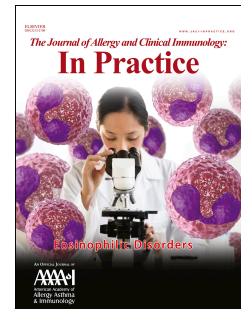


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Prevalence and Burden of Chronic Cough in the United States

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Glenmark, GossamerBio, Merck & Co., Inc., Mylan, Novartis, Principia, Regeneron/SanofiGenzyme and has served as a speaker for ALK, GlaxoSmithKline, Glenmark, Merck & Co., Inc., Myland, Optinose, Regeneron/SanofiGenzyme. Robert S Zeiger reports personal fees from Merck and Co., Inc., during the conduct of this study; additional personal fees from American Academy of Allergy, Asthma, and Immunology (AAAAI) as Deputy Editor of JACI: In Practice, American College of Allergy, Asthma and Immunology (manuscript), AstraZeneca, DBV Technologies, Genentech, Novartis, GlaxoSmithKline, Regeneron Pharmaceuticals, and UpTo-Date outside the submitted work; and grants to Kaiser Permanente Southern California (KPSC) from National Institutes of Health (NIH), ALK Pharma, Genentech, GlaxoSmithKline, MedImmune/AstraZeneca, and TEVA. Peter Dicpinigaitis has served as a consultant for Merck & Co., Inc., Bellus, Bayer, and Shionogi. Jonathan A Bernstein serves as a principal investigator and consultant for Merck & Co., Inc. and has served as a principal investigator, consultant, and speaker for AstraZeneca, Sanofi Regeneron, Novartis, Genetech, and has served as a speaker for GlaxoSmithKline and Optinose. Dr. Bernstein currently serves as the Editor-in-Chief of the Journal of Asthma. John J Oppenheimer has performed clinical research with GlaxoSmithKline, the NIH, and Regeneron and has served as a consultant for AstraZeneca, GlaxoSmithKline Novartis, Sanofi, Regeneron, and Abbvie. Dr. Oppenheimer is an associate editor of Annals of Allergy Asthma and Immunology and AllergyWatch and serves as a section editor of Current Allergy and Asthma Report. Nate A Way is an employee of Kantar LLC. Vicky W Li is an employee of Kantar LLC. Michael J Doane was an employee of Kantar LLC during the development and conduct of this study. Robert Boggs, Eduardo Urdaneta, Jessica P Weaver, Jonathan Schelfhout, and Eileen Fonseca are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and shareholders in Merck & Co., Inc., Kenilworth, NJ, USA.

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ABSTRACT

Background: Chronic cough is a common complaint but there is little population-based data on its burden in the United States.

Objective: To determine the prevalence of chronic cough and its burden on individuals and the healthcare system.

Methods: This was a survey of respondents who completed the 2018 National Health and Wellness Survey (NHWS) and questions about sleep and healthcare resource use. Chronic cough was defined as having a daily cough for ≥ 8 weeks. Respondents without chronic cough were selected through propensity score matching. Chronic cough prevalence was estimated using post-stratification sampling weights calculated using US Census data and post-data Horvitz-Thompson sampling weights to adjust for sampling bias.

Results: Of 74,977 NHWS respondents, 3,654 had experienced chronic cough in the previous 12 months, for a weighted prevalence of 5.0%. Respondents with chronic cough were older and more predominantly female than respondents without chronic cough (both $P < .001$). Compared with matched respondents without chronic cough, those with chronic cough had lower mean scores on the SF-36v2 physical ($P < .001$) and mental ($P < .001$) component summary scores. More respondents with chronic cough than matched controls experienced severe anxiety and severe depression in the past two weeks, work productivity impairment, impaired sleep quality and daytime sleepiness, as well as more emergency department visits and hospitalizations in the past 6 months ($P < .001$ for all comparisons).

75 **Conclusion:** The burden of chronic cough manifests itself as reduced health-related
76 quality of life, increased anxiety and depression, impaired sleep and work productivity,
77 and greater healthcare utilization.

HIGHLIGHTS

What is already known about this topic?

- Chronic cough is a common complaint in the United States.

What does this article add to our knowledge?

- The estimated prevalence of self-reported chronic cough among the US adult population is 5%.
- Compared with matched controls without chronic cough, respondents with chronic cough more often reported lower health-related quality of life.

How does this study impact current management guidelines?

- These results highlight the burden of chronic cough in the United States.

Key words. Cough/ Chronic Cough/ Chronic Disease/ Prevalence/ Quality of Life

89 **ABBREVIATIONS**

90 ED, emergency department

91 EQ-5D-5L, EuroQol 5-Dimension Health Questionnaire

92 GAD-7, General Anxiety Disorder 7-item scale

93 NHWS, National Health and Wellness Survey

94 PHQ-9, Patient Health Questionnaire 9-item scale

95 SF-36v2, Medical Outcomes Study 36-item Short Form Survey v2

96 WPAI, Work Productivity and Activity Impairment

INTRODUCTION

Coughing is a critical reflex to help clear the airways and prevent aspiration. However, when cough is no longer controlled and becomes persistent, it impacts quality of life. The importance of cough as a global clinical problem led to societies publishing guidelines on the diagnosis and management of cough [1-3]. These clinical guidelines categorize cough based on its duration, with chronic cough being daily or intermittent but lasting more than 8 weeks (in adults). In non-smokers, not taking an ACE-inhibitor, chronic cough is most commonly associated with certain comorbidities, such as upper airway cough syndrome (i.e., post-nasal drip), asthma, and gastroesophageal reflux disease [4]. However, some patients may continue to cough despite comprehensive investigation and treatment, in cases where no cause can be determined (termed unexplained chronic cough) or when cough persists despite treatment (refractory chronic cough) [5]. Hypersensitivity of airway sensory nerves, termed cough hypersensitivity, is hypothesized to contribute to the various categories of chronic cough [6].

In Finnish and UK cohort studies of the long-term prognosis of chronic cough, 46-86% of patients still suffered from the disorder 5-to-7 years after an initial interview [7, 8].

Demographic data from cough clinics in multiple countries indicate that patients are preponderantly female (two-thirds) with a mean age of 55 years [9]. Population-based surveys conducted in European countries support these demographics and suggest prevalence rates ranging from 4% to 12% [10-15]. In the United States there is little population-based data, and most information is from specialty cough clinics [16-22].

The primary objective of the present study was to provide unweighted and weighted prevalence estimates for chronic cough among adults in the United States, based on a population-based survey. The secondary objectives were to describe the

- 121 sociodemographic characteristics and health status of adults with chronic cough and to
122 measure its burden on patients.

METHODS

Study design

The National Health and Wellness Survey (NHWS) is a self-administered, internet-based questionnaire conducted annually in the United States and in other countries in a representative sample of each country's adult population. This survey collects information about demographics, health and wellness history, and healthcare use, and incorporates validated patient-reported health outcome instruments measuring quality of life, anxiety, depression, and work productivity and activity impairment. The 2018 NHWS also included questions about sleep impairment. Data from the US NHWS were collected in a survey between February to July 2018. A cross-sectional design was used to estimate disease prevalence and a case-control design for comparisons to describe respondents with chronic cough.

The protocol and questionnaire for the NHWS and the cough questionnaire were granted exemption from review by the Pearl Institutional Review Board. All respondents were informed of study details and provided their consent to participate. Each respondent was assigned a unique, anonymous code, and no identifiable personal information was collected.

Study sample

To be included in the US NHWS, respondents must be ≥ 18 years, able to read and write in English, state their age, gender, race/ethnicity, and provide informed consent.

Potential respondents were recruited through an existing, general-purpose (i.e., not healthcare-specific) web-based survey panel. All panelists explicitly agreed to be a panel member, register with the panel through a unique e-mail address, and complete an in-depth demographic registration profile. The 2018 US NHWS utilized a targeted quota

sampling of strata according to age, gender, and race/ethnicity, to ensure a demographic composition of the US adult population. Respondents were shown a list of conditions and asked, 'Which of the conditions have you experienced in the past twelve months?' Respondents with chronic cough were those answering 'yes' to the condition, 'chronic cough (daily, 8 weeks or longer)'. Respondents without chronic cough were those answering 'no' to the condition, 'chronic cough (daily, 8 weeks or longer)'. The wording was selected to align with the definition of chronic cough used in management guidelines, e.g., based on elapsed duration and a representation of frequency that indicated a persistent, on-going condition.

Study measures

Health-related quality of life was measured using two validated instruments, the Medical Outcomes Study 36-item Short Form Survey v2 (SF-36v2; Quality Metric, Lincoln, RI) and the EuroQol 5-Dimension Health Questionnaire (EQ-5D-5L™; EuroQol Research Foundation) [23, 24]. SF-36v2 physical and mental health component summary scores were calculated with the mean score set at 50 and the SD at 10; higher scores represent better health. The SF-6D health utility score, also derived from the SF-36v2, is a preference-based health utility index, with 0 representing death and 1 perfect health. The EQ-5D composite summary index was reported, with 1 reflecting the best possible health state and 0 representing death. Anxiety was measured with the General Anxiety Disorder 7-item scale (GAD-7), which measures the severity of symptoms of generalized anxiety over the prior 2 weeks [25]. Respondents were asked to rate the frequency of anxiety symptoms on a Likert scale ranging from 0 (not at all) to 3 (nearly every day), with scores ranging from 0 to 21. Severe anxiety symptoms are indicated by a score of 15-21. Depression was assessed with the Patient Health Questionnaire 9-item scale (PHQ-9) [26]. Respondents were asked to rate the frequency of symptoms of depression

in the last 2 weeks on a scale of 0 (not at all) to 3 (nearly every day). Summary scores range from 0 to 27, with values ≥ 20 representing severe depression.

The Work Productivity and Activity Impairment (WPAI) questionnaire is a 6-item instrument that measures the impact of a health state on work productivity over the prior 7 days [27]. It consists of 4 measures of impairment because of one's health: absenteeism (the percentage of work time missed), presenteeism (the percentage of hours of impaired performance while at work), total work productivity loss (a combination of absenteeism and presenteeism), and activity impairment (the percentage of impairment in daily activities outside of work) [27]. Only respondents who reported being employed provided data for work impairment. All respondents provided data for activity impairment.

To measure difficulties with sleep, respondents were asked (yes/no) to consider a list of sleep problems or symptoms and to indicate which they regularly experienced: difficulty falling asleep, waking during the night and not being able to get back to sleep, waking up several times during the night, waking up too early (i.e., before the alarm clock), sleep apnea (i.e., temporary absence of breathing), poor quality of sleep, daytime sleepiness, and/or difficulty staying awake.

Healthcare resource use was reported as all-cause visits to healthcare providers in the past 6 months. Visits ("yes/no" and number of visits) to general/family and specialty practitioners, the Emergency Department (ED), and hospitalizations were captured.

Data analysis

Outcomes are reported either as N (%) or mean (SD). Comparisons between earlier iterations of the NHWS and other established sources have been published previously [28-30]. To substantiate the representativeness of the 2018 NHWS sample, we

compared unweighted and weighted NHWS data to recent US government sources
(Table E1 in Online Repository).

Chronic cough prevalence was calculated as a proportion of the 74,977 2018 US NHWS
respondents and in demographic subgroups (male, female, age categories 18-49, 50-64,
and ≥ 65 years), and by smoking status (never smoked, or current/former smoker).

Smoking was defined as use of cigarettes or other tobacco products. Weighted
estimates were projected to the 2018 US population using post-stratification sampling
weights calculated using the US Census' International Data Base. Post-data collection
Horvitz-Thompson sampling weights were calculated to adjust for sampling bias,
specifically weights were assigned based on age, gender, race, and education.

NHWS respondents with chronic cough were matched 1:3 to respondents without
chronic cough, based on propensity score. Propensity scores were calculated using
logistic regression modeling, controlling for age (as a continuous variable), gender, and
the NHWS Charlson Comorbidity Index modified to exclude chronic obstructive
pulmonary disease (because it may contribute to chronic cough). Comparisons were
made using either two-tailed independent two-sample t-tests or the χ^2 test and in
bivariate analyses.

RESULTS

Prevalence of chronic cough

Of 74,977 respondents to the NHWS, 3,654 (4.9%) reported experiencing chronic cough in the previous 12 months (Table 1). Prevalence estimates weighted to the US adult population were within 0.2% of unweighted estimates. The weighted 12-month prevalence rate was 5.0% (Table 1), equivalent to 12.3 million US adults. The prevalence increased with age and was higher in females (5.2%) than in males (4.7%, $P=.01$), and in respondents with a history of smoking than in respondents who had never smoked (7.3% vs. 3.4%, $P<.001$).

Respondent characteristics

The mean (SD) age of respondents with chronic cough was 50.1 (17.4) years, and 60.4% were female. Patients with chronic cough were matched 1:3 with 10,962 respondents without chronic cough (Table 2). Respondents with chronic cough differed from matched controls in race/ethnicity ($P<.001$). Fewer chronic cough respondents were employed (45.8% vs. 51.5%), more had a household income below \$50,000 (56.8% vs. 48.8%), fewer had a college degree (35.8% vs. 43.9%), more were obese (39.6% vs. 33.7%), and fewer exercised regularly (55.8% vs. 64.2%; $P<.001$ for all comparisons).

Health-related quality of life

Respondents with chronic cough reported lower general health-related quality of life than the matched controls, as measured by scores on the SF-6D (0.62 vs. 0.71) and EQ-5D-5L (0.71 vs. 0.81) and had lower scores on the SF-36 physical (42.9 vs. 48.8) and mental (41.7 vs. 47.4) component summary scales ($P<.001$ for all comparisons; Table 3).

Respondents with chronic cough had experienced more symptoms of anxiety and depression in the prior two weeks than matched controls: GAD-7 score 6.6 vs 3.8 ($P<.001$) and PHQ-9 score 8.8 vs. 5.1 ($P<.001$). More than twice as many respondents with chronic cough than without reported severe anxiety (13.1% vs. 5.5%, $P<.001$) and severe depression (9.8% vs. 4.1%, $P<.001$; Table 3).

Greater percentages of respondents with chronic cough than matched controls regularly experienced sleep problems, as measured by each of the 8 items on the sleep questionnaire (Table 4). In addition, more chronic cough sufferers had been diagnosed with sleep apnea (15.8% vs. 10.4%, $P<.001$) and more were diagnosed with sleep difficulties other than sleep apnea, insomnia, or narcolepsy (12.8% vs. 6.3%, $P<.001$) compared with matched controls (data not shown).

Compared with matched controls, respondents with chronic cough experienced greater impairment in daily activities (44.8% vs. 27.1%, $P<.001$; Table E2 in Online Repository). Among those employed, respondents with chronic cough reported greater absenteeism (the percentage of work time missed; 13.8% vs. 6.6%), presenteeism (the percentage of hours of impaired performance while at work; 34.9% vs. 19.5%), and total work productivity loss (40.2% vs. 22.4%, $P<.001$ for all comparisons; Figure 1 and Table E2 in Online Repository).

Healthcare visits

Ninety percent of chronic cough respondents utilized healthcare services in the past 6 months, compared with 82.4% of matched controls ($P<.001$). Chronic cough respondents had 1.5 times the number of visits to healthcare providers (6.7 vs. 4.4, $P<.001$; Table E3 in Online Repository). More respondents with chronic cough sought care from family/general practitioners (63.1% vs. 55.9%), nurse practitioner/physician's

261 assistant (20.5% vs. 12.0%), pulmonologists (10.5% vs. 3.0%), gastroenterologists
262 (10.5% vs. 6.3%), and allergists (7.5% vs. 3.2%) than did matched controls, and
263 approximately twice as many visited an ED (25.5% vs. 14.5%) or were hospitalized
264 (16.2% vs. 8.8%) in the past 6 months ($P<.001$ for all comparisons; Table 3).
265 Conversely, healthcare provider specialties unrelated to the care of chronic cough were
266 visited by similar proportions of respondents in both groups, including dentists (35.4%
267 vs. 36.5%, $P=0.24$), gynecologists (17.1% vs. 16.8% of females, $P=0.77$), oncologists
268 (4.1% vs. 3.8%, $P=0.42$), and ophthalmologists (11.9% vs. 11.4%, $P=0.45$; data not
269 shown).

DISCUSSION

In the NHWS, the crude prevalence of chronic cough among US adults was 4.9% and the weighted prevalence was 5.0%. The prevalence was higher in females and increased with age. After matching on gender, age, and comorbidities, about one third (31%) of those with chronic cough were current smokers, compared with only 15% of controls. The matched groups with and without chronic cough contained similar proportions of Whites and Hispanic but differed in several sociodemographic characteristics. Those with chronic cough reported an increased frequency of obesity, decreased frequency of exercising, less education, poorer employment status, and lower household income.

In the present study, chronic cough was defined as cough lasting ≥ 8 weeks. This definition aligns with the chronic cough guidelines, defining chronic cough as a cough lasting > 8 weeks [2]. In the global epidemiological literature, a variety of definitions have been used, with cough ≥ 3 months being common [31]. Using these definitions, a pooled global prevalence of 9.6% was reported [32]. In population-based studies conducted in European countries in 2006-2020, the most frequently used definition was cough lasting > 8 weeks [11, 12, 14]; other definitions were cough of duration ≥ 12 weeks [10], greater than weekly coughing bouts [13], and daily or frequent problems with cough [15]. The range of estimated prevalence in these studies was 4%-12%. The prevalence among US adults of 5.0% reported here is within this range.

In the present NHWS study, 60.4% of respondents with chronic cough were female, the average age was 50.1 years, and 30.8% were current smokers. These values are comparable to those in population-based studies in European countries, where the percent females (median of means across 6 studies) was 60%-63%, the mean or

median ages were 51-64 years, and the percent of current smokers (median of study means) was 22% [10-15].

In studies based in US cough clinics the range of average percent females was 67%-87% and the range of mean ages was 55-61 years [16-19, 22, 33]. Current smokers were either excluded from US cough clinic-based studies [18, 22] or comprised less than 2.5% of the patient sample [19, 20]. In a worldwide survey of cough clinics, 66% were female, and the average age was 60-69 years (smoking status was not ascertained) [9]. Hence, the patients seen in specialty cough clinics are a select group that is more predominantly female and of older age than adults with chronic cough identified in population-based surveys. At the same time, current smokers, who typically make up 20%-30% of the population with chronic cough, were largely excluded from cough clinic-based studies.

In the present NHWS study, fewer respondents with chronic cough were employed and more had a household income below \$50,000 compared with matched controls. A similar observation was noted in population-based surveys in Denmark and the United Kingdom, where chronic cough was associated, respectively, with low income and lower social class [12, 13]. In a US cough clinic-based study, cough severity was associated with less education [18]. However, there is no confirmed causal relationship to help understand whether suffering from chronic cough is influenced by socioeconomic status (i.e., affordability concerns) or that suffering hinders the ability to improve economically.

By numerous measures, quality of life was significantly impaired in respondents with chronic cough. SF-36 physical and mental component summary scores were lower among chronic cough sufferers. There were symptoms of anxiety in over half of chronic cough sufferers, compared with one third of controls, and symptoms of depression in

about two thirds of chronic cough sufferers, compared with approximately one third in controls. More chronic cough sufferers had been diagnosed with multiple types of sleep disturbance, including sleep apnea, compared with controls, and work productivity and activity impairment were greater among chronic cough sufferers than among matched controls.

An impact of chronic cough on quality of life has been noted in other population-based surveys [11, 34]. Ninety-one percent of respondents to a pan-European internet survey reported being depressed because of their cough [11]. In a community-based survey in the United Kingdom, the majority of respondents with chronic cough reported psychological effects, including anxiety and depression, and most felt that the cough interfered with their social life [34]. Most US quality of life data come from cough clinic-based studies, which, with one exception [19], did not include controls without chronic cough. In US cough clinic-based studies chronic cough was associated with depressive symptoms [16], anxiety and depression [18], a poorer quality of life [17, 18], and sleep apnea or sleep disturbance [19, 22]. While one might expect to observe a worse quality of life among patients who persisted through the healthcare system to find themselves in a specialized cough clinic, our study supports that, even among the general population, chronic cough is associated with these same outcomes.

The results of this study may be contrasted with those of other conditions that impose a heavy burden on the sufferer and on society. A similar impact on daily life and work was observed among European migraine sufferers identified in the 2016 NHWS, who reported rates of absenteeism of 14.4%, presenteeism of 35.5%, total work productivity loss of 38.7%, and daily activity impairment of 44.2% [35]. In a multinational survey of employed adults with symptomatic asthma, respondents in the United Kingdom and Brazil, respectively, reported rates of absenteeism of 3.5%-17.4%, and total work productivity

impairment of 21%-59% [36]. The impact on work productivity is paralleled by an increased burden on healthcare use. In the present NHWS study, visits to the ED and hospitalizations were approximately twice as frequent among respondents with chronic cough than among matched controls. A similar result was observed in a US cough clinic-based study, which reported much higher rates of outpatient visits for respiratory events compared with matched controls, and a higher rate of ED visits for any cause [19].

The NHWS sample is broadly representative of the national adult population. However, it might underrepresent certain population sectors: the institutionalized, those with the most severe comorbidities and disabilities, and people without internet access. The self-reported nature of the NHWS is potentially associated with recall and self-presentation biases. To minimize recall bias, more recent timeframes were chosen for questions, i.e., the past week, two weeks, month, or six months. To avoid self-presentation bias, sensitive questions, e.g., about weight or income, had options of "Don't Know" or "Refuse to Answer", rather than responding in 'socially-appropriate' ways. The confidential nature of this survey may also have helped reduce self-presentation bias. Associations between the variables assessed and chronic cough were established in a matched subset of the NHWS population sample that was similar to respondents with chronic cough with respect to age, gender, and comorbidity burden. Nevertheless, the associations observed could be subject to confounding, e.g., in its association with chronic cough, lower income might be a surrogate for another variable, such as smoking status. Finally, the NHWS is a cross-sectional survey administered at one point in time, so that causal relationships cannot be inferred.

CONCLUSIONS

The 12-month weighted prevalence of self-reported chronic cough among adults in the United States was 5.0%, which represents on the order of 12.3 million individuals.

368 Relative to matched respondents without chronic cough, chronic cough was
369 accompanied by a poorer quality of life, increased symptoms of severe anxiety and
370 depression, a variety of sleep disturbances, impairment of work productivity and daily
371 living activities, and greater healthcare use.

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373 **Author contributions.**

374 Eli O Meltzer was responsible for interpretation of the data. Drafting the work and
375 revising it critically for important intellectual content.

376 Robert S Zeiger was responsible for interpretation of the data. Drafting the work and
377 revising it critically for important intellectual content.

378 Peter Dicpinigaitis was responsible for interpretation of the data. Drafting the work and
379 revising it critically for important intellectual content.

380 Jonathan A Bernstein was responsible for interpretation of the data. Drafting the work
381 and revising it critically for important intellectual content.

382 John J Oppenheimer was responsible for interpretation of the data. Drafting the work
383 and revising it critically for important intellectual content.

384 Nate A Way was responsible for interpretation of the data. Drafting the work and revising
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386 Vicky W Li was responsible for interpretation of the data. Drafting the work and revising it
387 critically for important intellectual content.

388 Robert Boggs was responsible for interpretation of the data. Drafting the work and
389 revising it critically for important intellectual content.

390 Michael J Doane was responsible for analysis of the data. Drafting the work and revising
391 it critically for important intellectual content.

Eduardo Urdaneta was responsible for interpretation of the data. Drafting the work and revising it critically for important intellectual content.

Jessica P Weaver was responsible for interpretation of the data. Drafting the work and revising it critically for important intellectual content.

Jonathan Schelfhout was responsible for interpretation of the data. Drafting the work and revising it critically for important intellectual content.

Eileen Fonseca was responsible for interpretation of the data. Drafting the work and revising it critically for important intellectual content.

All authors approve the final version to be published and agree to be accountable for all aspects of the work.

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495 Pavord I, et al. Asthma impacts on workplace productivity in employed patients who are

496 symptomatic despite background therapy: a multinational survey. J Asthma Allergy
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498

499 **TABLES**500 Table 1. Prevalence of chronic cough in past 12 months among US adults ^a

Characteristic	National Health and Wellness Survey (N=74,977)	Experienced chronic cough in prior 12 months, unweighted (N=3,654)	Experienced chronic cough in prior 12 months, weighted ^b (N=12,311,770)	P value ^c
Gender				0.01
Male	32,844 (43.8)	1,446 (4.4)	5,648,127 (4.7)	
Female	42,133 (56.2)	2,208 (5.2)	6,663,643 (5.2)	
Age category				
18-49	40,306 (53.8)	1,683 (4.2)	5,962,878 (4.4)	<.001
50-64	19,363 (25.8)	1,110 (5.7)	3,405,909 (5.7)	
≥65	15,308 (20.4)	861 (5.6)	2,942,983 (5.8)	
Smoking status				<.001
Never smoked	45,931 (61.3)	1,532 (3.3)	5,015,362 (3.4)	
Current or former smoker	29,046 (38.7)	2,122 (7.3)	7,296,408 (7.3)	

501 ^a Values presented as N (%).502 ^b Weighted to the US adult population (N=246,910,032)503 ^c P value for weighted values

504

505

506 Table 2. Characteristics of respondents with and without chronic cough in the past 12
 507 months

Characteristic	Chronic cough (N=3,654)	Matched without chronic cough ^a (N=10,962)	<i>P</i> value
	N (%)	N (%)	
Age (years) ^a			0.73
18-49	1,683 (46.1)	4,979 (45.4)	
50-64	1,110 (30.4)	3,403 (31.0)	
≥65	861 (23.6)	2,580 (23.5)	
Gender ^a			0.52
Female	2,208 (60.4)	6,690 (61.0)	
Male	1,446 (39.6)	4,272 (39.0)	
Race/ethnicity ^{b, c}			<.001
White	2,586 (70.8)	7,638 (69.7)	
Hispanic	345 (9.4)	964 (8.8)	
African American	295 (8.1)	1,123 (10.2)	
Asian	216 (5.9)	768 (7.0)	
Other ^d	212 (5.8)	469 (4.3)	
Employment status			<.001
Employed	1,672 (45.8)	5,644 (51.5)	
Not employed	1,982 (54.2)	5,318 (48.5)	
Education			<.001
College degree	1,309 (35.8)	4,810 (43.9)	
No college degree ^e	2,345 (64.2)	6,152 (56.1)	
Household income			<.001
<\$50,000 ^e	2,075 (56.8)	5,345 (48.8)	

≥\$50,000	1,579 (43.2)	5,617 (51.2)	
Insurance status			0.01
Insured	3,257 (89.1)	9,934 (90.6)	
Uninsured	397 (10.9)	1,028 (9.4)	
Comorbidities ^{a, f}			0.93
0	2,131 (58.3)	6,393 (58.3)	
1	782 (21.4)	2,371 (21.6)	
≥2	741 (20.3)	2,198 (20.1)	
Smoking status			<.001
Current smoker ^g	1,126 (30.8)	1,608 (14.7)	
Former smoker	996 (27.3)	2,859 (26.1)	
Never smoked	1,532 (41.9)	6,495 (59.3)	
Body mass index			<.001
Underweight	115 (3.1)	305 (2.8)	
Normal	972 (26.6)	3,355 (30.6)	
Overweight	1,002 (27.4)	3,187 (29.1)	
Obese ^g	1,447 (39.6)	3,697 (33.7)	
Not recorded	118 (3.2)	418 (3.8)	
Alcohol consumption			<.001
None	1,231 (33.7)	4,063 (37.1)	
≤1-3 times weekly	1,988 (54.4)	5,816 (53.1)	
>3 times per week	435 (11.9)	1,083 (9.9)	
Exercise ^h			
Yes	2,039 (55.8)	7,033 (64.2)	<.001
No	1,615 (44.2)	3,929 (35.8)	

^a Respondents from the NHWS population without chronic cough, propensity score matched (ratio 3:1) to chronic cough sample on age (continuous), gender, and modified Charlson Comorbidity Index.

511 ^b All race/ethnicity categories other than Hispanic are non-Hispanic.

512 ^c *P* values for bivariate comparisons of chronic cough versus matched

513 respondents without chronic cough by racial/ethnic group: Whites,

514 *P*=0.22; Hispanic, *P*=0.25; African American, *P*<.001; Asian, *P*<.001.

515 ^d American Indian and mixed race.

516 ^e No college degree or declined to answer. Household Incomes < \$50,000

517 or declined to answer.

518 ^f Comorbidities using the Charlson Comorbidity Index, modified to exclude chronic obstructive

519 pulmonary disease.

520 ^g *P*<.001 in bivariate comparison of currently smoke vs never or former smoker and of obese vs

521 not obese, respectively.

522 ^h Exercised vigorously at least one day in the past month for 20 or more minutes for the purpose

523 of improving or maintaining health, for losing weight, or for enjoyment.

524 Table 3. Health-related quality of life measures

Summary score			
	Chronic cough (N=3,654)	Matched without chronic cough ^a (N=10,962)	<i>P</i> value chronic cough vs. non-chronic cough
EQ-5D-5L Index, mean (SD)	0.71 (0.18)	0.81 (0.16)	<.001
SF-36v2, mean (SD)			
SF-6D Utility Index	0.62 (0.12)	0.71 (0.14)	<.001
Physical component	42.87 (10.76)	48.75 (10.19)	<.001
Mental component	41.69 (12.80)	47.37 (11.60)	<.001
GAD-7 anxiety score, mean (SD) ^b	6.58 (5.99)	3.83 (5.00)	<.001
Anxiety category, N (%)			<.001
None	1,656 (45.3)	7,463 (68.1)	
Mild	949 (26.0)	1,964 (17.9)	
Moderate	569 (15.6)	936 (8.5)	
Severe	480 (13.1)	599 (5.5)	
PHQ-9 depression score, mean (SD) ^c	8.84 (7.05)	5.10 (6.12)	<.001
Depression category, N (%)			<.001
None-minimal	1,260 (34.5)	6,718 (61.3)	
Mild	960 (26.3)	2,094 (19.1)	
Moderate	640 (17.5)	1,082 (9.9)	
Moderate-severe	436 (11.9)	621 (5.7)	
Severe	358 (9.8)	447 (4.1)	

525 ^a Propensity score matched to chronic cough sample on age, gender, and modified Charlson
526 Comorbidity Index.

527 ^b Anxiety symptoms over the prior 2 weeks on the GAD-7 scale of 0-21. A score of 15-21
528 represents severe anxiety.

529 ^c Depression symptoms over the prior 2 weeks on the PHQ-9 scale of 0-27. A score of 20-27
530 represents severe depression.

531

532

Table 4. Regularly experienced sleep problems ^a

Problem or symptom	Chronic cough (N=3,654)	Matched without chronic cough ^b (N=10,962)	<i>P</i> value
Difficulty falling asleep	1,720 (47.1)	3,419 (31.2)	<.001
Waking during night ^c	1,380 (37.8)	2,659 (24.3)	<.001
Waking up several times	1,504 (41.2)	2,766 (25.2)	<.001
Waking up too early	1,186 (32.5)	2,349 (21.4)	<.001
Sleep apnea	586 (16.0)	962 (8.8)	<.001
Poor quality of sleep	1,365 (37.4)	2,387 (21.8)	<.001
Daytime sleepiness	1,492 (40.8)	2,533 (23.1)	<.001
Difficulty staying awake	654 (17.9)	898 (8.2)	<.001

^a Values presented as N (%).^b Propensity score matched to chronic cough sample on age, gender, and modified Charlson Comorbidity Index.^c Waking during the night defined as waking during the night and not being able to get back to sleep.

540 **FIGURE LEGENDS**

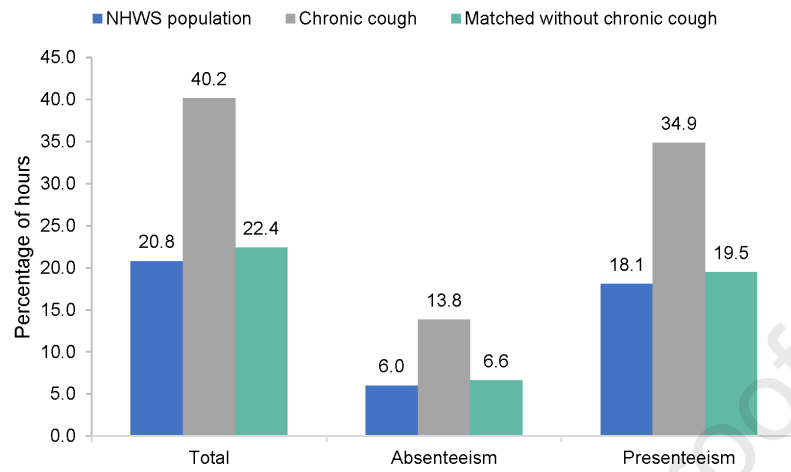
541 **Figure 1. Work productivity among employed respondents over the past week ^{a,b}**

542 NHWS, National Health and Wellness Survey

543 ^a $P < .001$ for all comparisons of chronic cough vs matched controls.

544 ^b Propensity score matched to chronic cough sample on age, gender, and modified Charlson

545 Comorbidity Index.



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Table E1. Comparison of characteristic profile of NHWS respondents and the US adult population

Characteristic	National Health and Wellness Survey Population N=74,977	National Health and Wellness Survey 2018 Weighted N=246,910,032	US Government Data ^{a, b, c}
Age (years), mean (SD) ^a	47.6 (17.4)	47.4 (0.08)	47.5 (18.5)
Age (years) category			
18-29	20.5%	21.1%	21.4%
30-39	17.1%	17.1%	17.1%
40-49	16.1%	17.2%	16.1%
50-64	25.8%	24.2%	25.2%
≥65	20.4%	20.4%	20.2%
Gender			
Female	56.2%	51.8%	50.8%
Male	43.8%	48.2%	49.2%
Race			
White	72.6%	73.2%	75.1%
African American	11.8%	13.4%	14.1%
Asian	8.7%	5.4%	6.8%
American Indian	0.9%	1.0%	1.7%
Hawaiian/Pacific Islander	0.4%	0.4%	0.4%
Mixed/Other	5.7%	6.8%	5.5%
Employment status ^d			
Employed	56.5%	NA	63.3%
Not employed	43.5%	NA	36.7%
Education			
No college degree ^e	54.3%	67.7%	67.5%
College degree	45.7%	32.3%	32.6%
Household income			
<\$25,000 ^f	23.0%	25.0%	19.6%
\$25,000-49,999	23.7%	25.4%	21.3%
\$50,000-74,999	18.9%	18.8%	17.4%
≥\$75,000	34.5%	30.9%	41.8%
Insurance status ^d			
Insured	89.4%	NA	90.0%
Uninsured	10.6%	NA	10.0%
Morbidities ^c			
Diabetes	9.6%	10.2%	9.5%
Migraine ^g	10.3%	10.0%	15.9%

NA, not available; SD, standard deviation

^a Age comes from US Census data, "Annual estimates of the resident population by single year and sex for the United States, Data through July 2017"^b US Census, American Community Survey, 2018 data. Gender & Race/Ethnicity from Table ID: DP05. Education from Table B06009. Income from Table ID: S1901. Insurance & Employment status from Table ID: DP03. Insurance Coverage from Table ID: S2701.^c Medical Comorbidities from National Center for Health Statistics, Centers for Disease Control (NCHS-CDC). National Health Interview Survey (2018 data, 18 years and older). Diabetes from Table A-4a. Migraine or severe headaches from Table A-5a.^d Note that the US Census data described in footnote B for Employment status includes those aged 16 years and older and Insurance status includes those aged 19 years and older whereas the NHWS includes ages 18 years and older.^e No college degree or declined to answer.^f Less than \$20,000 or declined to answer.^g NHWS reports percent of respondents which reported ever being diagnosed with migraines by their physician. As mentioned in footnote C, the comparator percent is for migraines or severe headaches experienced in the prior 3 months and which lasted at least a whole day.

Table E2. Work productivity and activity impairment over the past week

	NHWS population		Chronic cough		Matched without chronic cough ^a		<i>P</i> value chronic cough vs non-chronic cough
	N	Mean % (SD)	N	Mean % (SD)	N	Mean % (SD)	
Productivity impairment (% hours) ^b							
Absenteeism	40,561	6.0 (16.9)	1,611	13.84 (23.7)	5,398	6.6 (17.5)	<.001
Presenteeism	40,368	18.1 (26.1)	1,597	34.85 (29.7)	5,369	19.5 (26.7)	<.001
Total	40,561	20.8 (29.3)	1,611	40.15 (33.3)	5,398	22.4 (30.0)	<.001
Activity impairment (% hours) ^c	74,977	23.9 (28.5)	3,654	44.82 (30.2)	10,962	27.1 (29.6)	<.001

NHWS, National Health and Wellness Survey

^a Propensity score matched (ratio 3:1) to chronic cough sample on age, gender, and modified Charlson Comorbidity Index.

^b Results reported among employed respondents.

^c Results reported among all respondents.

Table E3. All-cause healthcare utilization in the past 6 months

	NHWS population (N=74,977)	Chronic cough (N=3,654)	Matched without chronic cough ^a (N=10,962)	<i>P</i> value chronic cough vs non- chronic cough
Visit type, N (%)				
Healthcare provider	58,494 (78.0)	3,289 (90.0)	9,029 (82.4)	<.001
General/family practitioner	38,570 (51.4)	2,304 (63.1)	6,128 (55.9)	<.001
NP/PA	7,557 (10.1)	748 (20.5)	1,318 (12.0)	<.001
Pulmonologist	1,682 (2.2)	385 (10.5)	325 (3.0)	<.001
Gastroenterologist	3,719 (5.0)	382 (10.5)	693 (6.3)	<.001
Allergist	2,291 (3.1)	274 (7.5)	356 (3.2)	<.001
Emergency Department	9,224 (12.3)	932 (25.5)	1,588 (14.5)	<.001
Hospitalized (inpatient)	5,386 (7.2)	591 (16.2)	963 (8.8)	<.001
Visit type, mean $\pm$ SD				
Healthcare provider	3.71 $\pm$ 5.69	6.66 $\pm$ 9.26	4.39 $\pm$ 6.41	<.001
General/family practitioner	0.87 $\pm$ 1.36	1.43 $\pm$ 1.87	1.00 $\pm$ 1.50	<.001
NP/PA	0.18 $\pm$ 0.81	0.46 $\pm$ 1.71	0.23 $\pm$ 0.85	<.001
Pulmonologist	0.04 $\pm$ 0.39	0.22 $\pm$ 1.35	0.05 $\pm$ 0.35	<.001
Gastroenterologist	0.08 $\pm$ 0.42	0.18 $\pm$ 0.71	0.10 $\pm$ 0.55	<.001
Allergist	0.07 $\pm$ 0.76	0.19 $\pm$ 1.12	0.08 $\pm$ 0.90	<.001
Emergency Department	0.23 $\pm$ 1.16	0.51 $\pm$ 1.31	0.27 $\pm$ 1.08	<.001
Hospitalized (inpatient)	0.14 $\pm$ 1.16	0.32 $\pm$ 1.12	0.16 $\pm$ 0.85	<.001

NHWS, National Health and Wellness Survey, 2018; NP, Nurse Practitioner; PA, Physician's Assistant.

^a Propensity score matched (ratio 3:1) to chronic cough sample on age, gender, and modified Charlson Comorbidity Index.