

RESPIPLUS™ PRESENTS

AUGUST 2021

CANADIAN CHRONIC COUGH INITIATIVE



EXECUTIVE SUMMARY



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In order to maintain anonymity and protect the privacy of individuals interviewed during this process, some names and identifying details have been changed.

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EXECUTIVE SUMMARY

Cough is the most common presenting symptom in the offices of both primary care physicians and respiratory specialists and is often a common presenting symptom for other specialists and health care professionals. Chronic cough – cough that lasts for 8 weeks or more – is one of the more challenging medical conditions to screen for and to treat because it often has multiple differential diagnoses and is occasionally due to more than one condition. For patients, chronic cough can be frustrating or even disabling and have a major impact on their quality of life.

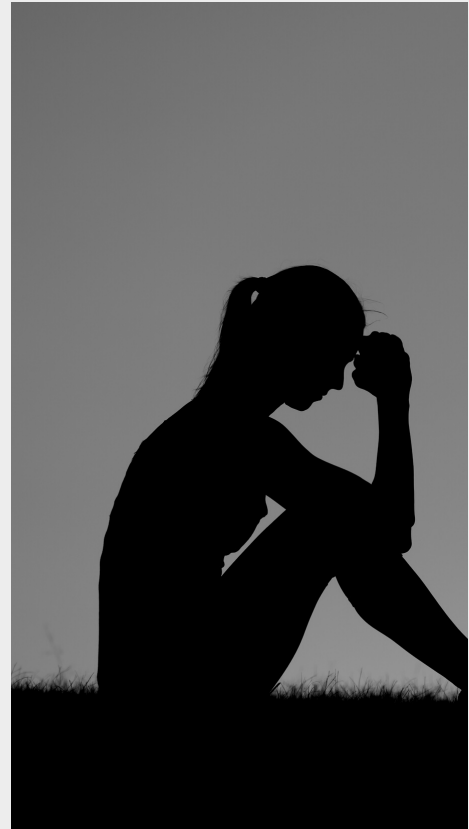
This report has been prepared by RESPIPLUS. Under the direction of leading clinicians and academics in the field of chronic cough and input from patients, RESPIPLUS has developed this report to raise awareness about this common but underdiagnosed and often improperly managed condition.

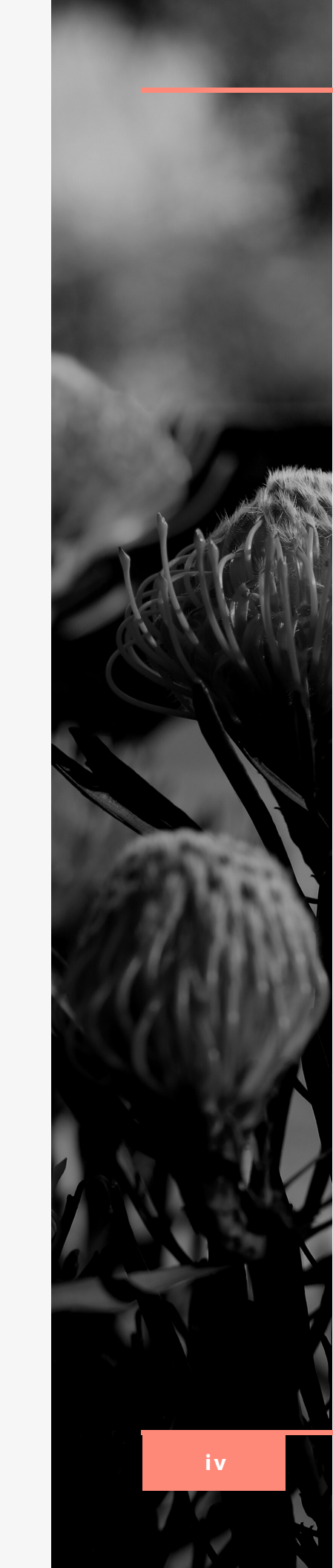
Various estimates for the global prevalence of chronic cough place the percentage from 5% to as high as 12%. Age- and gender-related differences in the incidence of chronic cough have also been noted with the condition being more common in females and in older populations.

THE IMPACT OF CHRONIC COUGH HAS BEEN ELOQUENTLY EXPRESSED BY SOME PATIENTS INTERVIEWED FOR THIS REPORT.

"I don't remember ever not coughing. I also wake up choking in my sleep. It's really, really hard to be in public, during COVID, when you could have a cough attack. I've been in places and having to run out of the store just so I can have my cough attack, because everybody looks at you like you're infectious and have COVID."

- Cathy, 53





Chronic cough places a burden on the health care system as a whole as patients often have to seek repeated visits with family physicians and various specialists. In a recent survey performed in 1,120 people with chronic cough, more than 70% of the subjects had sought more than 3 consultations in connection with their chronic cough.

At its most severe, chronic cough can lead to depression, anxiety, urinary incontinence, syncope, rib fractures, and dysphonia. Chronic cough has also been associated with sleep disorders and voice disorders.

For health care professionals responsible for screening, diagnosing and treating chronic cough there are a number of challenges, not the least of which is in properly defining the condition. Clinicians, researchers and guidelines have adopted a definition of chronic cough as one that has lasted 8 weeks or more in adults and 4 weeks or more in children. European Respiratory Society guidelines state: "The failure to recognize that the patient is suffering from the syndrome of chronic cough may lead to misdiagnosis with the patient labelled as suffering from recurrent chest infections, treatment resistant asthma or exacerbations of chronic obstructive pulmonary disease (COPD)."

Chronic cough can be caused by exposure to noxious stimuli such as cigarette smoke or air pollution or be caused by excessive stimulation of a normal cough reflex which can take place following inhalation of a

foreign body. It is also a symptom of several well-recognized chronic conditions.

1. Asthma
2. Non-asthmatic eosinophilic bronchitis (NAEB)
3. Gastroesophageal Reflux Disease (GERD)
4. Postnasal drip syndrome/ upper airways cough syndrome (UACS)

It is when the cough cannot be adequately explained by these conditions that issues become more complicated. A proportion of patients with chronic cough, particularly among adults, have persistent cough despite undergoing numerous tests and various treatments according to clinical practice guidelines. This condition has been described using a number of terms including idiopathic chronic cough, unexplained chronic cough and chronic refractory cough. One found 42% of patients presenting to a UK cough clinic have unexplained cough.

A growing understanding of the etiology of chronic cough is helping provide new approaches for therapy and defining targets for medications which could help treat the condition. The concept of cough hypersensitivity syndrome is now used to explain many cases of chronic cough and was first articulated by the European Respiratory Society (ERS) in 2011. Cough hypersensitivity syndrome is associated with hypersensitivity of the larynx and upper airways.

For family physicians, nurse practitioners, respiratory

therapists, respirologists and other specialists who deal with chronic cough in Canada, the challenges of properly diagnosing and treating chronic cough are many. Canadian family physicians report the frustrations felt by both themselves and patients when chronic cough is not properly investigated or treated. Even specialists in managing respiratory health report many patients are not properly diagnosed and end up being told that they will have to live with their condition.

Recent review articles propose a stepwise approach to assessing and managing chronic cough as follows:

1. Exclude and treat obvious causes
2. Investigate and treat common triggers of chronic cough
3. Exclude and treat rarer triggers of chronic cough
4. Manage unexplained chronic cough with speech therapy and/or neuromodulatory treatments

With no approved medications for uncontrolled chronic cough most specialist clinics management relies on using interventions with evidence of efficacy in clinical trials. In the UK, low dose morphine sulphate (MST) is often used, however, concerns about dependency have limited this use in Canada. Gabapentin or pregabalin have also been shown to be effective but can have significant side effects. Amitriptyline has also been used. Some patients may select speech and language therapy instead of medication. This intervention involves a multi-modality approach of education, reducing laryngeal irritation with relaxation exercises, cough suppression techniques and counselling. Those that benefit often have speech and language therapy as an adjunct to medication.

New therapies under investigation for treatment of chronic cough target specific receptors or channels in the peripheral sensory neurons.

The drug holding the most promise to be

the first therapy licensed for chronic refractory cough is gefapixant (MK-7264/AF-219) a selective antagonist of the P2X3 receptor. Phase 1 and 2 clinical trials evaluated more than 300 patients and demonstrated positive results for decreased mean daytime cough frequency, 24-hour cough frequency, and awake cough frequency.

Following the positive results from phase 1 and 2 trials, investigation of the drug continued with phase 3 clinical trials. Two parallel, double-blind, randomized, placebo-controlled trials (COUGH-1 and COUGH-2) were conducted to assess the efficacy and safety of gefapixant (15 mg or 45 mg twice daily) in patients with chronic cough. Results of COUGH-1 and COUGH-2 showed a statistically significant reduction in 24-hour cough frequency versus placebo at 12 weeks and 24 weeks in patients treated with gefapixant 45 mg twice daily. AEs reported were consistent with previous trials (dysgeusia occurring at a higher incidence with gefapixant 45 mg twice daily), and discontinuations of study drugs due to AEs were more frequent in the gefapixant 45 mg treatment arms.

In Canada, the ideal model of care for chronic cough involves appropriate and timely access to:

- Primary care - primary care physicians or nurse practitioners and pharmacists (screening)
- Secondary care - specialists (usually respirologists but also allergists, gastroenterologists and otolaryngologists)
- Tertiary care - cough clinics
- Other health care professionals - speech and language therapists, respiratory therapists, and specialized respiratory educators

Initial workup, diagnosis and treatment would be performed by primary care providers with referral to specialists when necessary. Patients with unexplained chronic cough or other more complex or



severe cases would be referred to interdisciplinary cough clinics. In addition to providing care, these clinics would also have a role in setting practice standards, conducting research, and training future respiratory specialists.

A consensus that patients with chronic cough should only wait two weeks to see a primary care provider and four months to see a specialist once referred for chronic cough are tempered with the recognition that wait times are currently often far longer due to the COVID-19 pandemic and the regional shortages of both general practitioners and specialists.

Given the complex and multifactorial nature of managing chronic cough it would be important that patients be fully engaged in their own care and have the knowledge and information to make important decisions about treatment. Physicians and all other professionals involved in providing care similarly would require the necessary education and training to provide the necessary care.

Patient education is seen as a critically important factor in better managing chronic cough in Canada.

“I THINK WE HAVE TO MAKE THEM AWARE THAT THEY'VE GOT A CONDITION AND THAT THERE'S SOMETHING THAT CAN BE DONE ABOUT IT, RATHER THAN JUST SUFFERING WITH IT,”

- Dr. Alan Kaplan (Family Physician)

Reference has also been made to the need to educate patients about non-pharmacologic approaches to managing chronic cough as well as drug therapies.

FOR THE PUBLIC AND PATIENTS A VARIETY OF INFORMATIONAL AND EDUCATIONAL TOOLS SHOULD BE CONSIDERED INCLUDING THE FOLLOWING:

- Self-help tools
- Online information modules
- Printed information sheets
- Podcasts and videos
- Webinars provided by experts