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Impact of Mental Health and Personality Traits on the Incidence of Chronic Cough in the Canadian Longitudinal Study on Aging (CLSA)

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ABBREVIATIONS:

BMI; body mass index, CLSA; Canadian Longitudinal Study of Ageing, COPD; chronic obstructive pulmonary disease,

ABSTRACT (250 Words)

Chronic Cough is a common troublesome condition, but risk factors for developing chronic cough are poorly understood. The aim of this study was to understand the relationship between mental health disorders, personality traits and chronic cough.

The Canadian Longitudinal Study on Aging is a prospective, nationally generalizable, random sample of adults aged 45-85 at baseline recruited between 2011-2015 and followed-up 3 years later. Chronic cough was defined a daily cough over the last 12 months. Incidental chronic cough was defined as those participants who reported new-onset chronic cough between baseline and follow-up 1. Current depressive symptoms and psychological distress was assessed using the Center for Epidemiologic Study Short Depression Scale (CESD-10) and Kessler Psychological Distress Scale (K-10) respectively. The 'Big-Five' personality traits were assessed using the Ten-Item Personality Inventory (TIPI). Relative risks are reported using a multi-variate mutually adjusted model.

At follow-up 1, 2,506 participants (11.1%) reported new-onset chronic cough during the approximate 3-year interval. Depressive symptoms [CESD≥10, RR 1.22(1.03-1.44)] and psychological distress [K-10≥22, RR 1.20(1.07-1.36)] at baseline were both independent predictors of a higher risk of incidental chronic cough. Prevalent and incidental chronic cough was also independently associated with an increased risk of developing depressive symptoms and psychological distress. Personality traits did not influence the development of chronic cough but did increase the risk of depressive symptoms and psychological distress.

This study shows that there is a bi-directional relationship between chronic cough, depressive symptoms and psychological distress and personality traits do not independently influence the development of chronic cough.

INTRODUCTION

Chronic cough is a common troublesome condition with a global prevalence ranging from 2-18%[1]. Cough is also the leading cause for ambulatory and primary care visits to physicians [2-4] and chronic cough lasting greater than 8 weeks is one of the commonest reasons for referrals to a pulmonologist[5]. Chronic cough is associated with significant impairment in the quality of life including physical, social and psychological domains[6]. Understanding the risk factors that lead to chronic cough could help identify at risk populations and knowledge of the consequences can help provide better care by providing a more holistic patient centred approach.

Risk factors for developing chronic cough from epidemiological studies from the general community and specialist cough clinics have identified an increase in the prevalence and incidence of chronic cough with aging, sex, current smoking, higher body mass index (BMI), respiratory airways diseases (asthma, chronic obstructive airways diseases, bronchiectasis), worsening lung function, airflow obstruction, and gastro-esophageal reflux disease (GERD)[7-9]. However, patients with chronic cough attending cough clinics, often have none of these conditions.

A number of cross-sectional studies have recognised depression and mood disorders as one of the most common co-morbidities associated with chronic cough[10-14]. However, it is not possible to determine if mental health disorders are a risk factor or a consequence from cross-sectional data. Current data from longitudinal studies are also inconclusive. The Rotterdam study found no increase in the incidence of chronic cough in those with high depressive symptom scores[15]. In contrast, descriptive data from the Canadian Longitudinal Study of Ageing (CLSA) recently demonstrated that participants with self-reported prior history of depression and anxiety had a greater incidence of chronic cough [8]. However, further analyses are required to determine if the association of mental health with chronic cough is independent on other covariates. Also, current symptoms of depression as well as psychological distress may be more relevant predictors of chronic cough than a previous lifetime history of depression or

anxiety. The impact of personality traits should also be considered, as these are considered important predictors of mental health disorders[16, 17].

The objective of this study was to investigate if mental health disorders and personality traits are independently associated with the development of chronic cough, and secondly, whether chronic cough is independently associated with the development of depressive symptoms and psychological distress.

STUDY DESIGN AND METHODS

Study Design and Population

The Canadian Longitudinal Study on Ageing (CLSA) is a large, nationally generalizable, stratified random sample of 51,338 Canadian men and women aged 45 to 85 years at baseline (2011-2015) from the 10 Canadian provinces[18]. Eligible participants had to be physically and cognitively able to participate on their own and not living in institutions such as long-term care facilities. Participants were recruited in the tracking cohort (n=21,241) and the comprehensive cohort (n=30,097). Participants in the comprehensive cohort were randomly selected from within 25–50 km of 11 data collection sites, which are located in seven provinces(n=30,097). In addition to completing interviews in-person, the comprehensive participants completed in-depth physical assessments. Details on the study design have been described elsewhere[19]. Each participant is followed every three years for 20 years or until death. The first follow-up was conducted between 2015 and 2018. The comprehensive data from baseline and follow-up 1 were included in the current analyses. This study was approved by the Hamilton integrated Research Ethics Board and by the CLSA scientific advisory board (Project ID: 1909024).

Chronic Cough definition

Definitions were based on responses from direct questioning of participants by trained research assistants at baseline and follow-up using standardised questionnaires. Participants at some sites in Ontario and Quebec were given a choice to complete the interview in English or French. The language used to complete the questionnaire was used as the dominant language of the participant in this study. Participants who self-reported as having a daily cough on most days in

the last 12 months were categorized as having a chronic cough at baseline or follow-up 1. Prevalent chronic cough was defined as those reporting chronic cough at baseline, whilst incident chronic cough was defined as those participants who did not report chronic cough at baseline but did at follow-up 1.

Assessment of Mental Health Disorders

The Center for Epidemiologic Study Short Depression Scale (CESD-10) was administered to assess depressive symptoms at baseline and follow-up 1[20].The short version is a 10-item questionnaire that assesses feelings in the past one week of being easily bothered, difficulty concentrating, depression, the effort required to perform activities, fearfulness, restless sleep, loneliness, hopefulness about the future and happiness. Each item has four possible responses; 0–rarely or never, 1–some of the time, 2-occasionally, 3-all of the time. The positive questions on happiness and hopefulness about the future are reversed scored and added to the other eight questions to provide a total range of 0-30, where a score of ≥10 indicates current depressive symptoms[20, 21].

The Kessler Psychological Distress Scale (K-10) was administered to identify the more severe range of psychological distress as it has been shown to predict a diagnosis of serious mental illness[22, 23]. Questions are based on a four-week recall of feeling tired out, nervous, unable to calm down, hopeless, restless or fidgety, unable to sit still, depressed, everything is an effort, unable to be cheered up, worthless. These ten questions are rated on a scale of 1 (none of the time) to 5 (all of the time) with a total possible score of 50, where a score ≥22 is considered high or very high psychological distress[23].

Assessment of Personality Traits

The Big Five Personality traits of openness, conscientiousness, extraversion, agreeableness, and emotional stability was measured using the Ten-Item Personality Inventory (TIPI)[24]. This is a 10-item questionnaire with two paired items for each Big Five trait. Each item is scored on a 7-point Likert Scale where 1 is ‘disagree strongly’, 4 is ‘neither agree nor disagree’, and 7 is ‘agree strongly’. Five of the ten items are reversed scored, added with its matching pair in the relevant

Big Five trait, and averaged to provide a single score for each domain out of 7. A score of <4 was considered low in that specific personality trait.

Statistical Analysis

Descriptive statistics for demographics and covariates are presented as categorical variables for incidental chronic cough and reported as frequencies and percentages. Covariates which impact the incidence of chronic cough were included in the core model; age, sex, smoking status, BMI, educational level, province, self-reported general health, interview language (French vs. English) and physician-diagnosed respiratory airways diseases (asthma, chronic obstructive pulmonary disease)[25].

Baseline CESD-10, K-10 and individual personality trait scores was added to the final mutually adjusted incidence model for chronic cough. The same covariates were used for incidental depressive symptoms and psychological distress. Incident depressive symptoms was considered in those participants who scored <10 at baseline but ≥10 at follow-up 1, and likewise for K10<22 at baseline and ≥22 at follow-up 1.

We employed Proc GENMOD in SAS (version 9.4) with Poisson distribution and log link for calculating the multivariable Relative Risk (RR) and assess the association of all covariates with the outcomes of incidental cough, depressive symptoms, and psychological distress. The analyses were also stratified by language (English vs. French).

RESULTS

Study Population and Demographics

The comprehensive cohort included 30,097 participants at baseline. A total of 29,972 completed the chronic cough question at baseline. At follow-up 1, 22,547 participants who did not report chronic cough at baseline completed the chronic cough question. In this follow-up sample who did not report baseline cough, 2,506 participants (11.1%, mean age 64.4 (S.D. 10.0)) reported new-onset chronic cough during the approximate 3-year interval. The proportion of participants with incidental chronic was higher with increasing age, in males, current smokers, was lowest in Quebec compared with Ontario (8.0% vs. 13.6% respectively)

(Table 1). There was a greater proportion of participants who developed chronic cough and scored lower (<4) on the agreeableness, conscientiousness, and emotional stability personality traits at baseline. Similarly, there was also a greater proportion who demonstrated higher depressive symptoms (CESD≥10: 15.2%) and psychological distress (K-10≥22: 16.0%) at baseline.

The Effects of Mental Health Disorders and Personality Traits on the Incidence of Chronic Cough

After adjusting for all the variables in the core model, depressive symptoms [CESD≥10, RR 1.22 (1.03-1.44)] and psychological distress [K-10≥22, RR 1.20 (1.07-1.36)] at baseline were both independent predictors of a higher risk of incidental chronic cough 3-years later by 22% and 20% (Figure 1, and Table E1). None of the five personality traits independently demonstrated any increased risk on the incidence of chronic cough. The effect of psychological distress and depressive symptoms was similar for prevalent chronic cough (Figure E1).

The CESD-10 individual item scores were further explored by sub-classifying into lack of positive affect (2 questions, maximum 6 points) and depressive affect scores (8 questions, maximum 16 points) with increasing cut-off values. A cut-off score of 1 for lack of positive affect was associated with a 12% increase in chronic cough [RR 1.12, (1.02-1.23)] whilst a cut-off of 8 for depressive affect scores demonstrated a 29% increase [1.29, (1.15-1.45) (Table E2).

The Effects of Chronic Cough on Depressive Symptoms

Compared with participants without chronic cough, those who had chronic cough at baseline, at follow-up-1 or both, had a greater proportion of participants with new depressive symptoms at follow-up 1 (CESD≥10, Table 2). A greater proportion of participants who developed depressive symptoms scored lower (<4) on the agreeableness, conscientiousness, emotional stability, and openness to new experiences personality traits at baseline. In addition, there was also a greater proportion who demonstrated higher psychological distress scores (K-10≥22:35.0%) at baseline.

After adjusting for all the variables in the core model, chronic cough at baseline, follow-up-1, or both were all independently associated with an estimated 27% and 22% increase in the risk of

incident depressive symptoms [RR 1.27 (1.06-1.52), RR 1.22 (1.04-1.43), RR 1.27 (1.07-1.50) respectively, Figure 2]. This was independent of the increased risk associated with a higher psychological distress score [K-10≥22, RR 3.13 (2.67-3.66)] at baseline, and lower scores (<4) on extraversion, conscientiousness, emotional stability, and openness to new experiences personality traits.

The Effects of Chronic Cough on Psychological Distress

Compared with participants without chronic cough, those who had chronic cough at baseline, at follow-up 1 or both, had a 1.5-2.5% greater proportion of participants with new onset symptoms of psychological distress at follow-up 1 (K-10≥2, Table 2). There was also a greater proportion of participants who developed symptoms of psychological distress and scored lower (<4) on the conscientiousness and emotional stability personality traits at baseline. In addition, there was also a greater proportion who demonstrated higher depressive symptoms scores (CESD≥10:13.0%) at baseline.

After adjusting for all the variables in the core model, chronic cough at baseline and follow-up 1, were both independently associated with an estimated 36% and 54% increase in the risk of incident psychological distress [RR 1.36 (1.06-1.76), RR 1.54 (1.25-1.90), respectively, Figure 3]. This was independent of the increased risk associated with a higher depressive symptom score [CESD≥10, RR 3.74 (3.20-4.38)] at baseline, and lower scores (<4) on conscientiousness, and emotional stability personality traits.

The Effects of English and French language on the Incidence of Chronic Cough

As the incidence of chronic cough was lowest in Quebec and highest in Ontario, the language the interview was conducted in was included in the core model for incidence of chronic cough. Compared to French speaking participants, those who were English speaking had a trend of 27% higher risk of incidental chronic cough [RR 1.27 (0.99-1.64), Table E1], independent of all other covariates in the model. Hence, the relative risk of all covariates including mental health disorders and personality traits for incident chronic cough were stratified based on English and French speaking (Table E1). Personality traits was not associated with an increased risk in either English and French speakers, however, only in English speakers was high depressive symptoms

[RR 1.30 (1.14-1.48)] and high psychological distress [RR 1.21 (1.00-1.47)] associated with an increased risk of developing chronic cough.

DISCUSSION

Healthcare professionals investigating and managing patients with refractory or unexplained chronic cough often question whether excessive coughing is due to an expression of an underlying mental health disorder or personality trait. The results of this study provide novel insights which suggest that there is a bidirectional relationship which is indirectly influenced by personality traits and also varies between English and French speakers. Depressive symptoms and psychological distress are independently associated with the development of chronic cough, but chronic cough also independently increases the risk of developing depressive symptoms and psychological distress. Personality traits do not directly influence the development of chronic cough, but may do so indirectly via their contribution to the development of depressive symptoms and psychological distress (Figure 4). Furthermore, the association of mental health disorders on the development of chronic cough was only found in English speakers but not in French speakers.

Understanding the mechanisms by which mental health disorders might influence coughing requires an appreciation of the neurophysiology of cough. Coughing is both under voluntary and involuntary control, but is widely recognised that the cough reflex is the archetypal airway defensive reflex which can be initiated by mechanical, chemical and thermal stimulation. Chronic cough is currently thought to be due to dysregulation of the peripheral and/or central nervous system[26, 27] and is often described as cough hypersensitivity syndrome[28] due to either; i) increased stimulation of the peripheral nerve terminals, ii) neuronal hyperexcitability of the afferent vagal nerve, brainstem and higher cortical projections[29-31] and/or iii) impaired central inhibitory control[31-33]. Recent studies suggest patients with chronic cough demonstrate a lack of voluntary cough suppression[34] and impairment in the descending inhibitory control neurons[32, 34]. Impairment in these inhibitory neurons have also been demonstrated in depression[35], but also irritable bowel syndrome[36], fibromyalgia[37], and chronic pain[38], which are also associated with chronic cough[15, 39, 40]. The neurotransmitters responsible for these inhibitory neurons to be functional are currently

thought to be endogenous opioids, endorphins, serotonin, norepinephrine, and dopamine[41-44]. Current guidelines suggest off-label use of low-dose opioids, pregabalin, gabapentin and amitriptyline for chronic cough, which would increase the levels of such neurotransmitters[45-47]. This is further supported by two studies demonstrating improvement in depressive symptoms after treatment of chronic cough[48, 49]. Therefore, depression and chronic cough have a shared neurobiology.

The idea that chronic cough increases depressive symptoms and psychological distress is conceptually more intuitive. The median cough frequency in patients with refractory or unexplained chronic cough recruited into clinical trials over a 24-hr period is approximately 20 coughs/hr, with more coughing during the daytime than night-time [50-54]. This high number of coughs results in impairment in physical, social, and psychological quality of life, including fatigue, exhaustion, chest pains, hernia, rib fractures, sleep disturbance, urinary incontinence in females and syncope in males[55-57]. Chronic cough significant impacts work-life with recent evidence showing increased time missed from work, absenteeism, and increased sick days [58]. These provide reasons why patients with chronic cough might develop depressive symptoms and psychological distress. Some of these symptoms are captured in cough quality of life questionnaires such as the Leicester Cough Questionnaire (LCQ) and Cough specific Quality of Life Questionnaire (CQLQ) used in clinical trials and recommended in clinical practice[59, 60].

Personality traits do not directly and independently influence chronic cough, but the fact that personality traits independently predict depressive symptoms and psychological distress is well described, and provides some internal validity of the measurement tools used in the CLSA[61]. The nature of the relationship between personality and depression has been highly debated with up to seven classical models described, divided into three groups. The first three (common cause, continuum/spectrum, precursor) suggest personality and depression are distinct but they arise from the same or similar etiological processes. The fourth and fifth (predisposition and patho-plasticity) imply personality directly affects the onset or maintenance of depression. The sixth and seventh models (concomitant and consequences) reverse the direction of causality by suggesting depression has a causal influence on personality. These concepts consider traits to be stable but other evidence suggests personality traits are dynamic and

amenable to change[62]. Genetic factors do contribute to long-term stability, but life stressors and changes in relationships and work/social roles can also influence a change in personality traits[63]. In contrast, pathological trait trajectories can also be reversed by positive life experiences[64]. This is important because if depressive symptoms could lead to chronic cough, it would be important to further evaluate the mediating processes and potentially modifiable risk factors between personality traits and depression.

It was recognised as early as 1975 that bilingual speakers responded to the CES-D10 questionnaire differently because the interviewee and interviewer may understand colloquial expressions differently [65]. Similarly, studies have shown inconsistent evidence of validity and reliability in the K-10 psychological distress scale amongst culturally diverse groups. In the CLSA, we have previously reported an overall lower incidence of chronic cough in French speakers compared with English speakers (under-review). This study also suggests that higher depression and psychological distress in French speakers does not significantly increase the risk of chronic cough. This could be due to lower numbers of French speaking participants with chronic cough, such that depressive symptoms and psychological distress have insufficient power to detect differences, or that language represents cultural norms, expectations, values, willingness to disclose information which can differ across English and French speaking cultures.

There are limitations to this study. First, depressive symptoms and psychological distress levels were assessed using questionnaires. Although these are validated for use in epidemiological studies, high scores may not always result in a clinical diagnosis of depression. Second, we currently do not have available complete analysable data on anti-depressant medication use, which could help ascertain the clinical validity of the high depressive symptoms scores. Third, the CESD-10 and K-10 have questions which relate to anxiety, but we have not analysed the independent effect of every item on the questionnaire as this was not the intended use of the questionnaires and cut-points for individual items are unknown. Fourth, the recall time period was different for each of the questionnaires – chronic cough was 12 months, depressive symptoms over the previous one week, and psychological distress over the previous four weeks. These different time intervals could result in an inadequate representation of patient symptoms over a three year time period between baseline and follow-up 1 where scores may

have changed over time, due to personal, social, and work stressors. Such factors are unaccounted for. We decided to use a baseline exposure model to investigate chronic cough. We have not analysed the change in mental health scores between baseline and follow-up 1. It is possible that someone improves in their depressive symptoms or psychological distress scores after baseline and then develops chronic cough 3 years later. Fifth, this is an epidemiological study from the general community and not from a specialist cough clinic, hence these findings may not be generalizable to patients attending a chronic cough clinic. Furthermore, detailed information about the cough severity, intensity, and therapeutic interventions were not available. The limitation of studying the effects of mental health disorder in a cough clinic, is that chronic cough has already occurred, and retrospectively assessing the effect of mental health and personality is extremely challenging. Only the impact of chronic cough on mental health over time can be assessed.

Conclusions

Personality traits of low emotional stability, conscientiousness, extraversion, and openness to experiences increase the risk of mental health disorders and psychological distress, which independently increase the risk of developing chronic cough. However, chronic cough also increases the risk of developing depressive symptoms and psychological distress.

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Guarantor Statement: P.R. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Data Availability Statement. Data are available from the Canadian Longitudinal Study on Aging (www.clsa-elcv.ca) for researchers who meet the criteria for access to de-identified CLSA data.

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Table 1: Descriptive Data on Incident Chronic Cough at Follow-Up 1 (n=22547).

		Incident chronic cough	
		Yes	No
		N (%)	N (%)
TOTAL		2506 (11.1)	20041 (90.9)
Age			
45-54		498 (8.2)	5605 (91.8)
55-64		810 (10.7)	6756 (89.3)
65-74		698 (12.9)	4705 (87.1)
75+		500 (14.4)	2975 (85.6)
Sex			
Male		1329 (12.2)	9571 (87.8)
Female		1177 (10.1)	10470 (89.9)
Smoking			
Never		1163 (9.4)	11227 (90.6)
Previous		1053 (12.1)	7638 (87.9)
Current		281 (21.0)	1056 (79.0)
Provinces			
Newfoundland & Labrador		186 (11.3)	1463 (88.7)
Nova Scotia		183 (9.4)	1767 (90.6)
Quebec		389 (8.0)	4466 (92.0)
Ontario		665 (13.6)	4234 (86.4)
Manitoba		275 (12.1)	1995 (87.9)
Alberta		278 (12.4)	1969 (87.6)
British Columbia		530 (11.3)	4147 (88.7)
Personality Trait Scores			
extraversion	low (<4)	857 (11.0)	6915 (89.0)
	high (≥4)	1585 (11.1)	12649 (88.9)
agreeableness	low (<4)	106 (13.3)	693 (86.7)
	high (≥4)	2339 (11.0)	18937 (89.0)
conscientiousness	low (<4)	108 (16.4)	551 (83.6)
	high (≥4)	2343 (10.9)	19111 (89.1)
emotional stability	low (<4)	236 (13.9)	1462 (86.1)
	high (≥4)	2216 (10.9)	18205 (89.1)
openness to experiences	low (<4)	239 (11.0)	1927 (89.0)
	high (≥4)	2184 (11.1)	17571 (88.9)
Depressive Symptoms Score			
CESD<10		2020 (10.4)	17330 (89.6)
CESD≥10		479 (15.2)	2671 (84.8)
Psychological Distress Score			
K-10<22		2208 (10.7)	18368 (89.3)
K-10≥22		232 (16.0)	1222 (84.0)

Table 2: Descriptive Data on Incident Depressive Symptoms and Psychological Distress at Follow-Up 1.

		Incident Depressive Symptoms (CESD≥10)		Incident Psychological Distress (K-10≥22)	
		Yes	No	Yes	No
		N (%)	N (%)	N (%)	N (%)
Personality Trait Score					
extraversion	low (<4)	713 (9.7)	6645 (90.3)	332 (3.9)	8186 (96.1)
	high (≥4)	1013 (7.0)	13395 (93.0)	533 (3.3)	15576 (96.7)
agreeableness	low (<4)	81 (11.0)	655 (89.0)	43 (4.9)	826 (95.1)
	high (≥4)	1647 (7.8)	19427 (92.2)	820 (3.4)	22997 (96.6)
conscientiousness	low (<4)	94 (19.4)	391 (80.6)	55 (9.3)	554 (90.7)
	high (≥4)	1643 (7.7)	19712 (92.3)	814 (3.4)	23298 (96.6)
emotional stability	low (<4)	258 (23.1)	859 (76.9)	183 (14.0)	1127 (86.0)
	high (≥4)	1478 (7.1)	19263 (92.9)	685 (2.9)	22731 (97.1)
openness to experiences	low (<4)	227 (11.3)	1777 (88.7)	101 (4.3)	2238 (95.7)
	high (≥4)	1495 (7.6)	18171 (92.4)	758 (3.4)	21423 (96.6)
Depressive Symptoms Score					
CESD<10				502 (2.3)	21446 (97.7)
CESD≥10				370 (13.0)	2471 (87.0)
Psychological Distress Score					
K-10<22		1473 (7.0)	19579 (93.0)		
K-10≥22		254 (35.0)	471 (65.0)		
Chronic cough Status					
No Chronic Cough		1227 (7.2)	15839 (92.8)	541 (3.0)	17677 (97.0)
Cough at Baseline only		149 (10.2)	1318 (89.8)	74 (4.5)	1564 (95.5)
Cough at FU-1 only		198 (10.0)	1773 (90.0)	120 (5.5)	2067 (94.5)
Cough at baseline and FU-1		195 (11.7)	1470 (88.3)	88 (4.7)	1785 (95.3)

Figure 1: The Independent Effects of Personality Traits, Depressive Symptoms and Psychological Distress on the Incidence of Chronic Cough. Complete model is mutually adjusted for all variables including age, sex, smoking status, BMI, educational level, province, self-reported general health, interview language, and physician-diagnosed respiratory airways diseases (asthma, chronic obstructive pulmonary disease).

Figure 1

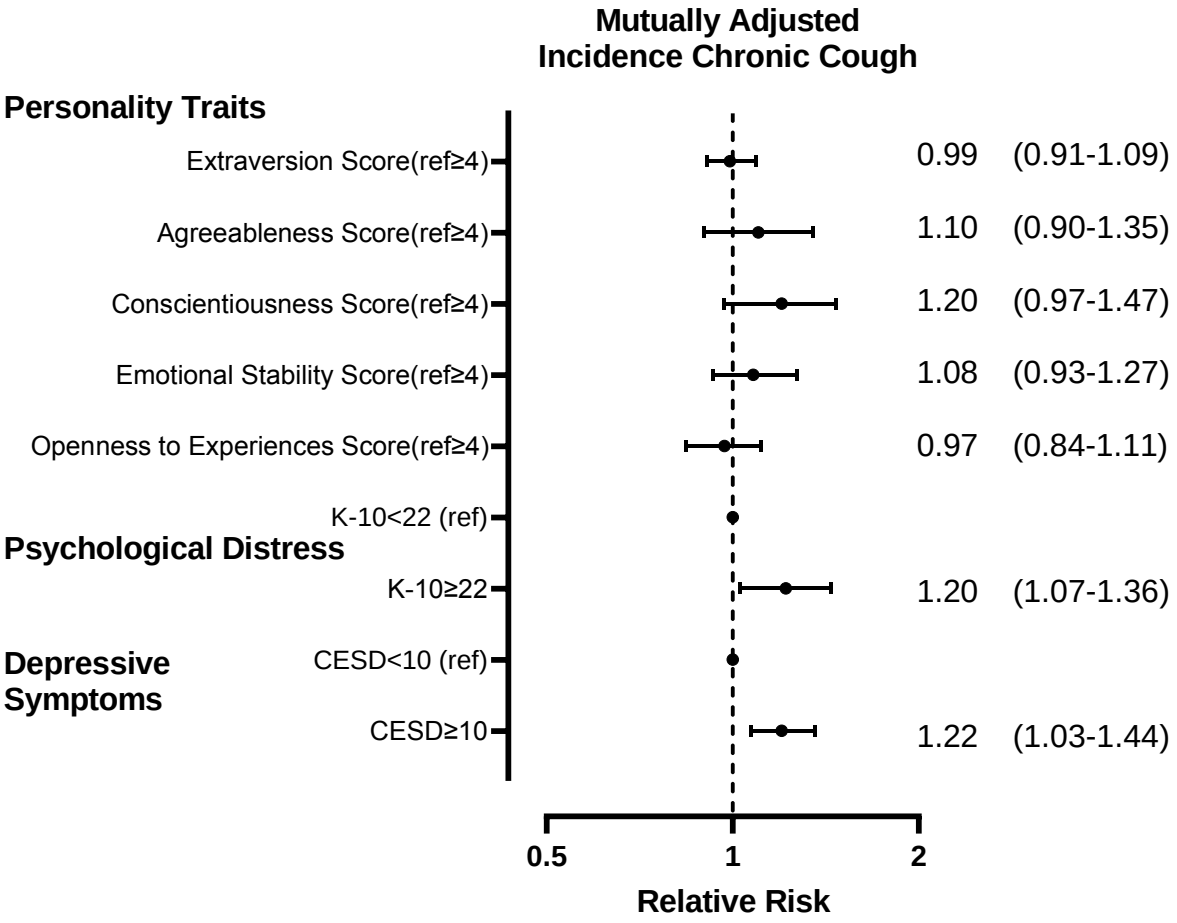

Figure 2: The Independent Effects of Chronic Cough, Personality Traits, and Psychological Distress on the Incidence of Depressive Symptoms. Complete model is mutually adjusted for all variables including age, sex, smoking status, BMI, educational level, province, self-reported general health, interview language, and physician-diagnosed respiratory airways diseases (asthma, chronic obstructive pulmonary disease)

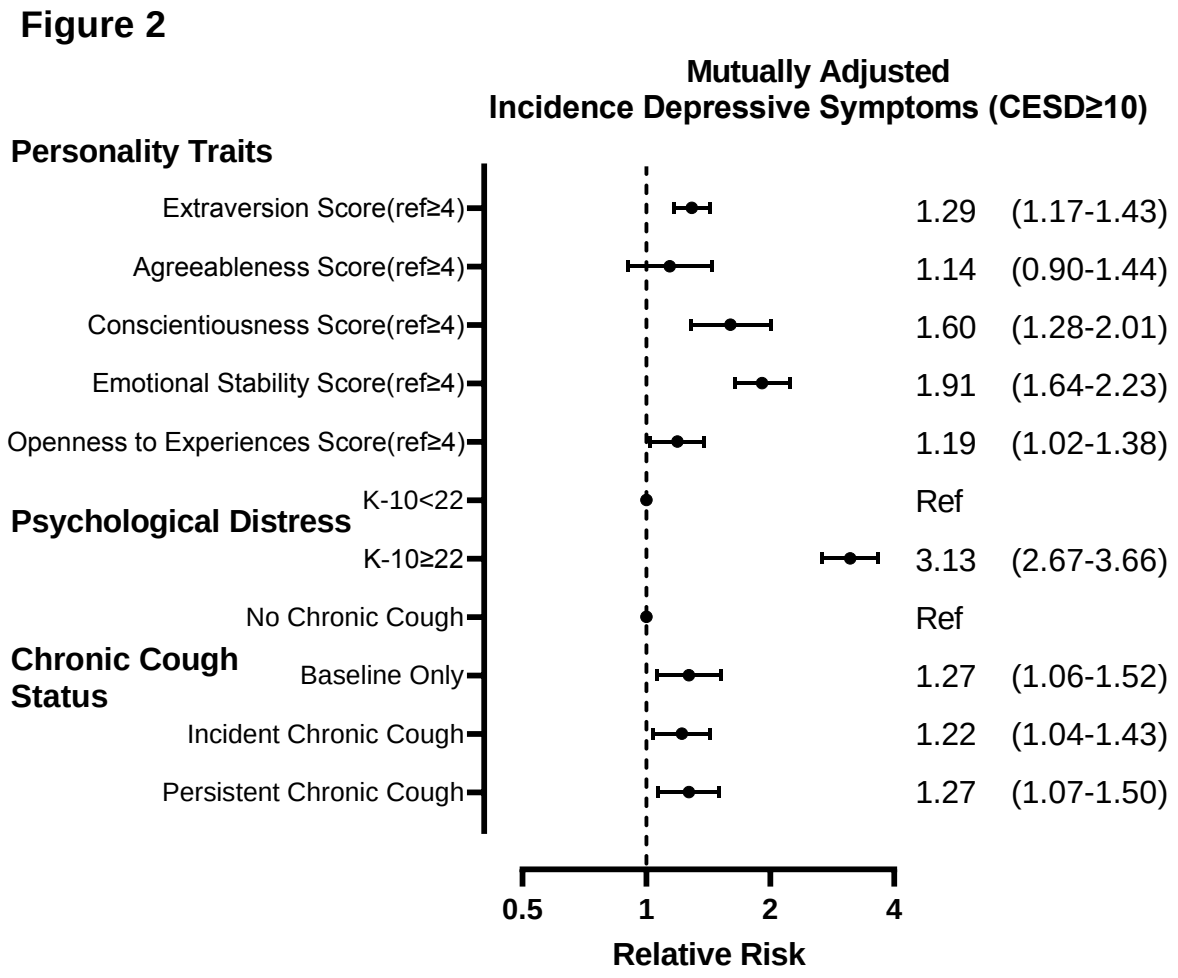

Figure 3: The Independent Effects of Chronic Cough, Personality Traits, and Depressive Symptoms on the Incidence of Psychological Distress. Complete model is mutually adjusted for all variables including: age, sex, smoking status, BMI, educational level, province, self-reported general health, interview language, and physician-diagnosed respiratory airways diseases (asthma, chronic obstructive pulmonary disease)

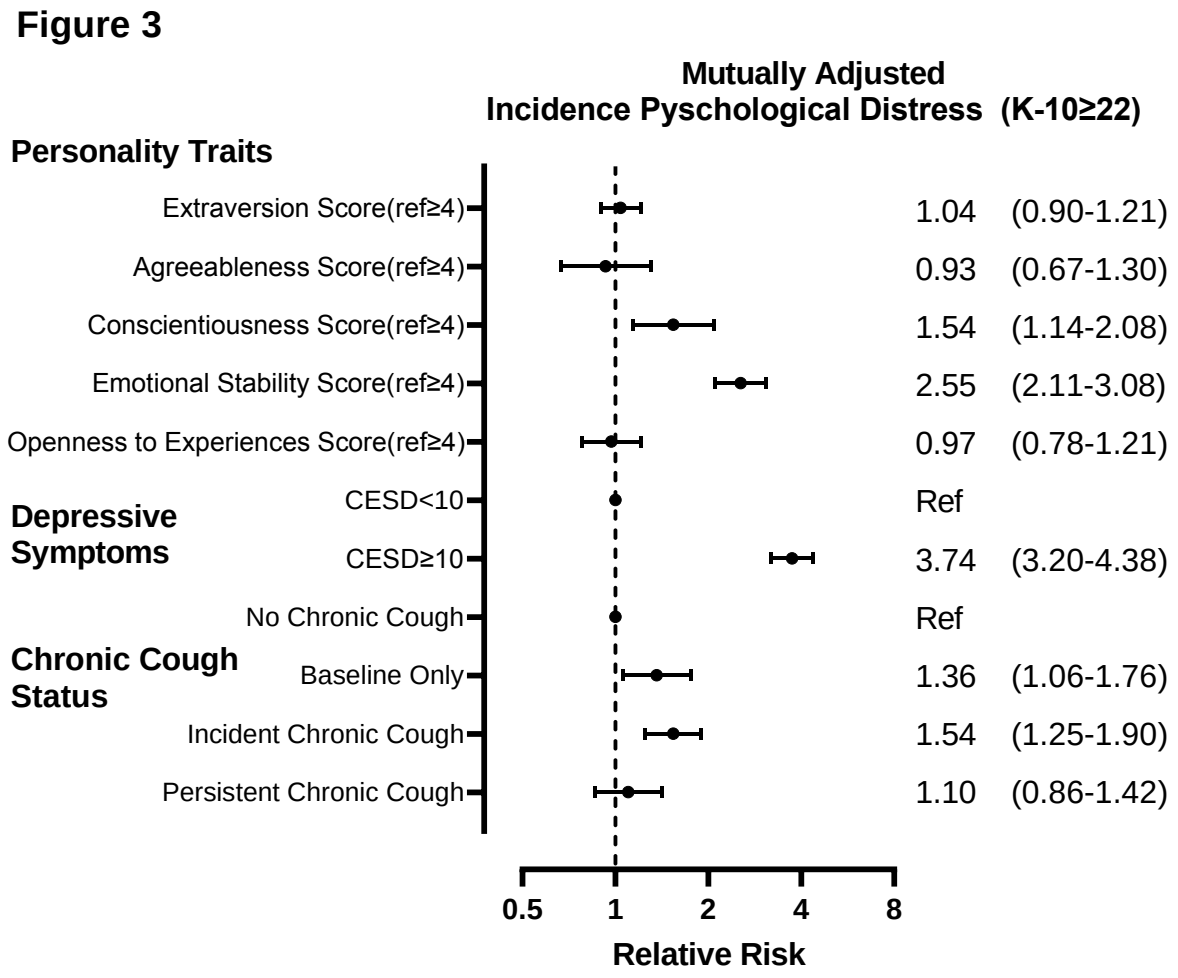

Figure 4: Summary of Findings

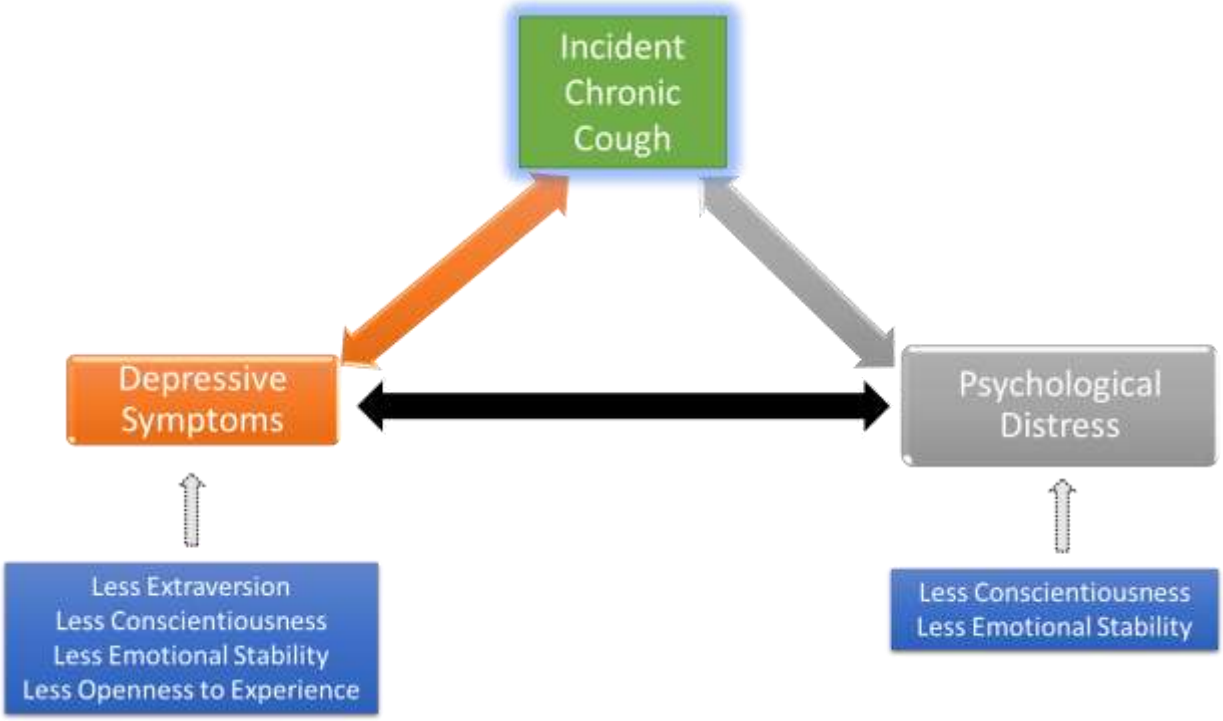

Table E1: Mutually Adjusted Incidence of Chronic Cough in all participants and stratified by English and French Speaking.

	ALL Participants			ENGLISH			FRENCH		
	Mutually adjusted model			Mutually adjusted model			Mutually adjusted model		
	RR	95% CI		RR	95% CI		RR	95% CI	
Time in years between baseline & FU1	1.10	0.94	1.28	1.11	0.94	1.32	1.04	0.71	1.53
Age Groups									
45-54	Ref			Ref			Ref		
55-64	1.29	1.15	1.45	1.28	1.12	1.45	1.34	1.01	1.78
65-74	1.64	1.45	1.85	1.69	1.48	1.93	1.37	1.00	1.88
75+	1.89	1.66	2.17	1.98	1.72	2.30	1.42	0.98	2.05
Sex									
Male	1.23	1.13	1.34	1.25	1.14	1.37	1.11	0.89	1.38
Female									
Highest education level (4 levels)									
< Secondary	Ref			Ref			Ref		
Secondary	0.91	0.74	1.12	0.89	0.70	1.13	0.98	0.64	1.50
Some post	0.83	0.67	1.04	0.82	0.64	1.05	0.93	0.50	1.75
Post secondary	0.82	0.69	0.98	0.82	0.67	1.00	0.83	0.59	1.17
Body mass index (WHO categories)									
Under wt.	0.93	0.54	1.61	0.82	0.42	1.58	1.25	0.45	3.48
Normal	Ref			Ref			Ref		
Overweight	1.23	1.11	1.37	1.21	1.08	1.36	1.34	1.03	1.76
Obese	1.44	1.28	1.61	1.43	1.26	1.61	1.50	1.13	2.00
Smoker									
Non-smoker	Ref			Ref			Ref		
Previous	1.14	1.05	1.25	1.17	1.07	1.29	0.99	0.78	1.26
Current	2.30	1.99	2.64	2.22	1.89	2.61	2.38	1.76	3.22
Province of residence									
Newfoundland & Labrador	0.83	0.70	0.99	0.82	0.69	0.98			
Nova Scotia	0.71	0.59	0.84	0.70	0.59	0.83			
Quebec	0.71	0.55	0.91	0.61	0.43	0.86	0.94	0.60	1.48
Ontario	Ref			Ref			Ref		
Manitoba	0.89	0.76	1.04	0.88	0.76	1.03			
Alberta	0.90	0.77	1.05	0.89	0.76	1.05			
British Columbia	0.88	0.78	0.99	0.87	0.77	0.98			
Perceived General Health									
Poor/fair	1.28	1.11	1.47	1.26	1.08	1.47	1.35	0.96	1.91
good/very good/Excellent	Ref			Ref			Ref		
Interview Language									

English	1.27	0.99	1.64						
French	Ref								
Chronic Respiratory Diseases									
No Asthma or COPD	Ref			Ref			Ref		
Asthma only	1.41	1.25	1.59	1.32	1.16	1.51	2.03	1.52	2.71
COPD only	1.52	1.24	1.85	1.33	1.06	1.66	2.90	1.86	4.52
Both Asthma and COPD	1.70	1.31	2.21	1.51	1.11	2.06	2.74	1.65	4.56
Personality trait Scores									
Extraversion Score(ref>=4)	0.99	0.91	1.09	1.00	0.91	1.10	0.99	0.79	1.23
Agreeableness Score(ref>=4)	1.10	0.90	1.35	1.17	0.94	1.44	0.68	0.33	1.38
Conscientiousness Score(ref>=4)	1.20	0.97	1.47	1.22	0.98	1.52	1.01	0.53	1.90
Emotional Stability Score(ref>=4)	1.08	0.93	1.27	1.06	0.88	1.27	1.15	0.83	1.60
Openness to Experiences Score(ref>=4)	0.97	0.84	1.11	0.97	0.83	1.13	0.94	0.69	1.28
Depressive Symptoms									
CESD<10	Ref			Ref			Ref		
CESD≥10	1.20	1.07	1.36	1.30	1.14	1.48	0.78	0.57	1.08
Psychological Distress Scale									
K-10<22	Ref			Ref			Ref		
K-10≥22	1.22	1.03	1.44	1.21	1.00	1.47	1.26	0.90	1.77

Table E2: Incidence of Chronic Cough based on lack of positive affect and depressive symptoms with increasing scores. Mutually Adjusted Model.

	Mutually adjusted model			Mutually adjusted model			Mutually adjusted model		
	RR	95% CI		RR	95% CI		RR	95% CI	
Time in years between baseline & FU1	1.11	0.95	1.29	1.11	0.95	1.30	1.12	0.96	1.30
Personality trait									
Extraversion Score(ref>=4)	0.99	0.90	1.08	0.99	0.91	1.09	1.00	0.92	1.10
Agreeableness Score(ref>=4)	1.10	0.90	1.35	1.10	0.90	1.35	1.11	0.90	1.35
Conscientiousness Score(ref>=4)	1.18	0.96	1.45	1.19	0.96	1.46	1.20	0.97	1.48
Emotional Stability Score(ref>=4)	1.06	0.91	1.25	1.06	0.91	1.25	1.09	0.93	1.27
Openness to Experiences Score(ref>=4)	0.96	0.84	1.11	0.97	0.84	1.12	0.97	0.84	1.12
Lack of Positive affect Scores	Cut-off: 1			Cut-off: 2			Cut-off: 3		
No	Ref								
Yes	1.12	1.02	1.23	1.05	0.95	1.16	1.09	0.96	1.23
Depressive affect Score	Cut-off: 6			Cut-off: 8			Cut-off: 10		
No	Ref								
Yes	1.19	1.08	1.32	1.29	1.15	1.45	1.14	0.98	1.32
Psychological Distress Score									
<22	Ref								
>=22	1.20	1.02	1.41	1.17	0.99	1.38	1.23	1.04	1.45

Figure E1: The Independent Effects of Personality Traits, Depressive Symptoms and Psychological Distress on the Prevalence of Chronic Cough. Complete model is mutually adjusted for all variables including age, sex, smoking status, BMI, province, self-reported general health, interview language, and physician-diagnosed respiratory airways diseases (asthma, chronic obstructive pulmonary disease).

Figure E1