Chronic cough in Germany: results from a general-population survey

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Shareable abstract (@ERSpublications)
Chronic cough is a prevalent condition in Germany among all age groups, regardless of sex, with highest rates in those 18–29 and ⩾50 years, and more frequent among current or prior smokers. Comorbidities are common in this population. https://bit.ly/3uiYj4w

Abstract

Background Chronic cough (CC) which is defined ⩾8 weeks is a common condition in clinical practice. However, estimates of prevalence and associated comorbidities in German adults and key subgroups of age and gender are lacking.

Methods Cross-sectional study based on a representative panel of 15 020 adult subjects of the general population who completed the German National Health and Wellness Survey, reporting CC and questions about comorbidities. Lifetime and 12-month prevalence are presented as unweighted estimates.

Results The lifetime CC prevalence was 6.5% (range across age groups 5.1%–8.3%) and the 12-month prevalence was 4.9% (range 3.7–5.7%). The prevalence of diagnosed CC was 2.8% (range 0.9–4.1%) and the prevalence of persons currently on any prescription to treat CC was 0.6% (range 0.2–1.4%). Respondents who experienced CC were 52.0±17.0 years old, with a higher prevalence in those aged 50 years and older. Persons with CC had higher morbidity scores and were diagnosed with an increased number of comorbidities, most frequently diagnoses of the respiratory system (71.0%), followed by digestive tract disorders (34.0%) and sleep disorders (37.6%).

Conclusions In a broadly representative sample of German adults, lifetime and 12-month prevalence of CC was greatest in current and former smokers and those older ⩾50 years of age. Comorbidities are frequent and may complicate management of these patients.

Introduction

Cough is one of the most common symptoms for patients seeking care from primary care specialists, allergists, otolaryngologists or pulmonologists [1]. While its exact characteristics are not always precisely defined [2, 3], the importance of cough as a global clinical problem has led multiple societies to publish guidelines on its diagnosis and management.

Similar to other societies, the German Respiratory Society guideline for chronic cough (CC) categorises cough based upon its duration [4–6]. Acute cough is present for less than 3 weeks and most often due to acute viral upper respiratory tract infection. A cough that has been present longer than 3 weeks is either sub-acute (up to 8 weeks) or chronic (CC; over 8 weeks) [7, 8].

CC negatively impacts quality of life directly due to the effect of cough on physical, social or psychological functioning or indirectly through associated comorbidities such as urinary incontinence, cough syncope and dysphonia leading to social isolation, depression, and difficulties in relationships [9].

CC often manifests in association with comorbidities, such as asthma, gastroesophageal reflux disease (GERD) and upper airway cough syndrome (previously called post-nasal drip syndrome) [10]. ZEIGER et al. [11]

reported that, among specialist-diagnosed CC patients, 44.1% exhibited GERD, 31.2% asthma, 24.3% obesity, 20.4% upper airway cough syndrome and 19.4% common cough complications.

Certain patients may continue to cough despite thorough investigation and treatment in cases where no cause can be determined (termed unexplained CC or idiopathic CC) or when cough persists despite treatment of existing underlying conditions (refractory CC) [12]. Increased exposure of the sensory nerve terminals to chemical irritants (*e.g.* prostaglandin-E2, ATP) or excess mucus may have a role in triggering cough [13]. Further, neuronal hypersensitivity of airway sensory nerves has been considered to cause cough, as many patients report singing, laughing, changes in temperature or noxious smells to trigger bouts of coughing [13].

There are currently no treatments approved by the European Medicines Agency for the treatment of refractory or unexplained CC. Given its prolonged nature, significant morbidity and lack of effective treatments, unexplained and refractory CC remains an unmet medical need.

Very little is known of the natural history of CC [5]. However, in recent years, substantial evidence on the epidemiology of CC has been collected [14]. The lack of reliable data on the prevalence of CC in Germany was noted as an important knowledge gap in the most recent German guideline [6]. Prevalence data has been particularly lacking in the general population, as many previously reported estimates of prevalence are derived from settings which require timely contact with a physician. A meta-analysis estimated that CC could impact as much as 12% of the European population [15]. There are some prevalence estimates as low as 4% in certain regions [16].

Furthermore, as there is no International Classification of Diseases-10 code for CC, the affected population is difficult to identify and has not been well studied. Therefore, in view of novel therapeutic approaches for CC, there is a need to better understand its prevalence as well as the characteristics, comorbidities and quality of life of these patients.

Thus, our study aimed to provide prevalence estimates for CC in Germany and to describe the characteristics, treatment patterns, healthcare resource use, and quality of life and health state patient-reported outcomes (PROs) of CC respondents in these countries relative to general population adults who have not experienced CC.

Methods

The National Health and Wellness Survey (NHWS; Kantar LLC, New York, USA) is a self-administered, internet-based questionnaire conducted annually in 12 regions in the world including Germany. This survey collects data regarding demographics, health and wellness history and healthcare utilisation, and incorporates validated patient-reported health outcome instruments measuring quality of life, anxiety, depression, work productivity and activity impairment. In Germany, roughly 15 000 adults (aged 18+) take part in the survey each year. Quota sampling, with strata by age and gender, is implemented to ensure that the demographic composition of the NHWS sample is representative of the adult German population. Comparisons between NHWS and other established country sources have been published previously [17–19]. All translations from US English to German were provided by GlobaLexicon (London, UK) and reviewed by Kantar Health.

The protocol and questionnaire for the NHWS was reviewed and approved 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 German 2020 NHWS, respondents had to be ⩾18 years, able to read and write in German, and state their age and gender. Potential respondents were recruited through an existing, general-purpose (*i.e.* not healthcare-specific) web-based survey panel. The 2020 NHWS, fielded in Germany between 30 December 2019 and 20 April 2020, utilised a targeted quota sampling of strata according to age and gender to ensure a demographic composition of the German adult population. A cross-sectional design was used to estimate disease prevalence and a case-control design for comparisons to describe respondents with CC. Respondents with and without CC were those answering, respectively, "yes" and "no" to the question: "Have you experienced daily CC for 8 weeks or longer within the past 12 months?" or "Have you ever experienced daily CC for 8 weeks or longer?". Those respondents were

further asked if they have ever been diagnosed with CC by a physician or are currently using a prescription medication to treat their CC. No medications nor therapeutic class lists were provided as prompts.

Study measures

To obtain a systematic overview of disease history, respondents were presented a comprehensive list of terms (partly with explanations). For example, the list comprised sleep conditions, with the terms "insomnia, narcolepsy, sleep apnoea, sleep difficulties (other)". Respondents were presented with the terms and asked to select those they have ever experienced, those experienced in the past year, and those for which they have received a diagnosis. The full list of terms is presented with the results in table 1.

Health-related quality of life was measured, e.g. the Medical Outcomes Study 12-item Short Form Survey v2 (SF-12v2; Quality Metric, Lincoln, RI) [20, 21]. SF-12v2 physical and mental health component summary scores were calculated with the mean score set at 50 and the standard deviation (SD) at 10; higher scores represent better health. Anxiety was measured with the General Anxiety Disorder 7-item scale (GAD-7), which measures the severity of symptoms of generalised anxiety over the prior 2 weeks [22]. 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. Depression was assessed with the Patient Health Questionnaire 9-item scale (PHQ-9) [23]. 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).

Data analysis

CC prevalence was calculated as a proportion of the 15 020 German 2020 NHWS respondents and in demographic subgroups (male, female, age categories 18–29, 30–39, 40–49, 50–64, 65–74 and ≥75 years), and by smoking status (use of cigarettes or other tobacco products: never smoked, or current/former smoker).

CC prevalence estimates were defined as follows:
- lifetime prevalence: report ever having had a CC (cough of ≥8 weeks); and
- 12-month prevalence: reporting of cough daily for ≥8 weeks in the past 12 months.

TABLE 1 Prevalence estimates of chronic cough (CC) in the National Health and Wellness Survey (NHWS) sample: lifetime, in past 12 months, diagnosed, drug treated (unweighted estimated)

		NHWS sample size	Lifetime[#]			12 months[¶]			Lifetime diagnosed[+]			Lifetime diagnosed and current user of a prescription medication to treat CC[§]		
			n	%	p-value*	n	%	p-value*	n	%	p-value*	n	%	p-value*
Total		15020	981	6.5		739	4.9		418	2.8		95	0.6	
Gender	Female	7741	518	6.7	0.412	397	5.1	0.223	248	3.2	0.001	45	0.6	0.415
	Male	7279	463	6.4		342	4.7		170	2.3		50	0.7	
Age group, years	18–29	2357	195	8.3	<0.001	113	4.8	<0.001	40	1.7	<0.001	8	0.3	<0.001
	30–39	2187	122	5.6		85	3.9		20	0.9		4	0.2	
	40–49	2288	116	5.1		84	3.7		46	2.0		9	0.4	
	50–64	4214	273	6.5		229	5.4		154	3.7		31	0.7	
	65–74	3330	234	7.0		191	5.7		136	4.1		34	1.0	
	75+	644	41	6.4		37	5.7		22	3.4		9	1.4	
Smoking status	Current/ Former smoker	8187	655	8.0	<0.001	526	6.4	<0.001	293	3.6	<0.001	68	0.8	<0.001
	Never smoked	6833	326	4.8		213	3.1		125	1.8		27	0.4	
Region[f]	East	4960	310	6.3	0.008	232	4.7	0.004	130	2.6	0.327	27	0.5	0.424
	North	1155	77	6.7		59	5.1		35	3.0		7	0.6	
	South	3665	205	5.6		147	4.0		90	2.5		19	0.5	
	West	5230	389	7.4		301	5.8		163	3.1		42	0.8	

*: comparison of subsample with total sample. #: prevalence estimates for ever being diagnosed with CC. ¶: prevalence estimates for experienced CC in past 12 months. +: prevalence estimates for ever being diagnosed with CC. §: prevalence estimates for ever being diagnosed and for currently using a prescription medication to treat their CC. f: South: Baden-Wuerttemberg, Bavaria; East: Berlin, Brandenburg, Lower Saxony, Mecklenburg-Western Pomerania, Saxonia, Saxonia-Anhalt, Thuringia; North: Bremen, Hamburg, Schleswig-Holstein; West: Hessia, North Rhine-Westphalia, Rhineland-Palatinate, Saarland; not specified: 10 respondents chose not to answer that question but also did not report CC.

Total and subgroup prevalence estimates by age, gender, smoking status and geographic regions (South: Baden Wuerttemberg, Bavaria; East: Berlin, Brandenburg, Lower Saxony, Mecklenburg-Western Pomerania Saxony, Saxonia-Anhalt, Thuringia; North: Bremen, Hamburg, Schleswig-Holstein; West: Hessen, North Rhine-Westphalia, Rhineland-Palatinate, Saarland) were calculated as unweighted and weighted estimates. As a sensitivity analysis, weighting was applied post-data collection using the Horvitz–Thompson method to align sample with age and gender composition of the German adult population using data reported in the 2019/2020 International Data Base of the US Census Bureau [24]. As weighted values did not relevantly differ from the unweighted values, only the latter are presented in this publication.

Propensity scores were used to match NHWS respondents with CC at a 1:3 ratio to respondents without CC. Propensity scores were calculated using age (as a continuous variable), gender, the NHWS Charlson Comorbidity Index modified to exclude chronic obstructive pulmonary disease (because it may contribute to CC), marital status, household income and an interaction term of marital status×household income. The interaction term was included as a reflection of socio-economic status, *e.g.* possible synergistic benefits from dual-income/partnered households, to control for the influence of an individual's ability to work irrespective of spousal income. Eligible controls were matched using a nearest neighbour approach on the logit with a caliper=0.25.

Results are presented as either N (%) or mean (SD). Between-group comparisons were conducted using two-tailed independent samples t-tests (Welch's t-test for unequal variances) for analysis of continuous variables, or the chi-quare tests for analysis of categorical variables. Respondents with CC in the past 12 months were compared to those without CC in terms of comorbidities and the named health-related quality of life scores.

Results were considered statistically significant at $p < 0.05$. All analyses were performed by Kantar Health LLC in SPSS (v.23), R (v.4.0.2) and/or SAS (v.9.4).

Results
Prevalence estimates
Out of the NHWS general population sample of 15 020 German respondents, 981 (6.5%) reported CC at any time during their lifetime. Across all (adult) age groups, the lifetime prevalence ranged from 5.1 to 8.3% ($p < 0.001$) (table 1). Past/present smokers reported a higher prevalence than non-smokers (8.0 *versus* 4.8%, $p < 0.001$). By the geographic region, prevalence rates ranged from 5.6 to 7.4% ($p = 0.008$) with prevalence highest in western Germany. The diagnosed prevalence 2.8% (range 0.9–4.1%, $p < 0.001$), and the current CC prescription medication user prevalence was 0.6% (range 0.2–1.4%, $p < 0.001$). The 12-month prevalence of CC in this sample was 4.9% (ranging from 3.7% to 5.7% across age groups, $p < 0.001$),

Respondent characteristics
Comparisons between respondents with and without CC in the past 12 months are presented in table 2. Matched respondents reporting CC were on average older than respondents without CC (52.1±17.0 *versus* 51.8±17.7; $p = 0.62$). The proportion of females was similar across groups (53.8% with CC and 56.3% without, $p = 0.240$). Differences between groups were noted for employment status (respondents with CC were less often employed), income (a similar proportion of respondents were in the middle income stratum but more respondents with CC were in the lower income stratum, $p < 0.001$), region and health insurance (see table 2).

Current medical conditions and comorbidities
Table 3 provides an overview on diseases and conditions in last 12 months as reported by respondents. In terms of organ systems, persons with CC reported most frequently medical diagnoses of the respiratory system (71.0% *versus* 29.9%, $p < 0.001$), also diagnoses by the digestive tract, the heart and blood system and sleep disorders were more common than in persons without CC (table 3).

Body mass index and comorbidity scores
Mean BMI was slightly higher in respondents with CC compared to those without 27.9 *versus* 27.1 kg·m^{-2} ($p = 0.004$). Also, the number of days with vigorous exercise was lower (5.0 *versus* 5.8 days, $p = 0.023$). Various patient-reported outcomes and scores are shown in table 4. In respondents with CC, the mean Charlson Comorbidity Score without COPD, the PHQ-9 score, the GAD-7 score and SF-12 physical component score and mental component score were significantly higher in persons with CC compared to those without (table 4).

TABLE 2 Characteristics in the subsample of respondents with chronic cough (CC) in the past 12 months *versus* the German adult general population subsample without CC

		Unmatched					Matched#					
		Total NHWS respondents	Respondents with CC in past 12 months	Respondents without CC in past 12 months	p-value		Total	Respondents with CC in past 12 months	Respondents without CC in past 12 months	p-value*		
n		15 020	739	14 281			2930	736	2194			
Age	Mean, SD	50.1 ±16.8	52.0±17.0	50.0±16.7	0.001*		51.8 ±16.7	52.1±17.0	51.8±17.7	0.62		
		n	%	n	%	n	%		n	%	n	%	

		Total NHWS n	Total NHWS %	CC n	CC %	without CC n	without CC %	p-value	Total n	Total %	CC n	CC %	without CC n	without CC %	p-value*
Age group, years	18–24	1276	8.5	66	8.9	1210	8.5	0.001*	232	7.9	65	8.8	167	7.6	0.443
	25–39	3268	21.8	132	17.9	3136	22		556	19	130	17.7	426	19.4	
	40–49	2288	15.2	84	11.4	2204	15.4		380	13	84	11.4	296	13.5	
	50–64	4214	28.1	229	31	3985	27.9		863	29.5	229	31.1	634	28.9	
	65–74	3330	22.2	191	25.8	3139	22		758	25.9	191	26.0	567	25.8	
	75+	644	4.3	37	5	607	4.3		141	4.8	37	5.0	104	4.7	
Gender	Male	7279	48.5	342	46.3	6937	48.6	0.223	1299	44.3	340	46.2	959	43.7	0.24
	Female	7741	51.5	397	53.7	7344	51.4		1631	55.7	396	53.8	1235	56.3	
Employment status	Employed full time/part time/ self-employed	8365	55.7	332	44.9	8033	56.2	0.000*	1384	47.2	329	44.7	1055	48.1	0.049*
	Homemaker/student/long-term disability/ not employed and not looking for work	1737	11.6	88	11.9	1649	11.5		374	12.8	88	12.0	286	13.0	
	Retired	4390	29.2	280	37.9	4110	28.8		1058	36.1	280	38.0	778	35.5	
	Not employed. but looking for work/ short-term disability	528	3.5	39	5.3	489	3.4		114	3.9	39	5.3	75	3.4	
Marital status	Married or living with partner	8329	55.5	390	52.8	7939	55.6	0.323	1556	53.1	389	52.9	1167	53.2	0.888
	Single/never married or divorced or separated or widowed	6614	44	345	46.7	6269	43.9		1361	46.5	343	46.6	1018	46.4	
	Decline to answer	77	0.5	4	0.5	73	0.5		13	0.4	4	0.5	9	0.4	
Household income (categorical)	Low (< €20,000)	3201	21.3	203	27.5	2998	21	<0.001*	824	28.1	202	27.4	622	28.4	0.53
	Medium (€20,000 - €49,999)	6350	42.3	315	42.6	6035	42.3		1285	43.9	315	42.8	970	44.2	
	High (≥ €50,000)	4133	27.5	168	22.7	3965	27.8		639	21.8	166	22.6	473	21.6	
	Decline to answer	1336	8.9	53	7.2	1283	9		182	6.2	53	7.2	129	5.9	
Level of education	Did not attend school or declined to answer	489	3.3	22	3	467	3.3	0.076	83	2.8	22	3.0	61	2.8	0.611
	Less than 4-year university degree	10 456	69.6	542	73.3	9914	69.4		2115	72.2	540	73.4	1575	71.8	
	4-year university degree or higher	4075	27.1	175	23.7	3900	27.3		732	25	174	23.6	558	25.4	
Smoking Status (cigarettes and other tobacco products)	Current smoker	4566	30.4	374	50.6	4192	29.4	<0.001*	1010	34.5	371	50.4	639	29.1	<0.001*
	Former smoker	3621	24.1	152	20.6	3469	24.3		737	25.2	152	20.7	585	26.7	
	Never smoked	6833	45.5	213	28.8	6620	46.4		1183	40.4	213	28.9	970	44.2	
Region	South	3665	24.4	147	19.9	3518	24.6	0.004*,¶	675	23	147	20.0	528	24.1	0.032*,¶
	East	4960	33	232	31.4	4728	33.1		961	32.8	231	31.4	730	33.3	
	West	5230	34.8	301	40.7	4929	34.5		1057	36.1	299	40.6	758	34.5	
	North	1155	7.7	59	8	1096	7.7		236	8.1	59	8.0	177	8.1	
	Not specified	10	0.1	0	0	10	0.1		1	0	-	0.01	1	0.0	

Continued

TABLE 2 Continued											
		Unmatched					Matched[#]				
		Total NHWS respondents		Respondents with CC in past 12 months		Respondents without CC in past 12 months	p-value	Total		Respondents with CC in past 12 months		Respondents without CC in past 12 months	p-value*
Health insurance type	Public, without additional private insurance	10 246	68.2	489	66.2	9757	68.3	0.06	2054	70.1	487	66.2	1567	71.4	0.001*
	Public, along with additional private insurance	2393	15.9	120	16.2	2273	15.9		465	15.9	119	16.2	346	15.8	
	Private insurance	1199	8	70	9.5	1129	7.9		202	6.9	70	9.5	132	6.0	
	Aid entitlement and additional private insurance	688	4.6	42	5.7	646	4.5		127	4.3	42	5.7	85	3.9	
	Other	151	1	10	1.4	141	1		30	1	10	1.4	20	0.9	
	None of the above	343	2.3	8	1.1	335	2.3		52	1.8	8	1.1	44	2.0	

Data are based on respondents who completed the 2020 Germany NHWS (National Health and Wellness Survey). *: t-test or chi-square statistic is significant at the 0.05 level. [#]: propensity score matched on age, gender, CCI modified to exclude COPD, marital status, household income, interaction term of marital status x household income; using 1:3 nearest neighbour on the logit, caliper=0.25. [¶]: given low sample size, "undefined" region was not included in the statistical comparison.

TABLE 3 Matched respondent experienced and physician-diagnosed conditions							
	Total NHWS respondents		Respondents with CC		Matched[#] respondents without CC		
n	15 020		739		2194		
	n	%	n	%	n	%	p-value*
Respondent-reported conditions experienced in prior 12 months							
Migraine	522	17.8	170	23.1	352	16.0	0.000*
Sleep conditions combined (at least one)	1412	48.2	520	70.7	892	40.7	0.000*
Insomnia	768	26.2	287	39.0	481	21.9	0.000*
Narcolepsy	52	1.8	39	5.3	13	0.6	0.000*
Sleep apnoea	252	8.6	114	15.5	138	6.3	0.000*
Other sleep difficulties	711	24.3	257	34.9	454	20.7	0.000*
Respondent-reported being diagnosed with condition by a physician during lifetime							
Cancer (any tumour, leukaemia, lymphoma, metastatic solid tumour)	183	6.2	40	5.4	143	6.5	0.068
Chronic pain due to rheumatoid arthritis	159	54.0	45	6.1	114	5.2	0.047*
Digestive tract (gastroesophageal reflux, heartburn, irritable bowel syndrome, ulcerative colitis, ulcers)	628	21.4	248	33.7	380	17.3	0.000*
Heart and blood (congestive heart failure, heart attack, mini-stroke/ transient ischaemia attack, peripheral vascular disease, stroke, diabetes Type I/II, latent autoimmune diabetes)	747	25.5	208	28.3	539	24.6	0.018*
Infectious diseases (AIDS, hepatitis B or C, HIV)	91	3.1	36	4.9	55	2.5	0.001*
Liver (chronic liver disease or cirrhosis)	63	2.2	28	3.8	35	1.6	0.000*
Neurological (hemiplegia, multiple sclerosis, Parkinson's disease)	76	2.6	24	3.3	52	2.4	0.057
Respiratory (allergies, asthma, hay fever, chronic bronchitis, CC COPD, emphysema)	1178	40.2	522	70.9	656	29.9	0.000*
Sleep (insomnia, narcolepsy, sleep apnoea, other sleep difficulties)	2828	18.8	278	37.6	2550	17.9	0.000*
Moderate or severe renal/kidney disease	32	1.1	5	0.7	27	1.2	0.191
Other (connective tissue disease or community-acquired pneumonia)	86	2.9	50	6.8	36	1.6	0.000*

CC: chronic cough; COPD: chronic obstructive pulmonary disease; NHWS: National Health and Wellness Survey. *: Chi-square statistic is significant at the 0.05 level. [#]: propensity score matched on age, gender, CCI modified to exclude COPD, marital status, household income, interaction term of marital status×household income; using 1:3 nearest neighbour on the logit, caliper=0.25.

TABLE 4 Matched general health scores and measures and report of weight and exercise							
	Total NHWS respondents		Respondents with CC		Matched* respondents without CC		p-value*
n	15 020		739		2194		
	Mean	SD	Mean	SD	Mean	SD	
CCI	0.87	1.31	1.16	1.39	0.77	1.27	0.000*
CCI–modified (without COPD)	0.73	1.23	0.80	1.26	0.70	1.21	0.068
PHQ-9 score[¶]	6.39	6.15	8.97	6.49	5.52	5.78	0.000*
GAD-7 score[¶]	4.73	4.72	6.75	5.15	4.06	4.36	0.000*
SF-12 physical component score[+]	46.33	10.11	42.75	9.52	47.53	10.02	0.000*
SF-12 mental component score[+]	46.27	10.77	42.75	10.45	47.53	10.59	0.000*
BMI[§]	27.29	6.51	27.93	7.03	27.08	6.31	0.004*
Numbers of days of vigorous exercise in the past month[f]	5.51	7.53	4.98	7.27	5.69	7.61	0.023*

BMI: body mass index; CC: chronic cough; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease; GAD-7: Generalized Anxiety Disorder questionnaire, 7-item; NHWS: National Health and Wellness Survey; PHQ-9: Patient Health Questionnaire, 9-item; SD: standard deviation; SF-12: Medical Outcomes Study 36-item Short Form Survey v2. *: t-test or chi-square statistic is significant at the 0.05 level. [#]: propensity score matched on age, gender, CCI modified to exclude COPD, marital status, household income, interaction term of marital status×household income; using 1:3 nearest neighbour on the logit, caliper=0.25. [¶]: PHQ-9 and GAD-7 are validated instruments to assess depressive symptoms over the prior 2 weeks (score range 0–27) and severity of generalised anxiety symptoms over the prior 2 weeks (score range 0–21), respectively. [+]The physical and mental health component summary scores were calculated with a mean score set at 50 and a standard deviation at 10; higher scores represent better health. [§]: BMI was collected for a subset of respondents who reported their height and weight, respectively N=2824 out of 2930; 707 out of 736; and 2117 out of 2194. BMI between 25 and <30.0 kg·m^{-2} indicates overweight. [f]: the question was "How many days in the past month did you exercise vigorously for at least 20 min for the purpose of improving of maintaining your health, with the purpose of losing weight, or for enjoyment?".

Discussion

According to this cross-sectional study, the 12-month prevalence of CC among adult respondents from a representative sample in Germany is 4.9%. Of these, almost half have been diagnosed by a physician and one tenth were currently using prescription treatment. Typically, respondents with CC have comorbidities, most frequently of the respiratory system; approximately one third have sleep disorders.

The present survey adds to a substantial body of evidence on CC. However, studies differ in terms of setting, age group, and prevalence of smoking. We used a cut-off of 8 weeks or greater for the CC definition, which is largely consistent with the recommended CC definition of >8 weeks in current North American and European clinical guidelines [5, 25]. Other studies applied other periods such as ⩾3 months, which might limit comparability of results.

Among the recently published studies on CC, the Rotterdam Study Group – a cohort of 9824 subjects aged ⩾45 years – found a self-reported prevalence of CC (daily coughing for at least 3 months during the preceding 2 years) of 10.9% [26]. In adult patients in the UK who were enrolled in a *Helicobacter pylori* screening program, a prevalence of 12% was reported [27]. A Canadian study showed in subjects aged 45 to 85 years self-reported prevalence of CC (coughed most days in the previous 12 months) was 15.8% at baseline and 17.1% at 3-year follow-up [28]. In the US, based on 75 000 National Health and Wellness Survey adult (⩾18 years) respondents, 5.0% had experienced CC (daily cough at least 8 weeks) in the previous 12 months [29].

Another study in Denmark (14 669 subjects, median age 58 years) found a point prevalence of 4% [16] and a study in Finland (mean age 51 years) of 7.2% [30]. The Respiratory Health in Northern Europe III cohort (n=13 500), a multi-centre study, reported non-productive CC in 7% and productive CC in 9% [31]. Based on a systematic review and meta-analysis, Song *et al.* [15] estimated the global CC prevalence at 10%, and the prevalence in Europe at 12%. However, there is no insight in the included data for the meta-analysis. As described above, there are notable differences in the design and population of mentioned studies that explain differences observed in CC prevalence.

When considering the age groups, we found the highest CC prevalence in the oldest (50+ years) and youngest (18–29 years) surveyed. Other studies have also reported higher rates of CC as persons age (Copenhagen [16], Rotterdam [26], Korea [32]). Interestingly, CC was more prevalent among 18–29-year-olds than among those aged 30–49 years. In other studies, the youngest adults have been reported in combination with persons in their thirties and sometimes with those up to age 49. For instance, Colak *et al.* [16] reported a nominally higher prevalence among Danish 20–39-year-olds than among those in their forties. Similarly, prior to adjusting for diagnostic proceures and other co-variables, a higher unadjusted prevalence was shown in Korea among 18–39-year-olds than those aged 40–64 years [32]. Combing the youngest adults with those in their third decade may temper the prevalence rate. Our study results were not stratified by age other than as reported for prevalence. It is therefore possible that owing to poorer economic circumstance and/or lower utilisation of healthcare services, this younger adult population has not addressed associated underlying conditions and/or that their behavioural choices, *e.g.*, smoking, may impact the rate of reported CC. The reasons for our observed higher prevalence rate among 18–29-year-olds remain unclear and could be assessed in future studies.

It has been reported that the cough reflex is more sensitive in women [33]. Some studies such as the Rotterdam study found a higher prevalence of CC in women [26]. In contrast, we did not find a statistically significant difference in the prevalence of CC between men and women in Germany. The higher prevalence in women reported elsewhere could be due, in part, to women being more willing to seek care for CC and are less likely to smoke. Interpreted with appropriate caution, our data suggests that patients with CC, on average, have a higher BMI as well as, and possibly correlated, fewer days of self-reported "vigorous exercise" than the general population.

In our study, the leading comorbidities in subjects with CC were respiratory disorders, which is consistent with the known epidemiology of cough and guideline-based evaluation recommendations. Typical conditions associated with CC are chronic obstructive pulmonary disease (COPD; *e.g.* the most important risk factor found in the Rotterdam study [26]), asthma or bronchiectasis (both are among the three top risk factors in the Copenhagen study [16]). Among the digestive tract disorders, GERD has been identified as independent risk factor in the Rotterdam study [26], the Copenhagen study [16], and the Korean National Health Survey [32]. As listed in table 3, subjects which reported CC also suffered from a relatively large variety of other medical conditions and comorbidities which have not necessarily previously been associated clinically with cough. The reasons for these observations remain speculative and cannot be

derived from the available data. While an increase in CC among people *e.g.* with "cancer", "congestive heart failure", "respiratory" conditions seems plausible, the increased prevalence in those with comorbid *e.g.* "migraine", "chronic pain" or "liver diseases" could be investigated in future studies.

We also found a higher prevalence of sleep disorders in subjects with CC. CC can be the sole presenting symptom of obstructive sleep apnoea in about one third of affected patients [34]. Furthermore, the relationship of sleep complaints to respiratory symptoms is well established, and cough symptoms have been associated with daytime somnolence in general population studies [35].

As reported in a previous study, CC was accompanied by increased symptoms of depression [36]. A complex relationship between psychomorbidity and CC has been described and psychological issues may be an aetiological factor in the development of CC (previously termed "psychogenic cough", now "somatic cough syndrome") [37]. Alternatively, psychomorbidity may be a result of CC in some respondents.

One of the strengths of our survey is the attempt to have an age and gender-representative sample. However, a few limitations need to be taken into consideration when interpreting the findings of our survey. Given the observational nature of the survey, no causal relationships between, *e.g.*, CC and the various comorbidities can be made [38]. Like other internet-based, patient-reported surveys, the NHWS sample likely under-represents people without access to or familiarity with electronic media, including the elderly, institutionalised patients, and those with severe comorbidities and disabilities which could make access to and ability to participate in online survey panels more difficult. The self-reported nature of the NHWS and cough module is also associated with potential corresponding biases, such as recall and self-presentation biases. Such biases could introduce additional measurement error. We analysed the general CC population which includes, among others, smokers and patients on angiotensin-converting enzyme inhibitors and did not confine the analysis to refractory or unexplained cough patients, which affects the reported prevalence estimates and gender ratios. Finally, as CC was defined by period prevalence (lifetime, 12 months) and not by point prevalence, there is the possibility of recall bias.
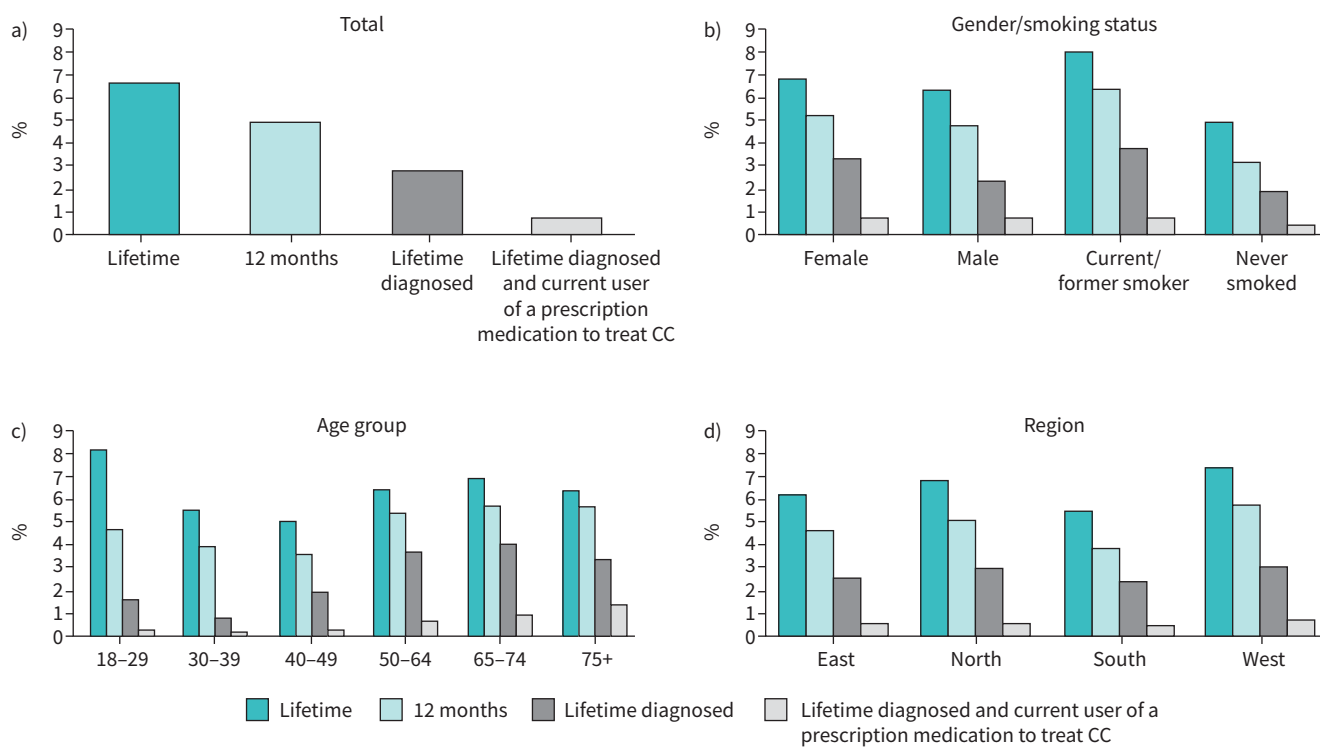

FIGURE 1 Prevalence estimates of chronic cough in the National Health and Wellness Survey (NHWS) sample: lifetime, in past 12 months, diagnosed, drug treated (unweighted estimated). CC: chronic cough.

In conclusion, CC is a prevalent condition in Germany among all age groups without gender preference, with highest rates in those 18–29 and 50 years and older and more frequent among those current or prior smokers. Comorbidities are common in this population, typically of the respiratory system, sleep disorders and depressive symptoms.

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