Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): A Population-based Study

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Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): A Population-based Study

Running title: Stress & COPD

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ARTICAL SUMMARY

Article focus

- The relationship between life event stress and chronic obstructive pulmonary disease (COPD).
- The impact of life event stress on the cognitive, mental and physical functioning of individuals with COPD.

Key messages

- Our findings showed that in individuals with COPD, life event stress unrelated to their illness experience had a worse effect in aggravating depressive symptoms and poor physical and mental functioning, more than in non-COPD individuals.

Strengths and limitations of this study

- The case definition for COPD in this study was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria.
- The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis.
- Definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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Abstract

Objectives: To study the relationship between life event stress and chronic obstructive pulmonary disease (COPD) and its impact on the mental and physical functioning of individuals with COPD, which are seldom investigated.

Design: Cross-sectional study.

Participants: A population-based sample (N=497) of individuals aged 65 and above with COPD (post-bronchodilatation $FEV_1/FVC<0.70$, N=136) and without COPD (N=277).

Outcome measures: We measured stressful life events, depressive symptoms (GDS), cognitive symptoms and function (CFQ, MMSE), and functional status (SF36-PCS and SF36-MCS) in participants with and without COPD.

Results: In two-way analysis of variance, event stress was associated with significant main effects on worse GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS scores ($p<0.001$), and with significant interaction effects in aggravating GDS score ($p<0.001$), SF36-PCS ($p=0.045$) and SF36-MCS ($p=0.034$) in participants with COPD more than in non-COPD participants, controlling for potential confounders. Main effect of COPD was found for FEV_1 ($p<0.001$) and CFQ ($p=0.02$).

Conclusions: Life event stress was found to aggravate worse mental health and impaired functioning in individuals with COPD, much more than in those without COPD. Psychosocial stress factors should not be ignored in clinical practice when there's a relapse or flare-up of COPD symptoms.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands out among chronic diseases with its high and rising prevalence and mortality [1], poor quality of life, frequent hospitalization and huge societal burden of care [2]. Because patients with COPD bear a heavy burden of psychological disturbances, psychiatric morbidity, and disability in daily living activities as well, the mental health of COPD patients has received growing attention in recent years.

Psychological factors are now recognized to play important roles in the etiology of chronic illness such as type II diabetes, coronary heart disease, gastroenterological disorders and obstetric outcomes [3]. The effects of chronic stress on the hypothalamic–pituitary–adrenal (HPA) axis and neuroendocrine profiles is known to result in depression, psychological burnout or post-traumatic stress disorder (PTSD) in all ages, but in late life, as well, there is growing evidence that it may also result in cognitive disorders ranging from mild cognitive impairment (MCI) to Alzheimer's disease [4]. Studies [5-7] have reported that psychological factors, such as anxiety and depressive symptoms, are common in COPD patients and are better predictors of COPD-related quality of life than pulmonary function.

Chronic stress in COPD patients include their illness experience of various difficulties in their emotional functioning, sleep and rest, physical mobility, social interaction, activities of daily living, recreation, work and finance. An extensive literature has described the stress and anxiety provoked by breathing difficulties/dyspnea in COPD, [8, 9] including muddled thoughts, heightened emotions, extreme fear and panic and decreased physical energy.

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The relationship between life event stress (extrinsic to illness-related experience) and COPD and the impact of stress on the mental and physical health and functioning of individuals with COPD has rarely been investigated [10, 11]. Life event stress relate to both the occurrence of negative life events and the appraisal and perception of the stressfulness of the event by the individual. Individuals with COPD may differ considerably from their non-COPD counterparts with respect to their psychological reaction to life situations they perceive as stressful, including the ways in which they deal with the various demands posed by their respective chronic illness. Thus stress cognition has a direct effect on mental health in patients with COPD [12]. Andenæs et al. (2006) [13] found that there is a continual interplay between subjective appraisals of stressful events and outcomes including psychological disturbances among COPD patients. The limited number of studies investigating the relationship between subjective stress and COPD thus warrants much further investigation [14].

The present study aimed to investigate the impact of life event stress on mental and physical health and functioning in a population-based sample (Singapore Longitudinal Aging Study) with and without COPD [15]. We hypothesized that in individuals with COPD, life event stress unrelated to their illness experience had a worse effect in aggravating depressive symptoms and physical and mental impairment than in non-COPD individuals. This was done by investigating the main effects of life event stress as well as the interaction between perceived life event stress and COPD in relation to depressive symptoms and SF-36 measures of mental and physical functioning.

METHODS

Study Design and Participants

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The participants in the study were an area subsample (*n*=497) from the Singapore Longitudinal Aging Study (SLAS-2), a prospective population-based cohort study of aging and health of community-dwelling elderly [16]. A whole population of all older adults aged 65 or older, who were residents in one district were identified from door-to-door census, and invited to participate in the study. Residents who were mentally or physically unable to give informed consent or participate were excluded. The response rate was 78.5%. All participants signed written informed consent for the study which was approved by the National University of Singapore Institutional Review Board.

COPD

We identified cases of COPD among the participants who had characteristic symptoms of COPD and spirometric evidence of chronic airflow obstruction (post-bronchial dilatation FEV1/FVC< 0.70), in accordance with the definition recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [17].

Ventilatory function testing was performed using a portable, battery operated, ultrasound transit-time based spirometer (Easy-One; Model 2001 Diagnostic Spirometer, NDD Medical Technologies, Zurich, Switzerland). Calibration was checked daily with a 3-L syringe. Forced expiratory maneuvers were performed with the respondent seated with recommended guidelines and standardization of procedures: at least three acceptable maneuvers, with forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) reproducible within 200 ml. Chronic airflow obstruction after bronchial dilatation was defined as FEV1/FVC < 0.70.

Questions from the British Medical Research Council Questionnaire on chronic respiratory symptoms were used to elicit symptoms characteristic of COPD: chronic

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cough and/or sputum lasting at least 3 months in the year and/or breathlessness on exertion.

Life Event Stress

Stressful life events and self-ratings of stress were measured by an 11-item life events inventory [18, 19] that excluded personal illness experiences directly related to COPD. The participants were asked to indicate yes or no as to whether any of eleven life events had occurred over the past year: spouse or partner die, a close friend or family member die or have a serious illness (other than your spouse or partner), major problems with money, a divorce or breakup, family member or close friend have a divorce or breakup, major conflict with children or grandchildren, major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events, a family member or close friend lose their job or retire, physically abused, verbally abused, or pet die". If the participant indicated a life event(s) had occurred, he/she was asked to appraise the event and indicate on a scale of 1 (did not upset me) to 3 (upset me greatly) the extent it upset them. Participants who did not report the occurrence of any life event or who indicated they were not affected by the event were grouped together as the "no/low stress experience" group. The scale provides a life event perceived stress score that ranged from 0 to 33 with a higher score indicating a participant experienced a greater number of more stressful events.

Depressive Symptoms

The presence of depressive symptoms was determined by the 15-item Geriatric Depression Scale (GDS-15) [20] validated for use in the local population [21]. The GDS was well suited for the study because it is largely free of the measurement artefact due to overlapping somatic symptoms of physical illness(es) and depression. Scores range

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from 0 to 15, and scores of 5 or more are indicative of depression.

Cognitive Function

Cognitive function was measured using the Cognitive Failures Questionnaire (CFQ) [22] and the Mini-Mental State Examination (MMSE) which are validated and widely used instrument to assess global cognitive functioning [23]. The CFQ uses a 5-point Likert-type scale (1 = Never, 5 = Very often) to evaluate self-reported cognitive problems (e.g.,"Do you need to re-read instructions several times?"). Higher CFQ scores indicate more frequent cognitive problems and higher MMSE scores (0 to 30) indicate better global cognitive functioning.

Physical and Mental Functioning

Physical and mental functional well-being was measured by the Medical Outcomes Study 36-item Short Form (SF-36) [24] which has been previously validated for use in Singaporeans [25]. Weighted summary measures of Physical Health Component Summary (PCS) scores and Mental Health Component Summary (MCS) scores were computed with higher scores indicating better physical and mental health functioning and quality of life.

Statistical Analysis

Data analysis was performed using the software package PASW Statistics version 18. The relationship between life event stress and depressive symptoms, cognitive function, physical and mental functioning was examined using two-way analysis of variance, with statistical significance set at $p<0.05$. The individual main effects of life event stress and COPD and their interaction on depressive symptoms, cognitive function, physical and mental functioning were investigated for participants with and without

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COPD, adjusting for important confounding variables including sex, age, ethnicity, smoking status, and number of chronic illness. For the outcome variables with significant interaction of life event stress and COPD, the simple effects of their relationships with life event stress score were investigated respectively in participants with and without COPD.

RESULTS

This study consisted of 497 participants with the average age of 72.1. Among the respondents, 32.9% had COPD, and 67.1% had no COPD. The proportion of respondents with stressful life events in the past one year was 43.4%. The socio-demographic and psychological characteristics of study participants with and without COPD are shown in Table 1. No significant difference in the number of stressful life events or perceived stress was observed between COPD and non-COPD participants.

Table 1 shows the scores of pulmonary and cognitive functions, depressive symptoms, physical and mental functioning in participants with and without COPD. In Table 2, two-way analysis of variance showed significant main effects of COPD for decreased post-bronchodilator FEV_1 ($p<0.001$) and higher CFQ scores ($p=0.020$) after adjustment of sex, age, ethnicity, smoking status, and number of chronic illness, indicating impaired pulmonary and cognitive functions in participants with COPD.

Significant main effects of stress were found for GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS ($p<0.001$) scores, and significant interactions of stress with COPD were found as well for GDS ($p=0.001$), SF36-PCS ($p=0.045$), and SF36-MCS ($p=0.034$) scores (Table 2). The simple effects of life event stress on GDS, SF36-PCS and SF36-MCS are shown for participants with and without COPD respectively (Figure 1).

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Increasing stress score was associated with higher GDS score, lower SF12-PCS and lower SF12-MCS scores in participants with COPD, more than in those without COPD after adjusting for potential confounders, indicating the association of life event stress with worse physical and psychological health in COPD.

Table 1. Socio-demographic, pulmonary and psychological variables of study participants aged 65 or older (Singapore Longitudinal Aging Study, SLAS)

	COPD		Non-COPD	
	N	%	N	%
Total	136	32.9	277	67.1
Sex				
Male	58	42.6	112	40.7
Female	78	57.4	163	59.3
Age (years, M±SD)	73.19	±5.87	71.23	±5.47
Ethnicity				
Chinese	121	89.0	241	87.6
Non-Chinese	15	11.0	34	12.4
Smoking				
Never smoker	77	57.6	211	77.3
Past smoker	29	21.6	41	15.0
Present smoker < 10 cigarettes daily	18	13.4	12	4.4
Present smoker ≥ 10 cigarettes daily	10	7.5	9	3.3
Number of chronic diseases	2.60	±1.30	1.65	1.25
Number of Negative Life Events	0.67	±0.98	0.74	±1.11
Life Event Stress Score	0.09	±0.16	0.10	±0.16
Post-bronchodilator FEV1	1.41	±0.05	1.70	±0.04
CFQ Score	36.1	±1.11	38.1	±0.98
MMSE Score	25.6	±0.32	26.2	±0.29
GDS Depression score	1.18	±0.19	1.14	±0.17
SF-36 PCS	45.0	±0.85	45.4	±0.75
SF-36 MCS	53.8	±0.82	53.9	±0.74

Figures in table denote mean ± SD or number and %.

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Table 2. Two-way ANOVA: Life event stress, COPD and mental and physical variables

	Main Effects of COPD		Main Effects of Stress		Interaction	
	F	P	F	p	F	p
Post-bronchodilator FEV1	17.458	<0.001	0.323	0.570	2.057	0.152
CFQ Score	5.424	0.020	1.927	0.166	2.514	0.114
MMSE Score	1.799	0.181	1.159	0.282	0.380	0.538
GDS Depression score	2.353	0.126	64.500	<0.001	10.970	0.001
SF-36 PCS	0.432	0.512	7.054	0.008	4.055	0.045
SF-36 MCS	0.659	0.417	14.710	<0.001	4.538	0.034

Adjusted variables: sex, age, ethnicity, smoking status, and number of chronic illness.

FEV1=Forced Expiratory Volume in the first second; CFQ=Cognitive Failure Questionnaire; MMSE=Mini-Mental State Examination; IADL=Instrumental Activities of Daily Living; GDS=the Geriatric Depression Scale; SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; MCS= Mental Health Component Summary.

DISCUSSION

The principal finding in this study indicated that life event stress was associated with more depressive symptoms, and worse mental and physical functioning in both COPD and non-COPD participants (main effects), but this effect was much more aggravated in COPD than in non-COPD individuals (interactive effect). To our knowledge,

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no other studies have reported demonstrating this relationship. These results suggest that individuals with COPD may be more susceptible to the adverse impact of life event stress than non-COPD individuals.

Using a macro-social approach, investigators have reported an ecological study of 50 states in the USA showing that higher levels of stressful events was associated with higher smoking prevalence as well as higher mortality from lung cancer and COPD. (11). To our knowledge, this is the only circumstantial evidence suggesting an etiological link between stress and the development of COPD. However, in our study, we found no significant associations between life event stress and COPD in support of this link at the individual level.

Among individuals with COPD in this study, it is given that the heavy burden of the disease and the illness experience from difficulties in breathing and exacerbations, emotional functioning, sleep and rest, physical mobility, social interaction, recreation, work and finance are in themselves a principal stressor [8, 9]. This may possibly have a knock-on effect on the frequency and perceived stressfulness of non-illness related negative life events encountered. However, we found that COPD participants actually did not report more life event occurrence or stress than non-COPD participants as a result. They thus appeared to experience the same number of life events and perceived them to be equally stressful as their non-COPD counterparts, but experienced differentially greater psychological distress and poorer daily life functioning as a result.

Given the complex nature of stress and its interaction with coping ability, an individual's internal psychological coping resources will determine how a negative life event is perceived and appraised and impact on wellbeing [26]. Given that the

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perception of stress were the same in both COPD and non-COPD individuals, differences in psychological coping ability does not appear to explain the greater psychological morbidity in COPD. This suggests the possibility that an underlying psychobiological basis [26] may explain why COPD patients are more vulnerable to the adverse health and functional impacts of stress. More studies are greatly needed given the small number of existing studies.

Our secondary finding of the main effects of COPD on FEV1 was expected and thus not surprising. However, the association of COPD with more frequent cognitive problems was interesting, although the results for MMSE score were not significant, possibly due to sample size limitation. These results are consistent with clinical and population studies that indicate significant cognitive effects of COPD on deficits in abstract reasoning, [27] complex visual motor process, [28] and verbal learning, [29] language,[30] attention, [31] information processing speed [31-33] and verbal learning and memory. [32, 33]

The present study has strengths and limitations. The case definition for COPD was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria. The measure of life event stress was modified to exclude illness-related stress from chronic diseases in this older population. The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis. A limitation of the study is that definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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In conclusion, the present study found that life event stress was associated with more depressive symptoms and worse mental and physical functioning in individuals with COPD, much more than in those without COPD. Further studies should explore the psychobiological mechanisms and the role of psychological interventions in COPD.

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DECLARATION OF INTEREST

The authors declare that there are no declarations of interest in relation to the current study. The authors are responsible for the writing and the content of this article.

DATA SHARING STATEMENT

There is no additional data available.

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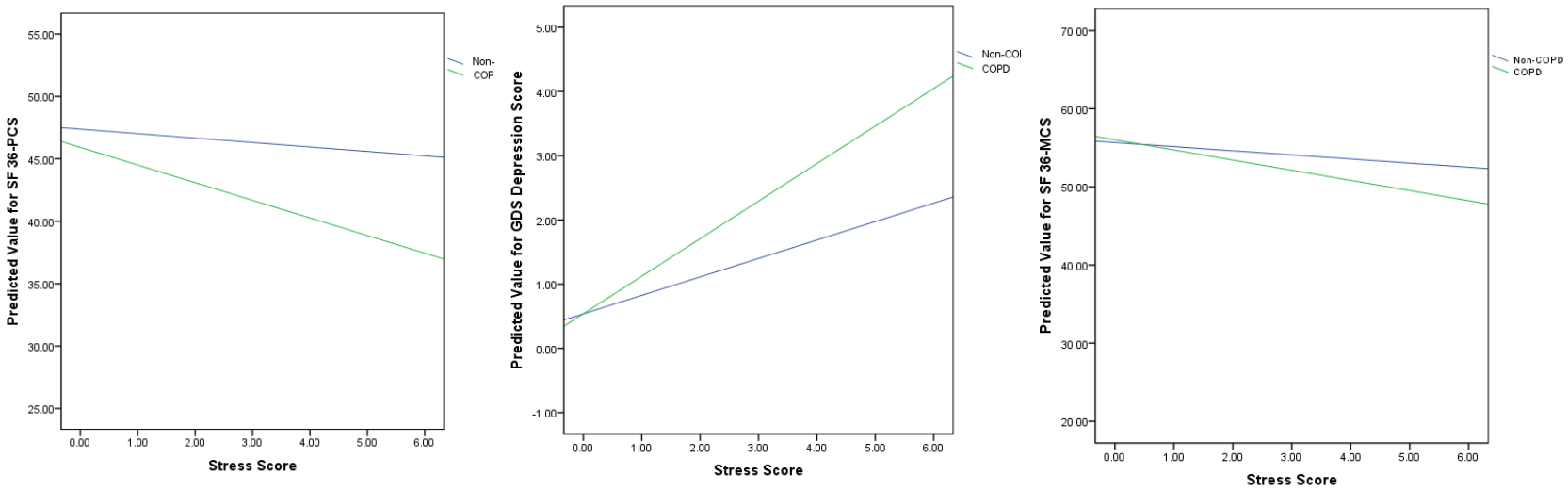

Figure 1. Predicted value for SF-36 PCS, GDS depression score and SF 36-MCS in participants with and without COPD

SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; GDS=the Geriatric Depression Scale; MCS= Mental Health Component Summary.

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ARTICAL SUMMARY

Article focus

- The impact of life event stress on the mental wellbeing and quality of life of individuals with chronic obstructive pulmonary disease (COPD).

Key messages

- Our findings showed that in individuals with COPD, life event stress had a greater detrimental effect on mental health and quality of life in comparison to non-COPD individuals.

Strengths and limitations of this study

- The case definition for COPD in this study was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria.
- The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis.
- Definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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Abstract

Objectives: To investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD

Design: Cross-sectional study.

Participants: A population-based sample (N=497) of individuals aged 65 and above with COPD (post-bronchodilatation $FEV_1/FVC<0.70$, N=136) and without COPD (N=277).

Measurements: We measured life event stress, depressive symptoms (GDS), cognitive symptoms and function (CFQ, MMSE), and physical and mental health functional status (SF36-PCS and SF36-MCS) in participants with and without COPD.

Results: In two-way analysis of variance controlling for potential confounders, life event stress was associated with significant main effects of worse GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS scores ($p<0.001$), and with significant interaction effects on GDS score ($p<0.001$), SF36-PCS ($p=0.045$) and SF36-MCS ($p=0.034$) in participants with COPD more than in non-COPD participants. Main effect of COPD was found for post-bronchodilator FEV_1 ($p<0.001$) and cognitive symptoms ($p=0.02$).

Conclusions: Our findings indicate that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands out among chronic diseases with its high and rising prevalence and mortality [1], poor quality of life, frequent hospitalization and huge societal burden of care [2]. Because patients with COPD bear a heavy burden of psychological disturbance, psychiatric morbidity, and disability in daily living activities [3, 4], the mental health of COPD patients has received growing attention in recent years.

Life event stress is increasingly recognized to play important roles in the development and outcomes of chronic illness such as type II diabetes, coronary heart disease, gastroenterological disorders and obstetric outcomes [5]. Stress is well known to result in depression, psychological burnout, post-traumatic stress disorder (PTSD) in all ages, as well as cognitive impairment in late life [6]. Among COPD patients, an intrinsic source of stress is directly related to their illness, involving the experience of anxiety and distress provoked by breathing difficulties [7, 8], including muddled thoughts, heightened emotions, extreme fear and panic and decreased physical energy, and various difficulties in emotional functioning, sleep and rest, physical mobility, social interaction, activities of daily living, recreation, work and finance. However, the impact of life event stress in general including those extrinsic to illness-related experience on the physical and mental functioning and quality of life of individuals with COPD in comparison to non-COPD individuals has rarely been investigated [9, 10, 6]. The aim of this study was to investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.

The present study analyzed data collected on COPD status, life event stress, and measures of pulmonary function, cognitive function, depressive symptoms and quality of in a population-based sample (Singapore Longitudinal Aging Study) [11] to

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investigate the effect of life event stress on psychological functioning and quality of life. We hypothesized that life event stress in the whole sample would be associated with depressive symptoms and poor quality of life (main effect), but would have a stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a greater detrimental effect on depressive symptoms and quality of life. A secondary relationship analyzed in two-way analysis of variance (ANOVA) was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function, based on the known effects of impaired pulmonary and cognitive function in COPD.

METHODS

Study Design and Participants

The participants in the study were a subsample recruited from one locality (Bukit Merah) in the South Central region of Singapore Longitudinal Aging Study (SLAS-2), a prospective population-based cohort study of aging and health of community-dwelling elderly [12]. We interviewed one participant from each household who were Singaporean citizens or permanent residents aged 65 or older who were able to give informed consent. Those who were too frail or ill and unable to complete the interview, for reasons such as from post-stroke aphasia, cachexia or profound dementia, were excluded. The participants who completed interviews and provided technically acceptable spirometric data (N=497) represented a response rate of 78.5% of the eligible participants. All participants signed written informed consent for the study which was approved by the National University of Singapore Institutional Review Board.

COPD

We identified cases of COPD among the participants who had characteristic symptoms of COPD and spirometric evidence of chronic airflow obstruction (post-

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bronchial dilatation FEV1/FVC< 0.70), in accordance with the definition recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [13].

Questions from the British Medical Research Council Questionnaire on chronic respiratory symptoms were used to elicit symptoms characteristic of COPD: chronic cough and/or sputum lasting at least 3 months in the year and/or breathlessness on exertion.

Ventilatory function testing was performed using a portable, battery operated, ultrasound transit-time based spirometer (Easy-One; Model 2001 Diagnostic Spirometer, NDD Medical Technologies, Zurich, Switzerland). Calibration was checked daily with a 3-L syringe. Forced expiratory maneuvers were performed with the respondent seated with recommended guidelines and standardization of procedures: at least three acceptable maneuvers, with forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) reproducible within 200 ml. Chronic airflow obstruction as defined as post-bronchial dilatation FEV1/FVC < 0.70.

Life Event Stress

Life event stress was measured by an 11-item life events inventory [14, 15] that excluded personal illness experiences directly related to COPD. The participants were asked to indicate yes or no as to whether any of eleven life events had occurred over the past year ("spouse or partner die, a close friend or family member die or have a serious illness (other than your spouse or partner), major problems with money, a divorce or breakup, family member or close friend have a divorce or breakup, major conflict with children or grandchildren, major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events, a family member or close friend lose their job or retire, physically abused, verbally abused, or pet die"). If the participant indicated (a) life event(s) had occurred, he/she was asked to appraise the event and indicate on a scale of 1 (did not upset me) to 3 (upset me greatly) the extent it upset

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them. Frequency of life event stress was calculated. The scale also provides a life event stress score appraised by the participant that ranged from 0 to 33 with a higher score indicating a participant experienced a greater number of more stressful events.

Depressive Symptoms

The presence of depressive symptoms was determined by a depression screening scale for elderly populations, the 15-item Geriatric Depression Scale (GDS-15) with scores ranging from 0 to 15 [16]. The GDS was well suited for the study because it is largely free of the measurement artefact due to overlapping somatic symptoms of physical illness(es) and depression. In validation studies in the local older population [17], translated versions of the GDS-15 have been found to be a valid and reliable screening tool for depression: Cronbach's alpha of 0.80, and intraclass coefficients of test-retest reliability of 0.83 and inter-rater reliability of 0.94. Using a GDS cutoff of >=5, the GDS-15 has a sensitivity of 0.97 and specificity of 0.95 (area under curve of 0.98) for determining major depressive disorder according to DSM-IV criteria. Depressive symptoms defined as such by GDS>=5 is clinically significant, and such cases including "sub-threshold" depression, had been shown in the same population to be associated with significantly poorer mental and physical health and functional status, and more healthcare resource utilization compared to non-cases and were similar to or worse than syndrome threshold cases of depression [18].

Cognitive Function

Cognitive function was measured using the Cognitive Failures Questionnaire (CFQ) [19] and the Mini-Mental State Examination (MMSE) which were validated and widely used instruments to assess global cognitive functioning [20]. The CFQ uses a 5-point Likert-type scale (1 = Never, 5 = Very often) to evaluate self-reported cognitive problems (e.g.,''Do you need to re-read instructions several times?"). Higher CFQ scores indicate more frequent cognitive problems and higher MMSE scores (0 to 30) indicate better

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global cognitive functioning, and MMSE scores of 23 or less are considered to be cognitively impaired.

Physical and Mental Functioning

Physical and mental functional well-being was measured by the Medical Outcomes Study 36-item Short Form (SF-36) [21] which has been previously validated for use in Singaporeans [22]. Weighted summary measures of Physical Health Component Summary (PCS) score and Mental Health Component Summary (MCS) score were computed with higher scores indicating better physical and mental health functioning and quality of life.

Statistical Analyses

Data analysis was performed using the software package PASW Statistics version 18. In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) and general linear model which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function. For the outcome variables with significant interaction of life event

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stress and COPD, the simple effects of their relationships with life event stress score were investigated respectively in participants with and without COPD. Statistical significance was set at $p<0.05$.

RESULTS

This study consisted of 497 participants with the average age of 72.1. Among the respondents, 32.9% had COPD, and 67.1% had no COPD. The proportion of respondents with stressful life events in the past one year was 43.4%. The socio-demographic and psychological characteristics of study participants with and without COPD are shown in Table 1. Participants with COPD were found to have higher mean age (t=3.328, $p=0.001$), higher proportion of smokers (χ^2 =20.586, df=3, $p<0.001$) and increased number of diseases (t=7.096, $p<0.001$). No significant difference in the number of life events or perceived stress was observed between COPD and non-COPD participants ($p>0.05$).

Table 1 shows that compared with those without COPD, participants with COPD had decreased post-bronchodilator FEV1 (t=6.185, $p<0.001$), MMSE score (t=3.090, $p=0.002$) and SF-36 PCS (t=2.726, $p=0.007$) score. There were no difference in CFQ and GDS depression scores between participants with and without COPD ($p>0.05$) in the whole sample. Next, we evaluated the effect of life event stress on GDS, CFQ, MMSE, SF-36 PCS and SF-36 MCS scores by subgroups of participants with COPD and without COPD. As shown in Table 2, two-way analysis of variance in general linear model showed significant main effects of life event stress for GDS (F=64.500, df=1, $p<0.001$), SF36-PCS (F=7.054, df=1, $p=0.008$) and SF36-MCS (F=14.710, df=1, $p<0.001$) scores, and significant interactions of life event stress with COPD were found as well for GDS (F=10.970, df=1, $p=0.001$), SF36-PCS (F=4.055, df=1, $p=0.045$), and SF36-MCS (F=4.538, df=1, $p=0.034$) scores. The simple effects of life event stress on GDS, SF36-

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PCS and SF36-MCS are shown for participants with and without COPD respectively in Figure 1. Increasing stress score was associated with higher GDS score, lower SF12-PCS and lower SF12-MCS scores in participants with COPD, more than in those without COPD after adjusting for potential confounders, indicating the association of life event stress with worse psychological distress and poorer quality of life among individuals with COPD, in comparison to non-COPD individuals. The other significant main effect found in two-way analysis of variance was of COPD for decreased post-bronchodilator FEV_1 (F=17.458, df=1, p<0.001) and higher CFQ scores (F=5.424, df=1, p=0.020) after adjustment of sex, age, ethnicity, smoking status, and number of chronic illness, indicating impaired pulmonary and cognitive functions in participants with COPD.

Table 1. Socio-demographic, pulmonary and psychological variables of study participants aged 65 or older (Singapore Longitudinal Aging Study, SLAS)

	COPD		Non-COPD		Significant Test	p
	N	%	N	%		
Total	136	32.9	277	67.1		
Sex						
Male	58	42.6	112	40.7	χ^2 =0.138, df=1	0.710
Female	78	57.4	163	59.3		
Age (years, M±SD)	73.19	±5.87	71.23	±5.47	t=3.328	0.001
Ethnicity						
Chinese	121	89.0	241	87.6	χ^2 =0.154, df=1	0.694
Non-Chinese	15	11.0	34	12.4		
Smoking						
Never smoker	77	57.6	211	77.3	χ^2 =20.59, df=3	<0.001
Past smoker	29	21.6	41	15.0		
Current smoker < 10 cigarettes daily	18	13.4	12	4.4		
Current smoker ≥ 10 cigarettes daily	10	7.5	9	3.3		
Number of chronic diseases	2.60	±1.30	1.65	1.25	t=7.096	<0.001
Number of Negative Life Events	0.67	±0.98	0.74	±1.11	t=0.609	0.543
Life Event Stress Score	1.02	±1.71	1.12	±1.78	t=0.525	0.600
Post-bronchodilator FEV1	1.42	±0.50	1.75	±0.52	t=6.185	<0.001
CFQ Score	38.0	±9.21	38.8	±9.83	t=0.733	0.464
MMSE Score	26.4	±3.26	27.4	±3.11	t=3.090	0.002
GDS Depression score	1.13	±2.04	0.84	±1.69	t=1.487	0.138
GDS≥5, % (n)	5.2	(7)	2.9	(8)	χ^2 =1.349, df=1	0.245
SF-36 PCS	44.6	±9.04	47.1	±7.21	t=2.726	0.007
SF-36 MCS	54.9	±7.83	55.1	±6.68	t=0.353	0.724

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Figures in table denote mean ± SD or number and %.
Smoker is defined as smoking ≥ 10 cigarettes daily

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Table 2. Two-way ANOVA: Life event stress, COPD and mental and physical variables

	Main Effects of COPD (df=1)		Main Effects of Stress (df=1)		Interaction (df=1)	
	F	*P*	F	*P*	F	*p*
Post-bronchodilator FEV1	17.458	<0.001	0.323	0.570	2.057	0.152
CFQ Score	5.424	0.020	1.927	0.166	2.514	0.114
MMSE Score	1.799	0.181	1.159	0.282	0.380	0.538
GDS Depression score	2.353	0.126	64.500	<0.001	10.970	0.001
SF-36 PCS	0.432	0.512	7.054	0.008	4.055	0.045
SF-36 MCS	0.659	0.417	14.710	<0.001	4.538	0.034

Adjusted variables: sex, age, ethnicity, smoking status, and number of chronic illness.
FEV1=Forced Expiratory Volume in the first second; CFQ=Cognitive Failure Questionnaire; MMSE=Mini-Mental State Examination; GDS=the Geriatric Depression Scale; SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; MCS= Mental Health Component Summary.

DISCUSSION

The principal finding in this study indicated that life event stress was associated with depressive symptoms and poor quality of life in both COPD and non-COPD participants (main effects), but showed a significantly stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a disproportionately greater detrimental effect. To our knowledge, no other studies have reported demonstrating this relationship.

It should be noted that participants with COPD actually did not report greater frequency of occurrence or perceived stress score of non-illness related life events than non-COPD participants. Instead, individuals with COPD appeared to experience the same number of non-illness related life events and perceived them to be equally stressful as their non-COPD counterparts, yet showed disproportionately greater psychological distress and poorer quality of life. These results suggest that individuals with COPD may be more vulnerable to the adverse impact of stressful events than non-COPD individuals.

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A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.

There are few studies that have investigated the relationship between cognitive appraisal of stressful events, coping strategies and psychological distress in COPD patients. A study by Andrenas and co-investigators [23] have assessed how hospitalized patients with acutely exacerbated COPD appraised and coped with a recent stressful event and their level of psychological distress. They reported that half of the respondents tended to perceive their stressful event as representing a threat, 26% as harmful, 7.6% as a loss, 4.3% as a challenge, and 11% characterized the stressful event in some other ways. However, the authors found that neither types of stressful event, stress intensity, primary or secondary appraisal, or number of coping strategies used were significantly related to psychological distress. Only problem-solving coping strategies were inversely related to psychological distress. This suggests that poor coping skills may be the principal psychological problem among COPD patients that contribute to their psychological distress and poor quality of life. However, further studies should be conducted.

Our secondary finding of the main effects of COPD on FEV_1 was expected and thus not surprising. However, the association of COPD with more frequent cognitive problems was interesting, although the results for MMSE score were not significant after adjustment in two-way ANOVA, possibly due to sample size limitation. These results are consistent with clinical and population studies that indicate significant

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cognitive effects of COPD on deficits in abstract reasoning [23], complex visual motor process [24], and verbal learning [25], language [26], attention [27], information processing speed [27-29] and verbal learning and memory [28, 29].

The present study has strengths and limitations. The case definition for COPD is accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria. Results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis. The measure of life event stress is modified to exclude illness-related stress from chronic diseases in this older population. However, a limitation of the life event inventory is inter-categorical variability and recall bias in the appraisal of the stressful life event [30]. In a cross-sectional study, interpreting the causal relationship between stress and the health-related functional outcomes can be uncertain. Further longitudinal studies are required.

Studies [31-33] have reported that mental health status, including anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. While it is increasingly being recognized that the identification and treatment of psychological disorders are important for improving patient centered outcomes in COPD patients, there should be commensurate attention to stressful life event(s) that trigger psychological disturbances and poor psycho-social functioning. Psychological interventions in COPD patients that include the identification of stressful life event and improving patients' coping skills may directly contribute to improving psychological functioning and quality of life in COPD patients.

In conclusion, the present study found that life event stress was associated with

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more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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DECLARATION OF INTEREST

The authors declare that there are no declarations of interest in relation to the current study. The authors are responsible for the writing and the content of this article.

DATA SHARING STATEMENT

There is no additional data available.

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Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): Associations with Mental Wellbeing and Quality of Life in a Population-based Study

Running title: Stress & COPD

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ARTICAL SUMMARY

Article focus

- The impact of life event stress on the mental wellbeing and quality of life of individuals with chronic obstructive pulmonary disease (COPD).

Key messages

- Our findings showed that in individuals with COPD, life event stress had a greater detrimental effect on mental health and quality of life in comparison to non-COPD individuals.

Strengths and limitations of this study

- The case definition for COPD in this study was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria.
- The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis.
- Definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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Abstract

Objectives: To investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD

Design: Cross-sectional study.

Participants: A population-based sample (N=497) of individuals aged 65 and above with COPD (post-bronchodilatation $FEV_1/FVC<0.70$, N=136) and without COPD (N=277).

Measurements: We measured life event stress, depressive symptoms (GDS), cognitive symptoms and function (CFQ, MMSE), and physical and mental health functional status (SF36-PCS and SF36-MCS) in participants with and without COPD.

Results: In two-way analysis of variance controlling for potential confounders, life event stress was associated with significant main effects of worse GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS scores ($p<0.001$), and with significant interaction effects on GDS score ($p<0.001$), SF36-PCS ($p=0.045$) and SF36-MCS ($p=0.034$) in participants with COPD more than in non-COPD participants. Main effect of COPD was found for post-bronchodilator FEV_1 ($p<0.001$) and cognitive symptoms ($p=0.02$).

Conclusions: Our findings indicate that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands out among chronic diseases with its high and rising prevalence and mortality [1], poor quality of life, frequent hospitalization and huge societal burden of care [2]. Because patients with COPD bear a heavy burden of psychological disturbance, psychiatric morbidity, and disability in daily living activities [3, 4], the mental health of COPD patients has received growing attention in recent years.

Life event stress is increasingly recognized to play important roles in the development and outcomes of chronic illness such as type II diabetes, coronary heart disease, gastroenterological disorders and obstetric outcomes [5]. Stress is well known to result in depression, psychological burnout, post-traumatic stress disorder (PTSD) in all ages, as well as cognitive impairment in late life [6]. Among COPD patients, an intrinsic source of stress is directly related to their illness, involving the experience of anxiety and distress provoked by breathing difficulties [7, 8], including muddled thoughts, heightened emotions, extreme fear and panic and decreased physical energy, and various difficulties in emotional functioning, sleep and rest, physical mobility, social interaction, activities of daily living, recreation, work and finance. However, the impact of life event stress in general including those extrinsic to illness-related experience on the physical and mental functioning and quality of life of individuals with COPD in comparison to non-COPD individuals has rarely been investigated [9, 10, 6]. The aim of this study was to investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.

The present study analyzed data collected on COPD status, life event stress, and measures of pulmonary function, cognitive function, depressive symptoms and quality of in a population-based sample (Singapore Longitudinal Aging Study) [11] to

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investigate the effect of life event stress on psychological functioning and quality of life. We hypothesized that life event stress in the whole sample would be associated with depressive symptoms and poor quality of life (main effect), but would have a stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a greater detrimental effect on depressive symptoms and quality of life. A secondary relationship analyzed in two-way analysis of variance (ANOVA) was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function, based on the known effects of impaired pulmonary and cognitive function in COPD.

METHODS

Study Design and Participants

The participants in the study were a subsample recruited from one locality (Bukit Merah) in the South Central region of Singapore Longitudinal Aging Study (SLAS-2), a prospective population-based cohort study of aging and health of community-dwelling elderly [12]. We interviewed one participant from each household who were Singaporean citizens or permanent residents aged 65 or older who were able to give informed consent. Those who were too frail or ill and unable to complete the interview, for reasons such as from post-stroke aphasia, cachexia or profound dementia, were excluded. The participants who completed interviews and provided technically acceptable spirometric data (N=497) represented a response rate of 78.5% of the eligible participants. All participants signed written informed consent for the study which was approved by the National University of Singapore Institutional Review Board.

COPD

We identified cases of COPD among the participants who had characteristic symptoms of COPD and spirometric evidence of chronic airflow obstruction (post-

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bronchial dilatation FEV1/FVC< 0.70), in accordance with the definition recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [13].

Questions from the British Medical Research Council Questionnaire on chronic respiratory symptoms were used to elicit symptoms characteristic of COPD: chronic cough and/or sputum lasting at least 3 months in the year and/or breathlessness on exertion.

Ventilatory function testing was performed using a portable, battery operated, ultrasound transit-time based spirometer (Easy-One; Model 2001 Diagnostic Spirometer, NDD Medical Technologies, Zurich, Switzerland). Calibration was checked daily with a 3-L syringe. Forced expiratory maneuvers were performed with the respondent seated with recommended guidelines and standardization of procedures: at least three acceptable maneuvers, with forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) reproducible within 200 ml. Chronic airflow obstruction as defined as post-bronchial dilatation FEV1/FVC < 0.70.

Life Event Stress

Life event stress was measured by an 11-item life events inventory [14, 15] that excluded personal illness experiences directly related to COPD. The participants were asked to indicate yes or no as to whether any of eleven life events had occurred over the past year ("spouse or partner die, a close friend or family member die or have a serious illness (other than your spouse or partner), major problems with money, a divorce or breakup, family member or close friend have a divorce or breakup, major conflict with children or grandchildren, major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events, a family member or close friend lose their job or retire, physically abused, verbally abused, or pet die"). If the participant indicated (a) life event(s) had occurred, he/she was asked to appraise the event and indicate on a scale of 1 (did not upset me) to 3 (upset me greatly) the extent it upset

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them. Frequency of life event stress was calculated. The scale also provides a life event stress score appraised by the participant that ranged from 0 to 33 with a higher score indicating a participant experienced a greater number of more stressful events.

Depressive Symptoms

The presence of depressive symptoms was determined by a depression screening scale for elderly populations, the 15-item Geriatric Depression Scale (GDS-15) with scores ranging from 0 to 15 [16]. The GDS was well suited for the study because it is largely free of the measurement artefact due to overlapping somatic symptoms of physical illness(es) and depression. In validation studies in the local older population [17], translated versions of the GDS-15 have been found to be a valid and reliable screening tool for depression: Cronbach's alpha of 0.80, and intraclass coefficients of test-retest reliability of 0.83 and inter-rater reliability of 0.94. Using a GDS cutoff of >=5, the GDS-15 has a sensitivity of 0.97 and specificity of 0.95 (area under curve of 0.98) for determining major depressive disorder according to DSM-IV criteria. Depressive symptoms defined as such by GDS>=5 is clinically significant, and such cases including "sub-threshold" depression, had been shown in the same population to be associated with significantly poorer mental and physical health and functional status, and more healthcare resource utilization compared to non-cases and were similar to or worse than syndrome threshold cases of depression [18].

Cognitive Function

Cognitive function was measured using the Cognitive Failures Questionnaire (CFQ) [19] and the Mini-Mental State Examination (MMSE) which were validated and widely used instruments to assess global cognitive functioning [20]. The CFQ uses a 5-point Likert-type scale (1 = Never, 5 = Very often) to evaluate self-reported cognitive problems (e.g.,''Do you need to re-read instructions several times?"). Higher CFQ scores indicate more frequent cognitive problems and higher MMSE scores (0 to 30) indicate better

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global cognitive functioning, and MMSE scores of 23 or less are considered to be cognitively impaired.

Physical and Mental Functioning

Physical and mental functional well-being was measured by the Medical Outcomes Study 36-item Short Form (SF-36) [21] which has been previously validated for use in Singaporeans [22]. Weighted summary measures of Physical Health Component Summary (PCS) score and Mental Health Component Summary (MCS) score were computed with higher scores indicating better physical and mental health functioning and quality of life.

Statistical Analyses

Data analysis was performed using the software package PASW Statistics version 18. In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) and general linear model which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function. For the outcome variables with significant interaction of life event

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stress and COPD, the simple effects of their relationships with life event stress score were investigated respectively in participants with and without COPD. Statistical significance was set at $p<0.05$.

RESULTS

This study consisted of 497 participants with the average age of 72.1. Among the respondents, 32.9% had COPD, and 67.1% had no COPD. The proportion of respondents with stressful life events in the past one year was 43.4%. The socio-demographic and psychological characteristics of study participants with and without COPD are shown in Table 1. Participants with COPD were found to have higher mean age (t=3.328, $p=0.001$), higher proportion of smokers (χ^2 =20.586, df=3, $p<0.001$) and increased number of diseases (t=7.096, $p<0.001$). No significant difference in the number of life events or perceived stress was observed between COPD and non-COPD participants ($p>0.05$).

Table 1 shows that compared with those without COPD, participants with COPD had decreased post-bronchodilator FEV1 (t=6.185, $p<0.001$), MMSE score (t=3.090, $p=0.002$) and SF-36 PCS (t=2.726, $p=0.007$) score. There were no difference in CFQ and GDS depression scores between participants with and without COPD ($p>0.05$) in the whole sample. Next, we evaluated the effect of life event stress on GDS, CFQ, MMSE, SF-36 PCS and SF-36 MCS scores by subgroups of participants with COPD and without COPD. As shown in Table 2, two-way analysis of variance in general linear model showed significant main effects of life event stress for GDS (F=64.500, df=1, $p<0.001$), SF36-PCS (F=7.054, df=1, $p=0.008$) and SF36-MCS (F=14.710, df=1, $p<0.001$) scores, and significant interactions of life event stress with COPD were found as well for GDS (F=10.970, df=1, $p=0.001$), SF36-PCS (F=4.055, df=1, $p=0.045$), and SF36-MCS (F=4.538, df=1, $p=0.034$) scores. The simple effects of life event stress on GDS, SF36-

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PCS and SF36-MCS are shown for participants with and without COPD respectively in Figure 1. Increasing stress score was associated with higher GDS score, lower SF12-PCS and lower SF12-MCS scores in participants with COPD, more than in those without COPD after adjusting for potential confounders, indicating the association of life event stress with worse psychological distress and poorer quality of life among individuals with COPD, in comparison to non-COPD individuals. The other significant main effect found in two-way analysis of variance was of COPD for decreased post-bronchodilator FEV_1 ($F=17.458$, $df=1$, $p<0.001$) and higher CFQ scores ($F=5.424$, $df=1$, $p=0.020$) after adjustment of sex, age, ethnicity, smoking status, and number of chronic illness, indicating impaired pulmonary and cognitive functions in participants with COPD.

Table 1. Socio-demographic, pulmonary and psychological variables of study participants aged 65 or older (Singapore Longitudinal Aging Study, SLAS)

	COPD		Non-COPD		Significant Test	*p*
	N	%	N	%		
Total	136	32.9	277	67.1		
Sex						
Male	58	42.6	112	40.7	$\chi^2=0.138$, df=1	0.710
Female	78	57.4	163	59.3		
Age (years, M±SD)	73.19	±5.87	71.23	±5.47	t=3.328	0.001
Ethnicity						
Chinese	121	89.0	241	87.6	$\chi^2=0.154$, df=1	0.694
Non-Chinese	15	11.0	34	12.4		
Smoking						
Never smoker	77	57.6	211	77.3	$\chi^2=20.59$, df=3	<0.001
Past smoker	29	21.6	41	15.0		
Current smoker < 10 cigarettes daily	18	13.4	12	4.4		
Current smoker ≥ 10 cigarettes daily	10	7.5	9	3.3		
Number of chronic diseases	2.60	±1.30	1.65	1.25	t=7.096	<0.001
Number of Negative Life Events	0.67	±0.98	0.74	±1.11	t=0.609	0.543
Life Event Stress Score	1.02	±1.71	1.12	±1.78	t=0.525	0.600
Post-bronchodilator FEV1	1.42	±0.50	1.75	±0.52	t=6.185	<0.001
CFQ Score	38.0	±9.21	38.8	±9.83	t=0.733	0.464
MMSE Score	26.4	±3.26	27.4	±3.11	t=3.090	0.002
GDS Depression score	1.13	±2.04	0.84	±1.69	t=1.487	0.138
GDS≥5, % (n)	5.2	(7)	2.9	(8)	$\chi^2=1.349$, df=1	0.245
SF-36 PCS	44.6	±9.04	47.1	±7.21	t=2.726	0.007
SF-36 MCS	54.9	±7.83	55.1	±6.68	t=0.353	0.724

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Figures in table denote mean ± SD or number and %.
Smoker is defined as smoking ≥ 10 cigarettes daily

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Table 2. Two-way ANOVA: Life event stress, COPD and mental and physical variables

	Main Effects of COPD (df=1)		Main Effects of Stress (df=1)		Interaction (df=1)	
	F	*P*	F	*P*	F	*p*
Post-bronchodilator FEV1	17.458	<0.001	0.323	0.570	2.057	0.152
CFQ Score	5.424	0.020	1.927	0.166	2.514	0.114
MMSE Score	1.799	0.181	1.159	0.282	0.380	0.538
GDS Depression score	2.353	0.126	64.500	<0.001	10.970	0.001
SF-36 PCS	0.432	0.512	7.054	0.008	4.055	0.045
SF-36 MCS	0.659	0.417	14.710	<0.001	4.538	0.034

Adjusted variables: sex, age, ethnicity, smoking status, and number of chronic illness.
FEV1=Forced Expiratory Volume in the first second; CFQ=Cognitive Failure Questionnaire; MMSE=Mini-Mental State Examination; GDS=the Geriatric Depression Scale; SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; MCS= Mental Health Component Summary.

DISCUSSION

The principal finding in this study indicated that life event stress was associated with depressive symptoms and poor quality of life in both COPD and non-COPD participants (main effects), but showed a significantly stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a disproportionately greater detrimental effect. To our knowledge, no other studies have reported demonstrating this relationship.

It should be noted that participants with COPD actually did not report greater frequency of occurrence or perceived stress score of non-illness related life events than non-COPD participants. Instead, individuals with COPD appeared to experience the same number of non-illness related life events and perceived them to be equally stressful as their non-COPD counterparts, yet showed disproportionately greater psychological distress and poorer quality of life. These results suggest that individuals with COPD may be more vulnerable to the adverse impact of stressful events than non-COPD individuals.

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A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.

There are few studies that have investigated the relationship between cognitive appraisal of stressful events, coping strategies and psychological distress in COPD patients. A study by Andrenas and co-investigators [23] have assessed how hospitalized patients with acutely exacerbated COPD appraised and coped with a recent stressful event and their level of psychological distress. They reported that half of the respondents tended to perceive their stressful event as representing a threat, 26% as harmful, 7.6% as a loss, 4.3% as a challenge, and 11% characterized the stressful event in some other ways. However, the authors found that neither types of stressful event, stress intensity, primary or secondary appraisal, or number of coping strategies used were significantly related to psychological distress. Only problem-solving coping strategies were inversely related to psychological distress. This suggests that poor coping skills may be the principal psychological problem among COPD patients that contribute to their psychological distress and poor quality of life. However, further studies should be conducted.

Our secondary finding of the main effects of COPD on FEV_1 was expected and thus not surprising. However, the association of COPD with more frequent cognitive problems was interesting, although the results for MMSE score were not significant after adjustment in two-way ANOVA, possibly due to sample size limitation. These results are consistent with clinical and population studies that indicate significant

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cognitive effects of COPD on deficits in abstract reasoning [23], complex visual motor process [24], and verbal learning [25], language [26], attention [27], information processing speed [27-29] and verbal learning and memory [28, 29].

The present study has strengths and limitations. The case definition for COPD is accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria. Results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis. The measure of life event stress is modified to exclude illness-related stress from chronic diseases in this older population. However, a limitation of the life event inventory is inter-categorical variability and recall bias in the appraisal of the stressful life event [30]. In a cross-sectional study, interpreting the causal relationship between stress and the health-related functional outcomes can be uncertain. Further longitudinal studies are required.

Studies [31-33] have reported that mental health status, including anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. While it is increasingly being recognized that the identification and treatment of psychological disorders are important for improving patient centered outcomes in COPD patients, there should be commensurate attention to stressful life event(s) that trigger psychological disturbances and poor psycho-social functioning. Psychological interventions in COPD patients that include the identification of stressful life event and improving patients' coping skills may directly contribute to improving psychological functioning and quality of life in COPD patients.

In conclusion, the present study found that life event stress was associated with

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more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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DECLARATION OF INTEREST

The authors declare that there are no declarations of interest in relation to the current study. The authors are responsible for the writing and the content of this article.

DATA SHARING STATEMENT

There is no additional data available.

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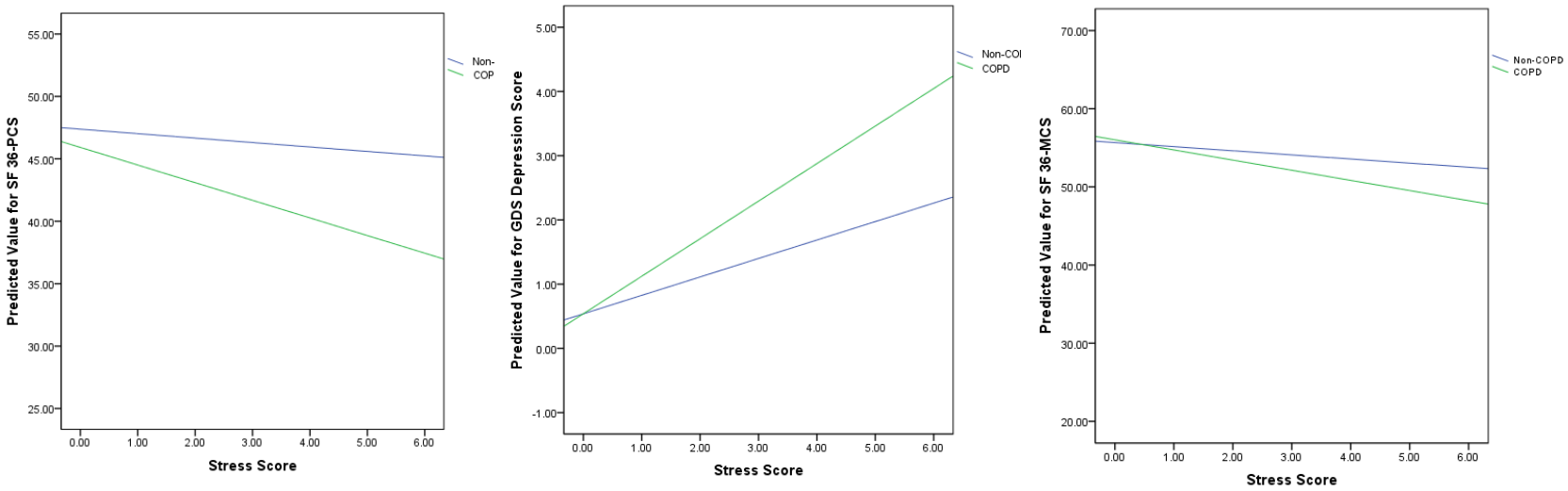

Figure 1. Predicted value for SF-36 PCS, GDS depression score and SF 36-MCS in participants with and without COPD

SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; GDS=the Geriatric Depression Scale; MCS= Mental Health Component Summary.

Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): Associations with Mental Wellbeing and Quality of Life in a Population-based Study

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Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): Associations with Mental Wellbeing and Quality of Life in a Population-based Study

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ARTICAL SUMMARY

Article focus

- The impact of life event stress on the mental wellbeing and quality of life of individuals with chronic obstructive pulmonary disease (COPD).

Key messages

- Our findings showed that in individuals with COPD, life event stress had a greater detrimental effect on mental health and quality of life in comparison to non-COPD individuals.

Strengths and limitations of this study

- The case definition for COPD in this study was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria.
- The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis.
- Definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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Abstract

Objectives: To investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD

Design: Cross-sectional study.

Participants: A population-based sample (N=497) of individuals aged 65 and above with COPD (post-bronchodilatation $FEV_1/FVC<0.70$, N=136) and without COPD (N=277).

Measurements: We measured life event stress, depressive symptoms (GDS), cognitive symptoms and function (CFQ, MMSE), and physical and mental health functional status (SF36-PCS and SF36-MCS) in participants with and without COPD.

Results: In two-way analysis of variance controlling for potential confounders, life event stress was associated with significant main effects of worse GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS scores ($p<0.001$), and with significant interaction effects on GDS score ($p<0.001$), SF36-PCS ($p=0.045$) and SF36-MCS ($p=0.034$) in participants with COPD more than in non-COPD participants. Main effect of COPD was found for post-bronchodilator FEV_1 ($p<0.001$) and cognitive symptoms ($p=0.02$).

Conclusions: Our findings indicate that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands out among chronic diseases with its high and rising prevalence and mortality [1], poor quality of life, frequent hospitalization and huge societal burden of care [2]. Because patients with COPD bear a heavy burden of psychological disturbance, psychiatric morbidity, and disability in daily living activities [3, 4], the mental health of COPD patients has received growing attention in recent years.

Life event stress is increasingly recognized to play important roles in the development and outcomes of chronic illness such as type II diabetes, coronary heart disease, gastroenterological disorders and obstetric outcomes [5]. Stress is well known to result in depression, psychological burnout, post-traumatic stress disorder (PTSD) in all ages, as well as cognitive impairment in late life [6]. Among COPD patients, an intrinsic source of stress is directly related to their illness, involving the experience of anxiety and distress provoked by breathing difficulties [7, 8], including muddled thoughts, heightened emotions, extreme fear and panic and decreased physical energy, and various difficulties in emotional functioning, sleep and rest, physical mobility, social interaction, activities of daily living, recreation, work and finance. However, the impact of life event stress in general including those extrinsic to illness-related experience on the physical and mental functioning and quality of life of individuals with COPD in comparison to non-COPD individuals has rarely been investigated [9, 10, 6]. The aim of this study was to investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.

The present study analyzed data collected on COPD status, life event stress, and measures of pulmonary function, cognitive function, depressive symptoms and quality of in a population-based sample (Singapore Longitudinal Aging Study) [11] to

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investigate the effect of life event stress on psychological functioning and quality of life. We hypothesized that life event stress in the whole sample would be associated with depressive symptoms and poor quality of life (main effect), but would have a stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a greater detrimental effect on depressive symptoms and quality of life. A secondary relationship analyzed in two-way analysis of variance (ANOVA) was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function, based on the known effects of impaired pulmonary and cognitive function in COPD.

METHODS

Study Design and Participants

The participants in the study were a subsample recruited from one locality (Bukit Merah) in the South Central region of Singapore Longitudinal Aging Study (SLAS-2), a prospective population-based cohort study of aging and health of community-dwelling elderly [12]. We interviewed one participant from each household who were Singaporean citizens or permanent residents aged 65 or older who were able to give informed consent. Those who were too frail or ill and unable to complete the interview, for reasons such as from post-stroke aphasia, cachexia or profound dementia, were excluded. The participants who completed interviews and provided technically acceptable spirometric data (N=497) represented a response rate of 78.5% of the eligible participants. All participants signed written informed consent for the study which was approved by the National University of Singapore Institutional Review Board.

COPD

We identified cases of COPD among the participants who had characteristic symptoms of COPD and spirometric evidence of chronic airflow obstruction (post-

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bronchial dilatation FEV1/FVC< 0.70), in accordance with the definition recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [13].

Questions from the British Medical Research Council Questionnaire on chronic respiratory symptoms were used to elicit symptoms characteristic of COPD: chronic cough and/or sputum lasting at least 3 months in the year and/or breathlessness on exertion.

Ventilatory function testing was performed using a portable, battery operated, ultrasound transit-time based spirometer (Easy-One; Model 2001 Diagnostic Spirometer, NDD Medical Technologies, Zurich, Switzerland). Calibration was checked daily with a 3-L syringe. Forced expiratory maneuvers were performed with the respondent seated with recommended guidelines and standardization of procedures: at least three acceptable maneuvers, with forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) reproducible within 200 ml. Chronic airflow obstruction as defined as post-bronchial dilatation FEV1/FVC < 0.70.

Life Event Stress

Life event stress was measured by an 11-item life events inventory [14, 15] that excluded personal illness experiences directly related to COPD. The participants were asked to indicate yes or no as to whether any of eleven life events had occurred over the past year ("spouse or partner die, a close friend or family member die or have a serious illness (other than your spouse or partner), major problems with money, a divorce or breakup, family member or close friend have a divorce or breakup, major conflict with children or grandchildren, major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events, a family member or close friend lose their job or retire, physically abused, verbally abused, or pet die"). If the participant indicated (a) life event(s) had occurred, he/she was asked to appraise the event and indicate on a scale of 1 (did not upset me) to 3 (upset me greatly) the extent it upset

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them. Frequency of life event stress was calculated. The scale also provides a life event stress score appraised by the participant that ranged from 0 to 33 with a higher score indicating a participant experienced a greater number of more stressful events.

Depressive Symptoms

The presence of depressive symptoms was determined by a depression screening scale for elderly populations, the 15-item Geriatric Depression Scale (GDS-15) with scores ranging from 0 to 15 [16]. The GDS was well suited for the study because it is largely free of the measurement artefact due to overlapping somatic symptoms of physical illness(es) and depression. In validation studies in the local older population [17], translated versions of the GDS-15 have been found to be a valid and reliable screening tool for depression: Cronbach's alpha of 0.80, and intraclass coefficients of test-retest reliability of 0.83 and inter-rater reliability of 0.94. Using a GDS cutoff of >=5, the GDS-15 has a sensitivity of 0.97 and specificity of 0.95 (area under curve of 0.98) for determining major depressive disorder according to DSM-IV criteria. Depressive symptoms defined as such by GDS>=5 is clinically significant, and such cases including "sub-threshold" depression, had been shown in the same population to be associated with significantly poorer mental and physical health and functional status, and more healthcare resource utilization compared to non-cases and were similar to or worse than syndrome threshold cases of depression [18].

Cognitive Function

Cognitive function was measured using the Cognitive Failures Questionnaire (CFQ) [19] and the Mini-Mental State Examination (MMSE) which were validated and widely used instruments to assess global cognitive functioning [20]. The CFQ uses a 5-point Likert-type scale (1 = Never, 5 = Very often) to evaluate self-reported cognitive problems (e.g.,''Do you need to re-read instructions several times?"). Higher CFQ scores indicate more frequent cognitive problems and higher MMSE scores (0 to 30) indicate better

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global cognitive functioning, and MMSE scores of 23 or less are considered to be cognitively impaired.

Physical and Mental Functioning

Physical and mental functional well-being was measured by the Medical Outcomes Study 36-item Short Form (SF-36) [21] which has been previously validated for use in Singaporeans [22]. Weighted summary measures of Physical Health Component Summary (PCS) score and Mental Health Component Summary (MCS) score were computed with higher scores indicating better physical and mental health functioning and quality of life.

Statistical Analyses

Data analysis was performed using the software package PASW Statistics (SPSS) version 18. In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) using generalized linear model [23] which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function. For the outcome variables with significant interaction

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of life event stress and COPD, the simple effects of their relationships with life event stress score were investigated respectively in participants with and without COPD. Statistical significance was set at $p<0.05$.

RESULTS

This study consisted of 497 participants with the average age of 72.1. Among the respondents, 32.9% had COPD, and 67.1% had no COPD. The proportion of respondents with stressful life events in the past one year was 43.4%. The socio-demographic and psychological characteristics of study participants with and without COPD are shown in Table 1. Participants with COPD were found to have higher mean age (t=3.328, $p=0.001$), higher proportion of smokers (χ^2 =20.586, df=3, $p<0.001$) and increased number of diseases (t=7.096, $p<0.001$). No significant difference in the number of life events or perceived stress was observed between COPD and non-COPD participants ($p>0.05$).

Table 1 shows that compared with those without COPD, participants with COPD had decreased post-bronchodilator FEV1 (t=6.185, $p<0.001$), MMSE score (t=3.090, $p=0.002$) and SF-36 PCS (t=2.726, $p=0.007$) score. There were no difference in CFQ and GDS depression scores between participants with and without COPD ($p>0.05$) in the whole sample. Next, we evaluated the effect of life event stress on GDS, CFQ, MMSE, SF-36 PCS and SF-36 MCS scores by subgroups of participants with COPD and without COPD. As shown in Table 2, two-way analysis of variance in general linear model showed significant main effects of life event stress for GDS (F=64.500, df=1, $p<0.001$), SF36-PCS (F=7.054, df=1, $p=0.008$) and SF36-MCS (F=14.710, df=1, $p<0.001$) scores, and significant interactions of life event stress with COPD were found as well for GDS (F=10.970, df=1, $p=0.001$), SF36-PCS (F=4.055, df=1, $p=0.045$), and SF36-MCS (F=4.538, df=1, $p=0.034$) scores. The simple effects of life event stress on GDS, SF36-

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PCS and SF36-MCS are shown for participants with and without COPD respectively in Figure 1. Increasing stress score was associated with higher GDS score, lower SF12-PCS and lower SF12-MCS scores in participants with COPD, more than in those without COPD after adjusting for potential confounders, indicating the association of life event stress with worse psychological distress and poorer quality of life among individuals with COPD, in comparison to non-COPD individuals. The other significant main effect found in two-way analysis of variance was of COPD for decreased post-bronchodilator FEV_1 (F=17.458, df=1, p<0.001) and higher CFQ scores (F=5.424, df=1, p=0.020) after adjustment of sex, age, ethnicity, smoking status, and number of chronic illness, indicating impaired pulmonary and cognitive functions in participants with COPD.

Table 1. Socio-demographic, pulmonary and psychological variables of study participants aged 65 or older (Singapore Longitudinal Aging Study, SLAS)

	COPD		Non-COPD		Significant Test	p
	N	%	N	%		
Total	136	32.9	277	67.1		
Sex						
Male	58	42.6	112	40.7	χ^2 =0.138, df=1	0.710
Female	78	57.4	163	59.3		
Age (years, M±SD)	73.19	±5.87	71.23	±5.47	t=3.328	0.001
Ethnicity						
Chinese	121	89.0	241	87.6	χ^2 =0.154, df=1	0.694
Non-Chinese	15	11.0	34	12.4		
Smoking						
Never smoker	77	57.6	211	77.3	χ^2 =20.59, df=3	<0.001
Past smoker	29	21.6	41	15.0		
Current smoker < 10 cigarettes daily	18	13.4	12	4.4		
Current smoker ≥ 10 cigarettes daily	10	7.5	9	3.3		
Number of chronic diseases	2.60	±1.30	1.65	1.25	t=7.096	<0.001
Number of Negative Life Events	0.67	±0.98	0.74	±1.11	t=0.609	0.543
Life Event Stress Score	1.02	±1.71	1.12	±1.78	t=0.525	0.600
Post-bronchodilator FEV1	1.42	±0.50	1.75	±0.52	t=6.185	<0.001
CFQ Score	38.0	±9.21	38.8	±9.83	t=0.733	0.464
MMSE Score	26.4	±3.26	27.4	±3.11	t=3.090	0.002
GDS Depression score	1.13	±2.04	0.84	±1.69	t=1.487	0.138
GDS≥5, % (n)	5.2	(7)	2.9	(8)	χ^2 =1.349, df=1	0.245
SF-36 PCS	44.6	±9.04	47.1	±7.21	t=2.726	0.007
SF-36 MCS	54.9	±7.83	55.1	±6.68	t=0.353	0.724

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Figures in table denote mean ± SD or number and %.
Smoker is defined as smoking ≥ 10 cigarettes daily

Table 2. Two-way ANOVA: Life event stress, COPD and mental and physical variables

	Main Effects of COPD (df=1)		Main Effects of Stress (df=1)		Interaction (df=1)	
	F	*P*	F	*P*	F	*p*
Post-bronchodilator FEV1	17.458	<0.001	0.323	0.570	2.057	0.152
CFQ Score	5.424	0.020	1.927	0.166	2.514	0.114
MMSE Score	1.799	0.181	1.159	0.282	0.380	0.538
GDS Depression score	2.353	0.126	64.500	<0.001	10.970	0.001
SF-36 PCS	0.432	0.512	7.054	0.008	4.055	0.045
SF-36 MCS	0.659	0.417	14.710	<0.001	4.538	0.034

Adjusted variables: sex, age, ethnicity, smoking status, and number of chronic illness.
FEV1=Forced Expiratory Volume in the first second; CFQ=Cognitive Failure Questionnaire; MMSE=Mini-Mental State Examination; GDS=the Geriatric Depression Scale; SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; MCS= Mental Health Component Summary.

DISCUSSION

The principal finding in this study indicated that life event stress was associated with depressive symptoms and poor quality of life in both COPD and non-COPD participants (main effects), but showed a significantly stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a disproportionately greater detrimental effect. To our knowledge, no other studies have reported demonstrating this relationship.

It should be noted that participants with COPD actually did not report greater frequency of occurrence or perceived stress score of non-illness related life events than non-COPD participants. Instead, individuals with COPD appeared to experience the same number of non-illness related life events and perceived them to be equally stressful as their non-COPD counterparts, yet showed disproportionately greater psychological distress and poorer quality of life. These results suggest that individuals

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with COPD may be more vulnerable to the adverse impact of stressful events than non-COPD individuals.

A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.

There are few studies that have investigated the relationship between cognitive appraisal of stressful events, coping strategies and psychological distress in COPD patients. A study by Andrenas and co-investigators [24] have assessed how hospitalized patients with acutely exacerbated COPD appraised and coped with a recent stressful event and their level of psychological distress. They reported that half of the respondents tended to perceive their stressful event as representing a threat, 26% as harmful, 7.6% as a loss, 4.3% as a challenge, and 11% characterized the stressful event in some other ways. However, the authors found that neither types of stressful event, stress intensity, primary or secondary appraisal, or number of coping strategies used were significantly related to psychological distress. Only problem-solving coping strategies were inversely related to psychological distress. This suggests that poor coping skills may be the principal psychological problem among COPD patients that contribute to their psychological distress and poor quality of life. However, further studies should be conducted.

Our secondary finding of the main effects of COPD on FEV_1 was expected and thus not surprising. However, the association of COPD with more frequent cognitive problems was interesting, although the results for MMSE score were not significant

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after adjustment in two-way ANOVA, possibly due to sample size limitation. These results are consistent with clinical and population studies that indicate significant cognitive effects of COPD on deficits in abstract reasoning [25], complex visual motor process [26], and verbal learning [27], language [28], attention [29], information processing speed [29-31] and verbal learning and memory [30, 31].

The present study has strengths and limitations. The case definition for COPD is accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria. Results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis. The measure of life event stress is modified to exclude illness-related stress from chronic diseases in this older population. However, a limitation of the life event inventory is inter-categorical variability and recall bias in the appraisal of the stressful life event [32]. In a cross-sectional study, interpreting the causal relationship between stress and the health-related functional outcomes can be uncertain. Further longitudinal studies are required.

Studies [33-35] have reported that mental health status, including anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. More studies of the effects of stress management and coping strategy in psychological interventions in COPD should be investigated in randomized controlled clinical trials.

It is increasingly being recognized that the identification of mood and anxiety disorders, and psychological and psychosocial interventions to improve mood and reduce anxiety are important for improving patient centered outcomes in COPD patients.

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However, in published clinical guidelines such as NICE, where the initial step care management by practitioners in primary care and general hospital settings includes low-intensity psychosocial interventions for patients with persistent subthreshold depressive symptoms or mild to moderate depression, there appears to be little attention given to identifying stressful life event(s) and supporting COPD patients experiencing stressful life events to prevent the onset of mood and anxiety disorders. In particular, group-based peer support, individual guided self-help based on cognitive behavioural therapy (CBT) principles or computerised CBT to reduce patients' vulnerability to stress may usefully include objective cognitive appraisal of stress, problem-solving coping skills, and relaxation therapy to help support COPD patients experiencing stressful life events.

In conclusion, the present study found that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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DECLARATION OF INTEREST

The authors declare that there are no declarations of interest in relation to the current study. The authors are responsible for the writing and the content of this article.

DATA SHARING STATEMENT

There is no additional data available.

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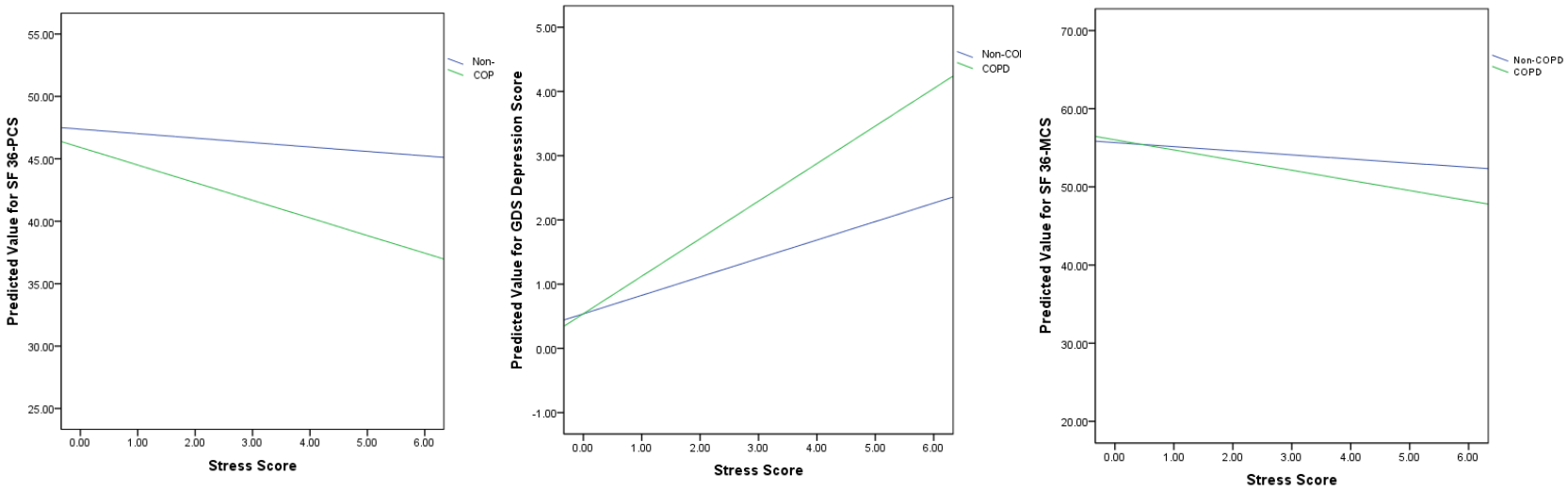

Figure 1. Predicted value for SF-36 PCS, GDS depression score and SF 36-MCS in participants with and without COPD

SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; GDS=the Geriatric Depression Scale; MCS= Mental Health Component Summary.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	*6-9*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): Associations with Mental Wellbeing and Quality of Life in a Population-based Study

Running title: Stress & COPD

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Tables: 2
Figure: 1

Key Words: Life event stress; COPD; Cognitive function; Physical and psychological well-being; Quality of life

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ARTICAL SUMMARY

Article focus

- The impact of life event stress on the mental wellbeing and quality of life of individuals with chronic obstructive pulmonary disease (COPD).

Key messages

- Our findings showed that in individuals with COPD, life event stress had a greater detrimental effect on mental health and quality of life in comparison to non-COPD individuals.

Strengths and limitations of this study

- The case definition for COPD in this study was accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria.
- The results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis.
- Definite causal inferences cannot be made from the cross-sectional findings in this study. Further longitudinal studies are required.

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Abstract

Objectives: To investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD

Design: Cross-sectional study.

Participants: A population-based sample (N=497) of individuals aged 65 and above with COPD (post-bronchodilatation $FEV_1/FVC<0.70$, N=136) and without COPD (N=277).

Measurements: We measured life event stress, depressive symptoms (GDS), cognitive symptoms and function (CFQ, MMSE), and physical and mental health functional status (SF36-PCS and SF36-MCS) in participants with and without COPD.

Results: In two-way analysis of variance controlling for potential confounders, life event stress was associated with significant main effects of worse GDS ($p<0.001$), SF36-PCS ($p=0.008$) and SF36-MCS scores ($p<0.001$), and with significant interaction effects on GDS score ($p<0.001$), SF36-PCS ($p=0.045$) and SF36-MCS ($p=0.034$) in participants with COPD more than in non-COPD participants. Main effect of COPD was found for post-bronchodilator FEV_1 ($p<0.001$) and cognitive symptoms ($p=0.02$).

Conclusions: Our findings indicate that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) stands out among chronic diseases with its high and rising prevalence and mortality [1], poor quality of life, frequent hospitalization and huge societal burden of care [2]. Because patients with COPD bear a heavy burden of psychological disturbance, psychiatric morbidity, and disability in daily living activities [3, 4], the mental health of COPD patients has received growing attention in recent years.

Life event stress is increasingly recognized to play important roles in the development and outcomes of chronic illness such as type II diabetes, coronary heart disease, gastroenterological disorders and obstetric outcomes [5]. Stress is well known to result in depression, psychological burnout, post-traumatic stress disorder (PTSD) in all ages, as well as cognitive impairment in late life [6]. Among COPD patients, an intrinsic source of stress is directly related to their illness, involving the experience of anxiety and distress provoked by breathing difficulties [7, 8], including muddled thoughts, heightened emotions, extreme fear and panic and decreased physical energy, and various difficulties in emotional functioning, sleep and rest, physical mobility, social interaction, activities of daily living, recreation, work and finance. However, the impact of life event stress in general including those extrinsic to illness-related experience on the physical and mental functioning and quality of life of individuals with COPD in comparison to non-COPD individuals has rarely been investigated [9, 10, 6]. The aim of this study was to investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.

The present study analyzed data collected on COPD status, life event stress, and measures of pulmonary function, cognitive function, depressive symptoms and quality of in a population-based sample (Singapore Longitudinal Aging Study) [11] to

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investigate the effect of life event stress on psychological functioning and quality of life. We hypothesized that life event stress in the whole sample would be associated with depressive symptoms and poor quality of life (main effect), but would have a stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a greater detrimental effect on depressive symptoms and quality of life. A secondary relationship analyzed in two-way analysis of variance (ANOVA) was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function, based on the known effects of impaired pulmonary and cognitive function in COPD.

METHODS

Study Design and Participants

The participants in the study were a subsample recruited from one locality (Bukit Merah) in the South Central region of Singapore Longitudinal Aging Study (SLAS-2), a prospective population-based cohort study of aging and health of community-dwelling elderly [12]. We interviewed one participant from each household who were Singaporean citizens or permanent residents aged 65 or older who were able to give informed consent. Those who were too frail or ill and unable to complete the interview, for reasons such as from post-stroke aphasia, cachexia or profound dementia, were excluded. The participants who completed interviews and provided technically acceptable spirometric data (N=497) represented a response rate of 78.5% of the eligible participants. All participants signed written informed consent for the study which was approved by the National University of Singapore Institutional Review Board.

COPD

We identified cases of COPD among the participants who had characteristic symptoms of COPD and spirometric evidence of chronic airflow obstruction (post-

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bronchial dilatation FEV1/FVC< 0.70), in accordance with the definition recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [13].

Questions from the British Medical Research Council Questionnaire on chronic respiratory symptoms were used to elicit symptoms characteristic of COPD: chronic cough and/or sputum lasting at least 3 months in the year and/or breathlessness on exertion.

Ventilatory function testing was performed using a portable, battery operated, ultrasound transit-time based spirometer (Easy-One; Model 2001 Diagnostic Spirometer, NDD Medical Technologies, Zurich, Switzerland). Calibration was checked daily with a 3-L syringe. Forced expiratory maneuvers were performed with the respondent seated with recommended guidelines and standardization of procedures: at least three acceptable maneuvers, with forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) reproducible within 200 ml. Chronic airflow obstruction as defined as post-bronchial dilatation FEV1/FVC < 0.70.

Life Event Stress

Life event stress was measured by an 11-item life events inventory [14, 15] that excluded personal illness experiences directly related to COPD. The participants were asked to indicate yes or no as to whether any of eleven life events had occurred over the past year ("spouse or partner die, a close friend or family member die or have a serious illness (other than your spouse or partner), major problems with money, a divorce or breakup, family member or close friend have a divorce or breakup, major conflict with children or grandchildren, major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events, a family member or close friend lose their job or retire, physically abused, verbally abused, or pet die"). If the participant indicated (a) life event(s) had occurred, he/she was asked to appraise the event and indicate on a scale of 1 (did not upset me) to 3 (upset me greatly) the extent it upset

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them. Frequency of life event stress was calculated. The scale also provides a life event stress score appraised by the participant that ranged from 0 to 33 with a higher score indicating a participant experienced a greater number of more stressful events.

Depressive Symptoms

The presence of depressive symptoms was determined by a depression screening scale for elderly populations, the 15-item Geriatric Depression Scale (GDS-15) with scores ranging from 0 to 15 [16]. The GDS was well suited for the study because it is largely free of the measurement artefact due to overlapping somatic symptoms of physical illness(es) and depression. In validation studies in the local older population [17], translated versions of the GDS-15 have been found to be a valid and reliable screening tool for depression: Cronbach's alpha of 0.80, and intraclass coefficients of test-retest reliability of 0.83 and inter-rater reliability of 0.94. Using a GDS cutoff of >=5, the GDS-15 has a sensitivity of 0.97 and specificity of 0.95 (area under curve of 0.98) for determining major depressive disorder according to DSM-IV criteria. Depressive symptoms defined as such by GDS>=5 is clinically significant, and such cases including "sub-threshold" depression, had been shown in the same population to be associated with significantly poorer mental and physical health and functional status, and more healthcare resource utilization compared to non-cases and were similar to or worse than syndrome threshold cases of depression [18].

Cognitive Function

Cognitive function was measured using the Cognitive Failures Questionnaire (CFQ) [19] and the Mini-Mental State Examination (MMSE) which were validated and widely used instruments to assess global cognitive functioning [20]. The CFQ uses a 5-point Likert-type scale (1 = Never, 5 = Very often) to evaluate self-reported cognitive problems (e.g.,''Do you need to re-read instructions several times?"). Higher CFQ scores indicate more frequent cognitive problems and higher MMSE scores (0 to 30) indicate better

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global cognitive functioning, and MMSE scores of 23 or less are considered to be cognitively impaired.

Physical and Mental Functioning

Physical and mental functional well-being was measured by the Medical Outcomes Study 36-item Short Form (SF-36) [21] which has been previously validated for use in Singaporeans [22]. Weighted summary measures of Physical Health Component Summary (PCS) score and Mental Health Component Summary (MCS) score were computed with higher scores indicating better physical and mental health functioning and quality of life.

Statistical Analyses

Data analysis was performed using the software package PASW Statistics (SPSS) version 18. In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) using generalized linear model [23] which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function. For the outcome variables with significant interaction

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of life event stress and COPD, the simple effects of their relationships with life event stress score were investigated respectively in participants with and without COPD. Statistical significance was set at $p<0.05$.

RESULTS

This study consisted of 497 participants with the average age of 72.1. Among the respondents, 32.9% had COPD, and 67.1% had no COPD. The proportion of respondents with stressful life events in the past one year was 43.4%. The socio-demographic and psychological characteristics of study participants with and without COPD are shown in Table 1. Participants with COPD were found to have higher mean age (t=3.328, $p=0.001$), higher proportion of smokers (χ^2 =20.586, df=3, $p<0.001$) and increased number of diseases (t=7.096, $p<0.001$). No significant difference in the number of life events or perceived stress was observed between COPD and non-COPD participants ($p>0.05$).

Table 1 shows that compared with those without COPD, participants with COPD had decreased post-bronchodilator FEV1 (t=6.185, $p<0.001$), MMSE score (t=3.090, $p=0.002$) and SF-36 PCS (t=2.726, $p=0.007$) score. There were no difference in CFQ and GDS depression scores between participants with and without COPD ($p>0.05$) in the whole sample. Next, we evaluated the effect of life event stress on GDS, CFQ, MMSE, SF-36 PCS and SF-36 MCS scores by subgroups of participants with COPD and without COPD. As shown in Table 2, two-way analysis of variance in general linear model showed significant main effects of life event stress for GDS (F=64.500, df=1, $p<0.001$), SF36-PCS (F=7.054, df=1, $p=0.008$) and SF36-MCS (F=14.710, df=1, $p<0.001$) scores, and significant interactions of life event stress with COPD were found as well for GDS (F=10.970, df=1, $p=0.001$), SF36-PCS (F=4.055, df=1, $p=0.045$), and SF36-MCS (F=4.538, df=1, $p=0.034$) scores. The simple effects of life event stress on GDS, SF36-

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PCS and SF36-MCS are shown for participants with and without COPD respectively in Figure 1. Increasing stress score was associated with higher GDS score, lower SF12-PCS and lower SF12-MCS scores in participants with COPD, more than in those without COPD after adjusting for potential confounders, indicating the association of life event stress with worse psychological distress and poorer quality of life among individuals with COPD, in comparison to non-COPD individuals. The other significant main effect found in two-way analysis of variance was of COPD for decreased post-bronchodilator FEV_1 (F=17.458, df=1, p<0.001) and higher CFQ scores (F=5.424, df=1, p=0.020) after adjustment of sex, age, ethnicity, smoking status, and number of chronic illness, indicating impaired pulmonary and cognitive functions in participants with COPD.

Table 1. Socio-demographic, pulmonary and psychological variables of study participants aged 65 or older (Singapore Longitudinal Aging Study, SLAS)

	COPD		Non-COPD		Significant Test	p
	N	%	N	%		
Total	136	32.9	277	67.1		
Sex						
Male	58	42.6	112	40.7	χ^2 =0.138, df=1	0.710
Female	78	57.4	163	59.3		
Age (years, M±SD)	73.19	±5.87	71.23	±5.47	t=3.328	0.001
Ethnicity						
Chinese	121	89.0	241	87.6	χ^2 =0.154, df=1	0.694
Non-Chinese	15	11.0	34	12.4		
Smoking						
Never smoker	77	57.6	211	77.3	χ^2 =20.59, df=3	<0.001
Past smoker	29	21.6	41	15.0		
Current smoker < 10 cigarettes daily	18	13.4	12	4.4		
Current smoker ≥ 10 cigarettes daily	10	7.5	9	3.3		
Number of chronic diseases	2.60	±1.30	1.65	1.25	t=7.096	<0.001
Number of Negative Life Events	0.67	±0.98	0.74	±1.11	t=0.609	0.543
Life Event Stress Score	1.02	±1.71	1.12	±1.78	t=0.525	0.600
Post-bronchodilator FEV1	1.42	±0.50	1.75	±0.52	t=6.185	<0.001
CFQ Score	38.0	±9.21	38.8	±9.83	t=0.733	0.464
MMSE Score	26.4	±3.26	27.4	±3.11	t=3.090	0.002
GDS Depression score	1.13	±2.04	0.84	±1.69	t=1.487	0.138
GDS≥5, % (n)	5.2	(7)	2.9	(8)	χ^2 =1.349, df=1	0.245
SF-36 PCS	44.6	±9.04	47.1	±7.21	t=2.726	0.007
SF-36 MCS	54.9	±7.83	55.1	±6.68	t=0.353	0.724

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Figures in table denote mean ± SD or number and %.
Smoker is defined as smoking ≥ 10 cigarettes daily

Table 2. Two-way ANOVA: Life event stress, COPD and mental and physical variables

	Main Effects of COPD (df=1)		Main Effects of Stress (df=1)		Interaction (df=1)	
	F	*P*	F	*P*	F	*p*
Post-bronchodilator FEV1	17.458	<0.001	0.323	0.570	2.057	0.152
CFQ Score	5.424	0.020	1.927	0.166	2.514	0.114
MMSE Score	1.799	0.181	1.159	0.282	0.380	0.538
GDS Depression score	2.353	0.126	64.500	<0.001	10.970	0.001
SF-36 PCS	0.432	0.512	7.054	0.008	4.055	0.045
SF-36 MCS	0.659	0.417	14.710	<0.001	4.538	0.034

Adjusted variables: sex, age, ethnicity, smoking status, and number of chronic illness.
FEV1=Forced Expiratory Volume in the first second; CFQ=Cognitive Failure Questionnaire; MMSE=Mini-Mental State Examination; GDS=the Geriatric Depression Scale; SF-36=36-Item Short-Form Healthy Survey; PCS=Physical Health Component Summary; MCS= Mental Health Component Summary.

DISCUSSION

The principal finding in this study indicated that life event stress was associated with depressive symptoms and poor quality of life in both COPD and non-COPD participants (main effects), but showed a significantly stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a disproportionately greater detrimental effect. To our knowledge, no other studies have reported demonstrating this relationship.

It should be noted that participants with COPD actually did not report greater frequency of occurrence or perceived stress score of non-illness related life events than non-COPD participants. Instead, individuals with COPD appeared to experience the same number of non-illness related life events and perceived them to be equally stressful as their non-COPD counterparts, yet showed disproportionately greater psychological distress and poorer quality of life. These results suggest that individuals

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with COPD may be more vulnerable to the adverse impact of stressful events than non-COPD individuals.

A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.

There are few studies that have investigated the relationship between cognitive appraisal of stressful events, coping strategies and psychological distress in COPD patients. A study by Andrenas and co-investigators [24] have assessed how hospitalized patients with acutely exacerbated COPD appraised and coped with a recent stressful event and their level of psychological distress. They reported that half of the respondents tended to perceive their stressful event as representing a threat, 26% as harmful, 7.6% as a loss, 4.3% as a challenge, and 11% characterized the stressful event in some other ways. However, the authors found that neither types of stressful event, stress intensity, primary or secondary appraisal, or number of coping strategies used were significantly related to psychological distress. Only problem-solving coping strategies were inversely related to psychological distress. This suggests that poor coping skills may be the principal psychological problem among COPD patients that contribute to their psychological distress and poor quality of life. However, further studies should be conducted.

Our secondary finding of the main effects of COPD on FEV_1 was expected and thus not surprising. However, the association of COPD with more frequent cognitive problems was interesting, although the results for MMSE score were not significant

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after adjustment in two-way ANOVA, possibly due to sample size limitation. These results are consistent with clinical and population studies that indicate significant cognitive effects of COPD on deficits in abstract reasoning [25], complex visual motor process [26], and verbal learning [27], language [28], attention [29], information processing speed [29-31] and verbal learning and memory [30, 31].

The present study has strengths and limitations. The case definition for COPD is accurately based on symptom and post-bronchial dilatation spirometric measures of chronic airflow obstruction that are diagnostic of COPD according to GOLD recommended criteria. Results from this general population-based study are largely free of clinical selection bias, and also controlled for important confounding by demographic and psychosocial variables in the analysis. The measure of life event stress is modified to exclude illness-related stress from chronic diseases in this older population. However, a limitation of the life event inventory is inter-categorical variability and recall bias in the appraisal of the stressful life event [32]. In a cross-sectional study, interpreting the causal relationship between stress and the health-related functional outcomes can be uncertain. Further longitudinal studies are required.

Studies [33-35] have reported that mental health status, including anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. More studies of the effects of stress management and coping strategy in psychological interventions in COPD should be investigated in randomized controlled clinical trials.

It is increasingly being recognized that the identification of mood and anxiety disorders, and psychological and psychosocial interventions to improve mood and reduce anxiety are important for improving patient centered outcomes in COPD patients.

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However, in published clinical guidelines such as NICE, where the initial step care management by practitioners in primary care and general hospital settings includes low-intensity psychosocial interventions for patients with persistent subthreshold depressive symptoms or mild to moderate depression, there appears to be little attention given to identifying stressful life event(s) and supporting COPD patients experiencing stressful life events to prevent the onset of mood and anxiety disorders. In particular, group-based peer support, individual guided self-help based on cognitive behavioural therapy (CBT) principles or computerised CBT to reduce patients' vulnerability to stress may usefully include objective cognitive appraisal of stress, problem-solving coping skills, and relaxation therapy to help support COPD patients experiencing stressful life events.

In conclusion, the present study found that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psycho-social support in this relationship.

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DECLARATION OF INTEREST

The authors declare that there are no declarations of interest in relation to the current study. The authors are responsible for the writing and the content of this article.

DATA SHARING STATEMENT

There is no additional data available.

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