

Chronic cough as a disease

Richard D. Turner ^{(1),2} and Surinder S. Birring^{3,4}

¹Princess Alexandra Hospital, Brisbane, Australia. ²School of Medicine and Dentistry, Griffith University, Southport, Australia. ³King's College Hospital, London, UK. ⁴Centre for Human and Applied Physiological Sciences, School of Basic and Medical Biosciences, Faculty of Life Sciences and Medicine, King's College London, London, UK.

Corresponding author: Richard Turner (richard.turner@health.qld.gov.au)



Shareable abstract (@ERSpublications)

Chronic cough should be considered a disease. The condition has distinct characteristics and is more than a symptom of other disorders. Approaching chronic cough as a disease should sharpen focus, increase understanding and improve patient outcomes. https://bit.ly/4chgfl3

Cite this article as: Turner RD, Birring SS. Chronic cough as a disease. *ERJ Open Res* 2024; 10: 00459-2024 [DOI: 10.1183/23120541.00459-2024].

Copyright ©The authors 2024

This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact permissions@ersnet.org

Received: 8 May 2024 Accepted: 19 June 2024

Abstract

Chronic cough is a frequent reason for medical consultation and has significant impact on quality of life. Due to the limited effectiveness of currently available treatments, and delays in accessing care, patients are often inadequately managed. There remains an overreliance by clinicians on outdated management algorithms, addressing chronic cough only as symptom of other medical conditions, and advocating investigation and trials of treatment of diseases which are often not present. This may lead to unnecessary cost, frustration and potential harm. Newer clinical guidelines in essence consider chronic cough as a disease in itself, resulting from afferent neuronal hypersensitivity and central nervous system dysfunction. Secondary factors which aggravate chronic cough (smoking, asthma, gastro-oesophageal reflux, *etc.*) are better considered as treatable traits associated with the primary disease process rather than direct "causes" of cough.

Explicitly approaching chronic cough as a discrete entity is consistent with the way in which "diseases" are generally characterised, and has advantages. The patient should be better able to understand their condition, and may have better confidence in attempts at management. The clinician should have better focus and avoid unfruitful treatments and investigation. In general, considering chronic cough as a disease should help to raise the profile of the condition, improve organisation of health service pathways, increase attention for research, and further the development of new treatments.

Introduction

Chronic cough is common and detrimental to quality of life. The global prevalence of cough of >8 weeks' duration is estimated at up to one in 10 people [1], and in many individuals troublesome frequent coughing may persist >15 years or a lot longer, despite attempts at treatment [2]. Adverse impacts on daily activities, wellbeing and psychological health are common [3].

Cough can clearly be associated with many diseases. This includes those which are significantly life-limiting, such as cancer. However, once easily diagnosable conditions associated with cough have been excluded or treated, patients can be left bereft of management options for cough which nevertheless persists. Part of this might be due to trivialisation or lack of interest from health practitioners who may see chronic cough as unimportant, thought of as merely a symptom of other conditions. In a large pan-European community survey, only 30% of >1100 people with chronic cough reported that their doctor had "dealt with their cough thoroughly" [3]. In public health systems, referrals for chronic cough to respiratory clinics are often given the lowest priority behind other conditions [4], and many health practitioners have limited knowledge of evidence-based approaches to chronic cough [5, 6]. The wider population may also underappreciate the significant physical, psychological and social morbidity associated with chronic cough [7, 8].



Much of the current clinical approach to chronic cough remains heavily influenced by an "anatomic diagnostic" paradigm. First proposed in the early 1980s, this idea posits that the large majority of chronic cough of no immediately obvious cause can be explained and successfully managed as one of three

disease processes affecting the main sites involved in cough reflex pathways: rhinosinusitis (of the nasopharynx), asthma (lower airways) and reflux disease (oesophagus) [9]. "Trials of treatment" were advocated for chronic cough on the basis of a rigid protocol [10], involving medications for this trio of conditions, potentially sequentially. Such practice has become widespread [11], even in the absence of specific evidence for those conditions, which are overdiagnosed as "causes" of cough [12]. A belief that chronic cough must be caused by overlooked diseases also led to recommendations for extensive investigation [13], in practice often a long, costly and frustrating process, especially for the patient [14], and potentially involving a number of different medical specialists [15].

Although very attractive and popular, initial data in support of anatomic diagnostic protocols were only from single-centre case series [16]. A big problem in assessing responses to treatments in chronic cough is a substantial placebo effect, even when measuring cough objectively [17]. Further issues are regression to the mean, and natural resolution of cough with time [18].

The accumulation of clinical experience over the past four decades, especially from specialist cough clinics, has made it very clear that many patients (>40% in some series) suffer with persistent chronic cough despite excluding or effectively addressing potential associated medical conditions [19]. Furthermore, compared to the effects of placebo on nonspecific chronic cough, carefully conducted prospective randomised clinical trials have not shown clear benefits of frequently used "anatomically directed" treatments such as proton pump inhibitor medication [20] and inhaled corticosteroids [21]. Consequently, "empirical trials" of treatment are not advocated for chronic cough in newer evidence-based guidelines [22, 23], and nor is extensive investigation if clinical features pointing to specific coexisting medical conditions are lacking [22].

Therefore, it is increasingly apparent that chronic cough is very often not merely a symptom of other disease. Rather, chronic cough may in many respects be better considered a disease in its own right. What follows is an examination of how approaching chronic cough as disease might be both justified and helpful.

Current concepts of chronic cough

Although chronic cough is associated with many diagnoses, cough is by no means universal in patients with diseases commonly stated to be "causes" of cough. For example, chronic cough may affect only two-thirds of patients with uncontrolled asthma [24], and <10% of those with chronic rhinosinusitis may have cough not attributable to other factors [25]. An association with gastro-oesophageal reflux events and cough exists, but is inconsistent and complex [26]. Chronic cough is more common in middle-aged women than other groups [27], an observation difficult to explain if cough was only a manifestation of other disease such as these. Furthermore, as described, chronic cough frequently exists in the absence of any other discernible pathology.

The current paradigm for chronic cough, among researchers and clinicians with a specialist interest, is that of a hypersensitivity disorder with features of vagal nerve neuropathy and central nervous system dysfunction [28, 29] (figure 1). There is much supportive evidence for this idea, from pre-clinical, physiological, neurobiological and clinical data, and from therapeutic trial outcomes [29]. The proposed





Downloaded from https://publications.ersnet.org on January 15, 2025 by guest. Please see licensing information on first page for reuse rights.

neuropathology has many similarities to chronic pain [30]. Clinically, patients often report features of hypersensitivity: coughing in response to low levels or no irritant exposure [31]. This can be demonstrated by measuring tussive responses to aerosolised solutions of diluted capsaicin and other compounds [32], during which a reduced ability to voluntarily supress cough may also be observed compared to healthy volunteers [33]. Increased airway nerve density changes have been documented in bronchial biopsy samples from individuals with chronic cough [34], and novel treatments targeting peripheral airway sensory receptors have proven efficacy in chronic cough, particularly antagonists of ATP-gated P2X3 ion channels [35, 36]. Functional magnetic resonance imaging has revealed cortical changes in those with chronic cough, including reduced activity in motor inhibitory pathways [37]. Chronic cough responds to centrally acting neuromodulator medications such as amitriptyline and gabapentin [38, 39].

A pathoneurophysiological basis for chronic cough is therefore beginning to emerge. In some cases, this may be underpinned by genetic variation, the best-studied example being cough associated with bi-allelic AAGGG repeat expansion sequences within the DNA polymerase-regulating gene *RFC1* [40]. This genetic variant is the cause of the neurological condition CANVAS (cerebellar ataxia with neuropathy and vestibular areflexia syndrome), although through mechanisms that are not yet clear [41]. Chronic cough is commonly associated with CANVAS, in the absence of other cough-provoking conditions, typically emerging years or decades before the classical neurological features of the disease [42, 43], and with clinical features of hypersensitivity as seen in chronic cough in other contexts [44].

Recent clinical guidelines for the management of chronic cough are very much more consistent with the idea of chronic cough as a disease rather than as a symptom of something else [22, 45]. In the absence of other symptoms, signs and risk factors for particular conditions associated with cough, investigation to seek evidence of other pathology should not be extensive but kept to a minimum; only chest radiography, spirometry, and measurement of fractional exhaled nitric oxide are probably essential in all, with further tests dependent on context [22]. An approach of seeking and managing treatable traits is now strongly advocated [46], in which relevant patient features and associated diagnoses (including smoking, angiotensin-converting enzyme (ACE) inhibitor medication, airways disease, gastro-oesophageal reflux, *etc.*) are generally considered aggravating factors for cough rather than "causes" in themselves [22, 45]. Treatments are then advocated and are of proven value directed at the putative disordered neuropathophysiological processes underlying cough hypersensitivity. Behavioural training and centrally acting neuromodulator medications are in various stages of development against afferent airway components of the cough reflex [36, 50, 51] (figure 1).

Cough as a disease

There is no generally agreed definition of disease: what may seem superficially a simple concept is difficult to pin down [52]. Disease may refer to a specific combination of signs and symptoms, a set of features associated with a disorder of organ function, or poor health associated with a specific cause [53]. The concept of disease also varies between health professionals, members of the public and health system funders or legislators [54]. Areas of difficulty and debate include where the line should be drawn between different "disease" entities, and what should be classed as more than "normal" population variation [55, 56].

Although the World Health Organization (WHO) publishes an International Classification of Diseases (ICD) [57], what actually constitutes disease is not explicitly stated. Furthermore, the document includes classification codes for other medical conditions, disorders, and clinical findings which most would not consider as "diseases", such as instrumentally assisted childbirth, or gunshot injuries. In this context chronic cough has its own entry in the ICD-10 in the USA and some other jurisdictions, code R05.3, under the category "symptoms and signs involving the circulatory and respiratory systems" [58]. While this is useful for billing purposes and to give the condition some recognition as a discrete entity, chronic cough has not yet reached the official status of "disease".

As described earlier, chronic cough is much more than a symptom. There is an understanding of underpinning pathophysiological processes, guidelines for chronic cough [22, 23, 45], specific treatments for the condition available and in development [51, 59], patient support information [60], groups for chronic cough (*e.g.* www.facebook.com/groups/ChronicCough/), and distinct referral pathways for patients within public health systems [4]. Cough can also be measured subjectively and objectively using methods which are now well established [61].

Approaching chronic cough as a discrete disease entity has many potential benefits. It should improve understanding for patients and their families, also helping patients in explaining the reason for coughing to

BOX 1 Chronic cough as a disease	
Characteristics of chronic cough consistent with distinct disease status	Potential advantages of considering chronic cough as a disease
Definable (cough lasting >8 weeks)	Improved understanding for patients, and validation of their concerns
Existing model of pathophysiological basis (combination of aggravating stimuli, afferent hypersensitivity and central nervous system dysfunction)	Increased focus for clinicians, with improved awareness of chronic cough management guidelines
Measurable (patient-rated and objective, e.g. cough frequency monitoring, cough reflex testing)	Better organisation of clinical services for chronic cough
Treatable, with specific interventions of proven efficacy (<i>e.g.</i> gabapentin, gefapixant, cough suppression training)	Increased funding and efforts for research
	Increased general profile of chronic cough in the medical community

concerned onlookers [8]. A specific disease label for a condition can help patients validate their chronic illness and increase confidence in treatment [62]. Treating chronic cough as a disease should also improve focus for clinicians, and help avoid unhelpful, costly, time-consuming, and even potentially harmful investigations and treatment trials. In turn, the profile of chronic cough generally should be increased, helping in the organisation of health services for patients with the condition, and in directing funding for research (box 1).

There is an argument that new diseases may be often defined under the influence of those with vested interests, particularly where states which were previously considered healthy are now considered not so, and where treatments might now be used where they were not previously considered necessary [55]. This does not hold for chronic cough, in which patients clearly do not meet the WHO definition of health ("a state of complete physical, mental and social well-being..." [63]), and who are already often being treated, but with medications which have limited efficacy for their underlying condition [11]. New pharmacological treatments for chronic cough are also likely to be highly regulated, and funded by public health budgets only according to certain criteria [59]. For the reasons outlined above, the reasons for considering chronic cough as a discrete disease outweigh any disadvantages of not doing so.

Nomenclature of chronic cough

One reason in which the idea of chronic cough as a disease has been slow to catch on may be terminology. This is a difficult area, in which there is debate and where consensus is sometimes lacking. Chronic cough is that which lasts >8 weeks [10]. Chronic cough of no discernible cause is termed unexplained or idiopathic [13, 19]. Refractory chronic cough is then that which may or may not be associated with another condition (such as asthma), but which persists despite adequately addressing associated pathology [64]. Cough hypersensitivity syndrome applies to the pathophysiological processes which are thought to underlie chronic cough in a large proportion of cases [28], referred to by some as a neuropathic cough [64]. These terms are sometimes used interchangeably, but may convey slightly different meanings, and lead to confusion [65].

The authors of the recent British Thoracic Society clinical statement on chronic cough suggest a clear workable solution to this semantic problem. They suggest using the general term refractory chronic cough to apply to all those patients in which cough has persisted >8 weeks and treatable traits have been adequately addressed [22]. Following clinical assessment the term (refractory) chronic cough can then be followed by "associated with" or "with features of" ACE inhibitor use, asthma, obstructive sleep apnoea, *etc.*, or refractory chronic cough with no treatable traits [22].

In our opinion, the term chronic cough is already familiar, and would apply to the overarching "disease", within which cough hypersensivity, refractory chronic cough and other terms have more specific meanings, some applying to particular cough phenotypes [66].

Conclusion

Thanks to increased clinical and research interest, much has changed in the understanding of and the approach to chronic cough over the past 20 years, culminating not least in the first novel drugs developed

and approved specifically for chronic cough, and clinical guidelines for management which are based on more evidence than ever before [67]. Despite this, many patients remain without effective treatment, even if recommended management approaches have been followed (which often is not the case). One simple step towards further advances for patients with chronic cough is the wider recognition of the condition as a discrete disease entity.

Provenance: Commissioned article, peer reviewed.

Conflicts of interest: R.D. Turner is an associate editor of this journal. Outside of the current work, but relevant to chronic cough in general, S.S. Birring reports consulting fees from Merck, Bellus Health, Trevi Therapeutics, Genentech, Nocion Therapeutics, Axalbion and NeRRe Therapeutics, honoraria from AstraZeneca, and an institutional grant from Merck.

References

- 1 Song W-J, Chang Y-S, Faruqi S, *et al.* The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. *Eur Respir J* 2015; 45: 1479–1481.
- 2 Koskela HO, Lätti AM, Purokivi MK. Long-term prognosis of chronic cough: a prospective, observational cohort study. *BMC Pulm Med* 2017; 17: 146.
- 3 Chamberlain SAF, Garrod R, Douiri A, *et al.* The impact of chronic cough: a cross-sectional European survey. *Lung* 2015; 193: 401–408.
- 4 Queensland Health. Chronic Cough Clinical Prioritisation Criteria. 2021. www.health.qld.gov.au/cpc/respiratoryand-sleep-medicine/chronic-cough. Date last accessed: 21 April 2024. Date last updated: 8 July 2021.
- 5 Ge H, Hong K, Fan C, *et al.* Knowledge, attitude, and practice of healthcare providers on chronic refractory cough: a cross-sectional study. *Heliyon* 2024; 10: e27564.
- 6 Leuppi JD, Guggisberg P, Koch D, *et al.* Understanding physician's knowledge and perception of chronic cough in Switzerland. *Curr Med Res Opin* 2022; 38: 1459–1466.
- 7 Birring SS, Prudon B, Carr A, *et al.* Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax* 2003; 58: 339–343.
- 8 Brindle K, Morice A, Carter N, *et al.* The "vicious circle" of chronic cough: the patient experience qualitative synthesis. *ERJ Open Res* 2023; 9: 00094-2023.
- 9 Irwin RS, Corrao WM, Pratter MR. Chronic persistent cough in the adult: the spectrum and frequency of causes and successful outcome of specific therapy. *Am Rev Respir Dis* 1981; 123: 413–417.
- 10 Morice AH, McGarvey L, Pavord I. Recommendations for the management of cough in adults. *Thorax* 2006; 61: Suppl. 1, i1–i24.
- 11 McGarvey LP, Harper G, Silvey M, *et al.* A real world study of cough burden and quality of life of UK patients who have undergone evaluation for chronic cough. *Curr Med Res Opin* 2023; 39: 1717–1728.
- 12 O'Hara J, Stocken DD, Watson GC, *et al.* Use of proton pump inhibitors to treat persistent throat symptoms: multicentre, double blind, randomised, placebo controlled trial. *BMJ* 2021; 372: m4903.
- 13 Pratter MR. Unexplained (idiopathic) cough: ACCP evidence-based clinical practice guidelines. Chest 2006; 129: Suppl. 1, 220S–221S.
- 14 Cho PSP, Shearer J, Simpson A, *et al.* Healthcare utilization and costs in chronic cough. *Curr Med Res Opin* 2022; 38: 1251–1257.
- **15** Slovarp LJ, Jetté ME, Gillespie AI, *et al.* Evaluation and management outcomes and burdens in patients with refractory chronic cough referred for behavioral cough suppression therapy. *Lung* 2021; 199: 263–271.
- 16 Irwin RS, Curley FJ, French CL. Chronic cough. The spectrum and frequency of causes, key components of the diagnostic evaluation, and outcome of specific therapy. *Am Rev Respir Dis* 1990; 141: 640–647.
- 17 Eccles R. The powerful placebo effect in cough: relevance to treatment and clinical trials. Lung 2020; 198: 13–21.
- 18 Yousaf N, Montinero W, Birring SS, et al. The long term outcome of patients with unexplained chronic cough. Respir Med 2013; 107: 408–412.
- 19 Haque RA, Usmani OS, Barnes PJ. Chronic idiopathic cough: a discrete clinical entity? Chest 2005; 127: 1710–1713.
- 20 Chang AB, Lasserson TJ, Gaffney J, et al. Gastro-oesophageal reflux treatment for prolonged non-specific cough in children and adults. *Cochrane Database Syst Rev* 2011; 1: CD004823.
- 21 Lee SE, Lee JH, Kim HJ, *et al.* Inhaled corticosteroids and placebo treatment effects in adult patients with cough: a systematic review and meta-analysis. *Allergy Asthma Immunol Res* 2019; 11: 856–870.
- 22 Parker SM, Smith JA, Birring SS, *et al.* British Thoracic Society clinical statement on chronic cough in adults. *Thorax* 2023; 78: s3–s19.
- 23 Marchant JM, Chang AB, Kennedy E, et al. Cough in children and adults: diagnosis, assessment and management (CICADA). Summary of an updated position statement on chronic cough in Australia. Med J Aust 2024; 220: 35–45.

- 24 Mincheva R, Ekerljung L, Bjerg A, *et al.* Frequent cough in unsatisfactory controlled asthma results from the population-based West Sweden Asthma study. *Respir Res* 2014; 15: 79.
- 25 O'Hara J, Jones NS. "Post-nasal drip syndrome": most patients with purulent nasal secretions do not complain of chronic cough. *Rhinology* 2006; 44: 270–273.
- Houghton LA, Smith JA. Gastro-oesophageal reflux events: just another trigger in chronic cough? *Gut* 2017; 66: 2047–2048.
- 27 Morice AH, Jakes AD, Faruqi S, *et al.* A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response. *Eur Respir J* 2014; 44: 1149–1155.
- 28 Morice AH, Millqvist E, Belvisi MG, *et al.* Expert opinion on the cough hypersensitivity syndrome in respiratory medicine. *Eur Respir J* 2014; 44: 1132–1148.
- 29 Chung KF, McGarvey L, Song W-J, *et al.* Cough hypersensitivity and chronic cough. *Nat Rev Dis Primers* 2022; 8: 45.
- 30 Arinze JT, Verhamme KMC, Luik AI, *et al.* The interrelatedness of chronic cough and chronic pain. *Eur Respir J* 2021; 57: 2002651.
- 31 Chung KF, McGarvey L, Mazzone SB. Chronic cough as a neuropathic disorder. *Lancet Respir Med* 2013; 1: 414–422.
- 32 Koskela HO, Nurmi HM, Birring SS. Utility of cough provocation tests in chronic cough and respiratory diseases: a comprehensive review and introduction of new reference ranges for the capsaicin test. Allergy Asthma Immunol Res 2021; 13: 833–849.
- 33 Cho PSP, Fletcher H V, Turner RD, et al. Impaired cough suppression in chronic refractory cough. Eur Respir J 2019; 53: 1802203.
- 34 Shapiro CO, Proskocil BJ, Oppegard LJ, *et al.* Airway sensory nerve density is increased in chronic cough. *Am J Respir Crit Care Med* 2021; 203: 348–355.
- **35** Turner RD, Birring SS. Chronic cough: ATP, afferent pathways and hypersensitivity. *Eur Respir J* 2019; 54: 1900889.
- 36 McGarvey LP, Birring SS, Morice AH, *et al.* Efficacy and safety of gefapixant, a P2X₃ receptor antagonist, in refractory chronic cough and unexplained chronic cough (COUGH-1 and COUGH-2): results from two double-blind, randomised, parallel-group, placebo-controlled, phase 3 trials. *Lancet* 2022; 399: 909–923.
- 37 Ando A, Smallwood D, McMahon M, *et al.* Neural correlates of cough hypersensitivity in humans: evidence for central sensitisation and dysfunctional inhibitory control. *Thorax* 2016; 71: 323–329.
- 38 Jeyakumar A, Brickman TM, Haben M. Effectiveness of amitriptyline versus cough suppressants in the treatment of chronic cough resulting from postviral vagal neuropathy. Laryngoscope 2006; 116: 2108–2112.
- 39 Ryan NM, Birring SS, Gibson PG. Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial. *Lancet* 2012; 380: 1583–1589.
- 40 Turner RD, Hirons B, Cortese A, *et al.* Chronic cough as a genetic neurological disorder? insights from cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS). *Lung* 2023; 201: 511–519.
- 41 Cortese A, Curro' R, Vegezzi E, et al. Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS): genetic and clinical aspects. Pract Neurol 2022; 22: 14–18.
- 42 Infante J, García A, Serrano-Cárdenas KM, *et al.* Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) with chronic cough and preserved muscle stretch reflexes: evidence for selective sparing of afferent Ia fibres. *J Neurol* 2018; 265: 1454–1462.
- 43 Guilleminault L, Chazelas P, Melloni B, et al. Repeat expansions of RFC1 in refractory chronic cough: a missing piece of the puzzle? Chest 2023; 163: 911–915.
- 44 Hirons B, Curro R, Abubakar-Waziri H, *et al.* Chronic cough characteristics in CANVAS. *Eur Respir J* 2023; 62: Suppl. 67, PA1912.
- 45 Morice AH, Millqvist E, Bieksiene K, *et al.* ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J* 2020; 55: 1901136.
- 46 Agusti A, Bel E, Thomas M, *et al.* Treatable traits: toward precision medicine of chronic airway diseases. *Eur Respir J* 2016; 47: 410–419.
- 47 Chamberlain Mitchell SAF, Garrod R, Clark L, *et al.* Physiotherapy, and speech and language therapy intervention for patients with refractory chronic cough: a multicentre randomised control trial. *Thorax* 2017; 72: 129–136.
- 48 Vertigan AE, Kapela SL, Ryan NM, *et al.* Pregabalin and speech pathology combination therapy for refractory chronic cough. *Chest* 2016; 149: 639–648.
- 49 Morice AH, Menon MS, Mulrennan SA, *et al.* Opiate therapy in chronic cough. *Am J Respir Crit Care Med* 2007; 175: 312–315.
- 50 Garceau D, Chauret N. BLU-5937: a selective P2X3 antagonist with potent anti-tussive effect and no taste alteration. *Pulm Pharmacol Ther* 2019; 56: 56–62.
- 51 Smith JA. The therapeutic landscape in chronic cough. *Lung* 2024; 202: 5–16.
- 52 Scully JL. What is a disease? EMBO Rep 2004; 5: 650–653.
- 53 Campbell EJ, Scadding JG, Roberts RS. The concept of disease. *Br Med J* 1979; 2: 757–762.

Downloaded from https://publications.ersnet.org on January 15, 2025 by guest. Please see licensing information on first page for reuse rights.

- 54 Tikkinen KAO, Leinonen JS, Guyatt GH, *et al.* What is a disease? Perspectives of the public, health professionals and legislators. *BMJ Open* 2012; 2: e001632.
- 55 Moynihan R. Medicalization: a new deal on disease definition. *BMJ* 2011; 342: d2548.
- 56 The Lancet Healthy Longevity. Is ageing a disease? Lancet Healthy Longev 2022; 3: e448.
- 57 World Health Organization. International Statistical Classification of Diseases and Related Health Problems (ICD). www.who.int/standards/classifications/classification-of-diseases. Date last accessed: 28 April 2024.
- 58 Millqvist E, Janson C, Bredin C. Refraktär och oförklarlig kronisk hosta har fått en egen ICD-10 kod. Hosta vanligaste orsaken till att söka läkarvård. [New ICD-10 code for refractory and unexplained chronic cough]. *Lakartidningen* 2023; 120: 22163.
- 59 European Medicines Agency. Lyfnua (Gefapixant). www.ema.europa.eu/en/medicines/human/EPAR/lyfnua. Date last accessed: 24 April 2024.
- 60 European Lung Foundation. Chronic Cough. https://europeanlung.org/en/information-hub/lung-conditions/ chronic-cough/ Date last accessed: 28 April 2024.
- 61 Turner RD, Birring SS. Measuring cough: what really matters? J Thorac Dis 2023; 15: 2288–2299.
- 62 Ogden J, Branson R, Bryett A, *et al.* What's in a name? An experimental study of patients' views of the impact and function of a diagnosis. *Fam Pract* 2003; 20: 248–253.
- 63 World Health Organization. Constitution of the World Health Organization. 1946. https://www.who.int/about/ governance/constitution. Date last accessed: 24 April 2024.
- 64 Gibson PG, Vertigan AE. Management of chronic refractory cough. *BMJ* 2015; 351: h5590.
- 65 McGarvey L, Gibson PG. What is chronic cough? Terminology. J Allergy Clin Immunol Pract 2019; 7: 1711–1714.
- 66 Mazzone SB, Chung KF, McGarvey L. The heterogeneity of chronic cough: a case for endotypes of cough hypersensitivity. *Lancet Respir Med* 2018; 6: 636–646.
- 67 Hirons B, Turner R, Cho PSP, et al. Chronic cough: is the end nigh? Breathe 2023; 19: 230165.