Systematic Review

Confounders effecting Quality of life of COPD patients in European Union :A systematic review

Abstract:

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disease characterized by restriction in expiratory airflow. It is among one of the major causes of illness and death globally. COPD causes severe negative effects on physical and mental health. It has a drastic effect upon the health-related quality of life of patients. Numerous factors contribute towards morbidity of COPD that include smoking, obesity, air pollutants and comorbid conditions (cardiovascular diseases, diabetes mellitus, arterial hypertension, infections).

Aims and Objectives: The current systematic review was conducted with the aim to determine the health related quality of life of COPD patients as well as the confounders of quality of life.

Methodology: A systematic review was conducted of 22 studies. The electronic databases used to search the articles were Pubmed, Scopus, Science Direct, ProQuest, Web of Science. Total 1880 studies were found, out of which only 22 studies met the inclusion criteria. All the studies included are within 2017-2022. Patients met inclusion criteria have less than 70% FEV1/FVC ratio and diagnosis of patients was according to the GOLD staging system. Majority study design were observational, some were cross sectional, experimental and randomized clinical trials. Mean age of patients observed was 40-85 years. To assess the quality of life of COPD patient specific questionnaires has been used like SGRQ, CAT, CCQ, EQ-5D-5L.

Results: Included studies shows that the quality of life of COPD is compromised physically as well as mentally. It is due to less physical activities, smoking habits, psychological issues, comorbidities like diabetes mellitus, cardiovascular diseases, arterial hypertension.

Conclusion: All the studies concluded that COPD patients diagnosed on basis of GOLD criteria and their quality of life is assessed via disease specific questionnaires that majorly includes SGRQ, CAT, CCQ, EQ-5D-5L. And it shows that quality of life of COPD decreases overall.

Keywords: Quality of life, COPD patients in European Union, assessment of HRQoL of COPD patients, CAT, SGRQ, acute exacerbations in COPD patients

Introduction:

Chronic obstructive pulmonary disease (COPD) is a restriction in expiratory airflow. Numerous anatomical abnormalities, such as fibrosis, restriction of the tiny airways, and lack of lung elastic recoil, can cause this. Airflow restriction is also occasionally caused by secretions, edema, and inflammation. (Spurzem and Rennard 2005)

One of the main causes of illness and death globally is chronic obstructive pulmonary disease, or COPD. Dyspnea, airflow restriction, skeletal muscle dysfunction, and co-morbidities all contribute to the functional decline and restrictions that COPD patients experience on a daily basis (Weldam, Schuurmans et al. 2013).The stated prevalence of COPD varies by area; in Europe, it is about 4%.(Cave, Atkinson et al. 2012)

Patients with this chronic illness experience severe negative effects on their physical and mental health, as it negatively affects systems and organs other than the lungs. This can result in pneumonia , pulmonary hypertension , and cardiovascular disease (CVD).(Cave, Atkinson et al. 2012)

The World Health Organization estimates that 210 million people worldwide suffer from COPD, and that the disease claimed 3 million lives in 2005. A substantial decline in quality of life (QoL) and high rates of morbidity and mortality are linked to COPD, particularly but not only in the later stages of the illness. According to the most recent estimates provided by the Global Burden of Disease Study, COPD ranked third globally in 2010 for causes of death.(Almagro and Castro 2013) Between 1994 and 2010, 2,348,184 fatalities were ascribed to COPD in the European Union. The prevalence of COPD in Europe has been reported to range between 4% and 10%. Forced expiratory volume in one second (FEV1) is used to determine the severity of COPD. Nevertheless, there is little correlation between FEV1 and the disease's clinical signs.For a more thorough evaluation of the severity of the disease, and standardized measurement of patient-related outcomes (such as health status) has been suggested.Patients with COPD have been found

to have high rates of diabetes, cardiovascular illness, and mental disorders (such as depression and anxiety). (Almagro and Castro 2013)

When it comes to inflammatory cells, mediators, inflammatory effects, and therapy response, the inflammatory process in COPD differs greatly from that in asthma.(Barnes 2000)COPD is of late onset, slowly progressive symptoms, poor response to inhaled therapy, and typically associated with long-term smoking, asthma typically has an early onset with intermittent symptoms, a good response to inhaled therapy, and is frequently associated with other allergy diseases. (Cukic, Lovre et al. 2012, Gibson and McDonald 2015)

Whereas COPD is caused by a Noxious Agent (primarily cigarette smoking), asthma is caused by a Sensitive Agent. While airflow restriction in asthma is fully reversible, it is not in COPD cases. Asthma is characterised by variable wheezing, while COPD is characterised by persistent symptoms. In asthma, bronchial hyperreactivity (BHR) is expressive, whereas in COPD, it is minimal. In cases of asthma, bronchodilators and corticosteroids are beneficial; in cases of COPD, they are essentially ineffective.(Cukic, Lovre et al. 2012)

It is acknowledged that one of the most prevalent and significant symptom of COPD is fatigue.(Hynninen, Pallesen et al. 2007)One of COPD's hallmark symptoms, dyspnea, can be a powerful inducer of anxiety. In the multivariable analysis, COPD was linked to an increased risk of anxiety. Anxiety was linked to worse health outcomes in COPD patients and make them avoid any physical activities.(Eisner, Blanc et al. 2010, Jarab, Alefishat et al. 2018)Research has indicated that malnourishment or low body weight is prevalent amongst people with COPD; it affects roughly 10-15% of patients with mild-to-moderate disease and 50% of patients with chronic respiratory failure and advanced stages of the disease.(Wouters, Creutzberg et al. 2002, Decramer, De Benedetto et al. 2005)Patients with COPD complained of a variety of symptoms and experienced a lower standard of living.(Yi, Ban et al. 2018)

Reduced dyspnea, increased exercise tolerance, enhanced quality of life, and averting future risks are the objectives of care for COPD patients.Drugs with anti-inflammatory qualities and both short- and long- acting bronchodilators are included in pharmacological approaches(Roche 2018).The bronchodilators may be used as needed or as a long-term maintenance treatment, depending on the severity of the illness.Inhaled corticosteroids are added to the treatment

regimen when the disease reaches a severe stage.Treating COPD at any stage of the disease is possible even though it cannot be cured. Along with recommendations for patient treatment, the guidelines that offer information to aid in the diagnosis of COPD also include risk-reduction tactics, lifestyle modifications, and medication recommendations.Supplemental oxygen can help patients with severe COPD who may also have hypoxemia and/or hypercapnia. This treatment can also increase the patients' ability to exercise.Participation in pulmonary rehabilitation, which is advised for all patients with COPD, is a beneficial adjunct to medication (Fromer 2011)

Previous studies related to quality of life in COPD patients tells the following: Loanna,et al described that chronic obstructive pulmonary disease (COPD) is a prevalent disease in the general population and a considerable burden for patients with the disease. This burden differs between patient groups. Some patients can live their lives almost untouched by the disease, while others are almost completely handicapped. One way to indicate the burden of the disease to patients is assessment of health-related quality of life (HRQoL) and health status. Quality of life (QoL) in general refers to the patient's ability to enjoy normal life activities(Tsiligianni, Kocks et al. 2011). Margarethe reported that health-related quality of life (HRQL) of COPD patients typically declines: The overall severity of COPD is influenced by symptoms such as cough, dyspnea, and sputum production, as well as by acute exacerbations of the disease and comorbidities that are common in COPD patients(Wacker, Jörres et al. 2016). Regis ,et Al described that patients with COPD have been found to have high rates of diabetes, cardiovascular illness, and mental disorders (such as depression and anxiety). According to reports, these comorbidities greatly raised the probability of treatment expenditures as well as death and hospitalizations for COPD patients.It has been observed that several respiratory characteristics, such as the degree of airflow restriction, dyspnea, and recurrent exacerbations, are independently linked to a lower quality of life (HRQoL). There is limited information available regarding the effects of other comorbidities, such as diabetes and cardiovascular disorders, on HRQoL. However, recent research have further revealed that COPD participants with anxiety and/or depression had decreased HRQoL(Burgel, Escamilla et al. 2013)

The questionnaires used to assess quality of life in COPD patients are as following. The Chronic Respiratory Questionnaire (CRQ)(Flokstra-de Blok, DunnGalvin et al. 2008),Severe Respiratory Insufficiency (SRI) instrument was studied in one study in oxygen dependant COPD

patients(Windisch 2008), COPD Assessment Test (CAT) was studied in eight studies in mainly pulmonary rehabilitation patients and in one study in primary care patients, St. George Respiratory Questionnaire (SGRQ) was studied in 26 papers in different settings (community, hospital, and pulmonary rehabilitation), Shorter form SF-12 (SF-12) was studied in one study in exacerbation patients(Menn, Weber et al. 2010), HRQOL was assessed using the EQ-5D-3L, which is a validated instrument, Clinical COPD Questionnaire (CCQ) was studied in eight studies. Utility measure EuroQol EQ5D was studied in five studies in hospital.(Duiverman, Wempe et al. 2008)

Methodology:

Study design:

Study protocols were according to the PRISMA flow diagram guidelines. This study is a literature review of about 22 studies from the Europeon Union. Study search is done by the electronic databases along with the manual search on Google scholar. The research is restricted to the English language. The study designs of the studies involved were cross sectional, corhort, observational, longitudinal, randomized, nonrandomized controlled and controlled perspective study.

In identification step, all the data collected is searched from different databases and registers like Pubmed, Scopus, Science Direct, ProQuest, Web of Science. Almost 1880 studies were searched from databases like 648 from Pubmed, 578 from Scopus, 340 from science direct, from ProQuest we got 200 and from Web of Science we found 114 studies. Out of 1880, after screening 750 studies were removed because of duplicate record. 25 studies were record renounced and were also removed from the record. 1105 studies left in record. After further screening 945 studies were again excluded from the records. 160 studies sought for retrieval out of which 43 studies did not have full text available and on this basis they were excluded from record. Studies remain in assessment for eligibility are 117 at this point. They are further filtered out. 40 studies got excluded because they didn't belong to Europeon Union. 25 studies screened out because they had no clear impact on quality of life in COPD patients. Further on 20 articles were not published in journals and 10 studies didn't explain any questionnaire for the quality of life of COPD patients. At last stage only 22 studies were included that met the criterias for review.

Inclusion Criteria

22 studies met the inclusion criteria. Criteria is as follows:

1- All the patients suffering from COPD
2- Population to be taken is from Europeon Union
3- Assessment of HRQoL of COPD patient is done in study
4- Studies that used specific questionnaires for assessing QoL
5- Age of patients is above 55 years
6- Studies were published in English language
7- The studies were published in peer reviewed journals
8- Measurement of FEV1/FVC value is done in studies
9- Patients classified according to GOLD staging system

Exclusion Criteria:

Exclusion criteria were as follows:

1- Patients having asthma are excluded
2- Articles that were related to oxygen therapy
3- Questionnaire that doesn't measure QoL of COPD patients were excluded
4- Study other than in English language was excluded
5- Studies other than from Europeon Union were excluded

Data Extraction

The data which was extricated from research studies included: study titles, authors, study year, university country, study design, mean age/gender, inclusion criteria, study population, questionnaire, result of QoL, factors that are causing reduced QoL.

Data Synthesis and Analysis

The effect of Chronic obstructive pulmonary disease on the patients' health has been investigated from all the studies. And how COPD reduces the quality of life of COPD patients and factors that are involved in reducing HRQoL has been assessed. Decrease in physical activities and exercise has been observed. Hypoxemia and dyspneais also seen in COPD patients.

Results:

The topic of our study is **"Systematic review of quality of life of COPD patients in Europeon Union"**. The studies included in this review were 22 in number. All the studies showed the assessment of quality of life in COPD patient. Shows all the factors and activities that reduces the quality of life. For the assessment of HRQoL, there are some specific and standard

questionnaires i.e. SGRQ, CAT, EQ-5D-3L etc. Data extracted includes study year, author, study design, inclusion criteria, sample population, age, gender, factors affecting QoL of patients.

Study Year:

Total 22 studies were conducted from 2017-2022. Out of which two studies were from year 2017, three studies from 2018, three studies from 2019, eight studies from 2020, two studies from 2021, and four studies from 2022 were taken.

Country:

All the studiestaken were from countries included in Europeon Union. Out of 22 studies, five studies were collected from Spain, three studies from Denmark, four studies from Germany, one from Austria and one from Netherlands. In a similar manner, one study was picked from each of these following:Bulgaria, Marbug, Hungary, the Solvak Republic, Sweden, and Poland.

Study Design:

In these 22 studies**,** fourteen studies belong to observational study design, eight studies from cross sectional study, one study from cohort clinical trial, four studies from observational longitudinal study, one from controlled prospective study, seven studies from experimental study design, six studies from randomized clinical trial, one from non-randomized clinical trial, and last from descriptive study (survey data) has been included.

Mean Age/Gender:

Both male and female subjects were participated in our study. Mean age of the subjects was between the range of 40-85.

Ratio of males were compartively greater than females.

Inclusion Criteria:

Patients with age >40 years who are diagnosed with GOLD criteria were selected in our study. FEV1/FVC ratio less than 70% of patients were included. Patients who received a diagnosis based on ATS/ERS were also included. Patients with a history of smoking 10–20 packs per day were chosen. The study included retired individuals with an HRQOL of 41.7% and married

patients with an HRQOL of 58.3%. Furthermore, the study included computer-illiterate people with more than two hospitalizations and patients with respiratory failure.

Study Population:

Study population shows the sample size of patients involved in studies and surveys. All the patients in studies participated gave written informed consent. The evaluation of patients has been done over the years from 1-5 year in differnet studies. And majority of patients were taken from hospital settings.

Maximum sample size includes 11,577 patients under study. One of the study based on real world analysis examined 3016 COPD patients over one year. Another study shows 543 patients in sample size examined over 5 years and at the end of period only 324 left.

Mostly sample includes geriatrics. Minimum sample size included was of 94 patients and its study period was 12 months, at the end of study 53 patients left.

Each Sample size further divided into two or three groups of control group, cohort group, pysical therapy group, self management group etc.

Questionnaire:

Different questionnaireare used for the assessment of health related quality of life in COPD patients. Out of 22 studies, 7 studies used St. George's Respiratory questionnaire (SGRQ). In these 7 studies, 5 studies used SGRQ alone and one study used it along with other questionnaires including EQ-5D-5L and Clinical COPD questionaries' (CCQ). One study used SGRQ, EQ-5D-5L, CCQ and also CAT to assess quality of life.

Further on, 8 studies used the questionnaire CAT. Out of 8, 4 articles used CAT questionnaire along with combination of different other questionnaires for the assessment of quality of life. These includes EORTC30, EQ-5D-5L, CCQ, mMRC, 15D QoL.

15D questionnaire is used in one study. Short form-12 and short form-36 health survey questionnaire are being used in the study of Germany and Sovak Republic respectively.

Clinical COPD questionnaire has been used in 3 of the studies in combination with different questionnaires.

In one study Chronic Respiratory Questionnaire (CRQ) is used. Two studies holds EQ-5D-3L and SRI questionnaire respectively.

One article from Ukarian and Poland, did not use particular HRQoLquestionnaire for COPD patients. They used Ukrainian version of World Health Organization (WHOQOL-100) questionnaire for the assessment of quality of life of COPD patients.

Total 3 studies used EuroQoL Five-Dimensional Five-Level Questionnaire (EQ-5D-5L) with combination with other questionnaires.

Results of quality of life:

Out of 22 studies, nine studies showed the reduced quality of life due to various factors.

Remaining studies showed the improvement in quality of life due to hospital admissions, increased physicalactivities, and use of drugs for exacerbation reduction, better organisational care, LWWCOPD intervention, supplementation and weight reduction.

Factors that causes reduction of quality of life:

Out of 22 studies, four studies discussed comorbidities as a factor of reduced quality of life along with COPD. Major diseases reported are Diabetes Mellitus, Cardiovascular diseases, Arterial hypertension, asthma, cystic fibrosis, orthopaedic diseases.

Smoking has been a prime factor of reducing the quality of life in COPD patients. Three studies majorly highlighted smoking and tobacco as a factor. Malnutrition and low HDL has also been discussed with this.

Two studies explainspsychiatric issues like depression and anxiety as a factor that reduces quality of life in COPD patients. Also reported that people who are married are reported with other factors majorly instead of depression and anxiety in reduced QoL.

One study from Denmark explained cancer of lung, neck and head as a factor of reduced quality of life in COPD patients.

One of the study has discussed obesity as a factor that plays a part in reducing quality of life.

Anemia has also been discussed as the reason in one study picked from Germany along with chronic respiratory failure in reducing the QoL of COPD patients.

Three studies described high degree of symptoms i.e. sever exacerbation, decreased physical activities, unemployment, ageing as a main factors in reducing or decreasing the quality of life.

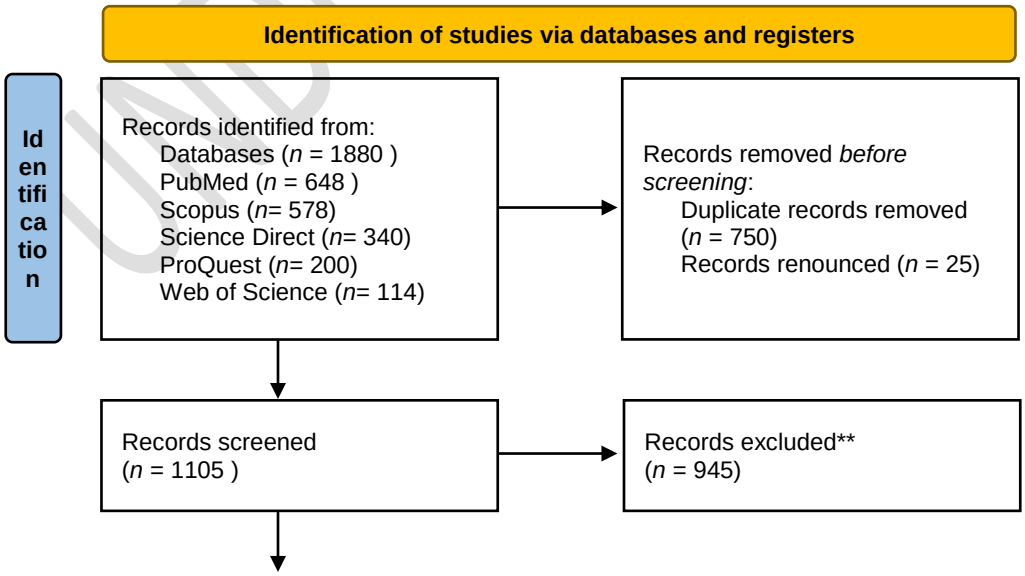
According to one study from Hungary, says high body mass index (BMI), less walk also leads to the same condition. Two studies from Spain described age, gender, traffic related air pollutants (NO2, PM2), residential distances to blue green spaces and pseudomonas aeroginosa for the severity of COPD and reduction of quality of life.

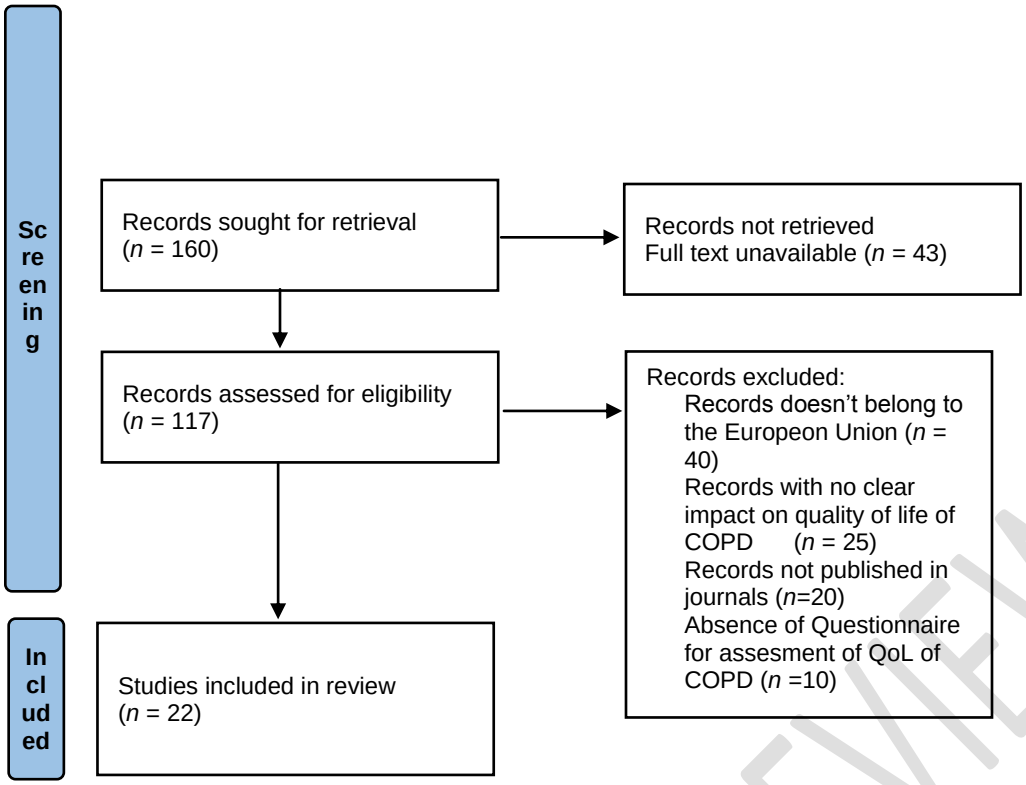
Lack of counselling and self-management has also been the reason for decreased QoL in one study.

One study collected from Sovak Republic says insufficient use of rehabilitations options and lack of research focused on mountain climate therapy are the factors.

Two studies didn't mention factors that causes the reduction of QoL. And one study described that hospitalization for exacerbations and physical activities can influence the health related quality of life.

Figure-1: PRISMA flow diagram for systematic review





*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit:http://www.prisma-statement.org/

Table 1. Quality assessment of included studies using AXIS tool.

AXIX tool items	Study 1 (Horner et al., 2020)	Study 2 (Mekov et al., 2022)	Study 3 (Tupper et al., 2018)	Study 4 (Brandl et al., 2018)	Study 5 (Szentes et al., 2020)	Study 6 (Huber et al., 2020)	Study 7 (Gottlieb et al., 2020)	Study 8 (Stöber et al., 2021)	Study 9 (Cosío et al., 2021)	Study 10 (Moitra S. et al., 2022)	Study 11 (Folch-Ayora et al., 2019)	Study 12 (Fekete M et al., 2022)	Study 13 (Steurer-Stey et al. 2018)	Study 14 (Kubincová et al. 2018)	Study 15 (Valentijn et al. 2021)	Study 16 (Lopez-Lopez et al. 2020)	Study 17 (Wollsching-S et al. 2021)	Study 18 (Persson et al. 2020)	Study 19 (Arndal et al. 2020)	Study 20 (Schenk et al. 2021)	Study 21 (Grygus et al. 2019)	Study 22 (Esteban et al. 2020)
Were the aims/objectives of the study clear?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the study design appropriate for the stated aim(s)?	Yes	No	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Was the sample size justified?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Was the target/reference population clearly defined?	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were measures undertaken to address and categorise non-responders?	No	No	No	No	No	Yes	Yes	Yes	No	No	Yes	No	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes
Were the risk factor and	Yes	No	No	Yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes

outcome variables measured appropriate to the aims of the study?																						
Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes
Were the basic data adequately described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Does the response rate raise concerns about non-response bias?	No	No	No	No	No	Yes	No	Yes	No	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes
If appropriate, was information about non-responders described?	No	No	No	No	No	Yes	Yes	Yes	No	No	Yes	No	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes
Were the results internally consistent?	Yes	No	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	yes	Yes	Yes	Yes
Were the results presented for all the analyses described in the methods?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the authors' discussions and conclusions justified by the results?	Yes	yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the limitations of the study discussed?	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes

Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	yes	No	No	Yes	No	No	Yes
Was ethical approval or consent of participants attained?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	Yes

Table-2: Study characteristcs of the included 22 studies

Sr. No.	Study	Study year	University / Country	Study design	Mean age / Gender	Inclusion Criteria	Study population	Questionnaire used	QoL	QoL-Confounders
1.	Quality of Life and Limitations in Daily Life of Stable COPD Outpatients (Horner et al., 2020)	2020	Kepler University Hospital, Department of Pulmonology, Austria	Cross-sectional study design	62.8% men; mean age 66.2 ± 0.3 (SE) years	Inclusion: age ≥40 years, a physician's diagnosis of COPD according to GOLD recommendations.	850 patients; mean FEV1%pred. 51.5 ± 0.6 (SE)) were analys ed.	St. George's Respiratory Questionnaire for COPD patients	Half of the patients (50.3%) reported not being able to do any sports and 78.7% stated that their respiratory symptoms did not allow them doing anything they would like to do.	Diabetes mellitus, Arterial hypertension, Cardiac disease, Smoking status
2.	Two-year mortality following a severe COPD exacerbation in Bulgarian patients (Mekov et al., 2022)	2022	Department of Occupational Diseases, Department of Pulmonary Diseases, Central Clinical Laboratory, Medical University Sofia Bulgaria	observational	*Mean age, years 65.1 (± 9.9) years * Male / Female= 108 (71.1%) / 44 (28.9%)	included patients had FEV1/FVC ratio < 0.70 fol-lowing administration of a bronchodilator.	152 consecutive COPD patients hospitalized for COPD exacerbation who gave written in-formed consent	CAT and mMRCquestiinarre	the presence of severe exacerbation, reduced quality of life, low BMI— increased mortality	Low HDL, Smoking
3.	Effect of tele–health care on quality of life in patients with severe COPD (Tupper et al., 2018)	2018	Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark	Randomized clinical trial	68-70 years old females	*Post-bronchodilator forced expiratory volume in 1 second [FEV1]/forced vital capacity ,0.7. *Post-bronchodilator FEV1,60% of predicted value.	281 (51.2%) patients gave written informed consent to study participation	15D Qolquestionnaire, CAT	A small improvement in the QoL	degree of symptoms and physical functioning
4.	Factors associated with generic health-related quality of life	2017	University of Regensburg, Regensburg, Germany	cross-sectional study, prospective patient cohort	65 years old (SD =8.85) 2/3 are male sex	Patients were recruited from primary care and specialist practices as well	206 COPD patients (60.7% male; mean age:	Short-Form 12 (SF-12) Health Survey Questionnaire	HRQol, is reduced by psychatric activities	Depression, anxiety

	(HRQOL) in patients with (COPD) (Brandl et al., 2018)			study		as from in- and outpatients from hospital settings	65.3 years)			
5.	Measuring quality of life in COPD patients: comparing disease- specific supplements to the EQ-5D-5L (Szentes et al., 2020)	2019	Ludwig-Maximilian's-University Munich, Germany	cross-sectional study	65± 5years	Analyzed patient-level information from DMP documentation and health insurance claims data. No more iclusion criteria is mentioned in study	1,350 participants	EuroQoL Five-Dimensional Five-Level Questionnaire (EQ-5D-5L), CAT, CCQ, SGRQ	Reduced qol is seen in patients	--
6.	The relationship between BMI and health-related quality of life in COPD (Huber M.B. et al., 2020)	2020	Institute of Health Economics and Health Care Management, Germany	Survey data (real-world evidence)	Age 65 ±5years, Female: 4,751 (41.0%), Male: 6,826 (59.0%)	Patients who participated in the COPD disease management program (DMP) in the respective year were included in this evaluation	11,577 patients	--	severe COPD might improve following weight reduction	Obesity
7.	Optimizing COPD treatment in patients with lung or head and neck cancer does not improve quality of life – a randomized, pilot, clinical trial (Gottlieb M et al., 2020)	2020	Copenhagen University Denmark	Experimental (randomized control trial)RCT	Age: 65±5 Females patients	Patients with an FEV1/FVC ratio <0.70, no significant beta-2-reversibility and no actual or pre-vious doctor-diagnosed asthma were eligible	114 patients	CAT and EORTC30 questionnaire	In this population of severely ill cancer patients, we did not find that this intervention, focusing on inhaled COPD medication, for the management of COPD had any convincing positive impact on the patients' perceived quality of life compared with usual care	Lung cancer, head and neck cancer
8.	Impact of Lung	2021	1-Helmholtz	Observational,	59.8% were male,	--	3016 COPD	EQ-5D-5L, (St.	FEV1 decrease	severe

	Function and Exacerbations on Health-Related Quality of Life in COPD Patients Within One Year: Real-World Analysis Based on Claims Data (Stöber et al., 2021)		Zentrum München, Neuherberg, Germany 2-IBE, Ludwig-Maximilians University Munich, Germany 3-Philipps-University Marburg, Germany	longitudinal study	mean age was 68.9 years,		patients	George's Respiratory Questionnaire (SGRQ), Clinical COPD Questionnaire (CCQ))	was associated with a significant but not minimal important difference (MID) deterioration in disease-specific HRQoL (mean change [95% CI]: CAT +0.74 [0.15 to 1.33])	exacerbation is significantly associated with an overall deterioration in disease-specific HRQoL.
9.	Implementation of an integrated care model for frequent-exacerbator COPD Patients (Cosío et al., 2021)	2020	Son Espases University Hospital – IDISBA Spain	Controlled prospective study	Age: 75±5years Male/Female = for standard care group 102 (77.3)/30 (22.7) And for ICM group 101 (71.6)/40 (28.4)	COPD patients diagnosed according to gold criteria with history of >2 AECOPD Required hospitalization and fulfilled inclusion criteria with no exclusion criteria for ICM	141 patients	CAT	Decreases ER and hospital admission and improves health status, but not mortality	Age, gender, pseudomonas aeroginosa are factors that causes severity of disease.
10.	Role of physical environment in health-related quality of life in patients with COPD (Moitra S et al., 2022)	2022	Pompeu Fabra University Barcelona, Spain	Cross sectional study (Randomized controlled trial)	Mean age of 69years 85% of males.	Patients approaching any of 33 primary care centres and five tertiary hospitals of five seaside and diagnosed with COPD according to ATS/ERS were recruited	Sample size was 407 geriatrics patients	CAT, CCQ	Reduced QoL in patients	Traffic related air pollutants (NO2 ,PM2) And residential distances to blue green spaces
11.	Patient education during hospital admission due to exacerbation of COPD	2018	University Jaume I, Castellon de la Plana, Spain	Controlled and randomized experimental study	Age: Mean±(SD) = 73.0 (9.4) Males: 94 (81.0) Females: 22 (19.0)	Patients diagnose with COD based on a history of smoking of 20 packs per year along with barely	Sample size was 446	SGRQ	Mean hrql score upon admission was 48.3+-20.0 Decreased in the IG on average by 6.83 points. CG	Smoking ,malnutrition

	(Folch-Ayora et al., 2019)					reversible air flow obstruction			barely shows changes in scores with avg reduction of 0.26 points Average drop of 15.76 in absolute change and an average drop of 23.99% in relative change	
12.	Effects of omega-3 supplementation on quality of life, nutritional status, inflammatory parameters, lipid profile, exercise tolerance and inhaled medications in COPD (Fekete M et al., 2022)	2022	Semmelweis University, Faculty of Medicine, Budapest, Hungary	CROSS SECTIONAL	**Age**: Omega3 consumer: 57.5-72.5 Omega3 non-consumer: 61-73 **Man**: Omega consumer=10 (52.63%) Omega3 non-consumer=180 (47.24%) **Woman**: Omega consumer= 9 (47.37%) Omega3 non-consuemr= 201 (52.76)	Inclusion criteria were: age ≥40 years and diagnosis of COPD [post-bronchodilation of forced expiratory volume in one second/forced vital capacity (FEV1/FVC) <70%].	400 patients	CAT	We observed better quality of life {CAT: 25 [21–30.5] vs. 26 [20–31]; P=0.519} , lower number of exacerbations in the previous half year [0 (0–1) vs. 1 (0–2); P=0.023], higher 6MWT values in the group with omega-3 supplementation	LESS WALK High BMI reduces the quality of life.
13.	Effects of the "Living well with COPD " intervention in primary care (Steurer-Stey et al. 2018)	2017	University of Zurich, Switzerland, University of Amsterdam, The Netherlands	prospectively planned, non-randomised controlled study	**Age years**: LWWCOPD group= 69.3±10.3 Control group= 67.1±10.0 **Male**: LWWCOPD= 28 (39.4%) Control= 225 (56.8%)	**Inclusion criteria** for both the mediX and ICE COLD ERIC cohorts were as follows: age ⩾40 years; a smoking habit (current or past) ⩾10 pack-years; a confirmed diagnosis of COPD; and a ratio (FEV1/FVC) ⩽0.70, with less than 12% and less than 200 mL increases in	467 patients; 71 in the LWWCOPD self-management group and 396 in the ICE COLD ERIC routine care control group	Chronic Respiratory Questionnaire domain	LWWCOPD intervention improved HRQoL to a clinically relevant extent and reduced COPD exacerbations	Lack of patient counselling and self-management

						FEV1, post dilatation, according to the GOLD & GOLD II–IV classifications . All participants be able to attend training sessions for 6 weeks.				
14.	The Effect of Pulmonary Rehabilitation in Mountain Environment on Exercise Capacity and Quality of Life in Patients with Chronic Obstructive Pulmonary Disease (COPD) and Chronic Bronchitis (Kubincová et al. 2018)	2018	Department of Physical Medicine, Balneology and Medical Rehabilitation, Medical Faculty of P. J. Šafárik University and L. Pasteur University Hospital in Košice, Košice, Slovak Republic	Observational comparison	Age (years) COPD 65.7±11.9	Comparing 2 groups of patients (patients with COPD and patients with CB) before initiation of the treatment with baseline measurements, and again after the intervention of 3 weeks of pulmonary rehabilitation in a mountain environment.	128 consecutive patients (90 diagnosed with COPD and 38 diagnosed with CB)	QoL questionnaire SF-36	there was a statistically significant **improvement after the intervention** in all the monitored subscales and summative scores in both CB patients and COPD patients (P<0.001 for all.	insufficient use of rehabilitation options lack of research focused on mountain climate therapy
15.	Cross-sectional study evaluating the association between integrated care and health-related quality of life (HRQOL) in Dutch primary care (Valentijn et al. 2021)	2020.	Department of Health Services Research, Maastricht University, Maastricht, The Netherlands	Cross-sectional study	Mean age of the participants was **62.1 (14.4) years**. **54.7%** of the sample were **female**	The majority of the participants were married (70.3 %) and almost half (49 %) were retired. Of the participants, 449 were categorisedin the high HRQOL group (58.3 %) and the remaining 321 were in the low HRQOL group (41.7%).	933 respondents participated	EQ-5D-3L	The present study showed that patients with a **better organi-sational care coordination experience were more likely to have a higher HRQOL.**	Unemployment and ageing were associated with lower HRQOL, and people who were married reported less anxiety and depression

16.	Results on health-related quality of life and functionality of a patient-centered selfmanagement program in hospitalized COPD: a randomized control trial (Lopez-Lopez et al. 2020)	2019	Department of Physiotherapy, University of Granada, Granada, Spain	Randomized clinical trial	**Age (years):** Control group=71.35±9.88 Physical therapy=71.20±11.53 Self management group=72.63±7.37	Patients of both sexes were included as long as they were older than 40 years of age, were diagnosed with severe COPD according to the criteria of the GOLD 3 or 4), were hospitalized due to acute exacerbation of COPD and agreed to participate.	a total of 66 patients were randomized in the three groups and performed the intervention with pre- and post-assessment.	The EQ-5D is a self-administered, health-related quality-of-life questionnaire	At 3 months, HRQoL shows **reductions in all subscores** in Control Group and Physical Therapy groups, while Self-Management group shows minimal maintenance of the values	cardiovascular disease, orthopedic diseases
17.	Anemia Severely Reduces Health-Related Quality of Life in COPD Patients Receiving Long-Term Home Non-Invasive Ventilation (Wollsching-Strobel et al. 2021)	2022	Witten/Herdecke University, Faculty of Health/School of Medicine, Germany	cohort study	**Age [years]=** 65.6 ± 8.1 **Female/male** [%] 46.1/53.9	Patients were only included if their chronic respiratory failure was primarily attributable to COPD. Regularly scheduled follow-up visits as well as those with acute problems	A total of **128** patients were enrolled for data analysis. Overall**, 32.8% of the patients were anemic**, while 4.7% had polycythemia	SRI	Overall, **32.8% of the patients were anemic,** while 4.7% had polycythemia.	Anemia plays a highly important role in reducing HRQL in patients with chronic respiratory failure,
18.	The Health Diary Telemonitoring and Hospital-Based Home Care Improve Quality of Life Among Elderly Multimorbid COPD and Chronic Heart Failure Subjects (Persson et al.	2022	Linköping, Linköping University, sweden.	cross-sectional study.	patients aged ≥65 years.	Elderly computer-illiterate subjects with ≥2 hospitalizations the previous year were included	**94patients** were enrolled of which 53 subjects completed the 12-month study period	St. Georges Respiratory Questionnaire (SGRQ)	the disease-**specific HRQoL was worsened at the 12 month**evaluation. At end-stage diseases subjects with COPD and CHF typically experience impaired functioning and	CHF

	2020)								impaired Qol.	
19.	Chronic rhinosinusitis in COPD: A prevalent but unrecognized comorbidity impacting health related quality of life (Arndal et al. 2020)	2020	Copenhagen University Hospital, Denmark	cross sectional study	**Age, mean (SD)=** 70.2 (8.9)	--	222 patients	CAT	CRS decreases HRQoL	asthma [1], bronchiectasis [2], cystic fibrosis [3] and primary ciliary dyskinesia The impact of CRS on HRQoL in COPD patients is comparable to CRS patients in general but significantly worse compared with COPD patients.
20.	Can simvastatin reduce COPD exacerbations? A randomised double-blind controlled study (Schenk et al. 2021)	2020	Medical University Vienna, Austria	randomised double-blind controlled study	Patients aged till 85 years/ Males	GOLD grade 2–4 were enrolled according to lung function criteria: ratio of forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC) <70% and FEV1 <80% predicted after bronchodilator use. They were current or former smokers with ⩾20 pack-years lifetime cigarette consumption.	208 patients	St George's Respiratory Questionnaire (SGRQ)	simvastatin at a dose of 40 mg daily significantly prolonged time to first COPD exacerbation and reduced exacerbation rate.	--
21.	The quality of life in COPD patients in the process of physical rehabilitation	2019	Nicolaus Copernicus University, Toruń, POLAND	randomised control trial (RCT)	**Adult** population**.** average age was **59.19 ± 0.74 years**		**124 patient. 64 (51.61%) males** and **60 (48.39%) females**	Ukrainian version of the World Health Organization Quality of Life Questionnaire	improvement of the overall quality of life increased indicators in problematic	--

	(Grygus et al. 2019)							(WHOQOL-100)	facets. decreased discomfort, decreased drug addiction, increased mobility, vital activity	
22.	Predictive factors over time of health-related quality of life in COPD patients (Esteban et al. 2020)	2020	Respiratory Department, Hospital Galdakao-Usansolo, Galdakao, Bizkaia, Spain	prospective observational longitudinal study	67years ±5 Males 308 Females 16	Patients were included in study if they diagnosed with COPD for at least 6months and had been stable for 6weeks. Other inclusion criteria were (FEV1) post-bronchodilator <80% of the predicted value and a FEV1/forced vital capacity ratio<70%	Geriatrics, 543 patients at start. Over 5year 324 left.	Saint George's Respiratory Questionnaire (SGRQ),	**PA** was related to a 13 to 35% better activity and impacts scores of HRQoL, depending on the level of PA, **hospitalizations** were related to 5 to 45% poorer HRQoL scores. **Pulmonary function was associated** with all HRQoL components, with an approximately **5% improvement in HRQoL**	Two key modifiable factors that influenced HRQoL were Physical Activity and hospitaliza-tions for exacerbation.

Discussion:

The state of health in individuals with COPD is impacted by numerous variables. However, because there are numerous questionnaires in use and some factors affect multiple sections or domains of the existing questionnaires, it is challenging to assess the degree of influence of each factor on health status. Several studies have also been conducted on evaluation of quality of life among COPD patients. This review evaluates the quality of life among COPD patients in European union countries and the effects of variable factors and different interventions on the quality of life.

This review presents that smoking is a prime factor of reducing the quality of life in COPD patients .Three studies majorly highlighted that smoking and tobacco as a cofactor .Similar results were shown by study conducted in chest disease research institute Kyoto ,Japan on 132 patients using Nottingham Health Profile as a general HRQL measure that reported air flow limitation, diffusing capacity ,life time cigarette consumption were significant predicators of HRQL in stable COPD patients.(Tsukino, Nishimura et al. 1996) In contrast a review article having databases from 2006 to 2007 from different countries of world by N.S.Godtfredson suggested that smoking cessation recommendation is not proportionate to degree of morbidity cause by smoking. . Smoking cessation in mild-to-moderate disease can prevent progression of disease severity; however, it is not known what characterizes smokers with different stages of COPD who choose to stop smoking compared with those who continue. (Godtfredsen, Lam et al. 2008)

This systemic review provides insight into the association of comorbidities and reduced quality of life in COPD patients .out of 22 studies four studies discussed comorbidities like Diabetes mellitus, cardiovascular disease, arterial hypertension, asthma, cystic fibrosis and orthopedic disease as factor of reduced quality of life . Similar results were shown in a systematic review by Manuel B.Huber,who concluded results from 25 studies of different parts of world ,in which it was clearly shown that certain comorbidities like CVD and diabetes worsen the quality of life in COPD patients.(Huber, Wacker et al. 2015) In contrast a cross sectional study conducted in 2002 in Netherland institute for health services research among 161 COPD patients and 395 asthma patients recruited from general practice reported that cardiac disease is associated with

HRQoL in asthma but not in COPD. The presence of hypertension is not associated with poor disease specific HRQoL in COPD patients. (Wijnhoven, Kriegsman et al. 2003)

The data from the studies also showed that the psychiatric issues like depression and anxiety are also the major factors that reduce the quality of life in COPD patients. Similar results were shown in a cross section analysis of data from the French COPD cohort initiatives BPCO ,data recorded in stable state and included spirometry ,dyspnea, mood disorders and comorbidities . The data suggested that in presence of dyspnea and exacerbations ,depression is the most important contributor to HRQoL impairment measured by SGRQ in COPD patients. (Burgel, Escamilla et al. 2013) In contrast a systematic review by Amy Baranaik in 2009 data collected from electronic journals and databases suggested that efficacy of psychological interventions to improve anxiety, depression and quality of life in COPD patients is relatively sparse.(Burgel, Escamilla et al. 2013)

Anemia has also been discussed as the reason in one study picked from Germany along with chronic respiratory failure in reducing the QoL of COPD patients .similar evidence shown in a retrospective study conducted by Marcello in Italy in which previous record of 105 patients analyzed .the study suggested that prevalence of anemia is 12.3% in COPD patients .anemia associated with reduction of exercise capacity, an increase of dyspnea and deterioration of quality of life. (Ferrari, Manea et al. 2015) In contrast a study conducted by Casanova et al in hospital Universitario Quiron Madrid on 130 COPD patients suggested that anemia prevalence was only 6.2% in patients ,it was less prevalent. (Echave-Sustaeta, Lozano et al. 2013)

The data from the studies in this review also depicted an association between nutritional status and the quality of life in COPD patients. Malnutrition increases dyspnea and exercise intolerance in COPD patients. BMI is closely related to dyspnea. Similarly , a prospective study conducted in department of chest diseases in IstanbulTurkey by Banu et al on 65 COPD patients also suggested that malnutrition is linked to a marked decrease in the strength and endurance of the respiratory muscles, an increase in airflow restriction, and an exacerbation of respiratory muscle dysfunction already present caused by hyperinflation. (Salepci, Eren et al. 2007). In contrast a prospective randomized controlled trial study conducted by Efthimiou et al in UK to investigate the effect of 3 months of oral supplementation in 14 poorly nourished outpatients with COPD reported that following three months of nutritional supplements, there were no differences in the

pulmonary functions of moderate-to-severe COPD patients who were undernourished compared to those who were well-nourished. (Efthimiou, Fleming et al. 1988)

The data from the study also showed that the cancer of head ,neck and lung also contribute to reduce the quality of life. This finding is similar to the retrospective study conducted in South Korea by Young soo-yi which reported that high prevalence of COPD was found in patients with non-small cell lung cancer with diminished quality of life. (Yi, Ban et al. 2018)

The data from the studies also suggest association between obesity and reduced health related quality of life in COPD patients. Similar results were shown by the cohort study conducted on 364 patients in Washington by Laura et al in which obese patients reported increased severity of dyspnea and overall poor health related quality of life. (Cecere, Littman et al. 2011) In contrast a cohort study conducted in France by Pierre on 633 patients reported that in presence of dyspnea ,depression was the most important factor in reducing quality of life while obesity has little effect in reducing quality of life. (Burgel, Escamilla et al. 2013)

This review also depicted an important factor traffic related air pollutant in reducing the quality of life in COPD patients .Similarly a cross sectional study conducted in Hong kong by Fong et al also described a strong association between the quality of air and the reduced quality of life in COPD patients. (Fong, Mui et al. 2010)

In same way a cross sectional study on 407 stable COPD patients conducted in spain by Moitra et al also showed that high residential exposure to traffic related air pollutants are associated with poorer quality of life in COPD patients. (Moitra, Foraster et al. 2022)

The study included in this review suggested that insufficient use of rehabilitation facilities has great impact in reducing the quality of life in COPD patients. Similarly a systematic review in Germany by Micheal et al interpreted that non pharmacological interventions like pulmonary rehabilitation and counseling has important role in improving the quality of life in COPD patients. (Hindelang, Kirsch et al. 2020)

CONCLUSION:

All the studies concluded that COPD patients diagnosed on basis of GOLD criteria and their quality of life is assessed via disease specific questionairres that majorly includes SGRQ, CAT,

CCQ, EQ-5D-5L. The study designs we included were observational , cross sectional , randomized, experimental and cohort. Overall, decrease in quality of life in patients of COPD has been seen and observed. Factors that contribute in this are comorbidities (cardiovacular diseases, aterial hypertension, psychotic disorders, diabetes mellitus, orthopedic diseases), obesity, traffic irritants, pollutants, anemia. Also one study claims lung, head and neck cancer to contirbute in the reduction of quality of life in COPD patients. This compromised life of COPD patients then leads to less physical activites, high BMI, less walking. Proper hospitalization and follow up can make the health a little better but cannot save a person from mortality.

LIMITATIONS OF THE STUDY

The current study is a systematic review of QoL of COPD patients from the regions of Europe. Therefore, it lacks the worldwide prospective.

ETHICAL APPROVAL

The current systematic review was conducted after getting ethical approval from the university's ethical review board with ethical protocol number: ERB-PHRMD-DPP/4529-A

INFORMED CONSENT

Not applicable

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