2), SF-36.	Work status, Illness perception	Age, Sex, Education, Physical activity, Self-efficacy
(Negi, Sarkar, Raval, Pandey, & Das, 2014)	126 patients	A cross-sectional study	Between November 2011 and April 2012	Hindi version of SGRQ	BMI, FEV1% predicted, FEV1/FVC%, MRC Dyspnea grade, Education, GOLD stage	Age, Sex, Area of residence, Smoking index, Seasonal variation
(Raheerison <i>et al.</i> , 2014)	430 patients	A multicenter cross-sectional observational study	September 2009 to November 2010	SGRQ-C	MRC dyspnea score, Number of treatments, Age, Anxiety, FEV1% predicted	Gold stage, Age, FEV1/FVC, BOD Index, No of exacerbation
(Abu Hassan, Abd Aziz, Hassan, & Hassan, 2014)	117 patients	NA	January to June 2013	CCQ	Smoking status, No of hospital admission due to COPD	No of days warded
(Justine, Tahirah, & Mohan, 2013)	100 patients	Cross-sectional correlational study	NA	SF-36 v2	Dyspnea score	Lung function
(Bentsen, Rokne, & Wahl, 2013)	100 COPD patients and 3594 general population	A comparative survey design	Between August 2005 and August 2007.	SF-36	COPD stage and severity	Age, Sex, Education level
(Obaseki, Erhabor, Awopeju, Obaseki, & Adewole, 2013)	50 patients	a cross-sectional study	NA	SGRQ	Breathlessness, Weight loss, Smoking pack /year	Age, Sex, Smoking status, GOLD stage, FEV1/FVC %, BMI
(Burgel <i>et al.</i> , 2013)	326 patients	Cross-sectional analysis	Between January 2005 and August 2009.	HADS SGRQ	FEV1%, Exacerbation/patient/year, Dyspnea, Low BMI, CAD/Comorbidity	Age, Smoking pack/year, Comorbidities, Current smokers, Sex
(Zamzam, Azab, El Wahsh, Ragab, & Allam, 2012)	40 patients	NA	NA	SGRQ	GOLD stage, FEV1% predicted	Smoking index
(Joseph, Pascale, Georges, & Mirna, 2012)	284 COPD patients from 2201 total sample	Cross-sectional study	Between October 2009 and September 2010	CCQ	Cumulative cigarette dose, Older age, having at least one smoker in the family, Lower education, Female gender, Any heart disease, Heating house by diesel, Cumulative waterpipe dose	COPD severity scoring
(Han <i>et al.</i> , 2011)	224 African American and 1049 Caucasian subjects with COPD	Descriptive design	NA	SGRQ	Pack-year smoking history, Younger age, Lower FEV 1% predicted, mMRC, The number of exacerbations	Race
(Sundh, Ställberg, Lisspers, Montgomery, & Janson, 2011)	1548 patients	Survey design/different setting	In 2005	CCQ	Educational level, BMI, Heart disease, GOLD stage	Sex, Age, Smoking status, comorbidities

Abbreviations: HRQoL, Health-Related Quality of Life; QoL, Quality of Life; SGRQ, St George's Respiratory Questionnaire; FEV1%, Forced Expiratory Volume in One Second; m MRC, Modified Medical Council Research Dyspnea scale; 6MWD, 6-minute walk distance; CAT, COPD Assessment Test; EQ5D, Euro Qol; CCQ, Clinical COPD Questionnaire; MOS SF-36, Medical Outcome Study of Short Form 36; QWB-SA, Self-Administered Quality of Well-Being Scale; MILQ, Multidimensional Index of Life Quality;

**Table 2.** Study characteristics of correlates and predictors between HRQoL and other variables (N = 22).

Author/ Date	Study Sample	Study design/ sampling	Study Purpose	Data Collection period	The instrument used to measure HRQoL	Main study results
(Ivziku, Clari, Piredda, De Marinis, & Matarese, 2019)	80 dyads	A cross-sectional descriptive design	To assess the influence of anxiety and depression on the physical and mental QoL in a patient with COPD and caregiver dyads	11 months from November 2016 to October 2017	GAD-7 Health Survey (SF-12)	This study found that psychological distress affects the QoL of COPD patients and caregivers consistently with prior research that used individual level of analysis and these results confirm the negative impact of anxiety and depression on the caregivers' mental QoL.
(Jarab, Alefishat, Mukattash, Alzoubi, & Pinto, 2018)	28 patients	Qualitative focused group	To explore patients' views and perceptions regarding COPD and its impact on their quality of life	NA	A qualitative study by the focused group and four themes emerged	In this qualitative study about patients' perspectives regarding COPD and its impacts on HRQoL, the evidence was COPD had a negative physical and psychological impact like anxiety on COPD patients.
(Brien <i>et al.</i> , 2018)	735 patients	a cross-sectional analysis of cohort study	To investigate factors associated with poor QoL, focusing on psychological measures potentially amenable to intervention	during the period of May 2012-June 2014	EQ-5D CAT GAD-7 scores	The study was evident that psychological factors like anxiety significantly contribute to disease-specific QoL impairment in COPD
(Quaderi & Hurst, 2018)	18 patients and 18 doctors	A qualitative method focused group/convenience sampling	To explore the unmet needs of patients from both patients and doctors managing COPD	In 2012	A qualitative study by the focused group and four themes emerged	This study aimed to explore the psychological impacts as an unmet need of patients that could potentially improve their quality of life from both patients' and doctors' perspectives whose managing patients with COPD. The study results showed most patients with COPD experienced difficulties in their psychosocial and physical functions such as breathlessness, fear, and helplessness that affect QoL and lead to social isolation.
(Kouijzer, Brusse-Keizer, & Bode, 2018)	20 form inpatient and outpatient	Qualitative semi-structured interview/purposive sampling	To explore the patient's perspective on the impact of fatigue on their daily lives and on treatment opportunities to tackle the burden of fatigue	NA	A qualitative study by the focused group and four themes emerged	The study findings indicate that patients with COPD perceive the impact of fatigue on their daily lives to be a key factor in decreasing their quality of life
(Stridsman <i>et al.</i> , 2018)	795 patients	Population-based study	To evaluate the association between fatigue and health-related quality of life HRQoL both among subjects with and without COPD	In 2014	FACIT-Fatigue EQ-5D CAT	In this population-based study, clinically relevant fatigue was associated with worse HRQoL among subjects with and without COPD when using the clinically useful generic instrument EQ-5D-VAS. Also, among subjects with COPD, clinically relevant fatigue was independently associated with anxiety
(Chen <i>et al.</i> , 2018)	91 patients	a cross-sectional study/a survey method	To assess the impact of fatigue and dyspnea symptoms on quality of life in individuals with COPD	January 2014 to May 2015	DI BFI CCQ	The symptoms of fatigue, Dyspnea, and anxiety were moderate to highly correlate with each other, and with HRQoL. Thus, all individuals have an impact on their health-related quality of life.

(Lim, Kim, Kim, & Kim, 2017)	130 patients	A descriptive cross-sectional design/convenient sampling	To identify symptom clusters and the effects on quality of life (QOL) in patients with COPD	Between November and December 2014	Korean version of the CAT	Symptom cluster 1 consisted of dyspnea, physical functional status, and dry mouth; symptom cluster 2 consisted of anxiety and depression, and symptom cluster 3 consisted of sleep disturbance and fatigue. Subgroup cluster analysis showed that COPD subjects with higher-scoring symptoms in symptom clusters 1, 2, and 3 had significantly poorer QOL.
(Pascal, Trofor, Lotrean, Filipeanu, & Trofor, 2017)	60 patients	an observational study	To assess anxiety, depression and panic disorders among patients diagnosed with COPD and to investigate their correlation with disease severity, QoL as well as tobacco use	Between January and September 2014	HADS CAT	The results indicated associations between anxiety, depression, panic attacks, and disease severity, as well as poor quality of life of patients with COPD, regardless of their current tobacco use status.
(Mewes, Rief, Kenn, Ried, & Stenzel, 2016)	502 patients	a cross-sectional online survey	To investigate the influence of psychological factors on HRQL and disability in COPD individuals recruited from the general population.	Between May and September 2012	Health Survey (SF-12) PHQ	High depression and anxiety were the main predictors of low mental HRQoL. an association was found between strong emotional reactions to COPD and low mental HRQoL
(Martinez <i>et al.</i> , 2016)	4097 patients	a cross-sectional analysis of data from participants with COPD in two cohorts	To explore factors associated with age-related differences in HRQL in COPD.	NA	SGRQ	Anxiety was associated with change and predicting HRQoL
(Paap, Bode, Lenferink, Terwee, & van der Palen, 2015)	13 Health care professionals	Qualitative study/face to face interview	To identify which domains of HRQoL are most important for patients with COPD from the perspective of healthcare professionals	From July through December 2013	Seven main themes emerged from the analysis of the open question	The study findings report the most frequently selected Patient-Reported Outcomes Measures (PROMs) domains which are fatigue, physical function, emotional support, anxiety, and depression that showed the most important domains to measure and associated with HRQoL among patients with COPD.
(Mehta <i>et al.</i> , 2014)	59 patients	a cross-sectional study	To study the association of psychiatric co-morbidities and QoL with the severity of COPD.	Between September and November 2013	HADS SGRQ	Patients with depression and anxiety disorders were likely to have a poorer quality of life represented by higher SGRQ scores. Also, patients with severe respiratory symptoms are more likely to suffer from anxiety disorders and depression and have a poorer quality of life.
(Miyazaki <i>et al.</i> , 2014)	336 COPD patients and 67 non-COPD subjects	an observational study	To investigate comorbid factors that may contribute to high CAT scores	Between April 2010 and December 2012	SF-36 version 2 CAT SGRQ HADS	There is a significant-good correlation with the SGRQ total score, all components of the SF-36, and CAT score with anxiety in the COPD patients.
(Al-Gamal, 2014)	67 patients and spouses	a cross-sectional, descriptive, correlational design/interview	To examine the relationships between anxiety, depression, and QoL of both Jordanian patients with COPD and their spouses	in 2011	QLI HADS	There was a significant negative correlation between total patient QoL scores and depression subscale score and anxiety sub-scale This indicated that patients with high psychological distress reported poor QoL.

(Burgel <i>et al.</i> , 2013)	326 patients	a cross-sectional analysis	To evaluate the independent contribution of comorbidities including mood disorders, metabolic and cardiovascular comorbidities to SGRQ scores	Between January 2005 and August 2009.	HADS SGRQ	The univariate data in this study indicated that COPD subjects with anxiety or depression had worse HRQoL
(Hoth <i>et al.</i> , 2013)	407 patients	Survey study/online survey	The primary objective was to determine whether ambiguity or complexity has a stronger impact on depressive symptoms, anxiety, quality of life, and breathlessness.	NA	MUIS HADS SGRQ	Uncertainty about physical symptoms which is ambiguity consistently predicted depression, anxiety, quality of life, and breathlessness over a two-year period among individuals with COPD while uncertainty about treatment and the healthcare system which is complexity did not have an independent effect on any of the previous outcome variables.
(Lou <i>et al.</i> , 2012)	1100 patients	A case-controlled study/A cluster-randomized sampling	To assess depression and anxiety in Chinese patients with COPD	Between March and May 2008	SGRQ HADS	Patients with COPD who had anxiety and/or depression had a poorer health-related quality of life
(Jiang & He, 2012)	96 patients	RCT	To explore the effects of an uncertainty management intervention on uncertainty, anxiety, depression, and QoL of COPD outpatients in China	10-month study duration	MUIS-A SGRQ STAI	This study suggests that an uncertainty management intervention is effective in improving uncertainty, anxiety, depression, and quality of life in COPD outpatients. It is provided the first evidence that uncertainty management can improve the QoL of COPD patients
(Baltzan <i>et al.</i> , 2011)	251 individuals	observational study/a secondary analysis of data collected during a randomized clinical trial	To determine whether patients with high fatigue differed in their response to pulmonary rehabilitation program compared to those with low reported fatigue both immediately after the program and 1 year after entry.		SGRQ CRQ 6MWD	In this study patients in both groups are improved similarly in their dyspnea, the 6MWD and endurance time after introducing a pulmonary rehabilitation program. However, high-fatigue patients had greater improvements in both the CRQ fatigue and the SGRQ scores. thus, this study suggests that high levels of fatigue are a common feature in patients with COPD
(Balcells <i>et al.</i> , 2010)	337 patients	a cross-sectional analysis/convenient sampling	To evaluate the association between anxiety and depressive symptoms and health-related quality of life (HRQoL), and to identify the effect modifiers of this relationship in patients with chronic obstructive pulmonary disease	between January 2004 and March 2006.	SGRQ HADS	This study showed a significant association between anxiety, depression or both and reduced HRQOL.
(Borge, Wahl, & Moum, 2010)	154 patients	a cross-sectional study	To explore the relationships between demographic and clinical variables and the symptoms of breathlessness, depression, anxiety, fatigue, sleeping difficulties and pain for patients with COPD.	from June 2006 to December 2007	HADS Lee Fatigue Scale (LFS) RQLQ	This study confirms breathlessness is associated with variables of anxiety and fatigue which affect the QoL in patients with COPD.

Abbreviation: CAT, COPD assessment test; HADS, Hospital Anxiety and Depression Scale; SGRQ, St George's Respiratory Questionnaire; PHQ, Patient Health Questionnaire; RCT, Randomized Clinical Trial; MUIS-A, Mishel's Uncertainty in Illness Scale-Adult version; STAI, State-Trait Anxiety Inventory; QLI, Quality of Life Index; FACIT-Fatigue, Functional Assessment of Chronic Illness-Fatigue; GAD-7, Generalized Anxiety Disorder 7-item scale; RQLQ, Respiratory Quality of Life Questionnaire; BFI, Brief Fatigue Inventory; DI, Dyspnea Inventory; CCQ, Clinical COPD questionnaire; CRQ, Chronic Respiratory Questionnaire.

### 3.1. Predictors Related to Sociodemographic and Clinical Variables

The correlation between HRQoL and age was discussed in several studies, and the results were controversial. Almost seven studies were reported a positive correlation between age and HRQoL [11] [23]-[28]. The SGRQ-c tool was used to measure the HRQoL primarily and the EQ-5D tool was the second. In addition, a few tools were developed by the study researchers. On the other hand, in SGRQ-c the impact of the score was high indicating more worsening of social function and psychosocial disturbances with aging, this could be clarified by the fact that aging is usually linked with impaired activity, depressive symptoms, and anxiety [17] [29] [30] [31]. On the contrary, nearly twelve studies were found a nonsignificant correlation between age and HRQoL indicating age didn't cause impaired HRQoL among those patients [19] [32]-[42].

The gender was correlated with HRQoL. A huge variation was between studies in predicting the gender correlation with HRQoL. Although many studies were found a correlation between two variables as shown in **Table 1**. The female patients had lower scores of HRQoL compared with male patients in the following studies [13] [24] [25] [26] [27]. The following five studies showed no significant correlation or difference between the two variables [16] [23] [33] [36] [43].

The educational level was correlated with impaired HRQoL indicating lower educational levels causing worse HRQoL in four studies [13] [25] [27] [33]. In contrast, five studies were showed no correlation between educational level and better HRQoL according to the type of HRQoL measures that have been utilized in these studies [11] [16] [23] [37] [38].

The comorbidities' status and type of disease as clinical variables were correlated with HRQoL. Moreover, the majority of studies should report more than two diseases to confirm the existence of comorbidities associated with HRQoL. The six studies have reported a correlation indicating the presence of two or more of the following diseases, ischemic heart disease or diabetes, or hypertension [11] [13] [17] [19] [23] [43]. While only two studies confirm the correlation between HRQoL with comorbidities status and types [31] [33]. However, many studies have reported the existence of comorbidities without explaining the type of comorbidities as it is shown in **Table 1**.

The severity of disease was considered the main factor to evaluate the disease progression and effectiveness of treatment. Sometimes it was linked with medication status and type of medication given to the patients through the course of treatment. The severity indicator factors are FEV1% predicted, GOLD staging, ABCD Criteria, CAT score, mMRC score, and FEV1/FVC%. Six studies were reported more than two factors as a predictor regarding the severity of disease [8] [15] [16] [17] [32] [44] while only three studies were reported not more than two factors that non predicting the HRQoL [17] [31] [42] [45]. However, most factors were reported, FEV1% predicted, FEV1/FVC%, CAT score, and GOLD stages.

Furthermore, the duration of disease, a number of hospitalizations, smoking behaviors and packs/year, and effect of weight measured by BMI were other clinical variables which discussed the correlation with HRQoL. Although many studies had confirmed these factors as a predictor, other studies reporting inconsistency with the same variables as not predicting factors as shown in **Table 1**. Moreover, there were widespread debates about the amount of smoke and behavior and it is a correlation with HRQoL. Six studies were reported no correlation between smoking behavior and the smoking indexes with HRQoL [15] [16] [17] [32] [39] [43], while in the following eight studies [11] [23] [27] [28] [38] [44] [46] [47] were reported an existence of correlation between smoking behaviors, smoking index, and HRQoL.

On the other hand, an old study carried out by Wijnhoven and his colleagues [48] reported a controversial result indicating better HRQoL in current smokers. The reasons that patients who are still smoking might be those with a less advanced stage of the disease. While another new study showed current smokers have a poorer quality of life (high total HRQoL score) compared with previous smokers [26].

Recently, new studied variables were discussed as a factors which correlates and predicting HRQoL, such as; type of work which was reported in one study [36], socioeconomic status in two studies [23] [24], nutrition type in one study [23], and the presence of family help and support in one study [24]. In contrast, the following studies were found type of works [23] [24] [25] [28] [37] [40], socioeconomic status [11] [25] [40], and living status [24] [25] [33] [38] not predicting the HRQoL in their population sample. Moreover, one study has reported the factors of areas of residency and seasonal variation effect. These factors were found not predicting the HRQoL [32]. Only one study has reported the correlation with pain, this factor was found not predicting the HRQoL [31].

A few studies have discussed the effectiveness of an interventional program. The 6MWD test is widely used among COPD patients. This test was correlated with lower scores of HRQoL in recent tow studies (best HRQoL) [17] [43]. Regarding the medication use was verified as a predictor of HRQoL. Shah and colleagues [23], Sharma and Joshi [25], Raheison and colleagues [34] demonstrated that deterioration in HRQoL was seen correlating with the number of prescribed medications, whereas other studies [8] [16] [47] were showed that the patients with the greatest impairment of HRQoL are those who are taking more than one medication, and those contained especially inhaled corticosteroids.

Together, numerous studies identified that lower education levels, more breathlessness, fatigue, lower BMI, anxiety, and depressive symptoms adversely affect the HRQoL. [10] [12] [15] [17] [49] [50]. In conclusion, the most common predictors of HRQoL among COPD patients were age, GOLD severity stage of the disease, dyspnea grade, and the number of exacerbations/hospitalizations. Other predicting factors include comorbidity, sex, body mass index, socioeconomic status, and educational level.

The Health-related quality of life was measured by using different generic and specific tools including general short-form (SF-12) health survey questionnaire which was utilized in three studies [16] [36] [51], MOS SF 36 was utilized in one study [33], and the specific one such as SGRQ-c was utilized in nine studies [8] [15] [17] [23] [24] [36] [37] [39] [43], EQ-5D was utilized in two studies [11] [13], Clinical COPD Questionnaire (CCQ) was utilized in four studies. [27] [28] [41] [46], and a newly developed one by study researchers was utilized in three studies [25] [26] [38]. The frequently utilized tool was the SGRQ-c through all reported studies. The SGRQ-c is a specific tool to measure the severity and HRQoL among patients with COPD. Out of all reported studies, most of the studies were solely used one tool to measure HRQoL, only two studies were used two types of tools in order to compare the level of HRQoL from two types of measurement and to report if there is a significant difference between each tool [33] [52]. Before it was common to see more than two types of tools were utilized to test HRQoL because of the need to cover all aspects of HRQoL, but now utilizing one specific tool is enough which covered the main aspects of HRQoL.

On the other hand, the majority of the study was utilized observational design in cross-sectional and longitudinal time series. The sample size was adequate the minimum in some studies was not less than 40 participants and the maximum, not more than 2734 participants. However, a few studies such as web-based surveys or prospective studies were failed to report the data collection period as shown in **Table 1**.

## **3.2. Correlates and Predictors between HRQoL and Other Variables**

### **3.2.1. Perceived Anxiety and Fatigue**

The patients with COPD experience a wide range of burdens which were represented with several symptoms, such as breathlessness, anxiety, and fatigue. These symptoms affect disease assessment and management. Fatigue was reported to be one of the most common symptoms among patients with COPD [53]. The patients with a chronic disease rated fatigue often as one of the key factors leading to reduced QoL [12]. However, the prevalence rate of fatigue was shown that almost half of all patients experienced abnormal fatigue: 23% mild and 24% severe fatigue in a study concerning the severity of fatigue in patients with stable, moderate to severe COPD [54]. While the prevalence rates for anxiety range from 17% to 51% [55]. Further, two studies supported that COPD patients have a higher incidence of anxiety 21% to 96% compared to 20% in the general population [50] [56]. Other studies were found that 90% of patients diagnosed with severe COPD suffered from severe breathing difficulty which was complicated by psychological distress related to anxiety and/or depression. The combination of factors resulted in an increased number of severe symptoms, hospitalization, and hospital mortality [56] [57].

Almost three studies discussed the correlation of HRQoL with fatigue. The qualitative study conducted by Kouijzer and colleagues [12], the authors pointed

out the purpose of the study was to examine the patient's perspective on COPD-related fatigue, the impact on activity daily life, and possible treatment opportunities to tackle the burden of fatigue. The study results showed the COPD-related fatigue causes a severe, negative impact on the physical, emotional, cognitive and social functioning of all participants. The negative impacts on daily functioning were negatively influenced by the HRQoL of patients leading to a heavy mental burden, decreasing patients' joy in life, and even in some cases their will to live. A qualitative study with face to face interviews was conducted to identify the domains of HRQoL from the perspectives of health care professionals. The study found fatigue and anxiety were the most important aspect correlated with impairment in HRQoL [10]. The two cross-sectional descriptive studies found a high correlation between disease symptoms like dyspnea, breathlessness with anxiety and fatigue which have an impact on the HRQoL among COPD patients [50] [58] [59].

Furthermore, a population-based study of (795) participants. The study was conducted to evaluate the correlation and compare between fatigue and HRQoL among COPD and Non-COPD patients. The study found clinically significant fatigue was correlated with worse HRQoL and independently correlated with anxiety [60]. Moreover, an observational study from secondary collected data was embedded within a randomized trial to test the effectiveness of pulmonary rehabilitation program on the level of activity and fatigue. The study results found that high fatigue patients had a greater improvement in both fatigue score in a chronic respiratory questionnaire and the SGRQ scores which indicate a high level of fatigue cause deterioration in the level of HRQoL with COPD patients [61].

Further studies about the correlation of HRQoL with anxiety, about five cross-sectional studies with an adequate sample size were conducted to evaluate the correlation between HRQoL and anxiety as shown in **Table 2**. Numerous studies had confirmed the results of COPD patients with anxiety had a poorer HRQoL and anxiety was the predictor of low mental HRQoL score [7] [19] [62]-[67]. Two qualitative studies with a focused group method were conducted. The studies aimed to explore patients' views and perceptions regarding COPD and their impacts on daily living. The results emerged four themes indicating that most patients with COPD experiencing difficulties in their psychosocial like anxiety and physical functions that affect their HRQoL and ultimately lead to social isolation [18].

On the other hand, fatigue was measured by using different tools including HADS were utilized in seven studies [4] [19] [64] [67] [68] [69] [70], STAI was utilized in one study [71], FACIT was utilized in one study [59], GAD-7 was used in two studies [7] [72], LFS was used in one study [50], BFI was used in one study [58]. The most frequently used tool was the HADS among all reported studies. This tool is a generic tool used to test anxiety and depression. Regarding fatigue, the GAD-7 was utilized as the most specific tool that has been used

among COPD patients.

### 3.2.2. Uncertainty among COPD

Uncertainty is defined as “inability to determine the meaning of illness-related events” [73]. However, if the expectations of health care providers differ from the expectations of patients, further confusion and patient uncertainty may be added [74]. Uncertainty about prognosis and symptoms is fundamental in living with a chronic health condition. COPD is characterized by breathlessness and airflow limitation that is not fully reversible. Thus, treatment focuses on managing symptoms and maintaining the HRQoL. The patients must recognize and appropriately understand their symptoms to take inhaler medications and seek evaluation for appropriate management [68]. There was a scarcity in the studies test a correlation of HRQoL with uncertainty. The old two studies were examined uncertainty among COPD patients based on a sample of (26) hospitalized patients [75] [76]. One more study has tested the effectiveness of a specific intervention to manage uncertainty [71]. In this study, the authors found a reduction in uncertainty and improvement in anxiety, depression, and quality of life among the intervention group.

A relatively recent longitudinal study over two years was used to determine which aspect of illness uncertainty (*i.e.*, ambiguity or complexity) has a significant correlation with psychological and selected clinical outcomes over a two year period among patients with COPD. The study results showed the greater uncertainty is correlated with more symptoms of depression and anxiety and reduced QoL. In addition, it was also correlated with worse physical symptoms (*i.e.*, pain and fatigue) [68]. Further studies are needed to investigate more about the uncertainty concept, and it is a correlation with HRQoL.

## 4. Discussion

The aim of this integrative review was to update, identify, and summarize kinds of literature that described HRQoL predictors and correlation of HRQoL with other variables limited to anxiety, fatigue, and uncertainty in patients with COPD. After a comprehensive search, the authors believe this is the first review conducted to cover the HRQoL correlations with variables of fatigue, anxiety, and uncertainty in specific and identifying between predicting and non predicting factors with HRQoL from (52) studies were included in this review. However, the previous review has described only the factors predicting the HRQoL, it was limited in the scope of articles, keywords of search engines, and searching coverage periods [77]. In the current study, **Table 1** “characteristics of the studies analyzing factors predicting the HRQL of patients with COPD” was included to evaluate the predictors of HRQoL across different studies. **Table 2** “study characteristics of correlates and predictors between HRQoL and other variables” was included to evaluate the correlation with HRQoL and other important variables. The tables were classified according to sample size, study design, data collection period, sampling methods, and type of tool used to measure

HRQoL. The two tables have presented a disagreement in the literature about the factors that predicting and non predicting the HRQoL among COPD patients.

The predictor factors were categorized according to factors related to demographic and clinical variables. What is new in this review, some related factors were examined which not discussed before in the literature. The factors were found as predictors of HRQoL such as; patient living status, work status and type, and help and support provider. Although numerous studies have been devoted to studying predictors of HRQoL and correlated factors in recent years among COPD patients, some HRQoL aspects remain unclear and need more investigations. A group of physical, emotional, and psychosocial factors was identified that correlated and altered of HRQoL. In conclusion, there is a discrepancy in the factors predicting and correlated HRQoL among COPD patients within the literature when utilizing specific tools to measure HRQoL.

Furthermore, this review identifies the instruments that had been used for collecting data indicating the SGRQ-c was the most utilized tool in the mentioned studies to measure HRQoL, the HADS to measure the anxiety, and the GAD-7 to measure fatigue, and the MUIS to measure uncertainty. Further, about the correlation with HRQoL, there was a significant correlation between anxiety, fatigue, and HRQoL among COPD patients. The literature still lacks clarity about the correlation of HRQoL with uncertainty among COPD patients. Further researches are needed to verify the validity of the reported correlation between HRQoL and other variables. In addition to a correlation with other sociodemographic and clinical variables to confirm the significant predictors.

Moreover, most of the reported studies have been carried out in developed countries. A few types of research have been carried out in developing countries. Cultural variations, pollution-related exposure, and special behaviors must be considered when disseminating the findings obtained from these studies. Contradicting findings are apparent in certain predictors of HRQoL as shown earlier in the provided tables. Additionally, the correlation with HRQoL was categorized according to correlation with perceived anxiety and fatigue and correlation with uncertainty. On the other hand, the studies included in this review were different in reporting quantitative and qualitative research design, sample size, and data collection methods and time period.

## 5. Limitations

Despite the important integrated findings in this review, the authors suggest that there are some limitations to be acknowledged. Excluding non-English language articles can minimize the chance of accessing some relevant literature. Additionally, most samples included participants from diverse cultural groups, complicating the generalizability of these studies, and making generalizations with respect to each study difficult. Finally, the heterogeneity among the studies in terms of the methodologies used and assessment tools makes it difficult to accu-

rately compare various aspects of the outcomes reported.

## 6. Conclusion

Health-related quality of life was low among patients with COPD. The HRQoL was decreased with the presence of anxiety and fatigue with COPD. There are many predictors that affect HRQoL with COPD. These predictors need more investigation and evaluation. The evaluation of HRQoL predictors among COPD patients should need to consider the measurement tools of HRQoL. The assessment of physical and psychological factors is important for improving COPD symptoms, preventing the consequent deterioration of HRQoL, and choosing the appropriate treatments. The literature demonstrated that HRQoL among COPD patients is apparent as an issue that needs further investigation from cultural perspectives. Certain predictors still have contradictory findings in the non-empirical literature. This review will expect to help in resolving discrepancies in the existing literature about predictors and correlated factors among COPD patients. It would be valuable to rule out which of these factors remain valid to predict HRQoL in a specific population and cultures. In clinical practice, screening for anxiety, fatigue, and uncertainty would refer potentially affected patients to specific care facilities for further assessment that may be promising approaches to improve the HRQoL among those patients. The findings from this review should encourage health care providers to explore carefully the predictors during patient history taking and interviews as an aid to help them understand why some patients may not respond to provided care options and why some of them are at high risk to a certain limit. This review will guide health care professionals to understand their patients in a more holistic manner.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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